A Multidisciplinary Study of the Interrelationships Among Alcohol Consumption, Physical Activity, Haematological Profiles and Psychological Well Being

Craig Sale, B.Sc. (Hons), M.Sc.

A thesis submitted in partial fulfilment of the requirement of Liverpool John Moores University for the degree of Doctor of Philosophy

May 2002

DECLARATION

I declare that the work in this thesis is entirely my own. I was involved in the design of experiments (with the assistance of my supervisors) and conducted all experimentation, data collection and subsequent analysis independently.

ABSTRACT

The thesis is composed of two studies designed to determine the interrelationships among alcohol consumption, physical activity, cardiorespiratory fitness, blood haematology and psychological well being. In study 1, 50 healthy subjects completed a questionnaire providing information on habitual physical activity and alcohol consumption. A venous blood sample was obtained from each subject and analysed for blood lipids, haemostatic variables and blood rheological indices. Results showed that drinking frequency was positively associated with high density lipoprotein (HDL) and apolipoprotein A1 (apo A1) ($p<0.05$). Recent alcohol consumption was significantly associated with plasminogen activator inhibitor-1 activity (PAI-1) ($p<0.05$), with moderate alcohol consumers having shortened prothrombin time (PT) ($p<0.05$) and higher tissue plasminogen activator activity (tPA) ($p<0.05$) when compared to light alcohol consumers. Those self-reporting higher physical activity and fitness levels exhibited lower mean values for low density lipoprotein (LDL) ($p<0.05$), apolipoprotein B (apo B) ($p<0.005$), total cholesterol/HDL ratio ($p<0.005$), plasma viscosity ($p<0.005$) and serum viscosity ($p<0.005$). Lower values of plasma ($p<0.05$) and serum ($p<0.05$) viscosity were also associated with higher weekly energy expenditures. Twenty-three subjects undertook further investigations and performed an incremental VO_{2max} test on a cycle ergometer. Two further blood samples were withdrawn post-exercise and following 30 minutes recovery. Whilst there were no significant associations between VO_{2max} and blood lipid levels, those subjects with high VO_{2max} exhibited longer thrombin time (TT) ($p<0.05$) and lower PAI-1 activity ($p<0.01$). Maximal exercise evoked significant increases in blood lipids ($p<0.005$), only when post-exercise data were not corrected for plasma volume changes. Maximal exercise was also followed by shortening of TT ($p<0.01$), PT ($p<0.005$) and activated partial thromboplastin time (APTT) ($p<0.005$), along with a reduction in fibrinogen concentration ($p<0.005$), but only following correction for plasma volume change. Significant increases in tPA activity ($p<0.005$) and D-dimer ($p<0.005$), with a concomitant reduction in PAI-1 activity ($p<0.005$) were observed following maximal exercise, even when post-exercise raw data were corrected for plasma volume changes. Although maximal exercise induced marked increases in blood rheological variables ($p<0.005$), adjustment of post exercise raw data for plasma volume loss significantly affected these changes. In study 2 questionnaires relating to the interrelationships among alcohol consumption, physical activity and psychological well being were administered on two occasions with 12 months intervening. Analyses were performed on 482 respondents from the first administration, 336 from the second, and 141 respondents who completed both questionnaires. Extraversion and neuroticism emerged as the significant predictors of psychological well being ($p<0.005$). Gender, alcohol expectancies and accommodation coping were the significant predictors of alcohol consumption ($p<0.05$), with alcohol consumption ($p<0.005$) significantly predicting alcohol related problems. Extraversion again emerged as the significant predictor of self-reported physical activity ($p<0.005$), whilst physical activity, avoidance coping ($p<0.05$) and social support seeking ($p<0.01$) significantly predicted the level of physical fitness ($p<0.005$). In conclusion, alcohol consumption was not related to blood haematological profiles or to the prediction of psychological well being. Habitual physical activity patterns were related to blood lipid and blood rheological profiles, with higher physical fitness being associated with hyperfibrinolysis. It was concluded that maximal exercise induces transient alterations in blood haematological profiles, but neither physical activity nor cardiorespiratory fitness, were significant predictors of psychological well being.

GLOSSARY OF TERMS

apo A1 – Apolipoprotein A1
apo B – Apolipoprotein B
APTT – Activated partial thromboplastin time
BMI – Body mass index
CAD – Coronary artery disease
CHD – Coronary heart disease
CVD – Cardiovascular disease
FDP – Fibrin degradation products
HDL – High density lipoprotein
HK – High molecular weight kininogen
LDL – Low density lipoprotein
LTPA – Leisure time physical activity
MI – Myocardial infarction
PAI-1 – Plasminogen activator inhibitor-1
PAI-2 – Plasminogen activator inhibitor-2
PK – Prekallikrenin
PT – Prothrombin time
TF – Tissue factor
TG – Triglyceride
tPA – Tissue plasminogen activator
TT – Thrombin time
UPA – Urokinase plasminogen activator
VLDL – Very low density lipoprotein

ACKNOWLEDGEMENTS

This thesis could not have been completed without the help, guidance and supports of my colleagues, friends and family to whom I owe much gratitude.

My sincerest thanks are extended to both Prof. Mahmoud El-Sayed (Director of Studies) and Prof. Andy Guppy (Senior Supervisor) whose advice, guidance and friendship were instrumental in the completion of this research.

This research would not have been possible without the many volunteers who gave up their time and in some cases their blood, without complaint. Their co-operation and compliance with the many aspects of the experimental procedures did not go unnoticed and my sincerest thanks are extended to you all.

Thanks are also extended to all my friends and colleagues at Liverpool John Moores University, whose support and encouragement made studying at LJMU an enjoyable and productive experience.

To my mum and my grandparents whose unselfish love, understanding and unwavering support provided the motivation to complete this thesis, especially during difficult times. It is impossible to put into words your contribution to this thesis but it undoubtedly could not have been completed without you.

Finally, I dedicate this thesis to the memory of my father who passed away during the early stages of the work (5th March, 1998) but who did, and still does much to inspire me in everything that I do.

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CHAPTER 1: INTRODUCTION

1.0. INTRODUCTION

1.1. Background to the Study

Coronary heart disease (CHD) is the most common cause of death in the UK, with 1 in 4 men and 1 in 5 women dying from the disease. Recent statistical information has indicated that CHD accounted for 135,000 deaths in the UK, with a further 35,000 deaths being related to other heart disorders/defects (British Heart Foundation, 2000).

A multitude of modifiable risk factors for cardiovascular disease have been identified, of which there are two main categories. The first category includes risk factors such as hyperlipidaemia, hyperfibrinogenaemia and hyperviscosity, which all contribute to the blood haematological profile and have been referred to as biological risk factors for cardiovascular disease (Dzau et al., 1991). The second category of risk factors includes elements of lifestyle, such as alcohol consumption, physical activity, smoking and diet (often termed health-related behaviours). Previous investigation has shown that a certain amount of interaction exists between these biological and lifestyle factors (Benfante et al., 1989; Wanemethee and Shaper, 1994; Boreham et al., 1999; Twisk et al., 1999). It should also be noted that certain lifestyle factors, such as alcohol consumption, physical activity and diet, could have a positive, as well as a negative, impact upon these biological risk factors (Blaxter, 1990).

Although all of these biological and lifestyle risk factors are important, and play a pivotal role in the pathogenesis of cardiovascular disease, the present study will only be confined to the examination of aspects of alcohol consumption and physical activity.

The results of several epidemiological investigations have suggested a relationship between lifestyle and cardiovascular health and disease (Dawber, 1980; Shaper and Pocock, 1987; Tunstall-Pedoe et al., 1989; Blaxter, 1990; Fowkes et al., 1991; MacAuley et al., 1996). Indeed the British Heart Foundation (2000) has reported that ~36-38% of CHD related deaths in the UK are due to physical inactivity. It has also been reported that 9% of deaths occurring from CHD in the UK could be avoided if sedentary individuals increased their level of physical activity (British Heart Foundation, 2000). Perhaps more difficult to estimate is the impact of alcohol consumption on cardiovascular health and disease as moderate levels of alcohol consumption is suggested to be cardio-protective (Maclure, 1993); whereas a high alcohol consumption would appear to elevate the risk of CHD, particularly in binge drinkers (British Heart Foundation, 2000).

Maclure (1993) reviewed clinical and epidemiological research, using a method of deductive meta-analysis, and concluded that current research suggests that moderate alcohol consumption could reduce the risk of developing CHD by between 30-60%. A U-shaped relationship between alcohol dose and the risk of

CHD was thus hypothesised. It was suggested that alcohol consumption could be preventative at low to moderate doses, but causative at higher doses.

Maclure (1993) suggested that moderate alcohol intake could have a positive effect on some of the biological indices pertinent to cardiovascular health and disease. Thus, it is of particular interest to examine both alcohol consumption and physical activity in relation to blood haematological profiles.

Alternative pathways exist to explain the protective role of low to moderate doses of alcohol consumption in cardiovascular disease (CVD). For example, it could be that psychological factors, associated with lower alcohol consumption, in contrast to those associated with abstinence or heavy drinking, might play a more important protective role than the alcohol dose itself (Criqui, 1987; Marmot et al., 1993). Further results from the Whitehall II study (Marmot, 1994; Stansfeld et al., 2002), have suggested the involvement of psychological factors, such as stress and perceived control, in the prediction of CHD among a sample of 10 000 white-collar workers. Several studies have also suggested links between CHD and psychological stress, coping strategies and elements of personality (Cooper and Payne, 1991).

Whilst a large body of research has identified a role for certain health related behaviours in the prediction of cardiovascular health and disease, these studies have tended, in the main, to concentrate on older populations. This is despite

evidence to suggest that atherosclerosis begins in early life (Misra, 2000) and that many of our adverse behaviour patterns are formed in childhood (Perry et al., 1994) and modified in young adulthood (Lee, 1999; Leslie and St. Pierre, 1999; Thiessen and Looker, 1999).

It has been suggested that the benefits of physical activity for cardiovascular health in the younger adult population remain uncertain (Andersen and Haraldsdottir, 1995). Therefore, cross-sectional investigations are needed to assess the relationship between physical activity and the biological factors affecting cardiovascular health and disease (Andersen and Haraldsdottir, 1995). Further evaluation is also required as to the relative importance of physical activity versus physical fitness in evoking changes in these biological factors.

Thus, the associations between health behaviour, blood haematology and psychological well being warrant further investigation. This is particularly important in younger populations, with whom end-points other than manifest disease must be used (Baranowski et al., 1992).

1.2. Project Aims:

The present study was designed to examine the interrelationships among established predictors of cardiovascular health and disease in young adults. In particular, the study examined the associations between selected health-related behaviours (alcohol consumption and physical activity), blood haematological

profiles (blood lipids, blood haemostasis and blood rheology) and psychological well being. Some of the potential underlying factors that may modify these associations were also investigated, particularly in relation to psychological well being. The impact of cardiorespiratory fitness (as assessed by VO_{2max}) on blood haematological profiles were also investigated.

To achieve these aims, the following objectives were established:

1. To determine the relationship between alcohol consumption and blood haematological profiles.
2. To determine the relationship between physical activity and blood haematological profiles.
3. To determine the relationship between cardiorespiratory fitness and blood haematological profiles.
4. To examine the effects of maximal exercise on blood haematology.
5. To examine the prediction of psychological well being from alcohol consumption, physical activity and fitness, whilst also considering the possible impact of individual differences, dispositional characteristics of the individual, personal control and coping strategies.
6. To examine possible psychological predictors of self-reported alcohol consumption and alcohol related problems.
7. To examine possible psychological predictors of self-reported physical activity and fitness.

CHAPTER 2: REVIEW OF THE LITERATURE

2.0. REVIEW OF THE LITERATURE

2.1. Introduction

This review of the literature will outline the extent to which CHD exists in the British population and its significant contribution to all-cause mortality statistics. The multi-factorial nature of CHD will be alluded to, with a brief outline of the progression of CHD from a series of risk factors through to congestive heart failure and sudden cardiac death.

This review will explain the categorisation of the risk factors for CHD into modifiable and non-modifiable factors and the subsequent sub-classification of modifiable risk factors into biological and lifestyle based risk. The remainder of this section will focus on the relationships between selected biological and lifestyle risk factors and CHD, as well as the effect of lifestyle on blood haematology and psychological well being.

Blood haematological factors associated with cardiovascular health and disease; such as blood lipid levels, blood haemostatic variables and blood rheological variables will be presented and discussed, as will the important psychological indices. Finally, an outline of the impact of both alcohol consumption and physical activity on cardiovascular health and disease will be provided, with particular emphasis on the effects of alcohol consumption and physical activity on blood haematological profiles and psychological well being.

2.2. Coronary Heart Disease Statistics

2.2.1. Coronary Heart Disease and Mortality

According to recent statistics (British Heart Foundation, 2000), cardiovascular disease is the main cause of death in the UK (250,000 deaths in 1998 alone). Approximately half of the CVD related deaths in the UK are due to CHD. This means that CHD by itself is the most common cause of death in the UK, with 1 in 4 men and 1 in 5 women dying from the disease. It has also been reported (British Heart Foundation, 2000) that CHD accounted for 135,000 deaths in the UK, with a further 35,000 deaths being related to other heart disorders/defects.

Furthermore, CVD is also one of the main causes of premature mortality (death under the age of 75 years) in the UK, as well as overall mortality. Evidence suggests that CVD is responsible for 38% of all premature deaths in men and 30% in women, causing over 80,000 premature deaths in the UK in 1998. Coronary heart disease is again the main cause of premature death in the UK, accounting for 26% of all premature deaths in men and 16% in women. Recent statistics identify CHD as the cause of over 50,000 premature deaths in one year alone (British Heart Foundation, 2000).

2.2.2. Coronary Heart Disease and Morbidity

There are four main sources with which to currently examine the possible morbidity statistics for CHD in the UK (British Heart Foundation, 2000).

1. **The World Health Organisation MONICA Project** (Tunstall-Pedoe et al., 1999)**:** This project has collected data on the incidence of myocardial infarction (MI) in 35 populations, across 21 countries from the 1980s to the mid 1990s. Results showed that both Belfast and Glasgow had high incidence rates for MI.

2. **Surveys of Self-Reported Health Status:** The Health Survey of England is a general survey that is conducted on a yearly basis. Results from 1998 showed that ~3% of adults report suffering from angina in the last 12 months, whilst ~0.4% report having suffered a heart attack in the same time period (Joint Health Surveys Unit, 1999).

The General Household Survey was a 10-year study including questions relating to longstanding sickness. In 1998 over 10% of adults reported having longstanding CVD, which was the second most commonly reported longstanding illness behind musculo-skeletal disorders. Although there have been no marked changes in the rates of self-reported morbidity from previous MI since 1988 in individuals under 65 years, reports suggest that rates have increased in older age groups (Office for National Statistics, 2000).

3. **Data Collected By General Practitioners:** The most recent survey by the Royal College of General Practitioners showed a 31% reduction in the number of people experiencing MI between 1981 and 1991 (Royal College of General Practitioners, 1995). This study further indicated that morbidity from heart failure is common in older age groups, with prevalence rates of 8% in men and 7% in women aged 75-84, this rises to 16% and 13% respectively in those aged over 85 years.

4. **Data Collected by the Department of Social Security:** This data is related to the number of people claiming incapacity benefit. Since 1994/1995 there has been a decrease in the number of days claimed because of CHD and other cardiovascular disorders in both men and women (Department of Social Security, 1995).

2.2.3. Summary

Cardiovascular disease is a major contributor to all-cause mortality statistics within the UK population. In particular, it is CHD, contributing ~50% of all CVD related deaths, that is the major threat. Of particular concern is the significant contribution of CHD to premature mortality statistics. In addition, CHD has a major influence on individual quality of life, with the number of people currently living with the disease in the UK being amongst the highest in the world. Whilst there may have been a significant improvement in the medical and surgical

treatment of CHD, the prevention of CHD remains a significant challenge to both medical and health-related research.

2.3. Coronary Heart Disease

Coronary heart disease is predominantly associated with coronary artery disease (CAD) which refers to alterations in the functional state of the coronary arteries, resulting in an inadequate coronary blood flow (Dzau et al., 1991). The resulting myocardial ischaemia leads to necrosis of the cardiac muscle, which precipitates myocardial infarction (MI), otherwise known as a "heart attack". Interestingly, many CAD patients experience recurrent transient symptoms of restricted blood flow to the myocardium (Dzau et al., 1991). The most common of these symptoms is transient bouts of chest pain, usually experienced during periods of exertion or emotional tension/stress. The chest pain experienced at these times is symptomatic of acute angina pectoris and individuals with this disorder are at a greater risk of subsequent MI (Dzau et al., 1991).

Myocardial infarction can lead to sudden cardiac death or, depending upon the severity of the damage, a loss of a portion of the cardiac muscle resulting in arrhythmia of the heart. Myocardial infarction is usually initiated by the formation of a blood clot (thrombus) in an atherosclerotic coronary artery (Dzau et al., 1991). This thrombus can dislodge and pass through the bloodstream until it finds an arterial lumen that is too small to pass through. At this point it becomes

stuck, and as a result restricts blood flow through the vessel, subsequently depriving the myocardium of necessary oxygen and nutrients (Dzau et al., 1991).

Thus, it is clear that CHD is a complex, multi-factorial disease, which develops through a chain of events beginning with the presence of certain risk factors and terminating in end-stage CHD (Dzau et al., 1991) (Figure 2.1.). The CHD risk factors, of which there are many, elicit negative changes in the heart and vasculature, which eventually become maladaptive or indeed pathological as they progress. For example, Dzau et al. (1991) cite coronary vascular obstruction and myocardial ischaemia as the ultimate consequences of maladaptive or pathological responses to increased intravascular pressure, serum lipid elevations, and other associated cardiovascular risk factors. As shown in figure 2.1., further maladaptive changes occur in the state of the heart in response to the ischaemic conditions it is placed under. These conditions, unless corrected, result in congestive heart failure and end-stage heart disease.

In summary, there are several potential stages of CHD, leading from a series of risk factors through to sudden cardiac death or congestive heart failure (Dzau et al., 1991). It is important to note that CHD is characterised by two distinctive stages. The first refers to atherosclerosis, which is slow to develop and usually precipitates the second stage. The second stage is coronary thrombosis, which can develop much more suddenly and precipitates MI.

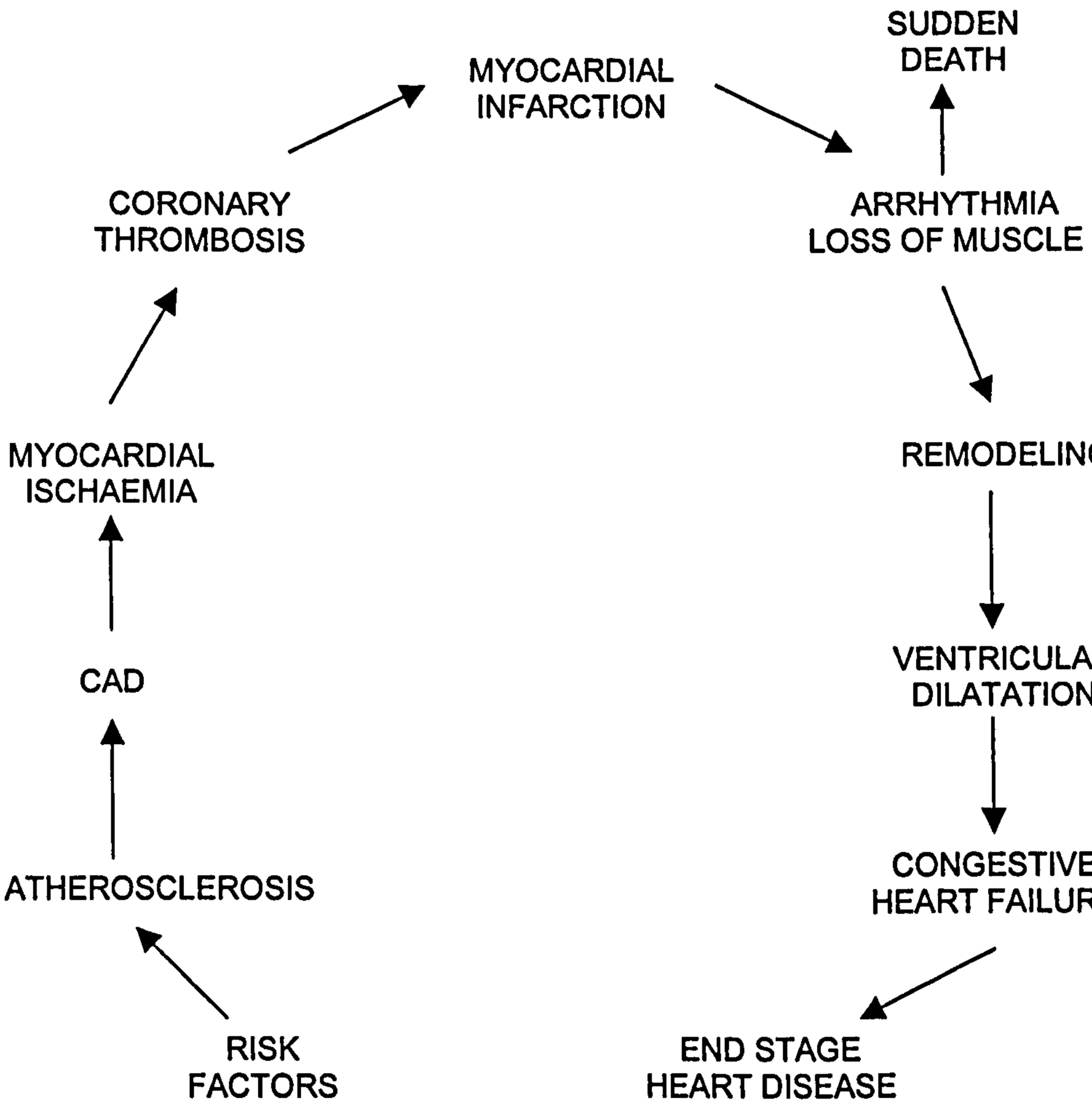


Figure 2.1. The chain of events involved in coronary heart disease (adapted from Dzau et al., 1991). CAD = coronary artery disease.

2.4. CHD Risk Factors

Multitudes of risk factors for the development of cardiovascular disease have been identified. Recent reports from a Danish cohort have identified risk factors including: age, sex, high cholesterol, low high-density lipoproteins (HDL), low low-density lipoproteins (LDL), high systolic blood pressure, smoking, high body mass index (BMI), diabetes, familial predisposition and previous heart disease

(Thomsen et al., 2001). Other additional risk factors have also been identified, and include indices of blood clotting (Smith et al., 2000), blood rheological factors (Junker et al., 1998), high alcohol consumption (Wanemethee and Shaper, 1999), lack of physical activity (Wanemethee and Shaper, 2001). Clearly some of these risk factors are modifiable whilst others are non-modifiable. In terms of disease prevention and the promotion of positive cardiovascular health it is the modifiable risk factors that are of most importance.

Of the modifiable risk factors for CHD there are two main categories: (a) the biological risk factors for cardiovascular disease and (b) the lifestyle/behavioural risk factors for cardiovascular disease (Benfante et al., 1989; Boreham et al., 1999; Twisk et al., 1999). It is the interaction between these two classifications of risk factors, which is of particular importance to current research. Indeed, it is suggested that CHD might be largely preventable by healthy lifestyles and effective management of the biological risk factors for CHD (British Heart Foundation, 2000).

Strong evidence now exists to suggest that atherosclerosis begins in childhood or adolescence (Misra, 2000). This would seem to coincide with the formation or development of many aspects of our lifestyle, particularly the development of our health related behaviour patterns (Perry et al., 1994). These behaviour patterns maybe further developed and modified as we enter adolescence and young adulthood (Leslie and St. Pierre, 1999; Thiessen and Looker, 1999). Indeed,

Raftopoulos et al. (1999) reported that when risk-related lifestyle factors are tracked from childhood into adulthood there was a significant link to the latter incidence of CHD.

Thus, it would seem pertinent to describe the relationship between lifestyle and CHD risk factors in the younger population with the overall goal being to establish guidelines for primary prevention strategies starting in adolescence or early adulthood. However, despite this need there still remains a dearth of information regarding the impact of lifestyle factors on the biological risk factors for CHD in younger populations (Berenson et al., 1997; Boreham et al., 1999).

The Northern Ireland Young Hearts Project (Boreham et al., 1993) was designed as a longitudinal investigation of CHD risk factors in young people. From this data, Boreham et al. (1999) examined the relationship between the development of biological risk factors for CHD in tandem with the development of key risk behaviours in a representative adolescent population. This study concluded that changes in lifestyle were associated with changes in the biological risk factors in adolescents. However, this study, probably because of the age of the participants (12-15 years), concentrated only on elements of physical activity and certain elements of the diet. Alcohol consumption was not considered and although smoking was measured only a very small proportion of the participants smoked. Furthermore, this study only reported on physical activity rather than

elements of cardiorespiratory fitness, which might be a more important predictor in a younger population (Andersen and Haraldsdottir, 1995).

The Coronary Artery Risk Development in Young Adults (CARDIA) study was a longitudinal study examining cardiovascular disease risk in a group of 18-30 years olds. This prospective study outlined the need for further investigation into the effects of lifestyle and other factors that influence, both favourably and unfavourably, cardiovascular disease risk in young adults (Friedman et al., 1988).

In summary, there are clearly well established risk factors for CHD, which have been broadly categorised in to those factors that can be modified and those that cannot. For obvious reasons, research has primarily focussed upon those risk factors that might respond to intervention, with these modifiable risk factors being further sub-classified into biological and lifestyle risk factors. Although some research evidence exists relating to the inter-relationships among biological and lifestyle risk factors in middle-aged and older adults, there remains little information relating to younger populations.

2.5. Blood Haematological Profiles and Cardiovascular Health and Disease

2.5.1. Blood Lipids

The term lipid refers to a heterogeneous group of biomolecules which are generally insoluble in water but which dissolve in non-polar solvents (i.e. chloroform). Lipids perform an array of functions within the body, most notably

acting as energy stores and as the structural components of membranes; although some even function as hormones (Gurr and Harwood, 1991).

The simplest forms of lipids are the fatty acids, which are a common constituent of most other lipids. Some fatty acids are found attached to proteins in the bloodstream as they are being transported, although most fatty acids within the body exist as a formative part of triglycerides (TG) (Brindley, 1985).

Triglycerides are the most common natural lipids found in the body and are formed by the esterification of glycerol with three (usually different) fatty acids. Triglycerides are the primary forms of storage of energy-providing compounds in humans but also provide insulation to the body and aid the transport of fat-soluble vitamins (Brindley, 1985). Triglyceride transport in the blood is facilitated by the presence of cholesterol (Nicolosi and Rogers, 1997). In addition, cholesterol also serves several other important functions. It acts as a precursor for bile acids, which are vital for fat digestion, it is an important structural component of membranes, and also forms part of some hormones such as corticosteroids, the estrogens, testosterone and calcitirol (Bloch, 1985). The cholesterol content of the body comprises that cholesterol which is synthesised within the body (primarily in the liver) and that which is consumed particularly in the form of animal-derived foods (Mead et al., 1986). Excretion of excess cholesterol is also the function of the liver, which disposes of any excesses either

directly, or in the form of bile acids (Mead et al., 1986). However, some cholesterol circulates through the bloodstream to be used, as the body needs it.

The transport of both TG (but not free fatty acids which are transported by albumin) and cholesterol is performed by the plasma lipoproteins (Skinner, 1996). The liver coats the cholesterol and TG with a shell of proteins and lipids producing a very low-density lipoprotein particle (VLDL) (Mead et al., 1986). Triglyceride and cholesterol is secreted from the liver in this way, in VLDL particles (Mead et al., 1986). Very low density lipoprotein particles are significantly smaller than the chylomicrons involved in exogenous lipid transport and contain phospholipid and cholesterol (the majority of which is esterified) (Mead et al., 1986). Approximately 40% of the VLDL protein structure is formed by apolipoprotein B (apo B), which is essential for VLDL secretion (Grundy, 1997). When the VLDL leaves the liver, lipoprotein lipase breaks down the TG in the VLDL to form fatty acids and glycerol (Brindley, 1985). These constituents are then released in to the bloodstream and are taken up by the body cells, where they are either oxidized or stored as adipose tissue (Brindley, 1985).

However, the VLDL does not disappear totally from the plasma at this stage (it has a half-life of ~2h in circulation), rather it begins to interact with high-density lipoproteins (HDL) (Mead et al., 1986). The VLDL is now termed an intermediate density lipoprotein as the density of the molecule has increased as TG is released (because fats are less dense than water). Much of the remaining VLDL

fraction eventually forms low-density lipoprotein (LDL) particles, predominantly composed of cholesterol (Mead et al., 1986). Low-density lipoprotein particles are absorbed from the bloodstream by receptors on cells, internalised and brokendown (Grundy, 1997). Most of the LDL is taken up by receptors on liver cells, which bind with LDL with high affinity (probably binding with apo B) (Grundy, 1997). Diets high in saturated fat and cholesterol can hamper this process by saturating the receptor sites with LDL, causing an accumulation in plasma (Grundy, 1997). Thus, the overall concentration of cholesterol in plasma tends to be proportional to LDL concentration. In many mammals there appears to be a rapid turnover of LDL from the blood although this process appears to be much slower in humans (Grundy, 1997).

The final essential component of lipid transport is HDL, which is the most dense lipoprotein, as a result of the high proportion of protein in its structure (90% apolipoprotein A [apo A], in two forms AI and AII) (Hemming and Hawthorne, 1996). Relatively little is known about its function, although it is thought that HDL scavenges cholesterol from peripheral tissues and from dying cells and then donates them back to lipoproteins, which then transport them back to the liver for excretion (Mead et al., 1986). It is via this pathway that peripherally formed cholesterol can be transported to the liver where it is converted to bile acids and excreted (Mead et al., 1986). Thus, it is thought that HDL plays a vital role in regulating cholesterol accumulation in peripheral tissues (Grundy, 1997).

2.5.1.1. Blood Lipids and CHD Risk

Moderate to severe elevations of both total cholesterol and LDL concentration in the blood is universally accepted as being causally related to the aetiology of atherosclerosis and CHD (Sharrett et al., 2001; Simons et al., 2001). The reduction of cholesterol and LDL levels in the blood significantly reduces the risk of CVD, as the administration of lipid-lowering therapy instigates a regression of atherosclerotic lesions (Brensike et al., 1984; Levy et al., 1984).

Previous reports have suggested that LDL concentrations in excess of 130mg.dl^{-1} warrant some form of intervention (Dzau et al., 1991). However, those individuals exhibiting other CHD risk factors may need a much lower level than this, particularly as elevated LDL levels further enhance the influence of other elements of atherogenic dislipidaemia (Grundy, 1997). Because there is a slow turnover of LDL in the plasma in humans, an accumulation of LDL molecules in the blood can occur. Low density lipoprotein molecules may then contribute to the formation of atherosclerotic lesions containing cells loaded with cholesterol (Heinecke, 1996).

Another element contributing to atherosclerotic dislipidaemia is hypertriglyceridemia (Grundy, 1997). Hypertryglyceridemia is also associated with the production of smaller LDL particles and a reduced HDL concentration in the blood (Grundy, 1997). Triglyceride levels begin to exert this effect at concentrations exceeding 150mg.dl^{-1}, although more normally

hypertriglyceridemia is a term reserved for concentrations above 200mg.dl^{-1} (Grundy, 1997).

In contrast cumulative research evidence has indicated that increases in HDL levels are cardio-protective (Dzau et al., 1991). However, the underlying mechanism responsible for this cardio-protective effect is not yet fully understood. Previous reports have suggested that the proposed cardio-protective effect of elevated HDL concentration occurs as a consequence of its role in reverse cholesterol transport (Skinner, 1996). Reverse cholesterol transport involves the efflux of cholesterol from peripheral tissues, promoted by small HDL particles or perhaps their apolipoproteins (Skinner, 1996). What is clear is that HDL levels below 35mg.dl^{-1} are indicative of a significantly elevated risk of cardiovascular disease (Grundy, 1997).

Two apolipoproteins, apo A1 and apo B have been linked with the CHD risk, as several studies have identified a reduced incidence of CHD in individuals with higher apo A1 levels (Kamboh et al., 1995; Gazzaruso et al., 1999). Conversely, apolipoprotein B levels have been positively linked with an increased incidence of CHD (Hamsten et al., 1986b).

In summary, atherogenic dislipdemia is characterised by the presence of several lipoprotein abnormalities, such as elevated LDL levels, high TG concentrations, small LDL particles and low HDL levels (Grundy, 1997). Whilst each of these

factors might be considered atherogenic in isolation, combinations of these lipid and lipoprotein abnormalities are usually observed. Thus, atherogenic dislipidaemia is indicative of an increased risk of CHD, at least on a par with moderate hypercholesterolemia, which is an independent CVD risk factor (Grundy, 1997).

2.5.2. Blood Haemostasis

Haemostasis refers to the way in which the body prevents blood loss. Physiological haemostatic mechanisms are most effective in dealing with injuries to the smaller blood vessels, as bleeding from a medium to large artery is unpreventable by the body. The normal vascular system maintains a delicate, yet dynamic balance between blood clot formation and clot lysis (El-Sayed et al., 2000). This balance is termed the haemostatic balance and prevents either internal or external bleeding from becoming too severe and also prevents pathological thrombosis. Thus, any alteration in the haemostatic balance can lead to excessive bleeding or pathologic thromboses (Mann, 1999).

Several factors acting in coalition maintain this equilibrium, including vasoconstriction of the blood vessel; platelet activation, adhesion and aggregation; blood coagulation and blood fibrinolysis. For the purpose of this study, emphasis will primarily be placed on blood coagulation and fibrinolysis.

Because of the complex nature of blood haemostatic mechanisms this review will describe mechanisms of blood coagulation and fibrinolysis separately, although it should be noted that both mechanisms interact closely to maintain the haemostatic balance.

2.5.2.1. Blood Coagulation

Blood coagulation represents the biological system via which the body permanently heals a vascular injury. It follows the processes of vasoconstriction and platelet plug formation and is designed to maintain haemostasis once normal blood flow has been restored (Mann, 1999). Blood coagulation is achieved via the interaction of several plasma proteins, protease zymogens, enzymes and cofactors that ultimately result in thrombin activation and the formation of fibrin when they are activated sequentially (Broze, 1995). The production of thrombin is rapid, occurring in under 5 minutes, and has been described as being semiautocatalytic because of its role in the feedback activation of other factors involved in the coagulation system (Mann, 1999).

Traditionally, two pathways of blood coagulation have been described and termed the intrinsic and extrinsic pathways (Figure 2.2.). The intrinsic pathway leads to thrombin generation using only the protein factors available in the circulating plasma, whilst the extrinsic pathway requires the presence of a lipid-dependent membrane glycoprotein which does not occur in plasma (Halkier, 1991). Recently, the traditionally held views about the coagulation processes

have been modified due to the fact that the intrinsic and extrinsic pathways for blood coagulation would appear to interact more closely than was initially thought (Roberts and Lozier, 1992).

The process of blood coagulation was originally reported to involve a cascade or waterfall of reactions (Macfarlane, 1964; Davie and Ratnoff, 1964). Whilst this theory remains relevant, others have suggested that for these reactions to proceed at physiologically relevant speeds, the presence of thrombin activated co-factors is required (Halkier, 1991). Thus, a more modern view of the coagulation process is that it involves a network of cyclic reactions.

The process of blood coagulation, in terms of the intrinsic pathway, begins with contact activation (Halkier, 1991). Contact activation involves the interaction of four proteins: factor XII, factor XI, plasma prekallikrenin (PK) and high molecular weight kininogen (HK) which interact with each other and with a negatively charged surface (where the majority of coagulative processes occur). For a review of the structure of these proteins and the mechanism of contact activation please refer to Halkier (1991). It should be noted that the exact mechanism responsible for contact activation is not completely understood, although the aim is quite clearly to convert the inactive factor XI to its active form, factor XIa (Halkier, 1991). Factor XIa in turn converts the inactive factor IX to factor IXa.

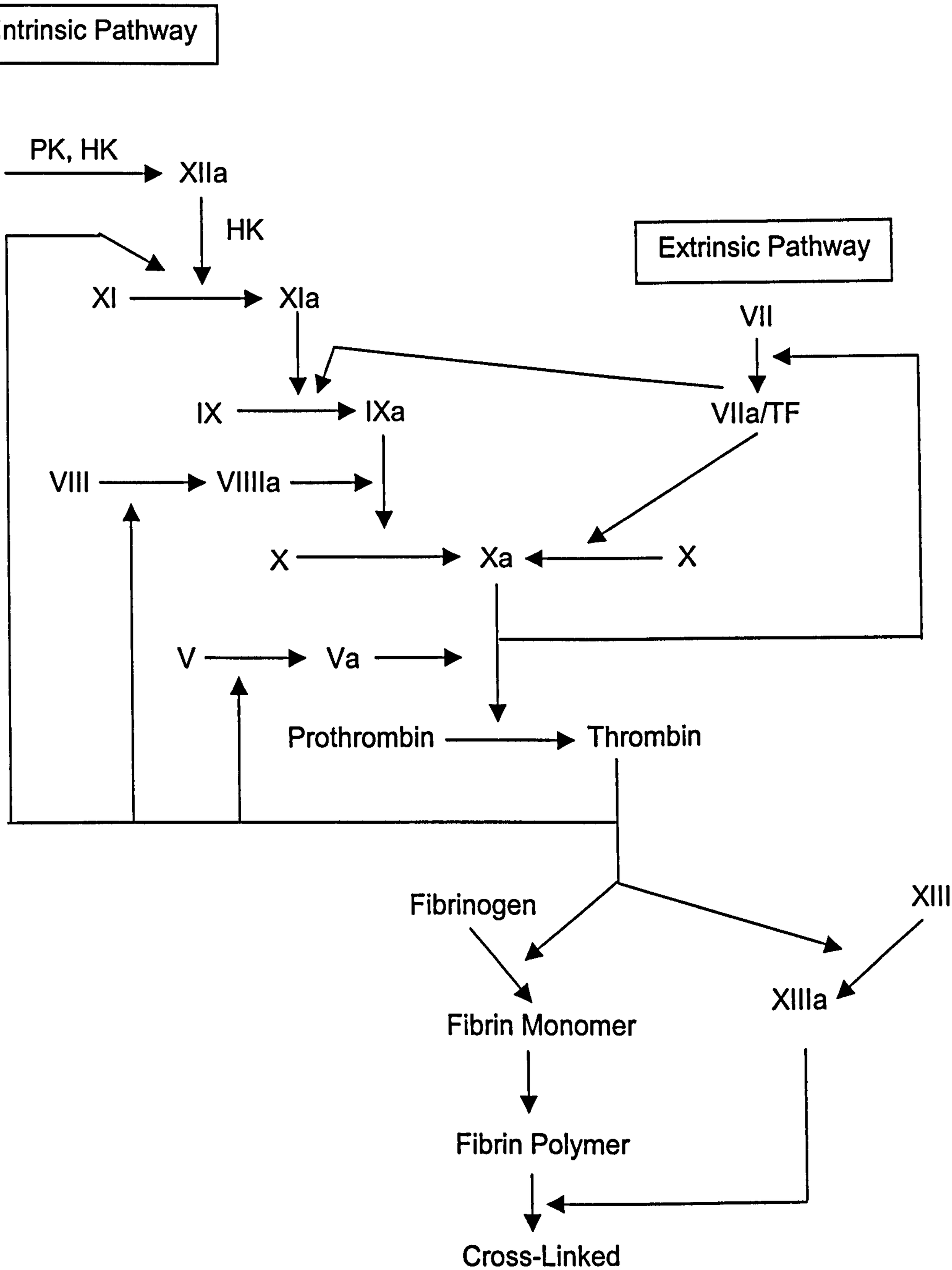


Figure 2.2. The interaction between the intrinsic and extrinsic pathways of blood coagulation (adapted from Roberts and Lozier, 1992). PK = prekallikrenin, HK = high molecular weight kininogen and TF = tissue factor

The next major step in the intrinsic pathway is the activation of factor X, which is brought about by the action of factor IXa (Halkier, 1991). In addition, the activation of factor X requires the presence of various co-factors in order for its conversion to occur at physiologically relevant speeds (Halkier, 1991). These co-factors include factor VIIIa, calcium and an anionic phospholipid. The primary function of factor Xa, once formed, is to convert prothrombin to thrombin (Mann, 1999). The activation of the conversion of prothrombin to thrombin by factor Xa again requires the presence of co-factors (calcium, phospholipid, and factor Va) (Halkier, 1991). The activation of thrombin eventually leads to the formation of the insoluble fibrin clot, via the conversion of fibrinogen into fibrin (Halkier, 1991). However, before discussing this in more detail the relevant activation's in the extrinsic pathway, which also results in the activation of factor X, will be discussed. The activation of factor X is the convergence point for both the intrinsic and extrinsic blood coagulation pathways (Halkier, 1991).

The activation of factor X via the extrinsic pathway requires the complex interaction of factor VIIa and its co-factors (tissue factor and calcium). Little is currently known with regards to this complex process, although it would appear that when factor VIIa binds with tissue factor it undergoes a conformational change which gives it an affinity for factor X (for a more in depth discussion of this issue please refer to Halkier, 1991).

In addition, it would appear that factor VIIa plus co-factors can also activate factor IX (Mann, 1999), thus providing some evidence of the previously mentioned inter-relationship between the intrinsic and extrinsic pathways. Indeed, it would appear that the proenzyme factor X is preferentially activated to factor Xa by the tissue factor/factor VIIa/factor IXa complex (Mann, 1999). The major problem with this theory is that this would not leave a role for the factor VIIIa-factor IXa mediated activation of factor X in the blood clotting pathways. However, the discovery of tissue factor pathway inhibitor (TFPI) provides a mechanism by which both of these pathways can work closely together in blood coagulation (Roberts and Lozier, 1992).

In this theory, the process of blood coagulation is activated by the exposure of tissue factor to factor VIIa which, as mentioned, results in the activation of both factor X and IX (Roberts and Lozier, 1992). It is at this point that TFPI works to prevent further factor Xa from being produced from factor VIIa and co-factors (Broze, 1998), although the reasons for this are not fully understood. This means that the only way that further factor Xa can be produced is via the intrinsic pathway involving factor IXa and factor VIIIa (Broze, 1998). This newer theory of blood coagulation means that the whole process is activated by tissue factor, rather than by contact activation.

The final step in blood coagulation is the formation of an insoluble fibrin clot and its covalent stabilisation (Halkier, 1991). The thrombin generated via both

intrinsic and extrinsic pathways catalyses the conversion of fibrinogen to fibrin (monomer), which binds in to a fibrin polymer structure (Halkier, 1991). In addition to its action on fibrinogen, thrombin also activates factor XIII (Halkier, 1991). Once formed factor XIIIa stabilises the fibrin clot by causing covalent cross-linking (Halkier, 1991).

2.5.2.2. Blood Coagulation and CHD Risk

Whilst a large body of evidence has suggested a role for the presence of elevated fibrinogen levels in the prediction of future CHD (Meade et al., 1986; Kannel et al., 1987; Smith et al., 2000), the relationship with other elements of the haemostatic system are less well observed. Several possible reasons for this exist, most notably the fact that the measurement of coagulation factors, such as FVII and FVIII, involve laborious analytical processes and as a result are difficult to measure accurately.

Examining clotting times, such as activated partial thromboplastin time (APTT), prothrombin time (PT) and thrombin time (TT) may provide some indication as to the potential clottability of the blood, should either of the blood clotting pathways be activated. In particular, the measurement of APTT provides and indication as to the global activation of the intrinsic blood coagulation pathway, whilst PT provides an indication of the global activation of the extrinsic pathway (El-Sayed, 1996). Thrombin time is an assay directly related to plasma fibrinogen concentration (El-Sayed, 1996).

There has been some interest in examining these indices in relation to the incidence and risk of CVD. Folsom et al. (1999) examined the risk of stroke in middle-aged subjects in relation to markers of haemostatic function, including APTT. Whilst there was some evidence of a reduced clotting time in those subjects with subsequent ischaemic stroke, the results failed to reach significance. However, when examining elements of peripheral atherosclerosis, Koksch et al. (1999) reported a lengthened PT and APTT in the patient group when compared to controls.

In summary, there exists a well-documented relationship between enhanced blood coagulation and the risk of CHD. In particular, a large body of evidence has identified a significant relationship between fibrinogen levels and CHD. However, the impact of other blood coagulation factors relating to the incidence of CHD are less well documented, although some evidence suggests a relationship between shortened blood clotting times and CHD.

2.5.2.3. Blood Fibrinolysis

The final process of blood clotting involves the formation of fibrin. Whilst this is a necessary process to staunch the flow of blood from vascular injury, it is also temporary and must be removed when the normal structure and function of the tissue is restored (Juhan-Vague et al., 1995). As its name suggests, fibrinolysis, or more accurately the fibrinolytic system, is the process by which the body

brings about the dissolution of the blood clot by controlling the enzymatic degradation of fibrin (Collen, 1980). The fibrinolytic system has great physiological importance, as demonstrated by the links between abnormal fibrinolysis and thrombosis on one end of the scale and with bleeding abnormalities on the other end of the scale (Lijnen and Collen, 1995).

One of the major components of the blood fibrinolytic system is plasminogen, an inactive proenzyme that can be converted to the active enzyme plasmin (Lijnen and Collen, 1995). Plasmin is the enzyme that degrades fibrin to the insoluble fibrin degradation products. In terms of the activation of plasminogen, two distinctly different plasminogen activators have been identified: tissue-type (tPA) and the urokinase-type (uPA) (Lijnen and Collen, 1995). These plasminogen activators are different as tPA mediated plasminogen activation is predominantly involved in the dissolution of fibrin in the circulation, whereas uPA seems to participate in pericellular proteolysis (Lijnen and Collen, 1995). For this reason the remainder of this review will concentrate primarily upon tPA, which has the most relevance to this study.

Inhibition of the blood fibrinolytic system may occur at the level of the activation of plasminogen or at the level of plasmin (Figure 2.3.). Specific plasminogen activator inhibitors (PAI-1 and PAI-2) lead to the inhibition of tPA and uPA, whilst α_2-antiplasmin inhibits the action of plasmin (Lijnen and Collen, 1995). The physiological processes of fibrinolysis are regulated via interactions between its

main components (Lijnen and Collen, 1995). In addition, the control over the synthesis and release of plasminogen activators and plasminogen activator inhibitors also help to regulate blood fibrinolysis (Lijnen and Collen, 1995).

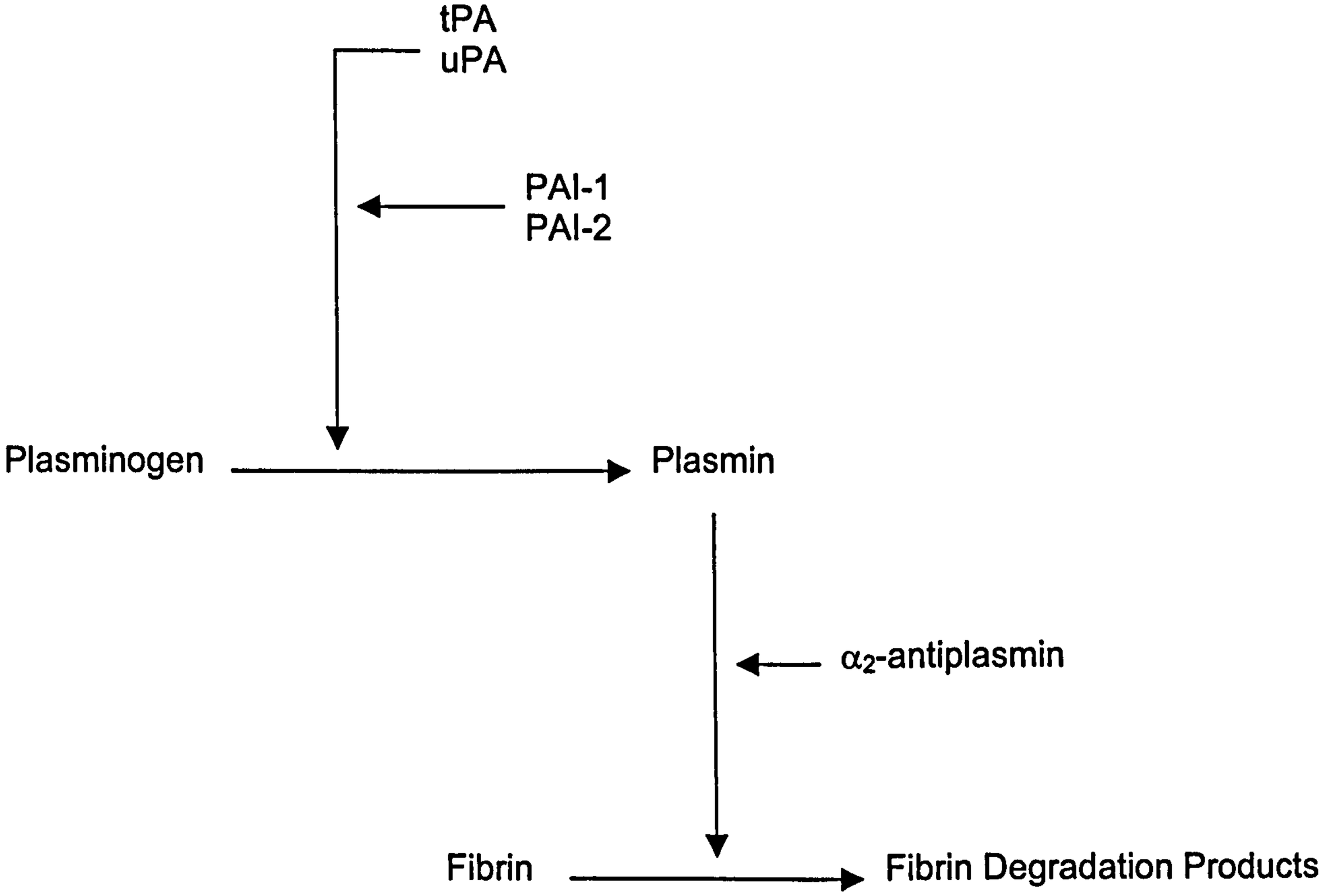


Figure 2.3. Schematic presentation of the fibrinolytic system (adapted from Lijnen and Collen, 1995).

2.5.2.3.1. Plasminogen

Human plasminogen is a single chain glycoprotein manufactured and secreted by the liver. Two slightly different forms of plasminogen exist and have been termed lys-plasminogen and glu-plasminogen (Lijnen and Collen, 1995). Both forms of plasminogen contain five homologous triple-loop structures called kringles, each of which contain structures called lysine-binding sites and aminohexyl-binding sites (Lijnen and Collen, 1995). Collen (1980) reported that these binding sites mediate the specific binding of plasminogen to fibrin and the interaction of plasmin with α_2-antiplasmin. Thus, these structures play a pivotal role in the regulation of blood fibrinolytic mechanisms.

2.5.2.3.2. Plasminogen Activators

Tissue plasminogen activator is synthesised and secreted from vascular endothelial cells in to the circulation (van Hinsbergh et al., 1991), where its concentration is normally between 0.2-2.0IU.ml^{-1} in normal healthy subjects. However, the half-life of tPA in the circulation is short (approximately 5 minutes) because of the rapid clearance of tPA by the liver. The results of previous reports have suggested that various stimuli, including catecholamine infusion, venous occlusion and exercise cause a rapid increase in the circulating tPA concentration (Lijnen and Collen, 1995; El-Sayed, 1995). Previous research has suggested that increases in tPA with exercise might be the result of elevations in

adrenaline as well as the result of decreased hepatic clearance due to a reduction in blood flow to the liver (Chandler et al., 1993).

Two separate phases, one slow, the other more rapid, have been identified in tPA mediated clot lysis (for review see Thorsen, 1992; Rijken, 1995). The slow phase is thought to involve the activation of plasminogen by single-chain tPA on the intact fibrin surface. The more rapid phase then takes place on a fibrin surface, which has already been partially degraded through the actions of plasmin (Rijken, 1995). This partial degradation exposes additional binding sites for both tPA and plasminogen on the superficial layer of the fibrin clot (Suenson et al., 1990), where massive concentrations of plasminogen have been measured (Sakharov and Rijken, 1994). A further reaction which may also assist in speeding up the degradation process is the conversion of the circulating single-chain tPA in to a two-chain tPA form by plasmin (Rijken, 1995).

2.5.2.3.3. Plasminogen Activator Inhibition

As previously mentioned, blood fibrinolysis is also regulated by specific inhibitors of plasminogen activation. The two most important inhibitors of plasminogen activation are PAI-1 and PAI-2 (Lijnen and Collen, 1995). Plasminogen activator inhibitor-1 is the most important inhibitor of single-chain tPA and two-chain tPA and can be measured in plasma at a concentration between 0-40IU.ml^{-1} (Lijnen and Collen, 1995). Plasminogen activator inhibitor-1 and tPA interact rapidly with each other, PAI-1 inhibiting the action of tPA by acting as a pseudo-substrate

(Lijnen and Collen, 1995). Plasminogen activator inhibitor-2 on the other hand is a rapid inhibitor of two-chain uPA and a slow inhibitor of two-chain tPA, although it does not inhibit single-chain tPA (Rijken, 1995). However, as PAI-2 is unmeasurable in normal human plasma, although it has been measured during pregnancy (Astedt et al., 1998), the remainder of this section will concentrate primarily upon PAI-1.

Although the source of PAI-1 in plasma was thought to be the vascular endothelial cells, subsequent investigation has shown that it is synthesised by a number of cell types including endothelial cells, magakaryocytes and hepatocytes (Rijken, 1995). Platelets also contain a high concentration of PAI-1 which is thought to be released upon platelet activation, although only 5% of the PAI-1 stored in platelets is the active form (Rijken, 1995). Despite the high concentrations of PAI-1 in platelets this source is not thought to contribute to plasma concentrations of PAI-1 (Rijken, 1995). Much of the variability in PAI-1 concentrations is thought to be due to the large diurnal effects on PAI-1, showing lower values later in the day (Andreotti and Kluft, 1991).

2.5.2.3.4. Plasmin

Plasminogen is converted to plasmin by cleavage of the Arg561-Val562 peptide bond (Lijnen and Collen, 1995). The plasmin molecule is a two-chain trypsin like serine proteinase composed of a heavy chain and a light chain (Lijnen and Collen, 1995). The primary function of plasmin is to cause the intravascular lysis

of fibrin, although it also causes the alteration of glu- to lys- plasminogen and inhibits selected coagulation factors including factors V, VII, and von Willebrand factor (Bachmann, 1994).

2.5.2.3.5. Plasmin Inhibitors

In addition to the inhibition of plasminogen, plasmin is also inhibited by α_2-antiplasmin. The plasma concentration of α_2-antiplasmin is 1μM, it is 13% carbohydrate, contains 464 amino acids and has a molecular weight of 67kDa (Holmes et al., 1987). α_2-antiplasmin reacts with plasmin by forming a 1:1 molar reversible complex. The inhibition of plasmin by α_2-antiplasmin occurs via two consecutive reactions (Lijnen and Collen, 1995), one a fast reaction resulting in the formation of a reversible inactive complex, the other a slower reaction resulting in and irreversible complex.

2.3.2.3.6. Fibrin/Fibrinogen Degradation

Once plasmin is formed it can degrade both fibrin and fibrinogen, with the resultant formation of both fibrin and fibrinogen degradation products. In other words, these protein fragments, termed fibrin degradation products (FDP), result from the proteolytic action of plasmin on fibrin or fibrinogen (Halkier, 1991). The plasmin catalysed cleavage of fibrinogen results in the formation of fragments D and E, which are considered as the final products of fibrinogenolysis (Halkier, 1991). The main difference between the degradation of fibrin in a clot and the degradation of fibrinogen is the presence of stabilising cross-links in the clot, this

means that the final products of fibrin degradation are slightly different to those of fibrinogen degradation (Halkier, 1991). In fibrin degradation the final products are fragment E and a dimer of fragment D (D-dimer) (Halkier, 1991). D-dimer is formed from the cross-linking of one fragment D with another fragment D released from adjacent fibrin molecule. The fibrin/fibrinogen fragments are not of fixed size but rather reflect their exposure to a greater, or lesser, amount of proteolytic shearing (Halkier, 1991). The measurement of FDPs in plasma is the most substantial evidence of continuing *in vivo* fibrinolysis (Rijken, 1995).

In summary the key components of blood fibrinolysis are:

- Plasminogen
- Plasminogen Activators
- Plasminogen Activator Inhibitors
- Plasmin
- Inhibitors of Plasmin
- Fibrin/Fibrinogen Degradation

Under normal physiological conditions the fibrinolytic system dissolutes the fibrin clot and is well controlled via specific interactions between the previously mentioned components. However, disruption of these normal physiological conditions may result in a disturbance of the balance between a profibrinolytic state and the inhibition of fibrinolysis, which on the one hand could lead to excessive bleeding, and on the other to a prothrombotic tendency of the blood

(El-Sayed, 1996). The more common of the two problems is a decreased fibrinolytic activity. Impaired synthesis and/or release of plasminogen activators may cause this via impairment of the function or synthesis of plasminogen, or via elevated PAI-1 levels (Juhan-Vague et al., 1995). All of these facts point towards a strong possible association between impaired fibrinolysis and the risk of CHD.

2.5.2.4. Blood Fibrinolysis and CHD Risk

Early investigations in to the possible associations between fibrinolytic function and CHD was based upon analyses such as euglobulin clot lysis time and fibrin plate lysis techniques (Korsan-Bengsten et al., 1972; Franzen et al., 1983). These studies clearly identified a role for impaired fibrinolytic function in the development of CHD. Although they provided excellent information regarding haemostatic function, these techniques reflected the simultaneous function of both fibrinolytic activators and inhibitors (Hamsten and Eriksson, 1995).

Increased PAI-1 activity levels have also been cited in several thrombotic disease states, including CAD and MI (Gram et al., 1987; Hamsten et al., 1987; Thompson et al., 1995; Kohler and Grant, 2000). In addition, previous research has reported that impaired fibrinolysis is a strong determinant of CHD in younger populations (Meade et al., 1993), particularly in those with hypertriglyceridemia (Hamsten et al., 1987). Hamsten et al. (1987) also examined the relationship between the recurrence of MI and plasma concentrations of PAI-1. Data showed

a positive relationship between PAI-1 and myocardial re-infarction after a period of 3 years. It should be noted however that the later finding contrasts with the results reported by Jansson et al. (1991) who failed to demonstrate a relationship between PAI-1 and myocardial re-infarction.

A further link between PAI-1 and CHD risk comes from the work of Juhan-Vague et al. (1991) who identified links between PAI-1 concentrations and insulin resistance, BMI, TG levels, insulin levels and systolic blood pressure. Although the mechanisms via which hyperinsulinaemia, insulin resistance and elevated PAI-1 levels are linked remains unclear.

Other research has not shown an association between either PAI-1 activity (Jansson et al., 1993) or clot lysis time (Meade et al., 1986) and MI, although a significant association between tPA antigen and CHD has been identified (Ridker et al., 1993; Haverkate, 1994; Thompson et al., 1995). There remains a question over which of the two parameters, PAI-1 or tPA antigen has the greater predictive value (Juhan-Vague et al., 1995). However, the elevated tPA levels in the circulation may more reflect an increase in the formation of tPA – PAI-1 complexes, and thus associations between increased tPA antigen levels and CHD are most likely mediated by PAI-1 levels and depressed fibrinolysis (Hamsten and Eriksson, 1995).

Several investigations have shown an elevation in circulating D-dimer levels in CVD patients (Herren et al., 1994; Danesh et al., 2001). This is clearly indicative of an *in vivo* hyperfibrinolysis in these patients. Thus, it would also be logical to assume that some degree of enhanced fibrin formation must also occur in CHD patients. It has been hypothesised that modest elevations in circulating D-dimer concentrations may reflect minor increases in blood coagulation as a consequence of thrombin formation, with a resultant increase in the turnover rate of cross-linked intravascular fibrin (Danesh et al., 2001). These, alterations have obvious importance for CHD risk.

In summary, the epidemiological, clinical and experimental evidence supports the hypothesised link between a disruption of the fibrinolytic system and CHD (Hamsten and Eriksson, 1995). In particular, elevated plasma concentrations of PAI-1 have been demonstrated in patients with varying degrees of CHD and associations among PAI-1 levels and metabolic and biological risk factors for CHD have been reported (Juhan-Vauge et al., 1995). However, it should be noted that it remains unclear whether impaired fibrinolysis is involved in the pathogenesis of CHD or merely occurs as a result of it.

2.5.3. Blood Rheology

The term haemorheology is used to describe the movement of blood through the vascular system. The rheological nature of human blood is governed by its viscous properties and by the interaction among several related variables. The

major determinants of blood rheology are whole blood viscosity, plasma viscosity, haematocrit, red blood cell deformability, red blood cell aggregation and fibrinogen concentration (El-Sayed, 1998). Whole blood viscosity is a universal measure of blood flow through the vascular system, with a more viscous blood providing a greater resistance to blood flow (Somer, 1966). This would mean that whole blood viscosity is a measure of the blood's internal frictions as it flows (El-Sayed, 1998).

Plasma viscosity is perhaps the major determinant of whole blood viscosity (El-Sayed, 1998). Previous reports have suggested positive associations between plasma viscosity and several plasma proteins, including plasma fibrinogen and globulins (Rand et al., 1970) as well as total protein concentrations (Rosenson et al., 1996). Indeed plasma fibrinogen concentration is thought to have the greatest effect on plasma viscosity levels as evidenced by the fact that plasma viscosity is usually ~20% greater than serum viscosity, although others have reported a difference of only ~7% (Jones et al., 1999). Carroll et al. (2000c) examined the biochemical predictors of plasma viscosity, showing the major predictors to be serum total protein and fibrinogen concentrations.

However, reports on the influence of albumin concentration on plasma viscosity are less clear (El-Sayed, 1998). Furthermore, other investigators have also reported associations between plasma lipid levels and plasma viscosity (Rosenson et al., 1996), as plasma viscosity was positively related to TG

concentration, whilst serum viscosity was positively associated with LDL cholesterol levels.

The term haematocrit refers to the volume of red blood cells existing in whole blood, expressed as a percentage. El-Sayed (1998) reported that there is a linear relationship between viscosity and haematocrit, although this linearity is only maintained over a specific haematocrit range of 20-60%. Beyond this range increases in viscosity become disproportionately higher with increasing haematocrit levels (Chien et al., 1966).

2.5.3.1. Blood Rheology and CHD Risk

Since the development of the appropriate techniques for the measurement of the rheological properties of human blood (for review see Harkness, 1971), the majority of research in this area has concentrated on the clinical impact of changes in the haemorheological profile. Existing research has indeed implicated alterations to the haemorheological profile in CVD (Rainer et al., 1987; Ernst et al., 1988; Koenig et al., 1988; Lowe et al., 1988; Neumann et al., 1989; Mares et al., 1991; Yarnell et al., 1991; Sweetnam et al., 1996; Kesmarky et al., 1998).

Lowe et al. (1980) showed a relationship between CAD and whole blood viscosity, plasma viscosity and plasma fibrinogen levels in 50 subjects aged between 30 and 55 years. They concluded that there was an association

between increased blood viscosity, but not plasma viscosity, and the extent of CAD in men. Similarly, Kesmarky et al. (1998) observed significant associations between whole blood viscosity and the extent of CAD, although in contrast to the data reported by Lowe et al. (1980) an association between CAD and plasma viscosity was also observed.

Junker et al. (1998) were the first to observe a significant relationship between plasma viscosity and the severity of CHD. Indeed, Junker et al. (1998) concluded that cardiovascular risk factors and CHD might be linked by plasma viscosity. In this study, coronary angiography was used to document changes in the atherosclerotic profile and this was related to plasma viscosity and other biochemical correlates. The study showed that in those subjects exhibiting 3 coronary vessels with stenoses, plasma viscosity was greater than in those subjects without stenosed vessels. Others have also reported similar findings (Kesmarky et al., 1998).

Initial analyses of the Framingham data showed an increase in CHD risk in subjects with high haemoglobin levels (Kannel et al., 1961). However, subsequent multivariate analysis of the same cohort appeared to show no such relationship (Truett et al., 1967). It is evident that a number of studies have shown elevated haematocrit levels in patients with coronary, cerebral and peripheral arterial disease (for review see Ernst, 1997). Ernst (1997), in a useful review of the current literature, concluded that the majority of epidemiological

investigations showed positive associations between haematocrit and CHD risk. Similarly, Kesmarky et al. (1998) also observed increased haematocrit levels in patients exhibiting multi-stenosed vessels, when compared to those without stenosed vessels or those with a single stenosed vessel.

In summary, many investigations have identified a link between components of blood rheology and the incidence of CHD. In particular, whole blood viscosity, plasma viscosity and fibrinogen appear to be significantly linked to CHD, although research evidence relating to the impact of other rheological variables on CHD risk are equivocal.

2.5.4. Psychological Well Being and Stress

Several theories of what constitutes both positive and negative psychological well being are evident from the literature (Ryff, 1989). Studies on psychological well being have included investigations of both general psychological well being and more situational psychological well being (particularly in relation to the workplace). Cooper (1986) and Warr (1990b) have proposed two of the more influential and well-recognised models of stress and psychological well being. Cooper (1986) suggests that stress interacts with several specific characteristics of the individual such as anxiety, neuroticism and personality. In this way, stress and these individual characteristics impact upon mental health and psychological well being. Warr (1990b) proposed an affective well being model based upon 3

continuums: anxiety-contentment, depression-enthusiasm and pleasure-displeasure. The approach to affective psychological well being was through two principal axes, which have been highlighted as the most important through non-occupational research (anxiety-contentment and depression-enthusiasm). The major types of affect maybe located anywhere along these axes and take into consideration feelings of both pleasure and arousal.

Whilst these models of psychological well being have tended to be employed in occupational research, and thus are considered situation dependent, other researchers have tended to examine more general aspects of psychological well-being. In particular, the other context-free measures of psychological well-being have tended to concentrate upon elements of life satisfaction, happiness, positive affect, negative affect, anxiety, depression, general dysphoria, self-esteem and other types of feeling (Goldberg, 1972; Diener, 1984).

Thus, a simple overview (albeit from an occupational setting) of the psychological well being (stress) process can be obtained from models such as Cooper (1986) (Figure 2.4.). As can be seen situational demands (sources of stress) operate through dispositional characteristics of the individual (such as personality and personal control) and coping styles to result in poor psychological well being and stress (mental ill health). Therefore, any research investigating psychological well being and stress should include measures of personality, personal control

(mastery) and coping style. As can be seen from figure 2.4. the anticipated long-term consequences of stress include physical ill health, such as CHD.

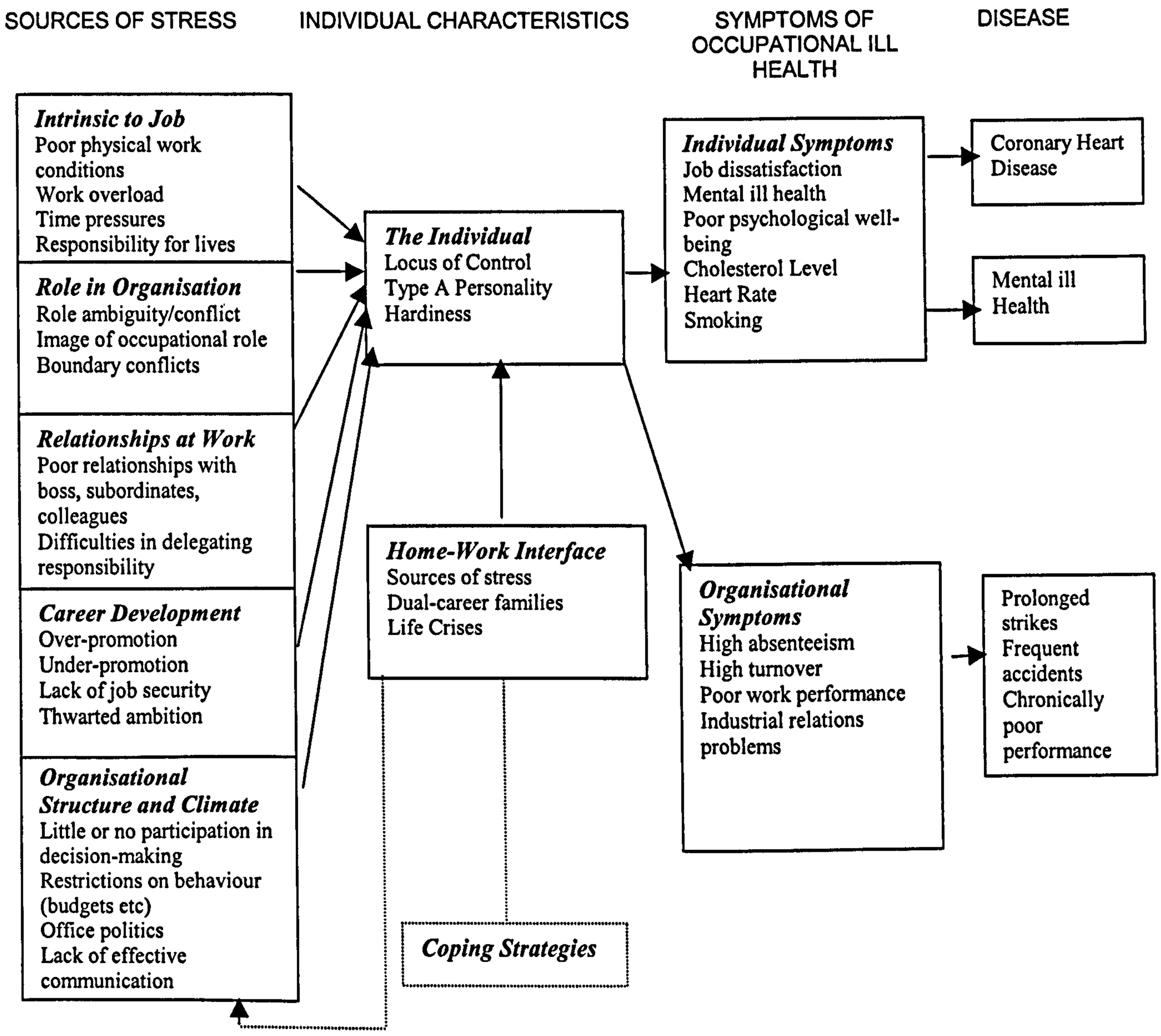


Figure 2.4. Model of occupational stress (adapted from Cooper, 1986).

2.5.4.1. Psychological Well Being and CHD Risk

Previous research has indicated a high correlation between perceived mental health status and medically assessed health status in predicting morbidity and mortality (Hooker and Siegler, 1992). However, recent review has questioned whether psychosocial factors are implicated in the aetiology of coronary heart disease or whether they merely affect survival among patients with existing disease (Hemingway and Marmot, 1999).

In terms of a relationship between psychological factors and CHD, stress, depression and anxiety have all previously been associated with the incidence of CHD, both before and after manifestation of the disease through MI (Troxler and Schwertner, 1985; Tennant, 1987; 1999). Indeed, other studies have suggested that work stress, lack of social support, depression, anxiety and personality are the most consistent psychological factors relating to the incidence of CHD (Hemingway and Marmot, 1999; British Heart Foundation, 2000). Cooper (1986) suggests that sources of stress can interact with several key characteristics of the individual, such as anxiety, neuroticism and type A personality patterns. According to Cooper (1986) these affects can, in turn, lead to mental ill health as well as several symptoms of physical ill health. In Cooper's model these include high blood pressure and heart rate, high cholesterol levels, smoking and high alcohol consumption. Clearly, these factors have been implicated in the biological risk for cardiovascular disease and may provide an indication of how

biological, psychological and lifestyle factors inter-relate to impinge upon cardiovascular health and disease.

However, given the difficulties with measuring these elements directly (particularly stress) and the equivocal findings relating to the impact of type A personality on CHD risk, others have considered it more appropriate to concentrate more on health related outcomes such as psychological well being (Kasl and Rapp, 1991). The benefit of measuring these psychological factors in relation to cardiovascular health and disease, as opposed to other psychological factors, lies in the superior instruments for the measurement of these factors.

Prospective investigations have indicated that emotional disturbance and hence poor psychological well being is a significant risk factor for coronary heart disease (Smith, 2001; Tennant and McLean, 2001). Previous research reviewing this association in more detail has revealed that several key psychological and psychosocial factors are implicated in the incidence of CHD (Goldstein and Niaura, 1992; Niaura and Goldstein, 1992). These studies reported that the major psychological factors playing a role in the development of cardiovascular disease were: negative affective states (such as anxiety and depression) certain negative behavioural characteristics, dispositional characteristics of the individual (such as personality) and poor coping style, allied to poor personal control. Others have also provided support for these conclusions (Hemingway and Marmot, 1999; Tennant, 1999).

In summary, it is clear that psychological factors may act alone or combine in clusters to impact upon CHD and that these factors might exert different effects at different stages of the life course (Hemingway and Marmot, 1999). The mechanism for a relationship between psychological well being and CHD might come from the affect that psychological factors have upon health related behaviour patterns. Alternatively, psychological factors might directly lead to key patho-physiological changes implicated in the aetiology of cardiovascular disease (Hemingway and Marmot, 1999).

2.6. Lifestyle Factors Influencing Cardiovascular Health and Disease

2.6.1. Alcohol Consumption and Cardiovascular Health and Disease

Maclure (1993) reviewed clinical and epidemiological research, using a method of deductive meta-analysis, concluding that current research data suggests that moderate alcohol consumption could reduce the risk of developing CHD by between 30-60%. A U-shaped relationship between alcohol consumption and the risk of CHD was thus hypothesised, with the suggestion being that alcohol is preventative at low to moderate doses but causative at high doses. Indeed, several studies, including the Framingham study (Shurtleff, 1970) and two health care group studies (Klatsky et al., 1977; Yano et al., 1977), have shown that consuming small quantities of alcohol resulted in the lowest death rates, whilst abstinence resulted in intermediate death rates, and heavy drinking resulted in

the greatest death rates. Several more recent research investigations have also indicated a reduced risk of sudden cardiac death with a light-moderate alcohol consumption as opposed to heavy drinking or abstinence (Wannamethee and Shaper, 1992; Albert et al., 1999).

Whilst there seems to be little argument that non-drinkers and heavy drinkers have higher cardiovascular mortality rates than moderate drinkers, some authors have questioned the interpretation of the U-shaped curve (Shaper, 1990). In particular, the assumption that light and moderate drinking is actually cardio-protective is debatable. Shaper (1990) highlights the fact that much of the problem stems from the failure of many of the previous studies to fully explore the nature of non-drinkers and heavy drinkers.

However, much research has led to the assumption that alcohol dose has a significant effect on cardiovascular health. Whilst this may be a valid hypothesis, alternative explanations exist for the protective role of low to moderate doses of alcohol. For example, it could be that other factors associated with low to moderate alcohol consumption, in contrast to those associated with abstinence or heavy drinking, might play a more important protective role than the alcohol dose itself (Criqui, 1987; Marmot et al., 1993). Clearly there is a need to examine the paths of association linking alcohol consumption to CHD, especially in the context of other health-related behaviours.

Despite these concerns the possibility exists that alcohol consumption patterns may influence the pathogenesis of coronary heart disease, particularly with regards to atherosclerosis. The actual role of alcohol in coronary heart disease has yet to be fully elucidated, although there is a possibility that patterns of alcohol consumption will have an affect on markers of CHD including, blood lipid profiles, blood haemostatic factors, blood rheological factors and psychological factors.

2.6.1.1. Alcohol Consumption and Blood Lipids

Sillanaukee et al. (2000) recently investigated the effects of self-reported alcohol consumption in relation to a wide range of lipid-based cardiovascular risk factors in middle-aged women. Their data showed that total cholesterol, HDL, LDL, TG, apo A1 and apo B concentrations were all positively correlated with self-reported alcohol consumption, although LDL concentrations were not. However, when alcoholic subjects were removed from the analysis only HDL and apo A1 concentrations remained significantly correlated with alcohol consumption. These results indicated that women consuming 20-40g.day^{-1} of alcohol, exhibited higher HDL and apo A1 concentrations, although in those women consuming >40g.day^{-1} all lipid concentrations increased, with the exception of LDL. Similar recent investigations have leant some support for these findings (Nanchahal et al., 2000). Indeed Nanchahal et al. (2000) reported a significant reduction in 10-year lipid-based cardiovascular risk profiles of women reporting the consumption of up to 22 units of alcohol per week.

A similar study, incorporating data from the Amsterdam Growth and Health Longitudinal Study reported no significant difference in total cholesterol concentrations between alcohol consumers and non-consumers (Koppes et al., 2000). However, a positive association between HDL concentration and alcohol consumption was observed in both males and females, although this association was modified by smoking status (i.e. the significant association was found in non-smokers but not in smokers). Importantly, this study also attempted to examine the isolated effects of beer, wine and spirit drinking on blood lipid concentrations, although no significant differences were observed.

Although several studies have observed an elevated HDL concentration with moderate alcohol consumption (Moore and Pearson, 1986; Gaziano et al., 1993; Riemens et al., 1997), the precise mechanism for this association remains unclear. Previous cross-sectional data supports the hypothesis of a dose-response relationship. Hulley and Gordon (1981) reported data which showed that social drinkers exhibited ~33% higher HDL levels than non-consumers.

In summary, it would appear that many recent investigations have supported an inverse relationship between alcohol intake and lipid-based cardiovascular risk in both men and women. In particular the postulated cardio-protective role of alcohol consumption would appear, at least in part, to be due to the role that alcohol consumption might play in elevating HDL levels. However, many of

these studies have failed to examine a wide range of consumption patterns, the different types of alcohol consumed, different age groups, with many also failing to remove ex-drinkers from their non-drinking category. Thus, further research is required relating to the impact of habitual alcohol consumption on blood lipids levels.

2.6.1.2. Alcohol Consumption and Blood Haemostasis

Another of the suggested mechanisms via which moderate alcohol consumption may have a positive impact upon CHD risk is by having a beneficial effect on blood haemostatic factors. However, much of the current evidence surrounding this effect is conflicting. Recent data produced from the Framingham Offspring Study showed significant reductions in fibrinogen, FVII and von Willebrand factor with light to moderate habitual alcohol consumption (Mukamal et al., 2001). This association was also most pronounced in those individuals who drank between 7 and 21 alcoholic drinks per week. However, those individuals who drank between 7 and 21 alcoholic drinks per week also exhibited a reduced fibrinolytic potential, as indicated by elevated PAI-1 and tPA antigen concentrations. Furthermore, they also reported that wine consumers were more likely to exhibit higher PAI-1 antigen levels, although none of the other haemostatic variables were affected by beverage type. From this study the authors concluded that light to moderate alcohol consumption was associated with a reduction in the bloods ability to clot, but higher consumption was related to impaired fibrinolytic potential (Mukamal et al., 2001). However, based on the data, this might seem a slightly

erroneous conclusion when faced with the fact that reduced blood coagulation and an impaired blood fibrinolytic potential were observed with the consumption of the same number of alcoholic drinks per week, although not necessarily the same units of alcohol.

El-Sayed et al. (1999a) reported no significant alterations in any of the haemostatic or fibrinolytic variables measured at rest, following the ingestion of $0.5g.kg^{-1}$ ethanol. However, a significant reduction in post-exercise fibrinogen concentration was observed when subjects had ingested ethanol, as opposed to placebo, prior to exercise.

The National Heart, Lung, and Blood Institute Family Heart Study reported data suggesting that whilst there was no difference in PAI-1 levels at different habitual alcohol intakes up to $14g.day^{-1}$ a greater intake of alcohol resulted in increased PAI-1 levels (Djousse et al., 2000). One of the more controlled investigations in to the effects of alcohol consumption on blood haemostatic and fibrinolytic factors compared low and normal alcohol consumption patterns in predominantly beer drinking male subjects (Dimmitt et al., 1998). When weekly alcohol intake was increased from 92ml to 410ml a decreased plasma fibrinogen concentration and platelet count were observed, although FVII levels increased. Increased weekly alcohol intake was also associated with increased tPA and PAI-1, although there was a reduction in the tPA/PAI-1 ratio indicating a proportionally greater increase in PAI-1 with elevated alcohol consumption. Other investigations have also

reported similar findings (Yarnell et al., 2000). These studies highlight the contradictory nature of much of the evidence relating to the effects of alcohol consumption on blood haemostasis and fibrinolysis to date. Clearly the observed reduction in plasma fibrinogen concentration with increased alcohol intake may relate to the purported beneficial effects for cardiovascular risk. However, the observed increase in FVII and in PAI-1 concentration provides evidence for an increased cardiovascular risk.

Other recent studies have reported on the negative effects of high alcohol consumption on blood fibrinolytic potential and the possible benefits of alcohol withdrawal. Delahouse et al. (2001) reported an enhanced fibrinolytic potential, particularly via a decreased PAI-1 concentration, following alcohol withdrawal in a group of alcoholic subjects. Numminen et al. (2000) reported that a large one off dose of alcohol, designed to mimic binge drinking, resulted in a 7-fold increase in PAI-1 concentrations. However, this study only examined this response in those subjects who were unused to this level of alcohol consumption. Others have shown significant fibrinogenolysis in response to exercise, although when exercise was performed following mild intoxication with alcohol a reduction in this fibrinogenolytic effect was observed (El-Sayed and Nieuwenhuizen, 2000).

In summary, research relating to the effects of alcohol consumption on elements of blood coagulation and fibrinolysis is equivocal. One possible reason for this is

differences in the measurement of alcohol consumption, with some studies reporting the effects of acute alcohol consumption, whilst others report on more habitual alcohol consumption or drinking frequencies. Other differences between studies are potentially the result of the varying indices of blood coagulation and fibrinolysis reported. As such, it would appear that the true effect of habitual alcohol consumption on blood coagulation and fibrinolysis remains to be fully established.

2.6.1.3. Alcohol Consumption and Blood Rheology

It is evident that alcohol consumption may have an impact on two of the main determinants of whole blood viscosity. Hamazaki and Shishido (1983) measured blood viscosity and plasma viscosity, before and after drinking at a dinner party, in 18 healthy volunteers. Results showed significant increases in both blood viscosity and plasma viscosity following alcohol consumption, which was attributed to changes in haemoconcentration. However, some questions may arise over the level of control and standardisation placed on consumption patterns in this experiment. Other studies have also reported an increase in viscosity alongside increasing alcohol consumption (Yarnell et al., 2000). In contrast, data from the Framingham Offspring cohort has shown a reduction in plasma viscosity with light to moderate alcohol consumption (Mukamal et al., 2001). This association was most evident at a drinking frequency of between 3-7 drinks per week. Other investigations have observed elevated haematocrit

concentrations with higher alcohol intakes (Stott et al., 1991; Wanemethee and Shaper, 1994).

In summary, limited evidence has indicated a significant impact of alcohol consumption on blood rheology. In particular studies would appear to indicate that increased alcohol consumption results in an increased blood rheological profile, particularly in relation to whole blood and plasma viscosity. However, further research is required to evaluate the effects of more habitual alcohol consumption on blood rheology.

2.6.1.4. Alcohol Consumption and Psychological Well Being

High alcohol consumption, leading to the manifestation of problem drinking patterns and alcohol abuse, remains a cause of both physical and mental ill health across many developed countries. However, it should be noted that alcohol consumption might both positively and negatively impact upon psychological well being (Graham and Schmidt, 1999).

Graham and Schmidt (1999) showed that a higher quantity and frequency of alcohol consumption was positively associated with poorer psychological well-being in older adults. There is some support for this finding, with previous research identifying links between alcohol misuse and poor psychological well being (Schonfeld and Dupree, 1991; Moos et al., 1993). In contrast, other research has failed to show a link between the level of alcohol consumption and

poorer psychological well being in both older (Borgatta et al., 1982; Saunders et al., 1991) and younger (Sale et al., 2001) adults. In addition, the frequency of drinking was not related to psychological well being in the Graham and Schmidt (1999) findings.

Whilst previous research has indicated links between alcohol use and psychological well being in middle-aged and older populations few have examined these associations in adolescents and younger adults (Hansell et al., 1999). Hansell et al. (1999) reported that the most probable reason for this is the absence of serious or chronic illnesses in this population. However, it would appear that this is missing a useful opportunity to measure these populations during a large developmental period, which is likely to have dramatic implications for their future mental health and psychological well being. Indeed, Hansell et al. (1999) go on to hypothesise that alcohol consumption impacts upon health in adolescent populations and may contribute to subsequent physical symptoms of ill health and psychological distress.

Other links between alcohol consumption and psychological well being may suggest a way in which poor physical and mental health may lead to subsequent alcohol use and misuse. Previous research has indicated that alcohol consumption and drinking behaviour might play a mediating role in the association between stress/distress and psychological well being (Hansell et al., 1999). Several studies have shown that alcohol consumption is used as a

means of coping with stress, and that by considering drinking as a coping behaviour we can adequately predict subsequent alcohol consumption (Cooper et al., 1988; Abbey et al., 1993; Evans and Dunn, 1995; Laurent et al., 1997) and alcohol related problems (Farber et al., 1980; Cooper et al., 1988).

Furthermore, several of these studies have identified links between the use of drinking to cope and more general coping strategies (Farber et al., 1980; Latack, 1986; Cooper et al., 1988), although there is some conflict over which of the more general elements of coping is linked to drinking to cope. For example, Latack et al. (1986) observed an association between alcohol use and symptom management type coping strategies, whilst Cooper et al. (1988) observed a significant association with the use of avoidance coping strategies. Clearly then there is a need to further investigate the complex interrelationships among alcohol consumption, drinking to cope and a wider range of more general coping strategies, in addition to possible associations with psychological well being.

It has also been suggested that drinking behaviour might itself be mediated by several dispositional characteristics of the individual, such as gender (Sale et al., 2001), personality (Williams and Clark, 1998; Sale et al., 2001), and perceptions of control (Haynes and Ayliffe, 1991; Seeman and Seeman, 1992). Thus, any examination of alcohol consumption and alcohol related problems in relation to psychological well being must also include the measurement and analyses of these variables.

In summary, there would appear to be a link between harmful levels of alcohol consumption and poorer psychological well being, which in turn might precipitate an even greater alcohol use. There is clearly a need to further investigate this relationship, especially in the context of additional psychological variables, which might play a mediating role.

2.6.2. Physical Activity and Cardiovascular Health and Disease

Physical activity is associated with a reduced cardiovascular morbidity and mortality in both men and women and in middle-aged and older individuals (Wanemethee and Shaper, 2001). However, the mechanism for this cardio-protective role is incompletely understood (Fagard, 1999; Wanemethee and Shaper, 2001). It would appear that the benefits of physical activity are probably multi-factorial in nature (Smith, 2001), perhaps both directly and indirectly impacting upon CHD risk (Andersen and Hippe, 1996). It has been suggested that the impact of physical activity is best evaluated by investigating its effects on other CHD risk factors (Andersen and Haraldsdottir, 1995). This section of the literature review will provide a synopsis of the recent literature examining the effects of physical activity on the blood haematological variables associated with cardiovascular health and disease.

In a recent meta-analytical report Williams (2001) stated that physical activity can be defined as voluntary movement produced by skeletal muscles that results in

energy expenditure, whereas cardiorespiratory fitness relates to the ability of the circulation and respiration to supply oxygen during sustained physical activity. Williams (2001) concludes that being unfit is a CVD risk factor distinctly different from inactivity. Thus, setting physical activity recommendations on the basis of fitness studies is inappropriate, as this demotes the status of physical fitness as a risk factor, whilst exaggerating the health benefits of moderate amounts of physical activity. Results are inconclusive with regards to the impact that less vigorous physical activity might have on CHD risk factors (Mensink et al., 1997). Andersen and Haraldsdottir (1995) also showed that favourable alterations in the CVD risk profile were associated with high cardiorespiratory fitness but not physical activity. As such, this section of the review of the literature will also report on recent literature examining the effect of both fitness and physical activity on the biological and psychological factors associated with cardiovascular health and disease.

Whilst the relationship between physical activity and cardiovascular health is well documented in the middle-aged and elderly population, the benefits in the younger population are still not well documented. Clearly this is an area which requires further investigation (Andersen and Haraldsdottir, 1995).

2.6.2.1. Physical Activity and Blood Lipids

Many of the early studies examining the effects of exercise on blood lipid levels concentrated mainly on total cholesterol and TG concentrations, and as such this

is where this section of the review will begin. Perhaps one of the reasons for the concentration of these early investigations on cholesterol was its purported links to CHD incidence at this time (Grundy, 1997). Whilst several investigations have reported reduced cholesterol concentrations in endurance trained subjects (Wood et al., 1977; Williams et al., 1986), many others have reported no significant difference (Tsopanakis et al., 1986; Durstine et al., 1987; Marti et al., 1991;Thompson et al., 1991; MacAuley et al., 1997). Slightly elevated plasma cholesterol concentrations have been observed in speed and power trained athletes when compared to controls (Farrell et al., 1982), although it should noted that others have not shown any significant differences in this subject group (Berg et al., 1980a; 1980b). It would appear that VO_{2max} is inversely related to plasma cholesterol concentrations (Leaf et al., 1997) although, in those studies where this statistic has been age and body mass adjusted, this relationship no longer appears (Montoye et al., 1978; Erikksen et al., 1981).

In general, cross-sectional data has shown that those participating in regular physical activity exhibit lower TG levels than less active or sedentary controls (Wood and Stefanick, 1990; Marti et al., 1991; Thompson et al., 1991). Cardiorespiratory fitness, as measured by VO_{2max}, has also been shown to be negatively related to TG levels (Leaf et al., 1997), although in contrast to the results observed with cholesterol, the relationship appears to remain significant even after adjusting for age and body mass (Hagan and Gettman, 1983). However, some other reports have failed to show such a relationship (Schwane

and Cundiff, 1979; Montoye et al., 1978). Both chronic (Thompson et al., 1988; Wood et al., 1991b) and acute (Siegel et al., 1970) bouts of endurance exercise have been shown to reduce plasma TG concentrations, particularly in those with elevated TG levels at baseline.

One of the major benefits of physical activity and exercise is the potential effect it has in increasing HDL levels. In general, cross-sectional investigations have indicated that endurance trained athletes exhibit higher HDL concentrations than more inactive controls (Tsopanakis et al., 1986; Durstine et al., 1987; Marti et al., 1991; Thompson et al., 1991). In contrast, longitudinal investigations have been less conclusive with regards to the effects of endurance training on HDL levels. Several studies have failed to show any significant difference in HDL levels with exercise training (Despres et al., 1988), particularly in those with lower HDL concentrations at baseline (Zmuda et al., 1998). However, others have reported significant changes in several subject groups (Marti et al., 1990; Blessing et al., 1995; Crouse et al., 1997; Halbert et al., 1999).

Moderate intensity exercise performance has been shown to produce significant increases in HDL concentrations in both sedentary young women (Imamura et al., 2000) and older hypertensive males (Kokkinos et al., 1998). Similarly, Pescatello et al. (2000) observed elevated HDL concentrations in more active elderly subjects. However, other studies exploring the effects of more long-term

moderate intensity intermittent exercise has failed to report sustained increases in HDL concentrations (Snyder et al., 1997).

Those studies investigating more habitual physical activity have tended to show increases in HDL concentration in those reporting higher physical activity levels (Marrugat et al., 1996; Wei et al., 1997; Yurgalevitch et al., 1998). However, Sowers et al. (1995) only observed this relationship in female, and not male, subjects; whilst other investigations have failed to observe this relationship at all (Fonong et al., 1996).

Although the impact of physical activity on LDL concentrations has been extensively studied, the results reported have been equivocal. Studies that have compared athletes to non-endurance trained subjects have in some cases reported no significant differences between the groups (Tsopanakis et al., 1986; Durstine et al., 1987; Marti et al., 1991;Thompson et al., 1991). Others have observed reduced LDL concentrations with greater physical activity, in a wide range of populations (MacAuley et al., 1996; Taimela et al., 1996; Schmidt et al., 1997; Pescatello et al., 2000). This has also been observed in the majority of exercise and exercise training studies (Crouse et al., 1995; Ponjee et al., 1995; Halbert et al., 1999). However, others have shown no effect of exercise training on LDL concentrations (Brownell et al., 1982; Despres et al., 1988; Thompson et al., 1988), unless subjects were obese at baseline (Nicklas et al., 1997).

There have been fewer studies examining the effects of physical activity and exercise on VLDL concentrations, although, in the main, results have suggested decreased concentrations following endurance exercise and training (Marti et al., 1991). Studies showing a significant reduction in TG levels with exercise training have also shown a significant reduction in VLDL concentration (Marti et al., 1991). Conversely, some studies not observing a reduction in TG concentration have not shown a significant reduction in VLDL levels (Nye et al., 1981), although in other studies a significant reduction in VLDL levels was reported even with no corresponding reduction in TG concentration (Despres et al., 1990). Previous research has shown a reduced VLDL concentration in athletes when compared to sedentary controls (Tsopanakis et al., 1986; Durstine et al., 1987; Marti et al., 1991). Berg et al. (1980a) has observed a significant negative correlation between VLDL concentration and VO_{2max}, whilst exercise training studies have observed reductions in VLDL (Marti et al., 1990).

Cross-sectional investigations have shown elevated apo A1 levels, but not apo A2 levels, in athletes compared to non-athletes (Thompson et al., 1983; Herbert et al., 1984). However, others have observed a significant relationship between predicted VO_{2max} and apo A1 level (MacAuley et al., 1997). Similarly, several investigations have observed increased apo A1 concentrations following periods of training (Stubbe al., 1983), particularly following weight loss from combined exercise and dietary management (Schwartz, 1987; Williams et al., 1992). However, others have shown no significant alterations in apo A1 with increasing

exercise levels in previously sedentary middle-aged men (Wood et al., 1983). Thompson et al. (1988) hypothesised that the increased apo A1 concentrations under training conditions may result from an increased half life.

In summary, there are equivocal research findings regarding the impact of both physical activity and fitness on blood lipid profiles. Differences in research findings are most likely due to (a) methodological differences relating to the type of physical activity or exercise regimens used, (b) the variety of assay techniques employed and (c) varying subject populations.

2.6.2.2. Physical Activity and Blood Haemostasis

The research evidence relating to the activation of the blood haemostatic system with exercise and training has been the subject of recent review (El-Sayed et al., 2000). The evidence currently available would suggest that exercise and training exert several powerful effects on blood haemostatic mechanisms in both patients and normal healthy individuals (El-Sayed et al., 2000).

Previous research has shown that exercise causes a reduction in both whole blood clotting time and APTT (Arai et al., 1990; Bartsch et al., 1990; Handa et al., 1992; Herren et al., 1992; Molz et al., 1993; Bartsch et al., 1995; El-Sayed et al., 1995), although the response of both PT and TT to exercise is not as well established (El-Sayed et al., 2000). Whilst Ferguson et al. (1987) reported a significant reduction in PT following exercise, several other studies have

observed no significant alterations (Rocker et al., 1990; Molz et al., 1993; El-Sayed et al., 1995). Although El-Sayed et al. (1995) did not show any significant alteration in PT, their data did show a significant reduction in TT post-exercise.

Studies on the impact of acute exercise on plasma fibrinogen levels have produced conflicting results (El-Sayed and Davies, 1995; El-Sayed et al., 1999b). Several studies have shown that fibrinogen concentration is elevated following acute exercise (Arai et al., 1990; Jooter et al., 1992; Suzuki et al., 1992), whilst other studies have reported significant decreases (Bartsch et al., 1990; Prisco et al., 1998). Yet more studies have reported no significant alterations (Watts, 1991; De Paz et al., 1992; Herren et al., 1992; Loon et al., 1992; Rankinen et al., 1994; El-Sayed et al., 1995). The conflicting data from these investigations is most likely due to differences in exercise protocol, levels of training, health status of the participants, the analytical methods used, and perhaps more importantly an inability to consider the dynamic nature of plasma volume during exercise (El-Sayed et al., 1999b).

Significant increases in FVIII activity following acute bouts of exercise at various intensities and durations have been reported (Arai et al., 1990; Hansen et al., 1990; El-Sayed et al., 1996). Both Arai et al. (1990) and Hansen et al. (1990) also observed that FVIII activity remained significantly elevated in to recovery. Despite the importance of these findings, the mechanism via which FVIII activity increases following acute exercise is not yet fully understood (El-Sayed et al.,

2000). El-Sayed (1993) hypothesised that it could either be due to the activation of FVIII in the circulation or alternatively to the release of stored or synthesised FVIII.

Research has shown that intensity plays a role in the relationship between exercise and the activation of blood coagulation (El-Sayed et al., 2000). Weiss et al. (1998) reported that exercise at ~68% VO_{2max} increased the formation of plasmin without causing the activation of blood coagulation. However, when the exercise intensity was increased to ~83% VO_{2max} the increase in plasmin formation was also accompanied by an increase in the markers of blood coagulation. Thus, it could be concluded from this study that more moderate exercise intensities might bring about an activation of blood fibrinolytic mechanisms *in vivo*, whilst higher intensity exercise results in the simultaneous activation of both coagulation and fibrinolytic mechanisms. However in contrast to these results, Schobersberger et al. (1996) showed that activation of blood coagulation occurred following an ultra-marathon race, perhaps indicating that exercise duration is also an important consideration. Schobersberger et al. (1996) also found that the increase in fibrinolytic activity was greater than the elevation in blood coagulation. Mustonen et al. (1998) also observed an increase in thrombin formation following submaximal exercise in patients with peripheral arterial occlusive disease, although no such increased was observed in healthy controls. It has been suggested that these recent results indicate that the activation of blood coagulation and fibrinolytic mechanisms are related to

exercise intensity as well as the health status of the population studied (El-Sayed et al., 2000).

The impact of less vigorous forms of physical activity on the haemostatic system is not as well documented, particularly in relation to habitual physical activity levels. Carrol et al. (2000a) measured plasma fibrinogen concentrations in relation to both leisure time physical activity and cardiorespiratory fitness in a group of middle-aged male subjects. Their data showed no significant association between either physical activity or predicted VO_{2max} and fibrinogen concentrations in these subjects. Previous studies (Lee et al., 1990; Folsom et al., 1991; Elwood et al., 1993), have shown that total leisure time physical activity is associated with lower plasma fibrinogen concentrations in other groups of middle-aged men. However, Lakka and Salonen (1993) showed that only high-intensity leisure time physical activity was associated with positive changes in plasma fibrinogen concentration.

Exercise of an intense nature causes the activation of blood fibrinolytic mechanisms (for review see El-Sayed et al., 2000), primarily due to the release of tPA from the vascular endothelial cells (El-Sayed et al., 1996). The activation of fibrinolytic activity with exercise would appear to be highly dependent upon the intensity of the exercise. The results reported by Andrew et al. (1986) showed that significant increases in fibrinolytic activity do not occur until the intensity of the exercise raises the heart rate above 50% of its maximum. Andrew et al.

(1986) and Davis et al. (1976) both showed that the greatest increases in fibrinolyitc activity occur at exercise intensities of between 70-90% of the maximum workload.

Results of previous research shows that both exercise intensity and duration are important in determining the duration of hyperfibinolysis in to recovery. Intense exercise has been shown to prolong hyperfibrinolysis for between 45-60 minutes (Ferguson et al., 1987), whereas hyperfibrinolysis has been prolonged for between 2 and 24 hours following long distance and marathon running (Hansen et al., 1990; Prisco et al., 1998). The fact that tPA activity and antigen levels increase following acute bouts of both aerobic and resistance exercise, is well-documented (Arai et al., 1990; Rocker et al., 1990; De Paz et al., 1992; Gough et al., 1992; Handa et al., 1992; El-Sayed et al., 1993; Molz et al., 1993; Vind et al., 1993; Szymanski and Pate, 1994; Rankinen et al., 1995; Schobersberger et al., 1996; Prisco et al., 1998), as is the fact that the exercise induced response of tPA is dependent upon exercise intensity (El-Sayed et al., 1993; Molz et al., 1993; Szymanski and Pate, 1994; Rankinen et al., 1995).

El-Sayed et al. (2000) suggested the possibility of groups of "poor responders" in terms of the tPA response to acute bouts of exercise. Whilst these poor responders are more prevalent in patients, they have also been observed among groups of healthy subjects (Rydzewski et al., 1990; Jansson et al., 1991; Hansen et al., 1994). El-Sayed et al. (2000) suggest that the ability to respond properly

to acute exercise corresponds to the capacity of the fibrinolytic system and that as a result poor responders may be at a greater risk of CVD when challenged by a stressor such as exercise.

Results pertaining to the influence of acute bouts of exercise on PAI-1 activity are more conflicting and not as well-documented as those for tPA (El-Sayed et al., 2000). Whilst the majority of studies have demonstrated a significant reduction in PAI-1 activity (Gough et al., 1992; Szymanski and Pate, 1994; De Paz et al., 1995; Rankinen et al., 1995; El-Sayed et al., 1996), other studies have failed to report any significant change (Vind et al., 1993; Prisco et al., 1998).

Studies have attempted to associate the *in vitro* changes in fibrinogen concentration with the *in vivo* changes in fibrin/fibrinogen degradation products (El-Sayed et al., 2000). D-dimer has been used as an *in vivo* marker of hyperfibrinolysis, with significant increases being observed following acute exercise (Molz et al., 1993; Prisco et al., 1998). El-Sayed et al. (2000) report that these results indicate that strenuous exercise results in *in vivo* hyperfibrinolysis, although it should be noted that other studies have failed to report significant changes in fibrin/fibrinogen degradation (Marsh and Gafney, 1982; Bounameaux et al., 1992). Thus, the actual effect of acute bouts of exercise on fibrin/fibrinogen degradation remains an unresolved issue and requires further investigation.

Very little is known regarding the effects of habitual physical activity on blood fibrinolytic variables. Data from the Northern Sweden MONICA study (Eliasson et al., 1996) reported a significantly increased tPA concentration in male subjects with higher levels of "vigorous" leisure-time physical activity. Greater leisure-time physical activity was also associated with a reduced PAI-1 activity in both males and females. They concluded that higher physical activity levels were associated with an enhanced fibrinolytic activity in subjects aged between 25-64 years. However, previous investigation did not show any significant associations between either leisure-time or work-time physical activity and blood fibrinolytic variables in a group of 54 year old men (Korsan-Bengtsen et al., 1973).

In summary, the available evidence suggests that the performance of an acute bout of exercise may result in the activation of blood coagulation and enhanced blood fibrinolysis. However, results relating to the impact of both exercise training and habitual physical activity measures are incomplete and conflicting, and thus require further investigation. Differences in results are most likely due to differences in training programmes and the assay techniques employed (El-Sayed et al., 2000).

2.6.2.3. Physical Activity and Blood Rheology

Plasma viscosity is one of several determinants of blood rheology and has an important role in the development of cardiovascular disease (El-Sayed, 1998; Junker et al., 1998). Increased plasma viscosity has been reported, at rest, in

both hypertensives (Letcher et al., 1981a) and chronic heart failure patients (Reinhart et al., 1998). Furthermore, previous research has shown that exercise elicits significant alterations in the blood rheological profile in both healthy subjects (Charm et al., 1979; Lecher et al., 1981b; Galea and Davidson, 1985; Martin et al., 1985; Brun et al., 1994) and in CVD patients (Toth et al., 1994; Reinhart et al., 1998).

Galea and Davidson (1985) investigated the haemorheological effects of marathon running. Their data on 14 marathon runners showed a significant reduction in red cell filterability and a concomitant increase in plasma osmolality. However, this study reported no significant alterations in either fibrinogen concentration or plasma viscosity. In contrast, Wood et al. (1991) reported increased plasma viscosity and fibrinogen concentrations following a 48km mountain race in 33 endurance trained subjects.

Toth et al. (1994) investigated the effects of peak exercise on haemorhological parameters in a group of ischaemic heart disease patients. Their data showed that maximal graded exercise on a treadmill caused significant increases in haematocrit, whole blood viscosity, plasma viscosity and fibrinogen concentration. Similar results have been reported following a VO_{2max} test (Martin et al., 1985). However, a similar investigation using graded maximal exercise on a treadmill in healthy subjects did not reported any significant changes in either

plasma viscosity levels or plasma fibrinogen concentrations (Letcher et al., 1981b).

Gueguen-Duchesne et al. (1989) reported significant increases in whole blood viscosity, plasma viscosity, haematocrit and total protein concentration following a combined exercise protocol incorporating cycling, arm cranking and treadmill running. Furthermore, similar results have been reported following less strenuous sub-maximal exercise (Brun et al., 1994), whilst Jones et al. (1999) reported a significantly increased plasma viscosity, but not plasma fibrinogen concentration, following both maximal and sub-maximal (70% VO_{2max} for 30 minutes) exercise.

The inconclusive reports from these studies might be a function of the differing methodologies of the investigations. In particular it would appear that exercise intensity and duration, as well as the specific testing procedures employed, might explain the inconsistent findings.

Martin et al. (1985) studied the effect of training status on blood rheological properties in 47 female subjects. The results of this study failed to show any relationship between training status and blood rheology, although it is interesting to note that plasma fibrinogen concentration was positively correlated with VO_{2max}. However, previous reports have suggested that plasma viscosity is lower in trained than in untrained subjects (Charm et al., 1979; Letcher et al.,

1981b; Ernst et al., 1985). Fendler and Matrai (1980) reported that the direction of exercise induced alterations in blood rheological properties depended on the fitness of the subject with well-trained subjects exhibiting a decrease in fibrinogen, plasma viscosity and whole blood viscosity and untrained subjects exhibiting an increase.

Whilst some experimental investigations have examined the effects of exercise on components of blood rheology, the possible effects that more general physical activity patterns might have on the rheological properties of blood has been largely ignored. Carroll et al. (2000b) reported that higher physical activity levels were associated with lower levels of haematocrit and plasma viscosity in a group on non-smoking middle-aged men. In terms of the lifestyle predictors of plasma viscosity, Carroll et al. (2000c) reported significant main effects of physical activity, predicted VO_{2max}, and adiposity. In a previous study, Koenig et al. (1997) examined the effects that both leisure-time and work-related physical activity had upon plasma viscosity. They concluded that leisure-time physical activity was associated with a lower plasma viscosity, although no such association was found with work-related physical activity.

In summary, alterations in plasma viscosity maybe one of the mechanisms via which physical activity and exercise protect against CHD. With this in mind the effects of physical activity and exercise on plasma viscosity and other components of the blood rheological profile need to be examined further.

2.6.2.4. Physical Activity and Psychological Well Being

In 1992 results published from the Allied Dunbar National Fitness Survey reported a strong positive relationship between physical activity and individuals perceptions of personal health and psychological well being. Further evidence of the beneficial effects of physical activity on aspects of mental health come from the various meta-analytical studies that have been published on this subject, although the majority of these are based on North American populations (for a detailed review of these refer to Mutrie and Biddle, 1995).

Previous research has shown exercise and physical activity to be important in the reduction of anxiety, depression, neuroticism, stress and would also appear to have other emotional effects such as increased self-esteem (Morgan and Goldston, 1987; Paffenbarger et al., 1994; Liao et al., 1995; Rostad and Long, 1996; Yeung and Hemsley, 1997). Clearly these benefits would provide a strong theoretical support for the beneficial effects of exercise and physical activity and the risk for CHD (Yeung and Hemsley, 1997).

Several theories have been used to describe these results, the most common of which is that those individuals who take up exercise feel better as a consequence. One of the possible mechanisms for this is that physical activity or exercise may assist in coping with stress. Indeed, Rostad and Long (1996) stated that exercise might be used in several ways as a coping strategy. For example, it may assist in regulating emotions by aiding relaxation, it may facilitate

problem-focussed coping strategies or it may simply provide means of distraction from the problem. One of the main problems with the current empirical studies focussing on the role of exercise behaviours as coping strategies for stress is that few have utilised measures of stress appraisal and coping processes in sufficient detail (Sale et al., 2000).

Ingledew et al. (1996) focussed on the links between health related behaviours and the use of problem-focussed, emotion-focussed and avoidance coping strategies. They reported strong links between exercise behaviours and the use of problem-focussed coping strategies, a finding, which is supported by the previous work of Rick and Guppy (1994). Subsequent research has also identified a link between habitual physical activity and the use of symptom reduction coping strategies (Sale et al., 2000).

However, others have hypothesised that dispositional characteristics of the individual, such as personality, might be more important in describing the above results, and as a result the relationship between physical activity and enhanced feelings of well being might be incidental rather than causal (Yeung and Hemesley, 1997). Previous research has indicated that exercisers exhibit different personality traits than non-exercisers. In particular it would appear that exercisers score higher on indices of extraversion and lower on neuroticism (Yeung and Hemesley, 1997). Similarly, Sale et al. (2000) reported a significant positive association between habitual levels of physical activity and extraversion

scores, although no relationship, positive or negative, was observed with neuroticism scores.

In summary, several well-controlled investigations have reported positive effects of physical activity and exercise on aspects of psychological well being, primarily in clinical populations (Scully et al., 1998). Caution would also seem pertinent when considering the direction of causality from much of this data, with some research suggesting any relationship might simply be incidental. In addition, several investigations would seem to have failed to consider possible mediating factors in the relationship between physical activity and psychological well being. Furthermore, there is less evidence relating to the impact of exercise and physical activity on psychological well being in non-clinical populations.

2.7. Overall Summary of the Review of Literature

Coronary heart disease is currently the single most common cause of death in both men and women in the UK, with the national death rate being among the highest in the world (British Heart Foundation, 2000). Coronary heart disease is multi-factorial in nature and progresses from a multitude of risk factors through to congestive heart failure or end-stage heart disease. As such the disease is considered as being largely preventable with the promotion of a healthy lifestyle and the appropriate management of the significant biological predictors of cardiovascular health and disease.

Several lifestyle factors, often termed health-related behaviours, have been implicated in the pathogenesis of CHD. In the main, research has identified a role for alcohol consumption, physical activity, smoking, and diet in the prediction of cardiovascular health and disease. One of the proposed mechanisms for this effect is the apparent association between these lifestyle factors and other biological factors associated with cardiovascular health and disease, such as blood haematological profiles. A potential role for psychological factors in the association between lifestyle and cardiovascular health and disease has also been hypothesised.

As such, this study is primarily concerned with the inter-relationships among two health related behaviours (alcohol consumption and physical activity), blood haematological profiles (blood lipid profiles, blood haemostatic variables, blood rheological indices) and psychological well being in a population of young, apparently healthy, adults. The principle behind the thesis is outlined by figure 2.5., with figures 2.6. and 2.7. outlining studies 1 and 2 respectively.

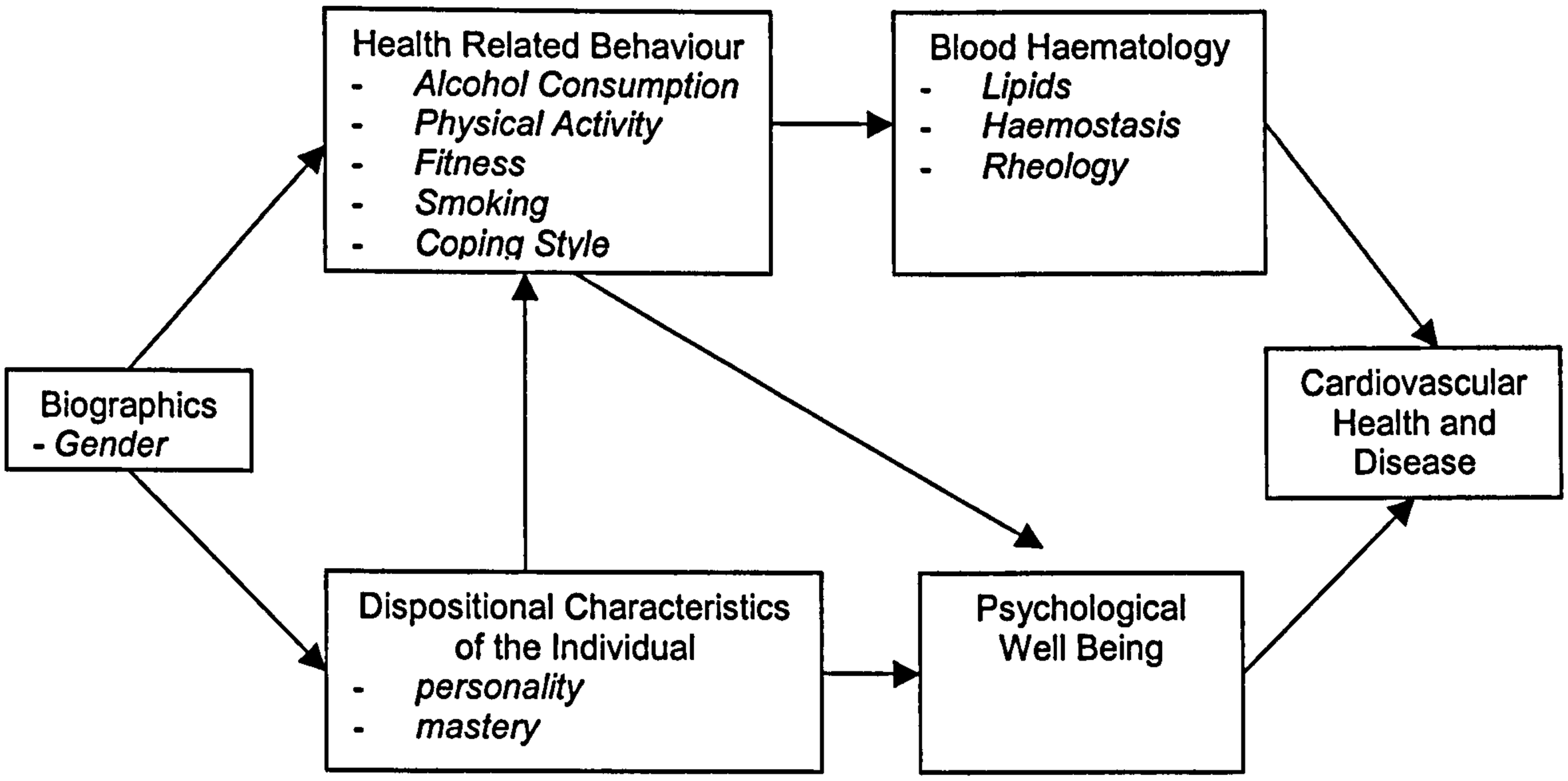


Figure 2.5. Schematic representation of the thesis.

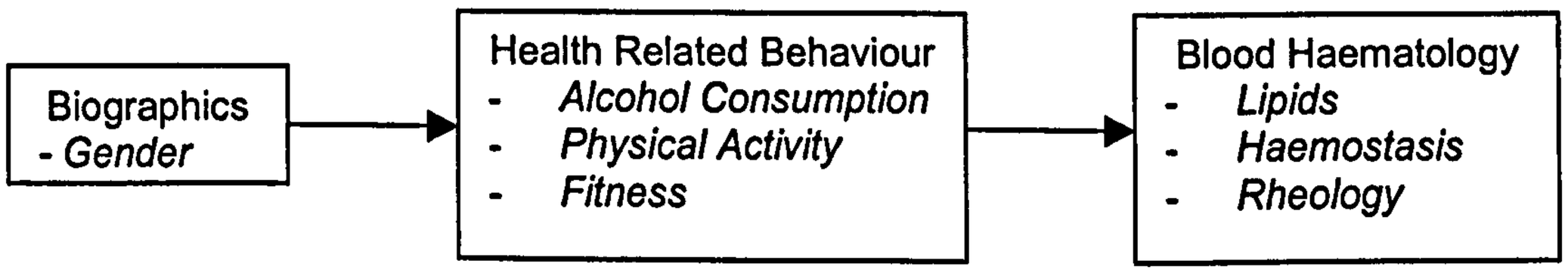


Figure 2.6. Schematic representation of study 1.

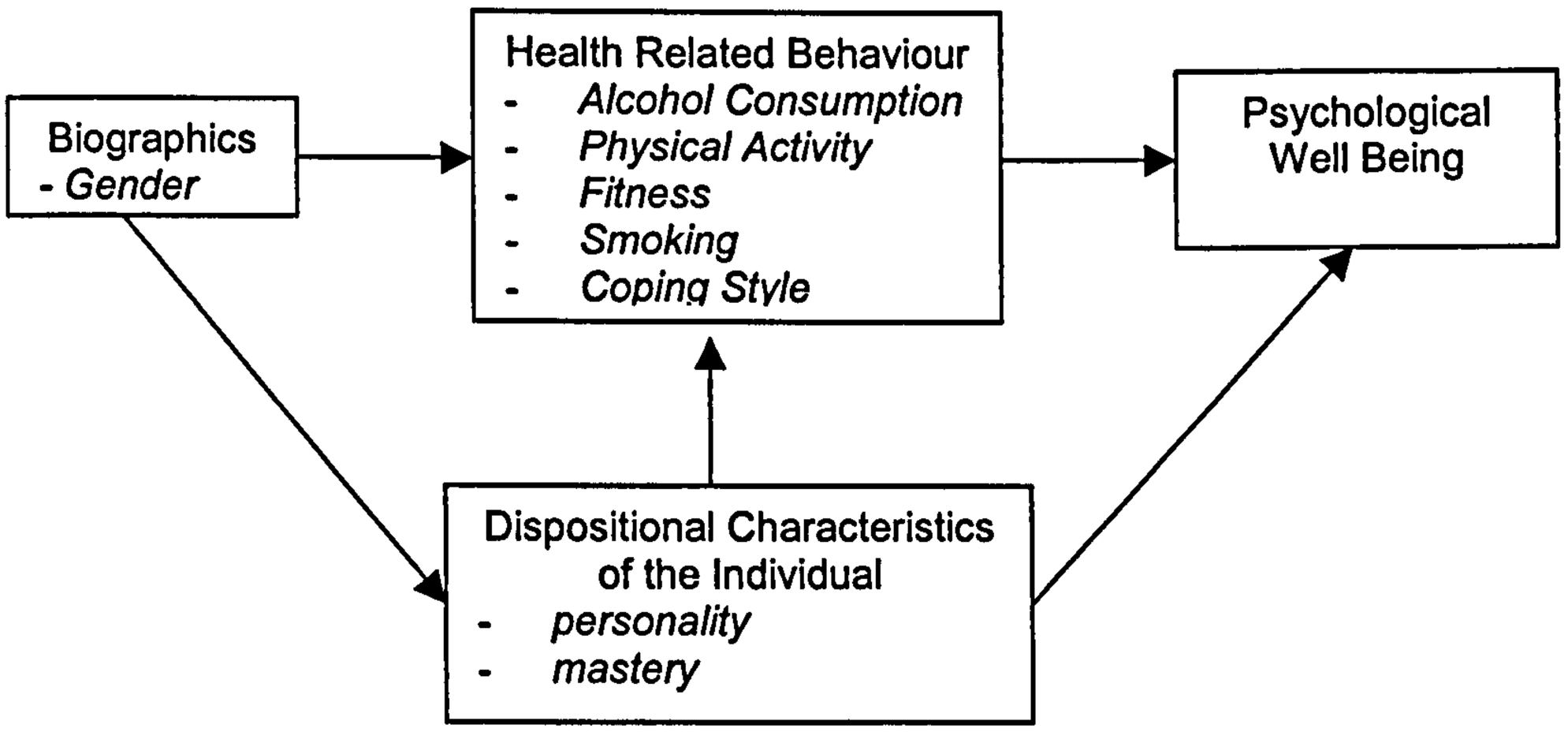


Figure 2.7. Schematic representation of study 2.

CHAPTER 3: STUDY 1 - THE EFFECTS OF ALCOHOL CONSUMPTION, PHYSICAL ACTIVITY AND FITNESS ON BLOOD HAEMATOLOGY

3.1. INTRODUCTION

Direct paths of association between alcohol consumption, physical activity and the risk of CHD have been hypothesised (Maclure 1993; Wanemethee and Shaper, 2001).

It has been shown that alcohol influences several blood haematological indices, which might explain a protective role (El-Sayed et al., 1999a). For example, it has been reported that alcohol consumption increases HDL concentration (Koppes et al., 2000; Sillanaukee et al., 2000), which may play a critical role in the progression of atherosclerosis. Another mechanism through which alcohol may protect against CHD is via favourable alterations in blood haemostasis (Mukamal et al., 2001), although existing evidence on this topic is both meagre and conflicting (El-Sayed et al., 1999a). Indeed, previous research has shown a negative impact of alcohol consumption on blood fibrinolytic mechanisms (Djousse et al., 2000). In addition, increases in plasma viscosity (Yarnell et al., 2000) and haematocrit concentration (Wanemethee and Shaper, 1994) have also been observed with increasing alcohol consumption, although others have indicated a reduction in plasma viscosity following moderate alcohol consumption (Mukamal et al., 2001).

The majority of previous studies were designed to examine the effects of an acute dose of alcohol rather than a detailed examination of the effects of habitual alcohol consumption on health and disease. This is important, as the possibility exists that the effects of alcohol consumption on some of the biological predictors of cardiovascular disease are of an acute and transient

nature. Thus, the inter-relationship among habitual alcohol consumption patterns and the biological predictors of cardiovascular health and disease warrants further investigation.

Research evidence also exists to support a positive impact of physical activity on blood haematological variables relating to cardiovascular health and disease (Wanemethee and Shaper, 2001). Research investigations have reported beneficial changes in blood lipid profiles (Leon and Sanchez, 2001), blood haemostasis (El-Sayed et al., 2000) and blood rheology (El-Sayed, 1998) with higher levels of physical activity and exercise.

However, Thompson et al. (2001) report that at least some of the beneficial alterations to blood haematology that are attributed to physical activity are the result of recent exercise. Thus, there is a question over which of these effects is acute and transient in nature and which are more chronic responses to habitual physical activity patterns (Thompson et al., 2001). Further investigation is also required to evaluate the relative importance of physical activity versus physical fitness in relation to the blood haematological variables associated with cardiovascular health and disease, particularly in younger adults (Andersen and Haraldsdottir, 1995).

Thus, the present study is designed to provide information on the impact of alcohol consumption, physical activity and fitness on the blood haematological variables associated with cardiovascular health and disease, particularly those related to blood lipids, haemostasis and rheology.

3.1.1. Aim of the Study

Study 1 can be divided in to two main parts, each of which was designed to examine a specific aim:

(a) The aim of part 1 was to examine the associations between habitual alcohol consumption, physical activity and blood haematology in young, apparently healthy, adults.

(b) The aim of part 2 was to examine the associations between cardiorespiratory fitness and blood haematology in a smaller cohort of subjects from part 1 of the study. In addition, the effects of an acute bout of maximal exercise on blood haematological profiles were also studied.

3.2. MATERIALS AND METHODS

3.2.1. Subjects: Study 1 (part 1)

Initially, ~200 subjects were recruited, via word of mouth, to participate in this cross-sectional study. However, many of these subjects (~ 150) were not included in the final analysis for a number of reasons, including (a) technical problems with equipment, (b) blood sampling and storing procedures, and (c) the failure of subjects to meet selection criteria for the experiment. Final statistical analyses were performed on 50 normal, apparently healthy subjects (35 male and 15 female). Subjects characteristics (mean±SD) were age: 24±3 years; height: 176.4±7.9cm; body mass: 75.0±12.2kg; BMI: 24±0.4kg.m^2; percentage body fat: 17±0.6%; resting heart rate: 60±2beats.min^{-1}; SBP: 125±2mmHg and DBP: 69±2mmHg. The Liverpool JMU Research Ethics Committee approved the study protocol and procedures and all subjects provided their written informed consent prior to their participation in the study.

All subjects were non-smokers and were not taking any medication prior to commencing the study. Although subjects reported no personal or family history of cardiovascular disease or hypertension, several of them reported previous family medical histories of high cholesterol, diabetes and obesity. All of these details were obtained by questionnaire (appendix A) and verbally confirmed by the subjects before experimental procedures commenced.

Female subjects were tested in the follicular phase of the menstrual cycle, between days 2 and 5. This was indicated in the questionnaire provided and

verbally confirmed with the subject before the commencement of testing. Whilst detailed data were collected relating to the use of hormonal contraceptives (either pill or injection based), it was considered impossible to completely control for the different types of hormonal contraception used. Six subjects reported that they were using hormonal methods of contraception. Of the 9 subjects reporting no current use of hormonal contraception, 5 subjects reported having used hormonal contraception within the previous 12 months.

3.2.2. Experimental Protocol for Study 1 (Part 1)

All experimental trials commenced at the same time of day (08:00-09:00), with laboratory temperature being 19^0C with a relative humidity of 45-50%. When reporting to the laboratory subjects were asked to complete a pre-test questionnaire which included questions on the demography of the sample, physical activity, smoking history, habitual alcohol consumption patterns, family medical history, normal dietary patterns and hormonal contraceptive use (for female subjects). Following this, the experimenter checked through the information provided and verbally confirmed with the subject that the selection of the subject was valid under the previously determined criteria (please refer to section 3.2.1.). It was also ensured that the subjects had not eaten for 12 hours, consumed caffeine or alcohol for 24 hours, and performed no exercise over the preceding 24 hours.

The subject remained in a seated position and in a relaxed state for a total of 30 minutes, at the end of which a 20ml venous blood sample was withdrawn, via a clean venipuncture, from a prominent vein in the antecubital fossa of the arm, with

no stasis. The major controls placed on the withdrawal of blood were: (a) the experimenter familiarised all subjects with the venipuncture technique prior to the commencement of experimental trials; (b) a qualified and experienced phlebotomist performed all venipunctures; (c) the venipuncture had to be single pass and clean and (c) all blood was withdrawn without the use of stasis.

Following the withdrawal of blood, the subject remained seated and relaxed for a further 10 minutes whilst applying pressure to the site of venipuncture. During this time the experimenter treated the blood samples according to the methods previously described in section 3.2.5.4..

Thereafter, resting blood pressure was taken, provided the subjects were feeling no ill effects of the venipuncture. After blood pressure measurement height, weight and skinfold thicknesses of the subjects were recorded.

3.2.3. Subjects: Study 1 (part 2)

A cohort of 23 male subjects from study 1 part 1 took part in part 2 of this cross-sectional experimental investigation. Subject characteristics (mean±SD) were age: 24±4 years; height: 180.4±5.8cm; body mass: 80.1±10.9kg; BMI: 25±2kg.m^{2}; percentage body fat: 14±3%; resting heart rate: 58±9beats.min^{-1}; SBP: 128±11mmHg and DBP: 70±9mmHg. The Liverpool JMU Research Ethics Committee approved the study protocol and procedures and all subjects provided their written informed consent prior to their participation in the study.

3.2.4. Experimental Protocol for Study 1 (Part 2)

All subjects who participated in study 1 part 1 were asked to further volunteer to take part in part 2. However only a small cohort of male subjects completed part 2 of the experimental trial. Following the recording of anthropometric indices, subjects were asked to perform a maximal cycle ergometry test to volitional exhaustion (VO_{2max} test).

The maximal test began with a standardised warm-up on the cycle ergometer at a power output of 150W for 5 minutes. Upon completion of the warm-up the subject was allowed sufficient time to stretch before being asked to begin the maximal exercise test itself. The maximal incremental exercise test commenced at a power output of 180W for a period of 2 minutes with the wattage being increased in 30W increments every 2 minutes until volitional exhaustion. A successful test was judged by several criteria as outlined in the BASES physiological testing guidelines (Bird and Davidson, 1997). Online gas analysis (Metamax, Cortex, Frankfurt, Germany) was used to measure the subjects expired gas throughout the maximal test. The online gas analysis system was calibrated as per manufacturer instructions. Heart rate was also monitored continually throughout the test and was recorded at 1-minute intervals from the beginning of the test. Two electric fans were placed either side of the subject to alleviate thermal stress.

Immediately following the maximal exercise test the subjects were again seated and another 20ml venous blood sample was withdrawn. The subject remained seated for a further 30 minutes following the exercise at which time a third 20ml venous blood sample was withdrawn. Once the blood flow from the third

venipuncture had been staunched, subjects were shown where they could shower and were subsequently taken for breakfast.

3.2.5. Experimental Tools

3.2.5.1. Pre-Test Questionnaire

The pre-test questionnaire was administered to all participants in order to obtain information on demography of the sample, physical activity, smoking history, habitual alcohol consumption patterns, normal dietary patterns, family medical history and hormonal contraceptive use (for female subjects). The questionnaire design was informed by previous questionnaires relating to health and lifestyle, such as the Liverpool Lifestyle Questionnaire.

3.2.5.1.1. Demographic Information

Information on age, gender, marital status, number of children, ethnic origin, religion, current employment, parents occupations, and educational background were obtained.

3.2.5.1.2. Physical Activity

Questions were designed to procure information on the habitual weekly physical activity of the subjects, based on recommendations made by Kriska and Caspersen (1997). Specific open-ended questions were posed relating to the type of activity performed (e.g. soccer, walking, gardening, jogging etc), the activity duration (reported in minutes), and the frequency of these activities per week. From this, the total time spent on leisure-time physical activity per week was

calculated. In addition, estimates of the weekly energy expenditure on leisure-time physical activity could be made, based on recommendations made by Kriska and Caspersen (1997). Other questions related to the frequency of the performance of "vigorous" and "less vigorous activities" lasting 20 minutes or more were asked, based on the Liverpool Lifestyle Questionnaire. Subjects were also asked to rate their physical activity and fitness, in relation to others of a similar age, along a 5-point Likert type scale ranging from "excellent" (coded as 1) to "very poor" (coded as 5).

3.2.5.1.3. Smoking History

Questions were asked relating to current and previous smoking habits in order to ensure that all subjects participating in this study were currently non-smokers.

3.2.5.1.4. Alcohol Consumption

The Alcohol Use Disorders Identification Test (AUDIT) was developed by the World Health Organisation (WHO) as a means of identifying individuals whose alcohol consumption has become harmful or hazardous to their health. Information relating to this scale and its use are provided in greater detail in section 4.2.2.9.1., and so it will not be discussed in duplicate here. In essence a high AUDIT score relates to a greater level of harmful/hazardous alcohol consumption.

Detailed information concerning the weekly habitual alcohol consumption patterns of the respondents was gained. Questions were related to the subjects' typical alcohol consumption over a 7-day week, their alcohol consumption on the Friday,

Saturday, and Sunday of the last weekend, and their typical weekends alcohol consumption (Friday, Saturday, Sunday). Respondents were asked to report both the type and amount of alcoholic beverage consumed, with these data then being converted to represent the units of alcohol consumed.

3.2.5.1.5. Dietary Patterns

Information was obtained on the frequency of consumption of various foods, normally associated with the adoption of a healthy diet (such as fresh fruit, salads, vegetables etc).

3.2.5.1.6. Family Medical History

Questions were asked in relation to the previous medical history of the subject and their families. In particular details were gained on previous heart disease, hypertension, high cholesterol and diabetes. If a positive response was indicated, the subject was then asked to provide information on which relative was a previous sufferer (e.g. mother, grandfather, etc).

3.2.5.1.7. Hormonal Contraceptive Use

Specific questions were asked relating to the current and previous use of hormonal methods of contraception. Information was obtained on the type and duration of hormonal contraceptive use.

3.2.5.2. Anthropometric Measures

3.2.5.2.1. Height

Body height measurements were recorded to the nearest 0.5cm with the use of a stadiometer (Seca, Germany). For this, subjects stood on a platform facing away from the stadiometer, the subject was asked to take a full breath in and hold it whilst the measurement was taken. The subject wore no shoes during this measurement.

3.2.5.2.2. Body Mass

Body mass was assessed to the nearest 0.1 Kg using a set of balance scales (Seca, Germany). The subject was clothed, wearing a pair of shorts and socks but no shoes or shirt.

3.2.5.2.3. Skinfold Thickness

Skinfold thickness was recorded at four sites (biceps, triceps, sub-scapula and supra-iliac) using Harpenden skinfold callipers (John Bull, England) and all measurements were taken from the right-hand side of the body with the subject standing in the anatomical position. Each of the four skinfold sites were anatomically identified as follows:

1. Biceps: taken from the anterior surface of the biceps midway between the anterior auxiliary fold and the antecubital fossa.

2. Triceps: taken as a vertical fold on the posterior midline of the upper arm, over the triceps muscle, halfway between the acrosion process and olecranon process.
3. Subscapular: taken as a diagonal fold stemming from the vertebral border, 2cm from the inferior angle of the scapulae.
4. Suprailiac: taken as a diagonal fold above the crest of the ilium.

Skinfold thicknesses were measured to the nearest 0.1mm, with three separate measurements being recorded from each site. The sum of all four skinfolds, plus the age and gender of the subject, were then used to calculate body density, as previously described by Durnin and Womersley (1974). Percentage body fat was then estimated from the body density results, using the Siri equation (Siri, 1956).

3.2.5.3. Collection and Treatment of Venous Blood

Venous blood (20ml) was withdrawn from a prominent vein in the antecubital fossa of the arm with no stasis. All samples were withdrawn using a sterile plastic syringe and 19-gauge needle. The experimenter, who had undergone a rigorous training course in phlebotomy, performed all venipunctures.

Venous blood (20ml) was aliquoted in to separate tubes containing several anticoagulants as follows:

- Six millilitres of whole blood was transferred to a tube containing tri-sodium citrate dihydrate (TCD), in the ratio 9 volumes whole blood to 1 volume TCD.

- From the above tube, 0.5 ml of TCD anticoagulated blood was transferred to a plastic tube containing acetate buffer solution (1 volume TCD blood to 1 volume acetate buffer solution) for the analysis of tPA activity.
- Ten millilitres of whole blood was transferred to two additional tubes containing a di-potassium ethylenediam inetetra-acetic acid (EDTA) anticoagulant coating, for the analysis of plasma viscosity and blood lipids.
- In the exercise condition only, 50μl of EDTA treated whole blood was added to a 1.5ml eppendorf tube, containing 150μl of perchloric acid, for the analysis of lactate concentration.
- The final 4ml of whole blood was added to a plain plastic tube containing no anticoagulant, for the production of serum.

3.2.5.4. Preparation of Venous Blood

The experimenter performed all preparation, treatment and analyses of venous blood samples, with all analyses being conducted in the biochemistry laboratories of Liverpool John Moores University.

Immediately following the collection and separation of venous blood, the TCD blood and the TCD plus acetate buffer sample were centrifuged (2000xg for 20 min at 4°C) for the production of platelet poor plasma as per manufacturers instructions. Once centrifuged, 400μl plasma was separated by pipette in to separate tubes and stored at -70°C for the subsequent determination of PAI-1 activity, Fibrinogen, TT, PT, and APTT. One tube containing 400μl of platelet poor plasma was briefly stored at room temperature before being analysed for D-dimer

concentration. The plasma from the tube containing whole blood plus acetate buffer solution was pipetted in to a tube. Hydrochloric acid was then added to this tube, in the ratio of 10μl HCl^- to 150μl of plasma. This tube was then also stored at -70°C for the subsequent analysis of tPA activity.

Aliquots of whole blood, anticoagulated with EDTA, were used for the measurement of lactate, haemoglobin and haematocrit. For lactate analysis, whole blood (50μl) was added to an Eppendorf tube containing perchloric acid (100μl). The Eppendorf tube was then centrifuged and the resultant supernatant was pipetted in to a further Eppendorf tube and stored at –70°C. The remainder of the EDTA anticoagulated blood was centrifuged (4000xg for 5 min at 20°C) and plasma separated as per manufacturers instructions. One and a half millilitres of plasma was added to a plain plastic tube and briefly stored at room temperature for the analysis of plasma viscosity. In addition, other plain plastic tubes, each containing 400μl of plasma, were stored at -70°C for the subsequent analysis of total cholesterol, TG, HDL and NEFA.

The whole blood added to a plain tube was placed in a water bath and incubated at 37°C. Once the clot was formed the tube was centrifuged (4000xg for 15 min at 20°C) and the serum pipetted in to three separate tubes. Serum (1.5ml) was then pipetted in to a plain plastic tube and briefly stored at room temperature for serum viscosity analysis. The remaining serum was pipetted in to two plain plastic tubes and stored at -70°C for the subsequent analysis of albumin, total protein, apo A1 and apo B.

3.2.5.5. Quality Control Procedures

- The water bath (Precitherm, Laboratory Mannheim, Germany) was allowed to run for a length of time to ensure stability of the designated temperature (37°C) prior to all testing. The temperature of the water was continuously checked using an external alcohol thermometer as well as the water bath thermostat.
- All pipettes were checked for the accuracy and precision of the dispensed volumes by weighing distilled water several times. All pipette tips were wiped with a clean tissue prior to expending the volume to avoid the addition of extra sample.
- Wherever possible, biochemical parameters were measured in duplicate.
- The separation of all plasma samples from the cells was conducted with great care to avoid error (avoiding cells, haemolysis).
- When using batches of reagents, care was taken to only use reagents of the same lot numbers. Also any reagent past the stated expiry date was not used.
- The centrifugation of all test samples was conducted at the appropriate speeds and temperatures, as per manufacturers instructions. The refrigerated centrifuge was allowed ample time to stabilise at the correct temperature where appropriate.
- The use of distilled, purified and sterile water was ensured where appropriate. In addition, all reagents were mixed precisely to manufacturers instructions to ensure homogeneity.
- The appropriate standards and controls were used to check the accuracy of all tests, as per manufacturers instructions.

3.2.5.6. Analytical Procedures for the Measurement of Blood Lipids

3.2.5.6.1. Analytical Procedures Using the Monarch Chemistry System

The Monarch Chemistry System is used to analytically quantify several different parameters contained within small volumes of plasma, serum, urine or cerebrospinal fluid. The system is able to utilise one, or more, of the following analytical techniques: spectrophotometry, potentiometry, and nephelometry/flourescence. In this study only spectrophotometry was used on EDTA treated plasma and serum for the quantification of total cholesterol, TG, NEFA, HDL, apo A1, apo B, albumin, total protein and lactate.

With spectrophotometry, the analyser utilises an optics module located within the system to analyse the samples by absorbance. Light, of a selected wavelength (controlled by a monochromator) is projected from a tungsten lamp through the top of a cuevette. Unabsorbed or unreflected light passes through the reaction substance and is filtered so that a narrow spectral band is directed toward a photomultiplier tube located below an optic filter. This tube measures the intensity of the light and transmits the data to the computer module, which in turn processes the data in to the required concentration or activity of the selected parameter.

There are several procedural guidelines to follow when using the Monarch Chemistry System for the analyses listed above. The following guidelines were strictly adhered to with each test:

- Plasma samples were prepared according to manufacturer instructions.
- All reagents were prepared and stored according to the manufacturer instructions and all reagents used throughout each test were from the same batch and were used prior to their listed expiration date.
- Each individual set of test parameters for the Monarch Chemistry system were set-up according to manufacturer instructions, in order to ensure measurement at the correct absorbance and at the correct sample to reagent ratio.
- The appropriate calibrators and standards were used to check the accuracy of each test.

3.2.5.6.2. Total Cholesterol

Total cholesterol was measured in plasma using an *in vitro* enzymatic method (INFINITY Cholesterol Reagent, Sigma Diagnostics, St. Louis, USA). The INFINITY reagent is based on the formulation first described by Alain et al. (1974), and the modification of Roeschlau et al. (1974).

The INFINITY reagent itself contains the following ingredients and active constituents:

- Cholesterol Oxidase (>100U.l)
- Cholesterol Esterase (>1250U.l)
- Peroxidase (>800U.l)
- 4-Aminoantipyrine (0.25mmol.l)

- Hydroxybenzoic Acid (10mmol.l)
- Buffer (pH6.6 at 25°C)
- Surfactant
- Sodium Azide (0.01%)

The cholesterol assay is based on a series of 3 reactions, as follows:

1. Cholesterol esters are enzymatically hydrolysed by cholesterol esterase (CE) to cholesterol and free-fatty acids:

$$\text{Cholesterol Esters} \xrightarrow{\text{CE}} \text{Cholesterol + Fatty Acids}$$

2. Free cholesterol is oxidised by cholesterol oxidase (CO) to cholest-4-en-3-one and hydrogen peroxide:

$$\text{Cholesterol} + O_2 \xrightarrow{\text{CO}} \text{Cholest-4-en-3-one} + H_2O_2$$

3. The hydrogen peroxide combines with hydroxybenzoic acid (HBA) and 4-aminoantipyrine (4AAP) in the presence of peroxidase (POD) to form a quinoeimine dye. The intensity of the solution colour is then measured at a dual wavelength of 500-550nm.

$$2H_2O_2 + \text{HBA} + \text{4AAP} \xrightarrow{\text{POD}} \text{Quinoneimine Dye} + 4H_2O$$

Subject plasma samples were thawed rapidly at 37°C before being separated in to 100µl aliquots, placed in the appropriate sample cups and added to the sample

ring (Instrumentation Laboratories, Warrington, England). The vial containing the ready to use INFINITY Cholesterol Reagent was then added to the Monarch reagent boat and placed in the appropriate carousel. Cholesterol was then analysed automatically using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England). The appropriate calibration solution (Cholesterol Calibrator, Sigma Diagnostics, St. Louis, USA) and quality control solution (Cardiolipid Control, Sigma Diagnostics, St. Louis, USA) were analysed to ensure the accuracy of results, as per manufacturers instructions. Thus, cholesterol concentration in the assay mixture is determined using the following equation:

Cholesterol = (absorbance of unknown / absorbance of calibrator) x calibrator value

Normal cholesterol levels are reported to be <200mg.dl^{-1} with a coefficient of variation of 2.1% for this method. High blood cholesterol levels are reported as being >240mg.dl^{-1} (to convert to mmol.l^{-1} divide mg.dl^{-1} by 38.46).

3.2.5.6.3. Triglycerides

The measurement of TG concentration in either plasma or serum, as part of a blood lipid profile, can be used in the diagnosis of hyperlipoproteinaemia. In addition, its measurement can help profile other diseases such as atherosclerosis, diabetes mellitus and other metabolic disorders.

Triglyceride concentration was measured using a method modified from the one originally reported by Bucolo and David (1973). In this study, the determination of plasma TG concentration utilised a method involving the enzymatic hydrolysis of TG to glycerol and free fatty acids, followed by the enzymatic measurement of the released glycerol, thus allowing an indirect measurement of the initial TG concentration.

In terms of the principle behind this form of measurement for TG, several enzymatic reactions are necessary. The enzymatic reactions involved in the TG assay are:

$$\text{Triglycerides} \xrightarrow{\text{Lipoprotein Lipase}} \text{Glycerol + Fatty Acids}$$

$$\text{Glycerol + ATP} \xrightarrow{\text{GK}} \text{G-1-P + ADP}$$

$$\text{G-1-P + NAD} \xrightarrow{\text{G-1-PDH}} \text{DAP + NADH}$$

$$\text{NADH + INT} \xrightarrow{\text{Diaphorase}} \text{Formazan + NAD}$$

Initially TG's are broken-down and hydrolysed to glycerol and fatty acids by lipoprotein lipase. The glycerol released is then phosphorylated by the action of ATP to form glycerol-1-phosphate and ADP. The catalyst for this reaction is

glycerol kinase. The glycerol-1-phosphate produced is subsequently oxidised to dihydroxyacetone phosphate (DAP) along with the concomitant reduction of NAD to NADH, in a reaction catalysed by glycerol-1-phosphate dehydrogenase (G-1-PDH). Oxidation of this NADH occurs along with the simultaneous reduction of 2-(p-iodophenyl)-3-p-nitrophenyl-5-phenyltetrazolium chloride (INT) to formazan (INTH) in the presence of diaphorase. Formazan is highly coloured and has an absorbance maximum at 500nm. Thus, the intensity of the colour produced is in direct proportion to the concentration of TG within the sample.

Before testing, the triglyceride (INT) reagent (Sigma Diagnostics, St. Louis, USA) was reconstituted with exactly 10ml distilled water. Following the addition of the distilled water, the stopper was added to the vial, the contents of which were mixed by inversion followed by a gentle swirling to facilitate diffusion of the contents. The vial was not shaken at any time during the test procedure as per manufacturer instructions. Subject plasma samples were thawed rapidly at 37°C before being separated in to 100µl aliquots and placed in the appropriate sample cups (Instrumentation Laboratories, Warrington, England). The vial containing the triglyceride (INT) reagent was then added to the Monarch reagent boat. Triglyceride was analysed automatically using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England), set to measure the absorbance of the test assay mixture at a wavelength of 500nm. The normal ranges for plasma triglyceride concentration in subjects under 30 years of age is 10-140 $mg.dl^{-1}$ (to convert to $mmol.l^{-1}$ divide $mg.dl^{-1}$ by 87.72), with a coefficient of variation of 2.5% for this method.

3.2.5.6.4. Non-Esterified (free) Fatty Acids

Non-esterified fatty acid concentration was measured in plasma using an *in vitro* enzymatic colourimetric method (NEFA C, Wako Chemicals, Neuss, Germany). This test works from the principle that NEFA, when treated with acyl-CoA synthase in the presence of ATP, magnesium cations, and CoA will form acyl-CoA as well as AMP and pyrophosphate (PPi). Secondly, the acyl-CoA is oxidised with the addition of acyl-CoA oxidase, producing hydrogen peroxide. The formation of a purple coloured liquid, with an absorption maximum of 550nm, is formed with the subsequent addition of peroxidase. Thus, NEFA concentration can be determined by measurement of the optical density of the liquid at 550nm.

Details of the reagents (NEFA C, Wako Chemicals, Neuss, Germany) used for this test are as follows:

- Colour Reagent A: Provided in dry form and contains: Acyl-coenzyme A sythetase (3U/vial), ascorbate oxidase (30U/vial), coenzyme A (7mg/vial), ATP (30mg/vial) and 4-aminoantipyrine (3mg/vial).
- Solvent A: An aqueous solution with the following ingredients: phosphate buffer pH 6.9 (0.05mol.l), magnesium chloride (3mmol.l), surfactant, stabilisers.
- Colour Reagent B: Provided in dry form and contains: acyl-coenzyme A oxidase (132U/vial) and peroxidase (150 U/vial)
- Solvent B: An aqueous solution with the following ingredients: MEHA (1.2mmol.l) and surfactant.

- NEFA Standard Solution: a known concentration of NEFA: oleic acid (1 mmol.l^{-1}), surfactant and stabilisers.

To fully prepare colour reagent A, exactly 10ml of solvent A was added to the colour reagent A vial. The contents were then mixed by gently inverting the vial as per manufacturer instructions until the contents were fully dissolved. Colour reagent B was prepared by adding precisely 20ml of solvent B to the colour reagent B vial. Again the contents were mixed by gently inverting the vial until the contents were dissolved.

Subject plasma samples were thawed rapidly at 37°C before being separated in to 100µl aliquots and placed in the appropriate sample cups (Instrumentation Laboratories, Warrington, England). Two 100µl aliquots of the ready prepared NEFA standard solution were also added to sample cups. The vials containing both colour reagent A and colour reagent B were added to their appropriate Monarch reagent boats. Non-esterified fatty acid concentration was analysed using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England). The coefficient of variation is 3% for this method.

3.2.5.6.5. High Density Lipoprotein

In recent years the measurement of HDL has been used alongside the measurement of other blood lipids, most notably cholesterol, as a tool for assessing an individuals risk of developing CHD. The importance of using HDL as an indicator of CHD risk has been highlighted by findings that showed a strong

negative relationship between HDL concentration in the plasma and the incidence of CHD.

For this study, HDL concentration was quantitatively determined from human plasma *in vitro*. Ready prepared reagents (EZ HDL Cholesterol Tests, Sigma Diagnostics, St. Louis, U.S.A.) were used, the details of which follow:

- EZ HDL Reagent 1: Goods buffer, pH 7.0 (30mmol.l) containing: 4AA (0.09mmol.l), POD (2400U.l), anti-human β-lipoprotein antibody (from sheep) and preservative
- EZ HDL Reagent 2: CHE (4000U.l), CO (20000U.l) and FDAOS (0.8mmol.l)

In addition to these reagents, the EZ HDL calibrator (Sigma Diagnostics, St. Louis, U.S.A.) was used, providing a known concentration of HDL cholesterol (53mg.dl, 1.37mmol.l).

The major reactions involved in the determination of HDL using the EZ HDL Cholesterol method are:

$$\text{LDL, VLDL, chylomicrons} \xrightarrow{\text{anti-human β-lipoprotein antibody}} \text{Antigen-Antibody complex}$$

$$\text{HDL} + H_2O + O_2 \xrightarrow{\text{CHE + CO}} \Delta^4\text{-cholestone} + \text{fatty acid} + H_2O_2$$

$$H_2O_2 + FDAOS + 4AA \xrightarrow{POD} \text{Blue Colour Complex}$$

The test principle assumes that the anti-human β-lipoprotein antibody in reagent 1 binds with all lipoproteins except HDL. Reagent 2 then acts to cause the formation of an antigen-antibody complex, thus blocking enzyme reactions. The cholesterol esterase (CHE) and cholesterol oxidase (CO) in reagent 2 only react with HDL. When reagent 2 reacts with HDL, hydrogen peroxide is produced, thus turning the liquid blue. The HDL concentration of the fluid can be ascertained by measuring the absorbance of the fluid at a wavelength of 600nm against the absorbance of the calibrator (also measured at 600nm).

Prior to analysis, the EZ HDL calibrator was reconstituted with exactly 3ml ddH_2O. The vial was swirled gently and left to stand for 15 minutes, according to manufacturer instructions. Following 15 minutes the vial was gently inverted to ensure full dissolution of the contents. A 100µl aliquot of the calibrator was added to the appropriate sample cup (Instrumentation Laboratories, Warrington, England). Subject plasma samples were thawed rapidly at 37°C before being separated in to 100µl aliquots, and placed in the appropriate sample cups. The vials containing both the EZ HDL Cholesterol reagents 1 and 2 were then added to the appropriate Monarch reagent boats. High-density lipoprotein concentration was analysed automatically using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England). The normal range of HDL concentrations in plasma is expected to be between 35mg.dl^{-1} and 60mg.dl^{-1} (to

convert to mmol.l^{-1} divide mg.dl^{-1} by 38.46), with a coefficient of variation of 4% for this method.

3.2.5.6.6. Low Density Lipoprotein and Very Low Density Lipoprotein

Both LDL and VLDL were estimated using standard equations as described previously by Friedewald et al. (1972). Low-density lipoprotein concentration was estimated from total cholesterol, HDL and TG values, using the following equation:

$$\text{LDL-C} = (\text{Total Cholesterol} - \text{HDL}) - (\text{TG} / 5)$$

3.2.5.6.7. Apolipoprotein A1

Apolipoprotein A1 represents approximately 60% of the protein structure of HDL protein mass. Apolipoprotein A1 concentrations have been used to aid the risk assessment of coronary artery disease (Kukita et al., 1984).

Apolipoprotein A1 concentration was measured using an immunoturbidimetric method of determination. The test principle revolves around the fact that apo A1 in serum combines with a specific antibody present in the reagent mixture, and forms and insoluble complex resulting in turbidity of the assay mixture. Thus, the amount of turbidity present is directly proportional to the amount of apo A1 present in the serum sample. The turbidity of the mixture is determined spectrophotometrically at a wavelength of 340nm. The actual concentration of apo A1 in the sample was determined using a standard calibration curve, obtained using multi-level apo A1 calibrators.

Ready-made reagents (Sigma Diagnostics, St. Louis, USA) were used for determination of apo A1 concentrations in this study, the details of which follow:

- Apo A1 Antibody Reagent: buffered solution containing goat antibodies to human apolipoprotein A-1; sodium azide (0.1%) as a preservative.
- Apo A1 Activator: surfactant solution, sodium azide (0.1%) added as preservative.
- Apo A1 Calibrators 1-5: Human serum containing 5 different concentrations of apo A1; sodium azide (0.1%) added as preservative.
- Apolipoprotein Serum Controls I and II: human serum containing apo A1; sodium azide (0.1%) added as preservative.

A working antibody reagent solution was made by adding 0.1ml of apo A1 activator to 10ml of apo A1 antibody reagent, as per manufacturer instructions. All other reagents were provided ready to use, although reagents were allowed to equilibrate to room temperature before use, as per manufacturer instructions.

Subject serum samples (serum was used to minimise non-specific turbidity, as per manufacturer instructions) were thawed rapidly at 37°C before being separated in to 100µl aliquots, and placed in the appropriate sample cups (Instrumentation Laboratories, Warrington, England). Apolipoprotein A1 calibrators and serum controls were also added to sample cups and placed in the appropriate position on the Monarch sample ring. The working antibody reagent solution was then added to the Monarch reagent boat, and placed in the appropriate position in the

analyser. Quantification of apolipoprotein A1 concentration was performed automatically by measuring the turbidity of the assay mixture against that of the apo A1 calibrators at 340nm, using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England). The expected range for apo A1 concentration is 73-169mg.dl^{-1}, with a coefficient of variation of 5% for this method.

3.2.5.6.8. Apolipoprotein B

Apolipoprotein B is the primary protein constituent of LDL, contributing approximately 90% of LDL protein mass. In recent times apo B levels have been utilised in the assessment of coronary heart disease risk, and have been suggested as a more sensitive biochemical marker than total cholesterol, TG, HDL and LDL (Naito, 1986; Kottke et al., 1986). Research has shown that coronary heart disease patients exhibit higher levels of apo B than do control subjects with no history of CHD (Kukita et al., 1984; Naito, 1986; Kottke et al., 1986).

Apolipoprotein B concentration was measured using an immunoturbidimetric method as reported by Rifai and King (1986). This test principle assumes that the apo B in the test sample combines with a specific antibody, contained within the reagent mixture (Sigma Diagnostics, St. Louis, USA). This forms an insoluble complex and results in turbidity of the assay mixture, with the amount of turbidity being directly proportional to the concentration of apo B in the sample. A spectrophotometer was used to measure the turbidity of the assay mixture at 340nm.

Ready-made reagents (Sigma Diagnostics, St. Louis, USA) were used for testing the samples in this study, the details of which follow:

- Apo B Antibody Reagent: Buffered solution containing goat antibodies to human apolipoprotein B. Sodium azide (0.1%) added as preservative.
- Apo B Calibrators 1-5: human serum containing 5 different concentrations of Apo B. Sodium azide added as preservative.
- Apolipoprotein Serum Controls I and II: Human serum containing Apo B. Sodium azide (0.1%) added as preservative.

All Apo B reagents were supplied ready to use, although reagents were allowed to equilibrate to room temperature before use, as per manufacturers instructions. Subject serum samples (serum was used to minimise non-specific turbidity, as per manufacturer instructions) were thawed rapidly at 37°C before being separated in to 100µl aliquots, and placed in the appropriate sample cups (Instrumentation Laboratories, Warrington, England). Apolipoprotein B calibrators and serum controls were also added to sample cups and placed in the appropriate position on the Monarch sample ring. The Apo B antibody reagent was then added to the Monarch reagent boat, and placed in the appropriate position in the analyser. Quantification of apo B concentration was performed automatically by measuring the turbidity of the assay mixture against that of the apo B calibrators at 340nm, using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England). The expected range of apo B concentration in human plasma is between 58-138mg.dl^{-1}, with a coefficient of variation of 5.1% for this method.

3.2.5.7. Analytical Procedures for the Measurement of Blood Coagulation

Measurements of fibrinogen concentration, TT, PT, and APTT were made using specific reagents and coagulometer (Coag-A-Mate XM) as supplied by Organon Teknika (North Carolina, USA).

The accurate measurement of these specific coagulation factors is dependent upon several things, including storage and thawing of blood samples, reagent quality, reagent volume, activation time, reaction temperature, and the clot detection system. As inaccurate data could occur from a failure to consider the above points, several specific precautions were taken in this study to ensure the accurate measurement of these coagulation factors:

1. Plasma was stored as per manufacturers instructions. Specifically, samples were both frozen and thawed rapidly to ensure the integrity of the samples. Samples were frozen rapidly at -70°C and thawed rapidly at 37°C to prevent denaturation of the coagulation proteins.
2. All reagents were mixed precisely to manufacturers instructions to ensure homogeneity of the data.
3. Any reagent not within the stated expiry date was not used and only reagents with the same batch numbers were used for each series of measurements.
4. The activation time for each of the specific assays was standardised to eliminate any variation in exposure time.
5. Verify Reference Plasma (Organon Teknika, North Carolina, USA) was used to calibrate the Coag-A-Mate and to ensure quality control before each series of measurements were made. Verify reference plasma is assayed human

plasma, the integrity of the constituents being assured by lyophilisation. Verify Reference Plasma is used as a control in coagulation assays and for the quantification of coagulation proteins.

6. The calibration curves for each of the specific assays were performed prior to each series of measurements, according to manufacturers instructions.

3.2.5.7.1. Fibrinogen

The method of Clauss (1957) was used for the quantification of fibrinogen in plasma. This method is based on the principle that when thrombin is added to a plasma sample, the fibrinogen within the sample is enzymatically converted to fibrin. Subsequently, the formation of a fibrin network is formed via polymerisation of the fibrin, following which a visible clot is formed when factor XIII (activated by thrombin) catalyses the formation of stabilising cross-bridges. The resultant time taken from the addition of thrombin to the formation of the clot is inversely proportional to the fibrinogen concentration.

The test procedure initially involves the determination of a four-point calibration curve using serial dilutions of the Verify Reference Plasma with Owren's Veronal Buffer (Organon Teknika, North Carolina, USA). In this study dilutions were made to produce values of 738mg.dl^{-1}, 369mg.dl^{-1}, 184.5mg.dl^{-1} and 92.25mg.dl^{-1} for the four-point calibration curve. Individual samples of plasma were then thawed rapidly at 37°C in a water bath. Samples were then diluted 1:10 with Owren's Veronal Buffer (0.1ml of sample to 0.9ml of buffer). Two hundred microlitres of each sample dilution was then added to the appropriate sample trays and warmed to 37°C for 2 minutes. One hundred microlitres of Fibriquik Thrombin Reagent

(Organon Teknika, North Carolina, USA) was then added to each sample tray. The thrombin reagent contains ~100NIHU.ml^{-1} of bovine thrombin with stabilisers and buffer. Following reconstitution with purified water, thrombin reagent was allowed to warm to room temperature (20-25°C) immediately prior to use, as per manufacturers instructions. Clot detection was commenced simultaneously with the addition of the thrombin reagent. The resultant fibrinogen concentrations were displayed by the Coag-A-mate shortly thereafter. The normal range for fibrinogen, reported by this instrument, is 146-380mg.dl^{-1} with a coefficient of variation of ~3%.

3.2.5.7.2. Thrombin Time

The role of thrombin in coagulation is to catalyse the polymerisation of fibrinogen to fibrin. Thus, the *in vitro* addition of thrombin to a sample of plasma would usually cause the formation of a blood clot. The TT test involves the addition of a known concentration of thrombin reagent to a set volume of plasma and the measurement of the time taken to clot formation.

The test procedure initially involves the rapid thawing of all test plasma samples at 37°C in a water bath. In addition, the Thromboquik Thrombin Reagent (3-4NIHU.ml^{-1} bovine thrombin, HEPES buffer, calcium chloride and stabilisers. Organon Teknika, North Carolina, USA), once reconstituted with 3ml purified water and mixed, was also warmed to 37°C for at least 2 minutes immediately before use. Two hundred microlitres of test plasma was added in duplicate to the appropriate test trays and warmed to 37°C for a further 2 minutes. Thereafter, 200µl of the thrombin reagent was forcibly added to the test plasma, with

simultaneous activation of clot detection. Results, recorded in seconds, were displayed by the Coag-A-Mate shortly after clot formation. The normal range for TT, as reported by the manufacturers, is 10.1-12.3, with a coefficient of variation of less than 3%.

3.2.5.7.3. Prothrombin Time

The PT test is used to screen for problems in the extrinsic pathway of blood coagulation (particularly sensitive to factors II, VII and X), although it is not sensitive to abnormalities in the intrinsic pathway. An abnormal or extended PT test is usually associated with a decreased level of the extrinsic clotting factors. Prothrombin time was determined by the method previously described by Hirsh and Hull (1987), using the following test procedure.

Tri-sodium citrate dihydrate anticoagulated test plasma was thawed rapidly at precisely 37°C in a water bath. A sufficient volume of Simplastin Excel S Thromboplastin Reagent (rabbit brain tissue thromboplastin, calcium ions and buffer; Organon Teknika, North Carolina, USA) was reconstituted with the appropriate dilutent (stabilisers, 0.05% sodium azide). The reconstituted reagent was shaken well to ensure complete rehydration and was mixed well prior to use to ensure homogeneity, as per manufacturers instructions. The thromboplastin reagent was then pre-warmed to 37°C by the coagulometer (any reagent being held at 37°C for longer than 60 minutes was discarded). One hundred microlitres of the test plasma was added, in duplicate, to the appropriate test trays and incubated at 37°C for 3 minutes. Two hundred microlitres of the pre-warmed thromboplastin reagent was then forcibly added to the test plasma, with

simultaneous activation of clot detection. The time to clot formation was the recorded (in seconds) and printed by the coagulometer. Normal values for PT using this method are 12-18 seconds, with a coefficient of variation of 0.4%.

3.2.5.7.4. Activated Partial Thromboplastin Time

The APTT test is universally accepted as a method of detection for abnormalities in the intrinsic coagulation pathway. In particular the APTT test is sensitive to deficiencies in factors II, VII, IX, X, XI and XII, as previously described by Brinkhouse and Dombrose (1980).

Test plasma was thawed rapidly at precisely 37°C in a water bath. Sufficient calcium chloride (0.025M) was prewarmed to 37°C in the coagulometer. Test samples (100µl) were then pipetted, in duplicate, in to the appropriate sample trays and incubated at 37°C for 3 minutes. The plasma was then activated by forcibly adding 100µl of Platelin LS Phospholipid Reagent (purified phospholipids, micronized silica, buffer, stabiliser and preservative; Organon Teknika, North Carolina, USA) and incubated at 37°C for 5 minutes. Following activation, 100µl of the pre-warmed calcium chloride was added to the sample trays, with simultaneous timing for clot detection. Clotting times were subsequently recorded (in seconds) and printed by the coagulometer. The normal range for APTT when using this method is 22.6-35.0 seconds, with a coefficient of variation of 0.9%.

3.2.5.8. Analytical Procedures for the Measurement of Blood Fibrinolysis

3.2.5.8.1. Tissue Plasminogen Activator Activity

Tissue plasminogen activator constitutes an important protein in the fibrinolytic pathway, and its activity plays an important part in the fibrinolytic system. The physiological role of tPA is to activate the conversion of plasminogen to plasmin, which in turn degrades fibrin to soluble fibrin degradation products (FDPs).

Tissue-plasminogen activator activity was determined using a specific photometric method (Quadratech, Molndal, Sweden) and microplate technique. The test principle stems from the fact that plasmin is formed when plasminogen is activated by tPA. The rate of this activation is in turn increased when tPA stimulator is present. Tissue plasminogen activator concentration is determined by measuring the amidolytic activity of plasmin on the chromogenic substrate S-2251. The release of p-nitroaniline (pNA) is determined at 405nm.

$$\text{Plasminogen} \xrightarrow{\text{tPA,tPA Stimulator}} \text{Plasmin}$$

$$\text{S-2251} \xrightarrow{\text{Plasmin}} \text{Peptide + pNA}$$

The specific coatest tPA reagents used in this method and their constituents are listed below:

- Tris Buffer Working Solution: Derived from diluting tris buffer stock solution 10 1:10 with sterile water, containing: tris 0.05mol.l, pH 8.3, containing detergent.
- Acetate Buffer Working Solution: Derived from diluting acetate buffer stock solution 1:3 with sterile water. Sodium acetate 0.2mol.l, pH 3.9.
- Tissue-plasminogen activator: tPA 10μg. Reconstituted with acetate buffer to obtain solution of exactly 5000IU.ml. Further diluted with tris buffer working solution (50μl tPA to 5ml tris buffer) to obtain a tPA concentration of 50IU.ml.
- tPA/PAI depleted plasma (human): reconstituted with 1ml sterile water.
- S-2251: chromogenic substrate (H-D-Val-Leu-Lys-pNA 2HCl) 11mg, with mannitol added as bulking agent. Reconstituted with 4ml tris buffer working solution to a concentration of 5mmol.l.
- Plasminogen (human): 1.5mg. Reconstituted with 4ml tris buffer working solution.
- tPA stimulator (human): 3mg human fibrin(ogen) fragments. Reconstituted with 1ml sterile water. Then diluted 1:5 with tris buffer working solution to form a tPA stimulator working solution.

The method of blood sample collection and treatment is particularly important with reference to the measurement of tPA activity. It is vital that citrated blood samples are mixed 1:1 with acetate buffer working solution, immediately following withdrawal, and that the resultant mixture is centrifuged within 2 minutes. In addition, it is vital that after centrifugation the plasma is separated from the cells

and treated with 10μl HCl (1mol.l) for every 150μl of acetate treated plasma. It is also vital that all samples are rapidly frozen to –70^{o}C.

The test procedure initially involved the careful preparation and storage of all reagents and standards according to manufacturers instructions. Following this, eight serial dilutions of the tPA standard were made, corresponding to concentrations of 0.25, 0.5, 1, 2, 4, 6, 8, and 10 IU.ml^{-1}. Each of the standards (100μl) were pipetted into the test wells of the microplate in duplicate, with blank controls being placed in the wells alongside the highest and lowest standards. Citrated, platelet-poor test plasma was thawed rapidly at 37°C, before being diluted 1:35 with sterile water (100μl plasma to 3.5ml sterile water). One hundred microlitres of each diluted plasma sample was added to the remaining microplate wells in duplicate. Immediately following this, 100μl of the assay mixture (1 volume plasminogen, 1 volume S-2251 chromogenic substrate, and 3 volumes tris buffer working solution) was added to each of the microplate wells. Fifty microlitres of the tPA stimulator working solution was then added to each of the wells, with the exception of those wells containing the blank controls (to which was added 50μl of tris buffer working solution). The microplate was then mixed and incubated at 37°C for 150 minutes, according to manufacturers instructions. Upon cessation of the incubation period, 50μl of acetic acid (20%) was added to each of the wells to stop all reactions from taking place. A microplate reader was then used to record the absorbencies at a dual wavelength of 405nm minus 490nm. The dual wavelength recording was used to compensate for any inherent variations in the microplate wells, according to manufacturers instructions. Tissue plasminogen activator activity values were derived from the standard curve and

the mean of the two readings was used for subsequent statistical analyses. Whilst tPA activity in plasma is variable, normal resting values in healthy individuals are between 0.2-2IU.ml, with a coefficient of variation of 3.9%.

3.2.5.8.2. Plasminogen Activator Inhibitor Activity

Increased levels of PAI-1 activity appear to be indicative of impaired fibrinolytic function and thrombotic diseases. Increased PAI-1 levels are also common during pregnancy and during sepsis.

Plasminogen activator inhibitor-1 was measured using an immunoactivity assay (Chromolize PAI-1, Biopool International, California, USA) and a microplate technique. In this assay active tPA is lypholised, while immobilised on the surface of the microplate well. Plasma samples containing PAI-1 are added to the test well and the active PAI-1 reacts with the bound tPA. An HRP-conjugated monoclonal antibody is added simultaneously. Following incubation, any unbound sample and conjugate are washed away, before an HRP-sensitive substrate is added in order to quantify PAI-1 activity. The intensity of the colour produced during this final step is directly proportional to the concentration of active PAI-1 in the sample.

The specific Chromolize PAI-1 reagents used in this method and their constituents are listed below:

- Microtest Strips: 12 tPA coated, 8-well strips.

- PET Buffer: phosphate, NaCl, EDTA, and tween 20 buffer substance sufficient for 1l solution. Reconstituted with 1l purified water and magnetically stirred for 15 minutes.
- PAI-1 Standard Plasma 0IU.ml: lypholised plasma with 0IU.ml PAI-1. Reconstituted with 250µl of purified water and gently agitated for 5 minutes.
- PAI-1 Standard Plasma 60IU.ml: lypholised plasma with 60IU.ml PAI-1. Reconstituted with 250µl of purified water and gently agitated for 5 minutes.
- Conjugate: 5ml HRP-labelled monoclonal anti-PAI-1 antibody. Reconstituted with 6ml PET buffer and agitated gently for 5 minutes. Reconstituted conjugate was stored in the dark until required for use.
- HRP Substrate Solvent: 20ml, phosphate/citrate buffer with hydrogen
- HRP Substrate: Dissolved in HRP substrate solvent (4ml-substrate solvent to each HRP substrate tablet). Made 15 minutes before use and stored in the dark until required.

The test procedure initially involved the careful preparation and storage of all reagents and standards according to manufacturers instructions. Following this, four serial dilutions of the PAI-1 standards were made, corresponding to active PAI-1 concentrations of 0, 15, 30 and 50 $IU.ml^{-1}$. The microplate wells were then reconstituted with 25µl of PET buffer, and incubated at ambient temperature for 2 minutes at a speed of 700rpm. Twenty-five microlitres of citrated, platelet-poor test plasma and the standards were added to separate test wells in duplicate. All samples and standards were added to the microplate wells within 15 minutes, as per manufacturers instructions. A further 25µl of conjugate was then added to each of the microplate wells. This procedure was completed within 1 minute, as

per manufacturers instructions. Following conjugate addition, the microplate was incubated, at ambient temperature, for 30 minutes on an orbital microtest plate shaker set at a speed of 700rpm. Following incubation, each of the microplate wells was washed using PET buffer. One hundred microlitres of HRP substrate was added to each test well and the plate was incubated, as above, for exactly 5 minutes. Following this incubation period the reaction was stopped by adding 100µl of sulphuric acid (1.6M) to each test well. An automatic microplate reader was used to measure the absorbance of the samples at a single wavelength of 492nm. Plasminogen activator inhibitor-1 activity was derived from the standard curve and the mean of the two readings was used for subsequent statistical analyses. The mean±S.D. PAI-1 activity in healthy individuals is 5.2±6.2 for males and 7±5.9 for females. The reported within-run coefficient of variation for PAI-1 activity is between 2.6-3.7% depending upon the standard used.

3.2.5.8.3. D-dimer

D-dimer was measured using a rapid immunoassay (immunofiltration) technique (Nycocard, Nycomed Pharma AS, Oslo, Norway). The major principle of this method involves a laminated test card containing a thin, porous membrane carrying monoclonal antibodies which react with D-dimer configured molecules. The actual membrane is covered by a plastic coating with holes cut in to it to create 6 test wells on each membrane. The porous membrane rapidly absorbs plasma applied to the test well, thus allowing the monoclonal antibodies to capture the D-dimer configured molecules. Subsequently, a conjugate is added which binds to the other antigenic sites available on the captured D-dimer molecules, the gold colloids of the conjugate forming an intensive stain. The intensity of red

colour visible on the membrane is related to the concentration of D-dimer configured antigens in the plasma.

Several ready to use reagents (Nycomed Pharma AS, Oslo, Norway) are needed for the test:

1. Washing Solution: buffered solution, pH 8, with BSA and detergents.
2. Conjugate: buffered solution containing anti D-dimer antibodies labelled with ultra-small gold particles.
3. Positive Control: buffered solution of fibrin degradation products, BSA and stabilisers.

The test procedure involves 5 main steps:

1. 50µl of washing solution was added to the test well and allowed to absorb in to the Nycocard membrane.
2. 50µl of platelet-poor citrated plasma, or control, was added to the pre-washed test well. Again the sample was allowed to absorb in to the membrane. If the absorbance took longer than 45 seconds then the test was repeated as this is reported to produce false high results.
3. 50µl of conjugate was added to the test well, and allowed to absorb in to the membrane.
4. A further 50µl of the washing solution was added to the test well.
5. The intensity of the red colour subsequently produced was recorded using the Nycocard Colour Densiometer Reader (Nycomed Pharma AS, Oslo, Norway). Normal D-dimer levels at rest are expected to be ~0.3mg.l^{-1}.

Several important precautions were taken to avoid inaccurate recording of D-dimer concentrations:

1. All citrated blood samples were centrifuged at 2000xg for 20 min, at 4°C to ensure only platelet-poor plasma was used.
2. Plasma samples were assayed immediately following centrifugation without being stored, as freezing was found to produce false high results.
3. All solutions added to the test wells were allowed to completely absorb in to the Nycocard membrane before the next solution was added.
4. If any of the solutions did not absorb in to the Nycocard within 45 seconds the assay was repeated. A failure of any solution, particularly of the conjugate or plasma, to absorb within 45 seconds was found to give a false high reading.

3.2.5.9. Analytical Procedures for the Measurement of Blood Rheology

3.2.5.9.1. Plasma and Serum Viscosity

Both plasma and serum viscosity were measured using a Coulter Viscometer II Capillary Viscometer (Beckman Coulter, USA). The viscosity of either plasma or serum is determined by propelling the required fluid, at a constant pressure, through a capillary tube of known size. The time taken for a known volume (0.5ml) of fluid to pass through the capillary is directly proportional to the viscosity of that fluid.

The appropriate start-up and shut down procedures were employed to ensure the viscometer was clean at all times, as per manufacturer instructions. Prior to each series of tests, the viscometer was calibrated, using the appropriate calibration

fluid (Beckman Coulter, USA). The reported calibration value was checked against the instillation calibration value (2550±2%). The calibration process was repeated if the calibration value was not within the acceptable range. Following calibration, the accuracy of the instrument was checked using the calibrator solution and high and low control solutions of known viscosities. When using this method the viscometer produces highly repeatable and reliable results with the coefficient of variation being less than 2% for this method.

Following centrifugation and separation both plasma and serum samples were stored at room temperature until analyses. Only fresh plasma and serum was analysed for viscosity as freezing was shown to result in false high values. Initially, plasma and serum samples 800µl were added to the sample cups, and placed in the carousel ring along with the calibrator solution and the high and low control solutions (these were used to further ensure the accuracy of results). The viscometer then automatically withdrew 0.5ml of sample, propelled it through the capillary tube, before producing a printout of the result in mpa.s^{-1}.

3.2.5.9.2. Haemoglobin

ß-Haemoglobin was measured in duplicate, using a ß-Haemoglobin photometer (Clandon, Angleholm, Sweden). In order to insure accurate, repeatable values, the photometer was first calibrated using the recommended control microcuvette in accordance with manufacturer instructions. Ethylenediam inetetra-acetic acid anticoagulated blood was drawn in to a specific microcuvette, coated with specific reagents causing a modified azidemethaemoglobin reaction. The photometer

measured and displayed the haemoglobin concentration using an absorbance method. In this study, two separate microcuvettes were each analysed twice to insure repeatability, with the average of all four values being used for statistical analyses.

3.2.5.9.3. Haematocrit

Micro-haematocrit was measured in duplicate using a micro-haematocrit reader (Hawksley, West Sussex, UK). EDTA anticoagulated blood was drawn in to specialised capillary tubes (Hawksley BS4316, West Sussex, UK) which were then centrifuged. Percentage haematocrit was then measured using the reader, with the average of the two values being used for statistical analyses.

3.2.5.9.4. Estimation of Plasma Volume Change

In study 1 (part 2), both post-exercise and recovery changes in plasma volume were estimated from haemoglobin and haematocrit values using the method of Dill and Costill (1974). The percentage changes in post-exercise and recovery plasma volume were then used to correct the respective results.

3.2.5.9.5. Albumin

Albumin was measured *in vitro* using an end-point bichromatic method, using IL Test Albumin Reagent (Instrumentation Laboratories, Warrington, England). This method is based on the fact that the albumin contained within the test sample binds to bromcresol green (BCG) resulting in a spectral change in the colour of the dye from yellow to green. The intensity of the resultant colour is directly

proportional to the albumin concentration in the sample, when measured at a dual wavelength of 620-690nm.

The albumin reagent comes ready to use and contains the following ingredients:

- Bromcresol Green (550μmol.l)
- Succinic Acid (150mmol.l)
- Surfactant
- Preservative

Initially subject serum samples were thawed rapidly at 37°C before being separated in to 100μl aliquots, placed in the appropriate sample cups and added to the sample ring (Instrumentation Laboratories, Warrington, England). The boat containing the ready to use Albumin Reagent was then added to the appropriate carousel. Albumin concentration was then analysed automatically using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England). The appropriate calibration solution (Referrl 3/C Calibrator, Instrumentation Laboratories, Warrington, England) and quality control solution (SeraChem, Instrumentation Laboratories, Warrington, England) were analysed to ensure the accuracy of results, as per manufacturers instructions. Thus, albumin concentration of the assay mixture was determined using the following equation:

Albumin = absorbance of sample x (calibrator value / absorbance of the calibrator)

The normal range for albumin concentrations in healthy humans is reported to be 3.9-5.0g.dl^{-1}, with a coefficient of variation of 2% for this method.

3.2.5.9.6. Total Protein

Total protein was measured *in vitro* using an end-point bichromatic method, using IL Test Total Protein Reagent (Instrumentation Laboratories, Warrington, England). This assay uses a modified biuret methodology whereby polypeptides react with supric sulfate in the biuret reagent to produce a stable lavender coloured complex. The intensity of the colour formed is directly proportional to the total protein concentration of the sample, at a dual wavelength of 550-690nm.

The total protein reagent comes ready to use and contains the following ingredients:

- Sodium Hydroxide (2mol.l)
- Potassium Iodide (9 $mmol.l^{-1}$)
- Cupric Sulfate (9 $mmol.l^{-1}$)
- EDTA (20mmol.l)

Initially subject serum samples were thawed rapidly at 37°C before being separated in to 100µl aliquots, placed in the appropriate sample cups and added to the sample ring (Instrumentation Laboratories, Warrington, England). The boat containing the ready to use Total Protein Reagent was then added to the appropriate carousel. Total protein concentration was then analysed automatically using the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England). The appropriate calibration solution (Referrl B Calibrator, Instrumentation Laboratories, Warrington, England) and quality control solution (SeraChem, Instrumentation Laboratories, Warrington, England) were analysed to ensure the accuracy of results, as per manufacturers instructions. Thus, total

protein concentration of the assay mixture was determined using the following equation:

TP = absorbance of sample x (calibrator value / absorbance of the calibrator)

The normal range for total protein concentrations in healthy humans is reported to be 6.4-8.3g.dl^{-1}, with a coefficient of variation of 3% for this method.

3.2.5.10. Blood Lactate

Lactic acid is produced as a result of the metabolism of carbohydrate. Muscle cells are the major contributory to the blood lactate concentration although some may also come from the erythrocyte itself. Blood lactate is metabolised by the liver and thus a measurement of blood lactate concentration reflects both lactate production and metabolism.

The specific assay for lactate (Gloster and Harris, 1962) is determined through the spectrophotometric measurement of NADH generation, at 340nm, in response to the catalytic action of lactate dehydrogenase (LD). The principle reaction behind the test is as follows:

$$\text{Pyruvate + NADH} \xleftrightarrow{\text{LD}} \text{Lactate + NAD}$$

When measuring lactate in this way the above reaction should be viewed from right to left in the presence of an excess of nicatinomide adenine dinucleotide

(NAD). In order to force the reaction to move in this direction only, the formed pyruvate must be trapped with hydrazine. Thus, an increased NADH formation to the left of the reaction is characterised by an increased absorbance at 340nm and is thus a measure of the original lactate concentration.

Ready made lactate reagents were used for the test (Sigma Diagnostics, St. Louis, USA). The reagents used were as follows:

- Lactate Dehydrogenase: LD (bovine heart) suspension in ammonium sulphate. Approximately 100U.ml when prepared.
- Glycine Buffer: glycine 0.6mol.l and hydrazine, pH 9.2 at 25°C.
- Nicatinamide adenine dinucleotide: NAD grade III, 10mg pre-weighed vial.

Initially, whole blood samples were added to perchloric acid to deproteinise the blood cells and then centrifuged to produce the test supernate. Before commencing the test, the reagent solution was mixed according to manufacturers instructions. Lactate dehydrogenase (100μl), glycine buffer (2ml) and distilled water (4ml) were added to the NAD coated vial and mixed by gentle inversion. Test samples were thawed and added to the appropriate sample cups (Instrumentation Laboratories, Warrington, England). Lactate concentration, as well as the concentration of the appropriate standard controls was measured automatically on the Monarch Chemistry System (Instrumentation Laboratories, Warrington, England) at a wavelength on 340nm.

3.2.6. Statistical Analyses

All data are presented as mean±SD and statistical significance was accepted at the $p<0.05$ level for all tests, unless otherwise indicated. Bivariate correlational analysis was used to examine the inter-relationships among alcohol consumption, physical activity and the biological factors associated with cardiovascular health and disease. Partial correlation analysis was also used to control for the effects of gender.

Differences in biological data relating to alcohol consumption patterns, drinking frequency and AUDIT score were analysed using one-way analyses of variance. Where significant differences occurred, Tukey's Post-Hoc analyses were performed.

The effects of an acute bout of maximal exercise on blood lipids, haemostasis and rheology were analysed using repeated measures one-way ANOVA. Significant differences were further analysed using paired t-tests with Bonferroni correction. Data were corrected for sphericity using the Greenhouse and Geiser method, where appropriate. All ANOVA data were tested for normality and for homogeneity of variance. Where the assumptions for parametric analyses were violated, data were analysed using Friedman tests. Post-hoc analyses was performed using Wilcoxon signed ranks tests with Bonferroni correction.

3.3. RESULTS

3.3.1. Alcohol Consumption Data

Weekly alcohol consumption of subjects was 27.2±25.1 units.wk^{-1}. When considering gender influences on habitual weekly alcohol consumption, males reported consuming 31.5±27.9 units.wk^{-1} and females reported consuming 17.7±11.5 units.wk^{-1}. The amount of alcohol consumed by subjects over the previous weekend was 13.4±15.4 units.

Wanemethee and Shaper (1992) classified a British population of middle-aged drinkers in to the following categories, based on their reported habitual weekly alcohol consumption: light drinkers (1-15 units.wk^{-1}), moderate drinkers (16-42 units.wk^{-1}) and heavy drinkers (>42 units.wk^{-1}). Using this classification, 22 of the subjects from this investigation were light drinkers, 18 were moderate drinkers and 10 were heavy drinkers. Alcohol consumption was 7.7±4.5 units.wk^{-1}, 25.4±6.1 units.wk^{-1} and 67.4±9.2 units.wk^{-1} in light, moderate and heavy drinkers respectively.

Results also showed that 16 subjects drank alcohol 2-4 times per month, 26 subjects consumed alcohol 2-3 times per week and 8 subjects ingested alcohol more than 4 times per week.

The AUDIT score was 11.5±6.0, with the mean±S.D. being 12.7±5.9 for males subjects and 9.9±5.8 for female subjects. When using the two cut-off points suggested by Claussen and Aasland (1993) to indicate hazardous (9-19 points) and harmful (>19 points) alcohol consumption, 18 subjects reported normal alcohol consumption, 24 subjects were designated as hazardous alcohol consumers and 8 were considered harmful alcohol consumers.

3.3.2. Alcohol Consumption and Blood Lipids

3.3.2.1. Bivariate Correlations

Table 3.3.1. provides descriptive data along with the bivariate correlation coefficients among habitual weekly alcohol consumption, alcohol consumption on the previous weekend, AUDIT score and blood lipid variables. No significant bivariate associations were shown between habitual weekly alcohol consumption and total cholesterol, TG, NEFA, HDL, LDL, VLDL, apo A1 and apo B. In addition, there were no significant associations between the total cholesterol/HDL or total cholesterol/LDL ratios and habitual alcohol consumption. All results remained non-significant even when partialling out the effects of gender.

No significant associations were observed between the alcohol consumed over the previous weekend and any of the blood lipid variables or ratios measured. This also remained the case after controlling for the effects of gender.

There were no significant bivariate associations between AUDIT score and any of the blood lipid variables or ratios measured. However, when examining item 1 from the audit questionnaire relating to drinking frequency (Table 3.3.1.), the data showed significant positive associations with both HDL ($r=0.31$; $p<0.05$) and apo A1 ($r=0.29$; $p<0.05$) concentrations, although both associations failed to remain significant having partialled out the effects of gender. The association between drinking frequency and the total cholesterol/HDL ratio was approaching significance ($r=-0.27$; $p=0.06$). None of the other blood lipid variables measured were significantly associated with drinking frequency.

Table 3.3.1. Correlation coefficients among alcohol consumption, alcohol related problems and blood lipid levels.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Alcohol Consuption (units.wk-1)														
2. Weekend Alcohol Consumption (units)	0.26													
3. AUDIT	0.81c	0.39c												
4. Drinking Frequency	0.81c	0.39c	0.61c											
5. Total Cholesterol (mg.dl-1)	0.10	0.14	0.07	-0.01										
6. TG (mg.dl-1)	-0.15	-0.05	0.06	0.06	-0.00									
7. NEFA (micmol.l-1)	0.11	-0.09	-0.08	0.07	0.14	-0.09								
8. HDL (mg.dl-1)	0.08	0.10	-0.06	0.31a	0.27	-0.34a	0.18							
9. LDL (mg.dl-1)	0.10	0.13	0.08	-0.14	0.96c	-0.11	0.10	-0.02						
10. VLDL (mg.dl-1)	-0.15	-0.05	0.06	0.06	-0.00	1.00c	-0.09	-0.34a	-0.11					
11. apo A-1 (mg.dl-1)	-0.01	0.12	-0.12	0.29a	0.19	-0.33a	0.07	0.90c	-0.06	-0.33a				
12. Apo B (mg.dl-1)	0.13	-0.06	0.10	0.16	0.59c	0.35a	-0.02	-0.21	0.59c	0.35a	-0.29			
13. Total Cholesterol/HDL	0.02	0.20	0.14	-0.27	0.54c	0.29a	-0.04	-0.65c	0.74c	0.29a	-0.67c	0.63c		
14. Total Cholesterol/LDL	-0.13	-0.10	-0.13	0.14	-0.59c	0.34a	-0.07	0.20	-0.74c	0.34a	0.19	-0.45c	-0.60c	
Mean	27.18	13.44	11.49	2.66	176.76	92.06	444.71	51.50	106.70	18.41	135.49	51.54	3.59	1.76
S.D.	25.01	15.46	6.01	0.77	36.75	38.17	237.74	12.37	35.82	7.63	13.91	15.13	1.03	0.45

a = $p<0.05$; b = $p<0.01$; c = $p<0.005$

3.3.2.2. Blood Lipid Profiles of Light, Moderate and Heavy Alcohol Consumers

One-way ANOVA showed no significant differences in total cholesterol, TG, NEFA, HDL, LDL, VLDL, apo A1 or apo B concentrations between light, moderate and heavy alcohol consumers (Table 3.3.2.). No significant differences between the levels of alcohol consumption were also shown for both the total cholesterol/HDL and the total cholesterol/LDL ratios.

Table 3.3.2. Blood lipid levels of light, moderate and heavy alcohol consumers.

Variable	Light Drinkers (1-15 units.week)	Moderate Drinkers (16-42 units.week)	Heavy Drinkers (>42 units.week)
Total Cholesterol ($mg.dl^{-1}$)	172.62±39.58	182.39±36.37	175.76±33.01
TG ($mg.dl^{-1}$)	96.26±38.58	92.65±38.98	81.80±37.89
NEFA ($\mu mol.l^{-1}$)	458.90±249.30	389.39±186.25	513.08±292.20
HDL ($mg.dl^{-1}$)	50.72±11.27	50.99±13.65	54.14±13.24
LDL ($mg.dl^{-1}$)	102.64±38.95	112.79±34.32	105.27±33.12
VLDL ($mg.dl^{-1}$)	19.26±7.72	18.53±7.80	16.36±7.58
Apo A1 ($mg.dl^{-1}$)	135.80±14.43	134.74±13.51	136.18±14.85
Apo B ($mg.dl^{-1}$)	50.68±13.84	52.31±14.66	51.95±20.61
Total cholesterol/HDL	3.51±0.96	3.77±1.13	3.43±1.04
Total Cholesterol/LDL	1.84±0.61	1.66±0.26	1.74±0.28

Values are mean±SD.

3.3.2.3. Drinking Frequency and Blood Lipids

One-way ANOVA showed significant differences across drinking frequencies for apo B ($F_{2,45}$=6.69; p<0.005). Post-hoc analysis revealed that those subjects drinking more than 4 times per week exhibited a significantly higher apo B concentration than those subjects drinking both 2-4 times per month (p<0.05) and those drinking 2-3 times per week (p<0.005). No significant differences in apo B concentration were shown between subjects who drank 2-4 times per month and those who drank 2-3 times per week. There were no other significant differences across drinking frequencies for any of the other blood lipid variables measured (Table 3.3.3.).

Table 3.3.3. Blood lipid levels of subjects reporting different drinking frequencies.

Variable	2-4 times per month	2-3 times per week	More than 4 times per week
Total Cholesterol ($mg.dl^{-1}$)	175.69±39.03	171.67±36.13	190.55±31.16
TG ($mg.dl^{-1}$)	98.87±46.24	86.49±33.21	100.06±40.49
NEFA ($\mu mol.l^{-1}$)	420.32±185.57	444.71±269.00	502.32±261.72
HDL ($mg.dl^{-1}$)	46.77±10.14	54.52±11.44	52.92±17.88
LDL ($mg.dl^{-1}$)	109.14±36.83	99.86±33.99	118.43±33.27
VLDL ($mg.dl^{-1}$)	19.77±9.25	17.30±6.64	20.01±8.10
Apo A1 ($mg.dl^{-1}$)	130.93±13.96	139.32±12.77	134.69±14.82
Apo B ($mg.dl^{-1}$)	51.50±15.27**a**	47.05±12.91**c**	69.61±10.21
Total cholesterol/HDL	3.89±1.09	3.25±0.86	3.82±0.99
Total Cholesterol/LDL	1.69±0.29	1.85±0.55	1.62±0.24

Values are mean±SD. **a** indicates significantly different from more than 4 times per week at the $p<0.05$ level and **c** indicates significantly different from more than 4 times per week at the $p<0.005$ level.

3.3.2.4. Blood Lipid Profiles of Subjects with Normal, Hazardous and Harmful Alcohol Consumption Patterns

One-way ANOVA showed no significant differences between normal, hazardous and harmful alcohol consumption patterns for total cholesterol, TG, NEFA, HDL, LDL, VLDL, apo A1 and apo B (Table 3.3.4.). In addition, no significant differences were also shown for both the total cholesterol/HDL ratio and the total cholesterol/LDL ratio.

Table 3.3.4. Blood lipid levels of subjects with normal, hazardous and harmful alcohol consumption patterns.

Variable	Normal (<9 points)	Hazardous (9-19 points)	Harmful (>19 points)
Total Cholesterol ($mg.dl^{-1}$)	175.44±39.93	175.41±32.50	190.84±43.84
TG ($mg.dl^{-1}$)	93.30±37.42	89.08±39.92	86.19±22.30
NEFA ($\mu mol.l^{-1}$)	449.05±221.26	431.69±271.01	489.69±192.76
HDL ($mg.dl^{-1}$)	50.44±11.77	53.52±12.88	48.37±13.44
LDL ($mg.dl^{-1}$)	106.34±39.35	103.60±29.64	125.24±42.06
VLDL ($mg.dl^{-1}$)	18.66±7.48	17.82±7.99	17.24±4.46
Apo A1 ($mg.dl^{-1}$)	134.68±15.35	138.06±12.08	129.10±16.59
Apo B ($mg.dl^{-1}$)	52.95±14.35	50.34±15.28	53.43±19.66
Total cholesterol/HDL	3.61±1.03	3.42±0.93	4.19±1.33
Total Cholesterol/LDL	1.81±0.65	1.74±0.26	1.59±0.26

Values are mean±SD.

3.3.3. Alcohol Consumption and Blood Haemostasis

3.3.3.1. Bivariate Correlations

Table 3.3.5. provides bivariate correlation coefficients among habitual weekly alcohol consumption, alcohol consumption on the previous weekend, AUDIT score and blood haemostatic variables. Also provided are descriptive data presented as mean±S.D.

No significant bivariate associations were shown between habitual weekly alcohol consumption and any of the blood coagulation variables measured, including fibrinogen, TT, PT, or APTT. In addition, there were no significant associations between the habitual alcohol consumption and any of the blood fibrinolytic variables measured, including tPA activity, PAI-1 activity and D-dimer.

There were no significant associations between the alcohol consumed over the previous weekend and blood coagulation (Table 3.3.5.). However, a significant positive association was observed between the level of alcohol consumed over the previous weekend and PAI-1 activity concentration ($r=0.35$; $p<0.05$). However, no other significant associations were observed between the level of alcohol consumed over the previous weekend and any of the other blood fibrinolytic indices measured, with all results remaining the same even after partialling out the effects of gender.

There was a negative association between AUDIT score and TT ($r=-0.35$; $p<0.05$); an association which remained even when partialling out the effects of gender. However, there were no other significant associations between AUDIT score and any of the other blood coagulation variables measured (Table 3.3.5.). The association between AUDIT score and tPA concentration was approaching significance ($r=0.27$; $p=0.06$), although none of the other blood fibrinolytic measures were significantly associated with AUDIT score.

There were no significant associations between drinking frequency and any of the blood coagulation or blood fibrinolytic variables measured. Furthermore, none of these results were affected by partialling out the effects of gender.

Table 3.3.5. Correlation coefficients among alcohol consumption, alcohol related problems and blood haemostatic variables.

	1	2	3	4	5	6	7	8	9	10	11
1. Alcohol Consuption (units.wk-1)											
2. Weekend Alcohol Consumption (units)	0.26										
3. AUDIT	0.81c	0.39c									
4. Drinking Frequency	0.81c	0.39c	0.61c								
5. Fibrinogen (mg.dl-1)	-0.01	-0.09	0.12	-0.05							
6. TT (s)	-0.17	-0.00	-0.35a	-0.19	-0.39c						
7. PT (s)	-0.17	-0.23	-0.19	-0.24	-0.56c	0.34a					
8. APTT (s)	0.03	-0.10	0.03	-0.22	0.03	0.28a	0.25				
9. tPA (IU.ml-1)	0.00	0.05	0.27	0.01	0.55c	-0.43c	-0.33a	0.22			
10. PAI-1 (AU.ml-1)	-0.02	0.35a	0.12	-0.09	0.06	0.03	-0.10	0.02	0.11		
11. D-dimer (mg.l-1)	-0.01	0.03	-0.09	-0.14	-0.13	-0.13	0.22	-0.12	-0.17	0.04	
Mean	27.18	13.44	11.49	2.66	284.68	10.46	16.17	30.04	1.85	7.36	0.25
S.D.	25.01	15.46	6.01	0.77	52.65	0.85	1.19	3.68	1.37	5.21	0.37

a = p<0.05; b = p<0.01; c = p<0.005

3.3.3.2. Blood Haemostatic Profiles of Light, Moderate and Heavy Alcohol Consumers

One-way ANOVA showed a significant difference in PT between light, moderate and heavy alcohol consumers ($F_{2,49}$=3.25; $p<0.05$). Post-hoc analysis showed a significantly shortened PT in moderate drinkers when compared with light drinkers ($p<0.05$). No significant differences between light, moderate and heavy alcohol consumers were shown for fibrinogen concentration, TT or APTT.

In terms of the fibrinolytic variables measured, one-way ANOVA showed a significant difference in the tPA activity concentrations of light, moderate and heavy alcohol consumers ($F_{2,49}$=3.72; $p<0.05$). Post-hoc analysis revealed a significantly greater tPA concentration in moderate drinkers when compared to light drinkers ($p<0.05$). There was also a trend towards a higher tPA concentration in moderate drinkers when compared to heavy drinkers ($p=0.09$). However, there were no significant differences between the levels of habitual weekly alcohol consumption for PAI-1 activity and D-dimer concentrations.

Table 3.3.6. Blood haemostatic variables in light, moderate and heavy alcohol consumers.

Variable	Light Drinkers (1-15 units.week)	Moderate Drinkers (16-42 units.week)	Heavy Drinkers (>42 units.week)
Fibrinogen ($mg.dl^{-1}$)	275.42±42.99	306.31±59.15	266.10±51.41
PT (secs)	16.55±0.89	15.63±1.09**a**	16.29±1.64
TT (secs)	10.75±0.92	10.17±0.83	10.37±0.52
APTT (secs)	29.59±3.43	30.56±4.24	30.10±3.39
tPA ($IU.ml^{-1}$)	1.50±1.09	2.51±1.72**a**	1.41±0.68
PAI-1 ($au.ml^{-1}$)	6.46±3.74	8.91±7.28	6.65±2.97
D-dimer ($mg.l^{-1}$)	0.30±0.42	0.24±0.36	0.18±0.23

Values are mean±SD. **a** = statistically significant difference from light drinkers at the $p<0.05$ level.

3.3.3.3. Drinking Frequency and Blood Haemostatisis

There were no significant differences across drinking frequencies for any of the blood coagulation variables measured (Table 3.3.7.). In addition there were no significant differences between different drinking frequencies and any of the blood fibrinolytic variables measured.

Table 3.3.7. Blood haemostatic variables across drinking frequencies.

Variable	2-4 times per month	2-3 times per week	More than 4 times per week
Fibrinogen ($mg.dl^{-1}$)	297.58±58.44	281.41±50.11	277.71±46.94
PT (secs)	16.28±0.89	16.25±1.23	15.37±1.45
TT (secs)	10.54±1.05	10.47±0.69	10.12±0.91
APTT (secs)	31.02±3.65	30.03±3.82	27.56±2.45
t-PA ($IU.ml^{-1}$)	1.88±1.57	2.07±1.38	1.12±0.40
PAI-1 ($au.ml^{-1}$)	8.28±3.65	7.40±6.55	5.39±2.73
D-dimer ($mg.l^{-1}$)	0.22±0.42	0.27±0.35	0.15±0.12

Values are mean±SD.

3.3.3.4. Blood Haemostatic Profiles of Subjects with Normal, Hazardous and Harmful Alcohol Consumption Patterns

One-way ANOVA showed a significant difference between normal, hazardous and harmful alcohol consumption patterns for TT ($F_{2,48}$=3.65; $p<0.05$). However, post-hoc analysis only revealed a trend towards an increased TT in those reporting normal alcohol consumption patterns when compared to those reporting both hazardous (p=0.07) and harmful (p=0.07) alcohol consumption patterns. No significant differences were observed between normal, hazardous and harmful alcohol consumption patterns for fibrinogen, PT or APTT.

No significant differences were observed between normal, hazardous and harmful alcohol consumption patterns for any of the fibrinolytic indices measured; including tPA activity, PAI-1 activity and D-dimer.

Table 3.3.8. Blood haemostatic variables in subjects with normal, hazardous and harmful alcohol consumption patterns.

Variable	Normal (<9 points)	Hazardous (9-19 points)	Harmful (>19 points)
Fibrinogen ($mg.dl^{-1}$)	275.41±40.46	286.23±54.21	297.17±77.44
PT (secs)	16.42±0.86	16.08±1.20	15.81±1.90
TT (secs)	10.88±0.83	10.33±0.71	10.09±0.90
APTT (secs)	29.85±3.19	30.40±3.85	30.24±4.12
t-PA ($IU.ml^{-1}$)	1.45±0.93	1.93±1.38	2.71±2.00
PAI-1 ($au.ml^{-1}$)	6.36±3.93	8.92±6.37	5.21±2.99
D-dimer ($mg.l^{-1}$)	0.22±0.28	0.29±0.45	0.22±0.29

Values are mean±SD.

3.3.4. Alcohol Consumption and Blood Rheology

3.3.4.1. Bivariate Correlations

Table 3.3.9. provides descriptive data and bivariate correlation coefficients among habitual weekly alcohol consumption, alcohol consumption on the previous weekend, AUDIT score and the blood rheological variables measured. No significant bivariate associations were shown between habitual weekly

alcohol consumption patterns and any of the blood rheological variables measured, including plasma viscosity, serum viscosity, haemoglobin, haematocrit, fibrinogen, albumin, or total protein.

No significant associations were also observed between the alcohol consumed over the previous weekend and any of the blood rheological variables measured. There were also no significant bivariate associations between AUDIT score, or drinking frequency, and plasma viscosity, serum viscosity, haemoglobin, haematocrit, fibrinogen, albumin, or total protein.

Table 3.3.9. Correlation coefficients among alcohol consumption, alcohol related problems and blood rheological variables

	1	2	3	4	5	6	7	8	9	10	11
1. Alcohol Consuption (units.wk-1)											
2. Weekend Alcohol Consumption (units)	0.26										
3. AUDIT	0.81c	0.39c									
4. Drinking Frequency	0.81c	0.39c	0.61c								
5. Plasma Viscosity (mpa.s-1)	0.06	-0.20	-0.03	0.05							
6. Serum Viscosity (mpa.s-1)	0.02	-0.17	-0.10	0.15	0.90c						
7. Haemoglobin (mg.dl-1)	0.19	0.07	0.13	0.04	-0.10	-0.09					
8. Haematocrit (%)	0.15	0.19	0.19	0.07	-0.13	-0.07	0.75c				
9. Fibrinogen (mg.dl-1)	-0.01	-0.09	0.12	-0.05	0.45c	0.22	-0.32a	-0.34a			
10. Albumin (g.dl-1)	-0.07	0.05	-0.10	-0.07	0.21	0.27	0.45c	0.41b	-0.03		
11. Total Protein (g.dl-1)	-0.08	0.01	-0.05	0.09	0.41b	0.48c	0.28	0.42b	0.16	0.67c	
Mean	27.18	13.44	11.49	2.66	1.57	1.46	141.00	43.28	284.68	5.18	6.38
S.D.	25.01	15.46	6.01	0.77	0.06	0.05	15.28	3.36	52.65	0.46	0.66

a = $p<0.05$; b = $p<0.01$; c = $p<0.005$

3.3.4.2. Blood Rheological Profiles of Light, Moderate and Heavy Alcohol Consumers

One-way ANOVA showed no significant differences between the level of habitual weekly alcohol consumption and any of the blood rheological variables measured, including plasma viscosity, serum viscosity, haemoglobin, haematocrit, fibrinogen, albumin and total protein.

Table 3.3.10. Blood rheological variables in light, moderate and heavy alcohol consumers.

Variable	Light Drinkers (1-15 units.week)	Moderate Drinkers (16-42 units.week)	Heavy Drinkers (>42 units.week)
Plasma Viscosity ($mpa.s^{-1}$)	1.57±0.07	1.57±0.05	1.57±0.07
Serum Viscosity ($mpa.s^{-1}$)	1.46±0.06	1.45±0.04	1.46±0.06
Haemoglobin ($mg.dl^{-1}$)	138.76±16.83	140.85±13.88	146.75±14.04
Haematocrit (%)	42.39±3.71	43.94±3.05	44.14±2.77
Albumin ($g.dl^{-1}$)	5.21±0.41	5.20±0.57	5.01±0.29
Total Protein ($g.dl^{-1}$)	6.38±0.69	6.49±0.65	6.01±0.52

Values are mean±SD.

3.3.4.3. Drinking Frequency and Blood Rheology

There were significant differences across drinking frequencies for both albumin ($F_{2,47}$=5.94; $p<0.01$) and total protein ($F_{2,47}$=3.18; $p<0.05$) concentrations. Post-hoc analyses revealed that those who drank alcohol more than 4 times per week exhibited greater albumin ($p<0.005$) and total protein ($p<0.05$) concentrations

than those who drank alcohol less frequently (2-3 times per week). In addition, the differences across drinking frequencies was approaching significance for haemoglobin ($F_{2,47}$=2.73; p=0.07). No other significant differences were shown for any of the other blood rheological variables measured.

Table 3.3.11. Blood rheological variables across drinking frequencies.

Variable	2-4 times per month	2-3 times per week	More than 4 times per week
Plasma Viscosity ($mpa.s^{-1}$)	1.58±0.06	1.56±0.07	1.60±0.07
Serum Viscosity ($mpa.s^{-1}$)	1.46±0.04	1.45±0.06	1.49±0.07
Haemoglobin ($mg.dl^{-1}$)	140.17±17.34	138.25±14.37	153.92±7.43
Haematocrit (%)	43.02±3.52	42.94±3.52	45.13±1.89
Albumin ($g.dl^{-1}$)	5.22±0.39	5.00±0.32**c**	5.70±0.70
Total Protein ($g.dl^{-1}$)	6.38±0.55	6.20±0.62**a**	6.99±0.81

Values are mean±SD. Significant differences from more than 4 times per week are indicated by **a**=p<0.05 and **c**=p<0.005.

3.3.4.4. Blood Rheological Profiles of Subjects with Normal, Hazardous and Harmful Alcohol Consumption Patterns

No significant differences were found between normal, hazardous and harmful alcohol consumption patterns for any of the blood rheological variables measured (Table 3.3.12.).

Table 3.3.12. Blood rheological variables in subjects with normal, hazardous and harmful alcohol consumption patterns.

Variable	Normal (<9 points)	Hazardous (9-19 points)	Harmful (>19 points)
Plasma Viscosity ($mpa.s^{-1}$)	1.58±0.07	1.56±0.06	1.57±0.07
Serum Viscosity ($mpa.s^{-1}$)	1.47±0.06	1.46±0.05	1.44±0.04
Haemoglobin ($mg.dl^{-1}$)	140.24±18.00	142.33±14.38	140.67±11.12
Haematocrit (%)	42.97±3.94	43.75±3.12	42.96±2.54
Albumin ($g.dl^{-1}$)	5.26±0.42	5.19±0.53	4.97±0.30
Total Protein ($g.dl^{-1}$)	6.42±0.69	6.45±0.70	6.14±0.36

Values are mean±SD.

3.3.5. Physical Activity and Self-Reported Fitness Data

Subjects reported spending 12.5±11.2h.wk^{-1} on physical activity which corresponded to a weekly energy expenditure of 3308.4±2480.6 kcal.wk^{-1}. In terms of the frequency of vigorous physical activity, 22% of the sample reported vigorously exercising less than once per week, 48% of the sample vigorously exercised 1-3 days per week and 30% of the sample reported vigorously exercising 4-6 days per week. Twenty-two percent of the sample also reported performing less-vigorous activity less than once per week, 44% 1-3 days per week, 18% 4-6 days per week and 16% reported the performance of less-vigorous physical activity everyday.

In terms of the self-reported physical activity levels of the subjects, 18% reported that their physical activity levels were excellent, 42% good, 24% fair and 16% poor. In terms of self-reported fitness, 16% reported excellent physical fitness, 40% good, 30% fair and 14% poor.

3.3.6. Physical Activity, Self-Reported Fitness and Blood Lipids

Table 3.3.13. provides descriptive data and bivariate correlation coefficients among physical activity, self-reported fitness and blood lipid levels. There were no significant bivariate correlations between weekly energy expenditure or total time spent on physical activity and any of the blood lipid variables measured. However, both self-reported physical activity and self-reported fitness were significantly associated with LDL (activity: $r=0.31$, $p<0.05$; fitness: $r=0.29$, $p<0.05$) and apo B (activity: $r=0.40$, $p<0.005$; fitness: $r=0.41$, $p<0.005$) levels, as well as the total cholesterol/HDL ratio (activity: $r=0.39$, $p<0.005$; fitness: $r=0.39$, $p<0.005$). Because of the scoring system for self-reported physical activity and fitness, this shows that subjects reporting a higher physical activity and fitness level had significantly lower LDL, apo B and total cholesterol/HDL ratio. All of these relationships remained significant even when partialling out the effects of gender. There were no other significant associations between either self-reported physical activity or fitness and any of the other blood lipid variables measured.

The frequency of vigorous physical activity was negatively associated with the total cholesterol/HDL ratio ($r=-0.29$, $p<0.05$), indicating a lower total cholesterol/HDL ratio in those reporting the more frequent performance of vigorous physical activity. However, this relationship failed to remain significant when controlling for the effects of gender. In addition, the correlation between vigorous physical activity and HDL level was approaching significance ($r=0.27$, $p=0.06$), indicating a trend towards higher HDL levels in those participating in more vigorous physical activity. No other significant correlations were shown between vigorous physical activity and other blood lipid variables.

A negative correlation was shown between the frequency of less vigorous physical activity and apo B concentrations ($r=-0.30$, $p<0.05$), even when controlling for the effects of gender. However, no other significant correlations were shown between less vigorous physical activity levels and any of the other blood lipid variables measured.

3.3.7. Physical Activity, Self-Reported Fitness and Blood Haemostasis

Table 3.3.14. provides descriptive data and bivariate correlation coefficients among physical activity, self-reported fitness and blood haemostatic variables. There were no significant correlations between either self-reported physical activity or fitness and blood coagulation or fibrinolytic variables.

Table 3.3.13. Correlation coefficients among physical activity, self-reported fitness and blood lipids

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. LTPA Energy Expenditure (kcal.wk-1)																
2. Total Time Spent on LTPA (h.wk-1)	0.73c															
3. Self-Reported Activity	-0.42c	-0.39c														
4. Self-Reported Fitness	-0.44c	-0.36b	0.93c													
5. Frequency of Vigorous LTPA	0.58	0.56c	-0.66c	-0.69c												
6. Frequency of Less Vigorous LTPA	0.25	0.38b	-0.50c	-0.49c	0.28a											
7. Total Cholesterol (mg.dl-1)	-0.08	0.10	0.24	0.22	-0.07	-0.01										
8. TG (mg.dl-1)	0.01	0.03	0.09	0.15	-0.08	-0.05	-0.00									
9. NEFA (micmol.l-1)	-0.05	0.25	0.19	0.18	0.04	0.17	0.14	-0.09								
10. HDL (mg.dl-1)	0.01	0.21	-0.24	-0.26	0.27	0.04	0.27	-0.34a	0.18							
11. LDL (mg.dl-1)	-0.09	0.02	0.31a	0.29a	-0.15	-0.01	0.96c	-0.11	0.10	-0.02						
12. VLDL (mg.dl-1)	0.01	0.03	0.09	0.15	-0.08	-0.05	-0.00	1.00c	-0.09	-0.34a	-0.11					
13. Apo A-1 (mg.dl-1)	-0.09	0.07	-0.22	-0.22	0.22	-0.01	0.19	-0.33a	0.07	0.90c	-0.06	-0.33a				
14. Apo B (mg.dl-1)	0.09	0.09	0.40c	0.41c	-0.15	-0.30a	0.59c	0.35a	-0.02	-0.21	0.59c	0.35a	-0.29			
15. Total Cholesterol/HDL	-0.05	-0.08	0.39c	0.39c	-0.29a	-0.01	0.54c	0.29a	-0.04	-0.65c	0.74c	0.29a	-0.67c	0.63c		
16. Total Cholesterol/LDL	-0.06	0.02	-0.22	-0.11	0.09	0.11	-0.59c	0.34a	-0.07	0.20	-0.74c	0.34a	0.19	-0.45c	-0.60c	
Mean	3308.38	21.37	2.38	2.42	3.08	3.28	176.76	92.06	444.71	51.50	106.70	18.41	135.49	51.54	3.59	1.76
S.D.	2480.64	11.17	0.97	0.93	0.73	0.99	36.75	38.17	237.74	12.37	35.82	7.63	13.91	15.13	1.03	0.45

a = $p<0.05$; b = $p<0.01$; c = $p<0.005$

Table 3.3.14. Correlation coefficients among physical activity, self-reported fitness and blood haemostatic variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. LTPA Energy Expenditure (kcal.wk-1)													
2. Total Time Spent on LTPA (h.wk-1)	0.73c												
3. Self-Reported Activity	-0.42c	-0.39c											
4. Self-Reported Fitness	-0.44c	-0.36b	0.93c										
5. Frequency of Vigorous LTPA	0.58	0.56c	-0.66c	-0.69c									
6. Frequency of Less Vigorous LTPA	0.25	0.38b	-0.50c	-0.49c	0.28a								
7. Fibrinogen (mg.dl-1)	-0.06	0.14	0.12	0.06	0.04	0.09							
8. TT (s)	0.19	0.06	-0.24	-0.23	0.19	0.16	-0.39c						
9. PT (s)	0.22	0.02	-0.19	-0.21	0.19	-0.04	-0.56c	0.34a					
10. APTT (s)	0.02	0.12	-0.10	-0.18	0.00	0.14	0.03	0.28a	0.25				
11. tPA (IU.ml-1)	-0.08	0.01	0.03	0.06	-0.25	-0.12	0.55c	-0.43c	-0.33a	0.22			
12. PAI-1 (AU.ml-1)	-0.11	-0.12	-0.13	-0.10	-0.01	0.01	0.06	0.03	-0.10	0.02	0.11		
13. D-dimer (mg.l-1)	0.06	0.04	0.18	0.09	0.01	-0.10	-0.13	-0.13	0.22	-0.12	-0.17	0.04	
Mean	3308.38	12.45	2.38	2.42	3.08	3.28	284.68	10.46	16.17	30.04	1.85	7.36	0.25
S.D.	2480.64	11.17	0.97	0.93	0.73	0.99	52.65	0.85	1.19	3.68	1.37	5.21	0.37

a = $p<0.05$; b = $p<0.01$; c = $p<0.005$

3.3.8. Physical Activity, Self-Reported Fitness and Blood Rheology

Table 3.3.15. provides descriptive data and bivariate correlation coefficients among physical activity, self-reported fitness and blood rheological variables. There were negative correlations between weekly energy expenditure and both plasma viscosity ($r=-0.31$, $p<0.05$) and serum viscosity ($r=-0.35$, $p<0.05$). This indicates that those with higher weekly energy expenditures had lower plasma and serum viscosity. Whilst the association with serum viscosity remained significant when controlling for gender, the association with plasma viscosity did not. None of the other blood rheological indices were significantly related to the weekly energy expended on physical activity.

There were also significant correlations between both self-reported physical activity and fitness and both plasma (activity: $r=0.42$, $p<0.005$; fitness: $r=0.41$, $p<0.005$) and serum (activity: $r=0.34$, $p<0.005$; fitness: $r=0.34$, $p<0.005$) viscosity. Those individuals self-reporting high physical activity and fitness levels had lower plasma and serum viscosity. There were no significant associations between either self-reported physical activity or self-reported fitness and any of the other blood rheological variables measured.

Furthermore, there were no significant correlations between either the frequency of vigorous physical activity, or less vigorous physical activity, and any of the blood rheological variables measured. In addition, no significant associations

were shown between the total hours spent on physical activity per week and any of the blood rheological variables measured.

Table 3.3.15. Correlation coefficients among physical activity, self-reported fitness and blood rheological variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. LTPA Energy Expenditure (kcal.wk-1)													
2. Total Time Spent on LTPA (h.wk-1)	0.73c												
3. Self-Reported Activity	-0.42c	-0.39c											
4. Self-Reported Fitness	-0.44c	-0.36b	0.93c										
5. Frequency of Vigorous LTPA	0.58	0.56c	-0.66c	-0.69c									
6. Frequency of Less Vigorous LTPA	0.25	0.38b	-0.50c	-0.49c	0.28a								
7. Plasma Viscosity (mpa.s-1)	-0.31a	-0.16	0.42c	0.41c	-0.12	-0.23							
8. Serum Viscosity (mpa.s-1)	-0.35a	0.21	0.34a	0.34a	-0.08	-0.25	0.90c						
9. Haemoglobin (mg.dl-1)	0.09	0.09	0.27	0.25	-0.13	-0.16	-0.10	-0.09					
10. Haematocrit (%)	0.06	-0.03	0.16	0.10	-0.02	-0.26	-0.13	-0.07	0.75c				
11. Fibrinogen (mg.dl-1)	-0.06	0.01	0.12	0.06	0.04	0.09	0.45c	0.22	-0.32a	-0.34a			
12. Albumin (g.dl-1)	0.30	0.31	0.04	0.03	0.27	0.04	0.21	0.27	0.45c	0.41b	-0.03		
13. Total Protein (g.dl-1)	0.19	0.19	0.03	-0.05	0.14	-0.04	0.41b	0.48c	0.28	0.42b	0.16	0.67c	
Mean	3308.38	12.45	2.38	2.42	3.08	3.28	1.57	1.46	141.00	43.28	284.68	5.18	6.38
S.D.	2480.64	11.17	0.97	0.93	0.73	0.99	0.06	0.05	15.28	3.36	52.65	0.46	0.66

a = $p<0.05$; b = $p<0.01$; c = $p<0.005$

3.3.9. Cardiorespiratory Fitness Data

Twenty-three male subjects (a cohort from study 1, part 1) also performed a VO_{2max} test in addition to measures taken in study 1 (part 1). Mean±SD absolute VO_{2max} was 3.7±0.5 $l.min^{-1}$ and relative was 47.61±8.97$mls.kg^{-1}.min^{-1}$.

3.3.10. Cardiorespiratory Fitness and Blood Lipids

Table 3.3.16. provides descriptive data and the bivariate correlation coefficients between cardiorespiratory fitness and blood lipid profiles. There were no significant bivariate associations between either absolute or relative VO_{2max} and any of the blood lipid variables measured.

3.3.11. Cardiorespiratory Fitness and Blood Haemostasis

Table 3.3.17. provides descriptive data and bivariate correlation coefficients between cardiorespiratory fitness and blood haemostatic variables. Results showed a significant positive bivariate association between cardiorespiratory fitness (absolute VO_{2max}: $r=0.41$, $p<0.05$; relative VO_{2max}: $r=0.44$, $p<0.05$) and TT. No other significant associations were shown for any of the other blood coagulation variables.

Whilst there was evidence of a significant negative association between relative VO_{2max} and PAI-1 activity ($r=-0.52$, $p<0.01$), there was no significant association

between absolute measures of VO_{2max} and PAI-1 (r=-0.31). No other significant associations were observed between cardiorespiratory fitness and any of the other blood fibrinolytic variables measured.

3.3.12. Cardiorespiratory Fitness and Blood Rheology

Table 3.3.18. provides descriptive data and bivariate correlation coefficients among cardiorespiratory fitness and blood rheological variables. No significant bivariate associations were observed between either absolute or relative VO_{2max} and any of the blood rheological variables measured.

Table 3.3.16. Correlation coefficients between cardiorespiratory fitness and blood lipids

	1	2	3	4	5	6	7	8	9	10	11	12
1. VO2max (l.min-1)												
2. VO2max (mls.kg-1.min-1)	0.69c											
3. Total Cholesterol (mg.dl-1)	-0.17	-0.41										
4. TG (mg.dl-1)	0.11	-0.13	0.31									
5. NEFA (micmol.l-1)	0.43	0.43	-0.09	-0.14								
6. HDL (mg.dl-1)	-0.28	-0.03	0.28	-0.24	-0.10							
7. LDL (mg.dl-1)	-0.09	-0.40	0.91c	0.15	-0.02	-0.06						
8. VLDL (mg.dl-1)	0.11	-0.13	0.31	1.00	-0.14	-0.24	0.15					
9. Apo A-1 (mg.dl-1)	-0.12	-0.28	0.03	-0.10	0.24	0.47a	-0.14	-0.10				
10. Apo B (mg.dl-1)	-0.06	0.18	0.72c	0.24	-0.32	0.12	0.68c	0.24	-0.41			
11. Total Cholesterol/HDL	0.18	-0.29	0.49	0.54b	0.02	-0.68c	0.70c	0.54b	-0.42a	0.45a		
12. Total Cholesterol/LDL	-0.10	0.32	-0.52	-0.04	-0.08	0.51a	-0.82c	0.04	0.39	-0.45a	-0.79c	
Mean	3.72	47.61	176.51	92.37	320.87	51.89	106.03	18.48	136.12	52.18	3.52	1.70
S.D.	0.48	8.97	29.73	40.41	160.50	11.58	26.40	8.08	12.92	17.16	0.84	0.20

a = $p<0.05$; b = $p<0.01$; c = $p<0.005$

Table 3.3.17. Correlation coefficients between cardiorespiratory fitness and blood haemostatic variables.

	1	2	3	4	5	6	7	8	9
1. VO2max (l.min-1)									
2. VO2max (mls.kg-1.min-1)	0.69c								
3. Fibrinogen (mg.dl-1)	-0.03	-0.18							
4. TT (secs)	0.41a	0.44a	-0.20						
5. PT (secs)	0.17	0.18	-0.44a	0.15					
6. APTT (secs)	0.08	0.27	-0.02	0.28	0.42a				
7. tPA (IU.ml-1)	-0.17	-0.22	0.57c	-0.47a	-0.17	0.30			
8. PAI-1 (AU.ml-1)	-0.31	-0.52b	0.36	-0.39	-0.30	-0.09	0.47a		
9. D-dimer (mg.l-1)	-0.21	-0.13	-0.01	-0.40	0.25	-0.15	-0.24	-0.04	
Mean	3.72	47.61	273.28	10.68	16.45	30.21	1.67	9.75	0.34
S.D.	0.48	8.97	50.50	0.78	0.95	3.74	1.40	6.06	0.46

a = p<0.05; b = p<0.01; c = p<0.005

a = p<0.05; b = p<0.01; c = p<0.005

Table 3.3.18. Correlation coefficients between cardiorespiratory fitness and blood rheological variables.

	1	2	3	4	5	6	7	8	9
1. VO2max (l.min-1)									
2. VO2max (mls.kg-1.min-1)	0.69c								
3. Plasma Viscosity (mpa.s-1)	-0.22	-0.12							
4. Serum Viscosity (mpa.s-1)	-0.21	0.04	0.91c						
5. Haemoglobin (mg.dl-1)	-0.26	-0.30	-0.19	-0.25					
6. Haematocrit (%)	-0.31	-0.38	0.17	0.06	0.50b				
7. Fibrinogen (mg.dl-1)	-0.03	-0.18	0.33	0.09	-0.14	0.03			
8. Albumin (g.dl-1)	0.32	0.12	0.31	0.21	0.23	0.12	0.22		
9. Total Protein (g.dl-1)	0.01	-0.07	0.62c	0.50a	-0.08	0.12	0.28	0.74c	
Mean	3.72	47.61	1.55	1.45	142.48	44.78	273.28	5.18	6.50
S.D.	0.48	8.97	0.06	0.05	14.94	2.18	50.50	0.34	0.64

a = $p<0.05$; b = $p<0.01$; c = $p<0.005$

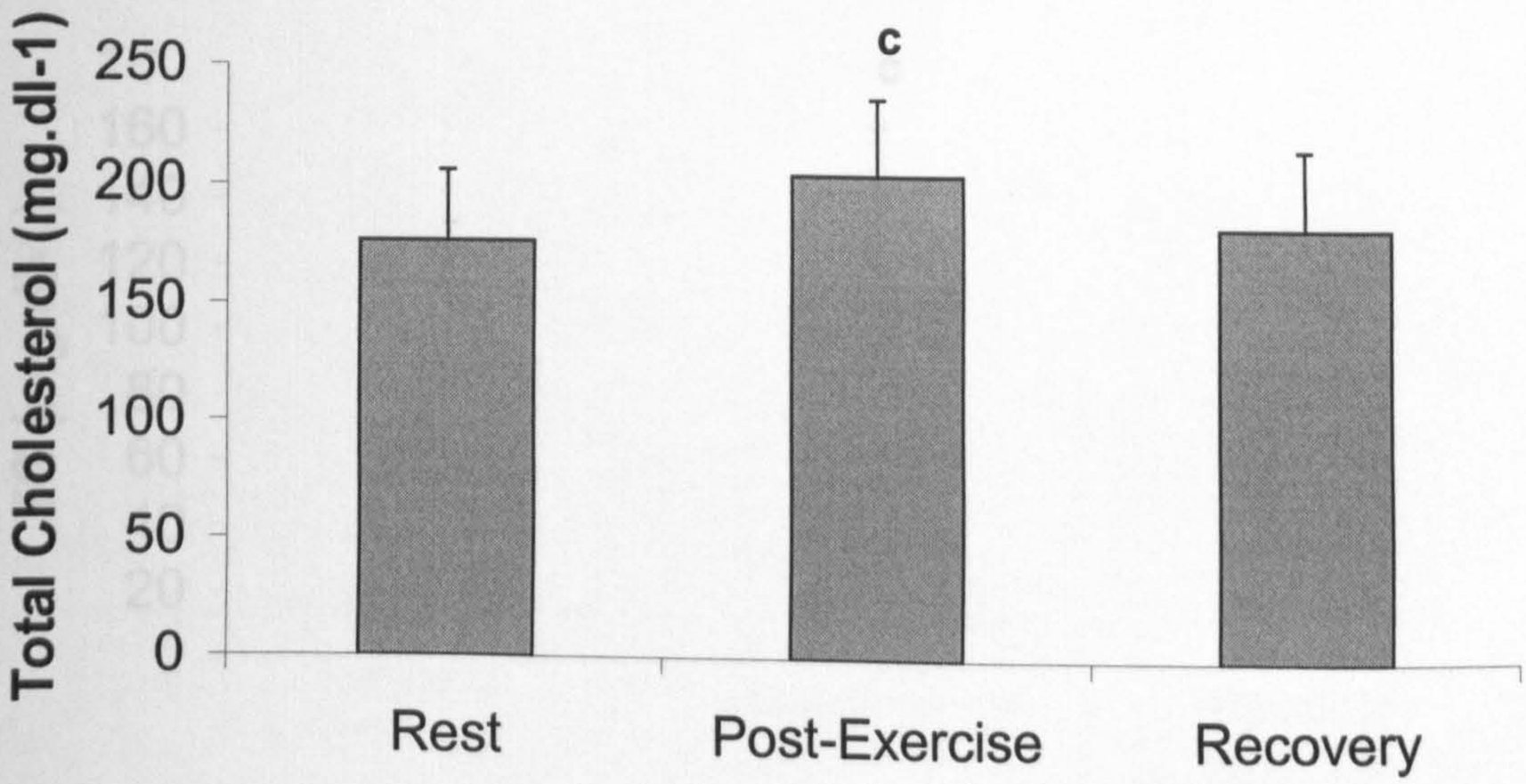
3.3.13. Maximal Exercise and Blood Lipids

There were significant differences between resting, post-exercise and recovery total cholesterol ($F_{1.4,29.8}$=23.83; p<0.005), TG (X^2_2=28.99; p<0.005), HDL ($F_{2,42}$=9.71; p<0.005), LDL ($F_{2,40}$=16.03; p<0.005) and VLDL (X^2_2=28.99; p<0.005) concentrations. Post-hoc analyses revealed a significant increase in total cholesterol (p<0.005), TG (p<0.005), HDL (p<0.005), LDL (p<0.005) and VLDL (p<0.005) concentrations following maximal exercise (Figures 3.3.1.A.; 3.3.2.A.; 3.3.3.A.; 3.3.4.A. and 3.3.5.A.). All blood lipid concentrations returned towards baseline following 30 minutes seated recovery.

When correcting post-exercise and recovery raw data for the effects of plasma volume change (Figures 3.3.1.B.; 3.3.2.B.; 3.3.3.B.; 3.3.4.B. and 3.3.5.B.), significant differences were observed between resting, post-exercise and recovery values for TG (X^2_2=6.37; p<0.05), LDL ($F_{2,40}$=24.26; p<0.005) and VLDL (X^2_2=6.37; p<0.05), although there were no significant differences in total cholesterol or HDL concentrations. Post-hoc analyses revealed that maximal exercise evoked a significant reduction in LDL levels immediately post-exercise (p<0.005), which remained even following 30 minutes seated recovery (p<0.005). However, post-hoc analyses failed to show any other significant differences between resting and post-exercise values, although TG (p<0.025) and VLDL (p<0.025) levels were significantly lower following recovery than at rest.

In addition, significant differences were shown between resting, post-exercise and recovery values for both the total cholesterol/HDL ($F_{2,42}$=33.26; p<0.005) and the total cholesterol/LDL ($F_{1.5,29.2}$=15.88; p<0.005) ratios (Figures 3.3.6. and 3.3.7.). Maximal exercise caused a significant reduction in the total cholesterol/HDL ratio (p<0.005), a result which remained even following 30 minutes seated recovery (p<0.005). Conversely, maximal exercise led to a significant increase in the total cholesterol/LDL ratio (p<0.005), an elevation which also remained significant following 30 minutes recovery (p<0.005).

A.



B.

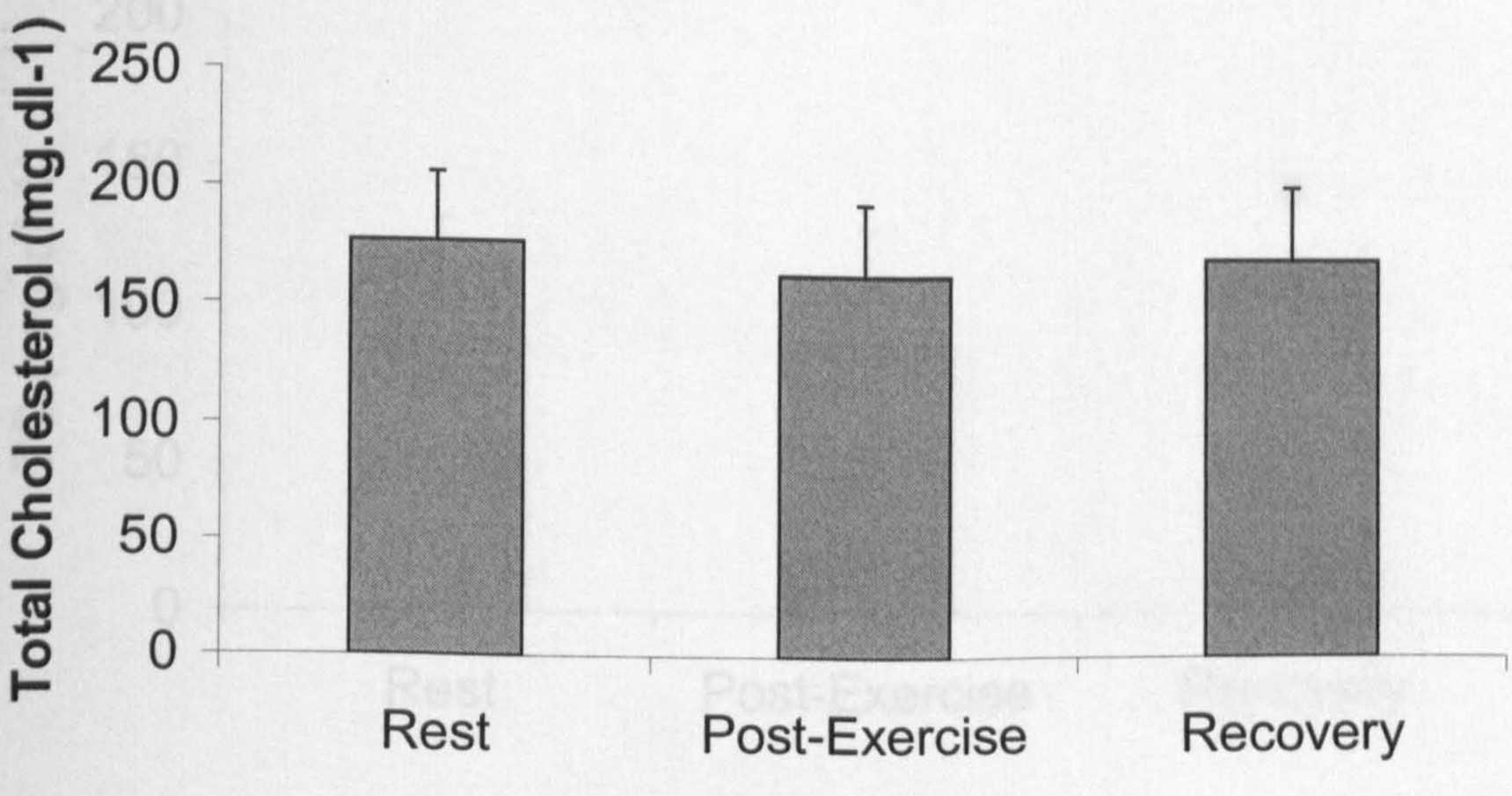
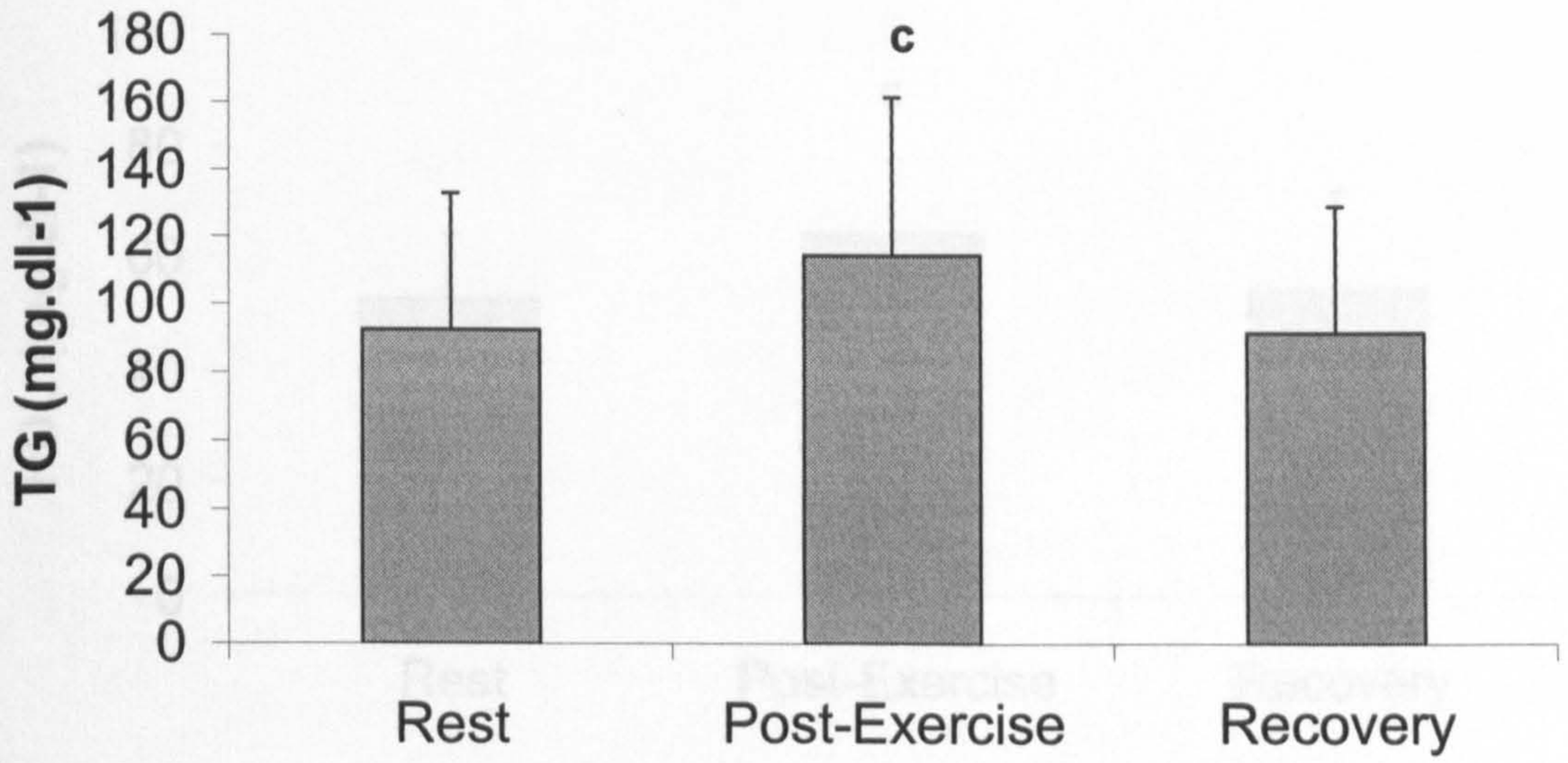


Figure 3.3.1. Total cholesterol concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

A.



B.

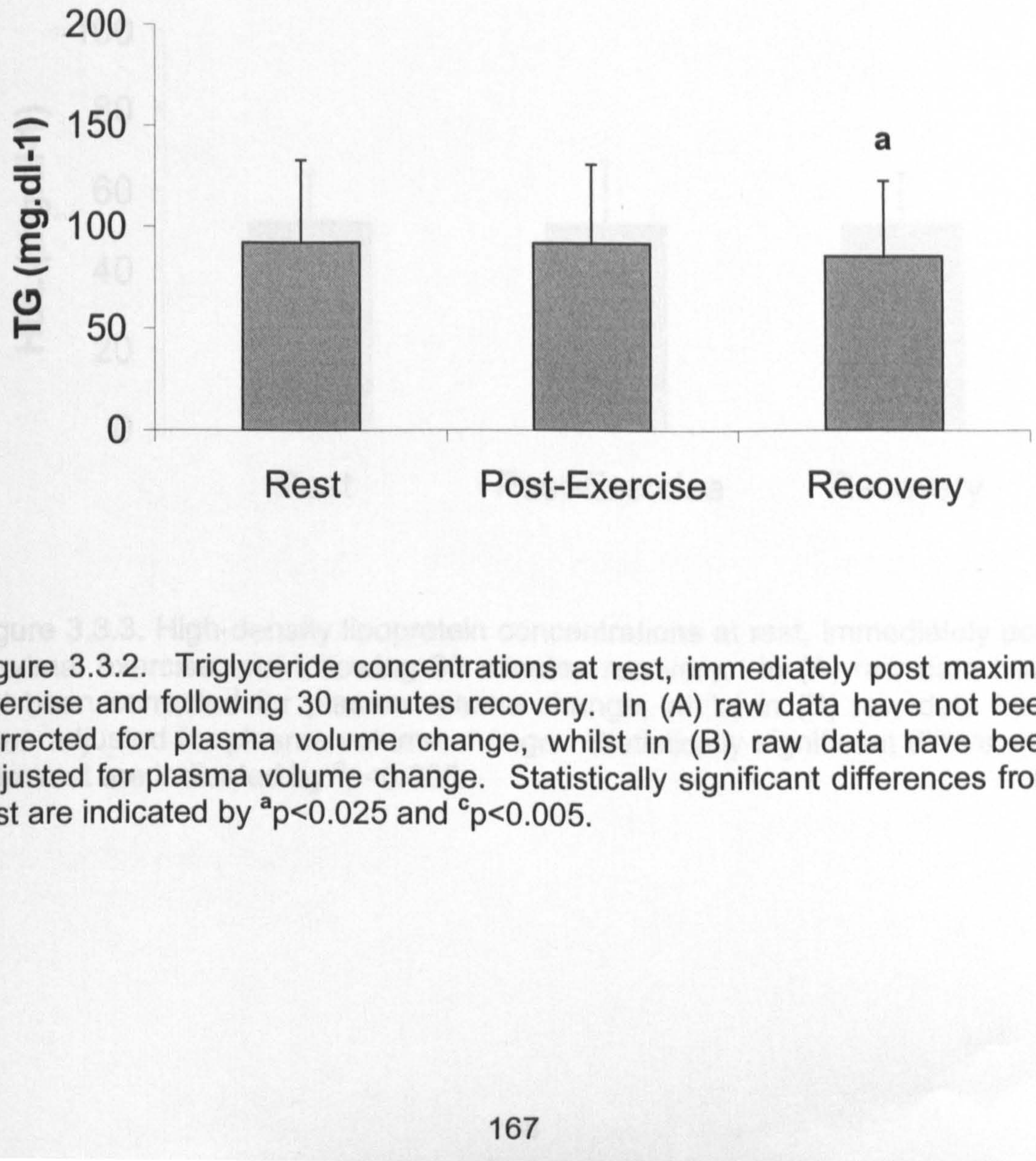
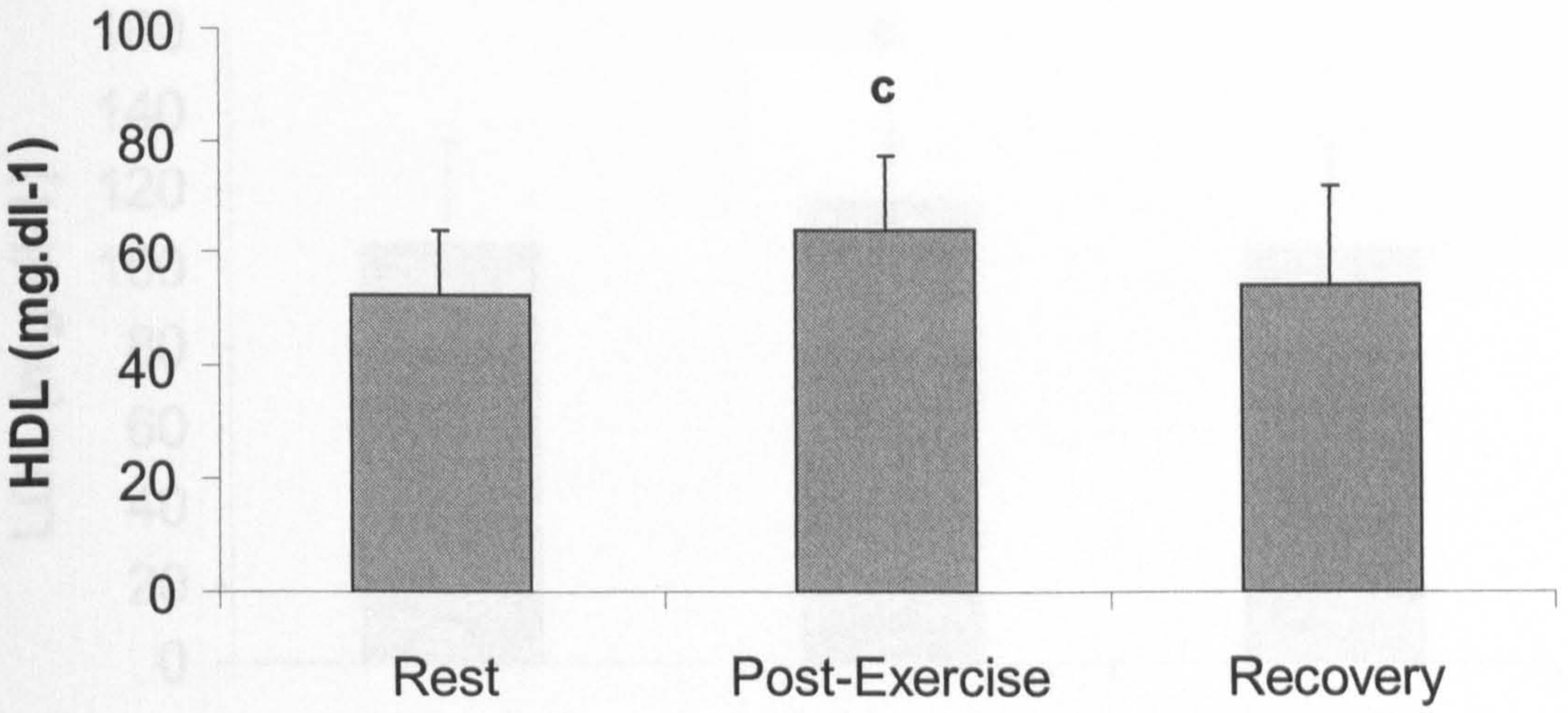


Figure 3.3.2. Triglyceride concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{a}p<0.025$ and $^{c}p<0.005$.

A.



B.

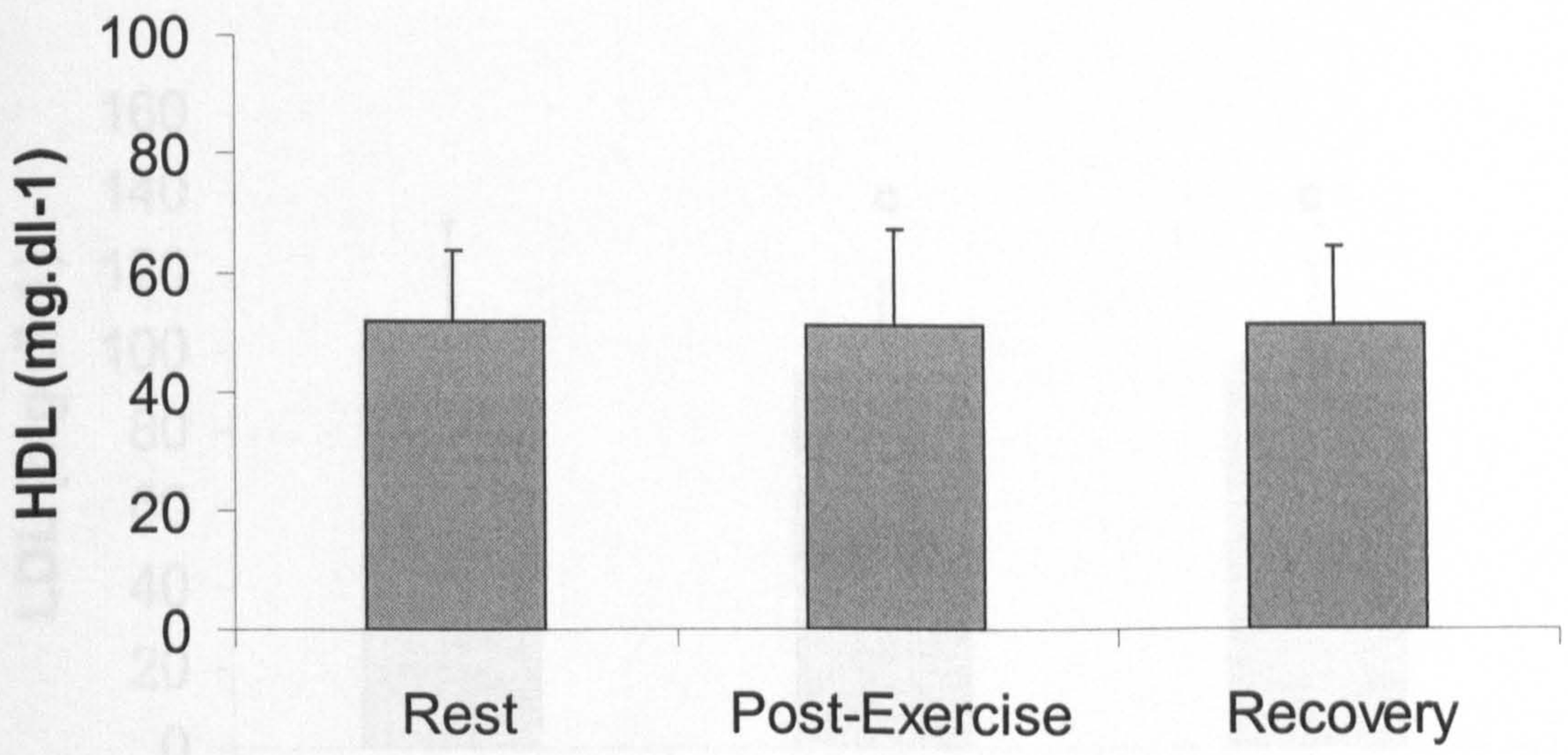
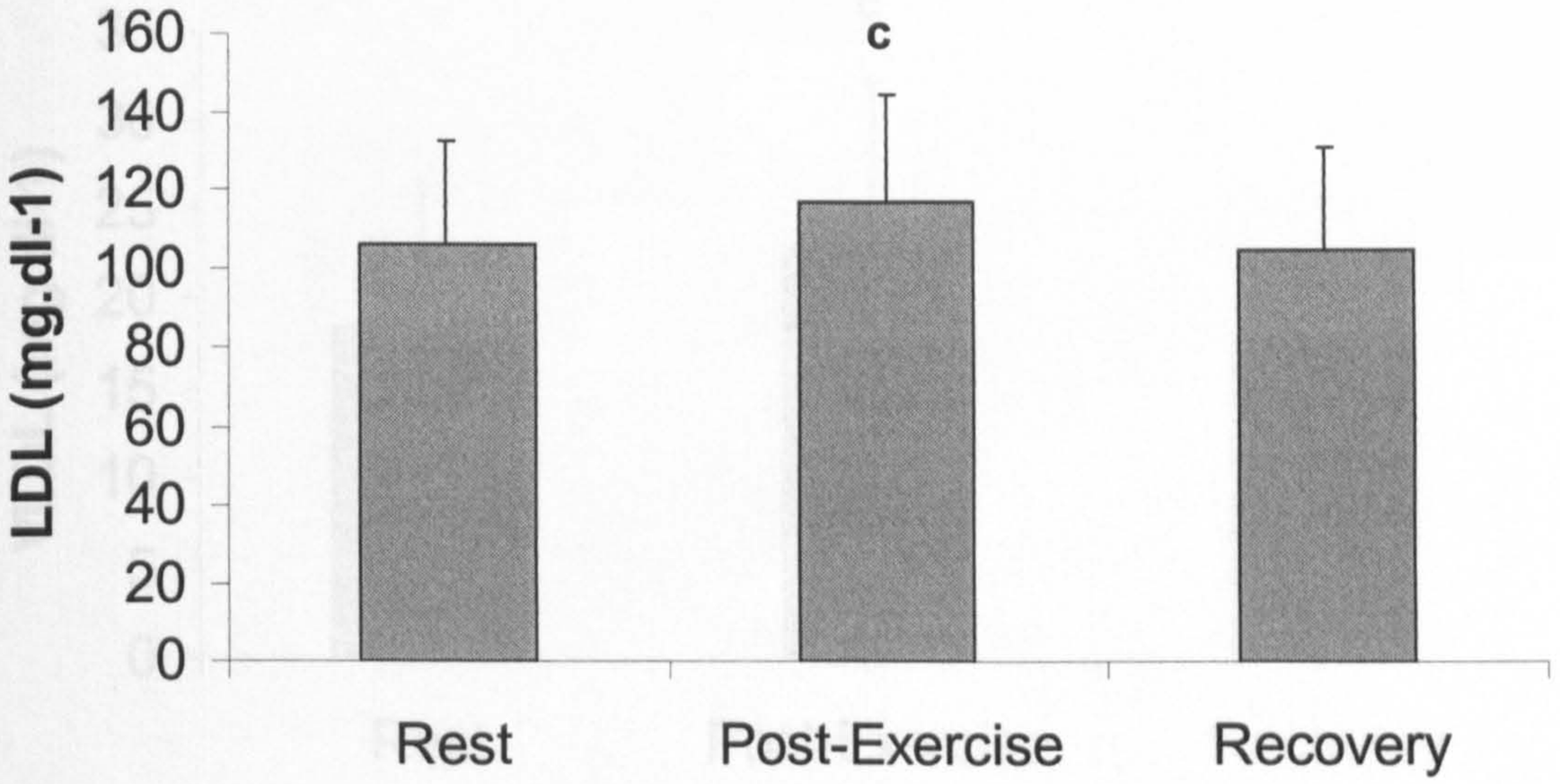


Figure 3.3.3. High-density lipoprotein concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

A.



B.

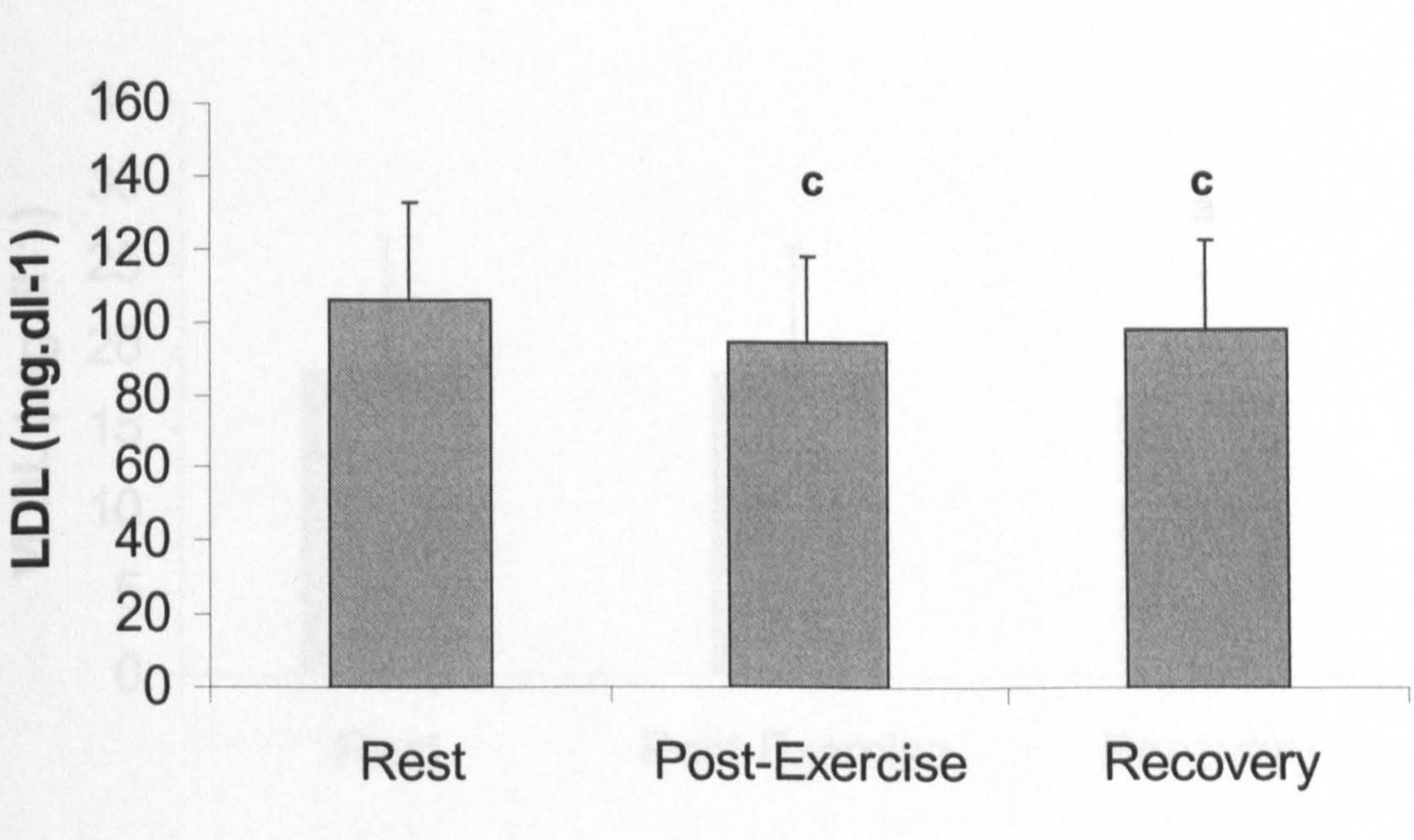
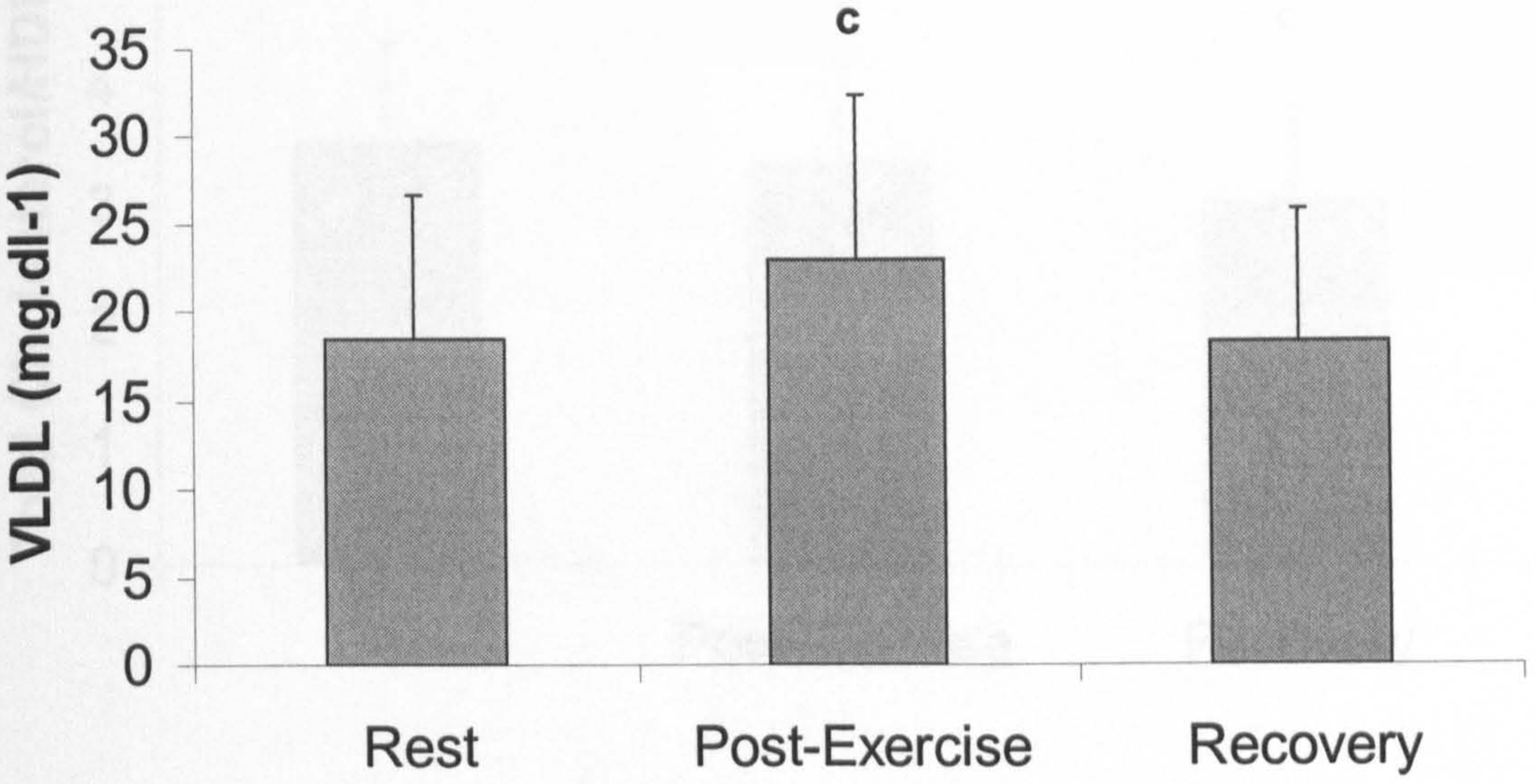


Figure 3.3.4. Low-density lipoprotein concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

A.



B.

Figure 3.3.5. Very low-density lipoprotein concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{a}p<0.025$ and $^{c}p<0.005$.

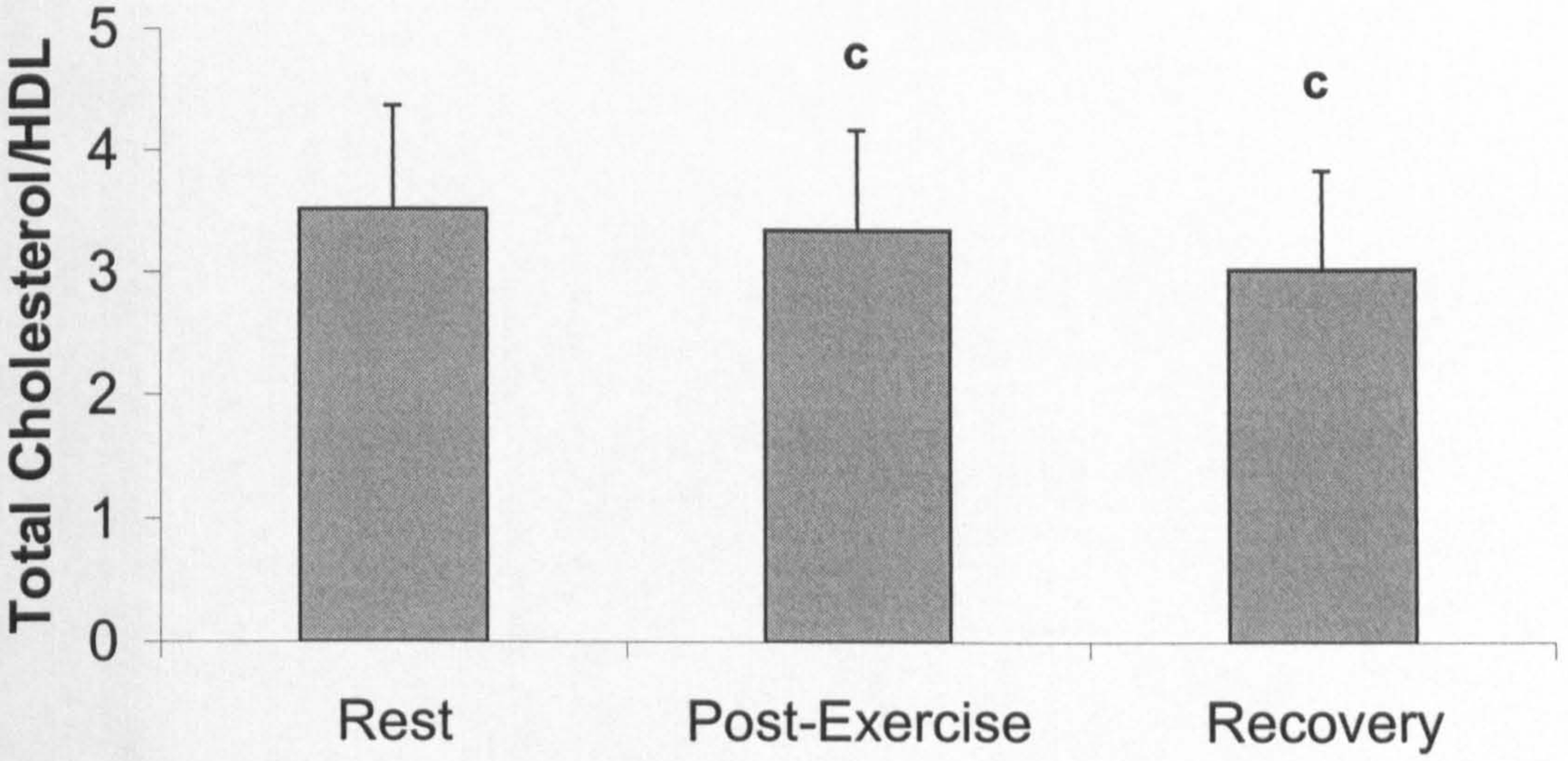


Figure 3.3.6. Total cholesterol/HDL ratio at rest, immediately post maximal exercise and following 30 minutes recovery. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

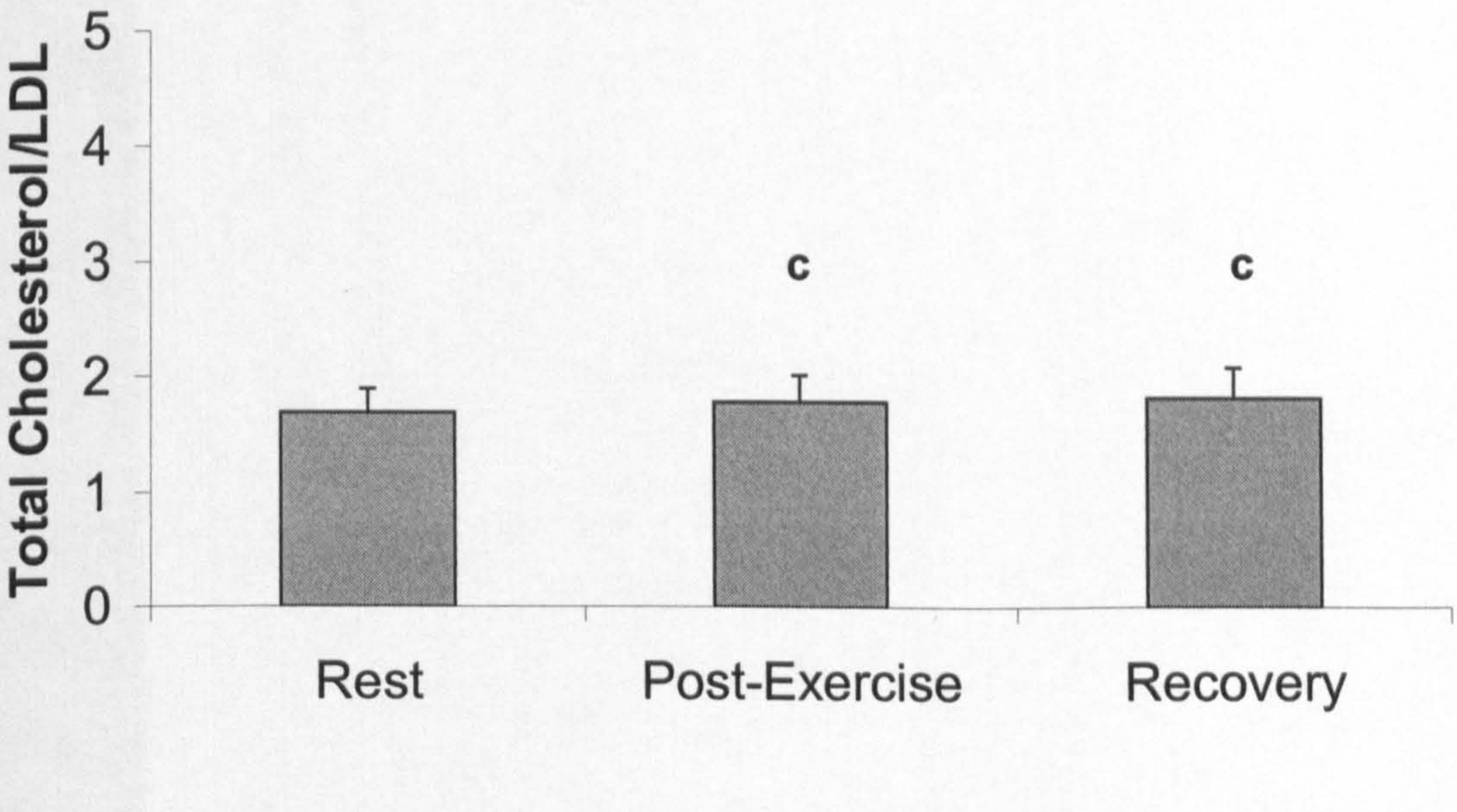


Figure 3.3.7. Total cholesterol/LDL ratio at rest, immediately post maximal exercise and following 30 minutes recovery. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

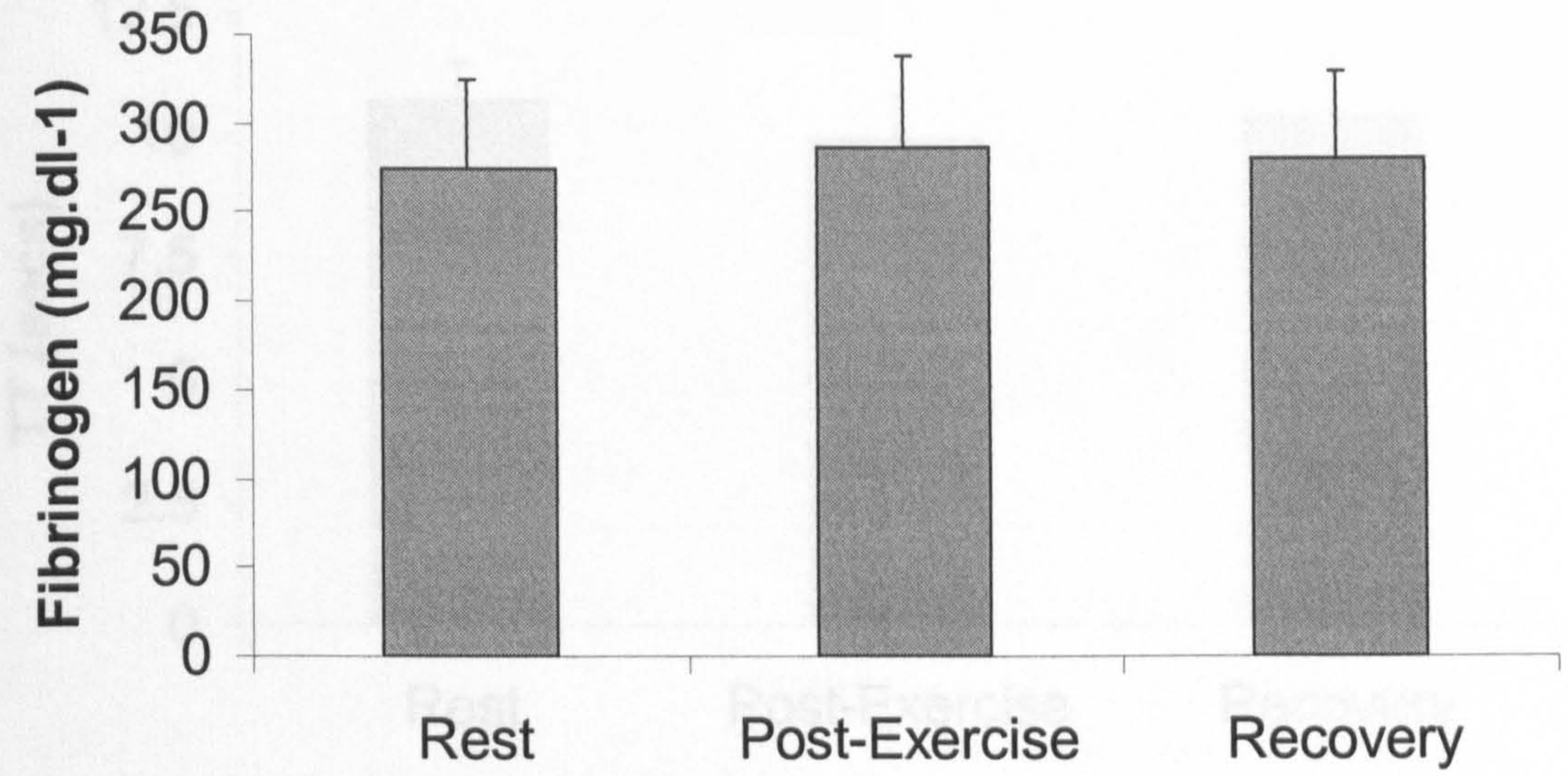
3.3.14. Maximal Exercise and Blood Coagulation

Although there was an ~5% increase in plasma fibrinogen concentration immediately following maximal exercise (286.79±52.28mg.dl^{-1}), when compared to resting values (273.28±50.50mg.dl^{-1}), this increase failed to reach the assigned level of significance (Figure 3.3.8.A.). Thus, plasma fibrinogen concentrations remained unaltered following maximal exercise and following 30 minutes seated recovery.

However, when raw data were corrected for exercise-induced changes in plasma volume (Figure 3.3.8.B.), repeated measures ANOVA showed significant changes in plasma fibrinogen concentration ($F_{2,44}$=19.60; $p<0.005$). Post-hoc analyses, showed a significant decrease in the plasma concentration of fibrinogen immediately after maximal exercise ($p<0.005$), with plasma fibrinogen concentrations returning towards resting values following 30 minutes seated recovery.

There were significant differences in TT ($F_{1.3,27.8}$=6.90, $p<0.01$), PT ($F_{2,44}$=26.89; $p<0.005$) and APTT ($F_{2,42}$=29.63, $p<0.005$) between resting, post-exercise and recovery values. Post-hoc analyses showed a significant decrease in TT ($p<0.005$), PT ($p<0.005$) and APTT ($p<0.005$) following maximal exercise, thus indicating significantly faster clotting times immediately post-exercise (Figures 3.3.9-3.3.11.). All clotting times remained significantly reduced, even following 30 minutes seated recovery.

A.



B.

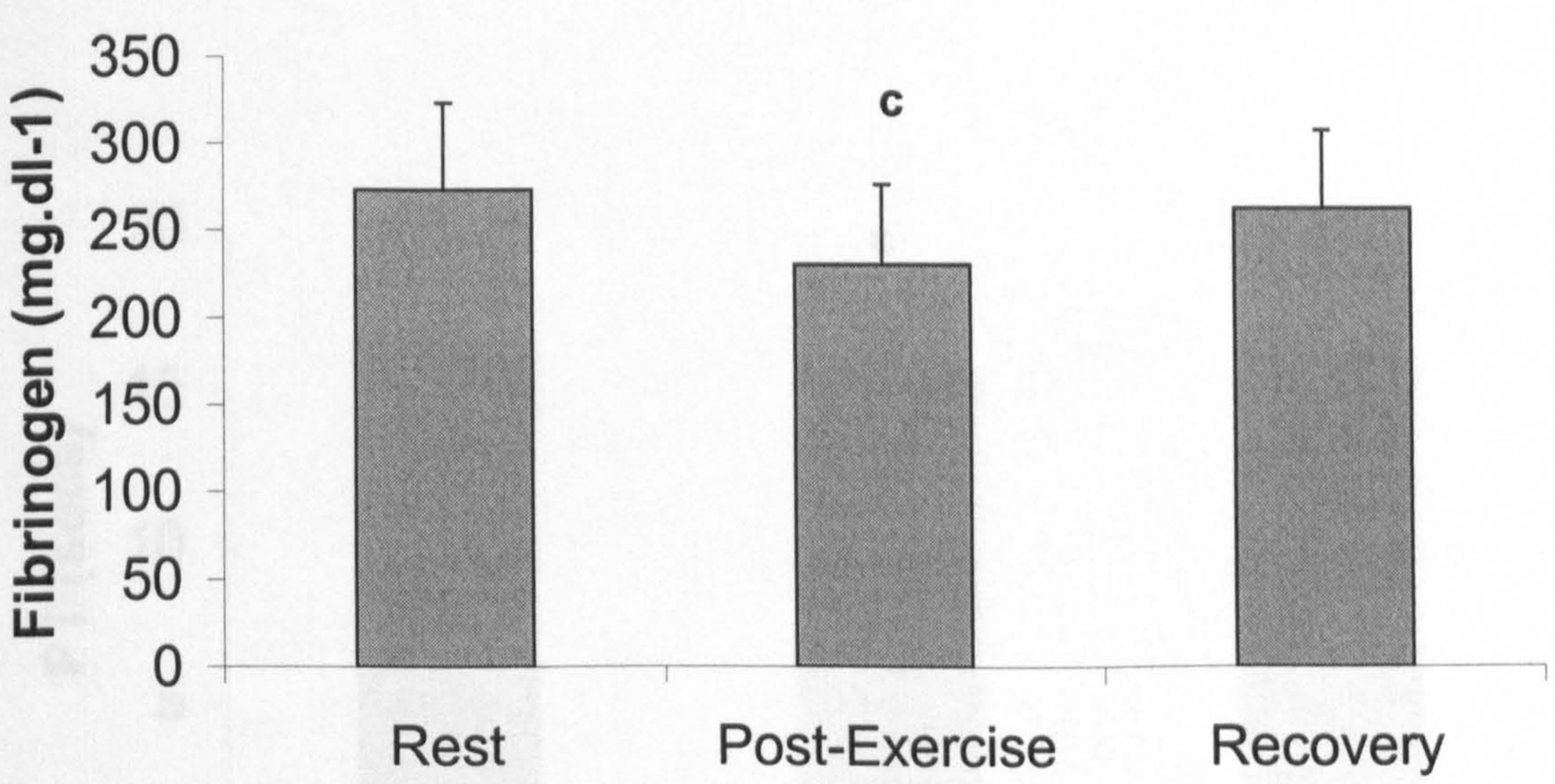


Figure 3.3.8. Plasma fibrinogen concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

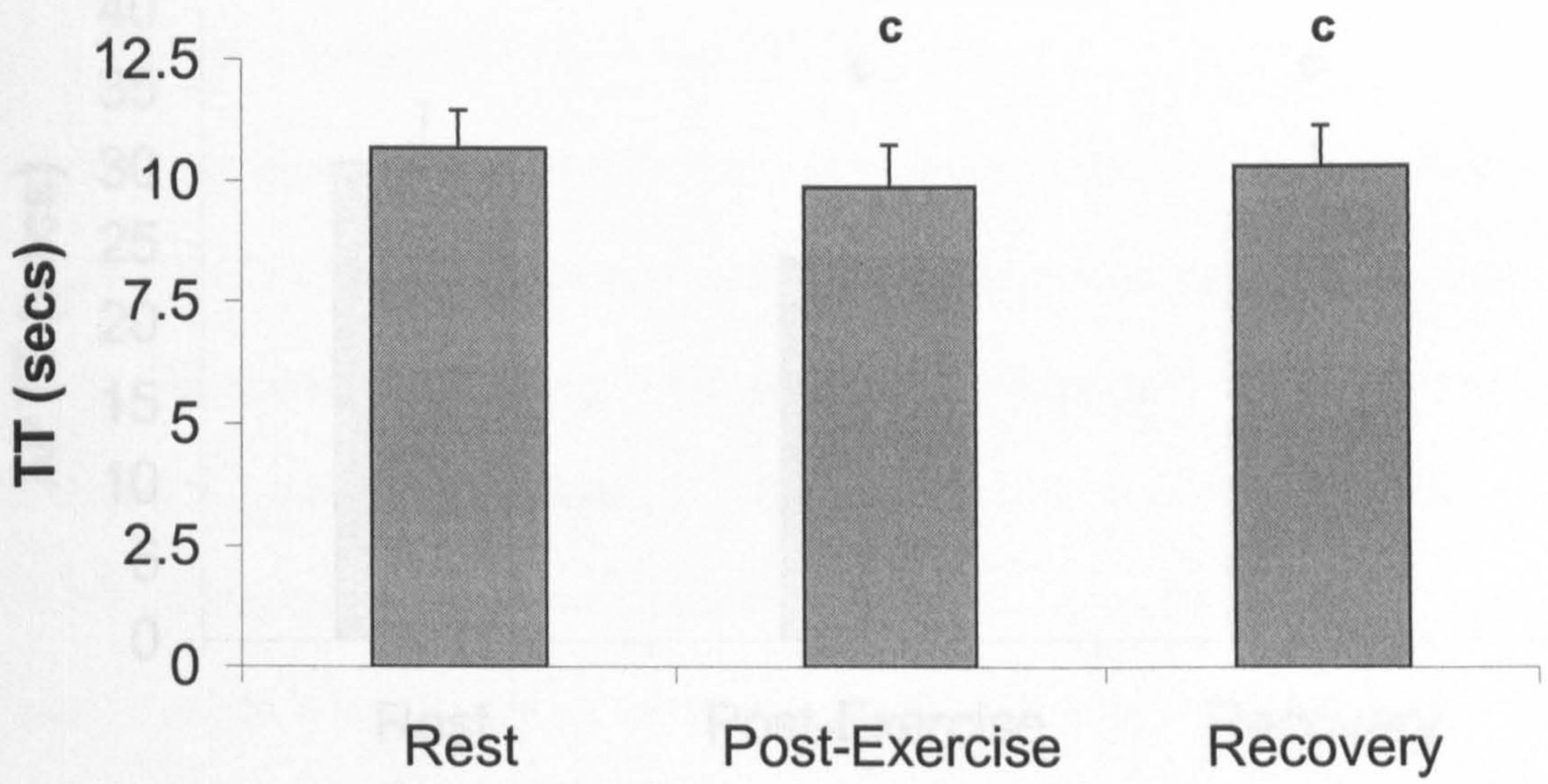


Figure 3.3.9. Thrombin time at rest, immediately post maximal exercise and following 30 minutes recovery. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

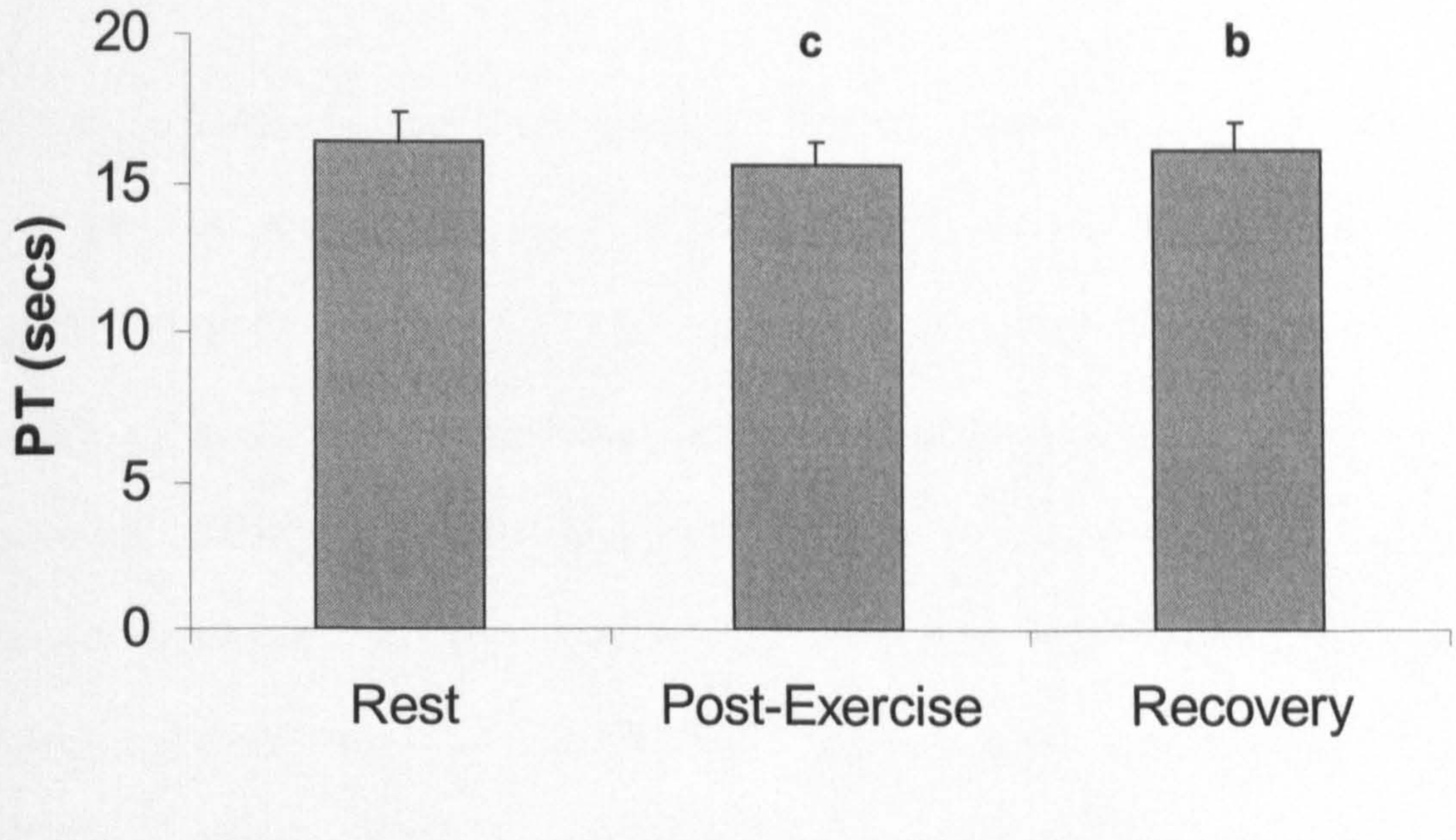


Figure 3.3.10. Prothrombin time at rest, immediately post maximal exercise and following 30 minutes recovery. Statistically significant differences from rest are indicated by $^{b}p<0.01$ and $^{c}p<0.005$.

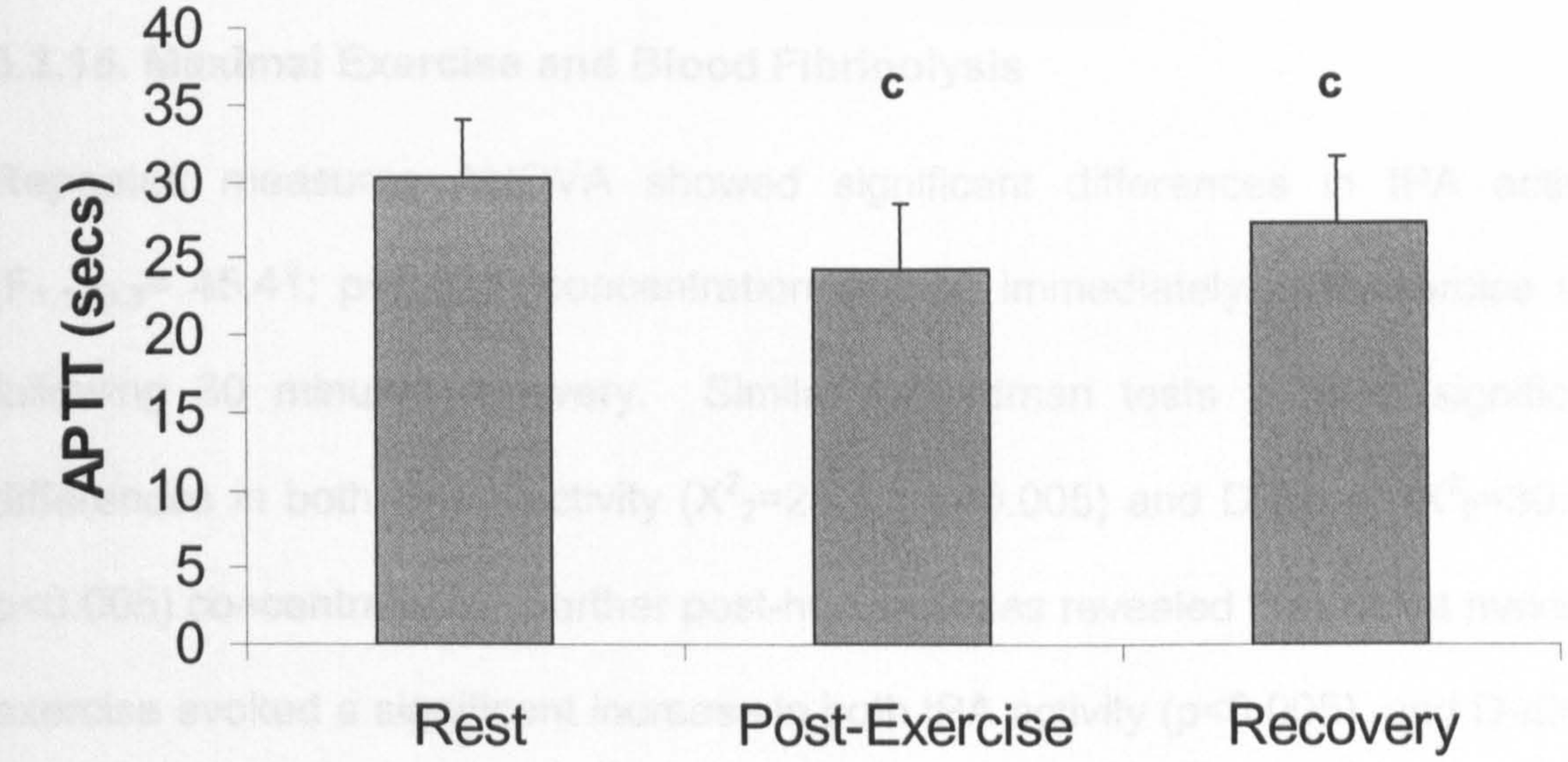


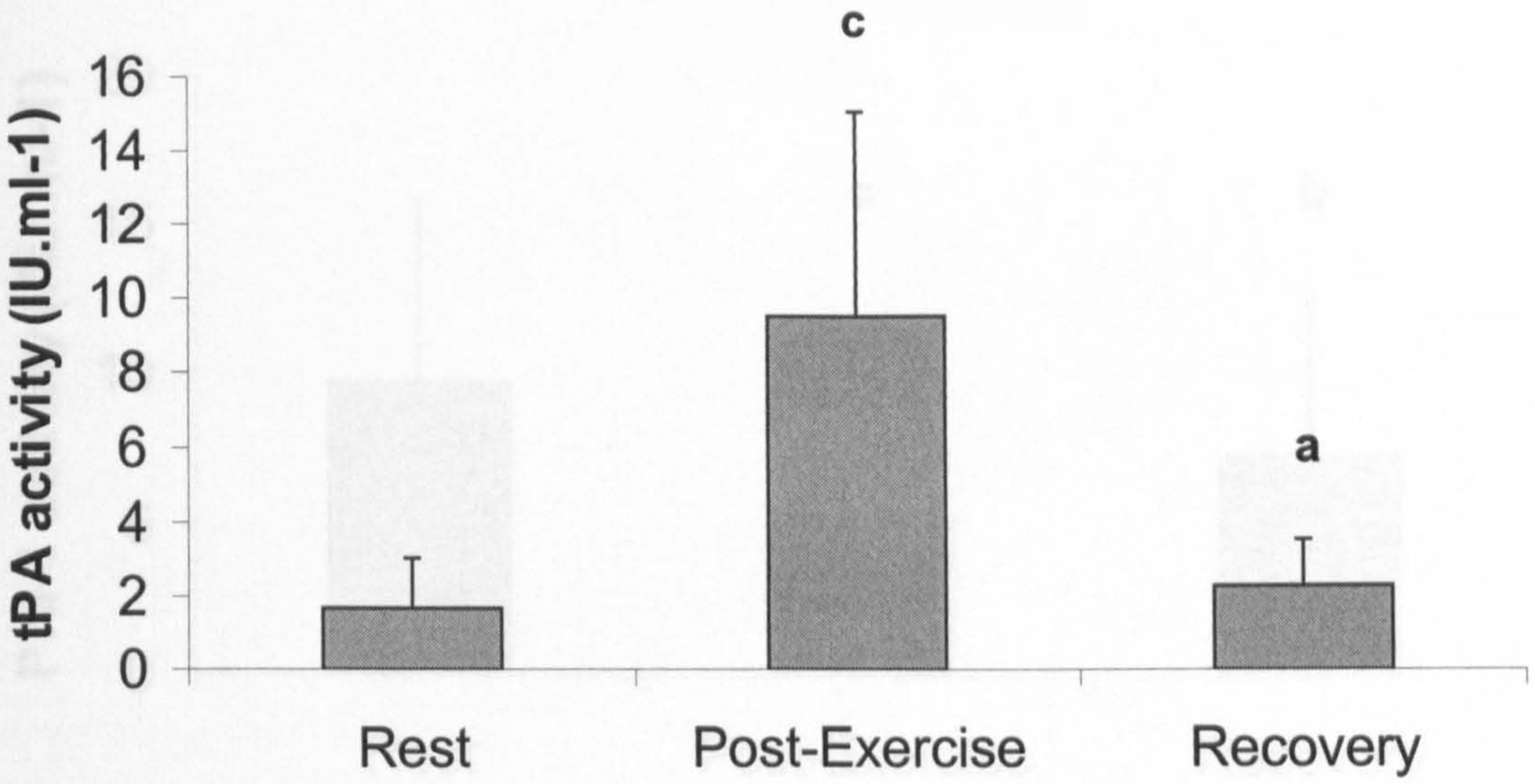
Figure 3.3.11. Activated partial thromboplastin time at rest, immediately post maximal exercise and following 30 minutes recovery. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

3.3.15. Maximal Exercise and Blood Fibrinolysis

Repeated measures ANOVA showed significant differences in tPA activity ($F_{1.1,23.3}$= 45.41; $p<0.005$) concentration at rest, immediately post-exercise and following 30 minutes recovery. Similarly Friedman tests showed significant differences in both PAI-1 activity (X^2_2=28.17, $p<0.005$) and D-dimer (X^2_2=30.03, $p<0.005$) concentrations. Further post-hoc analyses revealed that whilst maximal exercise evoked a significant increase in both tPA activity ($p<0.005$), and D-dimer concentration ($p<0.005$), there was a significant reduction in PAI-1 activity ($p<0.005$). Whilst there was a return back towards resting levels in D-dimer, tPA activity levels remained significantly elevated ($p<0.025$) and PAI-1 activity levels remained reduced ($p<0.005$) even following 30 minutes recovery (Figures 3.3.12.A.; 3.3.13.A. and 3.3.14.A.).

Significant differences remained between resting, post-exercise and recovery values for tPA activity ($F_{1.1,23.8}$= 39.78; $p<0.001$), PAI-1 activity (X^2_2=31.65, $p<0.005$), and D-dimer (X^2_2=11.57, $p<0.005$) concentrations following the correction of post-exercise and recovery raw data for plasma volume change (Figures 3.3.12.B.; 3.3.13.B. and 3.3.14.B.). Post-hoc analyses showed significant increases in both tPA activity ($p<0.005$) and D-dimer ($p<0.005$) following maximal exercise, whilst PAI-1 activity was significantly reduced ($p<0.005$). Following 30 minutes seated recovery there was an attenuation back towards resting levels for tPA activity and D-dimer, although PAI-1 activity levels remained significantly reduced ($p<0.005$).

A.



B.

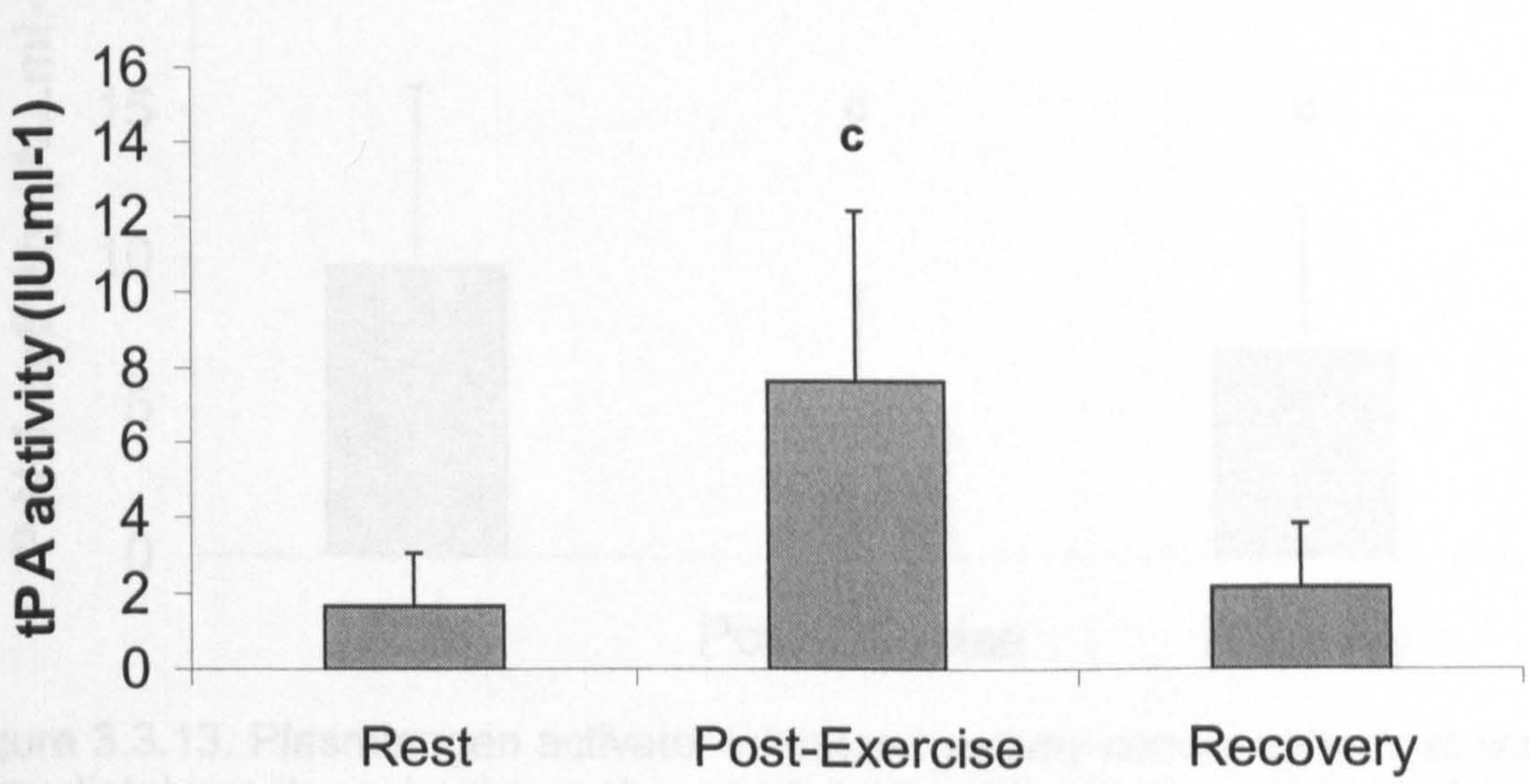
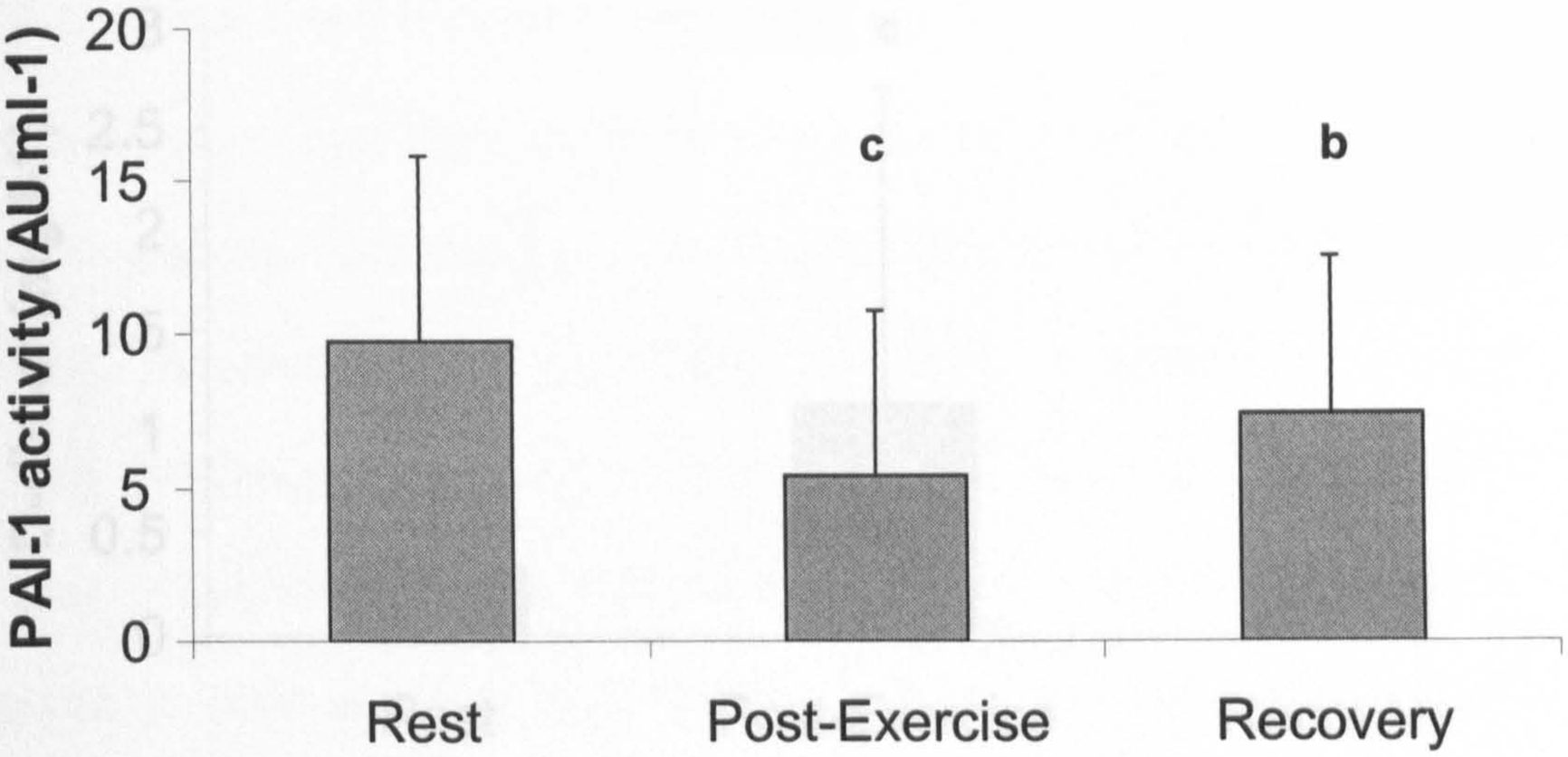


Figure 3.3.12. Tissue plasminogen activator activity concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{a}p<0.025$ and $^{c}p<0.005$.

A.



B.

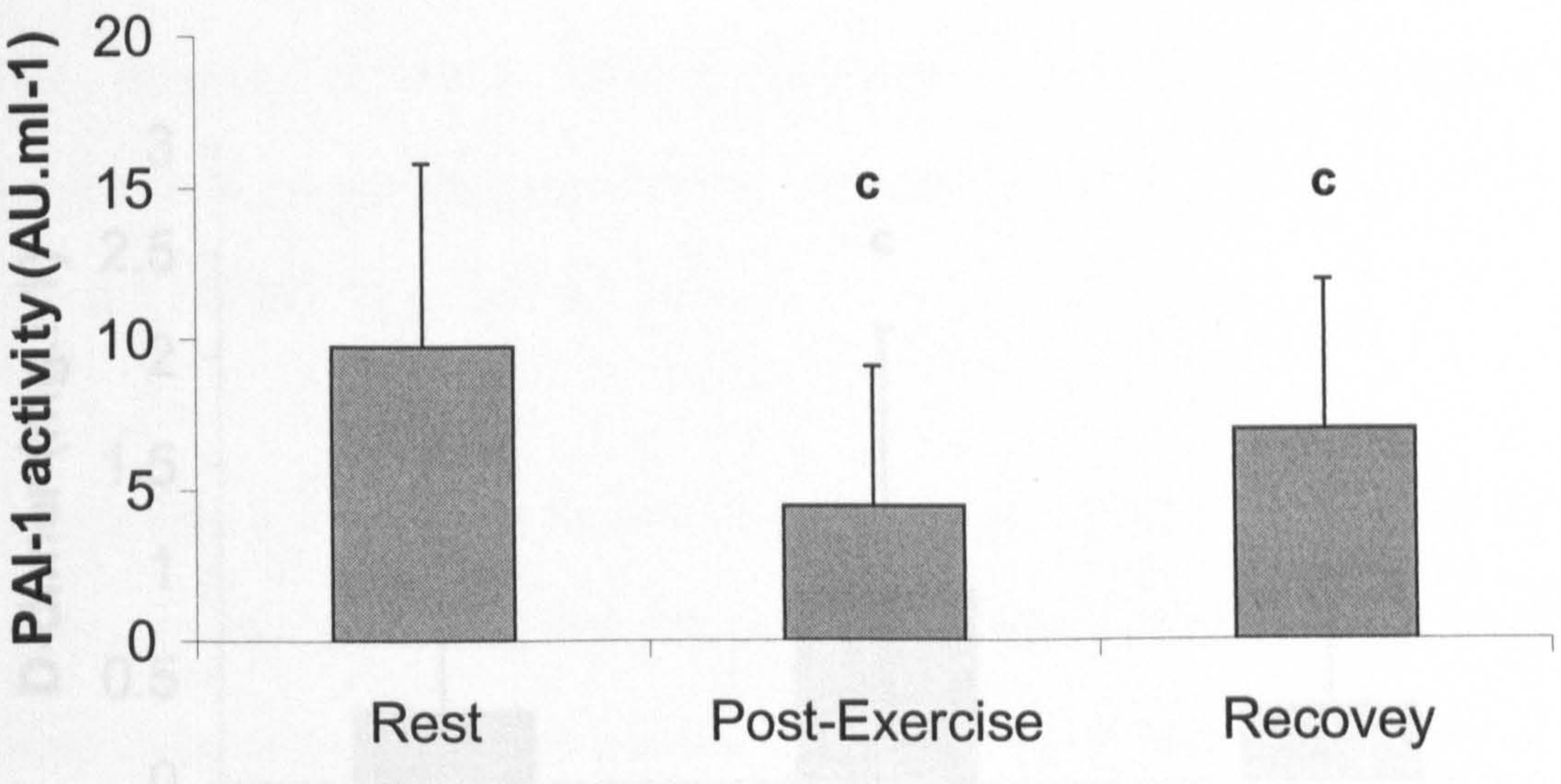
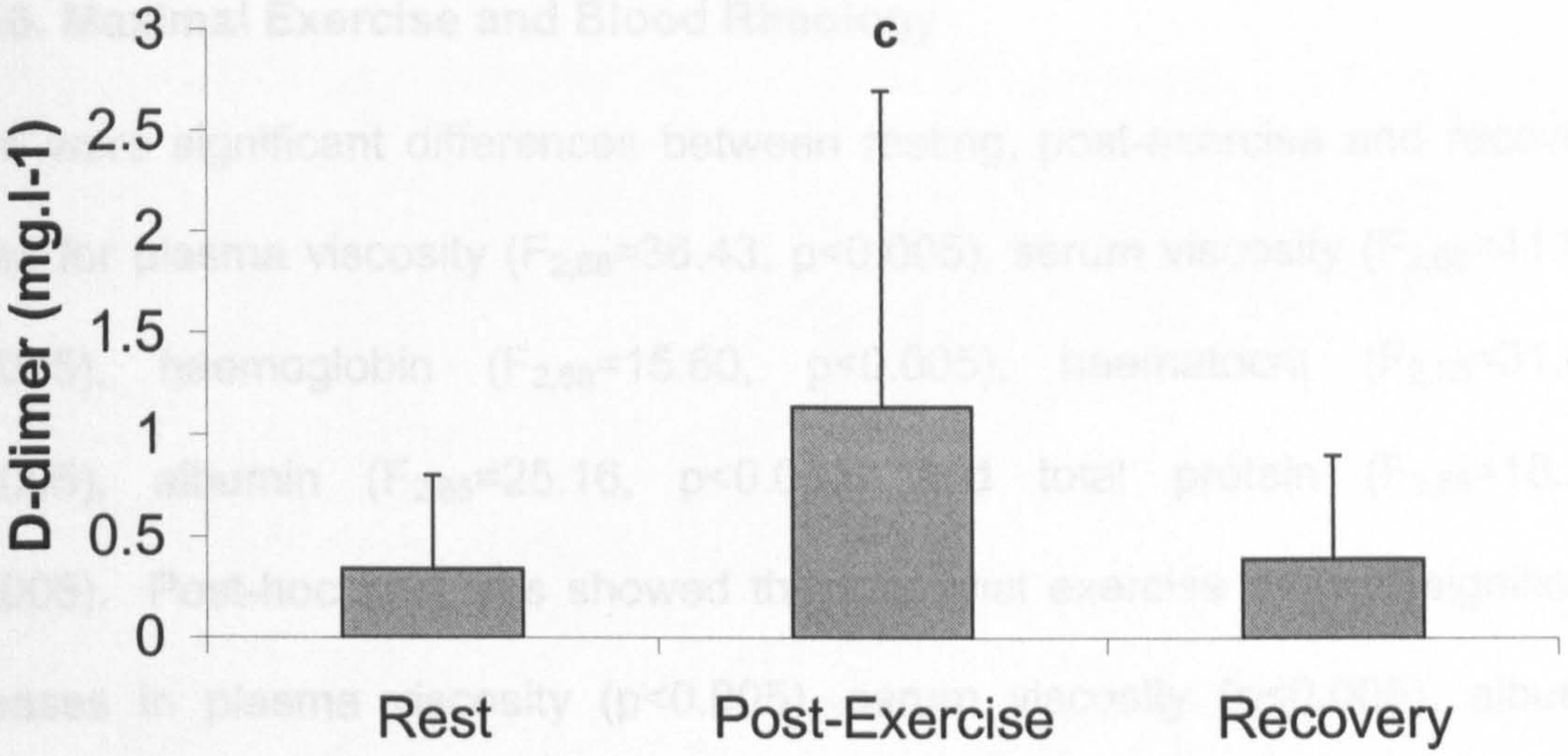


Figure 3.3.13. Plasminogen activator inhibitor-1 activity concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{b}p<0.01$ and $^{c}p<0.005$.

A.



B.

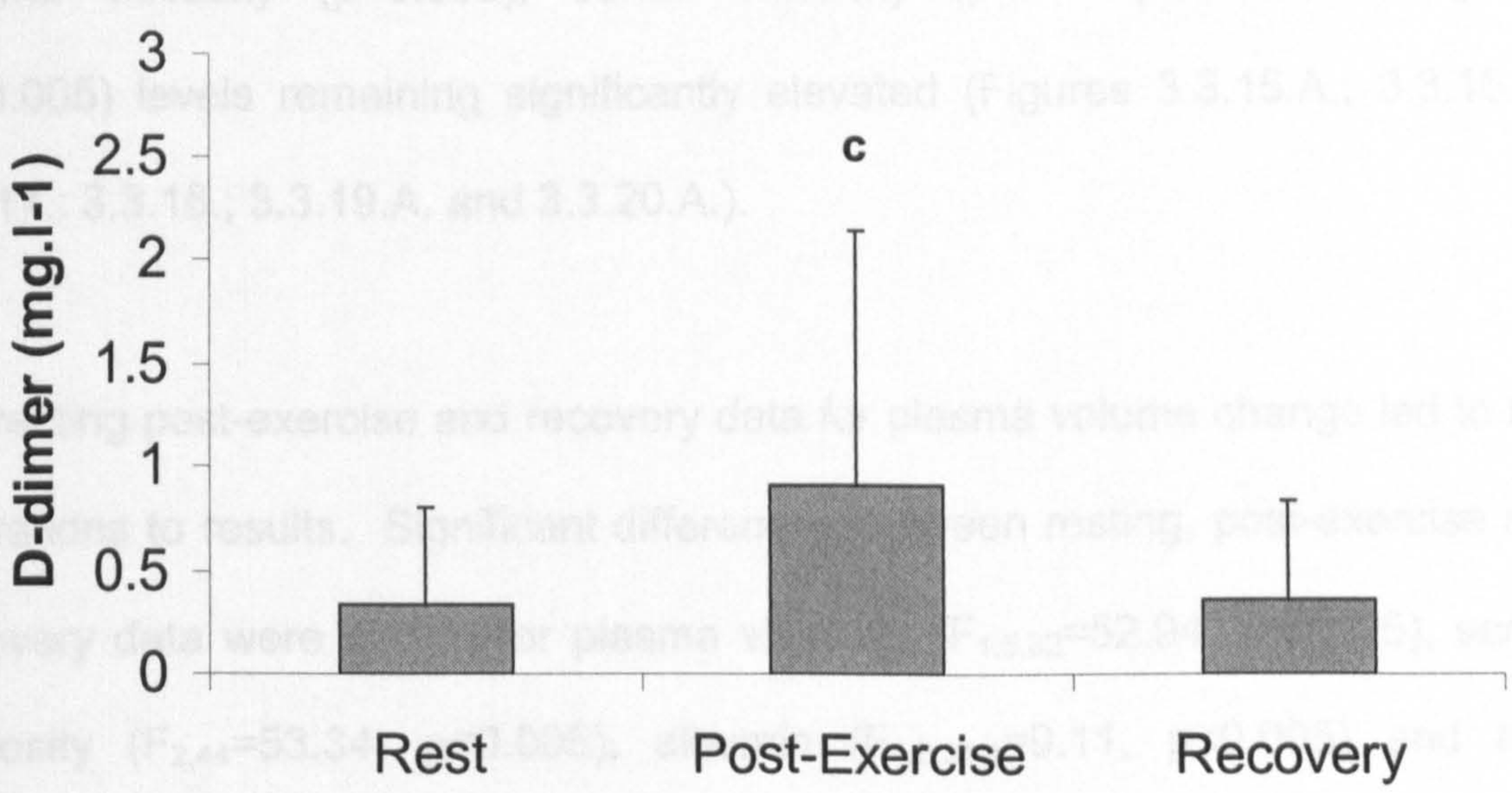


Figure 3.3.14. D-dimer concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

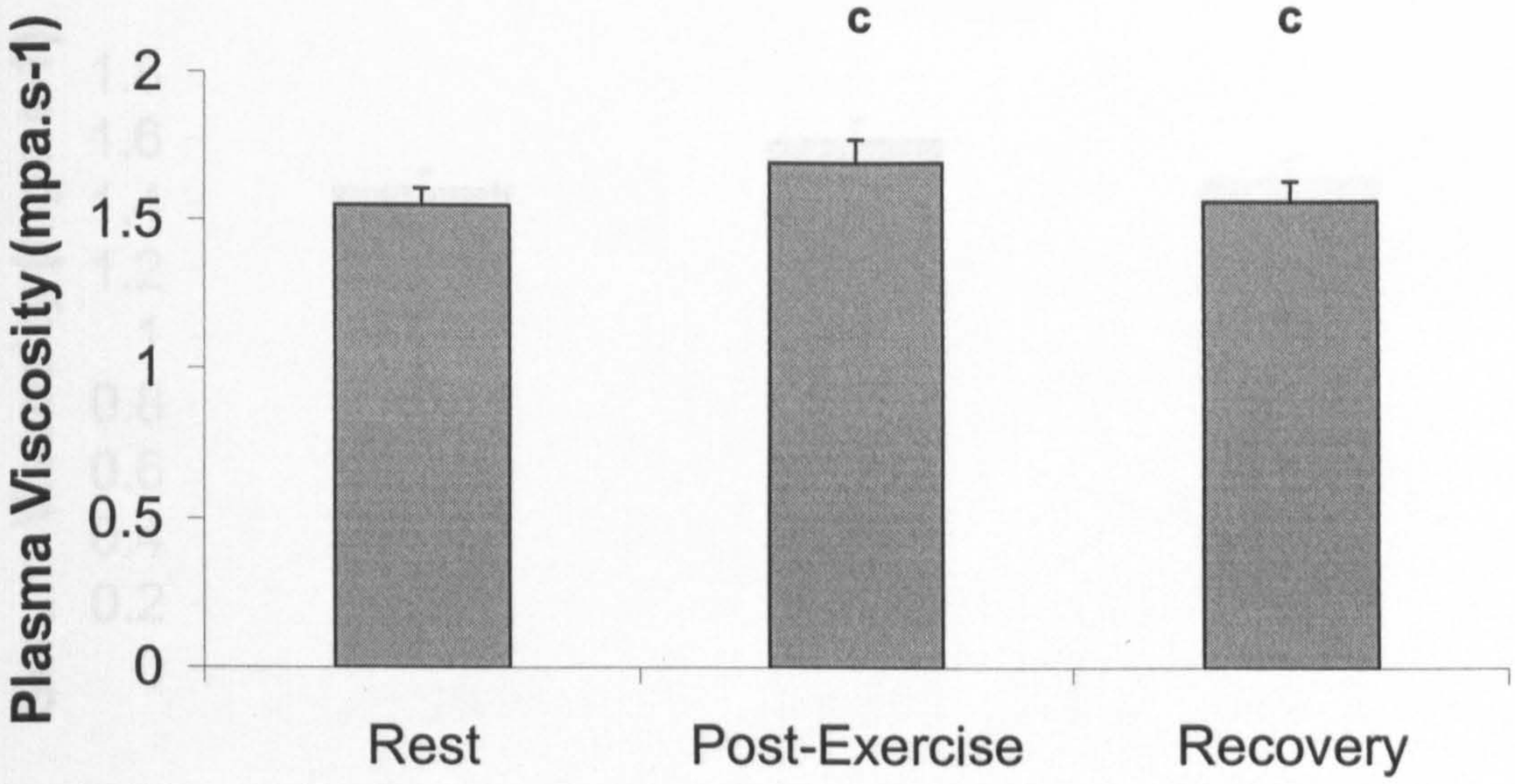
3.3.16. Maximal Exercise and Blood Rheology

There were significant differences between resting, post-exercise and recovery values for plasma viscosity ($F_{2,68}$=36.43, p<0.005), serum viscosity ($F_{2,68}$=41.60, p<0.005), haemoglobin ($F_{2,68}$=15.60, p<0.005), haematocrit ($F_{2,68}$=31.86, p<0.005), albumin ($F_{2,65}$=25.16, p<0.005) and total protein ($F_{2,65}$=18.29, p<0.005). Post-hoc analyses showed that maximal exercise evoked significant increases in plasma viscosity (p<0.005), serum viscosity (p<0.005), albumin (p<0.005), total protein (p<0.005), haemoglobin (p<0.005) and haematocrit (p<0.005). There was evidence of an attenuation back towards resting values following 30 minutes recovery for albumin, total protein and haematocrit, with plasma viscosity (p<0.005), serum viscosity (p<0.005) and haemoglobin (p<0.005) levels remaining significantly elevated (Figures 3.3.15.A.; 3.3.16.A.; 3.3.17.; 3.3.18.; 3.3.19.A. and 3.3.20.A.).

Correcting post-exercise and recovery data for plasma volume change led to key alterations to results. Significant differences between resting, post-exercise and recovery data were shown for plasma viscosity ($F_{1.5,32}$=52.94, p<0.005), serum viscosity ($F_{2,44}$=53.34, p<0.005), albumin ($F_{1.5,31.4}$=9.11, p<0.005) and total protein ($F_{2,42}$=3.67, p<0.05). Post-hoc analyses showed significant reductions in plasma viscosity (p<0.005), serum viscosity (p<0.005) and albumin (p<0.005) following maximal exercise, although the result for total protein concentration failed to reach the assigned levels of significance following Bonferroni correction (Figures 3.3.15.B.; 3.3.16.B.; 3.3.19.B. and 3.3.20.B.). Whilst 30 minutes seated

recovery resulted in a return of albumin concentration to baseline, plasma viscosity ($p<0.005$) and serum viscosity ($p<0.005$) remained significantly lower than at rest.

A.



B.

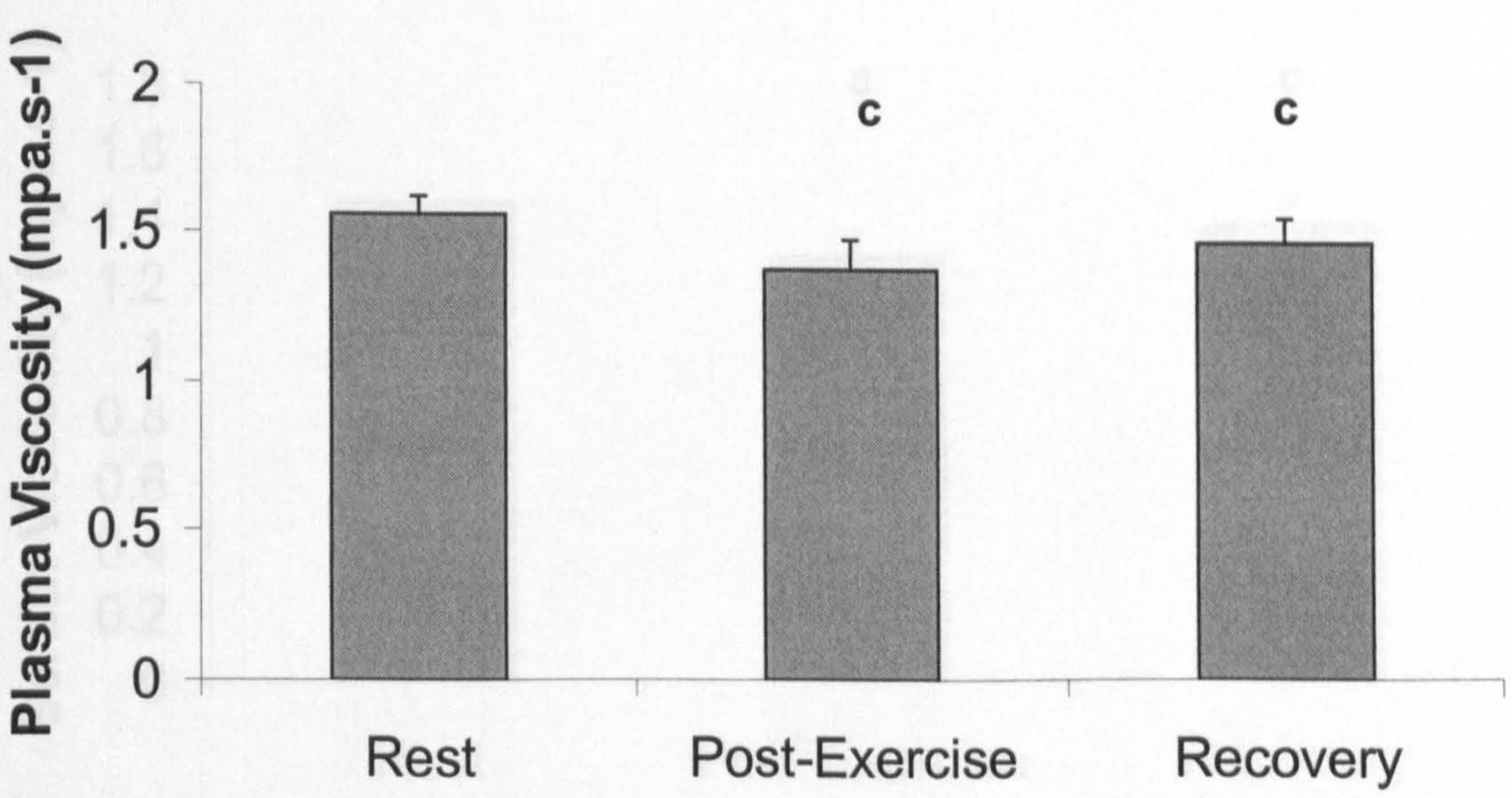
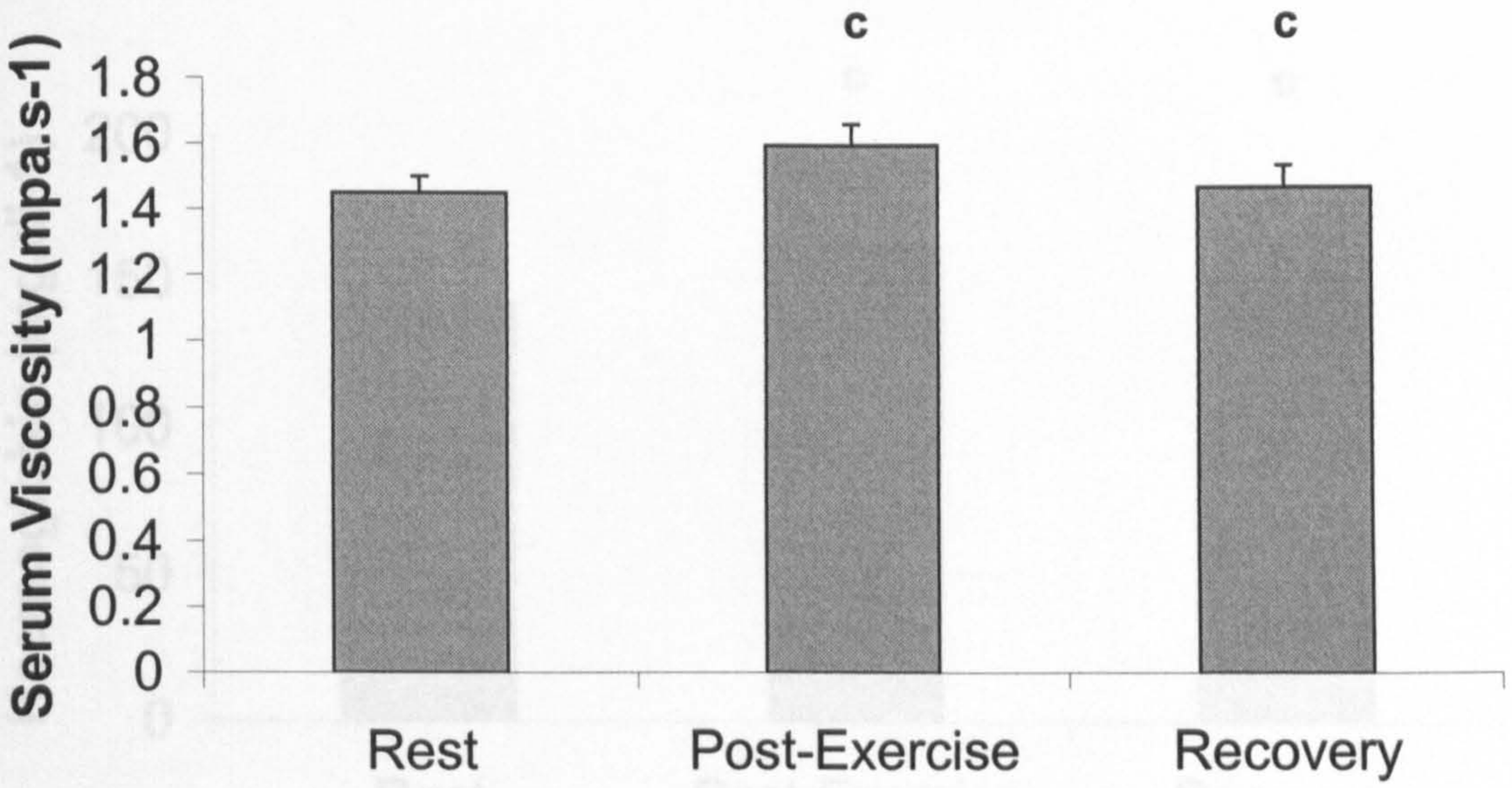


Figure 3.3.15. Plasma viscosity at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

A.



B.

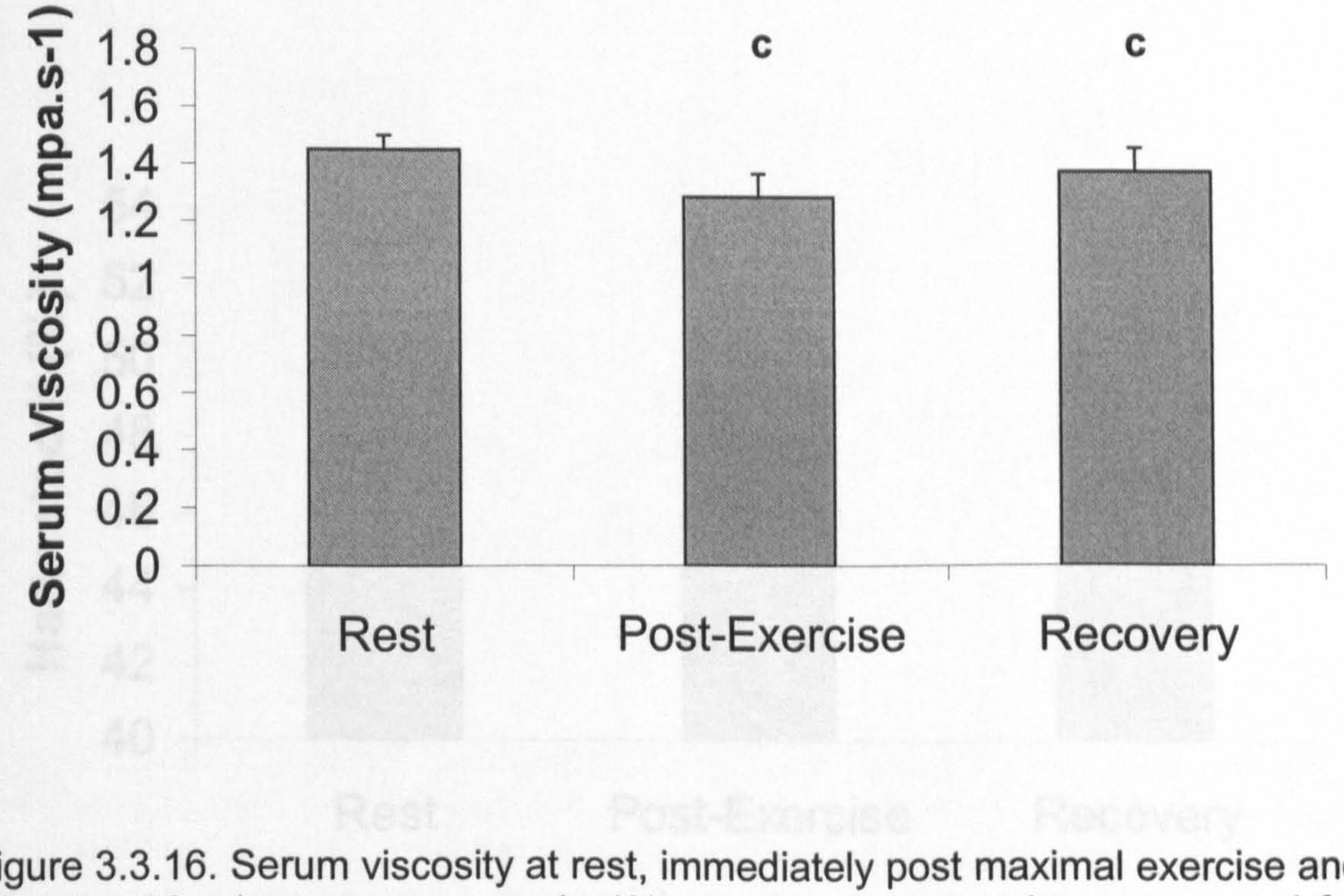


Figure 3.3.16. Serum viscosity at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

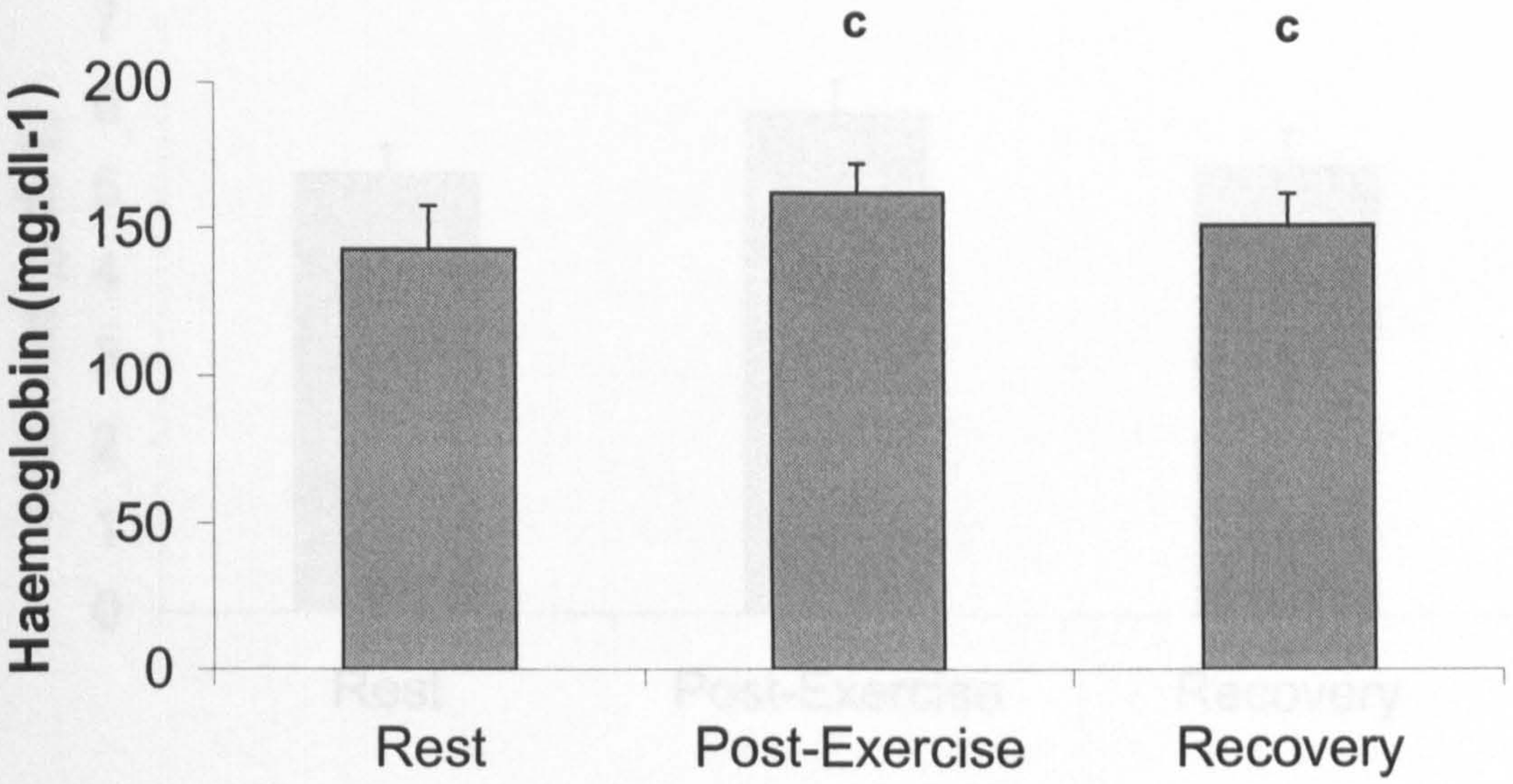


Figure 3.3.17. Haemoglobin concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

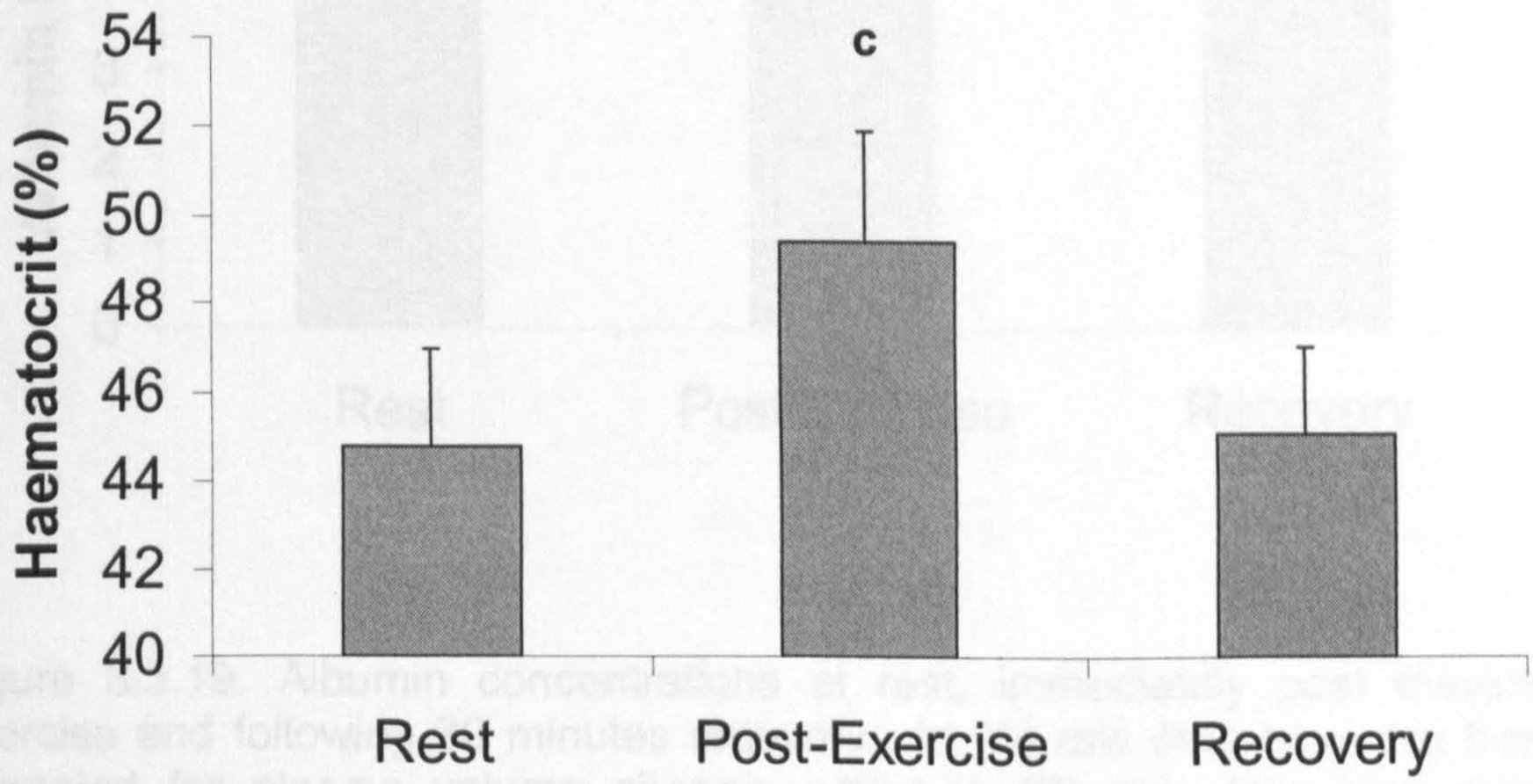
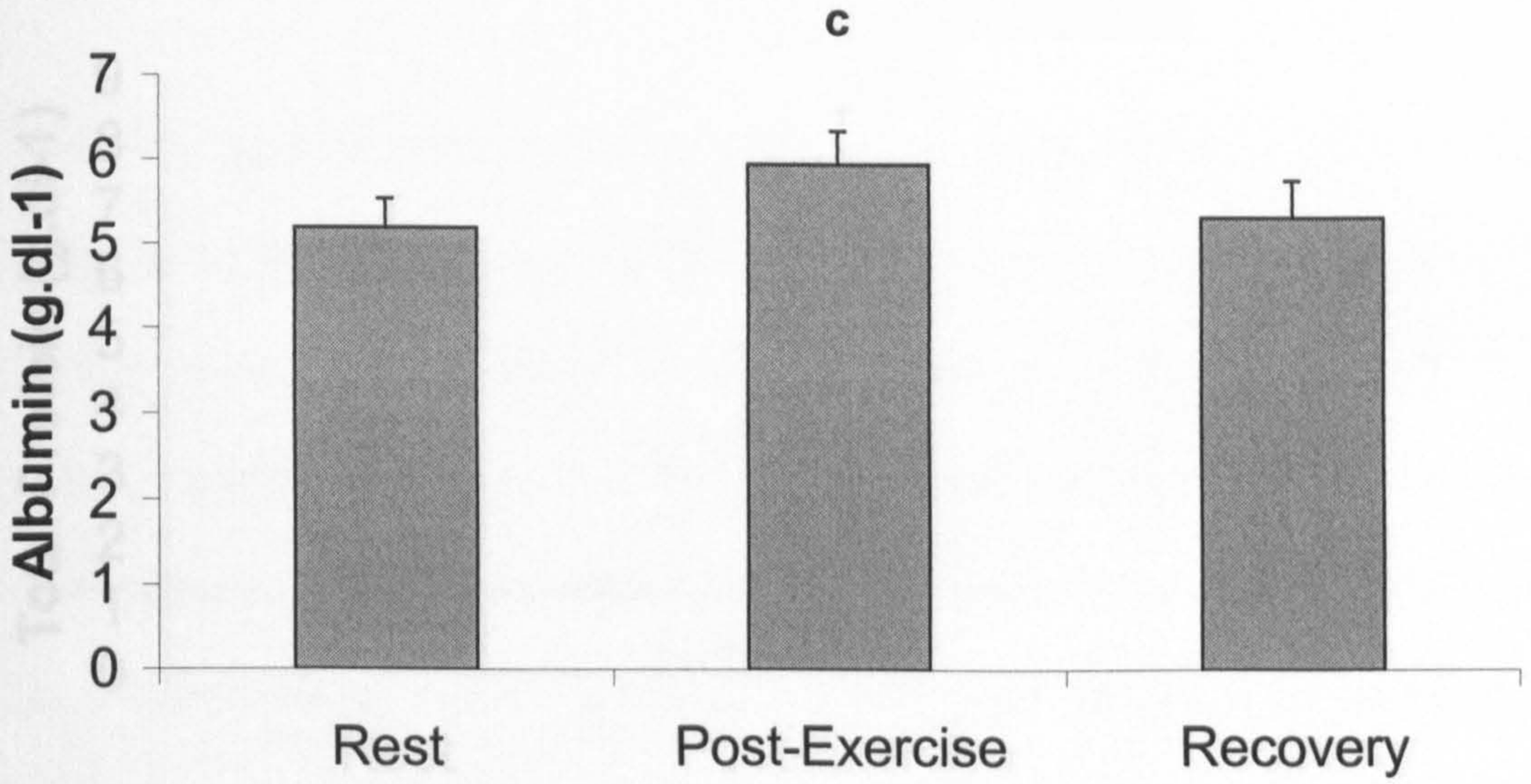


Figure 3.3.18. Haematocrit concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

A.



B.

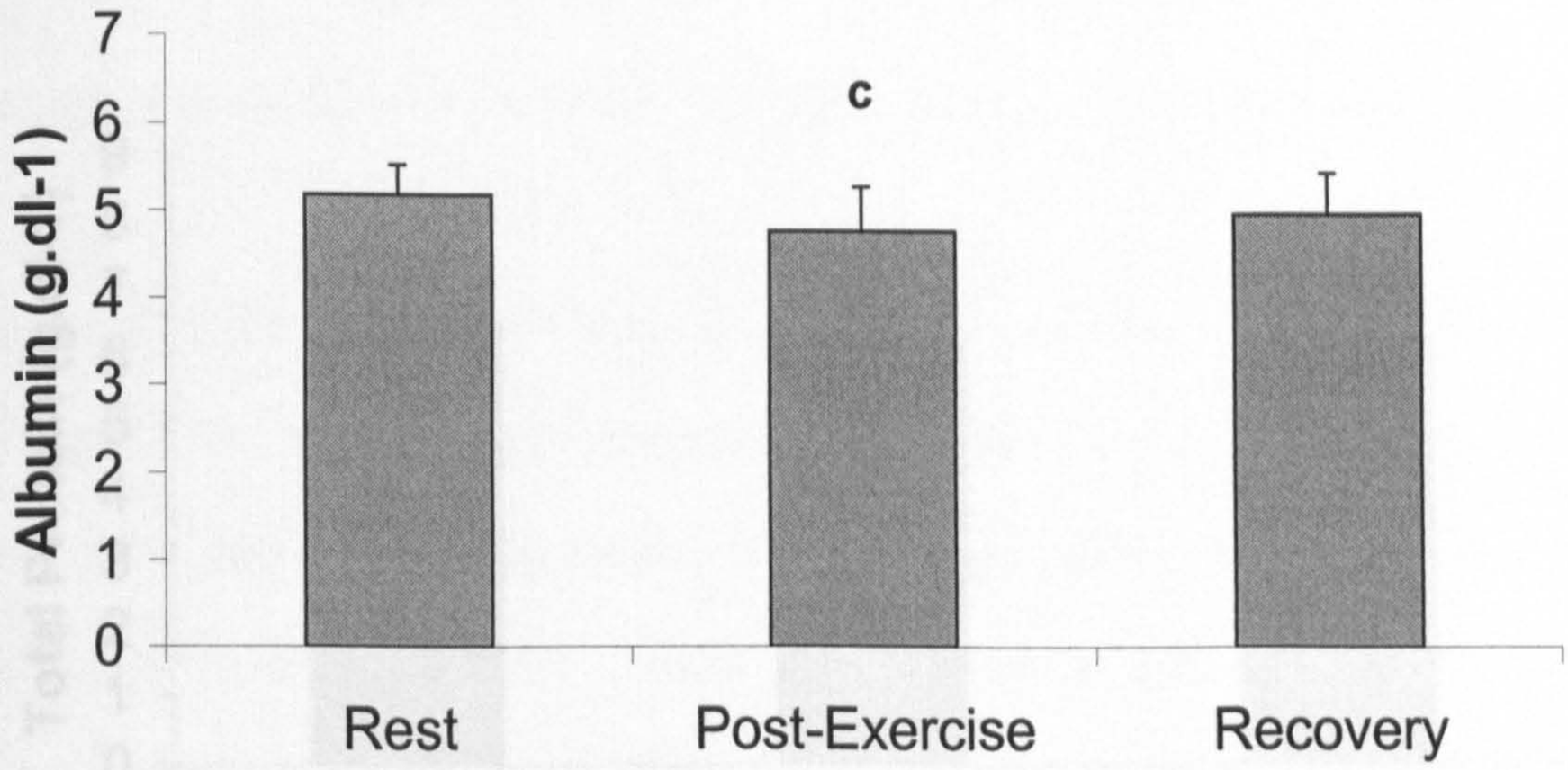
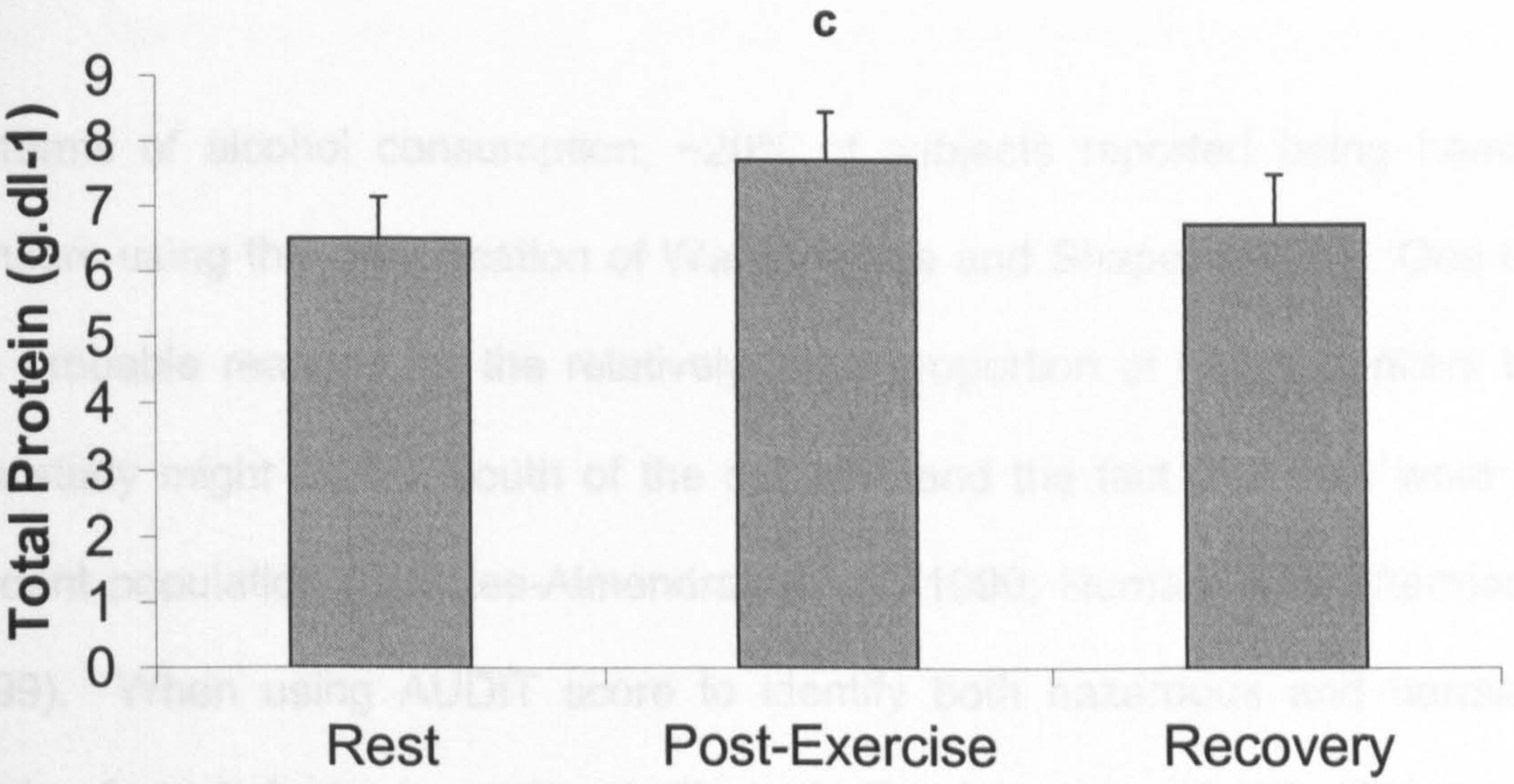


Figure 3.3.19. Albumin concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

A.



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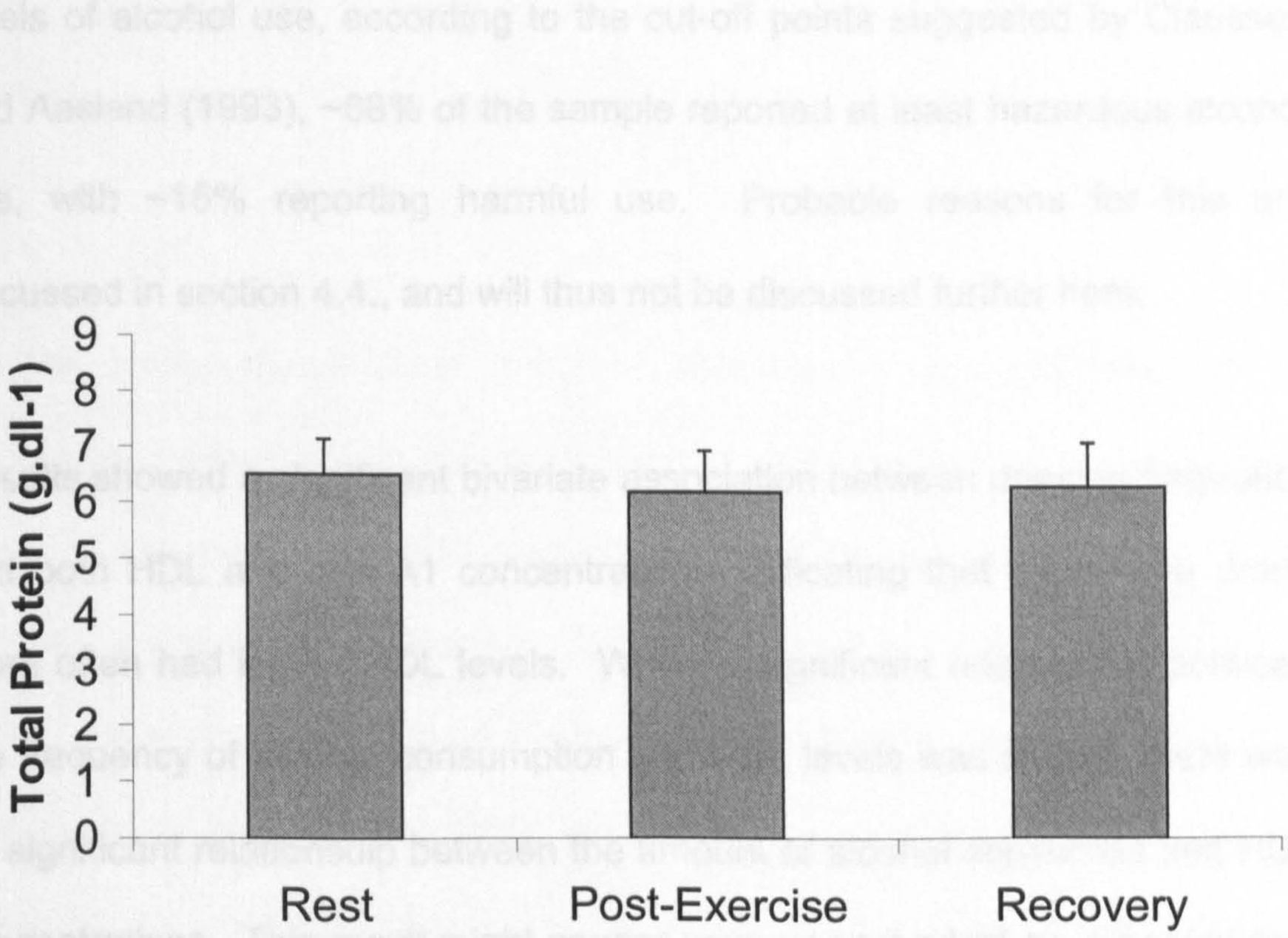

Figure 3.3.20. Total protein concentrations at rest, immediately post maximal exercise and following 30 minutes recovery. In (A) raw data have not been corrected for plasma volume change, whilst in (B) raw data have been adjusted for plasma volume change. Statistically significant differences from rest are indicated by $^{c}p<0.005$.

3.4. DISCUSSION

In terms of alcohol consumption, ~20% of subjects reported being heavy drinkers using the classification of Wanemethee and Shaper (1992). One of the probable reasons for the relatively large proportion of heavy drinkers in this study might be the youth of the subjects and the fact that they were a student population (Fuentes-Almendras et al., 1999; Humara and Sherman, 1999). When using AUDIT score to identify both hazardous and harmful levels of alcohol use, according to the cut-off points suggested by Claussen and Aasland (1993), ~68% of the sample reported at least hazardous alcohol use, with ~16% reporting harmful use. Probable reasons for this are discussed in section 4.4., and will thus not be discussed further here.

Results showed a significant bivariate association between drinking frequency and both HDL and apo A1 concentrations, indicating that those who drank more often had higher HDL levels. Whilst a significant relationship between the frequency of alcohol consumption and HDL levels was shown, there was no significant relationship between the amount of alcohol consumed and HDL concentrations. This result might appear unusual as it might be expected that those who drink more often might also consume more alcohol, although Hashimoto et al. (2001) reported similar findings, showing a significant association between drinking frequency and HDL concentration, and concluding that this association was independent of the level of alcohol consumption. It should be noted that the association between drinking frequency and HDL concentration in this study did not remain significant when

controlling for the effects of gender. In contrast, previous investigations have shown significant associations between self-reported alcohol consumption levels and blood lipid concentrations (Sillanaukee et al., 2000; Ruidavets et al., 2002). However, when alcoholic subjects were removed from the analyses in the study of Sillanaukee et al. only HDL and apo A1 remained significantly associated with alcohol consumption. Other research has also shown a significant association between alcohol consumption levels and HDL concentration (Gordon et al., 1981; Hulley and Gordon, 1981; Koppes et al., 2000), although the possible mechanisms responsible for this significant association were not alluded to.

Several investigations have indicated that one of the potential cardio-protective mechanisms of moderate alcohol consumption might occur as a result of elevated HDL concentrations when compared with light or heavy consumption (Moore and Pearson, 1986; Gaziano et al., 1993; Riemens et al., 1997). However, the results of this investigation failed to show any significant differences in HDL concentration when subjects were classified in to light, moderate or heavy alcohol consumers, or when classified according to different drinking frequencies. Furthermore, no significant differences between light, moderate and heavy alcohol consumers were observed for any of the other blood lipid variables measured. Differences between the results of this study and those of previous investigations are most likely due to the differences across subject characteristics or to other methodological differences.

No significant associations between alcohol consumption (either habitual or recent) or drinking frequency and markers of blood coagulation were shown in this sample of young, healthy adults. There was some evidence to suggest faster clotting times (as indicated by a shortened TT) in those individuals reporting greater alcohol misuse. However, if this were a true biological effect an association between alcohol misuse and fibrinogen concentration might be expected. As no such association was shown, any interpretation of the previous result must be made with an element of caution.

Another of the suggested mechanisms via which moderate alcohol consumption has been implicated in the reduction of cardiovascular risk is through a positive impact upon blood coagulation and fibrinolysis. Previous research has shown a reduction in the ability of the blood to clot with moderate levels of alcohol consumption (Goldberg et al., 1999; Agarwal and Srivastava, 2001; Schlienger, 2001). Although, others have indicated no significant alterations in blood coagulation mechanisms following the acute ingestion of a moderate dose of alcohol (El-Sayed et al., 1999a). Recent results from the Framingham Offspring Study (Mukamal et al., 2001) showed a significant association between habitual light to moderate alcohol consumption and lower plasma fibrinogen concentrations. Similarly, Dimmitt et al. (1998) also reported a reduced plasma fibrinogen concentration (as measured by thrombin clotting time) when 4 weeks of "usual" alcohol consumption was compared with 4 weeks of light alcohol consumption, in a

sample of 55 male subjects of varying ages. Thus, the results of this investigation were clearly not in agreement with those of Dimmitt et al. (1998) or Mukamal et al. (2001), as no significant differences were observed in either fibrinogen concentration or TT, when subjects were categorised as light, moderate or heavy drinkers. Differences between the results of this investigation and those of the above research again relate to differences in subject characteristics and measurement techniques.

However, this investigation showed that those individuals reporting moderate alcohol consumption exhibited significantly shortened prothrombin times. This result would appear to suggest that there is a greater potential for activation of the extrinsic blood-clotting pathway in moderate drinkers when compared to light drinkers. Similar findings were observed by Dimmit et al. (1998) who showed a significantly greater FVII concentration (as measured using one-stage prothrombin times) when alcohol intake was increased from low to "usual" levels. Dimmit et al. reported that this increase in FVII might help to compound the antifibrinolytic effect often observed in binge and heavy drinkers. This conclusion is somewhat surprising however as it could be suggested that Dimmit et al. did not measure either heavy or binge drinking per se. Furthermore, research investigating the effects of alcohol consumption on FVII levels is conflicting. Indeed Mukamal et al. (2001) showed a significant reduction in factor VII with more moderate alcohol consumption, in direct contrast to the results of this investigation and to those of Dimmit et al. (1998). Differences across studies are most likely due to

differences in the assay techniques, the classification of alcohol consumption and the subject populations.

Higher levels of recent alcohol consumption (previous weekend) were associated with elevated PAI-1 activity concentrations in this study. This indicates the potential for greater inhibition of blood fibrinolysis with high levels of recent, but not habitual, alcohol consumption. Similarly, Djousse et al. (2000) showed elevated PAI-1 activity concentrations in subjects with an alcohol intake in excess of 14g.day^{-1}, whilst Dimmit et al. (1998) also observed elevated PAI-1 concentrations when alcohol consumption was increased from low to more "usual" levels over an 8 week period. Furthermore, Numminen et al. (2000) reported elevated PAI-1 activity concentrations following a large acute dose of alcohol. The finding that recent, but not habitual alcohol consumption results in a potential inhibition of blood fibrinolysis has implications for those who "binge drink", particularly at the weekends or on special occasions, but whose habitual weekly alcohol consumption is not as high. In contrast to the results of the present study, other investigations have also shown elevated PAI-1 levels following increases in habitual weekly alcohol consumption (Yarnell et al., 2000).

Whilst the mechanism for an increase in PAI-1 activity with recent alcohol consumption is unclear, previous work has suggested that it might be related to elevations in TG concentration (Lin, 1997), as a high correlation between the two variables has been shown (Kozima et al., 1993; Dimmit et al., 1998).

This finding has led others to cautiously speculate that increased TG concentrations might result in the release of PAI-1 from the endothelium (Lin,1997), although the mechanism for this response was not alluded to. However, this theory cannot adequately explain the results of the present study as no significant correlation was observed between TG and PAI-1 activity concentrations. In addition, Dimmit et al. (1998) also reported that the significant elevation in PAI-1 concentration, shown with increasing alcohol consumption, remained even when controlling for TG levels. Thus, the exact mechanism responsible for the significant association between high recent alcohol consumption and elevated PAI-1 activity levels cannot be deduced from the data of the present study and requires further investigation.

No significant differences in PAI-1 activity concentration were shown when subjects were grouped into light, moderate or heavy drinkers. However, tPA activity concentrations were significantly elevated in moderate alcohol consumers when compared to both light and heavy drinkers. This would indicate an enhanced fibrinolytic potential in moderate alcohol consumers, a finding that might lend support to the purported links between moderate alcohol consumption and a reduction in the cardiovascular risk. Dimmitt et al. (1998) also observed an increased tPA activity concentration when weekly alcohol consumption increased from light to "usual" levels over an 8-week period. However, comparisons between the results of this study and those of Dimmit et al. (1998) must be made with caution, as it is not clear what level of consumption constituted "usual" alcohol intake in their study. The exact

mechanism responsible for significantly higher tPA activity concentrations in moderate alcohol consumers cannot be deduced from the data of the present study. Previously suggested mechanisms relating increases in tPA activity concentration with elevated TG concentrations (Dimmit et al., 1998) cannot explain the results of the present study as moderate alcohol consumers did not exhibit significantly higher TG concentrations than either light or heavy consumers.

This study showed no significant impact of either habitual or recent alcohol consumption on blood rheology. This was observed both within the bivariate analyses and when grouping subjects into light, moderate and heavy drinkers. Previous studies have also reported no significant associations between alcohol consumption and plasma viscosity (Fehily et al., 1982; Yarnell et al., 2000). In contrast, others have indicated increased plasma viscosity following acute alcohol consumption (Hamazaki and Shishido, 1983) and increased haematocrit with higher habitual consumption (Stott et al., 1991; Wanemethee and Shaper, 1994). Further studies have indicated a lower plasma viscosity in light drinkers, particularly at a drinking frequency of between 3-7 drinks per week (Mukamal et al., 2001).

Whilst this study did not show any significant effects of different drinking frequencies on plasma viscosity, individuals reporting a higher drinking frequency (>4 times per week) had elevated albumin and total protein concentrations when compared to those who drank less frequently. However,

the lack of a significant difference in plasma and serum viscosity across different drinking frequencies is perhaps confusing given the significant differences observed in albumin and total protein, which are considered two of the major determinants of plasma viscosity (El-Sayed, 1998; Carroll et al., 2000c). It should be noted however, that those individuals drinking more than 4 times per week had higher plasma and serum viscosity levels when compared to those drinking less frequently, but these differences failed to reach the assigned level of significance.

The weekly energy expended on physical activity in this investigation was 3308kcal.wk^{-1}. This level of energy expenditure is higher than has been reported in other investigations using a similar method of measurement (Leaf et al., 1997). The most probable reasons for differences between these studies are the youth of the population in this investigation and the fact that some were Sports Science students.

Subjects self-reporting a high physical activity and fitness had lower LDL and apo B concentrations. In line with these results, several previous investigations have shown reduced LDL concentrations with higher physical activity levels, across a wide range of populations (MacAuley et al., 1996; Taimela et al., 1996; Schmidt et al., 1997; Allison et al., 1999; and Pescatello et al., 2000). However, MacAuley et al. (1996) only showed a relationship between LDL concentrations and physical activity in the highest activity groups (representing the maximum physical activity) and not with habitual

activity (reflecting more consistent physical activity). Similarly, Ashton et al. (2000) reported a reduction in both LDL and apo B concentrations in those reporting a greater frequency of physical activity in a sample of 14077 female subjects. Others have also shown reduced apo B concentrations in younger subjects reporting higher physical activity (Craig et al., 1996). However, some have suggested that a significant relationship between LDL and physical activity has not been consistently demonstrated by cross-sectional, observational or randomised trial studies (for references see Taylor et al., 2002). One of the potential reasons for this is that the relationship between physical activity and LDL appears to be moderated by apolipoprotein E phenotype (Taimela et al., 1996).

Further results from this study did not show any significant associations between indicators of cardiorespiratory fitness and blood lipid concentrations. In contrast, Leaf et al. (1997) reported inverse associations between measures of cardiorespiratory fitness (as indicated by VO_{2max}) and total cholesterol, TG and LDL concentrations, although the mechanisms via which these alterations occurred was not alluded to. Differences between the results of this study and those of Leaf et al. (1997) might be explained by differences in sample size or by subject characteristics.

Results of this investigation also showed a reduction in the total cholesterol/HDL ratio in those reporting both higher vigorous physical activity and self-reported fitness. However, no significant association was shown

between cardiorespiratory fitness and HDL concentrations. This may indicate that HDL concentrations were increased more than total cholesterol concentrations in those individuals who report more vigorous physical activity. Previous results have indicated that increased physical activity is associated with an increase in HDL concentration (Marrugat et al., 1996; Wei et al., 1997; Yurgalevitch et al., 1998), although others have failed to observe this association (Fonong et al., 1996). Taylor et al. (2002) reported that whilst sports-related physical activity was significantly associated with higher HDL levels, leisure-time physical activity was not associated with any of the blood lipids measured. The results of this investigation also showed no significant effect of physical activity on blood lipid concentrations, but did show a strong trend ($p=0.06$) towards elevated HDL levels in those reporting a greater vigorous physical activity (generally related to sports performance). However, the study population of Taylor et al. (2002) was aged between 39 and 45, and the questionnaire used specifically distinguished between sport-related and leisure-time physical activity. Whilst this is an important distinction in a middle-aged population, much of the leisure-time physical activity of a younger population, particularly one containing Sports Science students, would be expected to be related to sports performance.

According to previous research, moderate intensity exercise is sufficient to produce significant increases in HDL concentrations, across a wide range of populations (Kokkinos et al., 1998; Imamura et al., 2000; Pescatello et al., 2000). However, others have reported no significant effect of moderate

intensity exercise on HDL levels (Snyder et al., 1997), with some researchers suggesting that increases in HDL concentration will only occur if the intensity of the exercise is sufficiently high. Indeed, it has been suggested that exercise that fails to generate weight loss (Fonong et al., 1996) or the expenditure of more that 1100kcal per exercise session (at 70% VO_{2max}) (Ferguson et al., 1998) will not affect HDL levels. In line with these results, Sgouraki et al. (2001) reported significantly elevated HDL concentrations following a single bout of maximal exercise. The results of this investigation clearly support the previous findings that an acute high intensity bout of exercise will significantly increase HDL concentrations, although this significant increase was no longer evident once post-exercise raw data were corrected for plasma volume changes.

In addition, maximal exercise resulted in significant increases in total cholesterol, TG and VLDL concentrations, although these differences did not remain once post-exercise raw data were corrected for plasma volume changes. Whilst a significant increase in LDL concentration was shown immediately after maximal exercise, a significant decrease was shown once post-exercise raw data had been corrected for the effects of haemoconcentration. Similarly, Crouse et al. (1995) reported significant reductions in LDL concentrations following a high intensity bout of exercise in hypercholesterolaemic men, but only when data were adjusted for changes in plasma volume. However, Davis et al. (1992) reported no significant alterations in blood lipid concentrations following acute bouts of both high

intensity (75% VO_{2max} for 60 minutes) and low intensity (50% VO_{2max} for 90 minutes) exercise, even when data were corrected for plasma volume changes. Other more recent investigations have also reported no significant effects of moderate exercise on blood lipid concentrations (Imamura et al., 2000).

This study showed no significant associations between physical activity and blood coagulation. In line with the results of this investigation, Carroll et al. (2000a) reported no significant associations between fibrinogen concentration and leisure-time physical activity or cardiorespiratory fitness. In contrast, others have shown reduced plasma fibrinogen concentrations in middle-aged subjects reporting higher levels of leisure-time physical activity (Lee et al., 1990; Folsom et al., 1991; Elwood et al., 1993). However, Lakka and Salonen (1993) reported that a reduced plasma fibrinogen concentration was only shown in those reporting greater levels of high-intensity physical activity. Whilst not observing an association with plasma fibrinogen concentration, a significant bivariate association was observed between both absolute and relative VO_{2max} and TT (but not with PT and APTT), thus indicating a lengthened blood clotting time in those with higher cardiorespiratory fitness. Lengthened thrombin time might be expected to occur in conjunction with lower fibrinogen concentrations, although results from this study did not find a significant association between cardiorespiratory fitness and plasma fibrinogen. Thus, there is some question over whether the observed

association between cardiorespiratory fitness and TT is of biological significance.

No significant associations were observed between physical activity and blood fibrinolysis. However, results showed that those individuals reporting a higher relative cardiorespiratory fitness exhibited a reduced inhibition of blood fibrinolysis, as evidenced by a lower PAI-1 activity concentration. Whilst previous data investigating physical activity and the fibrinolytic system are sparse (Scarabin et al., 1998), a similar study to this one, conducted on 21 nurses, reported no significant association between either weekly physical activity or VO_{2max} and either tPA or PAI-1 activity concentrations (Elich et al., 2000). Other larger population studies have shown significant reductions in PAI-1 activity in those reporting higher leisure-time physical activity (Eliasson et al., 1996; Scarabin et al., 1998), with possible explanations for this association relating to the impact of plasma TG and insulin concentrations on PAI-1 activity levels. In contrast to the results of this study, Eliasson et al. (1996) also showed significantly elevated tPA activity concentrations in those reporting higher leisure-time physical activity.

Maximal exercise resulted in significant alterations to blood haemostatic variables. In particular, there was a significant reduction in plasma fibrinogen concentration post-exercise, but only when raw data were corrected for the effects of exercise induced haemoconcentration. The results of this investigation agree with the findings of previous research, most notably those

of El-Sayed et al. (1999b) who also showed a significant reduction in post-exercise (both maximal and submaximal) plasma fibrinogen levels, following the correction of post-exercise raw data for the effects of plasma volume change. Exercise induced hyperfibrinogenolysis has been suggested as a possible mechanism for the observed reductions in plasma fibrinogen concentration. However, others have suggested that removal of fibrinogen from the plasma into the interstitial spaces, or an increased fibrin clot formation, might also explain these results (Martin et al., 1985). As the results of this study also showed a significant increase in D-dimer concentration following maximal exercise, there was evidence of *in vivo* hyperfibrinolysis. This might indicate an increase fibrin clot formation with maximal exercise, and thus might explain the observed reduction in fibrinogen concentration.

In contrast to the results of the present study, some research has shown significant increases in plasma fibrinogen concentrations post-exercise (Arai et al., 1990; Jooter et al., 1992; Suzuki et al., 1992), although the failure of these studies to report data corrected for exercise induced haemoconcentration might explain this discrepancy. However, other studies have failed to observe significant alterations in plasma fibrinogen concentrations following maximal exercise, even when post-exercise raw data were corrected for the effects of plasma volume change (De Paz et al., 1992; El-Sayed and Davies, 1995; Rankinen et al., 1995). Thus, it is unclear whether or not exercise causes a change in plasma fibrinogen concentration following exercise of differing intensities and duration's, in particular it is

unclear whether exercise induces a significant increase in plasma fibrinogen concentration or whether this effect is simply caused by haemoconcentration (El-Sayed et al., 1999b).

Significant shortening of APTT, PT and TT occurred following maximal exercise. Whilst the shortening of APTT is well reported following exercise (Arai et al., 1990; Bartsch et al., 1990; Handa et al., 1992; Herren et al., 1992; Molz et al., 1993; Bartsch et al., 1995; El-Sayed et al., 1995), the response of both PT and TT to exercise is less clear. Ferguson et al. (1987) has reported a significant shortening of PT following maximal treadmill exercise, although others have observed no such effect (Rocker et al., 1990; Molz et al., 1993;). El-Sayed et al. (1995) did not observe a significant effect of exercise on PT but did observe a significant shortening of TT. The results of this investigation are thus in agreement with the results of previous studies, most notably El-Sayed et al. (1995), which showed that maximal exercise resulted in an increased potential for activation of the intrinsic pathway for blood coagulation, as evidenced by a significantly shortened APTT. Results of this study also indicated that maximal exercise resulted in an increased potential for activation of the intrinsic pathway for blood coagulation, as evidenced by a significantly shortened PT. The significant reduction in thrombin time would be expected to indicate the potential for faster clot formation and hence significantly elevated fibrinogen levels. Although not significant, a 5% increase in plasma fibrinogen concentration was observed following maximal

exercise in this study, in line with previous investigations (Ferguson et al., 1979).

Activated partial thromboplastin time, PT and TT all remained significantly shortened following 30 minutes recovery, indicating the potential for a prolonged reduction in blood clotting times following maximal exercise. This finding is in line with previous research which has shown that changes in APTT persisted for 1 hour after maximal exercise (Ferguson et al., 1987), which was cautiously attributed to concomitant elevations in anaerobic metabolism. However, this is unlikely to adequately explain the results of Arai et al. (1990) who showed a significant shortening of APTT for 24 hours following a triathlon race, although potential reasons for this prolonged shortening of APTT post exercise were not alluded to.

An acute bout of maximal exercise also resulted in an enhanced potential for activation of blood fibrinolytic mechanisms, as evidenced by a significantly increased tPA activity concentration and a significantly reduced PAI-1 activity concentration. El-Sayed et al. (1995) reported that the increase in tPA following intense exercise was primarily related to the release of tPA from the vascular endothelial cells, most probably as a result of elevated adrenaline concentrations (Chandler et al., 1993). In addition, it might be that a combination of reduced PAI-1 concentration and reduced hepatic clearance of tPA (as a result of reduced hepatic blood flow) might also contribute to elevations in tPA activity post-exercise (Chandler et al., 1993). However, it is

noted that this cannot be directly inferred from the results of this study. Whilst an increase in both tPA activity and antigen have been shown following both aerobic and resistance type exercise (El-Sayed et al., 2000), results relating to the influence of acute bouts of exercise on PAI-1 activity concentrations are more conflicting. Some studies have reported no significant alterations in PAI-1 activity concentrations following exercise (Vind et al., 1993; Prisco et al., 1998), whilst others have reported significant reductions (Gough et al., 1992; Szymanski and Pate, 1994; Rankinen et al., 1995; El-Sayed et al., 1995).

Further evidence for the activation of both blood coagulation and blood fibrinolytic mechanisms following maximal exercise was indicated by significant increases in D-dimer concentration. Increases in D-dimer concentration relate to *in vivo* hyperfibrinolysis (Rijken, 1995). Thus, the results of this study would appear to indicate that maximal exercise not only increases the fibrinolytic potential but also causes an increase in fibrin formation. In particular, it would appear that maximal exercise results in an increased *in vivo* effect of plasmin, resulting in enhanced degradation of fibrin (Molz et al., 1993). Relatively few studies have examined the effect of exercise on D-dimer concentrations, although those that have tend to show either a significant increase (Molz et al., 1993; Prisco et al., 1998) or no significant change (Marsh and Gafney, 1982; Bounameaux et al., 1992) following acute bouts of exercise.

In line with the results of this investigation, both Carroll et al (2000b) and Koenig et al. (1997) reported significantly lower plasma viscosity in more physically active individuals. However, Koenig et al. (1997) reported that only leisure-time physical activity, and not work-related physical activity, was significantly related to reduced plasma viscosity. Others have reported a significantly lower plasma viscosity in trained individuals when compared to the untrained (Charm et al., 1979; Letcher et al., 1981b; Ernst et al., 1985). The favourable effects of high habitual physical activity levels on the viscosity of the blood, plasma and serum is most probably the result of a chronic expansion of the plasma volume (Koenig et al., 1997; Carroll et al., 2000b), as prolonged exercise and endurance training have previously been shown to result in significant haemodilution (Ernst, 1987; Convertino, 1991). Carroll et al. (2000b) also showed significantly lower haematocrit levels in more physically active individuals, although results from this investigation failed to support this finding.

In contrast to the results of Carroll et al. (2000b) there was no significant impact of more vigorous physical activity or indeed cardiorespiratory fitness on blood rheological variables in this study. Differences in the results of these studies was most likely due to the fact that Carroll et al. (2000b) examined a larger sample and used predicted VO_{2max} rather than a full protocol, as was used in this study. It should be noted however, that although laboratory measures of cardiorespiratory fitness were not associated with viscosity in this study, high self-reported fitness levels were associated with both lower

plasma and serum viscosity levels. Clearly, there is a difference between cardiorespiratory fitness and self-reported estimates of fitness in this study. This may indicate some degree of weakness in the single item scale used to identify self-reported fitness levels.

This study showed a significant impact of an acute bout of maximal exercise on blood rheology. As in this investigation, previous studies have shown significant increases in haematocrit and plasma viscosity following maximal exercise in both healthy individuals (Martin et al., 1985) and ischaemic heart disease patients (Toth et al., 1994). However, these studies also showed a significant increase in fibrinogen concentration following exercise, a result that was not observed in this investigation. Letcher et al. (1981b) did not observe any significant alterations in either plasma viscosity or fibrinogen concentrations following maximal graded treadmill running. In direct agreement with the results of this investigation, Jones et al. (1999) reported a significantly increased plasma and serum viscosity, but not plasma fibrinogen concentration, following both maximal and submaximal exercise. Jones et al. (1999) also observed significant reductions in these variables when post-exercise raw data were corrected for exercise induced haemoconcentration. In addition, Jones et al. showed significantly increased albumin and total protein concentrations in uncorrected data. However, in contrast to the results of this investigation, Jones et al. showed no significant differences between resting and post-exercise data following the correction for alterations in plasma volume, whereas significant reductions in both albumin and total

protein were observed in this investigation. Thus, the results of this study demonstrate that plasma and serum viscosity increase in response to an acute bout of maximal exercise in data uncorrected for plasma volume change, most probably due to a concomitant increase in plasma protein concentrations and significant haemoconcentration.

In conclusion, this study generally failed to show any beneficial effects of moderate alcohol consumption on blood lipids and blood rheology. Clearly the majority of previous research has identified a strong association between alcohol consumption and HDL concentration, across several diverse populations. However, the results of this investigation might question whether blood lipid concentrations, most notably HDL, are significantly associated with habitual alcohol consumption in a young, healthy adult population.

Moderate alcohol consumption was associated with an increased potential for blood coagulation via the extrinsic blood-clotting pathway. However results relating to blood fibrinolysis, indicated that higher alcohol consumption was associated with a decreased fibrinolytic potential as evidenced by an elevated PAI-1 activity level. In addition, those subjects reporting more moderate alcohol consumption had an elevated fibrinolytic potential, as evidenced by higher tPA activity concentrations when compared to those reporting light or heavy consumption.

This study supports previous findings showing beneficial blood lipid profiles in those individuals with higher habitual physical activity levels. However, this

study showed no significant relationship between measures of habitual physical activity and indicators of blood coagulation and fibrinolysis, although there was some evidence of a reduced inhibition of blood fibrinolysis in those with a higher cardiorespiratory fitness. Significant reductions in both plasma and serum viscosity were observed in those individuals reporting greater physical activity levels. There was also an acute modification of blood lipids, haemostasis and rheology following a single bout of high intensity exercise.

Differences between the results of studies relating to the effects of alcohol consumption and physical activity/fitness on blood haematology are most likely due to differences in the classification of alcohol consumption and physical activity, subject characteristics and assay techniques.

CHAPTER 4: STUDY 2 – ALCOHOL CONSUMPTION, PHYSICAL ACTIVITY AND PSYCHOLOGICAL WELL BEING

4.1. INTRODUCTION

There is a potential role that factors pertinent to mental health might play in the association between lifestyle and cardiovascular health and disease. Indeed, Marmot et al. (1994) clearly identified several potential links between alcohol consumption, mental health and CHD risk. However, this research failed to fully examine some of the psychological factors underlying the adoption of different alcohol consumption patterns. In particular, studies have failed to examine how the psychological factors underpinning the adoption of different alcohol consumption patterns might relate to a wider stress appraisal and coping framework; thus potentially missing out on some of the detail of this association (Guppy and Marsden, 1996).

Limited previous research has indicated that alcohol consumption might play a mediating role in the association between stress and psychological well being (Hansell et al., 1999). Several studies have observed links between alcohol consumption and coping behaviour, which might assist in the prediction of subsequent consumption patterns (Cooper et al., 1988; Abbey et al., 1993; Evans and Dunn, 1995; Laurent et al., 1997) and indeed alcohol related problems (Farber et al., 1980; Cooper et al., 1988). However, others have suggested that certain dispositional characteristics of the individual might be more important in predicting psychological well being (Haynes and Ayliffe, 1991; Seeman and Seeman, 1992; Williams and Clark, 1998) and that, as a result, the proposed relationships between alcohol consumption patterns and psychological well being might be coincidental rather than causal. Thus, there is a need for further investigation to examine the

interrelationships among alcohol consumption, psychological well being and potential mediators of this association, such as coping, mastery, personality and other individual differences.

Previous investigation has shown that physical activity has a positive impact on psychological well being (Paffenbarger et al., 1994; Yeung and Hemsley, 1997). Importantly, recent attempts have been made to place physical activity in the wider context of stress and coping processes, as reviewed by Rostad and Long (1996). Whilst several of the reviewed investigations highlighted the potential importance of such strategies in coping with stress, none of them incorporated measures of stress appraisal and coping processes in sufficient detail (Sale et al., 2000). Limited investigation has indicated that exercise may have benefit to the individual as it is positively linked with the use of more problem-focussed coping strategies (Rick and Guppy, 1994; Ingledew et al., 1996). Although others have again reported that dispositional characteristics of the individual might be more important in defining associations between physical activity and enhanced feelings of psychological well being (Yeung and Hemesley, 1997; Courneya and Hellsten, 1998; Sale et al.; 2000).

Thus, it is clear that whilst research has identified some significant links among alcohol consumption, physical activity and aspects of psychological well being, few studies have fully examined these associations in sufficient detail or alongside wider stress appraisal and coping processes. As such, there is a need to further investigate the complex associations among health-related behaviours and psychological well being, particularly with reference to

the use of more general coping strategies. There is also a need to examine these associations alongside important dispositional characteristics of the individual and other individual differences, which some have reported to be more important in the prediction of psychological well being.

4.1.1. Aim of the Study

Therefore, the specific aim of this investigation was to examine the prediction of psychological well being from selected health related behaviours, coping strategies, dispositional characteristics of the individual and other individual differences. A further aim of the present study was to expand upon previous research identifying associations among alcohol consumption and misuse, physical activity and the use of more general coping strategies, whilst again considering the potential effects of dispositional characteristics of the individual and other individual differences.

4.2. MATERIALS AND METHODS

4.2.1. Questionnaire Design and Procedure

A longitudinal research design was utilised in this study. Data were collected using self-completed questionnaires (appendix B) comprising, in the main, pre-published, validated and reliable public domain scales (see section 4.2.2.). The questionnaire design was informed by previous questionnaires relating to psychological well being in certain occupational groups (such as Brough, 1998).

In total there were two administrations of the same questionnaire spanning a one-year period, each administration was conducted between weeks 4-10 of each academic year. Questionnaires were administered in a supervised classroom setting post-lecture and thus, all respondents were students from Liverpool John Moores University. The sample was drawn from several different academic disciplines, including Sports Science, Health Science, Applied Psychology, Pharmacy, Engineering and Maritime Studies. The response to the questionnaire was voluntary and subjects were given written assurance that all individual responses would be treated anonymously and confidentially.

Respondents were asked to complete the questionnaire in silence, with no assistance from those sitting close to them. Respondents were also asked to provide their honest personal experiences relating to each question and were instructed to read each question carefully before answering.

At three separate stages in the development of the questionnaire, following significant changes in format, the questionnaire was piloted to ~30 respondents. On each occasion the comments made were used to slightly alter the wording of the questionnaire to make it more understandable to the target sample.

4.2.2. Materials

4.2.2.1. Section 1: Statistical Information

Information on age, gender, marital status, number of children, ethnic origin, religion, current employment, parents occupations, and educational background were obtained. This data was used as a tool for statistical comparison.

4.2.2.2. Section 2: Coping in General Life

The coping instrument used was the 20-item version of the Cybernetic Coping Scale (Edwards and Baglioni, 1993) with an additional 4 items from the Ways of Coping Check-List (Lazarus and Folkman, 1984). The combined 24-item scale provides information relating to the use of six general coping strategies. Each item was graded on a five point Likert scale (ranging from 'never' [coded as 1] to 'always' [coded as 5]), according to how often the respondent used a particular method to cope with the problems in their general life. Thus, a high score on each of the sub-scales indicates a high use of that specific coping strategy.

The 20-item Cybernetic Coping Scale (CCS) was developed from the cybernetic theory of stress, coping and well being (Edwards, 1988; 1992; Edwards and Cooper, 1988) which identifies stress as developing through a discrepancy between the perceived state and the desired state of the individual. The role of coping is seen as an attempt by the individual to reduce the negative effects of stress on psychological well being. This scale examines two main functions of coping: emotion focused coping and problem focused coping. These two coping functions can be further divided in to five coping factors relating to changing the situation (items 1, 7, 13, and 19), accommodation (items 2, 8, 14, and 20), devaluation (items 3, 9, 15, and 21), avoidance (items 4, 10, 16, and 22), and symptom reduction (items 5, 11, 17, and 23).

The original version of the CCS comprised 40-items. However, Edwards and Baglioni (1993) recommend the use of the 20-item version as it provides a valid representation of the cybernetic theories of coping, with little, if any, loss of information over the full 40-item version. The shorter nature of the scale also makes its use more viable with large survey based questionnaires such as the one employed by this study. Edwards and Baglioni (1993) reported that the reliability data for all scales measured in their study, including both 40 and 20 item variations, were 0.79 or higher. Cronbach's alpha coefficients yielded by this study (administrations 1 and 2 respectively) generally support the high internal consistency of the scale. Only the accommodation coping sub-scale produced a Cronbach's alpha coefficient of below 0.60

(administration 1). Cronbach's alpha coefficients for each of the sub-scales, following both administrations 1 and 2 respectively, were changing the situation 0.72 and 0.73; accommodation 0.57 and 0.61; devaluation 0.81 and 0.82; avoidance 0.78 and 0.75; symptom reduction 0.64 and 0.74.

The addition of four items from the Ways of Coping Checklist (WCCL) was used as a measure of the influence of social support as a coping strategy (items 6, 12, 18, and 24). The Cronbach's alpha coefficients yielded for the additional 4 items of the WCCL, representing the seeking of social support, were 0.72 and 0.79 from administrations 1 and 2 respectively. This is somewhat higher than the figure reported by Edwards and Baglioni (1993) who reported the internal consistency of the sub-scale as being 0.65, although this was based on the 6-item rather than the 4-item version of the sub-scale.

4.2.2.3. Section 3: Personal Control

A 7-item scale measuring mastery (Pearlin and Radabaugh, 1976) was included in the questionnaire in an attempt to identify perceived individual psychological control. This scale asks respondents to identify their level of agreement with each item using a four point Likert scale ranging from "strongly agree" (coded as 1) to "strongly disagree" (coded as 4). Thus, a high score on each item of this scale represented a greater degree of personal mastery, with items 6 and 7 being reverse scored.

Studies providing measures of the internal consistency of this scale have shown that the mastery scale devised by Pearlin and Radabaugh (1976) is psychometrically acceptable in terms of its internal consistency (Folkman et al., 1986; Thoits, 1987; Franks and Faux, 1990; Huyck, 1991). These studies have reported Cronbach's alpha coefficients of 0.74, 0.75, 0.78 and 0.80 respectively. The Cronbach's alpha coefficients of 0.72 and 0.79 that were reported from administrations 1 and 2 respectively lends support to the previous research reporting the good reliability of this scale.

4.2.2.4. Section 4: Well being in University Life

4.2.2.4.1. Section 4(a):

A 12-item scale incorporating adjectives designed to measure affective psychological well being (Warr, 1990b) was included in the questionnaire. The scale is based upon the two affective well being axes reported by Warr (1990b); namely anxiety-contentment (items 1-6) and depression-enthusiasm (items 7-12). The scale was made relevant to university students by asking them to indicate how often the respondent had felt the way the items described over the past few weeks at university. Respondents were asked to rate each of the 19-items along a 6-point Likert scale ranging from "never" (coded as 1) to "all of the time" (coded as 6). A high score thus indicates a greater perception of affective psychological well being with items 1, 2, 3, 7, 8, 9 being reverse scored.

Warr (1990b) reports Cronbach's alpha coefficients as 0.76 for anxiety-contentment and 0.80 for depression-enthusiasm, thus indicating a high

degree of internal consistency within the scale. However, an improved internal consistency within the scale was shown by this investigation with data yielding Cronbach's alpha coefficients of 0.87 and 0.91 for the anxiety-contentment sub-scale and 0.85 and 0.86 for the depression-enthusiasm sub-scale. Thus, reliability data from this study are in agreement with those reported by Sevastos et al. (1992) who also indicated a slightly improved reliability of the scale (0.82 for anxiety-contentment and 0.85 for depression-enthusiasm) from their sample of 3004 respondents.

4.2.2.4.2. Section 4(b):

A 16-item scale was incorporated in to this questionnaire to examine how each respondent had felt about their college work over the past few weeks. The scale used was developed by Warr (1990b) and comprised items relating to job competence (items 1-6), job aspiration (items 7-12), and negative job carry-over (items 13-16). Once again this scale was slightly altered to make it relevant to university students. This was achieved by substituting the word "job" for the words "academic work" in each of the 16 items. Although the scale was not re-validated following this change of wording, the original 1990 scale was designed as a means of measuring both job-related and non job-related well-being and was found to be psychometrically acceptable (Warr, 1990).

Each respondent was asked to indicate their degree of agreement with each item along a 5-point Likert scale ranging from "strongly disagree" (coded as 1)

to "strongly agree" (coded as 5). Items 3, 4, 5, 7, 9 and 10 were reverse scored.

A relatively high internal consistency was reported by Warr (1990b) for each of the sub-scales with Cronbach's alpha coefficients of 0.68 (job competence), 0.62 (job aspiration), and 0.78 (negative job carry-over). In this study data yielded similar Cronbach's alpha coefficients (0.65 and 0.67 for job competence; 0.59 and 0.59 for job aspiration; 0.80 and 0.81 for negative job carry over) to those of Warr (1990b).

4.2.2.5. Section 5: General Feelings

The 12-item improved short scale of extroversion (items 1, 3, 5, 7, 9 and 11) and neuroticism (2, 4, 6, 8, 10 and 12) from the Eysenck Personality Inventory was included in the questionnaire (Eysenck and Eysenck, 1964). The revised 12-item short version of the scale (Eysenck et al., 1985) asks respondents to indicate the extent to which each of the 12 items generally applied to the way in which they usually acted or felt. Responses were graded along a 4-point Likert scale ranging from "almost never" (coded as 1) to "almost always" (coded as 4). This scale indicated a good reliability for both the extraversion sub-scale (0.72 and 0.76 from questionnaire administrations 1 and 2 respectively) and for the neuroticism sub-scale (0.60 and 0.66 from questionnaire administrations 1 and 2 respectively).

4.2.2.6. Section 6: General Psychological Well Being

Well being in general life was assessed using the 12-item version of the General Health Questionnaire (GHQ-12), which provides a context-free measure of psychological well being. The GHQ is a well-known and extensively validated screening questionnaire for functional psychiatric illness (Goldberg, 1972; 1978). Although originally designed as a self-administered screening instrument for the detection of minor functional psychiatric illness among patients in a clinical setting; the GHQ (in both its 12 and 30 item variations) has been successfully applied as an indicator of mental health in other settings (Banks et al., 1980; Goodchild and Duncan-Jones, 1985; Marmot et al., 1993; Moyle, 1995; Parker et al., 1995).

Each respondent was asked to indicate their general level of health over the past few weeks, with the emphasis being placed upon recent health issues and not those concerning the past. Participants chose one of four possible alternatives to indicate their response to each of the 12 items. The four alternatives for items 1, 3, 5, 7, 9, and 11 were "better than usual "," same as usual "," less than usual", or "much less than usual". Whereas the four alternative responses for items 2, 4, 6, 8, 10, and 12 were "not at all", "no more than usual", "rather more than usual", or "much more than usual". Thus, a high score on the GHQ-12 indicates a lower state of psychological well being.

The GHQ has been used in several different formats including 12, 20, 30, 60, and 140 item variations. Due to the number of scales already included in this

questionnaire the smaller 12-item version of the GHQ was utilised as the shorter nature of the scale makes its use more viable with large survey based questionnaires, such as the one employed by this study.

Although shorter, the GHQ-12 remains a valid and reliable scale and has been successfully utilised by other researchers (Parkes, 1991; Daniels and Guppy, 1992; 1994; West and Reynolds, 1995; Guppy and Weatherstone, 1997). Furthermore, the internal consistency of the GHQ-12 is high, with Cronbach's alpha coefficients ranging from 0.80 to 0.90, as reported by several authors (Banks et al., 1980; Moyle, 1995; Parker et al., 1995). In addition, this study supports the high internal consistency previously reported for the GHQ-12, yielding Cronbach's alpha coefficients of 0.87 and 0.88 from administrations 1 and 2 respectively.

4.2.2.7. Section 7: Opinion of Self

The opinion respondents held about themselves was assessed using a ten item measure of self-esteem (Rosenberg, 1965). In this instance self-esteem can simply be seen as an individuals general perception of self-worth. Thus, respondents were asked to indicate their level of agreement with each of the 10 items relating to views people generally hold about themselves ("I feel that I'm a person of worth, at least on an equal basis with others" or "I take a positive attitude towards myself"). The respondents level of agreement with each of the items was assessed along a 4-point Likert scale ranging from

"strongly agree" (coded as 1) to "strongly disagree" (coded as 4), with items 1, 2, 4, 6 and 7 being reverse scored.

This is a well established and reliable scale with reports from large survey based studies indicating a high internal consistency for the scale. For example, Cooper et al. (1990) reported a coefficient alpha of 0.85, a finding which was supported by the data from this study which yielded Cronbach's alpha coefficients of 0.87 and 0.88 from questionnaire administrations 1 and 2 respectively.

4.2.2.8. Section 8: Coping and Life Events

4.2.2.8.1. Section 8(a)

This section was included in the questionnaire in an attempt to identify any major stressful events occurring in the respondents' life over the last year. The section simply asked the respondent to identify and briefly describe up to three events occurring within their lives over the last year that they have found stressful or difficult. This section was incorporated in to the questionnaire to provide a more detailed assessment of whether the stressful life events experienced by respondents in the previous year.

4.2.2.8.2. Section 8(b)

In this section respondents were simply asked to indicate whether they thought they had successfully coped with the stressful life events previously

listed. This section then further asked the respondent to list what method they thought they had used to cope with these stressful events. Again this section was incorporated in to the questionnaire to provide a more detailed assessment of how the individual had coped with any major stressful life events and how they had seen themselves coping with these events.

4.2.2.9. Section 9: Alcohol Consumption

4.2.2.9.1. Section 9(a):

The Alcohol Use Disorders Identification Test (AUDIT) was developed by the World Health Organisation (WHO) as a means of identifying individuals whose alcohol consumption had become harmful or hazardous to their health. The AUDIT was originally designed for use as a screening tool to detect harmful and hazardous alcohol consumption in primary health care settings (Saunders and Aasland, 1987; Babor et al., 1989), although it has been utilised for the detection of problem drinking in other populations, such as college students (Fleming et al., 1991), service industry personnel (Larsen, 1994) and the long-term unemployed (Claussen and Aasland, 1993). The 10-item AUDIT is a sensitive indicator of hazardous alcohol intake (Saunders et al., 1993) and alcohol abuse and dependence (Fleming et al., 1991; Claussen and Aasland, 1993a; 1993b).

The 10-item scale measures the frequency of drinking and alcohol intake (items 1-3), symptoms of alcohol dependence (items 4-6), adverse reactions to alcohol consumption (items 7-8), and signs of harmful alcohol use (items 9-10). Each of these items were graded along a 4-point scale, yielding a final

total of between 0 and 40. Several conflicting cut-off scores for hazardous and harmful alcohol consumption have been suggested. Originally when AUDIT was devised a cut-off score of 11 was recommended, with a person yielding a final score of 11 or above being classified as a positive case (Saunders and Aasland, 1987). However, Babor et al. (1989) recommended a lower cut-off score of 8 in order to fall in line with reductions in the recommended safe drinking limits. Claussen and Aasland (1993) used two further cut-off points of 8-9 to indicate hazardous consumption and 18-19 to indicate harmful consumption. For a more detailed review of choosing a cut-off score for the AUDIT questionnaire see Conigrave et al. (1995).

This study shows the AUDIT questionnaire to be a reliable scale, with Cronbach's alpha coefficients being 0.81 and 0.83 for questionnaire administrations 1 and 2 respectively.

4.2.2.9.2. Section 9(b):

This section was included in the questionnaire in an attempt to provide more information relating to individuals who did not drink. Thus, the first item incorporated here distinguishes between those respondents who have never consumed alcohol and those individuals who are ex-drinkers. The second and third items assess how long a respondent had not consumed alcohol for and how long the respondent was consuming alcohol before stopping. The final item asks the reason for the cessation of consuming alcoholic beverages.

4.2.2.9.3. Section 9(c):

This section was designed as a means of gaining more detailed information concerning the alcohol consumption patterns of the respondents. The section contains items regarding the respondents typical alcohol consumption over a 7-day week, their alcohol consumption on the Friday, Saturday, and Sunday of the last weekend, and their typical weekends alcohol consumption (Friday, Saturday, Sunday). Respondents were asked to report both the type and amount of alcoholic beverage consumed. These data were then converted to represent the units of alcohol consumed.

4.2.2.10. Section 10: Alcohol Expectancies

The scale used in this investigation assessed positive alcohol expectancies with the use of the abbreviated version of the Alcohol Effects Questionnaire (AEQ) (Rohsenow, 1983). This scale incorporated 6-items designed to examine a combination of six sub-scales, assessing expectancies for global positive effects of alcohol consumption, social and physical pleasure, sexual enhancement, aggression and power, social expressiveness, and relaxation and tension reduction in to a single six-item scale. Respondents assessed each of the six items on a two-point scale with the statements being rated as either true (coded as 2) or false (coded as 1). Thus, a high score relates to the perceived positive expectancies of alcohol and a low score relates to the perceived negative effects of alcohol.

Cooper et al. (1990) report the successful application of the abbreviated version of the AEQ to a large random sample of 1933 household residents in the USA. From this sample Cooper et al. (1990) reported the high internal consistency of the abbreviated AEQ, yielding a coefficient alpha of 0.82. However, data from this study only showed a relatively high internal consistency for the scale, with coefficient alphas for administrations 1 and 2 being 0.59 and 0.62 respectively.

4.2.2.11. Section 11: Alcohol Consumption and Coping

The consumption of alcohol as a means of coping was assessed using the drinking to cope scale of Polich and Orvis (1979). This is a 6-item scale whereby respondents report the frequency with which they use alcohol to cope with or to manage negative emotions ("to cheer up when you're in a bad mood" or "to help when you feel depressed and nervous"). Each of the 6 items were assessed along a 4-point frequency scale ranging from "almost never" (coded as 1) to "almost always" (coded as 4).

Cooper et al. (1990) report a coefficient alpha of 0.80 for this scale indicating the scale is a reliable measure with a high internal consistency. Data from this study also yielded high Cronbach's alpha coefficients of 0.82 and 0.87 respectively, thus supporting the existing reliability data for this scale.

4.2.2.12. Section 12: Physical Characteristics, Physical Activity and Smoking

In this section respondents were asked to provide some general information concerning their physical activity patterns. The section asked respondents for their height and weight, allowing for the computation of a body mass index score. The next six items asked respondents specific questions concerning their physical activity. Respondents were asked to rate both their activity levels and fitness along a 4-point Likert scale, with responses ranging from "sedentary" (coded as 1) to "highly active" (coded as 4) for the physical activity item and from "unfit" (coded as 1) to "very fit" (coded as 4) for the fitness item. These two single item scales were based on scales previously presented in BASES physiology testing guidelines (Bird and Davidson, 1997). In addition, respondents were asked what activities they did on a regular basis, how often they did them for and how many workout sessions they completed per week, based on recommendations made by Kriska and Caspersen (1997).

Smoking was assessed as a dichotomous variable with subjects reporting either "yes" (coded as 1) or "no" (coded as 2) to the question 'do you smoke'?. Further detail on the smoking habits of respondents was gained from additional items referring to how many cigarettes the respondents smoke, how often they smoke and what brand of cigarettes they smoke.

The final two questions on this scale referred to the subjects' general feeling of psychological well being over the last 12 months. These two items were

included as a subsidiary to the GHQ-12, which asked respondents about general well being over the past few weeks. The items asked whether respondents had been feeling unhappy and depressed and if they have been losing confidence in themselves over the last 12 months. Both items were assessed as a dichotomous variable with subjects reporting either "yes" (coded as 1) or "no" (coded as 2) to each of the questions.

4.2.3. Statistical Analyses

All data are presented as mean±SD and statistical significance was accepted at the $p<0.05$ level for all tests. Bivariate correlation analysis was used to examine the inter-relationships among alcohol consumption, physical activity and psychological well being and its correlates.

Hierarchical multiple regression analyses (MRA) were used in the prediction of general well-being, drinking to cope, alcohol consumption, alcohol problems, fitness and activity. Both step and final beta weights were reported, with a procedure of listwise deletion being employed to account for missing data.

4.3. RESULTS

4.3.1. Questionnaire Administration 1

4.3.1.1. Sample Description

A total of 894 questionnaires were administered, with 524 being returned (a response rate of 59%). However, 42 of these respondents were excluded from this sample as they provided insufficient information on a large portion of the questionnaire. Thus, statistical analyses were performed on a sample of 482 respondents. Of the 482 respondents 270 were male and 206 were female (6 respondents did not report gender). The age of the sample (mean±S.D.) was 25±7 years, with average height and bodymass of the sample being 173±45 cm and 69±13 kg respectively.

In terms of the domestic status of the sample, 67% of the sample were single, 22.4% of the sample were in a steady relationship, 8.3% of the sample were married, 1.5% of the sample were either divorced or separated and 0.2% of the sample were widowed. A further 0.6% of the sample failed to report domestic status. Four hundred and forty-four (92%) of the respondents reported having no dependent children and 35 (7%) reported having children, with 3 (1%) providing no data. Of the 35 respondents with children, 16 (46%) had 1 child, 14 (40%) had 2 children, 4 (11%) had 3 children and 1 (3%) had 4 children.

In terms of the ethnicity of the sample, 82% of the sample were Caucasian, 2.3% of the sample were Asian, 0.6% were Oriental, 0.6% were Afro-Caribbean and 12.7% of the sample reported some other ethnic origin. A further 1.8% of the sample failed to report ethnic origin. Of the respondents, 349 (72%) reported having no practicing religion and 128 (27%) reporting a practicing religion, with a further 5 (1%) providing no data.

Data relating to the typical drinking patterns of the sample showed that 6.8% of the sample reported that they were non-drinkers, a further 6.8% reported drinking monthly or less, 18.3% reported drinking 2-4 times per month, 43.6% reported drinking 2-3 times per week and 24.1% of the sample reported drinking 4 or more times per week. A further 0.4% failed to provide a response to this question.

In terms of the smoking habits of the respondents, 86 (17.8%) of the sample were smokers and 383 (79.5%) of the sample were non-smokers. Thirteen (2.7%) respondents failed to report smoking status.

In terms of physical activity 6% reported being sedentary, 34% moderately active, 37% active and 20% highly active. Three percent of the sample failed to report on their physical activity. With respect to self-reported fitness, 12% of the sample reported being unfit, 41% moderately fit, 34% fit and 10% very fit. Again 3% of the sample did not report their fitness.

4.3.1.2. Scale Descriptive Statistics

Scale means ± SD, as well as measures of internal consistency (Cronbachs alpha), are presented for each of the scales employed in statistical analyses (Table 4.3.1.). As can be seen, the majority of the scales have acceptable levels of internal consistency, with accommodation coping (α=0.57) being the lowest.

4.3.1.3. Bivariate Analyses

4.3.1.3.1. Health Related Behaviours in Relation to Psychological Well Being

No significant correlations were shown among alcohol consumption, physical activity and smoking. Habitual alcohol consumption was negatively correlated with the use of the changing the situation as a coping strategy ($r=-0.10$, $p<0.05$) and positively related to the use of both avoidance ($r=0.10$, $p<0.05$) and symptom reduction ($r=0.11$, $p<0.05$) as coping strategies. Habitual alcohol consumption was also positively correlated with AUDIT score ($r=0.23$, $p<0.005$) and negatively correlated with alcohol expectancies ($r=-0.14$, $p<0.01$), although no significant association was shown between habitual alcohol consumption and the reported use of drinking to cope. Furthermore, habitual weekly alcohol consumption was not significantly correlated with GHQ-12 score or anxiety-contentment and depression-enthusiasm scores. Thus, no association between alcohol consumption and measures of psychological well being were shown in this study. However, there was a significant positive correlation between alcohol

consumption at the weekend and anxiety-contentment ($r=0.14$, $p<0.01$). This would indicate that those who "binge" on alcohol at the weekends, but whose weekly alcohol consumption might not be as high, tend to report a greater sense of affective psychological well being.

Higher levels of physical activity were significantly associated with a greater use of both changing the situation ($r=0.14$, $p<0.01$) and symptom reduction ($r=0.15$, $p<0.005$) coping strategies. In contrast, those who reported higher physical activity levels reported reduced use of avoidance coping strategies ($r=-0.11$, $p<0.05$). In terms of general psychological well being, results indicated that those reporting higher physical activity levels also reported a greater sense of psychological well being ($r=-0.18$, $p<0.005$). Results also showed a positive correlation between physical activity and the general state of happiness ($r=0.13$, $p<0.01$) and confidence ($r=0.12$, $p<0.05$) over the preceding 12 months. Similarly, high levels of physical activity were positively associated with an increased sense of affective well being, on both the anxiety-contentment ($r=0.13$, $p<0.01$) and depression-enthusiasm scales ($r=0.24$, $p<0.005$). Furthermore, those individuals with higher habitual activity levels also reported a greater sense of self-esteem ($r=0.20$, $p<0.005$).

Smoking was not significantly correlated with any of the more general coping strategies. Similarly, no significant correlations were shown between smoking and general psychological well being, although there was a significant negative

correlation between smoking and anxiety-contentment (r=-0.12, p<0.05), indicating that respondents who smoked had a lower sense of affective psychological well being.

4.3.1.3.2. Individual Differences, Dispositional Characteristics of the Individual and Health Related Behaviour

With respect to individual differences in health behaviour, males reported significantly higher self-reported physical activity (r=-0.12, p<0.01) and fitness levels (r=-0.17, p<0.005) than females. However, there was no significant correlation between gender and habitual weekly alcohol consumption, although males reported a significantly greater alcohol consumption over a typical weekend (r=-0.12, p<0.005). No significant correlation was shown between smoking and gender, although females did report smoking more (r=0.15, p<0.05) and for longer (r=0.20, p<0.005).

There were no significant correlations between weekly alcohol consumption and either extraversion or neuroticism. However, there was a significant positive correlation between alcohol consumption at the weekend and extraversion (r=0.14, p<0.01). Habitual physical activity was positively correlated with extraversion (r=0.17, p<0.005) and negatively correlated with neuroticism (r=-0.19, p<0.005), indicating that extraverts tend to be more physical active. There was no significant relationship between smoking and either extraversion or

neuroticism, although there was a significant positive correlation between neuroticism and the amount of cigarettes smoked per week ($r=0.22$, $p<0.005$).

4.3.1.3.3. Individual Differences, Dispositional Characteristics of the Individual, Coping and Psychological Well Being

In terms of the relationships between gender and psychological well being, there was a significant positive correlation between gender and GHQ-12 score ($r=0.15$, $p<0.005$), showing that males reported a significantly higher sense of well being in general life. Males also reported a higher degree of affective psychological well being on the anxiety-contentment scale ($r=-0.12$, $p<0.005$), with no significant correlation shown between gender and depression-enthusiasm.

Females reported more frequent seeking of social support as a coping strategy ($r=0.10$, $p<0.05$). No further significant correlations were observed between gender and any of the other more general coping strategies. Both extraversion ($r=-0.26$, $p<0.005$) and neuroticism ($r=0.51$, $p<0.005$) were significantly related to GHQ-12 score, thus indicating that extroverts reported an enhanced sense of general psychological well being. These relationships remained significant even when controlling for the effects of gender (extraversion: $r=-0.27$, $p<0.005$; neuroticism: $r=0.52$, $p<0.005$). Similarly, extraversion was positively related to both anxiety-contentment ($r=0.28$, $p<0.005$) and depression-enthusiasm ($r=0.45$, $p<0.005$) scores, whilst neuroticism was negatively related to both anxiety-

contentment (r=-0.46, p<0.005) and depression-enthusiasm (r=-0.51, p<0.005) scores. Thus, those reporting high extraversion reported greater general and affective psychological well being whilst those reporting high neuroticism reported a reduced sense of affective well being.

Several significant associations were observed between elements of personality and the use of more general coping strategies. In particular, extraversion was positively correlated with the use of both symptom reduction (r=0.23, p<0.005) and seeking social support (r=0.18, p<0.005) as coping strategies, whilst neuroticism was negatively correlated with the use of changing the situation as a coping strategy (r=-0.10, p<0.05).

Table 4.3.1. Scale descriptive statistics and bivariate correlation coefficients for questionnaire administration 1

Alphas	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1. Age	-																											
2. Gender	-0.45c	-																										
3. BMI	-0.04	-0.07	-																									
4. Mastery	-0.14b	-0.07	-0.07	**0.72**																								
5. Extroversion	0.03	0.09a	0.06	0.23c	**0.72**																							
6. Neuroticism	-0.01	0.03	0.02	-0.33c	-0.25c	**0.60**																						
7. Changing the Situation	-0.15b	0.02	0.03	0.24c	0.07	-0.10a	**0.72**																					
8. Accomodation	-0.03	0.00	0.06	-0.03	0.04	0.00	0.21c	**0.57**																				
9. Devaluation	0.08	0.01	-0.04	-0.04	0.02	0.06	-0.05	0.38c	**0.81**																			
10. Avoidance	0.07	0.07	0.10	-0.12b	0.00	0.07	-0.18c	0.19c	0.56c	**0.78**																		
11. Symptom Reduction	0.00	-0.01	0.10a	0.14b	0.23c	-0.02	0.20c	0.03	0.01	-0.03	**0.64**																	
12. Seeking Social Support	0.02	0.10a	0.07	0.05	0.18c	-0.07	0.26c	0.15c	-0.06	-0.11a	0.34c	**0.72**																
13. Drinking to Cope	0.08	-0.04	0.11a	-0.16c	0 04	0.25c	-0.02	0.10c	0.09a	0.13b	0.03	0.01	**0.82**															
14. AUDIT	0.09	-0.06	0.04	-0.02	0.12b	0.16c	-0.05	0.06	0.07	0.10a	0.00	-0.09	0.50c	**0.81**														
15. Alcohol Expectancies	-0.13b	0.02	-0.07	-0.14b	-0.10a	-0.14b	0.09	-0.05	-0.11a	-0.08	-0.03	-0.00	-0.54c	-0.40c	**0.59**													
16. Habitual Alcohol Consumption	0.01	-0.03	-0.01	0.06	0.04	0.01	-0.10a	-0.05	0.02	0.10a	0.11a	0.04	0.09	0.23c	-0.14b	-												
17. Weekend Alcohol Consumption	0.10	-0.11a	0.07	0.07	0.14b	0.09	-0 02	0.04	0.05	0.09	0.12a	-0.04	0.34c	0.56c	-0.30c	0.25c	-											
18. Smoking	-0.07	0.02	0.02	-0.08	0.01	0.05	-0.07	-0.01	-0.06	0.00	-0.02	0.01	-0.06	-0.04	0.02	-0.02	-0.03	-										
19. Cigarettes Per Week	-0.30c	0.15a	0.05	-0.15a	0.03	0.22c	0.02	0.11	0.07	0.06	0.11	0.08	0.18b	0.04	-0.11	0.05	0 04	0.16b	-									
20. Duration of Smoking	-0.52c	0.20c	-0.01	-0.02	-0.03	0.16b	0.06	0.07	0 04	0.00	0.10	0.04	0.05	-0.06	-0.03	0.00	-0.05	0.20c	0.71c	-								
21. Physical Activity	0.01	-0.12b	-0.09	0.20c	0.17c	-0.19c	0.14b	0.06	-0.04	-0.11a	0.15c	-0.02	-0.11a	-0.01	0.10a	-0.05	-0.01	0.02	-0.13a	-0.04	-							
22. Fitness	0.08	-0.17c	-0.14b	0.13b	0.14b	-0.19c	0.16c	0.06	-0.07	-0.12a	0.06	-0.02	-0.14b	-0.06	0.07	-0.05	-0.12a	0.04	-0.14a	-0.11	0.72c	-						
23. Self-Esteem	-0.11a	-0.08	0.03	0.47c	0.39c	-0.47c	0.19c	-0.00	-0.04	-0.14b	0.15c	0.05	-0.17c	-0.05	0.11a	-0.03	0.04	-0.05	-0.06	-0.02	0.20c	0.21c	**0.87**					
24. GHQ-12	-0.04	0.15c	-0.02	-0.35c	-0.26c	0.51c	-0.07	-0.05	0.04	0 06	-0.06	0.01	0.21c	0.08	-0.11a	-0.06	-0.04	0.03	0.20c	0.12a	-0.18c	-0.18c	-0.53c	**0.87**				
25. Confidence	0.02	-0.08	0.07	0.26c	0.23c	-0.37c	0.00	-0.04	-0.04	-0.01	0.08	0.01	-0.21c	0.02	0.07	0.04	0.04	-0.08	-0.21c	-0.20c	0.12a	0.15b	0.36c	-0.44c	-			
26. Happiness	0.02	-0.04	0.03	0.22c	0.16c	-0.35c	-0.03	-0.04	-0.03	-0.04	0.03	-0.04	-0.16c	-0.02	0.06	-0.04	-0.04	-0.05	-0.20c	-0.17b	0.13b	0.17c	0.29c	-0.37c	0.58c	-		
27. Anxiety-Contentment	0.08	-0.13b	0.11a	0.30c	0.28c	-0.46c	-0.02	-0.01	0.02	0.00	0.07	-0.06	-0.06	0.11a	0.03	0.05	0.14b	-0.12a	-0.21c	-0.19c	0.13b	0.17c	0.48c	-0.60c	0.39c	0.36c	**0.87**	
28. Depression-Enthusiasm	0.02	-0.05	0.03	0.31c	0.45c	-0.51c	0.10a	0.04	-0.05	-0.10a	0.15c	0.07	-0.15c	-0.01	-0.03	-0.01	0.02	0.02	-0.16b	-0.10	0.24c	0.24c	0.51c	-0.61c	0.39c	0.40c	0.64c	**0.85**
Mean	75.34	1.47	23.56	21.32	15.50	10.45	13.49	12.11	11.55	10.97	14.06	13.82	10.54	21.64	9.54	25.99	16.27	2.11	17.95	1.63	2.74	2.44	31.95	10.80	1.79	1.63	23.38	26.89
S.D.	7.80	0.87	4.08	3.13	2 51	2.69	2.27	2.03	2.76	2.87	2.42	2.82	3.47	6.51	1.52	57.48	15.46	6.39	36.95	0.48	0.86	0.84	4.73	5.19	0.41	0.48	4.92	4.56

a=p<0.05; b=p<0.01 and c=p<0.005

4.3.1.4. Multivariate Analyses

Hierarchical multiple regression analyses (MRA) were used in the prediction of general well being, drinking to cope, alcohol consumption, alcohol problems, self-reported fitness and physical activity, with both step and final beta weights being reported. A procedure of listwise deletion was employed to account for missing data.

4.3.1.4.1. Prediction of General Psychological Well being

In terms of general psychological well being, the MRA predicted 37% of the variance in GHQ-12 scores. Results (Table 4.3.2.) indicated several significant predictors of GHQ-12, including gender, mastery, extraversion, neuroticism and the use of accommodation as a coping strategy. Each of these main effects was significant in the stepwise results and in the final MRA equation.

Table 4.3.2. Hierarchical multiple regression analyses predicting general psychological well being (GHQ-12 Score) from questionnaire administration 1.

Variable	Change R^2	Step Beta	Final Beta
Age	0.03b	-0.06	-0.07
Gender		0.16b	0.10a
Mastery	0.31c	-0.14b	-0.14b
Extraversion		-0.14b	-0.12a
Neuroticism		0.43c	0.43c
Smoking	0.01	-0.02	-0.01
Alcohol Consumption		-0.04	-0.03
Physical Activity		-0.08	-0.06
Changing the Situation	0.02	0.06	0.06
Accommodation		-0.14b	-0.14b
Devaluation		0.03	0.03
Avoidance		0.04	0.04
Symptom Reduction		-0.07	-0.07
Seeking Social Support		0.06	0.06
	$R=0.61$, $R^2=0.37$, $R^2_{ADJ}=0.35$, $F=14.02$, df14, 332, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.1.4.2. Prediction of Drinking to Cope, Alcohol Consumption and Alcohol Related Problems

In terms of the predictors of the use of drinking to cope, the final MRA equation accounted for 33% of the variance in drinking to cope scores. Stepwise analysis showed that there were significant main effects for alcohol expectancies and neuroticism, although the final MRA equation also identified gender as a significant predictor (Table 4.3.3.).

Table 4.3.3. Hierarchical multiple regression analyses predicting drinking to cope from questionnaire administration 1.

Variable	Change R^2	Step Beta	Final Beta
Age	0.02	0.08	-0.01
Gender		-0.08	-0.09a
Mastery	0.31c	-0.06	-0.06
Extraversion		0.05	0.05
Neuroticism		0.15c	0.15c
Alcohol Expectancies		0.50c	0.51c
Changing the Situation	0.01	0.06	0.06
Accommodation		-0.00	-0.00
Devaluation		-0.02	-0.02
Avoidance		0.09	0.09
Symptom Reduction		-0.00	-0.00
Seeking Social Support		0.02	0.02
	$R=0.58$, $R^2=0.33$, $R^2_{ADJ}=0.31$, $F=16.17$, df12, 392, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

In predicting alcohol consumption, the final equation accounted for 26% of the variance in alcohol consumption scores within the sample. There were significant main effects of gender, drinking to cope and extraversion in the prediction of alcohol consumption. Each of these variables was significant in both the stepwise and final MRA equations (Table 4.3.4.).

Table 4.3.4. Hierarchical multiple regression analyses predicting alcohol consumption from questionnaire administration 1.

Variable	Change R^2	Step Beta	Final Beta
Age	0.09c	0.04	-0.02
Gender		-0.30c	-0.28c
Mastery	0.14c	0.03	0.05
Extraversion		0.18c	0.17c
Neuroticism		0.06	0.06
Alcohol Expectancies		0.08	0.07
Drinking to Cope		0.27c	0.27c
Changing the Situation	0.02	-0.09	-0.09
Accommodation		0.01	0.01
Devaluation		-0.01	-0.01
Avoidance		0.05	0.05
Symptom Reduction		0.10	0.10
Seeking Social Support		-0.06	-0.06
	$R=0.51$, $R^2=0.26$, $R^2_{ADJ}=0.23$, $F=8.83$, df13,333, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

The final equation predicting alcohol related problems accounted for 48% of the variance in AUDIT scores within the sample. Significant stepwise main effects were observed for age, gender, alcohol expectancies, extraversion, neuroticism, alcohol consumption and drinking to cope. However, the contribution from gender failed to remain significant in the final MRA equation (Table 4.3.5.).

Table 4.3.5. Hierarchical multiple regression analyses predicting alcohol related problems from questionnaire administration 1.

Variable	Change R^2	Step Beta	Final Beta
Age	0.07c	0.13a	0.09a
Gender		-0.21c	-0.07
Mastery	0.28c	0.05	0.03
Extraversion		0.16b	0.10a
Neuroticism		0.15b	0.11a
Alcohol Expectancies		0.13a	0.11a
Drinking to Cope		0.39c	0.28c
Alcohol Consumption	0.13c	0.41c	0.40c
Changing the Situation	0.00	0.01	0.01
Accommodation		0.04	0.04
Devaluation		-0.01	-0.01
Avoidance		0.04	0.04
Symptom Reduction		-0.03	-0.03
Seeking Social Support		-0.02	-0.02
	$R=0.69$, $R^2=0.48$, $R^2_{ADJ}=0.46$, $F=20.91$, df14,315, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.1.4.3. Prediction of Self-Reported Fitness and Physical Activity

In terms of the predictors of fitness, the final MRA accounted for 55% of the variance in fitness scores within the sample. As illustrated by table 4.3.6. there were significant stepwise main effects of gender, BMI, extraversion, neuroticism, alcohol consumption and activity. However, only BMI and activity remained significant predictors in the final equation (Table 4.3.6.)

Table 4.3.6. Hierarchical multiple regression analyses predicting self-reported fitness from questionnaire administration 1.

Variable	Change R^2	Step Beta	Final Beta
Age	0.05c	-0.06	0.07
Gender		-0.17b	-0.07
BMI		-0.18b	-0.10a
Mastery	0.07c	0.05	-0.02
Extraversion		0.17b	0.07
Neuroticism		-0.13a	-0.03
Smoking	0.42c	0.04	0.04
Alcohol Consumption		-0.09a	-0.08
Physical Activity		0.68c	0.68c
Changing the Situation	0.01	0.06	0.06
Accommodation		0.03	0.03
Devaluation		-0.07	-0.07
Avoidance		0.01	0.01
Symptom Reduction		-0.01	-0.01
Seeking Social Support		-0.01	-0.01
	$R=0.74$, $R^2=0.55$, $R^2_{ADJ}=0.53$, $F=24.32$, df15, 299, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

The final MRA accounted for 19% of the variance in physical activity scores within the sample. Significant stepwise main effects were observed for age, gender, BMI, extraversion, neuroticism, and symptom reduction coping (Table 4.3.7.). In the final equation however, the contribution from age failed to remain significant.

Table 4.3.7. Hierarchical multiple regression analyses predicting self-reported physical activity from questionnaire administration 1.

Variable	Change R^2	Step Beta	Final Beta
Age	0.06c	-0.14a	-0.11
Gender		-0.19c	-0.22c
BMI		-0.13a	-0.15b
Mastery	0.09c	0.10	0.07
Extraversion		0.17b	0.16b
Neuroticism		-0.14a	-0.13a
Smoking	0.01	0.04	0.05
Alcohol Consumption		-0.09	-0.10
Changing the Situation	0.04a	0.03	0.03
Accommodation		0.07	0.07
Devaluation		0.04	0.04
Avoidance		-0.11	-0.11
Symptom Reduction		0.17b	0.17b
Seeking Social Support		-0.07	-0.07
	$R=0.44$, $R^2=0.19$, $R^2_{ADJ}=0.15$, $F=5.08$, df14, 302, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.2. Questionnaire Administration 2

4.3.2.1. Sample Description

Seven hundred and nineteen questionnaires were administered, with 406 being returned (a response rate of 57%). However, 70 of these respondents were excluded from this sample as they provided insufficient information on a large portion of the questionnaire and thus, statistical analyses were performed on a sample of 336 respondents. Of the 336 respondents 168 were male and 165 were female (3 respondents did not report gender). The age of the sample (mean±S.D.) was 25±6 years, with the height and bodymass of the sample being 170±14 cm and 69±12 kg respectively.

Descriptive statistics showed that 65.5% of the sample were single, 22.6% were in a steady relationship, 9.8% were married, 1.8% were divorced or separated and none were widowed. Only one person failed to report domestic status. Of the respondents, 311 (92.6%) reported having no dependent children and 24 (7.1%) reported having dependent children, with 1 (0.3%) failing to provide data.

Descriptive data indicated that 87.5% of the sample were Caucasian, 1.8% were Asian, 1.2% were afro-Caribbean, 0.3% were oriental, and 8.9% of the sample reported some other ethnic origin. A further 0.3% of the sample failed to report ethnic origin. Two hundred and forty-four respondents (72.6%) reported having

no practicing religion and 89 (27.5%) reported a practicing religion, with a further 3 (0.9%) providing no data.

Data relating to the habitual drinking patterns of the subjects showed that 7.1% of the sample were non-drinkers, 6% drank only monthly or less, 21.1% of the sample drank 2-4 times per month, 50.3% drank 2-3 times per week and a further 15.5% of the sample reported drinking 4 or more times per week.

Descriptive data relating to the smoking habits of the sample, showed that 54 respondents (16.1%) were smokers whilst 274 respondents (81.5%) were non-smokers. A further 8 respondents (2.4%) failed to report whether they smoked or not.

With respect to habitual physical activity, descriptive data showed that 15.2% of the sample reported being sedentary, 32.4% reported being moderately active, 42.3% reported being active and 12.5% reported being highly active. In terms of the self-reported fitness of the sample, 15.2% reported being unfit, 40.8% moderately fit, 34.5% fit and 7.7% reported being very fit. A further 1.8% of the sample failed to report on either activity or fitness.

4.3.2.2. Scale Descriptive Statistics

Scale means±SD, as well as measures of internal consistency (Cronbachs alpha), are presented for each of the scales employed (Table 4.3.8.). As can be

seen, all of the scales have acceptable levels of internal consistency, with accommodation coping (α=0.61) being the lowest.

4.3.2.3. Bivariate Analyses

4.3.2.3.1. Health Related Behaviours in Relation to Psychological Well Being

As was observed in the data from administration 1, alcohol consumption was negatively correlated with the use of changing the situation as a coping strategy ($r=-0.13$, $p<0.05$). In addition, alcohol consumption was also negatively correlated with the seeking of social support as a coping strategy ($r=-0.19$, $p<0.005$), although no other significant relationships were shown with any of the other general coping strategies. Alcohol consumption was positively associated with AUDIT score ($r=0.57$, $p<0.005$) and negatively associated with alcohol expectancies ($r=-0.26$, $p<0.005$). In contrast to the results of administration 1, alcohol consumption was also positively related to the use of drinking to cope ($r=0.37$, $p<0.005$). There was no significant relationship between alcohol consumption and general psychological well being (GHQ-12). In addition, there was no significant association between alcohol consumption and depression-enthusiasm, although a significant correlation was observed between alcohol consumption and anxiety-contentment ($r=0.12$, $p<0.05$).

There was a significant correlation between self-reported activity levels and smoking ($r=0.19$, $p<0.005$), indicating that those individuals who reported a high physical activity were less likely to be smokers. In addition, habitual physical activity was negatively related to both the amount of cigarettes smoked per week ($r=-0.17$, $p<0.005$) and the duration of smoking ($r=-0.18$, $p<0.005$).

In terms of the relationship between physical activity and the use of more general coping strategies, data showed that physical activity was associated with the use of symptom reduction as a coping strategies ($r=0.13$, $p<0.05$). However, there were no further significant correlations between physical activity and any of the other general coping strategies. There was a significant relationship between habitual physical activity levels and GHQ-12 score ($r=-0.19$, $p<0.005$), indicating that those reported higher physical activity levels also had an enhanced sense of psychological well being. In addition, positive correlations were observed between self-reported physical activity and scores on both the anxiety-contentment ($r=0.12$, $p<0.05$) and the depression-enthusiasm ($r=0.17$, $p<0.05$) scales. These results indicate that those individuals who reported a higher physical activity also reported a greater sense of both general and affective well being. In contrast to the results of administration 1, results from administration 2 showed no significant correlation between physical activity and both the general state of happiness and confidence of the respondents over the last 12 months. However, a significant relationship was observed between self-reported fitness and the general state of confidence over the last 12 months in this sample

(r=0.11, p<0.05). Higher levels of self-esteem were again reported by those individuals also reporting higher physical activity levels (r=0.12, p<0.05).

In contrast to the results from administration 1, there was a significant association between smoking and general psychological well being (r=-0.14, p<0.05). In addition, there was a significant relationship between smoking and the general state of both happiness (r=0.20, p<0.005) and confidence (r=0.17, p<0.01) of respondents over the last 12 months. Furthermore, smoking was also shown to be related to scores on both the anxiety-contentment (r=0.15, p<0.01) and depression-enthusiasm scales (r=0.17, p<0.01). These results indicate that those individuals who smoke also report a greater sense of both general and affective well being. There were no significant correlations between smoking and any of the general coping strategies.

4.3.2.3.2. Individual Differences, Dispositional Characteristics of the Individual and Health Related Behaviour

There were several significant correlations between gender and the health-related behaviours. Males reported significantly higher levels of both physical activity (r=-0.26, p<0.005) and fitness (r=-0.25, p<0.005) than females. Contrary to the results of administration 1, males also reported significantly higher habitual alcohol consumption (r=-0.27, p<0.005), as well as a greater consumption of alcohol at the weekend (r=-0.18, p<0.01). Also in contrast to the data reported

from administration 1, more males reported smoking than females ($r=-0.11$, $p<0.05$). However, there was no correlation between gender and both the amount of cigarettes smoked per week and the duration of smoking in those individuals that did smoke.

There were no significant relationships between extraversion and neuroticism and either habitual alcohol consumption or alcohol consumption at the weekend. Extraversion was positively related to both self-reported physical activity ($r=0.12$, $p<0.05$) and fitness ($r=0.13$, $p<0.05$), indicating that those reporting higher extraversion also reported a higher self-reported physical activity and fitness levels. However, neuroticism was not significantly associated with either physical activity or fitness, although it was significantly associated with smoking ($r=-0.14$, $p<0.05$) and the duration of smoking ($r=0.13$, $p<0.05$).

4.3.2.3.3. Individual Differences, Dispositional Characteristics of the Individual, Coping and Psychological Well Being

In terms of the relationships between gender and psychological well being, there was a significant positive correlation between gender and GHQ-12 score ($r=0.17$, $p<0.01$), showing that males reported a greater sense of general psychological well being than females. Similarly, males also reported a greater sense of affective well being on both anxiety-contentment ($r=-0.20$, $p<0.005$) and depression-enthusiasm ($r=-0.11$, $p<0.05$) scales. In addition, there was a

significant negative correlation between gender and self-esteem ($r=-0.11$, $p<0.05$), indicating that males also had a higher self-esteem. Females reported a more frequent use of seeking social support as a coping strategy ($r=0.25$, $p<0.005$). No other significant correlations were observed between gender and any of the other general coping strategies.

Both extraversion ($r=-0.23$, $p<0.005$) and neuroticism ($r=0.53$, $p<0.005$) were significantly related to GHQ-12 score, indicating that those reporting higher extraversion also reported an enhanced sense of general psychological well being. These relationships remained significant even when controlling for the effects of gender (extraversion: $r=-0.27$, $p<0.005$; neuroticism: $r=0.52$, $p<0.005$). Similarly, extraversion was positively correlated with both anxiety-contentment ($r=0.22$, $p<0.005$) and depression-enthusiasm ($r=0.39$, $p<0.005$). Conversely, neuroticism was negatively related to both anxiety-contentment ($r=-0.40$, $p<0.005$) and depression-enthusiasm ($r=-0.51$, $p<0.005$) scores.

Data also showed several significant associations between elements of personality and the use of more general coping strategies. Specifically, extraversion was positively related to both symptom reduction coping ($r=0.21$, $p<0.005$) and the seeking of social support ($r=0.18$, $p<0.005$), whilst neuroticism was positively related to avoidance coping strategies ($r=0.11$, $p<0.05$).

Table 4.3.8. Scale descriptive statistics and bivariate correlation coefficients for questionnaire administration 2

Alphas	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1. Age	-																											
2. Gender	-0.26c	-																										
3. BMI	-0.12a	-0.06	-																									
4. Mastery	-0.09	-0.10	-0.05	**0.79**																								
5. Extroversion	0.17b	0.15b	-0.06	0.30c	**0.76**																							
6. Neuroticism	-0 02	0.14b	-0.07	-0.40c	-0.30c	**0.66**																						
7. Changing the Situation	-0.15b	-0.03	-0.06	0.24c	0.08	-0.04	**0.73**																					
8. Accomodation	0.03	-0.09	-0.17	-0.07	0.04	0.02	0.33c	**0.61**																				
9. Devaluation	-0.00	-0.01	0.02	-0.08	0.08	-0.01	0.17b	0.41c	**0.82**																			
10. Avoidance	0.07	0.02	0.02	-0.24c	-0.03	0.11a	-0.05	0.29c	0.56c	**0.75**																		
11. Symptom Reduction	0.10	0.01	-0.09	0.30c	0.21c	-0.08	0.27c	0.06	0.02	-0.07	**0.74**																	
12. Seeking Social Support	-0.03	0.25c	-0.11	0.18c	0.18c	-0.01	0.26c	0.13a	0.01	-0.17c	0.39c	**0.79**																
13. Drinking to Cope	0.24c	-0.02	-0.02	-0.33c	-0.04	0.27c	-0.04	0.07	0.06	0.24c	0.00	-0.12a	**0.87**															
14. AUDIT	0.25c	-0.25c	0.09	-0.18c	-0.02	0.15b	0.01	0.13a	0.20c	0.25c	-0.08	-0.20c	0.54c	**0.83**														
15. Alcohol Expectancies	-0.28c	-0.08	-0.01	0.20c	-0.03	-0.17b	0.04	-0.05	-0.01	-0.14a	0.08	0.04	-0.51c	-0.37c	**0.62**													
16. Habitual Alcohol Consumption	0.20c	-0.27c	-0.12a	-0.07	0.08	0.04	-0.13a	-0.08	-0.02	0.02	-0.04	-0.19c	0.37c	0.57c	-0.26c	-												
17. Weekend Alcohol Consumption	0.20c	-0.18b	0.11	-0.15b	0.08	0.06	-0.01	-0.04	-0.01	0.03	-0.06	-0.16b	0.36c	0.55c	-0.27c	0.70c	-											
18. Smoking	0.06	-0.11a	0.10	0.01	0.04	-0.14a	-0.08	-0.00	-0.05	-0.02	-0.00	-0.05	-0.06	-0.02	0.01	-0.03	-0.05	-										
19. Cigarettes Per Week	-0.06	0.09	-0.07	-0.06	-0.05	0.11	0.05	-0.06	0.07	0.02	-0.02	0.02	0.09	0.08	-0.07	0.10	0.05	-0.82c	-									
20. Duration of Smoking	-0.18c	0.07	-0.07	0.01	-0.08	0.13a	0.08	0.03	0.05	0.03	-0.01	0.06	0.03	-0.00	0.09	-0.02	-0.03	-0.81c	0.77c	-								
21. Physical Activity	0.08	-0.26c	0.02	0.15b	0.12a	-0.08	0.07	-0.00	-0.04	-0.09	0.13a	-0.03	-0.10	0.06	0.07	0.05	0.01	0.19c	-0.17b	-0.18c	-							
22. Fitness	0.08	-0.25c	-0.06	0.14b	0.13a	-0.09	0.08	0.04	-0.06	-0.10	0.09	-0.07	-0.10	0.01	0.03	0.02	-0.02	0.22c	-0.19c	-0.22c	0.82c	-						
23. Self-Esteem	-0.06	-0.11a	-0.01	0.54c	0.30c	-0.53c	0.17b	0.00	-0.05	-0.19c	0.24c	0.19c	-0.30c	-0.15b	0.18c	-0.07	-0.08	0.08	-0.07	-0.05	0.12a	0.14b	**0.88**					
24. GHQ-12	0.03	0.17b	-0.06	-0.36c	-0.23c	0.53c	-0.04	0.02	-0.09	0.05	-0.08	-0.04	0.30c	0.15b	-0.13a	0.03	0.01	-0.14a	0.07	0.11	-0.19c	-0.19c	-0.49c	**0.88**				
25. Confidence	0.07	-0.07	0.05	0.28c	0.27c	-0.42c	-0.01	-0.02	-0.02	-0.08	0.05	-0.01	-0.25c	-0.12a	0.10	-0.05	-0.01	0.17b	-0.15b	-0.18c	0.10	0.11a	0.52c	-0.50c	-			
26. Happiness	0.03	-0.08	0.03	0.27c	0.21c	-0.45c	0.02	0.03	0.03	-0.01	0.07	0.02	-0.19c	-0.04	0.05	-0.00	-0.02	0.20c	-0.15b	-0.19c	0.05	0.06	0.39c	-0.43c	0.52c	-		
27. Anxiety-Contentment	0.10	-0.20c	0.04	0.25c	0.22c	-0.40c	-0.04	-0.07	0.07	0.01	0.06	-0.03	-0.07	0.02	0.04	0.12a	0.10	0.15b	-0.04	-0.15b	0.12a	0.14b	0.32c	-0.62c	0.33c	0.36c	**0.91**	
28. Depression-Enthusiasm	0.03	-0.11a	-0.03	0.40c	0.39c	-0.51c	0.11a	0.05	0.07	-0.07	0.16b	0.14a	-0.21c	-0.10	0.08	-0.01	-0.03	0.17b	-0.09	-0.17b	0.17b	0.17b	0.51c	-0.61c	0.41c	0.45c	0.63c	**0.86**
Mean	25.30	1.50	23.47	21.31	15.20	10.60	13.31	11.96	11.42	11.05	14.07	13.85	10.56	21.62	8.39	20.57	13.59	1.84	8.78	11.39	2.57	2.36	31.63	12.19	1.74	1.56	22.57	26.24
S.D.	5.54	0.50	2.83	3.32	2.54	2.84	2.36	2.07	2.71	2.60	2.51	2.91	3.83	6.55	1.58	17.89	12.43	0.37	26.27	31.87	0.85	0.84	4.90	5.47	0.44	0.50	5.67	4.72

a=p<0.05; b=p<0.01 and c=p<0.005

4.3.2.4. Multivariate Analyses

Hierarchical multiple regression analyses (MRA) were used in the prediction of general well being, drinking to cope, alcohol consumption, alcohol problems, self-reported fitness and physical activity. A procedure of listwise deletion was employed to account for missing data.

4.3.2.4.1. Prediction of General Psychological Well being

In terms of general psychological well being, the final MRA predicted 34% of the variance for GHQ-12 scores within the sample. Stepwise data showed significant contributions from gender, mastery and neuroticism (Table 4.3.9.). However, only mastery and neuroticism remained significant in the final MRA equation.

Table 4.3.9. Hierarchical multiple regression analyses predicting general psychological well being (GHQ-12 Score) from questionnaire administration 2.

Variable	Change R^2	Step Beta	Final Beta
Age	0.03a	0.01	0.02
Gender		0.16b	0.10
Mastery	0.29c	-0.12a	-0.15a
Extraversion		-0.10	-0.09
Neuroticism		0.44c	0.43c
Smoking	0.01	-0.02	-0.02
Alcohol Consumption		0.03	0.04
Physical Activity		-0.08	-0.08
Changing the Situation	0.02	0.06	0.06
Accommodation		0.05	0.05
Devaluation		-0.11	-0.11
Avoidance		-0.03	-0.03
Symptom Reduction		0.05	0.05
Seeking Social Support		-0.04	-0.04
	$R=0.58$, $R^2=0.34$, $R^2_{ADJ}=0.30$, $F=9.72$, df14, 265, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.2.4.2. Prediction of Drinking to Cope, Alcohol Consumption and Alcohol Problems

In terms of the predictors of the use of drinking to cope, the final MRA equation accounted for 38% of the variance in drinking to cope scores within the sample. Stepwise analysis showed that there were several significant main effects of age, alcohol expectancies, mastery, neuroticism and the use of avoidance coping strategies (Table 4.3.10.). However, the final MRA equation also identified gender as a significant predictor whilst the use of symptom reduction coping was also approaching significance (p=0.051).

Table 4.3.10. Hierarchical multiple regression analyses predicting drinking to cope from questionnaire administration 2.

Variable	Change R^2	Step Beta	Final Beta
Age	0.06c	0.25c	0.10a
Gender		-0.04	-0.11a
Mastery	0.29c	-0.21c	-0.21c
Extraversion		0.04	0.03
Neuroticism		0.15b	0.13a
Alcohol Expectancies		-0.41c	-0.41c
Changing the Situation	0.03a	0.05	0.05
Accommodation		-0.02	-0.02
Devaluation		-0.04	-0.04
Avoidance		0.14a	0.14a
Symptom Reduction		0.11	0.11
Seeking Social Support		-0.08	-0.08
	$R=0.62$, $R^2=0.38$, $R^2_{ADJ}=0.35$, $F=14.87$, df12, 294, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

With respect to the prediction of alcohol consumption, the final equation accounted for 26% of the variance in alcohol consumption scores within the sample. There were significant stepwise contributions from the main effects of age, gender, drinking to cope and extraversion (Table 4.3.11.). However, there was no significant contribution from age in the final equation.

Table 4.3.11. Hierarchical multiple regression analyses predicting alcohol consumption from questionnaire administration 2.

Variable	Change R^2	Step Beta	Final Beta
Age	0.12c	0.19c	0.06
Gender		-0.30c	-0.32c
Mastery	0.11c	-0.02	-0.00
Extraversion		0.12a	0.13a
Neuroticism		0.04	0.05
Alcohol Expectancies		-0.10	-0.10
Drinking to Cope		0.26c	0.27c
Changing the Situation	0.03	-0.06	-0.06
Accommodation		-0.11	-0.11
Devaluation		0.03	0.03
Avoidance		-0.04	-0.04
Symptom Reduction		-0.03	-0.03
Seeking Social Support		-0.05	-0.05
	$R=0.51$, $R^2=0.26$, $R^2_{ADJ}=0.22$, $F=7.21$, df13, 267, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

The final equation predicting alcohol problems accounted for 51% of the variance in AUDIT scores within the sample. As table 4.3.12. illustrates, significant stepwise main effects were observed for age, gender, alcohol expectancies, alcohol consumption and drinking to cope. However, only alcohol expectancies, drinking to cope and alcohol consumption remained significant in the final equation. In addition, the use of avoidance coping strategies was approaching significance as a main effect (p=0.06) in the final equation.

Table 4.3.12. Hierarchical multiple regression analyses predicting alcohol related problems from questionnaire administration 2.

Variable	Change R^2	Step Beta	Final Beta
Age	0.09c	0.20c	0.06
Gender		-0.23c	-0.10
Mastery	0.26c	-0.02	0.03
Extraversion		0.06	0.02
Neuroticism		0.08	0.08
Alcohol Expectancies		-0.15b	-0.11a
Drinking to Cope		0.40c	0.28c
Alcohol Consumption	0.13c	0.41c	0.42c
Changing the Situation	0.03a	0.07	0.07
Accommodation		0.01	0.01
Devaluation		0.05	0.05
Avoidance		0.11	0.11
Symptom Reduction		-0.06	-0.06
Seeking Social Support		-0.02	-0.02
	$R=0.71$, $R^2=0.51$, $R^2_{ADJ}=0.48$, $F=18.29$, df14, 247, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.2.4.3. Prediction of Self-Reported Fitness and Physical Activity

In terms of the predictors of fitness, the final MRA accounted for 66% of the variance in fitness scores within the sample. Significant stepwise main effects were observed for gender, BMI, extraversion, activity and the use of seeking social support coping strategies (Table 4.3.13.). However, it is of interest to note that only BMI, activity and the use of seeking social support coping strategies remained significant in the final MRA equation.

Table 4.3.13. Hierarchical multiple regression analyses predicting self-reported fitness from questionnaire administration 2.

Variable	Change R^2	Step Beta	Final Beta
Age	0.09c	0.09	-0.02
Gender		-0.27c	-0.03
BMI		-0.19b	-0.10a
Mastery	0.04a	0.03	-0.00
Extraversion		0.19b	0.08
Neuroticism		0.04	0.01
Smoking	0.52c	0.07	0.06
Alcohol Consumption		0.00	-0.01
Physical Activity		0.76c	0.77c
Changing the Situation	0.01	-0.01	-0.01
Accommodation		0.06	0.06
Devaluation		-0.05	-0.05
Avoidance		-0.02	-0.02
Symptom Reduction		0.00	0.00
Seeking Social Support		-0.09a	-0.09a
	$R=0.81$, $R^2=0.66$, $R^2_{ADJ}=0.64$, $F=30.09$, df15, 239, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

The final MRA accounted for only 18% of the variance in physical activity scores within the sample. Significant main effects were observed for gender, extraversion, smoking and symptom reduction coping (Table 4.3.14.). Each of these variables provided significant contribution to both stepwise and final MRA equations.

Table 4.3.14. Hierarchical multiple regression analyses predicting physical activity from questionnaire administration 2.

Variable	Change R^2	Step Beta	Final Beta
Age	0.10c	0.11	0.06
Gender		-0.30c	-0.30c
BMI		-0.12	-0.10
Mastery	0.03a	0.07	0.04
Extraversion		0.17b	0.16a
Neuroticism		0.05	0.07
Smoking	0.02a	0.15a	0.15a
Alcohol Consumption		-0.01	-0.01
Changing the Situation	0.02	0.02	0.02
Accommodation		-0.08	-0.08
Devaluation		-0.00	-0.00
Avoidance		0.05	0.05
Symptom Reduction		0.15a	0.15a
Seeking Social Support		-0.03	-0.03
	$R=0.42$, $R^2=0.17$, $R^2_{ADJ}=0.13$, $F=3.60$, df14, 240, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.3. Repeated Measures Data

4.3.3.1. Sample Description

Data files from administrations 1 and 2 were compared for date of birth, gender, height, domestic status, number of dependent children, educational qualifications, ethnic origin and religion. Only those subjects with comparable data for the majority of these variables were included in the repeated measures data set. From this combined data set, 141 respondents completed the questionnaire in both administrations 1 and 2.

Thus, repeated measures analyses were performed on a this sample of 141 respondents, with 53 (37.6%) respondents being male and 86 (61%) being female (2 respondents did not report gender). The average age of the sample was 25±7 (mean±S.D.) years, with average height and bodymass of the sample being 168±11 cm and 67±13 kg respectively.

Descriptive statistics showed that 61.1% of the sample were single, 26.2% were in a steady relationship, 10.6% were married, 2.1% were divorced or separated and none were widowed. Of the respondents, 127 (90.1%) reported having no dependent children and 14 (9.9%) reported having dependent children.

In terms of ethnicity, 87.2% of the sample were Caucasian, 2.8% were Asian, 0.7% were Afro-Caribbean, 0.7% were Oriental, and 8.5% reported some other ethnic origin. Of the respondents, 97 (68.8%) reported having no practicing religion, 43 (30.5%) reported a practicing religion and 1 (0.7%) provided no data.

Data relating to the habitual drinking patterns of the respondents showed that 5.0% were non-drinkers, 7.8% drank only monthly or less, 20.6% drank 2-4 times per month, 55.3% drank 2-3 times per week and a further 11.3% reported drinking 4 or more times per week.

Descriptive data relating to the smoking habits of the sample, showed that 23 respondents (16.3%) were smokers whilst 117 respondents (83.0%) were non-smokers. A further 1 respondent (0.7%) failed to report whether they smoked or not.

In terms of the self-reported physical activity of the sample, 11.3% of the sample reported being sedentary, 36.9% reported being moderately active, 42.6% reported being active and 9.2% reported being highly active. In terms of the self-reported fitness of the sample, 17.7% reported being unfit, 42.6% moderately fit, 33.3% fit and 6.4% reported being very fit.

4.3.3.2. Scale Descriptive Statistics

Table 4.3.15. provides the correlation coefficients of selected variables when correlating questionnaire administration 1 with administration 2. Clearly all measures were significantly related between questionnaires administrations 1 and 2.

Table 4.3.16. shows the correlations between each of the administration 2 variables, with the addition of the administration 1 outcome variables. Scale means ± S.D., as well as measures of internal consistency (Cronbachs alpha), are presented for each of the scales employed (Table 4.3.16.).

Table 4.3.15. Bivariate correlation coefficients between questionnaire administrations 1 and 2.

Variable	Correlation (r)
GHQ-12	0.37c
Happiness	0.38c
Confidence	0.42c
Anxiety-Contentment	0.51c
Depression-Enthusiasm	0.48c
Alcohol Consumption	0.50c
AUDIT	0.69c
Alcohol Expectancies	0.68c
Drinking to Cope	0.65c
Physical Activity	0.48c
Fitness	0.64c
Smoking	0.86c
BMI	0.49c
Changing the Situation	0.47c
Accommodation	0.34c
Devaluation	0.46c
Avoidance	0.40c
Symptom Reduction	0.50c
Seeking Social Support	0.56c
Mastery	0.46c
Self-Esteem	0.73c
Extraversion	0.75c
Neuroticism	0.74c

c=p<0.005

4.3.3.3. Bivariate Analyses

The majority of the correlation coefficients reported in table 4.3.16. will be similar, in significance (or non-significance), to those reported in section 4.3.2.3., with any changes in significance most likely being the result of a reduction in the number of cases used for analyses. Thus, so as to avoid repetition, only the correlation coefficients that relate to the outcome measures from questionnaire

administration 1 will be reported here, although all correlation coefficients can be viewed in table 4.3.16.

General psychological well being (GHQ-12) reported in questionnaire administration 1 was significantly related to the levels of mastery ($r=-0.26$, $p<0.01$), extraversion ($r=-0.18$, $p<0.05$) and neuroticism ($r=0.47$, $p<0.005$) reported in administration 2. No significant correlations were observed between GHQ-12(1) and any of the more general coping strategies from administration 2. In addition, no significant correlations were shown with smoking or alcohol consumption from administration 2, although GHQ-12(1) score was significantly correlated with the levels of both physical activity and fitness from administration 2. General psychological well being from administration 1 was also significantly related to reports of affective well being (anxiety-contentment: $r=-0.38$, $p<0.005$; depression-enthusiasm: $r=-0.37$, $p<0.005$) and the long-term feelings of confidence ($r=-0.32$, $p<0.005$) and happiness ($r=-0.29$, $p<0.005$) from administration 2.

The reported use of drinking to cope in administration 1 was significantly related to the levels of mastery ($r=-0.23$, $p<0.01$) and neuroticism ($r=0.27$, $p<0.01$) reported in administration 2, although not to extraversion. Again no significant correlations were observed with any of the more general coping strategies from administration 2. The reported use of drinking to cope(1) was also associated with alcohol consumption ($r=0.23$, $p<0.01$), alcohol problems ($r=0.44$, $p<0.005$)

and alcohol expectancies (r=-0.56, p<0.005) from administration 2. However, there were no significant associations with smoking, physical activity or fitness. Significant associations were also shown between drinking to cope(1) and administration 2 measures of self-esteem (r=-0.23, p<0.01), general well being (r=0.24, p<0.01) and depression-enthusiasm (r=-0.20, p<0.01), although not with measures of anxiety-contentment.

The habitual alcohol consumption, reported by respondents from questionnaire administration 1 was only significantly correlated with the smoking reported by respondents in administration 2 (r=-0.20, p<0.05) and not with any of the other reported measures from administration 2.

The reported level of alcohol related problems (AUDIT score) in administration 1 was significantly correlated with the neuroticism scores (r=0.30, p<0.005) reported in administration 2, although not with extraversion scores. In addition, there were no significant associations between AUDIT(1) and any of the more general coping strategies, or with levels of mastery. The AUDIT scores from administration 1 were positively correlated with administration 2 measures of drinking to cope (r=0.37, p<0.005) and alcohol consumption (0.37, p<0.005), whilst being negatively related to alcohol expectancies (r=-0.39, p<0.005). There were no significant correlations between AUDIT score from administration 1 and more general measures of psychological well being. However, in terms of affective measures of well being, there was a negative association between

AUDIT(1) score and levels of depression-enthusiasm ($r=-0.24$, $p<0.01$), but no significant relationship was observed with levels of anxiety-contentment.

Self-reported fitness from administration 1 was significantly correlated with the levels of mastery reported in administration 2 ($r=0.17$, $p<0.05$), but not with measures of extraversion or neuroticism. Self-reported Fitness(1) was also negatively associated with the use of devaluation coping strategies ($r=-0.27$, $p<0.01$) but not with any of the other more general coping strategies.

In terms of the health related behaviours, fitness(1) was significantly related to both physical activity(2) ($r=0.49$, $p<0.005$) and smoking(2) ($r=0.17$, $p<0.05$), although not to alcohol consumption(2). Self-reported levels of fitness from administration 1 were also significantly related to reports of general psychological well being ($r=-0.17$, $p<0.05$) and the long-term feelings of happiness ($r=0.19$, $p<0.05$) reported in administration 2. There was also a positive relationship between fitness(1) and measures of affective psychological well being in terms of depression-enthusiasm(2) ($r=0.18$, $p<0.05$), but not in terms of anxiety-contentment(2).

Reported physical activity from administration 1 was not significantly correlated with levels of mastery, extraversion or neuroticism from administration 2. Physical activity(1) was negatively associated with the use of devaluation coping strategies ($r=-0.27$, $p<0.01$) but was not significantly correlated with any of the

other more general coping strategies. In terms of the health related behaviours, activity(1) was significantly related to both fitness(2) ($r=0.53$, $p<0.005$) and smoking(2) ($r=0.19$, $p<0.05$), although not to alcohol consumption(2). There were no significant relationships between physical activity(1) and either general or affective measures of well being from administration 2.

Table 4.3.16. Scale descriptive statistics and bivariate correlation coefficients for repeated measures data

Alphas	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
1. Age	-																																	
2. Gender	-0.15	-																																
3. BMI	-0 09	-0 19a	-																															
4. Mastery	-0 03	-0 23b	-0 05	-																														
5. Extroversion	0 19a	0 02	-0 03	0 26b	-																													
6. Neuroticism	-0 04	0 17	0.11	-0 43c	-0 28c	-																												
7 Changing the Situation	-0.10	-0 06	-0 10	0 22b	0.11	-0 08	-																											
8 Accomodation	0 00	-0 08	0 04	-0.12	0 03	-0 01	0.26b	-																										
9 Devaluation	-0 05	0.10	0 03	-0 03	0.13	-0 15	0 30c	0 43c	-																									
10. Avoidance	0.05	0 06	0 04	-0 16	0 03	0.05	0 08	0.37c	0 63c	-																								
11. Symptom Reduction	0 04	-0 06	-0 02	0.21a	0.25b	-0 12	0.26b	-0.10	0 09	0.10	-																							
12. Seeking Social Support	0.05	0 13	-0 03	0.21a	0.24b	-0 15	0 23b	0.00	0.06	-0.11	0.50c	-																						
13. Drinking to Cope(2)	0.21a	-0 07	0 05	-0 25b	-0.12	0.24b	0 04	0 08	0.01	0 14	0.00	-0 05	-																					
14. AUDIT(2)	0.28c	-0 22a	0 17	0 02	0 12	0.11	0 05	0 08	0.13	0 13	-0 02	0 00	0.44c	-																				
15. Alcohol Expectancies	-0.32c	0 01	-0 10	0 09	-0 03	-0.13	0 01	-0 05	0 11	-0.03	0.05	0 07	-0 47c	-0 43c	-																			
16. Habitual Alcohol Consumption(2)	0.21a	-0 35c	0 22a	-0 01	0 04	0 10	-0 01	-0 13	-0.15	-0 11	-0 02	-0 07	0.27b	0 60c	-0 32c	-																		
17. Weekend Alcohol Consumption	0 25b	-0 29c	0 18	-0 08	0.10	0 10	-0 01	-0 11	-0 05	-0 02	0 01	-0 07	0.26b	0 53c	-0 34c	0.76c	-																	
18 Smoking	0.08	-0.23b	0 20a	0.04	0 10	-0.16	-0 13	-0 06	-0.12	-0 06	-0 05	-0 10	-0 07	0.03	0 07	0 08	0 05	-																
19. Cigarettes Per Week	-0 11	0 22a	-0 19a	-0 00	-0 01	0 07	0.18a	0 08	0 15	0 07	0 03	0 09	0 05	0.02	-0.09	-0 09	-0 08	-0 81c	-															
20. Duration of Smoking	-0.20a	0 23b	-0 18a	0 03	-0 14	0 16	0 17a	0 06	0 13	0 06	0.09	0 12	0 00	-0 06	0 06	-0 14	-0.13	-0 85c	0 84c	-														
21. Physical Activity(2)	0.12	-0.30c	0 00	0 18a	0.27c	-0 07	0 03	-0 07	-0.14	-0.12	0.07	-0 00	-0.12	0 04	0 10	0 09	0 07	0.20a	-0.17	-0.18a	-													
22 Fitness(2)	0.12	-0 32c	-0 09	0.17a	0 22b	-0.08	0.02	0 02	-0.12	-0 18a	0.01	-0 10	-0.08	0.07	0.06	0 09	0 11	0.22b	-0 15	-0.20a	0.79c	-												
23. Self-Esteem	-0 05	-0.21a	-0 16	0 53c	0 33c	-0.47c	0 23b	0 02	0.11	0 00	0 37c	0.29c	-0 07	0.04	0 07	-0 06	-0 09	0.04	0 04	-0 04	0.13	0.10	-											
24. GHQ-12(2)	-0 06	0.11	0 07	-0 43c	-0 42c	0 57c	-0.12	-0 08	-0 19a	-0 03	-0.17a	-0 21a	0.23b	-0 03	-0 07	0 08	0 03	-0 10	0 06	0 10	-0.17a	-0 15	-0 54c	-										
25 Confidence	0.08	-0.11	-0 01	0.29c	0 39c	-0.46c	0 05	0 04	0 10	0 04	0 16	0 01	-0 14	0 04	-0 09	-0 06	0.03	0.22b	-0.15	-0.32c	0 04	0 04	0 51c	-0.57c	-									
26. Happiness	0.05	-0 17a	0 08	0 29c	0.27b	-0.52c	-0 01	0 09	0.13	0.09	0.21a	0 06	-0.27c	-0.06	0 04	-0 05	-0.10	0 20a	-0.16	-0.18a	0 10	0 04	0 37c	-0 49c	0 46c	-								
27. Anxiety-Contentment	0.21a	-0 18a	0 06	0.25b	0 35c	-0 43c	-0 03	0 07	0 12	0 12	0 08	0 09	-0 00	0 03	-0.01	0 09	0 12	0 25b	-0 18a	-0 27c	0 10	0 11	0 33a	-0 59c	0 32c	0 37c	-							
28 Depression-Enthusiasm	0 06	-0 14	-0 04	0 37c	0 53c	-0 54c	0.14	0 18a	0 16	0.08	0.22b	0 31c	-0 21a	-0 05	0 10	-0 09	-0 06	0.18a	-0 08	-0 16	0 24b	0 19a	0.54c	-0 71c	0 46c	0 49c	0 70c	-						
29. Drinking to Cope(1)	0.15	0 04	0 19a	-0 23b	-0 01	0 27b	-0 05	0 04	0 03	0 07	-0.04	0 01	0 65c	0 44c	-0.56c	0 23b	0 29c	-0.16	0 13	0 08	-0.17	-0 13	-0.23b	0 24b	-0.15	-0.17	-0 07	-0 20b	-					
30. AUDIT(1)	0 16	-0 16	0 18	-0 05	0.04	0 30c	0 04	0 03	0 13	0 13	-0.05	-0 08	0.37c	0 69c	-0.39c	0 37c	0 40c	0 00	0 01	-0 06	-0.10	-0 04	-0 08	0 15	-0 03	-0 17	-0 15	-0 24b	0 49c	-				
31. Habitual Alcohol Consumption(1)	0 05	0 00	-0 05	-0 02	0 03	-0 08	0 07	-0 04	0 14	0 06	0 00	0 04	0 02	0.16	-0.15	0 05	0 06	-0 20a	0.12	0 09	-0 06	-0 03	0 06	-0 04	0 06	-0 12	-0 00	-0 02	-0 01	0.19a	-			
32. Physical Activity(1)	-0.01	-0 24b	-0 07	0 10	-0 00	-0.16	0 03	0 08	-0.18a	-0.16	0 07	0 07	-0 04	-0 06	0 09	-0 04	-0 02	0.19a	-0.17a	-0.22b	0 48c	0 53c	0.14	-0.14	0 04	0.12	0 07	0.10	-0 17	-0 13	-0 10	-		
33 Fitness(1)	0 07	-0 31c	-0 09	0 17a	0 13	-0 16	-0 00	0 07	-0 27b	-0 15	0 15	0 04	-0 04	-0 05	-0 07	0 05	0 07	0 17a	-0 15	-0 19a	0 49c	0 64c	0 18a	-0.17a	0 12	0 19a	0 10	0 18a	-0.20b	-0 16	-0 05	0 69c	-	
34 GHQ-12(1)	-0 03	0 22a	0 18a	-0 26b	-0 18a	0 47c	-0 06	-0 05	-0 06	-0 01	-0.12	-0 06	0 04	0.03	-0 05	0 02	-0 02	-0 15	0 09	0.15	-0.18a	-0 19a	-0.44c	0 37c	-0 32c	-0 29c	-0 38c	-0.37c	0 23b	0 15	-0 04	-0 20a	-0 24b	-
Mean	74 75	1 62	23 56	21 85	15 59	10 66	13 55	11 84	11 15	10.86	14 18	14 30	10 41	9.73	8 63	18 77	13 25	1 84	7 85	12 66	2 50	2 28	32 09	24 00	1.76	1 59	22 64	26.07	10 38	10 33	28 66	2.75	2 40	23.06
S.D.	6 67	0 49	3 04	3 22	2 52	2 99	2 40	2 00	2 83	2 56	2 41	2.79	3 64	5.76	1 50	17 33	11 50	0 37	24 81	33 77	0 82	0 83	4 80	5 56	0 43	0 49	5 80	5.11	3 66	6 32	99 00	0.85	0 82	5 35

a=p<0.05; b=p<0.01 and c=p<0.005

4.3.3.4. Multivariate Analyses

Hierarchical multiple regression analyses (MRA) were used in the prediction of administration 2 dependent variables (general well being, drinking to cope, alcohol consumption, alcohol problems, fitness and activity), with the corresponding outcome measures from administration 1 being added to the first block of the equation. The default statistical procedure of listwise deletion of missing data was employed. This procedure has been utilised effectively in analysing repeated measures survey data in relation to psychological well being (Zapf et al., 1996).

4.3.3.4.1. Prediction of General Psychological Well being

The final MRA predicted 46% of the variance for GHQ-12(2) scores within the sample. The stepwise results of the MRA showed that previous GHQ-12(1) score, extraversion and neuroticism were the significant predictors of GHQ-12 score (Table 4.3.17.). However, the contribution from the previous GHQ-12(1) score failed to remain significant in the final MRA equation (Table 4.3.17.).

Table 4.3.17. Hierarchical multiple regression analyses predicting general psychological well being (GHQ-12 score) from repeated measures data.

Variable	Change R^2	Step Beta	Final Beta
GHQ-12(1)	0.11c	0.33c	0.04
Age	0.00	-0.02	-0.01
Gender		-0.07	-0.01
Mastery	0.33c	-0.14	-0.16
Extraversion		-0.31c	-0.31c
Neuroticism		0.42c	0.40c
Smoking	0.00	0.03	0.02
Alcohol Consumption		0.03	0.02
Physical Activity		0.05	0.02
Changing the Situation	0.01	0.02	0.02
Accommodation		-0.02	-0.02
Devaluation		-0.03	-0.03
Avoidance		-0.07	-0.07
Symptom Reduction		0.05	0.05
Seeking Social Support		-0.07	-0.07
	$R=0.68$, $R^2=0.46$, $R^2_{ADJ}=0.39$, $F=6.21$, df15, 108, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.3.4.2. Prediction Drinking to Cope, Alcohol Consumption and Alcohol Related Problems

In terms of the predictors of the use of drinking to cope(2), the final MRA equation accounted for 51% of the variance in drinking to cope scores within the sample. Stepwise analysis showed that there were two significant main effects of gender, and previous use of drinking to cope(1), with both variables also being the only significant main effects in the final equation (Table 4.3.18.).

Table 4.3.18. Hierarchical multiple regression analyses predicting drinking to cope from repeated measures data.

Variable	Change R^2	Step Beta	Final Beta
Drinking to Cope(1)	0.42c	0.65c	0.53c
Age	0.03a	0.07	0.06
Gender		-0.14a	-0.16a
Mastery	0.05a	-0.11	-0.11
Extraversion		-0.10	-0.12
Neuroticism		0.05	0.03
Alcohol Expectancies		-0.13	-0.12
Changing the Situation	0.02	0.08	0.08
Accommodation		0.02	0.02
Devaluation		-0.10	-0.10
Avoidance		0.16	0.16
Symptom Reduction		0.01	0.01
Seeking Social Support		0.02	0.02
	$R=0.71$, $R^2=0.51$, $R^2_{ADJ}=0.45$, $F=9.46$, df13, 119, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

With respect to the prediction of alcohol consumption, the final equation accounted for 31% of the variance in alcohol consumption scores within the sample. Table 4.3.19. shows that there were significant stepwise contributions from the main effects of gender, neuroticism, alcohol expectancies and the use of accommodation coping strategies. However, the contribution from neuroticism did not remain significant in the final equation, although it was approaching significance (p=0.06)

Table 4.3.19. Hierarchical multiple regression analyses predicting alcohol consumption from repeated measures data.

Variable	Change R^2	Step Beta	Final Beta
Alcohol Consumption(1)	0.00	0.05	0.02
Age	0.16c	0.05	-0.09
Gender		-0.38c	-0.44c
Mastery	0.11b	0.02	-0.04
Extraversion		0.10	0.12
Neuroticism		0.21a	0.19
Alcohol Expectancies		-0.23a	-0.25a
Drinking to Cope		0.04	0.11
Changing the Situation	0.04	0.00	0.00
Accommodation		-0.21a	-0.21a
Devaluation		-0.01	-0.01
Avoidance		0.02	0.02
Symptom Reduction		-0.06	-0.06
Seeking Social Support		0.11	0.11
	$R=0.56$, $R^2=0.31$, $R^2_{ADJ}=0.21$, $F=3.12$, df14, 96, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

The final equation predicting alcohol problems accounted for 64% of the variance in AUDIT(2) scores within the sample. As table 4.3.20. illustrates, significant stepwise main effects were observed for previous AUDIT(1) score, alcohol expectancies and alcohol consumption, although only previous AUDIT(1) score and alcohol consumption remained significant in the final equation.

Table 4.3.20. Hierarchical multiple regression analyses predicting alcohol related problems from repeated measures data.

Variable	Change R^2	Step Beta	Final Beta
AUDIT(1)	0.46c	0.68c	0.49c
Age	0.03a	0.12	0.04
Gender		-0.11	-0.03
Mastery	0.03	0.01	0.06
Extraversion		0.06	0.04
Neuroticism		-0.01	-0.01
Alcohol Expectancies		-0.17a	-0.11
Alcohol Consumption	0.09c	0.35c	0.38c
Changing the Situation	0.03	-0.06	-0.06
Accommodation		0.06	0.06
Devaluation		0.05	0.05
Avoidance		0.08	0.08
Symptom Reduction		-0.07	-0.07
Seeking Social Support		0.13	0.13
	$R=0.80$, $R^2=0.64$, $R^2_{ADJ}=0.59$, $F=13.28$, df14, 106, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.3.4.3. Prediction of Self-Reported Fitness and Physical Activity

In terms of the predictors of fitness(2), the final MRA accounted for 78% of the variance in fitness scores within the sample. Significant stepwise main effects were observed for previously reported fitness(1) levels, extraversion, neuroticism, physical activity, the use of avoidance coping strategies and the use of seeking social support coping strategies (Table 4.3.21.). However, the contribution made by elements of personality (extraversion and neuroticism) failed to remain significant in the final MRA equation (Table 4.3.21.).

Table 4.3.21. Hierarchical multiple regression analyses predicting self-reported fitness from repeated measures data.

Variable	Change R^2	Step Beta	Final Beta
Fitness(1)	0.44c	0.66c	0.40c
Age	0.03	0.08	-0.00
Gender		-0.14	-0.01
BMI		-0.06	-0.06
Mastery	0.05a	0.04	0.05
Extraversion		0.21b	0.06
Neuroticism		0.16a	0.08
Smoking	0.22c	0.03	0.03
Alcohol Consumption		0.03	0.03
Physical Activity		0.58c	0.59c
Changing the Situation	0.05c	-0.01	-0.01
Accommodation		0.06	0.06
Devaluation		0.12	0.12
Avoidance		-0.18a	-0.18a
Symptom Reduction		-0.06	-0.06
Seeking Social Support		-0.16b	-0.16b
	$R=0.88$, $R^2=0.78$, $R^2_{ADJ}=0.74$, $F=20.16$, df16, 93, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

The final MRA accounted for 44% of the variance in self-reported physical activity(2) scores within the sample. Table 4.3.22. shows that significant stepwise main effects were observed for previous physical activity(1), age, gender and extraversion. However, only the contributions from previously reported physical activity(1) and extraversion remained significant in the final MRA equation (Table 4.3.22.).

Table 4.3.22. Hierarchical multiple regression analyses predicting physical activity from repeated measures data.

Variable	Change R^2	Step Beta	Final Beta
Physical Activity(1)	0.23c	0.47c	0.43c
Age	0.07a	0.17a	0.12
Gender		-0.18a	-0.16
BMI		-0.03	0.01
Mastery	0.11c	0.06	0.02
Extraversion		0.34c	0.33c
Neuroticism		0.15	0.13
Smoking	0.01	0.04	0.02
Alcohol Consumption		0.06	0.02
Changing the Situation	0.03	0.06	0.06
Accommodation		-0.16	-0.16
Devaluation		-0.03	-0.03
Avoidance		0.02	0.02
Symptom Reduction		0.94	0.35
Seeking Social Support		-0.08	0.39
	$R=0.67$, $R^2=0.44$, $R^2_{ADJ}=0.36$, $F=5.00$, df15, 94, $p<0.005$		

Values are mean±SD. a=p<0.05; b=p<0.01 and c=p<0.005

4.3.4. Summary of Results

General psychological well being was significantly predicted by dispositional characteristics of the individual such as personality (in particular neuroticism) and personal control (mastery) in both administrations 1 and 2. However, the only significant predictor of psychological well being in the repeated measures analysis was that of personality (extraversion and neuroticism). None of the health related behaviours emerged as significant predictors of psychological well being. Gender was a significant predictor of administration 1 psychological well being in the final analysis, although only the step beta was significant in administration 2. The use of accommodation as a coping strategy was also a significant predictor of general psychological well being in administration 1 but not in administration 2.

Alcohol expectancies, neuroticism and gender were the predominant predictors of the use of drinking to cope in administrations 1 and 2. Although personal control and the use of avoidance type coping strategies were significant predictors of administration 2 drinking to cope, they were not significant in administration 1. When controlling for administration 1 drinking to cope scores, the only other significant predictor of administration 2 drinking to cope was gender.

In predicting alcohol consumption from this data, individual differences (gender) and other dispositional characteristics of the individual (extraversion but not

neuroticism) were significant, alongside the use of drinking to cope. Interestingly however, repeated measures data revealed that alcohol expectancies and the use of accommodation coping strategies were the significant predictors of alcohol consumption, alongside gender; rather than extraversion and drinking to cope.

Alcohol expectancies, consumption and drinking to cope were the major predictors of alcohol related problems across administrations 1 and 2. Although, personality also emerged as a significant predictor of alcohol related problems in administration 1. Repeated measures data indicated that previously reported alcohol related problems alongside present alcohol consumption levels were the significant predictors of present alcohol related problems.

In terms of fitness, the significant predictors across administrations 1 and 2 were BMI and physical activity. Although the use of social support seeking as a coping strategy was also significant in administration 2. However, repeated measures data indicated that previous fitness levels and the use of both avoidance and social support seeking as coping strategies, as well as physical activity, were significant predictors of current fitness levels.

In terms of physical activity, the significant predictors from both administration 1 and 2 were gender, extraversion and the use of symptom reduction as a coping strategy. In addition, BMI and neuroticism were significant predictors in administration 1, whilst smoking was also significant in administration 2.

Repeated measures data indicated that only previous physical activity and extraversion were significant predictors of subsequent physical activity levels.

Thus, in relation to the model presented earlier (Figure 2.7., page 81), the extensive series of psychosocial results indicates only partial support for a strong role for health and general coping strategies in the prediction of psychological well being. Dispositional characteristics of the individual such as personality appear to have the largest influence on general psychological well being.

Whilst the above results seem to indicate a coherent set of findings, the response rates for both administrations of the questionnaire were disappointing, as was the number of repeated measures cases. These response rates were especially disappointing given the method of questionnaire administration. The most likely explanation for these low response rates is a lack of time for respondents to complete the questionnaire post-lecture. As such it might have been more beneficial to use allocated sessions to allow more time for completion of the questionnaire.

4.4. DISCUSSION

In terms of the longitudinal prediction of psychological well being in this population, the only significant predictors were elements of personality (extraversion and neuroticism). In particular, those reporting high extraversion also reported an enhanced sense of general psychological well being, whilst the opposite was true for those reporting higher neuroticism. Previous research has also identified elements of personality, particularly neuroticism, as being the most significant predictors of affective psychological well being (Yeung and Hemesley, 1997; Sale et al., 2000).

Others have indicated that because both extraversion and neuroticism have been used to reflect elements of both positive and negative affectivity respectively, it is logical to assume that they would be highly related to affective psychological well being (Parkes, 1990). However, previous research has indicated that the impact of such dispositional characteristics of the individual might be reduced using longitudinal data (Zapf et al., 1996; Daniels and Guppy, 1997). Indeed Sale et al. (2000) postulated that if time lagged well being measures were used as covariates in longitudinal analysis, the impact of trait measures, such as extraversion and neuroticism, on psychological well being would be reduced. Interestingly, the results of this investigation showed that even when time lagged well being data were used as a covariate in the prediction of subsequent psychological well being, the significant impact of personality remained significant. Thus, it would appear that extroverts might experience greater levels

of positive affect, whilst neurotics experience more negative affect and distress (Yeung and Hemesley, 1997). In agreement with Yeung and Hemesley (1997), the results of this study showed that personality is more persistent and relates to psychological well being over longer periods of time.

In terms of the cross-sectional results, other variables such as personal control, gender and the use of accommodation coping strategies also significantly contributed to the prediction of psychological well being. Previous research has identified a link between more general coping strategies and psychological well being (Rick and Guppy, 1994; Guppy and Weatherstone, 1997; Sale et al., 2000). The results of this investigation are partly in line with those of Rick and Guppy (1994) and Guppy and Weatherstone (1997) who both identified links between problem-focussed coping strategies (such as accommodation) and psychological well being. Results from administration 1 of this study showed that those reporting a greater use of accommodation as a coping strategy also reported an enhanced sense of psychological well being. This would indicate that those who attempt to modify their desires and expectations to fit in with the situation tend to report a greater perception of psychological well being than those who use some other coping strategy. However, the lack of a significant contribution from avoidance coping to the prediction of psychological well being in this study conflicts with the findings of both Guppy and Weatherstone (1997) and Sale et al. (2000). This is most likely due to differences in the coping measures employed by Guppy and Weatherstone (1997) and the fact that Sale

et al. (2000) reported the prediction of affective psychological well being, whist this study reported the significant predictors of more general psychological well being.

Those reporting higher mastery, and hence a greater personal control over the things that happen to them, also reported a greater sense of psychological well being. This finding is in agreement with other studies that have also reported a significant association between levels of mastery and psychological well being (Franks and Faux, 1990). In addition, males also reported higher perceptions of general psychological well being than females.

Interestingly this study failed to show any significant input from any of the health related behaviours (alcohol consumption, physical activity and smoking) in the prediction of general psychological well being. The fact that none of the health related behaviours significantly predicted psychological well being is somewhat surprising, particularly in light of the findings of previous research. This set of findings might reflect some weaknesses in the scales used to measure the health related behaviours, particularly in the use of self-report scales.

This investigation did not show any significant bivariate associations between alcohol consumption and general psychological well being, a finding which agrees with previous research on older adults (Borgatta et al., 1982; Saunders et al., 1991). Graham and Schmidt (1999) also failed to identify any significant

relationship between the frequency of alcohol consumption and psychological well being. However, in contrast to the results of the present study, Graham and Schmidt (1999) did show that those reporting higher habitual alcohol consumption had a lower perception of psychological well being.

Other investigations have shown links between alcohol misuse and poorer psychological well being (Schonfeld and Dupree, 1991; Moos et al., 1993). Some support for these observations was provided from the bivariate results from administration 2 of the questionnaire in this study, as those that reported more alcohol related problems also reported a lower perception of psychological well being (GHQ-12).

A significant bivariate association was shown between alcohol consumption and affective psychological well being in terms of anxiety-contentment, although not in terms of depression-enthusiasm. This indicates that those with higher alcohol consumption also report a greater sense of affective psychological well being in terms of anxiety-contentment scores. Links between alcohol consumption and measures of affective psychological well being have been identified previously in a similar sample (Sale et al., 2000).

This study showed that self-reported physical activity did not significantly predict general psychological well being (GHQ-12 score). However, bivariate results from both questionnaire administrations showed that those individuals who were

more physically active also reported a greater sense of general psychological well being. This finding lends support to previous research (Mutrie and Biddle, 1995; Yeung and Hemsley, 1997; Sale et al., 2000). Physically active individuals also reported having a higher sense of affective psychological well being in terms of lower anxiety and depression levels, as well as a greater self-esteem. These results confirm previous research findings suggesting a link between physical activity and reductions in anxiety and depression, as well as increased self-esteem (Morgan and Goldston, 1987; Paffenbarger et al., 1994; Liao et al., 1995; Rostad and Long, 1996; Yeung and Hemsley, 1997).

This study extended previous research (e.g. Ingledew et al., 1996) on links between health related behaviours (particularly alcohol consumption and physical activity) and more traditional dimensions of coping. In predicting alcohol consumption from cross-sectional data, both gender and extraversion (but not neuroticism) were significant, as was the use of drinking to cope.

The importance of drinking to cope in the prediction of alcohol consumption has been demonstrated previously by Cooper et al. (1990). This finding may explain the lack of a significant contribution from some of the more general coping strategies (in particular avoidance) to the prediction of alcohol consumption. In terms of the bivariate analyses, significant associations were shown between alcohol consumption and the use of changing the situation, symptom reduction, avoidance, and seeking social support as coping strategies. However, it should

be noted that only the use of changing the situation as a coping strategy was significantly associated with alcohol consumption across both administrations.

When using previous alcohol consumption as a covariate, repeated measures data revealed that alcohol expectancies, gender and the use of accommodation as a coping strategy were the significant predictors of current alcohol consumption. The fact that alcohol expectancies significantly predicts alcohol consumption patterns is consistent across the findings from previous research (Cooper et al., 1988; Evans and Dunn, 1995; and Laurent et al., 1997). Obviously there is a clear rationale for why those individuals who have high expectancies for the positive effects of alcohol also have higher habitual alcohol consumption levels.

The significant contribution of gender to the prediction of alcohol consumption has been demonstrated in the previous literature (Graham et al., 1998). In particular, results indicated that males reported greater alcohol consumption than females. Other reports have suggested that females might drink less than males because they expect a greater level of impairment due to the physiological reaction to alcohol (Jones and Jones, 1976). In addition, the traditional view is that females are more tightly sanctioned with respect to alcohol consumption and intoxicated behaviour (Marlatt and Rohsenow, 1980). However, this explanation is somewhat outdated and might not be sufficient to explain the lower alcohol consumption in female respondents in this study. In particular, because of the

age and nature of the sample population it is unlikely that such sanctions affected alcohol consumption in this sample. Perhaps a more up to date explanation as to why females consume less alcohol than males is due to the fact that women have a higher sensitivity to the toxic effects of alcohol and may also experience a greater level of cognitive impairment (Graham et al., 1998). One of the few studies in conflict with the finding that males consume more alcohol than females is that of Laurent et al. (1997), where the sample was very young (average age 15) and probably did not have established drinking patterns.

When predicting the use of drinking to cope, significant cross-sectional contributions from alcohol expectancies, avoidance coping, personal control, neuroticism and gender were shown. However, from these predictors only gender remained significant when time lagged data were analysed, using previous drinking to cope scores as a covariate. This result shows that males were more likely to use alcohol consumption as a means of coping, a result that might also contribute to the higher habitual alcohol consumption levels reported by male respondents.

In terms of the bivariate analyses, there was a significant association between drinking to cope and the use of avoidance type coping strategies across both administrations, whilst the reported use of both accommodation and devaluation coping strategies was significantly related to drinking to cope in one administration only. Thus, in line with previous research (Farber et al., 1980;

Latack, 1986; Cooper et al., 1988), there is some evidence of a link between the use of drinking to cope, alcohol consumption and some of the more general coping strategies.

However, there is some conflict within the existing literature as to which of the more general coping strategies is linked to alcohol consumption, and thus which ones might be important in further explaining the use of drinking to cope. For example, previous research has indicated that symptom management coping strategies significantly predict alcohol use (Latack et al., 1986), whilst others have reported that it is avoidance coping strategies that are most closely linked to the prediction of alcohol consumption (Cooper et al., 1988). However, Latack et al. (1986) did not measure general coping strategies alongside direct measures of drinking to cope, whereas Cooper et al. (1988) did measured drinking to cope but found no associations between this measure and any of the more general coping strategies. The results of this investigation provide an interesting addition to this debate, as the use of accommodation type coping strategies was shown to significantly predict lower alcohol consumption, whilst the use of more avoidance type coping strategies significantly predicted drinking to cope (although only in cross-sectional analyses). These findings would appear to highlight the potential benefits for the individual in having a wider range of coping strategies at their disposal.

In assessing alcohol related problems within the current sample, use was made of the AUDIT screening instrument, initially developed for use by the WHO. When using the two cut-off points suggested by Claussen and Aasland (1993) to indicate hazardous (9-19 points) and harmful (>19 points) alcohol consumption, approximately 47% of the sample reported hazardous consumption and 14% reported harmful consumption. Clearly there was a large proportion of the sample reporting some form of alcohol misuse in terms of either hazardous or harmful alcohol consumption. It could be that the sample used in this investigation contained an unusually high proportion of problem drinkers, or it could reflect difficulties with the scale. In particular, this unusual result might be reflective of the youth of the respondents and the fact that this was a student population, although previous reports using AUDIT in student populations did not show such a high proportion of problem drinkers (Fleming et al., 1991; Larsen, 1994). The AUDIT scale was designed and validated using a Scandinavian population, whose drinking patterns might be expected to be more conservative than a British population, although it is questionable whether cultural differences should be taken in to consideration when examining hazardous and harmful patterns of alcohol consumption. If the mean response for each item on the AUDIT score is calculated it would appear that respondents reported higher scores on the first three items of the scale (those items relating to alcohol consumption) when compared to the next seven items on the scale (those relating specifically to alcohol problems). Thus, it maybe that the relatively high AUDIT scores observed across this sample are in part due to high responses

relating to consumption and not specifically to the experience of alcohol related problems.

In the prediction of alcohol related problems, there were significant cross-sectional contributions from alcohol expectancies, consumption and drinking to cope. There was also some evidence of a role for personality (both extraversion and neuroticism) in the prediction of alcohol related problems from administration 1. Longitudinal data indicated that previously reported problem drinking as well as present alcohol consumption were the significant predictors of current alcohol related problems. Thus, there is evidence that alcohol consumption, alcohol expectancies and the use of drinking to cope are important in predicting alcohol related problems, supporting the previous literature (Cooper et al., 1988; Evans and Dunn, 1995).

There was a strong contribution from alcohol expectancies in the longitudinal prediction of alcohol consumption and in the cross-sectional prediction of both drinking to cope and alcohol related problems. Cooper et al. (1988) reported a stronger link between alcohol expectancies and drinking to cope than between expectancies and the other two outcome measures. In contrast, Evans and Dunn (1995) reported that alcohol expectancies were more important in determining alcohol related problems than alcohol consumption. Clearly there are some differences between the results of the investigations relating to the interrelationships among alcohol expectancies, consumption patterns, drinking to

cope and alcohol related problems. Distinct differences in the methods of measurement for each of the alcohol related variables, across the investigations is the most likely cause of these discrepancies. However, the fact that the current study shows alcohol expectancies as a significant longitudinal predictor of alcohol consumption, which in turn is a significant longitudinal predictor of alcohol related problems, is consistent with the theoretical model linking alcohol expectancies → alcohol consumption → alcohol related problems.

There is some evidence for a role of personality in predicting alcohol consumption patterns, drinking to cope and alcohol related problems, particularly in terms of the cross-sectional data. It would appear that whilst extraversion is a significant predictor of alcohol consumption, neuroticism is implicated in the prediction of drinking to cope, and both are implicated in the prediction of alcohol related problems. Clearly the link between extraversion and alcohol consumption might be reflective of both the youth of respondents and the social nature of the drinking associated with student based samples. Similar conclusions could be drawn from the results of Williams and Clark (1998), who also identified links between dispositional characteristics of the individual and alcohol consumption, drinking to cope and alcohol related problems. However, some care must be taken in comparing the results of the two studies, as Williams and Clark (1998) did not use traditional personality measures to reflect dispositional characteristics of the individual, nor did they use a standard measure of alcohol related problems, as was used in this study.

Previous research has reported that personality might be the most important factor in predicting physical activity patterns (Yeung and Hemesley, 1997). The results of this investigation would appear to support these findings, in that elements of personality, in particular extraversion, were shown to be the significant predictors of physical activity. This study would appear to show that exercisers exhibit different personality traits to non-exercisers, whereby exercisers score higher on indices of extraversion, a finding also shown by Yeung and Hemesley (1997). Yeung and Hemesley (1997) report that one of the reasons why personality might be predictive of physical activity is that individuals will endeavor to encounter situations consistent with their personalities. Thus, extraverts who need excitement and sensory stimulation will respond to physical activity, whilst the competition and social interaction of sport and exercise are not congruent with neuroticism, whereby the individual will attempt to avoid arousing situations (Yeung and Hemesley, 1997).

In terms of the bivariate analyses, there was a significant association between physical activity and the reported use of changing the situation, avoidance and symptom reduction coping strategies. However, it should be noted that only symptom reduction coping was significantly correlated across both administrations. This finding is in line with previous research which has reported strong links between physical activity and general coping strategies (Rick and Guppy, 1994; Ingledew et al., 1996; Sale et al., 2000). Both Rick and Guppy (1994) and Ingledew et al. (1996) reported links between physical activity and

problem focussed coping strategies. In addition, subsequent investigation on a similar sample to that used in this study, also showed a significant bivariate association between the use of symptom reduction coping and physical activity (Sale et al., 2000).

In terms of self-reported fitness, the significant predictors across administrations 1 and 2 were BMI and physical activity. Although the use of social support seeking as a coping strategy was also significant in administration 2 only. However, repeated measures data indicated that previous fitness levels, current physical activity levels and the use of both avoidance and social support seeking as coping strategies were significant predictors of current physical fitness. Thus, it would appear that there was a significant impact of the use of more general coping strategies on the prediction of physical fitness. This would indicate that those who exhibit more avoidance and social support seeking as coping strategies, and have a low physical activity also have lower self-reported fitness levels.

In summary, this investigation extends previous research relating to the links between health related behaviour (in particular alcohol consumption and physical activity) and more traditional dimensions of psychological well being and its correlates. This study has indicated that whilst there were some bivariate associations between health related behaviour and elements of psychological well being, the health related behaviours were not significant predictors of

general psychological well being. However, these findings should be viewed with some caution in light of the potential weaknesses of using single-item self-report scales in the measurement of the health related behaviours. The fact that psychological well being is not predicted by elements of health related behaviour could also be a consequence of the young and healthy nature of the population investigated.

Both individual differences and dispositional characteristics of the individual would appear to have the strongest impact in predicting both psychological well being and health related behaviour. Because of the strong impact of personality in the prediction of psychological well being, physical activity and alcohol consumption it could be concluded that previously found links between health related behaviour and enhanced levels of psychological well being might be incidental rather that causal, especially in those studies not examining personality. In particular, an extravert personality might lead an individual to participate in greater levels of physical activity, consume more alcohol and also to perceive greater levels of psychological well being.

There was some evidence to support a role for elements of coping and personal control (mastery) in the cross-sectional prediction of psychological well being, although they failed to remain significant in the analyses of longitudinal data.

This study also provides evidence for a theoretical model linking certain drinking motivations (such as drinking to cope and more notably alcohol expectancies) to alcohol consumption, which in turn links to alcohol related problems.

CHAPTER 5: SYNTHESIS OF FINDINGS

5.1. SYNTHESIS OF FINDINGS

The two studies of this thesis were designed to examine the interrelationships among alcohol consumption, physical activity, physical fitness, blood haematology and psychological well being, as outlined in figure 2.5..

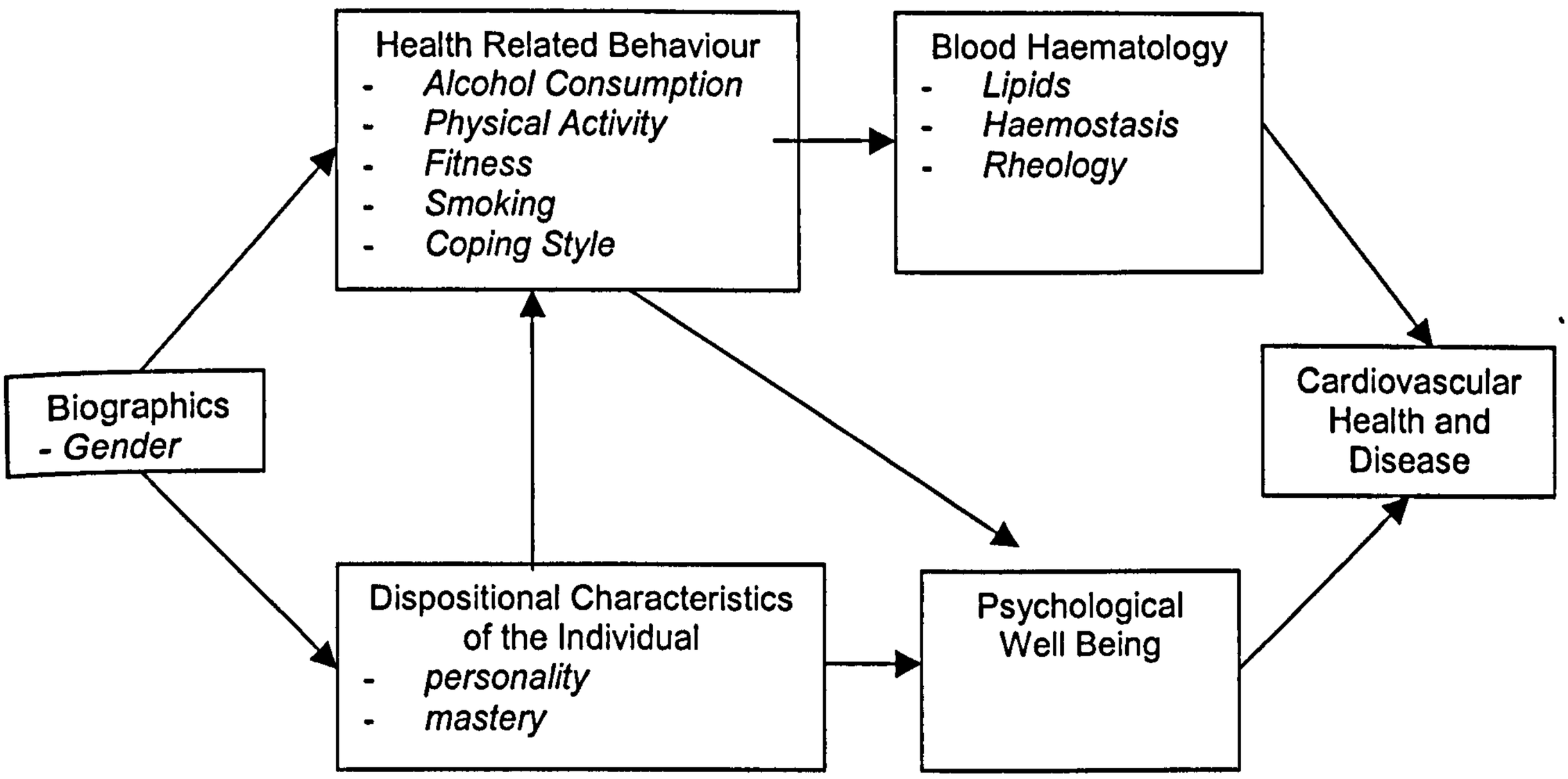

Figure 2.5. Schematic representation of the thesis.

Study 1 was designed to examine the interrelationships among alcohol consumption, physical activity, fitness and blood haematological profiles (Figure 2.6.).

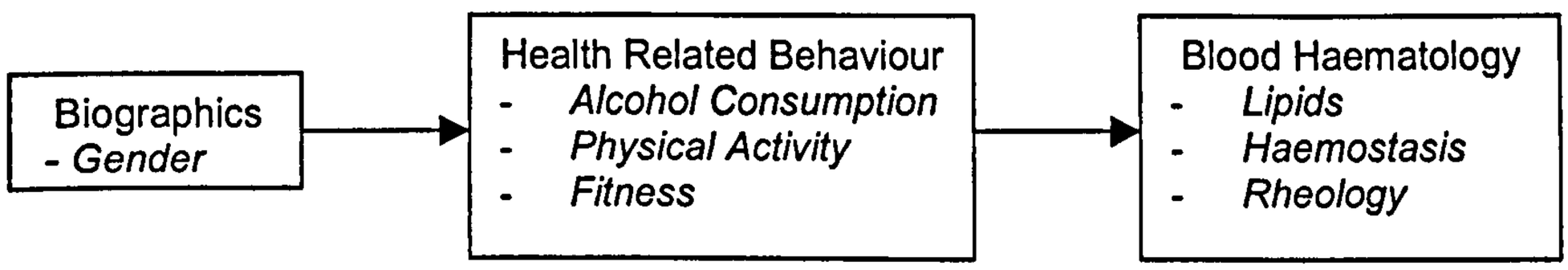

Figure 2.6. Schematic representation of study 1.

The results from study 1 showed that alcohol consumption was not significantly associated with blood lipid profiles. Furthermore, no significant differences in blood lipid profiles were found between light, moderate or heavy drinkers. However, those subjects who reported drinking more often, although not necessarily consuming more alcohol, had higher HDL and apo A1 levels.

An increased inhibition of blood fibrinolysis was shown with higher levels of recent alcohol consumption, as evidenced by higher PAI-1 activity concentrations. There were no other associations between alcohol consumption (habitual or recent) and blood haemostasis. Moderate alcohol consumption resulted in a greater potential for the activation of blood coagulation via the extrinsic blood coagulation pathway. Moderate drinkers also exhibited a greater potential for the activation of blood fibrinolysis when compared to light drinkers, as evidenced by elevated tPA activity concentrations. There were no significant associations between alcohol consumption (recent or habitual) and blood

rheological variables. However, those drinking more often, although not necessarily consuming more alcohol, had higher albumin and total protein concentrations.

Higher self-reported physical activity and fitness levels were associated with reduced LDL, apo B and total cholesterol/HDL ratio. Vigorous physical activity was also associated with a reduced total cholesterol/HDL ratio, probably due to the strong trend towards higher HDL levels in those self-reporting higher vigorous physical activity levels. An acute bout of maximal exercise evoked significant increases in total cholesterol, TG, HDL and VLDL concentrations. However, these significant increases no longer remained when post-exercise raw data were corrected for plasma volume change. Whilst a significant increase in LDL concentration was observed following maximal exercise in uncorrected data, a significant decrease was observed following correction for exercise induced haemoconcentration.

There were no significant associations between physical activity and blood haemostasis, although a high cardiorespiratory fitness was associated with elevated TT. As TT and fibrinogen are closely linked, the fact that fibrinogen was not correlated with VO_{2max} would cast some doubt on the certainty of whether this is a true biological effect, or whether it was merely a consequence of the small sample size (n=23). There was a reduced inhibition of blood fibrinolysis in subjects with higher cardiorespiratory fitness, as evidenced by lower PAI-1

activity concentrations. There was a significant decrease in the total cholesterol/HDL ratio following maximal exercise, whilst the total cholesterol/LDL concentration was significantly elevated.

An acute bout of maximal exercise evoked significant, but transient, alterations in blood coagulation and fibrinolysis. Reductions in fibrinogen levels were observed following maximal exercise, but only following correction for plasma volume change. In addition, maximal exercise evoked significant shortening of blood clotting times, indicating the potential for enhanced blood coagulation with acute bouts of high intensity exercise. Maximal exercise also resulted in an enhanced activation of blood fibrinolysis, as evidenced by increased tPA activity but reduced PAI-1 activity. There was also evidence of *in vivo* hyperfibrinolysis as indicated by elevated D-dimer concentrations.

Those individuals reporting higher habitual physical activity levels also exhibited reduced plasma and serum viscosity. Further, a high self-reported physical fitness, but not VO_{2max}, was associated with lower plasma and serum viscosity. The most likely explanation for these reduced plasma and serum viscosities in more physically active subjects is a chronic expansion of the plasma volume. An acute bout of maximal exercise resulted in increased plasma and serum viscosity in data uncorrected for plasma volume loss, most probably due to a concomitant increase in plasma protein concentrations and significant haemoconcentration.

Study 2 was designed to examine the prediction of psychological well being from alcohol consumption and physical activity, whilst also examining the impact of individual differences, dispositional characteristics of the individual and general coping strategies (Figure 2.7.).

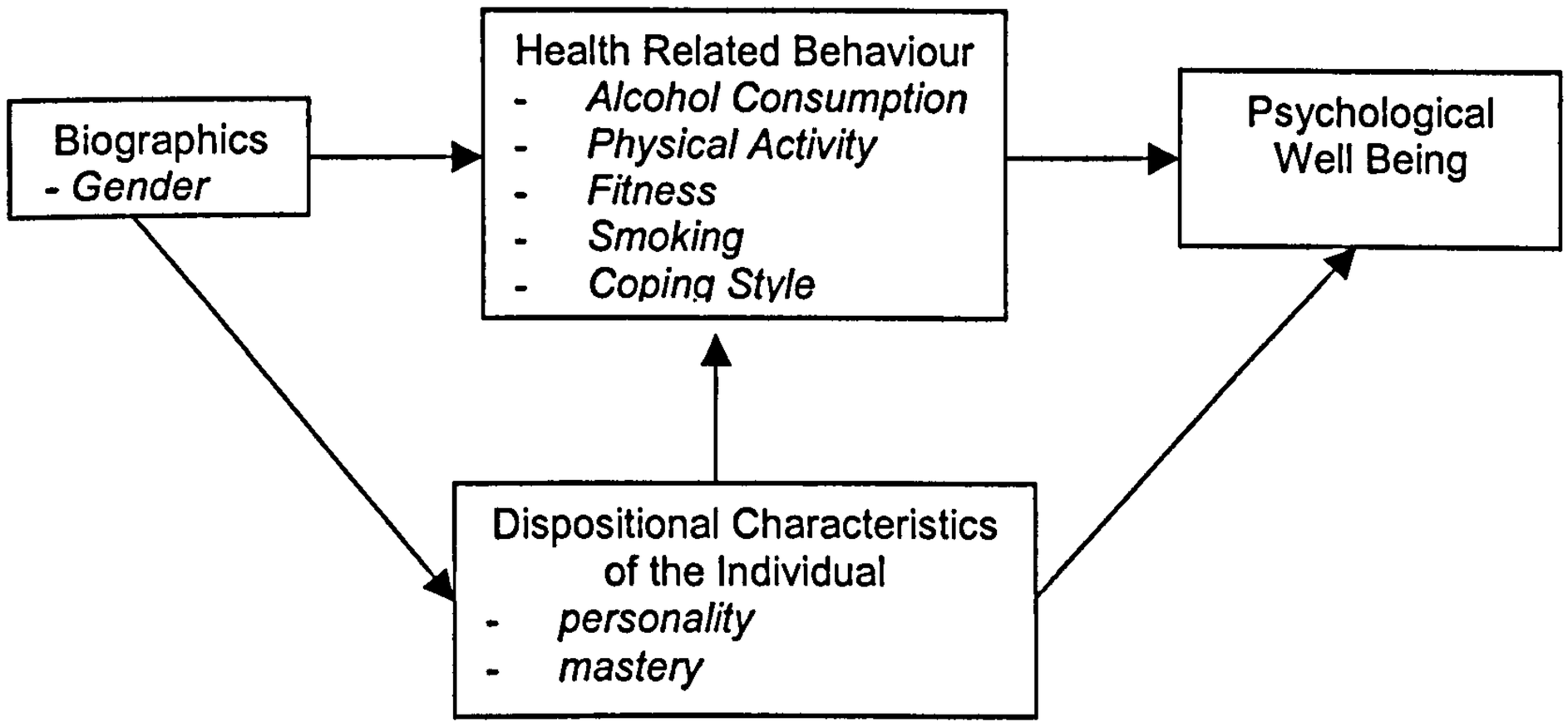

Figure 2.7. Schematic representation of study 2.

Results from study 2 showed that whilst there were some significant bivariate correlations between alcohol consumption, physical activity and psychological well being, there was no significant role for these health related behaviours in the prediction of psychological well being. Dispositional characteristics of the individual, such as personality, were the only significant predictors of psychological well being in the repeated measures analyses. In particular, results showed that extraverts had a higher sense of psychological well being,

with high neuroticism scores predicting a reduced sense of psychological well being.

However, some evidence of a role for accommodation coping (administration 1) and mastery (both administrations 1 and 2) in the prediction of psychological well being was evident from the cross-sectional data. Effective coping strategies can reduce the impact of stress on psychological well being, in this investigation those individuals who reported coping by adjusting their desires to meet the situation (accommodation) also reported a greater sense of psychological well being (administration 1 only). Furthermore, those who reported a greater perception of personal control over their circumstances (higher mastery) also reported an enhanced sense of psychological well being.

Individual differences, such as gender, and dispositional characteristics of the individual were also significant predictors of health related behaviour, in terms of alcohol consumption and physical activity. Male subjects reported higher alcohol consumption and extroverts reported greater physical activity. In addition, the reported use of accommodation coping strategies significantly predicted reduced alcohol consumption.

There was some evidence of a role for drinking motivations such as alcohol expectancies and drinking to cope (although only from cross-sectional data) in the prediction of alcohol consumption. In particular, those who reported higher

expectancies for a positive effect of alcohol also reported higher consumption, as did those who reported the use of drinking to cope. Only elevated alcohol consumption was significant in the prediction of alcohol related problems from the repeated measures data. Thus, this study indicates a possible theoretical model linking drinking motivations to alcohol consumption, which in turn links to alcohol misuse.

In summary, the aims of the two studies described in this thesis were realised as follows:

1. In general there was no evidence for a relationship between alcohol consumption and blood haematological profiles.
2. Self-reported physical activity, but not weekly energy expenditure, was correlated with lower LDL levels and total cholesterol/HDL ratio. The finding that the two methods of physical activity measurement were not in agreement is concerning and might reflect some weaknesses in the scales used. However, both self-reported physical activity and habitual weekly energy expenditure were associated with reduced plasma and serum viscosity levels. No significant correlations were shown between physical activity measures and blood haemostasis.
3. Self-reported fitness, but not VO_{2max} was significantly correlated with reduced LDL, total cholesterol/HDL ratio, plasma viscosity and serum viscosity. Higher cardiorespiratory fitness was associated with lengthened thrombin time and lower PAI-1 activity concentrations. The finding that the two methods

of fitness measurement were not in agreement is concerning and might reflect some weaknesses in the single-item scale used to indicate self-reported fitness.

4. An acute bout of maximal exercise resulted in transient alterations in blood haematological profiles. Some of these alterations were modified when post-exercise and recovery raw data were corrected for plasma volume changes.

5. Extraversion and neuroticism significantly predicted psychological well being. Although there were some significant bivariate correlations between alcohol consumption, physical activity and psychological well being, the health related behaviours did not significantly predict psychological well being. However, these findings must be viewed with some caution in light of the potential weaknesses of using single-item self-report measures of health related behaviour.

6. Male gender and high expectancies for a positive effect of alcohol were significant predictors of alcohol consumption. In addition, those who reported a greater use of accommodation coping also reported lower alcohol consumption. Alcohol related problems were significantly predicted by alcohol consumption.

7. Those who exhibited greater use of avoidance and social support seeking as coping strategies, and had lower physical activity levels also had lower self-reported fitness levels. High extraversion significantly predicted physical activity levels.

CHAPTER 6: OVERALL CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

6.1. OVERALL CONCLUSIONS

It is concluded that alcohol consumption was not related to blood haematological profiles, or to the prediction of psychological well being. Higher self-reported physical activity levels were related to blood lipid concentrations, whilst higher energy expenditures on physical activity were associated with blood rheological profiles. Whilst there was no association between physical activity and blood haemostasis, higher cardiorespiratory fitness was associated with an increased potential for blood fibrinolysis. Maximal exercise was associated with transient alterations in blood haematological profiles, but neither physical activity, nor fitness, were significant predictors of psychological well being.

It is recognised that there are limitations to the study design, particularly related to the small sample size in study 1, that consequently restrict the certainty of the conclusions which can be reported. It is possible that another detailed investigation examining the interrelationships among alcohol consumption, physical activity and haematological profiles, although incorporating a larger sample size and a non-student population, might show different results to those reported in this thesis. It is possible that a type I and/or type II error was committed, and a similar investigation with a larger sample size is required to confirm or refute the findings of the present study.

6.2. RECOMMENDATIONS FOR FUTURE RESEARCH

A number of issues have arisen from the present study. In particular, the following areas warrant further investigation:

1. The study should be repeated on a larger sample size.
2. Study 2 should be repeated on an older sample that may have more established alcohol consumption and physical activity patterns.
3. Study 2 should also be repeated with both shorter and longer gaps between questionnaire administrations.
4. There is a continued need for improved and refined methods of the measurement of physical activity, alcohol consumption and alcohol misuse by questionnaire.
5. Large, randomised and controlled trials are required to establish possible causal links between increases in blood lipids, in particular TG, and alterations in tPA and PAI-1 concentrations.
6. Further investigation is required to examine the combined effects of alcohol consumption and exercise on *in vivo* thrombin formation and fibrin generation.

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APPENDICES

APPENDIX A: Study 1 Pre-Test Questionnaire

Liverpool
John Moores University

Pre-Test Questionnaire

This pre-test questionnaire will contribute to a research project undertaken within the School of Human Sciences at the Liverpool John Moores University. The study you are involved in has been designed to examine the inter-relationships among alcohol consumption, physical activity and variables in the blood relating to cardiovascular health and disease.

The questionnaire asks several questions concerning you and your lifestyle, including questions on physical activity, diet, alcohol consumption, family medical history, and hormonal contraceptive use.

The results of this questionnaire will be treated in the strictest confidence and only the experimenter will see or have any further access to the details of individual questionnaires. The results reported in the PhD thesis or in subsequent publications will be represented as group data, your individual responses will not appear.

Remember: You are under no obligation to complete this questionnaire in whole or in part and you are free to withdraw from this study at any time.

Craig Sale B.Sc. (Hons), M.Sc.
Postgraduate Research Student
Research Institute for Sport and Exercise Sciences.
Liverpool John Moores University.
Room 2.25, Henry Cotton Campus,
Trueman Building, Webster Street, Liverpool. L3 3AF.
Tel : 0151 231 4341
e-mail: HUMCSALE@livjm.ac.uk

Demographic Information

The first part of this questionnaire is to gather data for ***statistical comparison only.***
PLEASE REPLY TO ALL THE ITEMS.

ITEMS	COMPLETE BOX
What is your **gender?**	[ ] Male [ ] Female
What is your **date of birth?**	...../...../.....
What is your current **domestic status?** *(Tick a box)*	[ ] Married (or cohabiting.) [ ] Not married or cohabiting (but in a steady relationship) [ ] Divorced or Separated [ ] Widowed [ ] Single
Do you have any **dependent children?** *(If **YES** please specify how many)*	[ ] Yes [ ] No No. of dependent children:.....
In terms of educational qualifications :- a. How many GCSE's / 'O' levels (or equivalent) do you have at grades A-C. b. Howmany 'A' levels do you have? c. What subjects did you take at 'A' level?	
Do you have a job **outside of college hours?**	[ ] Yes [ ] No
If yes what is your **job title?**	.....
Is this **part-time** or **full-time?**	[ ] Full-time [ ] Part-time
What are your parents occupations?	Father..... Mother.....
What is your **ethnic origin?**	[ ] Caucasian [ ] Afro-Caribbean [ ] Asian [ ] Oriental
Do you have a **practising religion?** *f **YES** please specify which religion)*	[ ] Yes [ ] No Religion:.....

Physical Activity

(a) Which of the following best describes your ***usual practice.***

PLEASE TICK ONE BOX ONLY FOR EACH QUESTION.

ITEMS	COMPLETE BOX
Do you think you take enough exercise?	[ ] Yes [ ] No
During the day, on an average weekday, do you spend **most** of your time: *(Tick one box only)*	[ ] Sitting Down (e.g. driving or at a desk) [ ] Engaged in moderate activity (e.g. walking, light-lifting, houswork) [ ] Engaged in vigorous activity (aerobic, digging, heavy-lifting, jogging)
What sporting or exercise activities do you engage in each week? (i.e. walking, jogging, aerobics, soccer, gardening)	1..... 2..... 3..... 4..... 5..... 6.....
For **each** of the activites listed above, how many minutes do you spend on each activity per workout?	1..... 2..... 3..... 4..... 5..... 6.....
For **each** of the activites listed above, how many workouts do you do per week?	1..... 2..... 3..... 4..... 5..... 6.....

Physical Activity (continued)

On average, how often do you undertake **vigorous** sport or recreational activities which last 20 minutes and make you **breathless** (e.g. jogging, aerobics, football, tennis)	[ ] Never [ ] Less than once a week [ ] 1 to 3 days a week [ ] 4 to 6 days a week [ ] Every day of the week
On average, how often do you undertake **less vigorous** sport or recreational activities **in addition** to your normal daily activities (e.g. walking, yoga, gardening)	[ ] Never [ ] Less than once a week [ ] 1 to 3 days a week [ ] 4 to 6 days a week [ ] Every day of the week
How would you describe your **fitness** compared to other people of your age?	[ ] Excellent [ ] Good [ ] Fair [ ] Poor [ ] Very poor
How would you describe your level of **physical activity** compared to other people of your age?	[ ] Excellent [ ] Good [ ] Fair [ ] Poor [ ] Very poor
How would you describe your **health** compared to other people of your age?	[ ] Excellent [ ] Good [ ] Fair [ ] Poor [ ] Very poor

Smoking History

The following section will ask you questions concerning you smoking habits.

ITEMS	COMPLETE BOX
Which of the following statements best describes you?	[ ] I have never smoked [ ] I used to smoke occasionally but don't smoke now [ ] I used to smoke everyday but don't smoke now [ ] I smoke occasionally but not everyday [ ] I smoke every day
If you **do smoke** how long have you been smoking for?	
If you **used to smoke** how long were you smoking for before quitting?	
If you **used to smoke** how long has it been since you last smoked?	
If **you do smoke** how many cigarettes, cigars or tobacco do you smoke each week?	
What brand of cigarettes, cigars, or tobacco do you smoke?	

Alcohol Consumption

(a) This section is concerned with ***your drinking habits.***

PLEASE REPLY TO ALL THE ITEMS.

Circle your choice for each item on the table

ITEMS					
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times per month	2-3 times per week	4 or more times per week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 -9	10 or more
3. How often do you have 6 or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
5. How often during the last year have you failed to do what is normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
6. How often during the last year have you needed a drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
9. Have you or someone else been injured as a result of your drinking?	No	Yes but not in the last year	Yes during the last year		
10. Has a relative, friend, or doctor been concerned about your drinking or suggested you cut down?	No	Yes but not in the last year	Yes during the last year		

(b) If you replied ***NEVER*** to question 1 of section (a) please answer the next 4 questions.

1. Have you ever consumed a drink containing alcohol?	Yes	No			
2. How long has it been since you have had a drink containing alcohol?	Less than 3 months	6 months - 1 year	1 year - 2 years	2 years - 5 years	more than 5 years
3. For how long were you consuming drinks containing alcohol before quitting?	6 months	1 year	2 years	3 years	more than 3 years
4. For what reason did you stop consuming drinks containing alcohol?					

(c) If you replied that you ***DO DRINK ALCOHOLIC DRINKS*** to question 1 of section (a) (i.e. responses 2-5) then please answer the next 4 questions.

What is your average alcohol consumption during a 7 day week? *For example :* type : John Smiths Bitter amount : 4 cans type : Red wine amount : 1 bottle type : Vodka amount : 3 shots type : Hooch amount : 4 bottles	type..... amount..... type..... amount..... type..... amount..... type..... amount..... type..... amount.....
If you think of last weekend (fri, sat, sun). How much alcohol did you consume.....	
Friday.....	type..... amount..... type..... amount..... type..... amount..... type..... amount..... type..... amount.....
Saturday.....	type..... amount..... type..... amount..... type..... amount..... type..... amount.....
Sunday.....	type..... amount..... type..... amount..... type..... amount..... type..... amount..... type..... amount.....
Is this typical of a usual weekends alcohol consumption?	[ ] Yes [ ] No
If not please give a typical weekends alcohol consumption.....	type..... amount..... type..... amount..... type..... amount..... type..... amount..... type..... amount.....

Dietary Patterns

The following section will ask you questions concerning you dietary habits.

(a) How often do you eat the following foods?

ITEMS	Never	Less than once a week	1 or 2 days per week	Most Days	Once a day	More than once a day
Fresh fruit in summer	1	2	3	4	5	6
Fresh fruit in winter	1	2	3	4	5	6
Salads in summer	1	2	3	4	5	6
Salads in winter	1	2	3	4	5	6
Green vegetables	1	2	3	4	5	6
Fish (all kinds)	1	2	3	4	5	6
Poultry (e.g. chicken, turkey	1	2	3	4	5	6
Red Meat (e.g. beef lamb, pork)	1	2	3	4	5	6
Processed meat (e.g. burgers, susages, pies, pastes, pate)	1	2	3	4	5	6
Cheese	1	2	3	4	5	6

(b) Please respond to all of the following questions.

Do you eat a special diet? *(If **YES** please specify)*	[ ] Yes [ ] No diet.....
What kind of bread do you eat?	White..... Brown..... Wholemeal.....
What kind of spreading fat do you use at home?	Butter..... Hard Margarine..... Soft Margarine..... Low Calorie Spread..... None.....
What type of cooking fat do you use at home?	Lard, butter or other animal fat..... Vegetable Oil..... Olive Oil..... Other (please specify).....
What type of milk do you normally use?	Full Cream..... Semi-Skimmed..... Skimmed..... None..... Other (please specify).....

General Health

(a) Which of the following best describes your ***usual state of health.***

PLEASE TICK ONE BOX ONLY.

I am very healthy	
I am reasonably healthy, but could do better	
I am sometimes healthy, sometimes not	
I am not very healthy	
I am definitely unwell, ill and in poor health	
I find it hard to say, I am not really sure	

Family Medical History

The following section will ask you questions concerning your family history.

Have you ever been told by a doctor that you have, or have had: High Blood Pressure Angina A Heart Attack or Stroke High Cholesterol Level Diabetes Mellitus	 [ ] Yes [ ] No [ ] Yes [ ] No [ ] Yes [ ] No [ ] Yes [ ] No [ ] Yes [ ] No
Has anybody in your family suffered from heart trouble? (e.g. heart attack, stroke, heart disease, angina) (If Yes, which relation[s])	[ ] Yes [ ] No .....
Has anybody in your family suffered from high blood pressure? (If Yes, which relation[s])	[ ] Yes [ ] No .....
Has anybody in your family died from heart trouble? (If Yes, which relation[s])	[ ] Yes [ ] No .....
Has anybody in your family suffered from high cholesterol levels? (If Yes, which relation[s])	[ ] Yes [ ] No .....
Has anybody in your family suffered from diabetes mellitus? (If Yes, which relation[s])	[ ] Yes [ ] No .....

Hormonal Contraceptive Use

The following section will ask **female respondents only** about the use of hormonal contraceptives. It is necessary to collect this information because contraceptive use can markedly affect the variables being measured in the blood for this experiment.

ITEMS	COMPLETE BOX
Do you use any form of hormonal contraception? (i.e. oral, intravenous, intrauterine)	[ ] Yes [ ] No
If you replied **yes** to the above question what brand of contraception do you use?	
For how long have you been using this form of contraception?	
If less than **6 months**, what brand of contraception, **if any**, were you using previously	
If you replied **no** to the above question, have you previously taken any form of hormonal contraception?	
If YES what brand of contraception did you previously use?	
For how long did you use this form of hormonal contraception before ceasing?	
How long has it been since you last used hormonal contraception?	
How many days has it been since the onset of your last menstrual cycle?	

APPENDIX B: Study 2 Survey on Alcohol Consumption, Physical Activity and Well Being

Liverpool
John Moores University

Survey of Alcohol Consumption, Physical Activity and Well Being

This survey will contribute to a research project undertaken within the School of Human Sciences at the Liverpool John Moores University. The survey asks several questions concerning your alcohol consumption, physical activity and psychological well being.

You will be contacted again during the next academic year and asked to complete the same survey again. You are under no obligation to complete this, or indeed the following survey. However, your co-operation would be greatly appreciated and the results of this study will hopefully contribute to current research concerning alcohol consumption, physical activity and their relationship to physical and psychological well being.

There are no right or wrong answers to the questions in the survey but what is of most value are your honest personal experiences, as best apply to the questions posed. Complete anonymity of questionnaire data is assured. It is important to remember that it is your opinion that is of most value so please answer all the questions by yourself with no assistance from others sitting close to you. Please read the general information and the questions carefully before answering.

Thank-you for your time and co-operation.

Craig Sale B.Sc. (Hons), M.Sc.
Postgraduate Research Student
Research Institute for Sport and Exercise Sciences.
Liverpool John Moores University.
Room 2.25, Henry Cotton Campus
Trueman Building, Webster Street
Liverpool. L3 3AF.
Tel : 0151 231 2474
e-mail : HUMCSALE@LIVJM.AC.UK

Section 1: Statistical Information

The first part of this questionnaire is to gather data for STATISTICAL COMPARISON ONLY.

PLEASE REPLY TO ALL THE ITEMS.

ITEMS	COMPLETE BOX
What is your **gender?**	[ ] Male [ ] Female
What is your **date of birth?**	...../...../.....
What is your current **domestic status?** *(Tick a box)*	[ ] Married (or cohabiting.) [ ] Not married or cohabiting (but in a steady relationship) [ ] Divorced or Separated [ ] Widowed [ ] Single
Do you have any **dependent children?** *(If YES please specify how many)*	[ ] Yes [ ] No No. of dependent children:.....
In terms of educational qualifications :-	
a. How many GCSE's / 'O' levels (or equivalent) do you have at grades A-C.	
b. How many 'A' levels do you have?	
c. What subjects did you take at 'A' level?	
Do you have a job **outside of college hours?**	[ ] Yes [ ] No
If yes what is your **job title?**	.....
Is this **part-time** or **full-time?**	[ ] Full-time [ ] Part-time
What are your parents occupations?	Father..... Mother.....
What is your **ethnic origin?**	[ ] Caucasian [ ] Afro-Caribbean [ ] Asian [ ] Oriental [ ] Other
Do you have a **practising religion?** *If YES please specify which religion)*	[ ] Yes [ ] No Religion:.....

Section 2: Coping in General Life

Section 2 is concerned with how you GENERALLY cope with problems in YOUR LIFE.

PLEASE REPLY TO ALL THE ITEMS.

Use these response choices to answer the items below:

RESPONSE CHOICES				
1 Never	**2 Rarely**	**3 Sometimes**	**4 Often**	**5 Always**

Circle your response choice for each item on the table:

ITEMS	CIRCLE YOUR CHOICE				
1. I try to change the situation to get what I want.	1	2	3	4	5
2. I make an effort to change my expectations.	**1**	**2**	**3**	**4**	**5**
3. I try to convince myself that the problem was not very important after all.	1	2	3	4	5
4. I try to keep myself from thinking about the problem.	**1**	**2**	**3**	**4**	**5**
5. I try to let off steam.	1	2	3	4	5
6. I talk to someone to find out more about the situation.	**1**	**2**	**3**	**4**	**5**
7. I focus my efforts on changing the situation.	1	2	3	4	5
8. I try to convince myself that the way things were, was in fact acceptable.	**1**	**2**	**3**	**4**	**5**
9. I tell myself the problem was unimportant.	1	2	3	4	5
10. I try to turn my attention away from the problem.	**1**	**2**	**3**	**4**	**5**
11. I try to relieve my tension somehow.	1	2	3	4	5
12. I accept sympathy and understanding from someone.	**1**	**2**	**3**	**4**	**5**
13. I work on changing the situation to get what I want.	1	2	3	4	5
14. I try to adjust my expectations to meet the situation.	**1**	**2**	**3**	**4**	**5**
15. I tell myself the problem wasn't so serious after all.	1	2	3	4	5
16. I refuse to think about the problem.	**1**	**2**	**3**	**4**	**5**
17. I try to get it off my chest.	1	2	3	4	5
18. I ask a relative or friend I respect for advice.	**1**	**2**	**3**	**4**	**5**
19. I try to fix what was wrong with the situation.	1	2	3	4	5
20. I try to adjust my own standards.	**1**	**2**	**3**	**4**	**5**
21. I tell myself that the problem wasn't such a big deal after all.	1	2	3	4	5
22. I try to avoid thinking about the problem.	**1**	**2**	**3**	**4**	**5**
23. I try to relax.	1	2	3	4	5
24. I talk to someone about how I was feeling.	**1**	**2**	**3**	**4**	**5**

Section 3: Personal Control

This section asks about the DEGREE of CONTROL OR INFLUENCE you have over YOUR LIFE.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS	STRONGLY AGREE	AGREE	DISAGREE	STRONGLY DISAGREE
1. I have little control over the things that happen to me.	1	2	3	4
2. There is really no way I can solve some of the problems I have	**1**	**2**	**3**	**4**
3. There is little I can do to change many of the important things in my life.	1	2	3	4
4. I often feel helpless in dealing with the problems of life.	**1**	**2**	**3**	**4**
5. Sometimes I feel that I'm being pushed around in life.	1	2	3	4
6. What happens to me in the future mostly depends on me.	**1**	**2**	**3**	**4**
7. I can do just about anything I really set my mind to.	1	2	3	4

Section 4: Well-being in University Life

(a) Please rate the following 19 items, concerning how often you have been feeling the way the item describes over the PAST FEW WEEKS AT UNIVERSITY.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS	Never	Occasionally	SOME of the time	MUCH of the time	MOST of the time	ALL of the time
1. Tense	1	2	3	4	5	6
2. Uneasy	**1**	**2**	**3**	**4**	**5**	**6**
3. Worried	1	2	3	4	5	6
4. Calm	**1**	**2**	**3**	**4**	**5**	**6**
5. Contented	1	2	3	4	5	6
6. Relaxed	**1**	**2**	**3**	**4**	**5**	**6**
7. Depressed	1	2	3	4	5	6
8. Gloomy	**1**	**2**	**3**	**4**	**5**	**6**
9. Miserable	1	2	3	4	5	6
10. Cheerful	**1**	**2**	**3**	**4**	**5**	**6**
11. Enthusiastic	1	2	3	4	5	6
12. Optimistic	**1**	**2**	**3**	**4**	**5**	**6**
13. Anxious	1	2	3	4	5	6
14. Comfortable	**1**	**2**	**3**	**4**	**5**	**6**
15. Motivated	1	2	3	4	5	6
16. Angry	**1**	**2**	**3**	**4**	**5**	**6**
17. Aggressive	1	2	3	4	5	6
18. Annoyed	**1**	**2**	**3**	**4**	**5**	**6**
19. Placid	1	2	3	4	5	6

(b) The following 16 items ask about how things have been going at college over the PAST FEW WEEKS.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
1. I can do my academic work well.	1	2	3	4	5
2. With my academic work, I make a special effort to keep trying when things seem difficult.	**1**	**2**	**3**	**4**	**5**
3. I am not very interested in my academic work.	1	2	3	4	5
4. I find my academic work quite difficult.	**1**	**2**	**3**	**4**	**5**
5. I often have trouble coping with my academic work.	1	2	3	4	5
6. I enjoy doing new things in my academic work.	**1**	**2**	**3**	**4**	**5**
7. I sometimes think I am not very competent at my academic work.	1	2	3	4	5
8. I like to set myself challenging targets in my academic work.	**1**	**2**	**3**	**4**	**5**
9. I prefer to avoid difficult activities in my academic work.	1	2	3	4	5
10. I am not very concerned how things turn out with my academic work.	**1**	**2**	**3**	**4**	**5**
11. I can deal with just about any problem in my academic work.	1	2	3	4	5
12. I feel I am better than most people at tackling difficulties with my academic work.	**1**	**2**	**3**	**4**	**5**
13. After I leave university, I keep worrying about work problems.	1	2	3	4	5
14. I find it difficult to unwind at the end of a university day.	**1**	**2**	**3**	**4**	**5**
15. I feel used up at the end of a university day.	1	2	3	4	5
16. Being in university makes me feel quite exhausted at the end of the day.	**1**	**2**	**3**	**4**	**5**

Section 5: General Feelings

(a) Try to decide which option below best represents your USUAL WAY of acting or feeling. There are no right or wrong answers, your IMMEDIATE REACTION is what is important.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS	ALMOST NEVER	QUITE SELDOM	QUITE OFTEN	ALMOST ALWAYS
1. Do you like plenty of excitement and bustle around you?	1	2	3	4
2. Does your mood go up and down?	**1**	**2**	**3**	**4**
3. Are you rather lively?	1	2	3	4
4. Do you feel "just miserable" for no good reason?	**1**	**2**	**3**	**4**
5. Do you like mixing with people?	1	2	3	4
6. When you get annoyed do you need someone friendly to talk to?	**1**	**2**	**3**	**4**
7. Would you call yourself happy-go-lucky?	1	2	3	4
8. Are you troubled about feelings of guilt?	**1**	**2**	**3**	**4**
9. Can you let yourself go and enjoy yourself a lot at a lively party?	1	2	3	4
10. Would you call yourself tense or "highly strung"?	**1**	**2**	**3**	**4**
11. Do you like practical jokes?	1	2	3	4
12. Do you suffer from sleeplessness?	**1**	**2**	**3**	**4**

Section 6: General Psychological Well Being

We would like to know how you have felt in GENERAL, OVER THE PAST FEW WEEKS. Remember that we want to know about PRESENT AND RECENT complaints, NOT those you had in the past.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

HAVE YOU RECENTLY:-	**CIRCLE YOUR CHOICE**			
1. Been able to concentrate on whatever you are doing?	Better than usual	Same as usual	Less than usual	Much less than usual
2. Been losing confidence in yourself?	**Not at all**	**No more than usual**	**Rather more than usual**	**Much more than usual**
3. Felt that you were playing a useful part in things?	More so than usual	Same as usual	Less useful than usual	Much less useful
4. Lost much sleep over worry?	**Not at all**	**No more than usual**	**Rather more than usual**	**Much more than usual**
5. Felt capable of making decisions about things?	More so than usual	Same as usual	Less so than usual	Much less capable
6. Felt constantly under strain?	**Not at all**	**No more than usual**	**Rather more than usual**	**Much more than usual**
7. Been able to face up to your problems?	More so than usual	Same as usual	Less able than usual	Much less able
8. Felt that you couldn't overcome your difficulties?	**Not at all**	**No more than usual**	**Rather more than usual**	**Much more than usual**
9. Been able to enjoy your normal day-to-day activities?	More so than usual	Same as usual	Less so than usual	Much less than usual
10. Been feeling unhappy and depressed?	**Not at all**	**No more than usual**	**Rather more than usual**	**Much more than usual**
11. Been feeling reasonably happy all things considered?	More so than usual	About same as usual	Less so than usual	Much less than usual
12. Been thinking of yourself as a worthless person?	**Not at all**	**No more than usual**	**Rather more than usual**	**Much more than usual**

Section 7: Opinion of Self

This section asks about the VIEWS that you hold about YOURSELF.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS	STRONGLY AGREE	AGREE	DISAGREE	STRONGLY DISAGREE
1. I feel that I'm a person of worth, at least on an equal basis with others	1	2	3	4
2. I feel that I have a number of good qualities	**1**	**2**	**3**	**4**
3. All in all, I am inclined to feel that I am a failure	1	2	3	4
4. I am able to do things as well as most other people	**1**	**2**	**3**	**4**
5. I feel I do not have much to be proud of.	1	2	3	4
6. I take a positive attitude toward myself	**1**	**2**	**3**	**4**
7. On the whole, I am satisfied with myself	1	2	3	4
8. I wish I could have more respect for myself	**1**	**2**	**3**	**4**
9. I certainly feel useless at times	1	2	3	4
10. At times I think I am no good at all	**1**	**2**	**3**	**4**

Section 8: Coping and Life Events

(a) It is well recognised that certain life events can be perceived as being stressful. Please can you identify and describe THREE EVENTS that have occurred within the LAST YEAR that you have found the most stressful or difficult. If there have NOT been any stressful life events then PLEASE INDICATE THIS in the box below and CONTINUE TO THE NEXT SECTION.

Event 1	
Event 2	
Event 3	

(b) We would like to know if you think that you have successfully coped with the stressful life events that you have OUTLINED ABOVE (if there were any) and we would also like to know what method(s) you used to cope with these events.

Do you feel that you successfully coped with.....	Event 1.... Yes/No Event 2.... Yes/No Event 3.... Yes/No
What method(s) did you use to cope with Event 1?	
What method(s) did you use to cope with Event 2?	
What method(s) did you use to cope with Event 3?	

Section 9: Alcohol Consumption

(a) This section is concerned with your USUAL DRINKING HABITS.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS					
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times per month	2-3 times per week	4 or more times per week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	**1 or 2**	**3 or 4**	**5 or 6**	**7 -9**	**10 or more**
3. How often do you have 6 or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?	**Never**	**Less than monthly**	**Monthly**	**Weekly**	**Daily or almost daily**
5. How often during the last year have you failed to do what is normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
6. How often during the last year have you needed a drink in the morning to get yourself going after a heavy drinking session?	**Never**	**Less than monthly**	**Monthly**	**Weekly**	**Daily or almost daily**
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?	**Never**	**Less than monthly**	**Monthly**	**Weekly**	**Daily or almost daily**
9. Have you or someone else been injured as a result of your drinking?	No	Yes but not in the last year	Yes during the last year		
10. Has a relative, friend, or doctor been concerned about your drinking or suggested you cut down?	**No**	**Yes but not in the last year**	**Yes during the last year**		

(b) If you replied NEVER to question 1 of section 9(a) please answer the next 4 questions.

1. Have you ever consumed a drink containing alcohol?	Yes	No			
2. How long has it been since you have had a drink containing alcohol?	**Less than 3 months**	**6 months - 1 year**	**1 year - 2 years**	**2 years - 5 years**	**more than 5 years**
3. For how long were you consuming drinks containing alcohol before quitting?	6 months	1 year	2 years	3 years	more than 3 years
4. For what reason did you stop consuming drinks containing alcohol?					

(c) If you replied that you DO DRINK ALCOHOLIC DRINKS to question 1 of section 9(a) (i.e. responses 2-5) then please answer the next 4 questions (continues over-leaf).

What is your average alcohol consumption during a 7 day week? *For example :* type : John Smiths Bitter amount : 4 cans type : Red wine amount : 1 bottle type : Vodka amount : 3 shots type : Lemonade Hooch amount : 4 bottles	type..... amount..... and type..... amount..... and type..... amount.....
If you think of last weekend (fri, sat, sun). How much alcohol did you consume.....	
Friday..... *Where did you drink.....*	type..... amount..... and type..... amount..... and type..... amount.....
Saturday..... *Where did you drink.....*	type..... amount..... and type..... amount..... and type..... amount.....
Sunday..... *Where did you drink.....*	type..... amount..... and type..... amount..... and type..... amount.....

Is this typical of a usual weekends alcohol consumption?	[ ] Yes [ ] No
If not please give a typical weekends alcohol consumption.....	type..... amount..... and type..... amount..... and type..... amount.....

Section 10: Alcohol Expectancies

This section is concerned with what EFFECT YOU EXPECT drinking alcohol to have.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS		
1. Drinking makes the future seem brighter	AGREE	DISAGREE
2. Having a few drinks is a nice way to celebrate special occasions	**AGREE**	**DISAGREE**
3. After a few drinks I am more sexually responsive	AGREE	DISAGREE
4. If I'm feeling restricted in any way, a few drinks make me feel better	**AGREE**	**DISAGREE**
5. If I have a couple of drinks it is easier to express my feelings	AGREE	DISAGREE
6. Alcohol enables me to fall asleep more easily	**AGREE**	**DISAGREE**

Section 11: Alcohol Consumption and Coping

This section is concerned with the USE OF DRINKING ALCOHOL as a means of coping with pressure.

PLEASE REPLY TO ALL THE ITEMS.

Circle your response choice for each item on the table:

ITEMS *DO YOU DRINK .....*	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
1. To forget your worries?	1	2	3	4
2. To relax?	**1**	**2**	**3**	**4**
3. To cheer up when your in a bad mood?	1	2	3	4
4. To help when you feel depressed and nervous?	**1**	**2**	**3**	**4**
5. To feel more self-confident and sure of yourself?	1	2	3	4
6. To relieve boredom?	**1**	**2**	**3**	**4**

Section 12: Physical Characteristics, Physical Activity and Smoking

This section is concerned with your physical characteristics and your usual physical activity and smoking patterns.

PLEASE REPLY TO ALL THE ITEMS.

What is your height?	.....			
What is your body mass?	.....			
How would you describe your physical activity compared to others of your age?	sedentary	moderately active	active	highly active
How would you describe your fitness levels compared to others of your age?	**unfit**	**moderately fit**	**fit**	**very fit**
What activities do you engage in on a regular basis?				
What is the average number of miles you would cover during each workout?				
How many minutes on average do you spend on each workout?				
On average, how many workouts do you do per week?				
Do you smoke? ***(If YES please specify how many per week)*** **How long have you been smoking for?** **What brand of cigarette do you smoke?**	**[ ] Yes [ ] No**			
Over the last 12 months have you been feeling unhappy and depressed?	**[ ] Yes [ ] No**			
Over the last 12 months have you been losing confidence in yourself?	**[ ] Yes [ ] No**			

APPENDIX C: Relevant Publications and Abstracts

1. El-Sayed, M.S.; **Sale, C.**; Jones, P.G.W. and Chester, M. (2000). Blood haemostasis in exercise and training. *Medicine and Science in Sports and Exercise*, 32(5), 918-926.
2. El-Sayed, M.S.; Jones, P.G.W. and **Sale, C.** (1999). Exercise induces a change in plasma fibrinogen concentration: fact or fiction?. *Thrombosis Research*, 96(6), 467-472.
3. **Sale, C.**; Jones, P.G.W.; Chester, M. and El-Sayed, M.S. (1999). Exercise induces a change in plasma fibrinogen concentration: fact or fiction?. 4th Annual Congress of the European College of Sports Science, Rome 14-17 July 1999.
4. Jones, P.G.W.; **Sale, C.**; Chester, M. and El-Sayed, M.S. (1999). Does exercise induce effective changes in blood rheology. 4th Annual Congress of the European College of Sports Science, Rome 14-17 July 1999.
5. **Sale, C.**; Guppy, A. and El-Sayed, M.S. (2000). Individual differences, exercise and leisure activity and affective well-being. Ergonomics, 43(10), 1689-1697.
6. **Sale, C.**; Guppy, A. and El-Sayed, M.S. (1999). Exercise and health related behaviours, personality and psychological well-being (abstract). 4th Annual Congress of the European College of Sports Science, Rome 14-17 July 1999.
7. **Sale, C.**; Guppy, A. and El-Sayed, M.S. (1999). Individual differences, exercise and leisure activity and affective well-being (abstract). *Journal of Sports Sciences*, 17, 923. The Fourth International Conference on Sport, Leisure and Ergonomics, Wirral 17-19 November 1999.

Blood hemostasis in exercise and training

MAHMOUD S. EL-SAYED, CRAIG SALE, PETER G. W. JONES, and MICHAEL CHESTER

Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, ENGLAND; and Cardiothoracic Centre, Broadgreen Hospital, Broadgreen, Liverpool, ENGLAND

ABSTRACT

EL-SAYED, M. S., C. SALE, P. G. W. JONES, and M. CHESTER. Blood hemostasis in exercise and training. *Med. Sci. Sports Exerc.*, Vol. 32, No. 5, pp. 918–925, 2000. Formation of the blood clot is a slow but normal physiological process occurring as a result of the activation of blood coagulation pathways. Nature's guard against unwanted blood clots is the fibrinolytic enzyme system. In healthy people, there is a delicate dynamic balance between blood clot formation and blood clot dissolution. Available evidence suggests that exercise and physical training evoke multiple effects on blood hemostasis in normal healthy subjects and in patients. A single bout of exercise is usually associated with a transient increase in blood coagulation as evidenced by a shortening of activated partial thromboplastin time (APTT) and increased Factor VIII (FVIII). The rise in FVIII is intensity dependent and continues into recovery. The effects of acute exercise on plasma fibrinogen have yielded conflicting results. Thus, the issue of whether exercise-induced blood hypercoagulability *in vitro* mirrors an *in vivo* thrombin generation and fibrin formation remains disputable. Exercise-induced enhancement of fibrinolysis has been repeatedly demonstrated using a wide range of exercise protocols incorporating various exercise intensities and durations. Moderate exercise appears to enhance blood fibrinolytic activity without a concomitant activation of blood coagulation mechanisms, whereas, very heavy exercise induces simultaneous activation of blood fibrinolysis and coagulation. The increase in fibrinolysis is due to a rise in tissue-type plasminogen activator (tPA) and decrease in plasminogen activator inhibitor (PAI). The mechanism of exercise-induced hyperfibrinolysis is poorly understood, and the physiological utility of such activation remains unresolved. Strenuous exercise elicits a transient increase in platelet count, but there are conflicting results concerning the effect of exercise on platelet aggregation and activation. Few comprehensive studies exist concerning the influence of exercise training on blood hemostasis, making future investigation necessary to identify whether there are favorable effects of exercise training on blood coagulation, fibrinolysis, and platelet functions. **Key Words:** COAGULATION, FIBRINOLYSIS, PLATELET FUNCTION, ACUTE EXERCISE, PHYSICAL TRAINING

Although blood is hypercoagulable after strenuous exercise, probably due to an increase in Factor VIII (FVIII) (3,37,50), the level of other clotting factors does not appear to be altered. Exercise-induced shortening of whole-blood clotting times and activated partial thromboplastin time (APTT) is well documented (3,5,7,37,48,52,73). However, results reported on prothrombin time (PT) and thrombin time (TT) in response to exercise have been controversial. Research has shown both a significant shortening (39) and no significant difference in PT (37,73,91) after exercise. More recently, El-Sayed et al. (37) have demonstrated that exercise significantly shortens TT. Changes in APTT and PT persist from 1 to 24 h postexercise (3,91).

EFFECTS OF ACUTE EXERCISE ON BLOOD COAGULATION, FIBRINOLYSIS, AND PLATELET FUNCTIONS

Blood coagulation changes in response to acute exercise. Exercise bouts of varied intensity and duration have all induced significant increases in FVIII coagulant activity (3,37,50). Additionally, increases in FVIII coagulant activity and antigen have been positively associated with exercise intensity (2), and this increase persists into recovery (3,50). Significant increases in FVIII activity were also observed after resistance exercise, and these increases were positively correlated to the volume of weight lifted (32).

The mechanism by which exercise increases FVIII is not fully understood. It may either be due to activation within the circulation or to the release of stored or freshly synthesized FVIII (32). *In vitro* exposure of FVIII to catalytic concentrations of thrombin induced a significant increase in FVIII (55), suggesting that this increase might also be associated with thrombin formation. The stimulus responsible for exercise-induced increases in FVIII seems to be mediated via the β-adrenergic receptor pathway because β blockade blunts this increase (19).

Studies investigating the effects of acute exercise on plasma fibrinogen concentration have produced conflicting results (36). A number of these studies have shown that exercise using different protocols had no significant effects on plasma fibrinogen (24,37,52,67,89,119). However, others have either reported significant increases (3,59,104) or significant decreases (5,84). Differences in exercise protocol, training status, subject health, and the analytical methods used for the assessment of plasma fibrinogen are probably responsible for the reported inconsistencies.

0195-9131/00/3205-0918/0
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Submitted for publication December 1998.
Accepted for publication May 1999.

Exercise causes an activation of blood coagulation, although it is disputable whether this leads to significant *in vivo* thrombin generation and fibrin formation. Weiss et al. (120) examined the relationship between exercise intensity and the activation of coagulation and fibrinolysis. They showed that exercise at ~68% $\dot{V}O_{2max}$ increased plasmin formation without corresponding increases in the markers of blood coagulation activation. Similarly, exercise at ~83% $\dot{V}O_{2max}$ was associated with an increase in plasmin formation, although this was accompanied by a concomitant increase in markers of blood coagulation. Thus, moderate exercise appears to enhance *in vivo* blood fibrinolysis, whereas very heavy exercise activates blood fibrinolysis and blood coagulation simultaneously. Long-term exercise such as marathon running was followed by an activation of blood coagulation, as indicated by the formation of thrombin and cross-linked fibrin (96). It should be noted, however, that the acceleration of blood coagulation was smaller than the activation of blood fibrinolysis. Patients with peripheral arterial occlusive disease exhibited increased thrombin formation postsubmaximal exercise, although no such increase was shown in healthy controls (76). These recent results would suggest that markers of the activation of blood coagulation and indicators of enhanced fibrinolysis are related to exercise intensity and the health of the populations studied.

Thrombin-antithrombin complex (TAT) and prothrombin fragments 1+2 (PTF1+2) have been utilized as markers of blood coagulation activation in exercise. Significantly increased TAT has been observed after long-distance running (5,84) and postmaximal incremental cycling (29). This coincided with a significant increase in PTF1+2 concentration (7,12,52,84,85).

In vivo hypercoagulability may also be linked with the formation of fibrinopeptide A (FPA). However, exercise studies on this marker of hypercoagulability have produced conflicting results. A significant increase of FPA was found after exhaustive exercise (7,85), although other studies have demonstrated no significant change (5,52). These discrepancies may be attributed to differences in exercise protocol, training status, and the analytical methods used. Therefore, evidence suggesting that acute physical exercise in healthy subjects leads to increased thrombin generation and fibrin formation *in vivo* remains debatable.

Mandalaki et al. (69) studied blood coagulation inhibitors and reported a significant decrease in antithrombin III activity postmarathon run. Huisveld et al. (56) confirmed this reduction in antithrombin III postexercise and further reported a reduction in the blood fibrinolysis inhibitors α_2-antiplasmin and C_1-inactivator. Other studies have reported no significant change in antithrombin III concentrations after exhaustive exercise (3,5,24,52). Research evidence regarding the effects of exercise on these markers of blood coagulation and fibrinolysis are insufficient to draw a valid conclusion.

Blood fibrinolytic changes in response to acute exercise. It is generally accepted that intense exercise induces significant activation of fibrinolysis as a consequence of tissue plasminogen activator (tPA) release from the vascular endothelial cells (37). Evidence is also available to suggest that plasma levels of urinary-type plasminogen activator (uPA) increase significantly postexercise (27,111). It should be noted, however, that peak levels of uPA and tPA do not coincide in time or magnitude in response to maximal exercise (111). This may signify independent mechanisms regulating exercise-induced increases in the level of uPA and tPA. Large increases (75–250%) in fibrinolytic activity are not apparent until heart rate reaches 50% of maximum (2), with the greatest increase occurring between 70% and 90% of maximal workload (2,21). Although this hyperfibrinolysis is transient, reports have been conflicting concerning its return to baseline levels postexercise with a time course of 45 to 60 min after intense exercise (6,39), 2 h after long distance running (50), and 24 h postmarathon (84).

Tissue-type plasminogen activity and antigen levels have been shown to increase significantly following several different exercise protocols (3,24,45,48,73,84,89,91,96,105), and this increase seems to be intensity dependent (73,89,105). Similar to endurance exercise, resistance exercise increased plasminogen activator activity (32,113), and this increase was again intensity dependent (32).

Research has indicated the presence of "poor responders" among groups of healthy subjects, although more often among patients (49,58,92). These individuals demonstrate a diminished fibrinolytic response to exercise (32). It is suggested that the ability to respond adequately to physical exercise represents the capacity of fibrinolytic potential. Consequently, poor responders are probably at greater risk of atherosclerotic vascular disease when challenged with exercise.

The mechanism responsible for and the biological significance of exercise-induced hyperfibrinolysis is not entirely understood. Adrenoreceptor stimulation was suggested as a possible pathway for the release of plasminogen activator (35) because β blocking with propranolol partially decreases the normal fibrinolytic response to exhaustive exercise (31). This explanation seems unlikely because, during exercise, tPA release occurs before an increase in adrenaline, suggesting that the main release of tPA is mediated by some other nonadrenergic mechanism, possibly vasopressin (30).

Studies have demonstrated a significant reduction of plasminogen activator inhibitor (PAI-1) activity after aerobic and anaerobic exercise (25,37,45,89,105). Maximal treadmill exercise in normoxemic and hypoxemic conditions significantly decreased PAI-1 activity (102). Resistance exercise also produced a similar reduction (32). Other studies have failed to detect any change in PAI-1 after exhaustive aerobic (84) and isometric (113) exercise protocols. As it is the case with tPA response, the PAI-1 response to exercise is related to the training status of the individual (106).

Attempts have been made to relate the activation of fibrinolysis with changes in fibrinogen concentration measured *in vitro* and with alterations of the markers of fibrinogen and/or fibrin degradation *in vivo*. Significant increases

in fibrin/fibrinogen degradation products (Fb/FgDP) have been demonstrated following various exhaustive exercise protocols (39,84). The plasma Fb/FgDP response appears to be related to exercise intensity and the training status of the individual (24,25).

An increased level of another *in vivo* marker of hyperfibrinolysis, D-dimer, was observed when submaximal exercise was followed by short-term maximal exercise (73), and after endurance exercise (3,5,84,91). These results suggest that strenuous exercise results in hyperfibrinolysis *in vivo*. This is not a uniformly reported finding because other studies (12,70) have failed to demonstrate changes in Fb/FgDP in response to exercise. Therefore, the actual effect of exercise on Fb/FgDP has yet to be resolved.

Platelet functions in response to acute exercise. Strenuous exercise results in an increased platelet count (thrombocytosis) ranging from 18% to 80% (4,7,18,43,116). This increase has been ascribed to a fresh release of platelets from the vascular beds of the spleen, the bone marrow, and from intravascular pools found in the pulmonary circulation and lungs (13,94).

Although physical activity is widely recognized as being beneficial to health, attempts to relate the effects of exercise to changes in platelet aggregation and functions have produced conflicting results. Strenuous exercise increases platelet aggregation in response to various aggregatory agents such as adenosine diphosphate (ADP) (8,42,77,82,110), collagen (18,61,93,110), and adrenaline (94). In addition, Winther and Reine (121) observed a postexercise increase in platelet aggregability in stable angina patients.

Research has demonstrated significant increases in plasma β-thromboglobulin (βTG) (7,17,41,52,77,80,107,110,116) and platelet factor 4 (PF4) (45,116), indicating enhanced platelet aggregation. Enhancement of *in vivo* platelet release, occurring in response to exercise, if it occurs, is considered minimal because the reported changes in βTG have remained within the physiological range (110). Furthermore, Lemne et al. (65) reported that, in response to strenuous exercise, βTG was higher in hypertensives than in sedentary age-matched controls, possibly due to the greater synthesis postexercise of antiaggregatory prostanoid prostacyclin. Maximal cycling (8,42,116) and maximal treadmill running (18) have also resulted in significant platelet activation, as indicated by an increased sensitivity to ADP-induced aggregation. Other markers pertinent to platelet activation such as alpha-granule membrane protein (GMP-140) (80) and thromboxane B_2 (TXB_2) (80,107) were also increased postexercise.

Exercise-induced activation of platelets might be linked with anaerobic metabolism (18) because activation of blood platelets seems to be more pronounced in exercise above, but not below, the anaerobic threshold (18,43,116). It has been proposed that exercise-mediated elevation of catecholamines is the common pathway for enhanced platelet aggregation (14,108). In support of this theory, selective β blockade has resulted in inhibition of platelet activation postexercise (53,121). In contrast, Wallen et al. (114) reported no effect of β blockade on platelet function in exercising stable angina patients and hypertensives. Furthermore, an increased catecholamine response to static exercise has been observed without a detectable change in ADP-induced platelet aggregation, PF4, or βTG. Therefore, the influence of increased catecholamines is questionable, although it might be that the mechanism mediating platelet activation in static exercise is different from that operating during dynamic exercise. During exercise, the preaggregatory release of catecholamines is concomitant with an enhanced release of the antiaggregatory prostanoid prostacyclin. This has been found in healthy subjects (82) and diabetics (62,75).

Increased platelet aggregation may be mediated by internal calcium stores because attenuated platelet aggregability has been reported in response to high doses of calcium-channel blockers (64,87,99,114). This may have implications for exercise, particularly resistance exercise, because of the importance of calcium in muscle function.

Significantly decreased adrenaline-, ADP-, and collagen-induced platelet aggregation have been reported postmarathon (90). Decreases in platelet aggregation have also been reported in young healthy subjects in response to strenuous cycling (20) and submaximal exercise (15), although not in patients with stable angina pectoris (116). However, Gleerup et al. (41) observed lower βTG and PF4 concentrations in borderline hypertensives postexercise. The mechanism responsible for this exercise-induced reduction of platelet aggregability is not fully understood. However, it might be linked with the release of antiaggregatory prostanoid prostacyclin, which inhibits platelet aggregation (10,82), or to the release of tPA, which desegregates platelets (68).

In contrast, aerobic exercise has been reported to produce no significant alterations in platelet aggregability, as indicated by unaltered TXB_2 and βTG concentrations (18,28,107) or by a monoclonal antibodies binding technique (60). Similarly, exhaustive isometric exercise had no effect on ADP-induced platelet aggregation or on the release of βTG and PF4 (113). Furthermore, no significant changes in GMP-140 and TXA_2 were observed after treadmill exercise in normal healthy subjects, although changes were reported in coronary heart disease (CHD) patients (80).

Exercise studies addressing female populations have reported no exercise-induced changes in βTG- and ADP-induced aggregation (1,51), possibly because menstrual phase was not accounted for. Mixed-gender studies have also failed to consider the menstrual phase of female participants (43,60,109). Wang et al. (118) reported variations in platelet adhesiveness and ADP-induced platelet aggregation during midfollicular and midluteal phases, although submaximal exercise suppressed these markers. Currently, no published research exists investigating the effect of exercise on platelet functions in postmenopausal women or the transition with menopause.

It is currently unclear whether platelet functions are altered in older individuals with exercise. Gonzales et al. (44) reported no effect of age on platelet count or βTG in sedentary individuals postexercise. Likewise, Todd et al. (107) observed no significant differences in βTG between

young and middle-aged men after treadmill running. However, TXB_2 was significantly higher in the middle-aged group 30 min into recovery, suggesting that older men may exhibit enhanced platelet activation postexercise. In contrast, Gleerup et al. (41) reported significantly decreased *in vivo* platelet aggregability postexercise in healthy young but not in middle-aged healthy males.

Discrepancies in results pertaining to platelet functions may be explained by methodological variations, such as exercise protocol, analysis techniques, dietary effects, the inability to analyze measurements across time, and the use of different populations. As a result, it is not possible to draw conclusions regarding the influence of acute exercise on platelet aggregation and functions. However, some investigators believe that the enhancement of platelet functions during strenuous exercise in sedentary individuals may precipitate thrombosis in the coronary microcirculation and thus augment the risk of primary cardiac arrest (100).

TRAINING EFFECTS OF EXERCISE ON BLOOD COAGULATION, FIBRINOLYSIS, AND PLATELET AGGREGATION

Physical training and blood coagulation. Little information seems to be available regarding the effects of exercise training on blood coagulability. Cross-sectional data of PT and APTT as overall measures of blood coagulability showed no difference among sedentary individuals, joggers, or marathon runners, either at rest or postexercise (39). These results are in agreement with those reported in athletes and nonathletes who exhibited similar TT at rest (119). Likewise, a longitudinal study (37) demonstrated no significant change in TT or PT after 3 months of endurance training. When physical activity level was assessed by a questionnaire, a lower APTT, but not TT, was found in active compared with nonactive individuals (63). Physical training in postmyocardial infarction patients seems to suppress blood coagulability because APTT at rest is significantly longer after training in these patients (104).

Resting levels of FVIII activity and FVIII antigen do not change with training in sedentary individuals (11,83,88,112) or endurance-trained athletes (119). However, postmyocardial patients lowered their resting levels of FVIII activity and FVIII antigen after 4 wk of physical training (104). The normal increase in FVIII activity postexercise also seems to be unaltered after 12 wk of standardized aerobic training (37). These meager results suggest that FVIII activity and FVIII antigen levels at rest or after exercise remain unchanged in response to training in normal healthy subjects, although not in cardiac patients.

Plasma fibrinogen level is one of the main determinants of whole-blood viscosity and plays a pivotal role in the blood clotting mechanism (37). High levels of plasma fibrinogen are usually found in patients suffering from CHD (16,72). The relationship between plasma fibrinogen and exercise training has been recently reviewed (33) and will only be briefly discussed here. Epidemiological studies have implicated a favorable association between physical training and plasma fibrinogen levels (34,49). However, available longitudinal evidence is conflicting, with some research suggesting that physical training may reduce plasma fibrinogen concentration in patients (122) and in elderly males but not in young males (103). Surprisingly, and in contrast to these results, plasma fibrinogen concentration increased significantly in elderly males postintensive training, and this coincided with a significant rise in C-reactive protein. It was concluded that vigorous training in elderly males might cause a chronic increase in acute-phase reactant proteins such as fibrinogen (97). Unlike elderly males, recent evidence suggested that the training effects on plasma fibrinogen in elderly females appears to be negligible (26). No valid conclusion regarding the effect of training on plasma fibrinogen could be drawn from the above reports, and further investigations are required.

Physical training and blood fibrinolysis. Thrombosis plays a significant role in the pathogenesis of acute myocardial infarction, unstable angina, and sudden cardiac death (47). Although the reduction in cardiovascular risk associated with regular physical activity has been repeatedly reported (66,71,98), the pathway(s) via which this occurs is not fully understood and remain speculative. It is suggested that this may be linked with exercise-induced favorable effects on blood fibrinolysis (9,37,50,91). However, it is important to note that the effect of physical training on parameters pertinent to blood fibrinolysis have produced inconsistent results. For example, no relationship between physical training status and resting fibrinolytic activity has been reported when blood fibrinolysis was assessed by global methods such as euglobulin clot lysis time and fibrin plate methods (39,63). However, when more specific techniques were used, higher resting tPA activity and tPA antigen levels were found in inactive compared with active individuals (24,106). Comparable results were reported in which PAI activity was decreased after 8 months of training, but this decrease failed to reach the designated level of significance ($P > 0.05$) due to large group variances and seasonal variations (23).

Higher PAI values were found in postmyocardial infarction patients compared with the elderly, and also in athletes compared with age-matched sedentary individuals and elderly sportsmen (101). Evidence is also available to suggest that exercise rehabilitation programs are associated with significant reductions in PAI levels in cardiac patients but not in healthy controls (38,104). Three months of detraining seems to reverse the favorable reduction in PAI activity observed posttraining (46). Two studies on the effect of exercise training on blood fibrinolysis in non–insulin-dependent diabetics have produced varying results. An increase in the resting level of blood fibrinolysis was demonstrated after training in one study (95) but not in the other, in which blood fibrinolysis was unaltered at rest or in response to exercise (54).

Enhanced fibrinolysis in response to exercise seems to be related to the training status of the individual (39). This concept was confirmed by recent evidence (24,106), which showed higher tPA release and lower tPA/PAI complex after exercise in physically trained subjects compared with untrained individuals. Diminished fibrinolytic activity, due to an increase in PAI, is often seen in patients with myocardial ischemia, although this diminishes after exercise rehabilitation (81,101). However, Estelles et al. (38) showed no significant effect of training on PAI activity in cardiac patients. This discrepancy may be attributed to methodological differences, particularly the exercise intensity and duration as well as the analytical techniques used for the measurement of PAI activity. It is interesting to note that the subjects who did not participate in the exercise rehabilitation program and acted as controls exhibited increased PAI activity (38). The increase in PAI activity after training in the control group is intriguing, and the exact mechanism responsible for this was not adequately explained. Therefore, rehabilitative exercise programs may prevent further disturbances in blood fibrinolysis in cardiac patients.

Earlier studies suggested that the favorable effects of training on blood fibrinolysis appear to be age related because higher fibrinolytic potential was observed posttraining in older but not in younger subjects. For example, elderly subjects exhibited an increase in tPA and a decrease in PAI activity (103) and PAI antigen (97) after different training programs. In contrast to data reported in elderly subjects (103), recent evidence suggests that physical training can also favorably affect blood fibrinolysis in the young (112).

No valid conclusion can be reached regarding the exact effects of physical training on blood coagulation and fibrinolysis. This is undoubtedly due to variations in the training programs used, the populations studied, and the analytical methods used.

Physical training and platelet functions. Clinical studies have indicated that platelets play an important role in the pathogenesis and progression of cardiovascular diseases (78,123). Epidemiological research has suggested that physical conditioning may play a role in the prevention of cardiovascular diseases (40,57,74,79,86). However, the effects of exercise training on platelet aggregation and function have not been adequately studied, and the results reported are either controversial or incomplete (22,44,83,115,117)

Exercise training in healthy individuals could reduce the risk of cardiovascular disease via suppressing platelet adhesiveness and aggregation. Indeed, 8 wk of endurance exercise increases aerobic capacity, and this was associated with a decrease in resting and postexercise platelet adhesiveness and aggregation (117). These results are in agreement with earlier reports that showed a significant decrease in platelet responsiveness with exercise training (22). Nevertheless, these favorable effects of training on platelet aggregability are transient and may disappear with detraining (117).

Although the etiology of impaired platelet function with age is complex, physical training may curtail the detrimental effects of age on platelet function (44). Studies on the effect of training on markers pertinent to platelet activation *in vivo*, such as PF4 and βTG, have produced conflicting results. During the course of endurance training for 9 months PF4 concentration, but not βTG, increased progressively in both male and female subjects (83). These data indicate that training may be associated with undesirable *in vivo* platelet activation, probably due to an increased younger platelet population. In contrast, individuals who exercise regularly or who are physically fit exhibited lower βTG levels at rest compared with sedentary controls (22,44). Reduced platelet aggregation at rest and in response to exercise was also reported in previously sedentary women after training (115). These favorable changes in platelet aggregation with training occurred simultaneously with an increase in plasma nitric oxide level, leading the authors to suggest that platelet aggregation may be mediated via the nitric oxide pathway.

After consideration of the meager results reported above, it is not possible to draw a valid conclusion on the exact effects of physical training on platelet aggregation and function, and future experimental trials are needed.

CONCLUSION

Abnormal hemostatic profiles are known to have clinical and prognostic relevance in cardiovascular disease. Previous research on blood hemostasis is based on the assumption that exercise may favorably affect the hemostatic and fibrinolytic systems. Available evidence suggests that acute exercise causes activation of blood coagulation, acceleration of blood fibrinolysis, and induces alterations in platelet functions. However, information regarding the effects of physical training on blood hemostasis is incomplete and mostly fragmented. In addition, the mechanisms via which these changes occur remain to be elucidated, and the results reported should be viewed as preliminary research findings. This is undoubtedly due to differences in training programs, populations studied, and the analytical methods used. The hypothesis regarding the favorable influence of training on blood hemostasis should be further examined, and available studies should be replicated. Several questions related to exercise and blood hemostasis, particularly platelet aggregation and functions, remain unanswered and warrant future investigation. For example, it would be of interest to assess the possible impact of exercise training on blood hemostasis in relation to the incidence of ischemic heart disease. Although blood coagulation and fibrinolysis are strongly related mechanisms, training effects could be different in different populations. The combined influence of diet and exercise on blood hemostasis is another topic that warrants further investigation.

Address for correspondence: Prof. Mahmoud. S. El-Sayed, The Research Institute for Sport and Exercise Sciences, School of Human Sciences, Liverpool John Moores University, The Henry Cotton Campus, Webster Street, Liverpool, L3 2ET, England. E-mail: M.ElSAYED@LIVJM.ac.uk.

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Pergamon

Thrombosis Research 96 (1999) 467–472

THROMBOSIS RESEARCH

REGULAR ARTICLE

Exercise Induces a Change in Plasma Fibrinogen Concentration: Fact or Fiction?

Mahmoud S. El-Sayed, Peter G.W. Jones and Craig Sale
Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, England.

(Received 11 May 1999 by Editor D. Prisco; revised/accepted 12 July 1999)

Abstract

This study examined the effect of exercise on plasma fibrinogen concentrations with simultaneous measurements of plasma volume changes. Eight moderately active males aged 26.6±3.6 years (mean±SD) completed maximal (VO_2max) and submaximal (75% VO_2max for 30 minutes) exercise trials separated by 7 days. Venous blood samples were obtained at rest, immediately postexercise, and following 30 minutes of recovery. Whole blood was analysed for haematocrit and haemoglobin, while citrated plasma was assayed for fibrinogen levels. Values of haematocrit and haemoglobin before and after exercise were utilised for the estimation of plasma volume changes. Plasma volume decreased ($p<0.05$) immediately following both maximal (−17.7±5.1%) and submaximal (−14.3±4.1%) exercise. Exercise resulted in decreased plasma fibrinogen levels (maximal exercise: from 266.3±14.5 to 222.2±23.9 mg·dL^{-1}; submaximal exercise: from 239.5±45.4 to 209.7±42.4 mg·dL^{-1}) only when postexercise raw data were corrected for the contraction of plasma volume. It is concluded therefore that changes in plasma volume in response to exercise should be taken into account when interpreting exercise effects on plasma fibrinogen concentration. © 1999 Elsevier Science Ltd. All rights reserved.

Key Words: Plasma fibrinogen; Plasma volume changes; Submaximal and maximal exercise

There is an association between haemostatic factors and the risk of hypertension, unstable angina, myocardial infarction, and sudden cardiac death [1]. Hyperfibrinogenaemia is recognised as an independent risk factor for both coronary heart disease [2] and hypertension [3]. Indeed, Meade et al. [4] reported that the standardised regression effects for plasma fibrinogen level and cholesterol were similar when predicting fatal ischaemic heart disease.

Although the relationship between plasma fibrinogen and exercise has been extensively studied [5], the evidence available is conflicting. Some studies have shown that exercise has no significant effect on plasma fibrinogen [6–12]. Others have indicated either an increase [13] or a decrease [14–16] following exercise. A change in plasma fibrinogen concentration may occur as a consequence of a transient fluid shift into (haemodilution) or out of (haemoconcentration) the intravascular space.

Haemoconcentration occurs in response to intense exercise, with a linear relationship existing between the amount of plasma transferred from the vascular tree and exercise intensity [17]. It is hypothesised that an inability to consider the dynamic nature of plasma volume during exercise in relation to alterations in plasma fibrinogen levels is one of the main causes of the discrepancy in the

Abbreviations: Hct, haematocrit; Hb, haemoglobin; ANOVA, analysis of variance.

Corresponding author: Prof. Mahmoud. S. El-Sayed, The Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, The Henry Cotton Campus, Webster Street, Liverpool, L3 2ET, England. Tel: +44(151)231 4321; Fax: +44(151)231 4353; e-mail: <M.S.ElSAYED@livjm.ac.uk>.

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PII S0049-3848(99)00140-1

reported literature (for review see [5]). In some of these studies, postexercise fibrinogen data were corrected for plasma volume contraction [7,8,11–13,18–20]. However, other investigators either did not adjust postexercise raw data for changes in plasma volume [21] or did not heed this aspect [9,10,16,22–24].

This study was conducted to examine the effect of both maximal and submaximal exercise on plasma fibrinogen concentrations, with simultaneous measurements of changes in plasma volume. Alterations in plasma volume were calculated from measurements of haematocrit (Hct) and haemoglobin (Hb) both before and after exercise.

1. Materials and Methods

1.1. Subjects

Eight moderately active (VO_2max: 50.0±6.1 mL·kg·minute^{-1}) male subjects (age: 26.6±3.6 years) volunteered to participate in this study. Individuals who smoked or were suffering from thrombotic or cardiovascular disorders were not allowed to participate. Subjects were also free from any medications prior to and during the study; none of the subjects had a positive family history of coronary heart disease. Prior to the experiment, subjects underwent habituation sessions to familiarise themselves with the laboratory environment, testing protocol, and blood sampling procedures. Approval for the experimental protocol was obtained from the institution's Human Ethics Committee. All subjects provided written consent after having read and understood the details of the experiment.

1.2. Experimental Design

Maximal and submaximal exercise trials were separated by 7 days. Subjects were requested to attend the laboratory after an overnight fast, having abstained from exercise and alcohol for 24 hours and caffeine for 12 hours preceding each trial. The two exercise tests were conducted at the same time of day (8:00 to 9:00 a.m.). The laboratory had an ambient temperature of 20 to 22°C and a relative humidity of 45–50%. Subjects were requested to maintain the same dietary pattern during the 48 hours preceding the test and this was verbally confirmed prior to testing.

Prior to exercise subject height (179.9±6.8 cm), body mass (76.7±5.7 kg), skinfold thickness (percentage body fat: 12.9±2.1, using Harpenden Skinfold Calipers, West Sussex, England), and resting blood pressure (systolic: 124.0±8.0, diastolic: 59.0±6.0 mm·Hg^{-1}, using Dynamap vital signs monitor 8100T, Critikon, Tampa, FL, USA) were recorded. The maximal exercise test commenced with a 5-minute warm-up period at a power output of 150 W. Thereafter, power output was increased by 30 W every 2 minutes until volitional exhaustion. Electric fans were placed in front of and around the subject to alleviate thermal strain. It was judged that the subjects had attained their VO_2max when the following criteria were met: (a) a plateau in VO_2 uptake with increasing power, (b) a final respiratory exchange ratio of 1.1 or above, and (c) a heart rate within 5 beats·min^{-1} of age predicted maximum. Heart rate was measured continuously by telemetry (RE 3000, Polar Electro, Kempele, Finland). A mouthpiece with two-way valve connected to a wide-bore tubing allowed the collection and analysis of expired air (Metabolic Measurement Cart 2900, Sensor Medics, Yorba Linda, CA, USA). The submaximal exercise trial consisted of cycling for 30 minutes at a power output corresponding to 75% VO_2max.

1.3. Blood Sampling and Analytical Procedures

After reporting to the laboratory, subjects were requested to remain quietly in a seated position for 30 minutes, after which a venous blood sample (15 mL) was removed. All venous blood was taken from a prominent superficial vein in the anticubital fossa using a clean venipuncture with minimal stasis. Two further blood samples, each 15 mL, were withdrawn immediately postexercise and 30 minutes into recovery. Whole blood was aliquoted equally into three chilled 5-mL tubes containing 3.8% trisodium citrate dihydrate (nine volumes of blood to one volume of citrate), a dipotassium ethylenediamine tetra-acetic acid (EDTA) coating, or no anticoagulant.

Citrated blood was mixed and then centrifuged at 2000×*g* for 20 minutes. Plasma was separated and frozen at a temperature of −70°C for subse

quent fibrinogen assay (COAG-A-MATE XM of Organon Teknika, Durham, NC, USA). Duplicate samples were assayed for Hb (Hemocue, Angelholm, Sweden) and Hct (Hawksley, Sussex, England) levels, which were used for the calculation of changes in plasma volume using the method of Dill and Costill [25].

1.4. Statistical Analyses

The statistical analyses were carried out using two-way analysis of variance (ANOVA) with repeated measurements to compare variables at rest, postexercise, and into recovery for both maximal and submaximal exercise trials. When ANOVA indicated the presence of a significant difference, Tukey's post-hoc test was employed. Statistical significance was accepted at an alpha level of $p<0.05$. Values are mean±SD.

2. Results

2.1. Plasma Volume Changes following Exercise and into Recovery

Immediately postexercise there was a significant decrease ($p<0.05$) in mean plasma volume levels in response to both maximal (−17.7±5.1%) and submaximal (−14.3±4.1%) exercise trials. Although the plasma volume contraction following maximal exercise was greater than that observed in response to submaximal exercise, this difference did not reach the designated level of significance. At the end of the recovery period, plasma volume was largely restored to the preexercise level.

2.2. Plasma Fibrinogen Concentrations

Compared to levels at rest, plasma fibrinogen levels remained unaltered after both maximal and submaximal exercise trials, and following 30 minutes of seated recovery (Figure 1A). No significant sampling time (rest, postexercise, or recovery) by exercise condition (maximal and submaximal) interaction was found for fibrinogen. However, when the raw data were adjusted for exercise-induced plasma volume changes, marked alterations in the concentration of plasma fibrinogen were found (Figure 1B). The ANOVA showed a significant difference ($p<0.05$) in plasma fibrinogen concentrations at rest, immediately postexercise, and into recovery, with no significant difference between maximal and submaximal exercise trials. Further post-hoc analysis showed a significant decrease ($p<0.05$) in fibrinogen level immediately postexercise, but a return to the preexercise level at the end of 30 minutes of recovery. This occurred similarly during both maximal and submaximal exercise trials.

3. Discussion

The results of the present study showed a significant decrease in plasma fibrinogen concentration in response to maximal and submaximal exercise protocols. This decrease only occurred when postexercise raw data were corrected for exercise-induced haemoconcentration. These results agreed with a number of studies that have examined the effects of exercise on plasma fibrinogen concentration [14,26,27]. Bartsch et al. [15] examined plasma fibrinogen concentration in 19 well-trained, male long-distance runners in response to a 100-km race. Total serum protein was significantly higher whereas fibrinogen levels were significantly lower after the race. Exercise-induced hyperfibrinogenolysis was suggested as a plausible mechanism mediating fibrinogen reduction after the race. It is known that prolonged exercise is usually associated with an expansion of plasma volume [25]; therefore, it is suggested that the decrease in fibrinogen level found in the study of Bartsch and coworkers may also have been due to haemodilution. This explanation is based on two observations: (a) postexercise blood sampling was delayed for between 5 and 53 minutes, and (b) subjects ingested fluid during the race and this may have induced a hyperhydration status in the athletes with a resultant dilutional effect on plasma fibrinogen. Removal of fibrinogen from the plasma by transudation into the interstitial spaces and increased fibrin clot formation also have been suggested as mediating factors for a reduction in plasma fibrinogen following exercise [14].

Comparable findings have been reported by Osterud et al. [27], who examined plasma fibrinogen concentration following a different prolonged exercise protocol (Holmenkollen 50-km cross-coun-

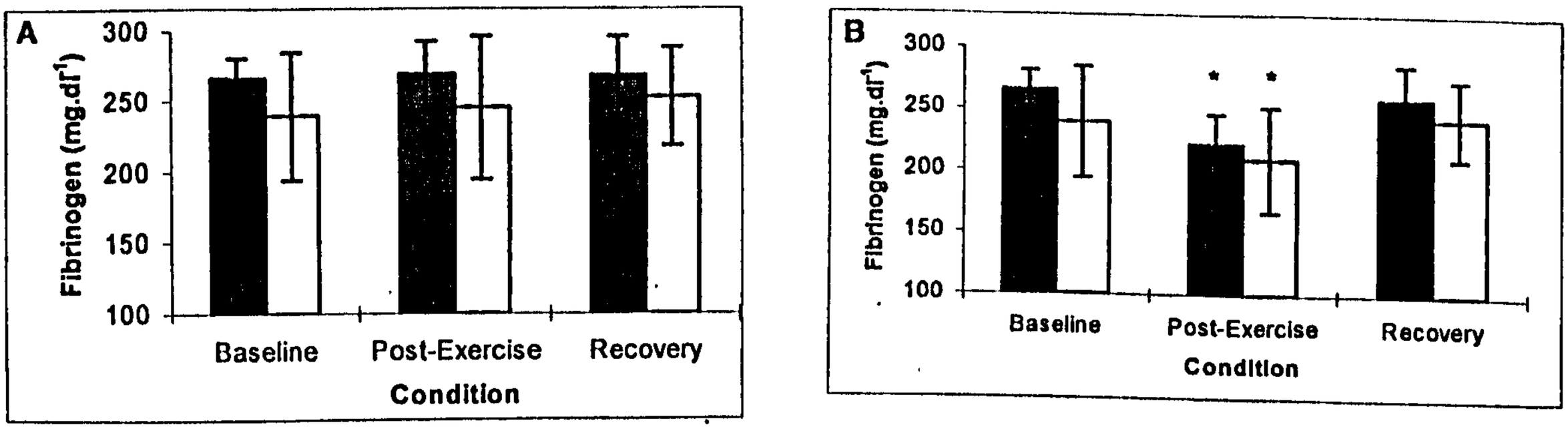

Fig. 1. Plasma fibrinogen concentrations at baseline, immediately postexercise and in recovery for both maximal (solid bars) and submaximal (open bars) exercise conditions. In (A) raw data have not been corrected for plasma volume change, while in (B) raw data have been adjusted for plasma volume change. *Statistically significant difference between resting and postexercise values ($p<0.05$).

try skiing race) in 31 male and female elite skiers. Although fibrinogen levels were relatively low among the skiers (210±20 mg·dL^{-1} for males and 230±20 mg·dL^{-1} for females), its concentration decreased significantly in males to a value of 190±20 mg·dL^{-1} following the race. No postexercise data were reported for women and, in addition, it is not clear whether or not the raw data were adjusted for plasma volume changes in this study. Although the fall in plasma fibrinogen concentration postexercise observed in the present study is similar to that reported by previous authors [14,15], the magnitude of this reduction is small and might be a reflection of limited exercise-induced hyperfibrinogenolysis. This assumption is based on the evidence reported by Collen et al. [28], who noted a shortened half-life of radiolabeled fibrinogen, thus suggesting that exercise induces small but significant fibrinogenolysis. However, others have failed to confirm this finding [29].

In contrast to the results of the present study, some evidence indicates that exercise induces a significant increase in plasma fibrinogen concentration in moderately trained subjects. However, this increase was mainly due to exercise-induced haemoconcentration [13,19]. Similar responses occurred in normal untrained subjects [8] as well as in patients with pulmonary disease [30], cardiovascular disease [31], and diabetes [9]. When postexercise fibrinogen values were adjusted for plasma volume loss, both a multistage maximal treadmill exercise stress test [7] and maximal cycling exercise [11,12] failed to evoke a significant change in plasma fibrinogen levels. Similarly, plasma fibrinogen levels did not alter significantly after long-distance running [6] or exhaustive exercise [28].

Although some of the above studies have indicated no change in fibrinogen concentration in response to exercise, other investigators have found an increase [13,21,32]. A delayed increase in plasma fibrinogen concentration was found after long-distance running, which only reached the assigned level of significance ($p<0.05$) 2 and 4 hours after exercise [32]. No explanation was offered for this delayed increase in plasma fibrinogen. It should be noted that either no allowance was made for plasma volume changes in these studies [21], or this aspect was unheeded [10,23]. Therefore, it is unclear whether or not exercise induces an actual increase in circulating fibrinogen or only an apparent increase due to haemoconcentration. The most likely mechanism for the increase described above is a reduction in plasma volume. This explanation is based on the evidence that acute exercise brings about a transfer of blood fluid to and from the interstitium, depending on exercise intensity and duration, and this may affect the relative concentration of plasma fibrinogen.

We recognise that there are limitations to our study design, particularly the small sample size that consequently restricts the certainty of the conclusion reached. It is possible that a type II error was committed and a larger sample size might be required to confirm or refute the results of the present study.

Although both maximal and submaximal exer-

se induced a significant decrease in plasma fibrinogen concentration, parallel changes in fibrinogen mass may have also occurred; however, this cannot be deduced from the data of the present study. The exact mechanism for the decrease observed in plasma fibrinogen concentration is not completely known, but it might be linked to an enhanced rate of fibrinogen catabolism (hyperfibrinogenolysis), or possibly to removal of fibrinogen from the plasma into the interstitial spaces. Further investigations are required to examine plasma fibrinogen concentration with simultaneous measurements of fibrin/fibrinogen degradation products and/or thrombin activation. The results of these investigations would shed further light on the exact effect of and the mechanisms responsible for exercise-induced changes in plasma fibrinogen levels.

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4th Annual Congress
of the European College of Sport Science
Rome, 14-17 July 1999

EXERCISE INDUCES A CHANGE IN PLASMA FIBRINOGEN CONCENTRATION: FACT OR FICTION ?

C. Sale[1], P.G.W. Jones[1], M. Chester[2], M.S. El-Sayed[1]

[1]Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, and [2]Cardiothoracic Centre, National Refractory Angina Centre, Liverpool, England

Hyperfibrinogenemia is recognised as a significant independent risk factor for CHD (Koenig et al. 1997) with a predictive value similar to that for serum cholesterol (Curran et al. 1998). Although the relationship between exercise and plasma fibrinogen has been studied and recently reviewed (El-Sayed 1996), the evidence available is conflicting. One potential reason for this could be an inability to account for the interaction between plasma fibrinogen level and exercise-induced changes in plasma volume. Therefore, the following study was conducted to examine the effect of both maximal and submaximal exercise on plasma fibrinogen concentrations, with simultaneous measurements of plasma volume changes (Dill and Costill 1974).

Eight moderately active male subjects (age, mean±SD; 26.6±3.6 years) completed submaximal (VO2max for 30 minutes) and maximal (VO2max) exercise trials, which were separated by 7 days. Venous blood samples were obtained at rest, immediately post-exercise, and following 30 minutes recovery. Whole blood was measured for haematocrit (Hct), haemoglobin (Hb) and lactate; while citrated plasma was assayed for fibrinogen levels, using a clotting method as described by Clauss (1957). Values of Hct and Hb before and after exercise were utilised for the estimation of plasma volume changes.

Plasma volume decreased significantly ($P<0.05$) immediately following both submaximal (-14.3±4.1%) and maximal exercise (-17.7±5.1%) trials. Although the contraction of plasma volume, post maximal exercise, was greater than that found post submaximal exercise, this difference failed to reach the assigned level of significance ($p>0.05$). The statistical analyses of the raw data, without correction for plasma volume changes, showed no significant differences in plasma fibrinogen level at rest, immediately post-exercise or following recovery. However, when raw data were corrected for the exercise induced contraction of plasma volume, both maximal (from 266.3±14.5 $mg.dl^{-1}$ to 222.2±23.9 $mg.dl^{-1}$) and submaximal (from 239.5±45.4 $mg.dl^{-1}$ to 209.7±42.4 $mg.dl^{-1}$) exercise trials induced significant decreases ($P<0.05$) in plasma fibrinogen concentration.

It is concluded, therefore, that plasma fibrinogen level was decreased immediately after exercise, only when raw data were adjusted for plasma volume loss. However, the biological validity of adjusting raw data for plasma volume shifts is debatable because the native plasma fibrinogen level is the most important factor that determines the haemostatic and rheologic characteristics of the blood post-exercise.

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4th Annual Congress
of the European College of Sport Science
Rome, 14-17 July 1999

Does Exercise Induce Effective Changes in Blood Rheology ?

P.G.W. Jones[1], C. Sale[1], M. Chester[2], M.S. El-Sayed[1]

[1]Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, and [2]Cardiothoracic Centre, National Refractory Angina Centre, Liverpool, England

Disturbances in blood rheology are recognised as both risk factors and predictors for cardiovascular disease (Junker et al. 1998). Despite the recognised benefits of exercise on CHD risk, only a few studies have examined the effects of exercise on blood rheological properties (El-Sayed 1998). Therefore, the present study was designed to examine the influence of exercise on the three main determinants of blood rheology namely; haematocrit, haemoglobin and plasma viscosity.

Eight healthy male subjects (age, mean ± SD; 26.6±3.6 years) performed maximal and submaximal (70% VO_2max for 30 min) exercise trials on two separate occasions, with 7 days intervening. Venous blood samples were obtained at rest, immediately post-exercise, and following 30 min recovery. Whole blood was analysed for haematocrit, haemoglobin, and lactate; whilst citrated plasma was assayed for fibrinogen levels. Capillary viscometry was used for the determination of both plasma and serum viscosity. Serum was also assayed for total protein and albumin levels. Haematocrit and haemoglobin levels were used for the calculation of plasma volume changes (Dill and Costill 1974).

Plasma volume decreased significantly following both maximal (-17.7±5.1%) and submaximal (-14.3±4.1%) exercise trials. Results showed a lower serum viscosity than plasma viscosity at rest (average of two resting values was –7.4±0.9%), and this difference remained constant post-exercise (maximal: -6.8±2.5%; submaximal: -6.2±3.3%) and following 30 min seated recovery (maximal: -6.7±1.3%; submaximal: -5.7±2.4%). Significant increases ($p<0.05$) in plasma and serum viscosity, but not in fibrinogen level, were found immediately post-exercise. However, when raw data were corrected for exercise-induced changes in plasma volume, both plasma (maximal: from 1.54±0.03 to 1.42±0.07 mpa·s^{-1}; submaximal: from 1.55±0.04 to 1.46±0.08 mpa·s^{-1}) and serum (maximal: from 1.44±0.01 to 1.32±0.02 mpa·s^{-1}; submaximal: from 1.45±0.01 to 1.35±0.02 mpa·s^{-1}) viscosity decreased significantly ($p<0.05$). Likewise, when post-exercise fibrinogen raw data were corrected for the estimated plasma volume change, a significant decrease ($p<0.05$) was observed (maximal: from 266.3±15.1 to 222.2±24.7 mg·dl^{-1}; submaximal: from 239.5±47.0 to 209.7±43.9 mg·dl^{-1}). In addition, a significant increase ($p<0.05$) in serum total protein and albumin levels were found post-exercise for uncorrected, but not corrected raw data. All the blood rheological parameters measured in response to both maximal and submaximal exercise trials were similar in magnitude and showed no statistically significant differences.

It is concluded that both maximal and submaximal exercise induce a significant decrease in plasma and serum viscosity, and the main mechanism responsible for this is exercise-induced plasma volume contraction. No significant correlation was found between plasma fibrinogen concentration and plasma viscosity and this maybe attributed to a type 2 error because of the small sample size.

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ERGONOMICS, 2000, VOL. 43, NO. 10, 1689–1697

Individual differences, exercise and leisure activity in predicting affective well-being in young adults

C. SALE†, A. GUPPY‡* and M. EL-SAYED†

†Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK

‡Department of Psychology, Middlesex University, Enfield EN3 4SF, UK

Keywords: Well-being; Coping; Physical activity; Health behaviours; Individual differences.

This study focuses on the prevalence of exercise and health-related leisure activities (smoking, drinking), across groups of subjects, defined by personality and gender, in relation to subjective well-being. Results from a cross-sectional survey of 187 participants are reported. Males ($n=80$) reported more drinking ($p<0.001$) and smoking ($p<0.001$) than females, though they also reported higher habitual physical activity levels ($p<0.001$). Females ($n=107$) reported more frequent use of social support coping ($p<0.01$). There was a positive association between extraversion and self-reported habitual physical activity as well as alcohol consumption (even when controlling for gender). Neuroticism was not related to any of the exercise and leisure activity variables. Multiple regression analyses predicted 34% of variance for the depression-enthusiasm and 39% of the variance for the anxiety-contentment measures of affective well-being. Neuroticism ($p<0.001$) and avoidance coping ($p<0.05$) were the only significant predictors of both anxiety-contentment and depression-enthusiasm. It is concluded that the influence of individual differences such as personality and gender on coping behaviour and well-being is consistent with social learning theory research. Limitations of cross-sectional research designs necessitate caution with inferring causal paths. Recommendations for future research are presented concerning the use and value of repeated measures designs within research into exercise and well-being.

1. Introduction

There have been recent attempts to place exercise and health-related behaviours in the wider context of stress and coping processes. Rostad and Long (1996) reviewed a range of empirical studies, focusing on the role of exercise behaviours as coping strategies for stress. While the general conclusion suggested positive support for the efficacy of such strategies in coping with stress, none of the studies reviewed have incorporated measures of stress appraisal and coping processes in sufficient detail.

Rick and Guppy (1994) identified several exercise and health-related coping strategies regularly used by a sample of over 600 white collar employees. Taking regular exercise was reported as a frequent means of coping with work stress by 30% of employees. Other health behaviours, such as maintaining a healthy diet, were

*Author for correspondence. e-mail: a.guppy@mdx.ac.uk

Ergonomics ISSN 0014-0139 print/ISSN 1366-5847 online © 2000 Taylor & Francis Ltd
http://www.tandf.co.uk/journals

frequently reported by nearly half of the sample. Factor analysis of the reported coping strategies identified a leisure activity oriented dimension encompassing 'taking regular exercise', 'turning to hobbies and pastimes', 'eating a healthy diet' and 'expending energy'. This factor was in addition to other more commonly reported coping dimensions such as problem-oriented coping, avoidance and social support seeking. The health and exercise coping dimension was significantly related to problem-focused coping, social support seeking and the use of formal relaxation methods. It was also significantly related to reported mental health, though use of formal relaxation methods was not significantly related to mental health.

Ingledew *et al.* (1996) considered health-related behaviours as well as more traditional measures of coping behaviour. Their main aim was to establish the relationship between the dimensions of coping that have been identified in research over the past 20 years and the health-related behaviours. They reported 'clear clusters' of exercise behaviours as well as the use of problem-focused, emotion-focused and avoidance coping. Their results indicated that exercise coping was significantly related to problem-focused coping, thus supporting the earlier findings of Rick and Guppy (1994), though no associations between exercise coping and well-being were reported by Ingledew *et al.* (1996).

Various researchers have suggested that exercise may be linked with dispositional characteristics of the individual, such as personality and perceived locus of control. For example, Courneya and Hellsten (1998) reported that exercise behaviour was positively linked with extraversion, and negatively correlated with neuroticism, within a student sample. Personality factors were related to the different types of exercise behaviours that participants adopted, with extraverts preferring to exercise with others rather than alone. An element to this research concerned the motives for exercising. Neuroticism was the only factor to correlate with the motivating factors of physical appearance and weight control. The personality dimension of 'openness' was solely related to exercise used as a mental health/stress relief coping strategy.

Some gender-based differences in general coping behaviours have been reported in previous research. Rick (1995) found that females were less likely to use regular exercise as a means of coping with stress, though they were significantly more likely to use social support coping strategies. Ingledew *et al.* (1996) reported that females were more likely to use eating and emotion-focused coping strategies, though they did not find significant gender differences in the adoption of exercise activity as a coping behaviour.

In predicting well-being from coping, a large number of studies have indicated the positive impact of problem-focused coping and the potentially negative impact of coping strategies such as avoidance (Parkes 1990, Rick and Guppy 1994). Previous research has also identified positive links between exercise activity and affective well-being. Rostad and Long (1996) discussed the positive impact of exercise-related programmes on measures such as state anxiety and depression. Yeung and Hemsley (1997) reported significant associations between reported physical activity and both positive and negative affect measures. However, in subsequent regression analyses, they found that trait measures such as neuroticism and extraversion were more important predictors of well-being.

Therefore, the objectives of the present study were to expand upon the previous research identifying a link between exercise and general coping behaviours; and to explore the direct effects of exercise and the use of general coping strategies on psychological well-being, while controlling for the effects of personality and individual differences.

2. Methods

2.1. *Measures*

Seven scales were used in this questionnaire-based study. Brief details of each of the scales employed are given below. As the questionnaire used here mainly incorporated well established, prevalidated scales, only a relatively small pilot study was employed. At three separate stages in the development of the questionnaire, following significant changes in format, the questionnaire was piloted to 30 respondents.

2.1.1. *Demographic information*: Information was obtained on age (year of birth) and gender (one male, two females).

2.1.2. *Coping in general life*: The 20-item version of the Cybernetic Coping Scale (Edwards and Baglioni 1993) with an additional four items from the Ways of Coping Check-List (Lazarus and Folkman 1984) were incorporated to yield general coping strategies but not specific coping responses. The items were selected to represent the coping dimensions of changing the situation, accommodation, devaluation, avoidance, and symptom reduction (from the CCS) and social support seeking (from the WCCL). Each item was graded on a five-point Likert scale, according to how often the respondent used a particular method to cope, with the scale ranging from 'never' (=1) to 'always' (=5).

2.1.3. *Affective well-being*: A 12-item scale incorporating adjectives designed to measure job-related well-being (Warr 1990) was included in the questionnaire. The scale is based on the two well-being axes reported by Warr (1990); namely job-related anxiety-contentment and job-related depression-enthusiasm. The scale was altered to make it applicable to university students by asking them to indicate how often the respondent had felt the way the items described over the past few weeks at university. Respondents were asked to rate each of the 12-items along a six-point frequency scale ranging from 'never' (=1) to 'all of the time' (=6). A high score thus indicates a greater perception of personal well-being.

2.1.4. *Personality*: Extraversion was assessed using the six-item improved short scale of extraversion from the Eysenck Personality Inventory (EPI) (Eysenck and Eysenck 1964). Neuroticism was assessed using the corresponding six-item measure of neuroticism from the EPI. Responses were graded along a four-point frequency scale ranging from 'almost never' (=1) to 'almost always' (=4).

2.1.5. *Habitual alcohol consumption*: This was designed as a means of gaining detailed information concerning the typical alcohol consumption patterns of respondents. Respondents were asked to report their typical weekly (7 days) alcohol consumption, recording both the type and amount of alcoholic beverage consumed. These data were then converted to represent the total number of units of alcohol consumed over the typical 7-day period. This methodology is similar to that used in a large number of investigations ranging from general population studies (Wilson 1980) to cross-national investigations of drink driving (Guppy and Adams-Guppy 1995). While it is acknowledged that there may be under-reporting of consumption through self-reported measures (Midanik 1992), it is felt less likely that correlational analyses are affected by such bias compared with estimates of population means.

2.1.6. *Physical activity*: Respondents were asked to rate their habitual activity levels along a four-point Likert type scale, with responses ranging from 'sedentary' (=1) to 'highly active' (=4).

2.1.7. *Smoking*: Smoking was assessed as a dichotomous variable with subjects reporting either 'yes' (=1) or 'no' (=0) to the question 'do you smoke?'.

2.2. *Procedures*

Cross-sectional data were collected over 3 weeks corresponding to weeks 4–6 of the second university academic semester. Data were collected by means of a self-completed questionnaire, administered in a classroom setting following lectures. The response to the questionnaire was voluntary and subjects were given written assurance that all individual data would be treated confidentially and anonymously. The local institution's Ethics Committee approved the study. All data were analysed using the Statistical Package for the Social Sciences (SPSS).

3. Results

3.1. *Sample*

Two-hundred and sixty-one questionnaires were administered, with 190 of these being completed and returned (response rate=72%). Three participants were excluded from this sample because they provided incomplete data on many of the questions. Thus, statistical analysis was performed on 187 respondents (80 males, 107 females; mean age 24±9 years). All respondents were students from the Psychology, Health Studies, Nursing, Engineering and Sports Science courses at Liverpool John Moores University.

3.2. *Scale-descriptive statistics*

The scale means±SD, as well as measures of internal consistency (Cronbach's Alpha), are presented for each of the scales employed (table 1). As can be seen, the majority of the scales have reasonable levels of internal consistency, with accommodation coping (I=0.57) being the lowest.

3.3. *Relationship between coping, exercise and health behaviours, and well-being*

Intercorrelations (table 1) identified some significant relationships between the coping and health-related behaviours and the measures of individual differences. Although males reported significantly more drinking ($r=-0.34$, $p<0.001$) and smoking ($r=-0.27$, $p<0.001$), they also reported higher habitual physical activity levels than females ($r=-0.29$, $p<0.001$). Females reported more frequent use of social support coping ($r=0.23$, $p<0.01$), with these findings remaining statistically significant even after controlling for the effects of personality. There was a positive correlation between extraversion and self-reported habitual physical activity ($r=0.19$, $p<0.01$), as well as alcohol consumption ($r=0.37$, $p<0.001$), even when controlling for gender. Neuroticism did not significantly correlate with any of the exercise and leisure variables once gender had been partialled out.

Extraversion was significantly related to measures of anxiety-contentment ($r=0.28$, $p<0.001$) and depression-enthusiasm $r=0.26$, $p<0.001$), as was neuroticism (anxiety-contentment: $r=-0.56$, $p<0.001$; depression-enthusiasm: $r=-0.51$, $p<0.001$). Neuroticism shared nearly 30% of the variance in anxiety-contentment scores. Significant positive correlations with anxiety-contentment were also identified

Table 1. Correlation coefficients, scale means (±SD) and Cronbach's Alpha coefficients for each of the scales used.

Alpha	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Anxiety-contentment	**0.90**													
2. Depression-enthusiasm	0.72[c]	**0.85**												
3. Gender	−0.32[c]	−0.22[b]	–											
4. Extraversion	0.28[c]	0.26[c]	−0.19[a]	**0.74**										
5. Neuroticism	−0.56[c]	−0.51[c]	0.33[c]	−0.27[c]	**0.65**									
6. Alcohol consumption	0.22[b]	0.13	−0.34[c]	0.37[c]	−0.14	–								
7. Activity	0.20[b]	0.11	−0.29[c]	0.19[b]	−0.10	0.04	–							
8. Smoking	−0.13	−0.13	−0.27[c]	−0.03	0.12	0.07	−0.13	–						
9. Changing the situation	0.09	0.15[a]	0.05	0.20[b]	−0.09	0.02	0.00	0.01	**0.73**					
10. Accommodation	0.00	0.11	−0.09	0.09	0.05	−0.09	0.06	−0.10	0.13	**0.57**				
11. Devaluation	0.08	0.06	0.03	−0.02	−0.02	−0.05	0.07	0.13	−0.06	0.24[c]	**0.87**			
12. Avoidance	−0.08	−0.10	0.02	0.05	−0.01	0.02	−0.09	0.03	−0.19[b]	0.16[a]	0.45[c]	**0.82**		
13. Sympton reduction	0.08	0.13	0.03	0.16[a]	0.02	0.02	0.17[a]	0.03	0.25[c]	0.29[c]	0.09	0.03	**0.82**	
14. Seeking social support	−0.12	−0.08	0.23[b]	0.11	0.18[a]	−0.08	−0.01	0.00	0.22[b]	0.17[a]	−0.11	−0.11	0.42[c]	**0.77**
Mean	3.81	4.43	1.57	3.09	2.23	18.15	2.66	1.76	3.43	3.06	2.94	2.81	3.56	3.51
SD	0.95	0.77	0.50	0.62	0.54	13.57	0.82	0.43	0.54	0.52	0.96	0.75	0.65	0.72

[a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$.

for alcohol consumption ($r=0.22$, $p<0.01$), habitual physical activity ($r=0.20$, $p<0.01$). Problem-focused coping (changing the situation) was significantly correlated with depression-enthusiasm ($r=0.15$, $p<0.05$). Gender was significantly related to both anxiety-contentment ($r=-0.32$, $p<0.001$) and depression-enthusiasm ($r=-0.22$, $p<0.01$) with males reporting higher affective well-being.

Following gender-based interaction analyses in other areas of research on well-being (Laurent *et al.* 1997), interaction terms were calculated for gender and the two personality dimensions. These were correlated with the coping and health-related measures, with the main effects of gender and personality partialled out (reflecting procedures described by Cohen and Cohen 1983). The only significant interaction term revealed that habitual physical activity was associated with the gender × extraversion interaction term, although this was only a weak effect ($r=0.18$, $p<0.05$). Further examination of the simple effects revealed that, for females, extraversion was significantly related to physical activity ($r=0.32$, $p<0.001$).

Hierarchical multiple regression analyses (MRA) identified significant predictors of affective well-being scales. MRA predicted 39% of the variance for anxiety contentment and 34% of the variance for depression-enthusiasm. Neuroticism and avoidance coping significantly predicted levels of anxiety-contentment, once other variables had been statistically controlled (table 2). Neuroticism and avoidance coping also significantly predicted depression-enthusiasm (table 2).

4. Discussion

The present results extend the findings of Ingledew *et al.* (1996) on links between health-related behaviours (exercise, smoking, drinking) and more traditional dimensions of coping. However, evidence of significant correlations was limited, with only the frequency of habitual physical activity being significantly correlated

Table 2. Multiple regression analysis predicting anxiety-contentment and depression–enthusiasm.

	Anxiety-contentment		Depression-enthusiasm	
Variable	Standardized regression coefficient	p	Standardized regression coefficient	p
Gender	−0.04	0.61	0.01	0.95
Extraversion	0.07	0.31	0.11	0.15
Neuroticism	−0.47	0.00	−0.46	0.00
Alcohol consumption	0.11	0.12	0.04	0.56
Activity	0.08	0.24	0.01	0.87
Smoking	0.07	0.30	0.07	0.29
Changing the situation	0.01	0.92	0.05	0.52
Accommodation	−0.02	0.79	0.11	0.13
Devaluation	0.13	0.08	0.08	0.28
Avoidance	−0.15	0.04	−0.16	0.03
Sympton reduction	0.09	0.20	0.10	0.21
Seeking social support	−0.07	0.37	−0.08	0.28
	$R=0.62$; $R^2=0.39$; $R^2_{ADJ}=0.34$; $F=8.63$; d.f.=12,163; $p<0.00$		$R=0.58$; $R^2=0.34$; $R^2_{ADJ}=0.29$; $F=6.91$; d.f.=12,163; $p<0.00$	

with 'symptom reduction coping'. This lack of relationship between drinking and smoking behaviour and the coping dimensions such as avoidance could well reflect weaknesses in the measures used. Cooper *et al.* (1988, 1992) emphasized the distinction between alcohol consumption and the use of alcohol as a coping strategy. Furthermore, Polich and Orvis (1979) described measures of alcohol use as a coping strategy, which has qualitative advantages over simple measures of consumption. Thus, a more precise measure of how smoking and drinking are used to cope could improve the current methodology.

The results provided some support for the impact of individual differences on the use of coping behaviours, particularly health-related behaviours. The link between gender and social support coping has been reported previously (e.g. Rick and Guppy 1994), as has the finding that males have higher alcohol consumption patterns (e.g. Evans and Dunn 1995). These probably reflect wider processes of socialization and the development of expectations coping efficacy and normative beliefs (Abrams and Niaura 1988). The finding that males reported more frequent habitual physical activity contradicts research reported by Ingledew *et al.* (1996) and Ransford and Palisi (1996) where substantial gender differences were not observed, particularly with younger samples. It is possible, however, that the high proportion of sports science students in the present sample may be responsible for this anomalous finding.

The observation that extraversion was significantly related to drinking and habitual physical activity, as well as the reported frequency of the use of problem-focused coping (and to a lesser extent, symptom reduction coping) persisted after controlling for the effects of gender. The 'gender × extraversion' interaction term indicated that the strong association between extraversion and physical activity applied only to females. To some extent the link between extraversion and exercise supports the findings reported by Courneya and Hellsten (1998), though the lack of an association for neuroticism contradicts their results. While there is no sufficient explanation for such contradictory results within two similar student samples, it is clear from a number of studies (Daniels and Guppy 1994, Zapf *et al.* 1996) that the stability, as well as the interpretability, of relationships among measures in such studies would be better achieved with the use of repeated measures data sets.

From the multivariate analyses, in both cases the two significant contributors to the equations were neuroticism and avoidance coping. These findings support the previous literature, particularly Yeung and Hemsley (1997) that neuroticism was the strongest predictor of affective well-being. The negative contribution of avoidance coping is in line with Guppy and Weatherstone (1997), although the lack of a significant contribution from 'problem-focused coping' measures to the multiple regression analysis contradicts the findings of Rick and Guppy (1994) and Guppy and Weatherstone (1997). While to some extent this contradiction is felt to be related to differences in the coping measures used, there was a significant bivariate correlation between problem-focused coping ('changing the situation') and affective well-being (depression-enthusiasm). Further, from the bivariate analyses, both alcohol consumption and habitual physical activity were significantly related to affective well-being (anxiety-contentment). While the positive correlation between habitual physical activity and well-being is supported by, for example, Yeung and Hemsley (1997), the positive correlation between alcohol consumption and well-being conflicts with, for example, Graham and Schmidt (1999). The significant positive association between these two variables was rendered non-significant when the effects of gender were partialled out.

To some extent the significance of measures such as extraversion and neuroticism in predicting affective well-being in cross-sectional surveys is as anticipated. Various researchers have utilized extraversion and neuroticism as measures of dispositional positive and negative affectivity respectively (e.g. Parkes 1990), logically expecting high correlations with indicators of well-being. Consideration of the merits of repeated measures designs in well-being research (Zapf *et al.* 1996, Daniels and Guppy 1997) suggests that the influence of such traits may be reduced when time lagged well-being measures are used as covariates for current levels of well-being. Thus, with the development of more sophisticated methodologies, it may be less likely that trait measures have strong predictive power, once the effects of time-lagged outcome variables have been entered into prediction equations (Zapf *et al.* 1996).

The present research has extended the findings from several other recent reports in relation to exercise, coping and psychological well-being. The relationships between exercise behaviours, health behaviours (such as smoking and drinking) and other active and passive coping behaviours were examined. In a further extension of the work reported by Ingledew *et al.* (1996), such patterns of behaviour were related to outcome measures of psychological well-being. The role of personality in exercise, exemplified by Courneya and Hellsten (1998), was also expanded in the current study. While the value of the current empirical contribution can be seen in the light of such reports, and particularly where there may be an integration of research lines, there are limitations in the strength of conclusions that can be drawn from single phase, cross-sectional research designs. As Zapf *et al.* (1996) indicated, there may be confusion about causality in significant associations as well as difficulty in determining the influence of unmeasured variables. It is anticipated that the later stages of the current research programme, which will include repeated measures data, will link coping and exercise patterns more clearly, with subsequent perceptions of efficacy and well-being.

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4th Annual Congress
of the European College of Sport Science
Rome, 14-17 July 1999

EXERCISE AND HEALTH-RELATED BEHAVIOURS, PERSONALITY AND PSYCHOLOGICAL WELL-BEING

C. Sale, A. Guppy, M.S. El-Sayed

Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, England

A number of recent papers have attempted to place exercise and health behaviours in the context of wider stress and coping processes. Rostad and Long (1996) focused upon the role of exercise behaviours as coping strategies for stress across a range of empirical studies. Although the general conclusion positively supported the efficacy of such strategies in coping with stress, it was clear that all the studies reviewed lacked the appropriate measures to consider stress appraisal and coping processes in detail. Rick and Guppy (1994) reported that taking regular exercise was frequently cited as a means of coping with work stress. Other health related behaviours, such as maintaining a healthy diet, were also frequently cited by approximately 50% of the sample. It was also found that exercise and health coping factors were significantly related to self-reported mental health, as well as to problem focused coping. Similar findings were reported by Ingledew et al. (1996) who showed that exercise coping was significantly related to problem focused coping, although no associations between coping and well-being were reported. Other studies have suggested that the adoption of exercise and health behaviours may be linked with an individuals dispositional characteristics, such as personality and perceptions of control. For example, Courneya and Hellsten (1998) reported that exercise behaviour was positively linked with extraversion, and negatively correlated with neuroticism in a student sample. Thus, the objectives of the present study were: (a) to expand upon previous research linking exercise and health behaviours with other forms of coping, (b) to examine associations between personality, perceptions of control and exercise behaviours, and (c) to explore the effects of exercise and coping on well-being directly, whilst controlling for the effects of personality differences.

This study examined exercise and health related behaviours (drinking and smoking) in a sample of 187 University students, in relation to reported coping behaviour, perceived control and well-being.

The results indicated that there were significant positive relationships between exercise behavior and well-being ($p<0.01$), symptom reduction coping ($p<0.05$), perceived control ($p<0.001$) and extraversion ($p<0.01$). Smoking was negatively related to well-being and exercise, but positively correlated with the use of devaluation coping. Alcohol consumption was negatively related to accommodation coping ($p<0.05$) and to extraversion ($p<0.001$), as well as being positively correlated with well-being ($p<0.01$). Multiple regression analysis indicated that 40% of the variance in well-being scores could be predicted by the variables. The two strongest predictors in the equation were perceived control and neuroticism. Further regression analyses (using just the health related behaviors) indicated that around 10% of the variance in well-being could be predicted, with self-reported physical activity and drinking both significant contributors to the equation.

Thus, whilst health and exercise behaviours seem related to other forms of coping, these links were not strong. Furthermore, while all three health behaviours were significantly associated with psychological well-being, their overall influence on mental health was much smaller than the dispositional characteristics of personality and perceived control.

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must be considered relevant factors that are conditioned by the presence of opposition.

The horizontal velocity at the moment of receiving the ball was greater when there was opposition, which could indicate that the spatial awareness developed by players should be greater when facing opposition. Therefore, using an opponent in shooting practice can improve spatial awareness by making more demands on perceptive mechanisms. In terms of the organization of the action in memory, it was observed that players modify their movements in the final phase of the jump shot in the presence of an opponent, thus reflecting the adaptability of the neuromuscular system to contextual variations. This reorganization produced in the final phase of the jump shot confirms that the shot is no mere copy of the physical movement that persists throughout the process, but that it must be redefined each time according to the playing situation, feedback defining the conditions in which the action takes place. This means that the players can use the information derived from the first stage of the action to readjust the segments in the later phases.

We conclude that shooting practice in various contexts could improve the capacity of the motor programme to adapt to new situations, as well as augmenting retention of the movement. So far as shooting training is concerned, attention must be focused on the initial phase of the movement, the stationary phase, which is the most automatic and where least variability has been found. However, in the ball release phase, players can make adjustments to the segments according to the context in which the shot is being taken, so that any attempt to automatize a specific final movement could be counterproductive.

Individual differences, exercise and leisure activity and affective well-being

C. Sale, A. Guppy and M.S. El-Sayed

Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK

Attempts have been made to describe the relationship between exercise and health-related activities and various indicators of mental health (Rick and Guppy, 1994: *European Work and Organizational Psychologist*, 4, 121–137). Although some research has emphasized the links between health and leisure activities and more traditional coping measures (Ingledew *et al.*, 1996: *British Journal of Health Psychology*, 1, 263–281), other empirical studies have focused on the relationship between individual differences, such as sex and personality, and health and exercise behaviour (Courneya and Hellsten, 1998: *Personality and Individual Differences*, 24, 625–633). From these studies, it would seem that health and exercise behaviours are positively associated with well-being, whereas social exercise behaviour is more commonly reported by those with extrovert characteristics. In this study, we focused on the relative use of exercise and health-related leisure activities (e.g. smoking, drinking) across groups of individuals defined by personality and sex in relation to subjective well-being measures.

Results from a cross-sectional survey of 187 participants are reported. Males ($n = 80$) reported significantly more drinking (18.35 ± 13.57 units; $r = -0.34$, $P < 0.001$) and smoking (44 smokers, 143 non-smokers; $r = -0.27$, $P < 0.001$), but also reported high habitual physical activity levels (10 sedentary, 77 moderately active, 70 active, 30 highly active; $r = -0.29$, $P < 0.001$). Females ($n = 107$) reported more use of social support coping, with these findings remaining statistically significant ($r = 0.23$, $P < 0.01$) even after controlling for the effects of personality. Further findings emphasized the positive association between extraversion and self-reported habitual physical activity ($r = 0.19$, $P < 0.05$) as well as alcohol consumption ($r = 0.37$, $P < 0.001$) (even when controlling for sex). Neuroticism was not found to be correlated with any of the exercise and leisure variables, once sex had been partialled out. Hierarchical multiple regression analyses were used to identify significant predictors of affective well-being scales, predicting 34% of the variance for depression–enthusiasm and 39% of the variance for anxiety–contentment. Depression–enthusiasm was significantly predicted by neuroticism ($\beta = -0.46$, $P < 0.001$) and avoidance coping ($\beta = -0.16$, $P < 0.05$). Levels of anxiety–contentment were also significantly predicted by neuroticism ($\beta = -0.47$, $P < 0.001$) and avoidance coping ($\beta = -0.15$, $P < 0.05$), once other variables had been controlled for statistically.

The results provide support for the impact of individual differences on the use of coping behaviours, particularly health-related behaviours. Only limited evidence was found for significant associations between health-related behaviours and traditional dimensions of coping, with only physical activity being significantly correlated with tension-reduction coping ($r = 0.17$, $P < 0.05$). Psychological well-being was significantly predicted by neuroticism and avoidance-coping strategies, rather than by any of the health-related behaviours.

The effect of cricket ball colour and illuminance levels on the catching behaviour of professional cricketers

K. Scott, D. Kingsbury, S. Bennett, K. Davids and M. Langley

Department of Exercise and Sport Science, The Manchester Metropolitan University, Alsager, UK

In recent years, there have been many alterations to the equipment and technology in professional cricket, including the introduction of white balls during day–night one-day matches. The aim of the present study was to assess simulated slip-catching performance and movement initiation time in professional cricketers when ball colour and illuminance levels differ.

Five male professional cricketers aged 28 ± 4 years (mean $\pm$ *s*) volunteered to catch a total of 60 cricket balls, 20 (10 red and 10 white) under three illuminance levels (571, 1143 and 1714 lux). The participants stood with hands on thighs and were required to perform two-handed catches. Balls were projected from a ball machine at 20 $m \cdot s^{-1}$ over a distance of 8.4 m, to the participant's dominant side. To enhance sensitivity of catching performance, an established catching scale was used. On the 0–5 scoring scale, a complete