

# SOCIAL COGNITION IN EPILEPSY

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## Abbreviations

AED	Antiepileptic drug
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
BA	Broadman's area
BF	Bifrontal
CBZ	Carbamazepine
CR	Conditional Reasoning
DLPFC	Dorsolateral prefrontal cortex
EEG	Electroencephalogram
EI	Emotional intelligence
FER	Facial emotion recognition
FHI	Frontal Head Injury
FL	Frontal lobe
FLE	Frontal lobe epilepsy
FSIQ	Full Scale Intelligence Quotient
HADS	Hospital Anxiety and Depression Scale
HC	Healthy Controls
IBE	International Bureau for Epilepsy
IGE	Idiopathic generalised epilepsy
ILAE	International League Against Epilepsy
IQ	Intelligence Quotient
LT	Left temporal lobe
JME	Juvenile myoclonic epilepsy
LTLE	Left temporal lobe epilepsy
LF	Left frontal lobe
LFT	Left fronto-temporal
LH	Left hemisphere
MME	Mini Mental State Examination
MTLE	Medial temporal lobe epilepsy
MTL – HS	Mesial temporal lobe epilepsy with hippocampal sclerosis
MTS	Medial temporal sclerosis
MRI	Magnetic resonance imaging

NC	Normal control group
OFC	Orbito-frontal cortex
PHT	Phenytoin
QoL	Quality of life
QOLIFE-31	Quality of Life in Epilepsy 31
PFC	Prefrontal cortex
PWE	People with epilepsy
RF	Right frontal lobe
RFT	Right fronto-temporal
RH	Right hemisphere
RT	Right temporal lobe
RTLE	Right temporal lobe epilepsy
SD	Standard deviation
SPECT	Single-photon Emission Computerised Tomography
TASITS	The Awareness of Social Inference Task
ToM	Theory of mind
ToHN	Theory of Human Nature
TL	Temporal lobe
TLE	Temporal lobe epilepsy
WAIS	Wechsler Adult Intelligence Scale
WASI	Wechsler Abbreviated Scale of Intelligence
WCNN	Walton Centre for Neurology and Neurosurgery
WST	Wason Selection Task
WTAR	Wechsler Test of Adult Reading
WHO	World Health Organisation
VGB	Vigabatrin
VM	Ventromedial
VM PFC	Ventromedial prefrontal cortex

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## ABSTRACT

Some of the psychological problems associated with epilepsy have their origins in the ability of people with epilepsy (PWE) to engage in meaningful and appropriate social interactions. PWE often report difficulties in social settings, yet there is a paucity of research investigating the socio-cognitive skills of this group. This thesis aimed to investigate these skills and relate them to the patient's perceived impact of epilepsy on their social competence. An additional objective was to see whether studying social cognition in focal epilepsy might provide some insight into the organic basis of social cognitive abilities in the normal population.

The thesis consists of four separate studies which aimed to investigate social cognition and social functioning in patients with focal epilepsy. With this in mind, a test battery assessing a range of skills linked to social cognition was administered to a cross section of experimental groups (N=95). These included patients with seizure foci in the right frontal lobe (RF), left frontal lobe (LF), right temporal lobe (RT), left temporal lobe (LT) and a group with idiopathic generalised epilepsy (IGE). A normal control group (NC) and a frontal head injured (FHI) group with no epilepsy were also recruited for the study.

In Studies 1 and 2 theory of mind (ToM) deficits were apparent in people with RF and LT epilepsy. These groups demonstrated impairment in the appreciation of false belief and deception at first and second order levels of intentionality. They also exhibited deficits in the appreciation of pragmatic language when attempting to infer the meaning underlying hints given by story characters. These impairments were in part attributable to deficits in narrative memory in the LT group. In Study 3



embedding problems within a social context significantly facilitated conditional reasoning in the NC, LT and RF groups but not in the other experimental groups. This finding was unexpected and suggests a double dissociation between ToM and social conditional reasoning. Study 4 investigated the extent to which socio-cognitive impairment was associated with the perceived impact of epilepsy on everyday social functioning. No statistically significant relationship between these variables was found, although a significant negative correlation between education level and impact of epilepsy was observed.

Taken together the findings suggest that impairment in ToM may be a particular feature of right frontal lobe pathology and that social conditional reasoning and ToM may be functionally dissociated. PWE do not appear to have insight into their social functioning difficulties, which may well reflect underlying pathology. In light of this, future research should obtain objective measures of social competence from 'significant others'.

This is the only series of studies to date to assess social cognition in people with frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE) within the same design. It is also the first time that social conditional reasoning in epilepsy has been systematically assessed and represents one of the largest lesion studies within the field of social cognition. It is hoped that some of the test material used in the thesis, may prove to be a useful and inexpensive clinical resource to help identify PWE who are at risk of reduced social competence, and in localising the site of seizure foci in patients during clinical audit, particularly where anterior foci are suspected.

## **Chapter 1: General Introduction**

The purpose of this brief introduction is to provide a general overview and to give the reader an insight into how the research idea for this thesis was developed.

The themes to be addressed in this research were in part informed by observing the symptoms and behaviours exhibited by patients with epilepsy who were attending the Walton Centre for Neurology and Neurosurgery (WCNN) in Liverpool. The WCNN is a tertiary referral unit and the majority of patients attending clinics at the WCNN have refractory epilepsy (characterised by difficult to manage seizures). A number of these patients were being assessed to see if they were viable candidates for surgery. A recurrent difficulty reported by epilepsy patients attending the WCNN was that they experienced a number of difficulties in relation to social functioning. Such difficulties have been reflected in the wider epilepsy population where people with epilepsy often report difficulties in social settings, such as problems in forming friendships, stigmatisation, educational underachievement, low self-esteem and restricted opportunities for social activities (Austin & de Boer, 1997; Baker, Brooks, Buck, & Jacoby, 1999; Collings, 1990; Fisher et al, 2000; Jacoby, Baker, Steen, Potts & Chadwick, 1996; Mittan, 1986).

Exactly why this clinical group experience problems in social situations was unclear but likely to be a consequence of a number of complex interrelated psychosocial factors that impact upon the person with epilepsy. Such factors include the experience of stigma, unemployment or underemployment, anxiety and depression, cognitive dysfunction, poor self esteem, social isolation and difficulties in interpersonal relationships (Austin & de Boer, 1997; Corcoran & Thompson,



1992; Collings, 1990; De Souza & Salgado, 2006; Fisher et al, 2000; Grabowska-Grzyb, Jędrzejczak, Nagańska & Fiszler, 2006; Jacoby et al., 2006; Mensah, Beavis, Thapar & Kerr, 2007; Morrell, 2002; Suurmeijer, Reuvekamp & Aldenkamp, 2001; Thompson & Corcoran, 1993). The impact of these factors on the quality of life of people with epilepsy is discussed in detail in Chapter 3.

Some of the behaviours exhibited by people with epilepsy have parallels with those seen in other conditions, such as Asperger's syndrome and autism. Social cognitive dysfunction in autism has been well established and theory of mind (ToM) deficits are believed to be a core feature of the disorder. Corcoran, Mercer & Frith (1995) and Frith & Corcoran (1996) discovered that people with schizophrenia had social cognitive deficits which were dependent on their current symptom profile. Patients in remission or with symptoms of passivity did not exhibit any socio cognitive deficits, whilst those with paranoid delusions, negative features and incoherence were impaired on ToM tasks. This research spurred a plethora of studies in the area of schizophrenia and ToM during the late 1990's and early 2000's. At this time it was becoming very apparent that social cognitive dysfunction was present in a number of clinical populations and was not just specific to autism, consequently research investigating socio-cognitive functioning in other clinical populations increased in prevalence. Social cognitive deficits in these clinical populations may be in part due to the neural structures implicated in such disorders, consequently lesion studies and structural and functional imaging studies trying to localise social cognitive function in the brain were also emerging, a review of lesion and neuroimaging research in relation to social cognition is detailed in Chapter 4 of the thesis.

As well as the psychosocial factors mentioned above, this thesis intended to consider whether some of the psychosocial problems associated with epilepsy had their origins in the ability of people with the condition to engage in meaningful and appropriate social interactions. People with epilepsy (PWE) often report difficulties in social settings, yet to date there had been little research investigating the socio-cognitive skills of this group. It is possible that the neural disruption caused by recurring seizures in focal epilepsy could in some way be linked to brain areas that are implicated in social cognitive functioning. Consequently some people with epilepsy (PWE) may be more prone to such psychosocial difficulties depending on their seizure foci. With this in mind a review of the literature (see Chapter 5) revealed that before 2000 there had been no published studies which had investigated social cognition in epilepsy, social cognition was an important but neglected area of study in the field of epilepsy. This apparent gap in the literature prompted the research questions which are the focus this thesis.

The thesis is divided in to two sections. The first section consists of five introductory chapters which review relevant literature. The second section consists of a description of the general method, five empirical chapters and a general discussion. Chapter 2 will provide the reader with a general overview of epilepsy so that discussion of epilepsy related variables in subsequent chapters will be clear to the reader. Chapter 3 will address psychological difficulties such as cognitive dysfunction and the prevalence of anxiety and depression in PWE, this is relevant to the thesis as such difficulties can impact on how the participants perform on the measures used in the empirical studies. Beyond this, the overall aim of this chapter is to provide the reader with a general overview of the sort of factors that can



impede social functioning in PWE. The literature outlined in Chapter 3 is particularly relevant to subsequent empirical chapters which will investigate social cognitive functioning in epilepsy. Socio-cognitive skills may be particularly relevant to being able to identify and resolve psychosocial difficulties, thereby reducing the impact of epilepsy on the quality of life of PWE. This aspect will also be addressed in the subsequent empirical chapters of this thesis. Specifically it is intended to establish the extent to which deficits in social cognitive skills identified in the early empirical chapters of this thesis determine the perceived impact of epilepsy on the everyday lives of PWE.

Chapter 4 will provide an overview of social cognition with a particular focus on ToM. With particular emphasis on lesion studies, research investigating the neural basis of ToM will be discussed in detail. Chapter 5 will review all the literature to date which has specifically assessed social cognition in epilepsy, as research in this area is particularly pertinent to the objectives of the thesis. Chapter 6 will outline the general design and methodology of the thesis. Both Chapter 4 and Chapter 5 are especially relevant to the first two empirical chapters of the thesis (Chapters 7 & 8) which use measures of ToM to assess social cognition in epilepsy, in relation to seizure foci. The third empirical study assesses social conditional reasoning (Chapter 9) which has been linked to ToM performance in previous research (Corcoran & Frith, 2005; Ermer, Guerin, Cosmides, Tooby & Miller, 2006). The fourth and final study (Chapter 10) will investigate whether perceived difficulties in social functioning in PWE is reflected in their performance on the socio-cognitive measures which have been investigated in the first three empirical studies.

The primary objective of this thesis is to investigate whether some of the social difficulties that people with epilepsy report may be a consequence of problems with social cognition, including ToM. The thesis consists of five separate studies which aim to investigate social cognition/functioning in patients with focal epilepsy. With this in mind, a test battery assessing a range of skills linked to social cognition/functioning was administered to different experimental groups of patients with epilepsy. These included patients with seizure foci in the right frontal lobe (RFL), left frontal lobe (LFL), right temporal lobe (RTL), left temporal lobe (LTL) and a group with idiopathic generalised epilepsy (IGE). A normal control group and a frontal head injured (FHI) group with no epilepsy were also recruited for the study.

An additional objective of the thesis was to see whether studying social cognition in focal epilepsy might provide some insight into the organic basis of social cognitive abilities in the normal population. As Kirsch (2006) argues ‘because it is intimately involved with dysfunction in salient anatomical regions, intractable focal epilepsy provides a natural window into social cognitive functioning’ (p. 72).

Understanding the role that social cognition plays in underpinning social behaviour in people with epilepsy, will hopefully assist in identifying patients who may be at risk of reduced social competence. Consequently the findings set out in this thesis might contribute towards the development of more effective psychological interventions in patients who are experiencing social cognitive deficits. Such interventions will enable the smoother functioning of such individuals in society.



## **Chapter 2: Epilepsy**

### ***Chapter outline***

This chapter will outline the history of epilepsy, more modern conceptions of what characterises epilepsy, its prevalence and incidence rates and the criteria for classifying seizures and epileptic syndromes. Aetiology of epilepsy and how it is managed with particular emphasis on drug therapy and the side effects associated with taking anti epileptic medication will be discussed. The chapter aims to provide an account of the physiological characteristics and the theoretical and practical perspectives which underlie the condition, thereby permitting a more complete understanding of the research literature in this area. This should also facilitate the understanding of the discussion of quality of life issues in epilepsy in Chapter 3 and research which has investigated social cognition in PWE in Chapter 5.

### ***2.1 Historical background***

Epilepsy has been regularly documented since antiquity, in different parts of the world and in different cultures (International League Against Epilepsy (ILAE, 2003a). The word epilepsy comes from the Greek verb '*epilambanein*', which means to be seized or taken by surprise (ILAE, 2003a). Historically, all diseases were regarded as a form of punishment, curses from the gods or evil spirits and epilepsy was seen as a means of retribution for sin. Depending on the common popular belief at the time, PWE were believed to be possessed by demons, to be insane or associated with the divine and supernatural. Such misconceptions have meant that epilepsy has been surrounded by stigma, superstition and prejudice.

Many religions have regarded the epileptic as being possessed. The New Testament (Mark 14-29) clearly describes a young boy who has a tonic-clonic seizure and refers to the seizure as a 'deaf and dumb spirit' that possesses the boy. In the 2<sup>nd</sup> and 3<sup>rd</sup> centuries physicians and philosophers associated epilepsy with the lunar phases and this bred the misunderstanding that epilepsy was a form of lunacy (Chadwick, 1997). The belief that epilepsy was contagious goes back to Roman times when epileptics were spat on to ward away demons and avoid infection. This idea was still prevalent during the 13th century when Berthold of Regensburg wrote that the infection was contagious through the patient's 'evil' breath (ILAE, 2003a). The idea that epilepsy was infectious still prevailed in the 18<sup>th</sup> century (De Boer, 1995).

Throughout history many laws have discriminated against PWE. The Code of Hammurabi, dated 1780 B.C, declared that a person with epilepsy was not allowed to marry and could not be a member of a jury or a witness in court (ILAE, 2003a). Despite advances in clinical research and treatment, legislation which stigmatises people with epilepsy still exists in some countries or has only recently been revoked. Stemming from the eugenics movement, prohibiting marriage was seen as a way of preventing procreation and often sterilisation of PWE was encouraged. Until 1956 PWE in the United States were prohibited from marriage in 17 states and 18 states provided for sterilisation (Epilepsy Foundation of America, 1992). In the United Kingdom a similar law on the prohibition of marriage existed until 1970 (ILAE, 2003a).



Contrary to previous superstitious explanations, the Hippocratic collection of medical writings (400 BC) was the first attempt at a scientific explanation of epilepsy (Chadwick, 1997). These writings suggested that epilepsy was an organic disorder caused by an excess of phlegm and could be treated with diet and drugs as opposed to magic. It was during the 18<sup>th</sup> century when the idea of epilepsy as a physical disorder as opposed to a disorder of the soul began to gain credence. In the 19<sup>th</sup> Century the first asylums were built to accommodate both psychiatric and epileptic patients (Masia & Devinky, 2000). Ironically this created opportunities for patients with epilepsy to be closely studied and enhanced people's understanding of the disorder. In 1875 John Hughlings Jackson was the first neurologist to acknowledge that epilepsy was an organic disorder where disruption to electrical activity was responsible for causing a seizure (Brodie & Schachter, 2001).

Historical representations of epilepsy have been plagued with negativity and misconception, which has lead to fear and condemnation of the disorder within society. Despite advances in understanding epilepsy, myths and misconceptions about epilepsy are still prevalent in today's society (Baxendale & O'Toole, 2007). How these misconceptions contribute towards the experience of stigma and psychosocial difficulties in people with epilepsy will be discussed in more detail in Chapter 3.

## ***2.2 What is epilepsy?***

Epilepsy is one of the most common neurological disorders affecting people in Britain. It is the second most common reason for referral to a neurologist in the

United Kingdom, with headache and migraine being the most common (Hopkins, Menken & De Fries, 1989). It is the most prevalent serious neurological disorder in the world (Brodie & Schachter, 2001).

A seizure is defined as ‘an episode of neuronal hyperactivity’ (Jacoby & Baker, 2000, p.13). Seizures are transient episodes ‘of neurological dysfunction brought about by abnormal, synchronous and excessive discharges of cerebral neurons’ (Oxbury, Polkey, and Duchowny, 2000, p.11).

Epilepsy is an umbrella term which incorporates a constellation of different seizures and syndromes. It is evident by recurrent, typically unprovoked epileptic seizures (Guberman and Bruni, 1999). Many definitions of epilepsy focus on the unprovoked and recurrent nature of seizures. This is significant because not everyone who has a seizure is considered to have epilepsy. Some individuals are more sensitive and have a lower threshold to electrical discharges in the brain. Consequently there are individual differences in how susceptible people are to having a seizure. Seizures caused as a consequence of systemic disturbances such as a rise in body temperature (febrile seizures), a lack of blood supply (anoxic seizures) as a consequence of illness, trauma or injury, or single isolated seizures do not necessitate a diagnosis of epilepsy (Baker and Jacoby, 2001).

### ***2.3 Incidence and prevalence of epilepsy***

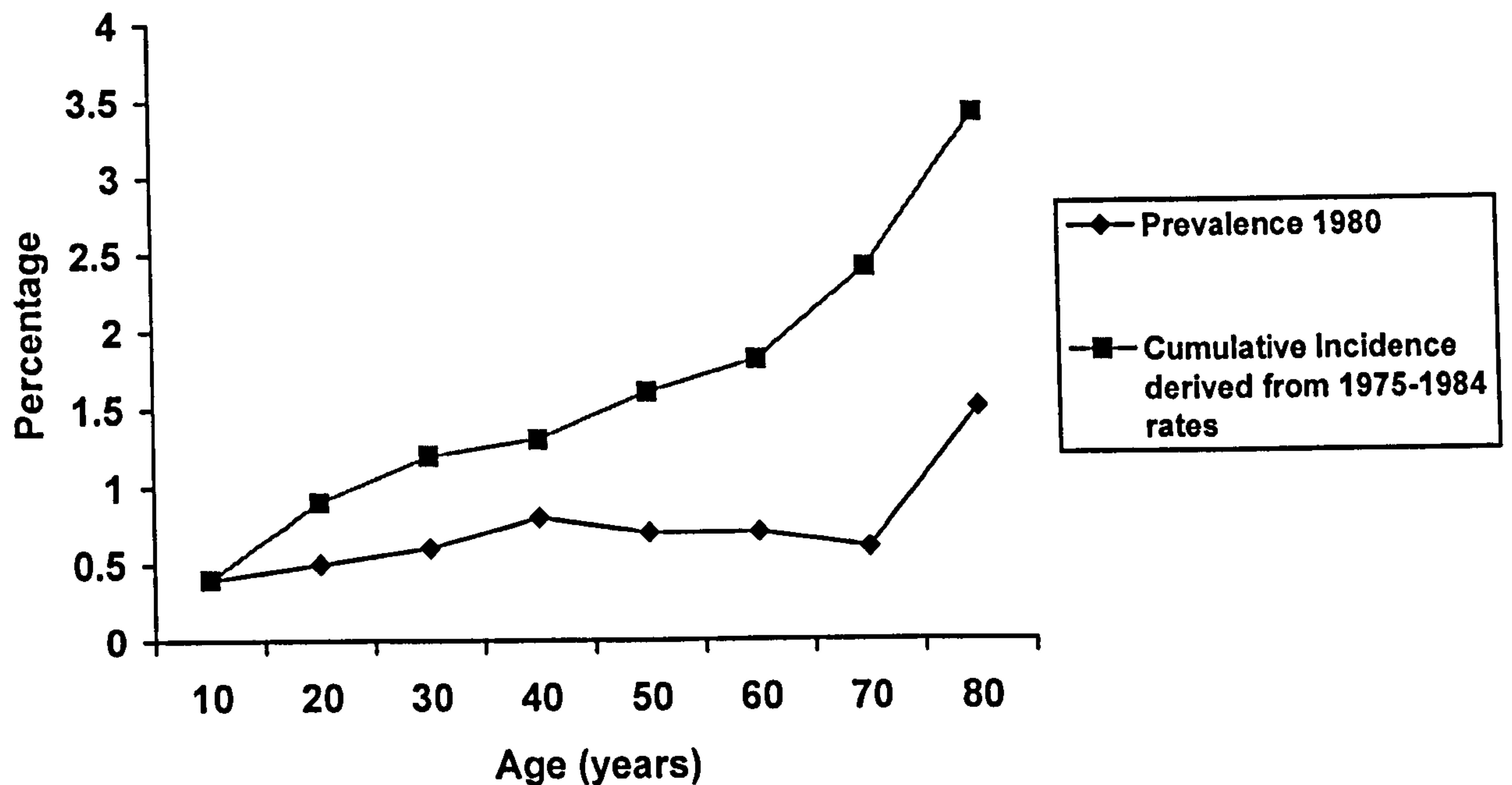
Epilepsy has an age adjusted incidence (annual rate of new cases) of between 20 and 50 per 100,000 and a prevalence (proportion of active cases within a given



population at any one time) of 4 to 10 per 1,000, (Chadwick, 1997). This means that as many as 29,000 people will be diagnosed with epilepsy each year and that there are as many as half a million people with epilepsy in the United Kingdom (Chadwick, 1997). In the region of 50 million people have epilepsy worldwide and 80% of PWE live in developing countries with little if any access to treatment (Brodie & Schachter, 2001; de Boer, Mula & Sander, 2008).

Most epidemiology studies concur that the highest incidence rates of epilepsy are in the early and later years of life (Oxbury, Polkey, and Duchowny, 2000). Porter (1993) reports that over 75% of people with epilepsy experience seizures before they are 18. The most extensive epidemiological study to date was conducted in Rochester, Minnesota. The incidence of epilepsy and unprovoked seizures was recorded for all residents between 1935-1984 (see Figure 1). Incidence of Epilepsy by ILAE seizure type was also recorded (see Figure 2); seizure type will be discussed in detail in 2.4.

Cumulative incidence refers to the amount of people within a given population who develop epilepsy over a set period of time. The cumulative incidence rate for developing epilepsy changes over the life course according to age. The chances of developing epilepsy from birth until the age of 20 is in the region of 1%, while the highest incidence rate is 3% and occurs in the elderly above the age of 70 (Baker & Gorry, 2001). This increase is mainly due to the risk of cerebrovascular disease (Hopkins & Shorvon, 1995). In the Rochester study, a significantly higher number of males than females were found to develop epilepsy (Hauser, Annegers & Kurland, 1993).



*Figure 1: Prevalence and cumulative incidence of epilepsy in Rochester, Minnesota. Adapted from (Hauser & Annegers, 1993).*

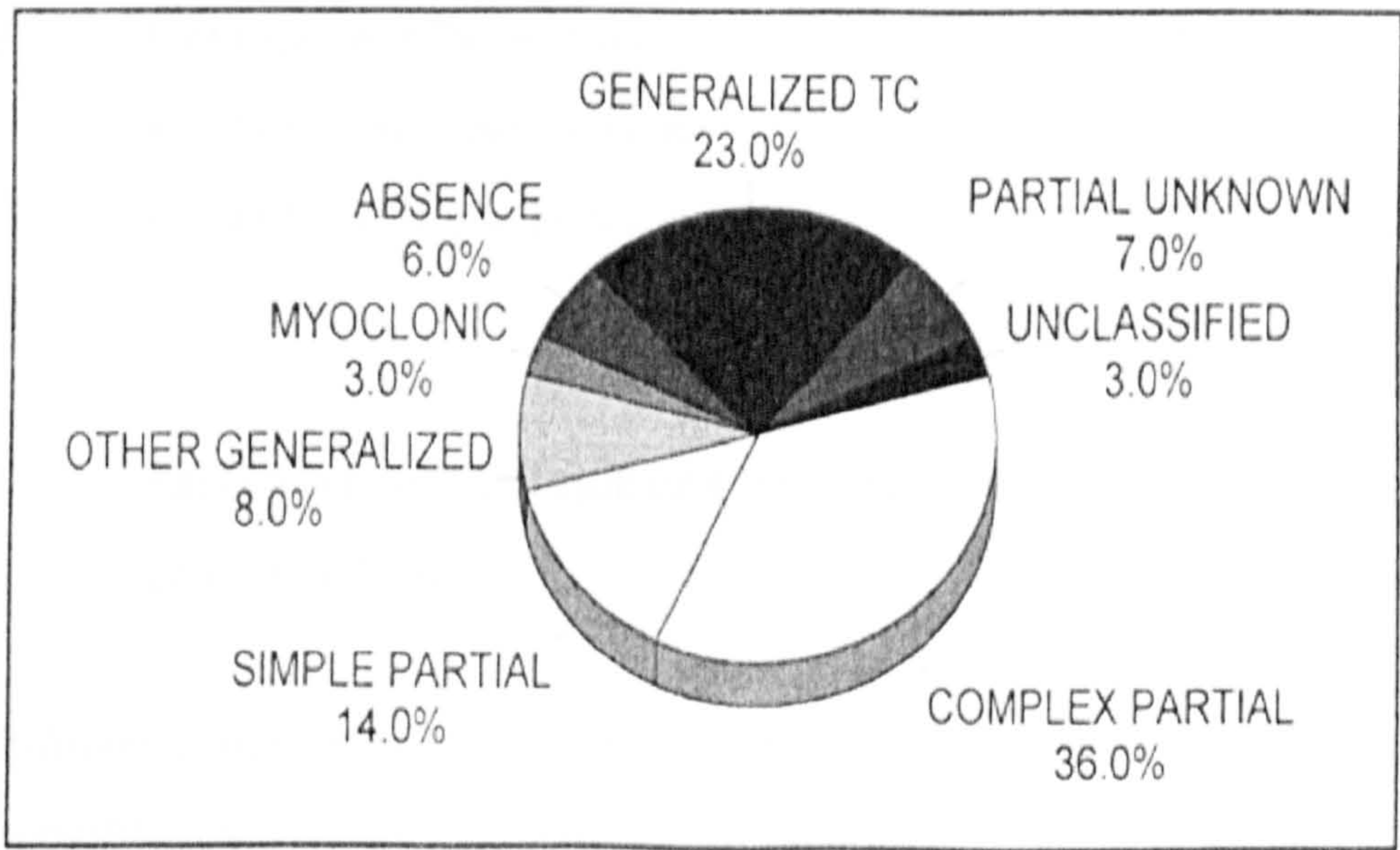
#### **2.4 Classification of seizures and epilepsy**

Engel (1989) proposes that the term epileptic focus is used ‘to refer to the cortical area that appears to be the major source of interictal epileptiform EEG discharges’ (p. 2). ‘Discharges can be focal, implying a single epileptiform abnormality, bilateral or independent, suggesting abnormalities in both hemispheres; multifocal, suggesting three or more abnormalities; or diffuse (either widespread or generalised), where there is no apparent epileptic focus’, (Engel, 1989, p. 2).

The most widely used way of classifying seizures is based on the guidelines of The Commission on Classification and Terminology of the International League against Epilepsy ILAE (1981). Seizures can be defined in terms of their symptoms and their locus of origin and are classified under four main headings; partial (local,



focal) seizures, primary generalised seizures, unclassified seizures and prolonged or repetitive seizures (status epilepticus) see Table 1. It is worthy of note that in 2006 the ILAE developed a revised list of seizure classifications which requires more detailed information especially in relation to focal seizures. However, the ILAE (2008) recognise that the information required for the 2006 list is not always readily available and that the 1981 classification system is suitable for most purposes. The majority of the research discussed throughout this thesis has utilised the 1981 classification system.



**Figure 2:** Proportion of incidence cases of epilepsy in Rochester, Minnesota, (1935-1984) stratified by ILAE seizure type. TC =tonic-clonic seizures.  
Taken from Hauser, Annegers & Rocca (1996).

*Table 1: Seizure Classification (Modified from the Commission on Classification and Terminology of The International League Against Epilepsy, 1981).*

---

I.	<b><i>Partial seizures (focal, local)</i></b>
A.	<b>Simple partial seizures (consciousness not impaired)</b> <ul style="list-style-type: none"><li>• with motor symptoms</li><li>• with sensory symptoms</li><li>• with autonomic symptoms</li><li>• with psychic symptoms</li></ul>
B.	<b>Complex partial seizures (consciousness is impaired)</b> <ul style="list-style-type: none"><li>• with simple partial onset</li><li>• without simple partial onset, altered awareness/memory from onset.</li></ul>
C.	<b>Partial seizures (simple or complex) evolving to secondary generalisation</b>
II.	<b><i>Primary generalised (convulsive or non convulsive, involve both hemispheres)</i></b>
(A)	(i) Typical absence seizures (ii) Atypical absence seizures
(B)	Myoclonic seizures
(C)	Clonic, tonic and tonic-clonic seizures
(D)	Atonic seizures
III.	<b><i>Unclassified seizures (inadequate or incomplete data)</i></b>
IV.	<b><i>Prolonged or repetitive seizures (status epilepticus)</i></b>

---



### ***2.4.1 Partial seizures***

Partial seizures are focal in nature and have clinical or electroencephalographic evidence of a localised onset (Baker & Jacoby, 2001). Partial seizures are subdivided into three categories, (simple partial, complex partial and partial evolving to secondary generalisation) (Oxbury, Polkey, and Duchowny, 2000). In contrast, generalised seizures have no evidence of localised onset and usually occur with no warning. A patient may be prone to more than one type of seizure.

Simple partial seizures are localised and consciousness is maintained. The seizure is usually restricted to one hemisphere and the symptoms are related to the focal area of the brain where the seizure occurs. These seizures can be sub divided into motor seizures where patients can experience a motor event such as jerking of a limb, sensory seizures involving sensory, somatosensory, gustatory or vertiginous symptoms, autonomic seizures which may involve manifestations such as sweating, vomiting or flushing and less commonly psychic seizures which can involve dysphasia, impaired memory, altered affect, déjà vu and jamais vu. Simple partial seizures rarely involve both hemispheres whereas complex partial seizures frequently involve bilateral hemispheric activation. Complex partial seizures are also localised but consciousness is impaired. These seizures may be accompanied by psychic disturbance and automatisms such as lip smacking, chewing, swallowing and verbal utterances. Often the patient may experience an aura before the seizure and post-ictal confusion after the seizure.

Both complex and simple seizures are defined by their locus of origin in the brain. Seizures can be frontal, temporal, parietal and occipital in origin. Temporal and

frontal lobe seizures are the most common. Seizures are accompanied by particular motor and sensory symptoms depending on the seizure foci as highlighted by Chadwick (1997) and summarised in Table 2.

*Table 2: Motor and sensory symptoms associated with focal seizures (taken from Chadwick, 1997).*

Frontal Lobe	Jacksonian Seizures (tingling in hand or arm)
	Adversive seizures (eyes or head turn to one side)
Temporal Lobe	Strange smells or tastes
	Altered behaviour
	Déjà vu
	Lip smacking or chewing movements
Parietal	Tingling or jerking of the leg, arm or face
Occipital	Flashing lights or spots

Both types of partial seizure may cease remaining focal in nature or both may spread and evolve into a generalised motor seizure. These seizures are called secondary generalised seizures and can be tonic-clonic, tonic or clonic.

**2.4.2 Generalised seizures**

Generalised seizures are not localised in nature and can be convulsive (tonic-clonic, clonic, tonic, atonic, myoclonic seizures) or non-convulsive (absence seizures).

Combinations of the different types of generalised seizures may occur within one patient.

The most well known form of generalised seizures are tonic-clonic seizures. These seizures involve a sudden contraction of muscles (tonic) followed by jerking movements (clonic) where the muscles relax and contract intermittently, after this phase the person may stay unconscious or fall into a deep sleep (see Table 3). Tonic seizures can occur without the clonic phase and vice versa.

Absence seizures are non convulsive seizures that often begin in childhood or early adolescence. They have a sudden onset and cessation. Loss of consciousness is very brief disrupting the patients foregoing behaviour after which normal activity is resumed. In some instances automatisms, clonic, atonic and tonic events may be evident, these are referred to as atypical absence seizures.

Repetitive seizures, where one seizure cannot be distinguished from another or where consciousness is not recovered between seizures is called 'status epilepticus', this type of attack can be life threatening.

Myoclonic seizures are characterised by a clonic jerking movement of the muscle which often occurs whilst falling asleep or upon waking. Atonic seizures (or drop attacks) involve nodding of the head or a person falling to the floor due to a sudden decrease in muscle tone.



**Table 3: Tonic and clonic phase of generalised seizures (Gastaut & Broughton, 1972).**

---

***Tonic Phase***

1. Usually lasts from 10 to 20 seconds
- 2. Begins with brief flexion:
  - a. muscles contract
  - b. the eyelids open; eyes look up
  - c. the arms are elevated, abducted, and externally rotated; elbows are semi-flexed
  - d. the legs are less involved but maybe flexed
3. The extension phase is more prolonged:
  - a. involves first the neck and back
  - a tonic cry may occur and lasts 2-12 seconds
  - c. the arms extend
  - d. the legs are extended, abducted and externally rotated
4. The tremor begins:
  - a. the tremor is a repetitive relaxation of the tonic contraction
  - b. starts at 8 per second, gradually coarsens to 4 per second
  - c. leads to the clonic phase

***Clonic phase:***

1. Usually lasts about 30 seconds
  2. Begins when the muscular relaxations completely interrupt the tonic contraction
  3. Brief violent flexor spasms of the whole body
  4. The tongue is often bitten
-



## ***2.5 Epilepsy syndromes***

Once seizure type has been diagnosed, aetiology is ascertained in order to classify the epilepsy into a syndrome. In 1985 the Commission on Classification and Terminology of the ILAE devised a classification system based on epilepsy syndromes (this was later revised in 1989). A syndrome is a disorder characterised by a cluster of signs and symptoms customarily occurring together (Baker & Jacoby, 2001). Effective classification of seizures and syndromes is imperative for appropriate therapy and prognosis. The epilepsy syndrome is determined by whether the epilepsy is localised-related or generalised and both these groups are subdivided by whether the epilepsy is idiopathic, symptomatic or cryptogenic.

Idiopathic epilepsies are thought to be genetic and have no known cause except that which may arise from a possible hereditary condition. In idiopathic epilepsy the epilepsy itself is the primary disorder.

Symptomatic epilepsies are caused by a recognisable postnatal acquired brain pathology such as infection or trauma or by perinatal complications and the epilepsy itself is a secondary disorder. Aetiology may be established using magnetic resonance imaging (MRI) and single-photon emission computerised tomography (SPECT) which can identify distinct areas of damage within the brain that may relate to specific cognitive deficits.

Cryptogenic epilepsies are thought to have an underlying structural cause though this cause has not been established by current diagnostic procedures. These

epilepsies are thought to be symptomatic and with advances in brain imaging techniques the diagnosis of cryptogenic epilepsies will decrease.

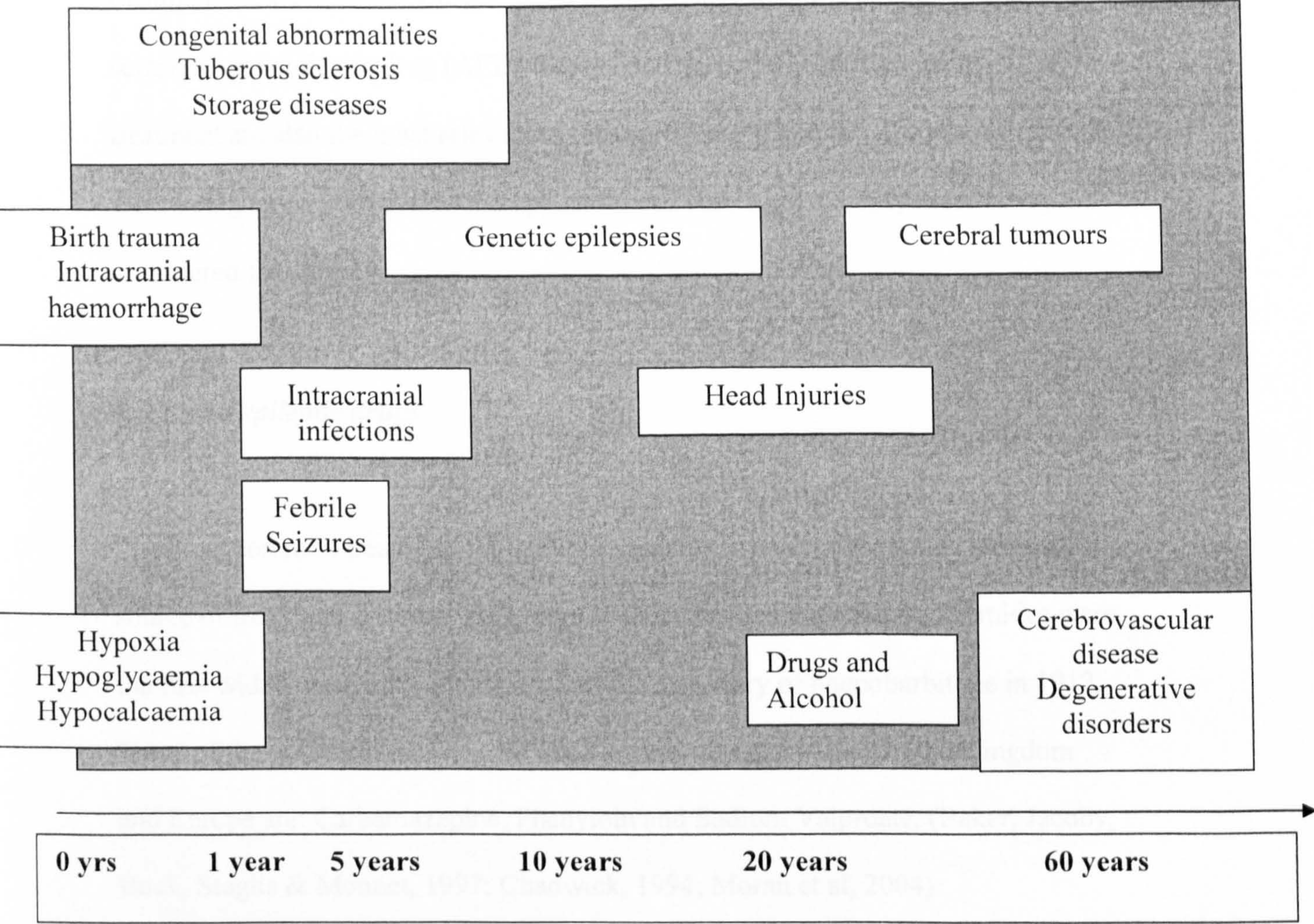
**2.6 Aetiology of epilepsy**

After determining seizure type and syndrome the final stage in the diagnostic process is to determine underlying aetiology. Epilepsy can be caused by almost any form of cerebral pathology such as birth trauma, head injury, infection, tumours, congenital defects, exposure to toxic agents, degenerative disorders and cerebrovascular disease. Seizure history and investigative techniques such as EEG, MRI and SPECT are important in helping establish aetiology. Radiological techniques typically detect underlying pathology in 85% of cases (Oxbury, Polkey, and Duchowny, 2000). The main causes of seizures and epilepsy in children and adults are displayed in Table 4. The aetiology of epilepsy tends to vary in accordance with age as seen in Figure 3

*Table 4: Main causes of seizures in children and adults (Taken from Porter, 1993).*

<i>Infants and children</i>	<i>Adults</i>
No definite cause determined	No definite cause determined
Birth and neonatal injuries	Vascular lesions
Vascular insults other than above	Head trauma
Congenital or metabolic disorders	Drug or alcohol abuse
Head injuries	Neoplasia
Infection	Infection
Neoplasia	Heredity
Heredity	





**Figure 3:** Aetiology of epilepsy at different ages (adapted from Brodie & Schachter, 2001).

**2.7 Treatment of epilepsy**

There are a number of potential therapies available to people with epilepsy, examples include vagus nerve stimulation, special diets and cognitive behavioural techniques aimed at reducing psychosocial factors which may trigger seizures. The evidence for the efficacy of these approaches is not convincing (Baker & Gorry, 2001). Section 2.7.1 and 2.7.2 have focussed on summarising two forms of



treatment which have demonstrated the most efficacy in terms of controlling seizures; anti epileptic drug (AED) therapy and surgery. These two forms of treatment are also the most relevant to the current sample in the study as all patients were being treated with AED therapy and those with focal epilepsy were being considered for surgery.

### ***2.7.1 Anti epileptic drugs***

The most common treatment for epileptic seizures is medication and is the usual source of treatment if two or more unprovoked seizures are evident. Bromides were the first widely used anticonvulsant until the discovery of phenobarbitone in 1912. Three of the most commonly prescribed anticonvulsants in the United Kingdom and Europe are: Carbamazepine, Phenytoin and Sodium Valproate, (Baker, Jacoby, Buck, Staglis & Monnet, 1997; Chadwick, 1994; Moran et al, 2004).

The choice of initial anti epileptic drug (AED) is usually dependent on seizure type, most drugs are found to more effective for particular seizure types (see Table 5). Other important factors include epilepsy syndrome, underlying aetiology (if known), age of onset, seizure frequency and comorbid conditions. The clinician must assess the benefit and risk factors to the individual whilst taking account of the individual needs of the patient.

*Table 5: Antiepileptic drugs of choice in adolescents and adults (adapted from Brodie & Schachter, 2001).*

Seizure type	Drug(s) of first choice	Drug(s) of second choice
Partial	Carbamazepine Phenytoin	Lamotrigine* Oxycabazine* Sodium Valproate
Tonic- clonic	Sodium Valproate Carbamazepine Phenytoin	Lamotrigine* Oxycabazine*
Absence	Sodium Valproate	Ethosuximide Lamotrigine*
Myoclonic	Sodium Valproate	Lamotrigine*
Unclassified	Sodium Valproate	Lamotrigine*

NB: Lamotrigine and oxycarbazepine are regarded as first-line drugs in some countries.

There are many inter-related factors effecting quality of life in epilepsy but the most important factor is freedom from seizures (Jacoby, 1992). The primary aim of AED treatment is to reduce the severity and frequency of seizures whilst minimising the level of side effects. Clinicians aim to do this using the simplest drug regime and monotherapy is the preferred approach for new patients to avoid toxicity. Introducing one drug at low dosage and gradually increasing this will reduce the chances of unwanted side effects and monotherapy is effective in approximately 70% of newly diagnosed cases (ILAE, 2003b). Polytherapy is the alternative for patients who have seizures that are more difficult to manage and consequently this approach produces more side effects due to the different drug

interactions. For some patients who usually suffer from refractory epilepsy (difficult to manage) adequate seizure control can only be achieved using polytherapy. To minimise the level of side effects to the patient, blood serum levels of AEDs need to be carefully monitored. AED therapy (first or second choice of drug) enables approximately 60% of people with epilepsy to become seizure free (Brodie & Schachter, 2001). (See Table 6 for indications of use and side effects for the main AEDs.)

Non compliance in AED treatment is prevalent and problematic with up to one third of patients occasionally not taking their medication (Buck, Jacoby, Baker, Chadwick, 1997). To overcome such issues clinicians need to make sure that patients fully understand the long term benefits of AED treatment. Medial temporal lobe epilepsy (MTLE) is the most common type of epilepsy and presents the most difficulty in relation to drug therapy (Kent et al, 2006), surgery may be a consideration in such cases of refractory epilepsy.



**Table 6. Main antiepileptic drugs, indications for use and common side-effects (adapted from Chadwick and Usiskin, 1987; BMA, 1997).**

Generic Name	Trade Name	Indications for use	Adverse Effects
Carbamazepine	Tegratol /Tegratol retard	Simple and complex partial, primary or 2nd generalised tonic-clonic.	Dose-related: dizziness, double vision, ataxia, drowsiness, unsteadiness, nausea, and vomiting
Clobazam	Frisium	Occasional use: tonic-clonic and partial seizures	Dose-related: drowsiness and sedation
Clonazepam	Rivotol	Status epilepticus	Dose-related: sedation, ataxia, behavioural problems and psychosis, inflammation of veins if given intravenously
Diazepam	Valium/ Diazemulus/ Stesolid	Status epilepticus	Dose-related: sedation
Ethosuximide	Zarontin/ Emeside	Atypical and typical absence	Dose-related: nausea, drowsiness, dizziness, unsteadiness, may exacerbate tonic-clonic seizures. Allergic rashes. anorexia, behavioural changes.
Felbamate	Felbatol	Partial with and without 2nd generalisation; primary generalised, tonic clonic; atypical absences; atonic seizures.	Anorexia, nausea, insomnia, headache, dizziness, fatigue and weight loss.
Gabapentin	Neurontin	Partial with or without secondary generalisation	Fatigue, somnolence, dizziness and ataxia.

Phenobarbitone	Prominal/ Liminal/ Garenal	Effective in: primary and 2nd generalised tonic-clonic and partial seizures	Dose-related: drowsiness, unsteadiness. Allergic: rashes. Chronic toxicity: tolerance habituation, withdrawal seizures, adverse effects on cognitive functioning.
Phenytoin	Epanutin	Primary and 2nd generalised tonic-clonic, simple and complex partial seizures	Dose-related: drowsiness, unsteadiness, slurred speech, occasionally abnormal movement disorders. Allergic: rashes, swelling of lymph glands, hepatitis. Chronic toxicity: gum swelling, acne, coarsening of facial features, hirsutism, folate deficiency.
Primidone	Mysoline	Primary and 2nd generalised tonic-clonic and partial seizures	Dose-related: drowsiness, unsteadiness. Allergic: rashes. Chronic toxicity: tolerance, habituation, withdrawal seizures, adverse effects on cognitive functioning.
Sodium Valporate	Epilim/ Epilim Chrono	All idiopathic generalised epilepsies. Effective in partial, primary and 2nd generalised tonic clonic, typical absence, atonic and myoclonic seizures	Dose-related: tremor, irritability, restlessness, occasional confusion. Allergic: gastric intolerance, liver damage. Chronic toxicity: weight gain, and hair loss.
Topiramate (TPM)	Topamax	Partial and 2 <sup>nd</sup> generalised seizures	Somnolence, fatigue, psychomotor slowing, difficulty with concentration, confusion and paresthesias.
Lamotrigine (LTG)	Lamictal	Partial and generalised seizures	Rash, headache, blood dyscrasia, ataxia, asthenia, diplopia, nausea, vomiting.



### **2.7.2 Surgery**

Intractable (also referred to as refractory) epilepsy is prevalent in 20-40% of people diagnosed with epilepsy despite the use of appropriate drug therapy (Oxbury, 2000).

Intractable epilepsy is defined as:

‘a continuation of seizures beyond two years despite treatment with three of phenobarbital, phenytoin, carbamazapine, sodium valproate or lamotrigine taken at ‘optimal’ doses either individually or in combination’ (Oxbury, 2000, p. 475).

Surgery is an option for those with intractable epilepsy. The most successful surgery outcome is reported when the seizure foci is localised to the anterior temporal lobe and MRI confirms medial temporal sclerosis (MTS), with 70-80% of patients experiencing a reduction in seizures (Brodie & Schachter, 2001). The degree of surgical success is greatly reduced where PWE have frontal lobe foci, with only 30-40% of patients experiencing a marked reduction in seizures (Brodie & Schachter, 2001). Procedures can be functional, such as disconnecting the corpus callosum (although this procedure is rarely carried out in practice now). This does not cure the epilepsy but will prevent the spread of seizures from one hemisphere to the other (Baker & Gorry, 2001) see Table 7. Procedures can also be resective (such as temporal lobe resections e.g amygdalohippocampectomy) which are intended to be curative because they remove the epileptogenic focus (Baker & Gorry, 2001). Given the epileptogenic seizure foci, the impact that surgery will have on the person’s quality of life must be clearly established before surgery is considered. To determine epileptic focus various methods



are used such as EEG, MRI, and videotelemetry. It is especially important to establish the functional capacity of the hemisphere where the resection will take place. This is measured with the use of baseline neuropsychological evaluation (tests of memory and intellectual functioning) and by sodium amytal (WADA) testing (Baker & Gorry, 2001). During the Wada test one hemisphere is anaesthetised at a time to determine lateralisation of speech and mneumonic function. Neuropsychological assessment attempts to establish seizure focus by making inferences based on the performance of PWE on certain neuropsychological tests, thereby mapping structure with function. The success of surgery has increased over time due to developments in pre-surgical assessment and surgical techniques (Smith, Chadwick, Baker, Davis & Dewey, 1993). This is in the most part due to advances in the technology used in the diagnosis of patients (Saunder, Hart, Johnson & Shorvon, 1990).

*Table 7: Types of epilepsy surgery and their indications, taken from Brodie & Schachter, 2001.*

Procedure	Indication
Focal resection	Partial-onset seizures arising from respectable cortex
Corpus callosotomy	Tonic, tonic or tonic-clonic seizures with falling and injury, large non-resectable lesions, or secondary bilateral synchrony.
Hemispherectomy	Rasmussen’s syndrome or other unilateral hemisphere pathology in association with functionally impaired contralateral hand
Subpial transections	Partial-onset seizures arising from unresectable cortex

## ***2.8 Side effects and cognitive dysfunction related to AEDs***

AEDs have undesirable physical and cognitive side effects, some of which have been outlined in relation to dose in Table 6. Chadwick (1994) classified four different types of toxicity in relation to AEDs, acute dose related toxicity, acute idiosyncratic toxicity, chronic toxicity and teratogenicity. Acute dose related toxicity is non specific encephalopathy in relation to high blood concentrations. This is characterised by sedation and nystagmus (involuntary eye movement) and as blood concentration levels increase; ataxia, dysarthria (motor speech disorder) and eventually confusion and drowsiness. Acute idiosyncratic toxicity is rare and unpredictable and can result in allergic skin reactions which may or may not be accompanied by fever and in extreme cases Steven-Johnson syndrome (serious skin condition which can be life threatening) and acute liver failure. If such reactions occur the AED will be withdrawn with immediate effect. Chronic toxicity can impact on any system such as the nervous system, skin, liver, blood, immune system, endocrine system, bone, connective tissue and can cause complications during pregnancy. Teratogenicity relates to the impact of taking AEDs whilst pregnant which can result in congenital malformations and dysmorphia (psychiatric condition involving obsessive body dissatisfaction).

Baker, Buck, Spalgis and Monnet (1997) conducted a European study investigating the side effects of AEDs in over five thousand people with epilepsy and found that only 12% of respondents reported being free of side effects. The most commonly reported effects were memory problems, fatigue, problems concentrating, sleepiness, nervousness, agitation and difficulty in thinking clearly. In a large community study in



America, Fisher et al. (2000) found that one in five PWE stated that the side effects of AEDs and their cost was the worst thing about having epilepsy.

All of the major AEDs have been associated with cognitive impairment which for the majority of AEDs has been regarded as mild to moderate (Aldenkamp, 2001). Children and the elderly are particularly susceptible to the adverse effects that AEDs can have on cognition (Aldenkamp & Baker, 2001; Hirsch, Schmitz & Carreño, 2003). The impact that cognitive impairment can have may vary according to age because particular functions may be important to the individual at different times of life.

Aldenkamp (2001) emphasises the importance of learning in children, driving ability in adults (where reaction time and processing speed may be paramount to safety) and where impairments can impact on functions that may already be weak (such as memory in the elderly). When assessing cognitive impairment in relation to AED treatment it is important to note that a number of epilepsy related variables may also be impacting on cognitive functioning. These include seizure type, aetiology, frequency of seizures, age of onset, brain lesions and psychosocial factors (Hessen, Lossuis, Reinvang & Gjerstad, 2006).

Certain cognitive functions are particularly sensitive to AED use such as information processing speed, memory, attention, motor fluency and reaction time, (Aldenkamp et al, 1993; Gallassi et al, 1992; Hessen, et al., 2006; Meador et al, 1991, 1993; Thompson, Huppert & Trimble, 1980; Thompson & Trimble, 1981). Memory dysfunction is the most commonly reported side effect of epilepsy and taking AED's (Baker, Nashef & van Hout, 1997; Motamedi & Meador, 2004; Thompson & Corcoran, 1992).



In the last 30 years 100 studies have investigated the impact of AED therapy on cognitive function (Hessen et al., 2006). Despite a plethora of research in the area, the magnitude of cognitive dysfunction and how this differs across different AED's is not well established. Hessen et al. (2006) attribute this to a number of methodological flaws. Differences in selection methods for participant recruitment, choice of test instruments, reporting of results, and test administration have made it difficult to conduct a proper evaluation of findings across studies. Small sample sizes have reduced the statistical power of findings, many studies have not recruited suitable control groups or randomised the effect of treatment. Assessing the effects of a specific AED are compounded by using participants on polytherapy, the only way to overcome this would be to use a randomised, double blind, placebo controlled withdrawal study of seizure-free participants on monotherapy who are tested after several months of stable treatment (Hessen et al., 2006). Hessen et al. (2006) did exactly this and tested 150 participants who had been free of seizures for 2 years or more, they concluded that discontinuation of AED therapy would enhance cognitive performance in patients receiving monotherapy, particularly where complex cognitive processing under time pressure was required, as in tasks requiring divided attention, rapid language processing and form discrimination.

Aldenkamp (2001) reviewed studies that had assessed the cognitive sequelae associated with particular AEDs. The review focussed on the most commonly prescribed AEDs at the time; phenobarbitone, phenytoin, carbamazepine and valproate (see Table 8 for a summary of the review).

The impact of AEDs on cognitive functioning must be considered when assessing patient performance on psychological tests. While it is clear that this presents a potential confound in the research conducted as part of this thesis, the potential for this is lessened by the fact that no AED in the present sample was overrepresented in any one experimental group (see Table 15 Chapter 6).

*Table 8: Absolute cognitive side effects of established AEDs (taken from Aldenkamp, 2001).*

Type of AED	Type of impairment	No. subjects
<b>Phenobarbitone</b> MacLeod et al., 1978	Short term memory	19 (e)
<b>Phenytoin</b> Smith & Lowrey, 1975 Thompson et al.,1980 Thompson et al.,1981 Meador et al., 1991 Meador et al., 1993	Memory/mental speed Memory Memory/attention/mental speed Attention/mental speed Impairment of memory	10 (nv) 8 (nv) 8 (nv) 21 (nv) 15 (nv)
<b>Carbamazaine</b> Thompson et al.,1980 Meador et al., 1991 Meador et al., 1993 Aldenkamp et al., 1993	No impairment Mental speed/attention Impairment of memory No impairment	8 (nv) 21 (nv) 15 (nv) 56 (e)
<b>Valproate</b> Thompson & Trimble, 1981 Craig & Tallis, 1994 Prevey et al., 1996 Aldenkamp et al., 1993	Mental speed No impairment Mild psychomotor slowing Psychomotor slowing	10 (nv) 12 (e) 18 (e) 17 (e)

e, epilepsy; nv, volunteers.

## ***2.9 Chapter Summary***

Historical misconceptions of epilepsy have lead to many of the psychosocial problems that people with epilepsy experience and primarily the impact that stigma induces (this will be discussed in more detail in Chapter 3). Despite educational efforts, stigma and myths surrounding epilepsy are still prevalent in today's society (Baxendale & O'Toole, 2007).

Seizures can be caused by cerebral pathology or systemic disturbances but a diagnosis of epilepsy is not considered until two or more unprovoked seizures are evident. Diagnosing epilepsy has three important stages where the clinician must identify seizure type, epilepsy syndrome and if possible the underlying aetiology. Seizure type can be classified under two main categories depending on whether the seizures are localised (partial) or generalised. Epilepsy syndromes determine whether there is a distinguishable underlying cause (symptomatic) or not (cryptogenic or idiopathic) and underlying aetiology is investigated via the use of brain imaging techniques and thorough neuropsychological evaluation. The most common form of treatment is anti epileptic drug therapy which aims to control seizures whilst minimising unwanted physical and cognitive side effects. The most commonly reported side effect of AED treatment is memory deficits. Problems with attention and speed of information processing are also commonly cited, although for most AEDs, cognitive impairment is deemed to be mild or moderate (Aldenkamp, 2001). For those with intractable epilepsy, surgery may be a consideration.



Dodrill (1980) found a more significant impairment on neuropsychological tests in epilepsy patients reporting higher levels of psychosocial problems. The empirical chapters of the thesis will explore the impact that epilepsy has on social cognitive functioning in epilepsy and whether perceived impact of epilepsy on psychosocial functioning is in line with socio cognitive performance. To set this in context, Chapter 3 will focus on discussing psychosocial and cognitive functioning in epilepsy.

## **Chapter 3: Epilepsy, Psychosocial and Cognitive Functioning**

### ***Chapter outline***

This chapter will provide an overview of the psychosocial problems that PWE experience as consequence of epilepsy and its treatment. Psychosocial problems will be discussed in light of how they impact on quality of life. The chapter will discuss the stigma, myths and stereotypes that PWE encounter and the implications of these for important psychological outcomes including anxiety, depression, self esteem, sense of mastery and cognitive dysfunction. The latter part of the chapter will focus on psychosocial factors including social isolation, interpersonal and family relationships and employment. The overall aim of this chapter is to provide the reader with a general overview of the sort of factors that can impede social functioning in PWE.

### ***3.1 Psychosocial impact of epilepsy and its treatment, on quality of life***

PWE have more problems of a social nature than the general population (Austin & de Boer, 1997). The most important determinant of quality of life and psychosocial functioning in people with epilepsy is freedom from seizures, (Jacoby, 1992). This finding is reflected in the psychosocial problems that are evident in people with refractory epilepsy and the improvement in scores on quality of life measures after successful surgery (Baker, Nashef, van Hout, 1997; Baker, Smith, Dewey, Jacoby & Chadwick, 1993; Malmgren, Sullivan, Ekstedt, Kullberg & Kumlien, 1997; Vickrey et al., 1992). It is important to note that studies which assess psychosocial functioning in PWE often focus on clinical samples who may have refractory epilepsy so the precise

nature of psychosocial functioning in all PWE is difficult to gauge (Austin & de Boer, 1997). Factors that have been associated with an increased risk of social dysfunction include, severe and frequent seizures, a chronic form of the condition, the comorbid presence of other conditions, educational underachievement, negative attitudes towards epilepsy and a lack of family support (Austin & de Boer, 1997).

The psychosocial problems that are faced by the person with epilepsy particularly in relation to employment and relationships are not always a consequence of seizure activity but more often the result of discrimination and misconceptions about the disorder (ILAE, 2003a). People with epilepsy live under the ‘sword of Damocles’, never knowing when and where a seizure may occur, whether they may lose consciousness without warning and if ultimately their seizures can be controlled. This uncertainty can render the individual with vulnerability in social situations. PWE have stated that uncertainty and fear of having a seizure are the worst things about having the epilepsy (Fisher et al., 2000).

Whilst to some degree all chronic medical conditions will influence a person’s quality of life, the impact may be particularly apparent in the person with epilepsy (ILAE, 2003f). Children with epilepsy have been found to have more social problems than children with other chronic disorders such as diabetes or bronchial asthma (Aper et al., 1991; Austin, Smith, Risinger, McNelis, 1994; Matthews, Barabas, Ferrari, 1982). The uncertainty associated with epilepsy and the social stigma of having the disorder have obvious consequences for the quality of life of PWE (ILAE, 2003f). Psychosocial difficulties experienced by PWE have been found to exist across cultures, with reduced quality of life reported in Canada, and with lower school attendance and performance



in the Netherlands. In China PWE have encountered difficulties in finding a partner (due to negative family attitudes about having the disorder). Elsewhere, in countries as diverse as Ecuador, Ethiopia and Kenya, PWE have experienced social isolation and exclusion, as well as difficulties in finding employment and in maintaining intimate and family relationships (ILAE/IBE/WHO, 1999; Wiebe, Bellhouse, Fallahy & Eliasziw, 1999)

The issues that will be discussed in the present chapter concern the impact of psychosocial factors on the quality of life of PWE. These are eloquently summarised in a quotation from Billod (cited in ILAE, 2003a, p.12):

‘The epileptic is avoided, on all faces he reads his sentence to isolation. Everywhere he goes, menacing and insurmountable obstacles arise to his obtaining a position, to his establishing himself, to his relationships and to his very livelihood; he has to say goodbye to his dreams of success, for the masters even refuse him work in their shops; goodbye to his dreams of marriage and fatherhood, goodbye to the joys of the domestic hearth. This is death to the spirit’

### ***3.1.1 Myths, Stereotypes and Stigma***

Myths, misconceptions and stereotypes in relation to epilepsy find their origins in how epilepsy has been portrayed and documented throughout history (refer to section 2.1). These have served to create and propagate the stigma that surrounds epilepsy.

Current myths and misconceptions about epilepsy are still prevalent in society, particularly in individuals who do not know someone with epilepsy, (Baxendale & O'Toole, 2007). As ILAE (2003a) highlights, despite attempts to educate people in relation to epilepsy the media often contribute to the problem by 'disseminating inaccurate information' (p.13). In particular television and cinematic portrayal of characters with epilepsy have worked to 'perpetuate many of the ancient myths surrounding the condition' (Baxendale & O'Toole, 2007, p.192.). Baxendale and O'Toole (2007) argue that characters are often depicted as dangerous, possessed by demons and insane, who may foam at the mouth and become violent during a seizure. People with epilepsy are seen as requiring immediate medical assistance to stop seizures and putting something in the mouth of someone during a seizure is believed to prevent them from swallowing their tongue.

As well as reinforcing negative stereotypes Baxendale and O'Toole (2007) argue that misrepresentations of epilepsy misguide the public to the best course of action to treat a seizure if they witness one. This in turn may leave epilepsy sufferers at risk if they have a seizure in public (such as misguided well-wishers putting something in their mouth). Baxendale and O'Toole (2007) found that one in three of the 4605 members of the general public they surveyed would attempt this course of action if they saw someone having a seizure. Long, Reeves, Moore, Roach & Pickering (2000) report a higher percentage with 41% of their sample reporting that this course of action was appropriate, such misconceptions regarding first aid are perpetuated by misrepresentation in the media (Krauss, Gondek, Krumholz, Paul and Shen, 2000).



Krauss et al. (2000) studied English print media stories about epilepsy between 1991 and 1996. Thirty-one percent of the stories presented were inaccurate in some way, 14% contained scientific inaccuracies, 9% exaggerated the benefits of treatment and 5% exaggerated the risks associated with seizures. Many stories reinforced historical misrepresentations of epilepsy by associating it with demonic possession and divine intervention. Clearly misunderstanding about the nature of epilepsy and how to help someone when they have a seizure may impact on self perceptions of PWE in society and in turn how society perceives PWE. Misperceptions within society may lead to prejudice, discrimination and stigma towards PWE and consequently PWE may be more socially isolated, feel more stigmatised and have reduced self esteem.

Scambler (1989) distinguishes between two different types of stigma that are prevalent in PWE. These are 'enacted' stigma where PWE are discriminated against and 'felt' stigma where the person with epilepsy is fearful of exposure to 'enacted stigma'. There is often a disparity between actual enacted stigma and felt stigma in PWE (ILAEE employment, 2003) where felt stigma is more apparent than enacted stigma (Jacoby, 1994). The manner in which the individual perceives stigma is a very subjective process and varies greatly across PWE. Factors such as personality, the effectiveness with which the individual copes with the condition, years of education, perceived discrimination in gaining and retaining employment and the restrictions PWE feel as a consequence of having the condition, all potentially impact on felt stigma (Lee, Yoo & Lee, 2005; Ryan, Kempner, & Emlen, 1980).

There are a number of clinical features of epilepsy that can impact on feelings of stigma and psychosocial sequelae. Seizure type can have a very influential impact on



the psychosocial consequences of epilepsy such that tonic clonic seizures due to their dramatic nature can potentially be more stigmatising (Jacoby et al., 1996). Seizures that are not well controlled have been associated with increased feelings of stigma (Baker, Brooks, Buck & Jacoby). Jacoby et al. (1996) found that 62% of PWE experiencing frequent seizures reported feeling stigmatised by their disorder. The equivalent percentages were 40% for those who had seizures less often than once a month and 25% for PWE in remission. Jacoby et al (1996) also found that perceived stigma was significantly affected by current seizure activity, age at onset, current age and duration of epilepsy. Age of onset explained variation in scores on perceived stigma. Felt stigma in PWE was also evident in a large European cross cultural study by Baker, Brooks, Buck & Jacoby (2000) which found that 51% of a sample of over 5000 PWE felt stigmatised by having epilepsy. The strongest predictor of felt stigma in this study was perceived impact of epilepsy as measured by the Impact of Epilepsy Scale (Jacoby, Baker, Smith, Dewey & Chadwick, 1993) (this measure is used in Study 4 of the thesis). Age of onset, country of origin, the risk of injury as a result of having epilepsy and feelings about life also significantly affected stigma scores. There were cross cultural differences in the perceived impact of epilepsy and felt stigma which the authors argue may highlight a disparity in the experiences of PWE in different countries and cultures. In a further review of the literature, Smeets, van Lierop, Vanhoutvin, Aldenkamp and Nijhuis (2007) concluded that stigma (both felt and enacted) had a negative influence in gaining and retaining employment.

Stigma has a wide impact on the psychosocial functioning in PWE affecting interpersonal relationships, employability, health and quality of life in general (Morrell, 2002). The presence of stigma in PWE is multifactorial. The ability of

parents to cope with the diagnosis and the extent to which they are overprotective of young PWE, may cause increased feelings of stigma in the child (Goodyer, 1988; Scambler and Hopkins, 1986), and may well have longer term consequences for the child's self esteem in later life (McCollum, 1981).

Stigma contributes greatly to the burden endured by PWE and is often the reason why PWE conceal their disorder (Morrell, 2002). Stigma leads to discrimination and PWE have been exposed to discrimination and prejudicial behaviour over many centuries and in many countries (de Boer et al., 2008). 'The history of epilepsy can be summarised as 4000 years of ignorance, superstition and stigma, followed by 100 years of knowledge, superstition and stigma' (Kale, 1997, p.2). Such prejudicial behaviour is still prevalent within society. A recent study by Jacoby and Jacoby (2005) found that 36% of PWE were refused one or more types of insurance in the UK. Such discrimination deprives PWE of the right to adequately provide for themselves and their family in the event of a problem. This in turn can undermine self-esteem and adversely affect relationships.

In one study which assessed 445 PWE, the perception of felt stigma was dependent on whether the individual experienced limitations in their everyday life or had suffered discrimination at work (Ryan, Kempner & Emlen, 1980). The number of years in school was negatively correlated with felt stigma in this study indicating that increased education in someway lessens felt stigma.



Chaplin et al. (1992) found that the psychosocial consequences of epilepsy are most closely linked to the severity of the disorder in the early stages of diagnosis and Morrell (2002) argues that effective medical intervention at this time will work to reduced perceived stigma in the individual. Recent studies demonstrate that there has been an improvement in public attitudes towards PWE and views have become less stigmatised (Jacoby, Gorry, Gamble & Baker, 2004; Jacoby, Gorry & Baker, 2005; Jacoby, Snape & Baker, 2005;).

### ***3.2 Psychopathology, Anxiety and Depression***

PWE are at greater risk of psychopathology, anxiety, depression and suicide than the general population and they are also more likely to be socially dysfunctional than those without the condition (Jacoby et al., 1996; ILAE, 2003c; Mensah et al., 2007; Pompili, Giradi, Rupeto, & Tatarelli, 2005; Pompili, Giradi & Tatarelli, 2006). Depression and suicide are 4-5 times more prevalent in PWE than the general population (Brodie & Schachter, 2001). Anxiety and depression often coexist in the general population (Mensah et al., 2007) and this is especially the case in PWE. Anxiety and depression are the most prevalent psychiatric features in epilepsy, with anxiety being the most frequently reported psychiatric problem (Arnston, Drodge, Norton, & Murray, 1986; Betts, 1981; Collings, 1990; Jacoby et al., 1996). As PWE are living with a chronic condition they may be more prone to feel demoralised and consequently may have a more pessimistic outlook on life which can in turn impact on affect and mood. Psychiatric and psychological disorders are under diagnosed and treated in PWE (de Boer et al., 2008).



Clinical features of epilepsy that have been found to impact on psychopathology include seizure frequency, age of onset, seizure type, duration of epilepsy and aetiology (Jacoby et al., 1996). Jacoby et al. (1996) examined the impact of these variables in an unselected population of PWE in the UK. Increased seizure activity was significantly related to anxiety and depression. Longer duration of epilepsy and older age of onset were also significantly correlated with depression. Jacoby et al. (1996) suggest that the age of onset effect may be attributable to the need to adapt to the condition and the implications it may have on employment prospects and the ability of the PWE to provide for their family. Research has suggested that parental over protectiveness may in part facilitate psychopathology in children with epilepsy (Ferrari, Matthews & Barabas, 1983).

A diminished sense of mastery is a core feature of epilepsy which can mediate feelings of anxiety and depression (Brier, Fuchs & Brookshire, 1998; Hermann & Wyler, 1989; Salgado & Souza, 2001). Because of their unpredictable nature, seizures engender an external locus of control since PWE feel that they have little in the way of control over their life and this can serve to perpetuate and intensify feelings of anxiety and depression (de Souza & Salgado, 2006). Table 9 summarises some of the psychiatric difficulties that PWE display and how they are more prevalent than in the general population.

**Table 9: Rates of prevalence of some psychiatric disorders in patients with epilepsy as compared with those in the general population (taken from de Boer et al., 2008).**

	Patients with Epilepsy	General Population
Depression	11-60%	Dysthymia 3.3% Major depression 4.9-17%
Psychosis	2-9%	Schizophrenia 1% Schizophrenia disorder 0.2%
ADHD	12-37%	4-12%
General anxiety disorder	15-25%	5-7%
Social phobia	15-20%	10-12%
Panic disorder	2-21%	0.5-3%

**3.2.1 Anxiety**

How anxiety manifests itself and how it is related to epilepsy is summarised in figure

4. Increased feelings of anxiety in PWE can be manifested in a number of ways.

Anxiety may be present prior to and during seizures activity, fear of having a seizure may induce feelings of anxiety (Mittan & Locke, 1982) and the stigma associated with having epilepsy may make PWE more anxious (Arnston et al., 1986). PWE may develop agoraphobia and social phobia due to the unpredictability of seizures and the possibility that they may occur at any time, in awkward places and in difficult circumstances (Thompson, 2000).

Anxiety has been associated with a number of epilepsy related factors, such as earlier age of onset, poor seizure control, presence of side effects of AEDs and increased seizure activity and seizure severity (Mensah, et al., 2007; Smith, Baker, Dewey, Jacoby & Chadwick, 1991; Jacoby, et al., 1996). Seizure severity was the most

significant predictor of anxiety in a study which assessed quality of life in patients with refractory partial seizures (Smith et al., 1991).

As well as epilepsy related factors psychosocial factors play an important part in mediating anxiety in PWE. Vasquez and Devinsky (2003) argue that anxiety may be a consequence of the unpredictability of epilepsy, restricted social activities, low self esteem, stigma and rejection from society

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As an ictal phenomenon (i.e. anxiety as seizure or seizure component):

- (i) As a simple partial seizure alone,
  - (ii) As an aura component of a complex partial seizure
  - As an anticipatory fear associated with an aura heralding a seizure;
  - As an anticipatory fear of having a seizure without premonitory warning;
  - As a secondary neuropsychiatric after-effect of seizure, i.e., a postictal event;
  - As an interictal manifestation of the same underlying aetiological mechanism as the primary seizure disorder;
  - As an adverse consequence of antiepileptic treatment;
  - As an adverse consequence of intrapsychic maladaptation to having epilepsy;
  - As an adverse consequence of social maladaptation to having epilepsy;
  - As an unrelated comorbid primary psychiatric disorder.
- 

*Fig. 4. The association between epilepsy and anxiety (taken from Goldstein & Harden, 2000).*



### **3.2.2 Depression**

The existence of a relationship between epilepsy and depression has been documented since antiquity. As Goldstein and Harden (2000) highlight, recognition of this relationship has been noted before 2000BC in Indian Ayurvedic writing. In an early review of evolving historical perspectives Lewis (1934, cited in Goldstein & Harden, p.228.) cites a quote from Hippocrates' writing:

'Melancholics ordinarily become epileptics, and epileptics melancholics: of these two states what determines direction is the direction the malady takes; if it bears upon the body, epilepsy, if upon the intelligence, melancholy'

How depression manifests itself and how it is related to epilepsy is summarised in figure 5. The symptoms of depression are apparent in 40-60% of PWE (Grabowska-Grzyb et al., 2006). A number of epilepsy related factors have been associated with depression. Having focal epilepsy has been associated with depression (Forsgren & Nystrom, 1999) and Grabowska-Grzyb et al. (2006) found that having complex partial seizures was also positively correlated with the experience of depression. These authors also found that depression was more common in people with TLE with a focus in the dominant hemisphere. This may be particularly apparent in people with mesial temporal sclerosis (Quiske, Helmstaedter, Lux & Elger, 2000). High seizure frequency and refractory epilepsy have been shown to be associated with feelings of depression as have certain types of AED (Kanner & Balanov, 2002; Schmitz, Robertson & Trimble, 1999; Mendez, Cummins & Benson, 1986). The nature of the relationship between epilepsy and depression may be bi-directional such that history of depression

is often much more common in people who later have a seizure (Forsgren & Nystrom, 1999; Hesdorffer, Ludvigson, Hauser & Olafsson, 1989).

Some of the psychosocial factors that mediate depression in PWE are the patient's ability to adjust to the diagnosis, the experience of stigma and discrimination, feelings of uncertainty and a lack of control due to the unpredictable nature of seizures and a lack of social support (Chaplin, Yepez, Shorvon & Floyd, 1990; Dell, 1986; Jacoby, 1994; Hermann & Whitman, 1989; Mungas, 1982; Scambler, 1987).

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1. Depressive reaction to acquiring the label of epilepsy
  2. Depressive reaction to social or family problems of epilepsy
  3. Prodromal depressive feelings before a seizure
  4. Depressive feelings as an aura
  5. Depressive feelings as an ictal state
  6. Postictal depressive feelings
  7. Depressive twilight state
  8. Epileptic depressive delirium
  9. Endogenous depression unrelated directly to seizures, but possibly to their increase in frequency
  10. Depressive symptoms occurring in association with other mental illnesses, particularly a paranoid or schizophrenic psychosis.
- 

*Fig. 5. The association between epilepsy and depression (taken from Betts, 1981).*

### ***3.3 Self-esteem, sense of mastery and self efficacy***

Clinical features such as seizure severity have been identified as the most significant predictor of self esteem and locus of control in a study which assessed quality of life in



patients with refractory partial seizures (Smith et al., 1991). Baker, Spector, McGrath and Soteriou (2005) found that seizure frequency was negatively related to self esteem in adolescents. Those who reported higher levels of knowledge about epilepsy also reported higher levels of self esteem, which may have important implications for treatment intervention.

Poor self esteem has been found to be prevalent in PWE in a number of studies (Collings, 1990; Fisher et al., 2000; Jacoby et al., 1996; Levin, Banks & Berg, 1988) and appears to be a common feature of the disorder. Clearly the prevalence of poor self esteem among PWE has important implications for psychosocial functioning. Collings (1990) conducted a study in the UK and Ireland on 392 PWE and found that these individuals felt that they would have higher self esteem if they did not have epilepsy. PWE rated their behaviours as significantly more unpredictable, handicapped, lacking in maturity, and adaptability. They perceived themselves as lacking in value, and dependability, less stable, and less able to cope with life. These PWE also saw themselves as unsuccessful, less well adjusted and less happy compared to healthy volunteers. Employment also has an important influence on self esteem. For example, unemployed PWE have lower self esteem than those that are employed (Chaplin, 2005; Lee, 2005; Jahoda, 1982).

Baker et al. (1993) found a relationship between anxiety, depression and sense of mastery scores in relation to self esteem. People who had low self esteem scored higher on the anxiety and depression elements of the HADS and lower on the sense of mastery measure. Parental over protectiveness may reduce feelings of autonomy and independence such that PWE feel a reduced sense of control in their life (McCollum,



1981). Increasing knowledge about epilepsy through educational programmes has been successful in increasing self esteem (Snead et al., 2004). Individual and family counselling may also help to increase feelings of self esteem in PWE (Morrell, 2002).

The heightened uncertainty associated epilepsy and its treatment may cause the person with epilepsy to feel that they have little control over their lives and consequently they may experience a reduced sense of mastery. Consistent with this PWE have been found to have a poorer sense of mastery in comparison to normal controls (De Vellis, De Vellis, Wallston & Wallston, 1980).

Poor sense of mastery has been linked to a range of psychological variables in PWE, such as anxiety, low self esteem, an increased likelihood of committing suicide and feelings of helplessness (Arnston et al., 1986; Baker et al., 1993; Matthews and Barabas, 1981).

Schachter (2005) argues that self mastery may be influential in reducing the impact of stigma and improving compliance to medication regimes. He cites a study by Dilorio et al. (2004) in which self efficacy and patient satisfaction accounted for most of the variance in managing medication in a study of PWE.

### ***3.4 Cognitive dysfunction related to epilepsy***

One of the most debilitating aspects of being diagnosed with epilepsy is the impact that recurrent seizures can have on cognitive functioning and daily life. In a study by Fisher et al. (2000) PWE ranked cognitive impairment one of the biggest problems with

having the disorder. Common cognitive deficits in people with epilepsy are intellectual decline, reduced information processing speed, reduced reaction time, attentional deficits and memory impairments (Aldenkamp, Dreifuss & Renier, 1995; Corcoran & Thompson, 1993; Helmstaedter, Kurthen, Lux, Reuber, & Elger, 2003; Moore & Baker, 2002).

Memory is the most frequently reported problem in PWE (Thompson & Corcoran, 1992; Corcoran & Thompson, 1993) and deficits ‘can range from poor concentration and minor forgetfulness to gross clouding of consciousness and disorientation’ (de Boer et al., 2008, p.542.). People with TLE and especially MTLE are particularly vulnerable to memory deficits. Such deficits appear to be most apparent in those who have had epilepsy for a longer duration (Hendriks, Aldenkamp, van der Vlugt, Alpherts & Vermeulen, 2002).

Up to a quarter of PWE have learning disabilities and a half of people with learning difficulties have epilepsy (de Boer et al., 2008). Learning can be heavily affected because seizures can effect the individual’s level of alertness as well as the short term storage of information. Nocturnal seizures may well interrupt sleep and interfere with the consolidation of memory (de Boer et al., 2008). Such difficulties can clearly have an impact on educational progress and academic attainment.

For the majority of seizure types, Aldenkamp and Bodde (2005) emphasise that cognitive impairment arising from seizure activity can be reduced or reversed by effective seizure control. Therefore early detection of the cognitive consequences of seizure activity and effective seizure control are paramount in preventing long term



cognitive dysfunction (Aldenkamp & Arends, 2004; Kent et al., 2006). This may be especially relevant to children with epilepsy, where the negative impact of seizures on cognitive functioning may accumulate overtime (Aldenkamp & Arends, 2004). Early detection may be especially problematic for those with non convulsive seizures that may go undetected.

Many seizure related variables can impact on cognitive functioning, these include seizure type, seizure frequency, the age of onset, aetiology, duration of epilepsy, the type and number of AEDs, interictal EEG discharges and the site of the seizure foci (Jokeit & Schacher, 2004; Oxbury, 2000). The nature of cognitive impairment will vary according to the location of the seizure foci. Of particular relevance to the present thesis are TLE and FLE and the cognitive deficits associated with foci in these regions will now be discussed.

#### ***3.4.1 Differentiating cognitive impairment between FLE and TLE***

Differences in test performance between TLE and FLE are not apparent in all studies and it should be noted that neuropsychological tests have been criticised for not effectively distinguishing between FLE and TLE (Exner et al., 2002).

Upton & Thompson (1996) found that FLE were impaired in relation to TLE on the Stroop task and cost estimation (estimating the price of common objects) but the Wisconsin Card Sort task (WCST) did not reveal any differences between the groups. Similarly Hermann, Wyler and Richey (1988) found that people with TLE made perseverative errors on the task similar to those seen in patients with frontal lobe involvement.



Helmstaedter, Kemper & Elger (1996) compared the cognitive capabilities of people with FLE and TLE. Factor analysis revealed that the test battery tapped four distinct functions, speed and attention for timed tasks, memory span, motor coordination, and response inhibition and maintenance. People with FLE performed significantly worse on tests assessing response inhibition and motor control in comparison to people with TLE. However, Exner et al. (2002) found no differences in performance between FLE and TLE on measures of associative learning, general intelligence, mnemonic functioning, attention and information processing speed. Equally no differences were observed in set shifting, abstract conceptualisation or visuospatial processing of faces. The only difference observed was that FLE were impaired on verbal STM span in relation to TLE. Exner et al. (2002) highlight that test performance should be interpreted with caution when trying to differentiate between FLE and TLE especially prior to surgery. This is particularly pertinent to executive tasks such as the WCST. Corcoran and Upton (1993) administered a modified version of the WCST and found that people with hippocampal sclerosis were more impaired on this task in comparison to people with unilateral TLE or FLE (Corcoran & Upton, 1993). They attributed impairment to the heavy working memory requirements of the task and the central role that the hippocampus plays in relation to working memory.

Discriminating cognitive dysfunction between TLE and FLE in neuropsychological testing can be problematic for a number of reasons. Cognitive dysfunction is not just mediated by seizure foci but also the amount of underlying pathology, the propagation pattern of seizures and their frequency. Seizure type is also influential, in that people with MTLE who have secondary generalised seizures are more likely to have general

impairments in functions associated with the prefrontal lobes (Jokeit, Seitz & Markowitsch, 1997). An EEG study has provided evidence that seizures that originate from the MTLE have a tendency to spread to the ipsilateral frontal lobe (Lieb, Dasheiff & Engel, 1991). Therefore such seizures may impact on executive functioning.

Conversely the frontal lobes are the largest part of the cortex and are connected to many other brain regions, therefore seizure propagation which is particularly rapid in FLE (Williamson, 1992) may disrupt cognitive functioning in other cortical regions such as those that may be reliant on the functional integrity of the temporal lobes (Exner et al., 2002).

### ***3.4.2 Temporal Lobe Epilepsy (TLE)***

MTLE is the most common focal epilepsy syndrome, and is characterised by focal seizures that cause epileptogenic mesial (medial) temporal lesions (usually hippocampal sclerosis) which are often resistant to AED therapy (Schacher et al., 2006). MTLE is also typically characterised by an early age of onset and a history of febrile seizures (Helmstaedter, 2001).

The range of cognitive functions that can be compromised in people with repeated MTLE seizures include intelligence, learning, visuo spatial functions, problem solving, memory function and academic attainment (Herman, Seidenberg, Schoenfeld and Davies, 1997; Hermann & Seidenberg, 2002). If the dominant hemisphere is affected then language deficits can also be apparent (Kent et al., 2006). People with TLE report word finding difficulties. For example, Mayeux, Brandt, Rosen and Benson, (1980) found that people with LTLE were impaired in comparison to a RTLE and a generalised epilepsy group. This lateralisation effect has been replicated in a number of



studies (Davies et al., 1994; Ellis, Hiram, Cardno, & Kay, 1991; Hermann & Wyler, 1988; Hermann, Wyler & Somes, 1991; Hermann, Seidenberg, Haltiner & Wyler, 1992; Sass et al., 1992; Saykin et al., 1995). Early age of onset has also been associated with deficits in word finding in TLE (Bell et al., 2001).

Due to the damage and loss of neurons that recurrent seizures cause to the hippocampal system, so it is not surprising that memory dysfunction is one of the most documented deficits in MTLE (Alessio et al., 2006). Deficits are apparent in the immediate recall of short stories in logical memory tasks and in delayed recall in both verbal and non verbal memory tasks (Corcoran & Thompson, 1993; Thompson & Corcoran, 1992). In PWE who complained of memory problems the top five reported daily problems were, finding a word that was on the 'tip of the tongue', losing things, going back to check that that one has done something, forgetting that one was told something or forgetting people's names (Corcoran & Thompson, 1993).

Researchers have also distinguished differences in the type of memory impairment associated with right and left seizure foci. Verbal memory impairments are most often observed in people with MTLE who have a predominant left seizure focus while non verbal or visuospatial impairments are typically found in those with a predominant right seizure focus (Barr et al., 1997; Baxendale et al., 1998; Hermann & Seidenberg, 2002; Hermann, Wyler, Richey & Rea, 1987; Moore & Baker, 1996; Sass et al., 1992; Selwa et al, 1994). Research has also suggested that left hippocampal damage in MTLE may have more detrimental effects on memory function than right hippocampal damage (Baxendale, 1995., Rausch & Babb, 1993). This may be because people with left hippocampal lesions also exhibit more extra-hippocampal damage rendering them more susceptible to cognitive dysfunction (Bonilha et al, 2007). Jokeit, Damen, Zang,



Janszky and Ebner (2001) suggest that seizures in the MTL may disrupt the consolidation of memory and this is why they have such an impact on memory function. Consistent with this proposition Blake, Wroe, Breen and McCarthy (2000) found that people with LTLE had accelerated long term forgetting of verbal material. This impairment may be indicative of the effect that seizures have on the consolidation of new information in the long term (Shulman, 2000).

Cognitive deficits have been found to be more severe in LTLE than RTLE. Moore and Baker (2002) found that people with LTLE were impaired in verbal intelligence, general intelligence, attention span and expressive language in comparison to those with RTLE

Specific demographic variables relevant to epilepsy have also been shown to affect memory. Kent et al. (2006) discovered that the longer the duration of MTLE and the younger the person was when they were diagnosed, the greater the impact on verbal memory. Their findings imply that early seizure control could help to reduce the long term impact that recurrent seizures have on memory function in TLE. Helmstaedter, et al. (2003) did a longitudinal study investigating the long term impact of TLE on memory function in patients who were being treated with AEDs or surgery. They concluded from their findings that memory deficits can cease or improve if seizures are adequately controlled.

The impact that age of seizure onset and duration of MTLE have on memory function have been documented in a number of studies (Alessio et al, 2004., Dikmen, Matthews & Harley, 1975., Lespinet, Bresson, N’Kaoua, Rougier, Claverie, 2002). Higher

seizure frequency has also been another influential demographic factor in relation to memory deterioration (Aldenkamp et al., 1996). The influence of AEDs has already been highlighted in 2.7.1

### ***3.4.3. Frontal Lobe Epilepsy (FLE)***

Generally studies investigating the impact of focal epilepsy on cognition concentrate on TLE. There are few neuropsychological studies that have attempted to assess the behavioural characteristics and the nature of impairment in FLE (Farrant et al., 2005; Helmstaedter et al., 1996; McDonald et al., 2005; Morris & Cowey, 2000; Shulman, 2000). FL seizures are the second most prevalent type of seizure that are subject to surgical intervention and 15% of refractory epilepsy cases are due to FLE (Farrant et al. 2005; Helmstaedter, 2001). Of all patients that undergo surgical treatment for epilepsy, 18% have FLE (Hosking, 2003).

FLE does not impair intellectual functioning per se but removal of epileptogenic tissue in the frontal lobe has improved IQ performance (Milner, 1975). Post operative scores on the WAIS were improved despite large proportions of tissue being removed. This may be indicative of the fact that epileptogenic tissue in the FL can diminish general cognitive functioning (Morris & Cowey, 2000). Indeed Milner suggests that epileptogenic tissue may in fact cause disruption to the functions of other cortical tissue. However, the improvement in post operative scores has also been attributed to the effect of repeat testing (Morris & Cowey, 2000).



In general memory is not impaired in FLE unless the memory task has an executive component such as organising the material to be remembered (Delaney, Rosen, Mattson, Novelly, 1980; Morris & Cowey, 2000).

Deficits in response inhibition as assessed by various forms of the Stroop Task have been evident in FLE (Corcoran & Upton, 1993; Helmstaedter, Gleissner, Zentner & Elger, 1998; Helmstaedter et al., 1996). Such deficits are reflected in people with lesions of the FL (Demakis, 2004; Stuss, Floden, Alexander, Levine, Katz, 2001). McDonald et al. (2005) investigated response inhibition and set shifting in a group of people with FLE, TLE and normal controls by using variations of the Stroop Task. They found that FLE and especially those with LFLE were impaired on response inhibition in comparison to NC. They also found that when they increased the executive demands of the task by testing two or more executive skills (response inhibition and set shifting) at the same time it exacerbated the impairments in FLE patients. However, whether this outcome reflects the increased difficulty of the task as opposed to increased executive demands remains unclear. The authors suggest that LFLE impairment may be particularly apparent due to the role that the left PFC plays in supporting the executive control functions that are required for verbal response inhibition. The TL group and particularly those with left MTS (mesial temporal sclerosis) also exhibited executive dysfunction on the response inhibition/set shifting task which the authors suggest may be mediated by seizure frequency (which was related to errors in the task), propagation of seizures to the FL or the demands of the task on working memory.

The effects of seizure activity in FLE can be diverse due to widespread, bilateral and fast propagation of seizures (Farrant et al., 2005; Helmstaedter et al., 1996; Shulman, 2000). Consequently seizures can cause general cognitive disruption in the prefrontal cortex (Farrant et al., 2005). Morris and Cowey (2000) suggest that people with FLE exhibit mild executive dysfunction in comparison to people with frontal neurosurgical lesions.

### ***3.5 Social Factors***

#### ***3.5.1 Social isolation, interpersonal & family relations***

Social isolation is far more common in PWE (Austin & de Boer, 1997; ILAE, 2003c). Social isolation may well be a consequence of a number of factors, such that PWE may isolate themselves for fear of having a seizure in public, may have reduced opportunities for social interaction with others because of difficulties in gaining and retaining employment and because of parental over protectiveness. Fisher et al. (2000) found that PWE reported fear as the worst thing about having epilepsy, such fears included fear of being involved in a car accident, of having a seizure in public, of embarrassment in public and fear of losing employment. Twenty-four percent of the sample worried about social stigma, fear of the reaction of others to their disorder, shame and loneliness. Clearly such fears may discourage PWE from participating fully in social activities. Mittan (1986) found that fear of injury as a consequence of having a seizure in public was a commonly cited reason for staying at home in a fifth of PWE. Reduced opportunities for social interaction may result in less chance of developing friendships and relationships and this has been reflected in the disparities in marital status in PWE in comparison to controls (Arnston et al. 1986; Collings, 1990).



Baker et al. (2005) measured levels of social anxiety in a group of adolescents with refractory epilepsy in relation to knowledge about having epilepsy. Surprisingly, they found that social anxiety was not related to seizure frequency but directly related to knowledge, such that lower levels of knowledge lead to increased levels of anxiety. Using educational interventions to increase medical knowledge of epilepsy has been successful in improving quality of life (Snead et al., 2004).

Thompson (2000) reports that in a survey of young people with refractory epilepsy the biggest area of dissatisfaction was social isolation and particularly in forming friendships and participating in social activities outside of the family home. Social networks and friendship are important sources for social support and will have a great impact on the individual's ability to cope with having epilepsy and being part of society.

Epilepsy can greatly affect the ability of PWE to develop and continue relationships (Fisher et al, 2000). In a UK study by Jacoby et al. (1996) seizure frequency was associated with marital status, where less people with frequent seizures were married and more reported their status as divorced/separated or single. A distinct trend in the data in relation to time since last seizure was found, as the time since the last seizure increased so did the likelihood that the person with epilepsy would be married or widowed. Age of onset of epilepsy was also an influential factor in explaining marital status where people who were younger at the onset of epilepsy were less likely to marry. Collin, Labiner and Yerby (1998) report that limited social opportunities result in lower birth rates in men and women with epilepsy. Parental over protectiveness may interfere with the development of important life skills and render the child with less

confidence and independence (Austin & de Boer, 1997; Lothman, Pianta & Clarson, 1990).

Epilepsy can have psychosocial consequences for all family members. Stress, marital difficulties, restriction to social life, low self esteem and psychopathology have all been reported within the families of PWE (Ellis, Upton & Thompson, 2000). Family stress, the available support from extended family members, family mastery, being female and seizure frequency were found to be significant predictors of social functioning in children with epilepsy (Austin, Risinger & Beckett, 1992). Clearly the importance of family variables is highlighted in this study, the nature of the relationship is unclear, epilepsy may be causing family stress because of family reactions to the disorder or the child's psychosocial functioning may be a reaction to the family environment. Another factor which may limit participation in social activities and independence, is not being able to drive (Dean & Austin, 1996).

Williams, Steel & Sharp (2003) assessed parental anxiety and its impact on the quality of life of children with epilepsy in two hundred parents. Parental anxiety had a direct relationship with decreased quality of life in children. The authors suggested that respite, social support groups and increased education about the risks associated with seizures and how parental behaviour may impact on the development of the child may alleviate the problem. Thompson and Upton (1992) found that carers of PWE were unhappy with how their role restricted their personal and social life and felt that respite and more social support were needed.

Austin and de Boer (1997) argue that PWE find it very hard to develop friendships. Exactly what facilitates this difficulty is hard to determine. This may be the result of a



number of interrelated factors such as, the attitudes of PWE towards having the disorder (Austin & de Boer, 1997) the attitude of others towards the condition, the reduced social opportunities through employment and being unable to drive, reduced self esteem or social skills. It may well be a consequence of a number of complex interrelated factors.

### ***3.5.2 Education and Employment***

Evidence of underachievement in school children with epilepsy is apparent, in general young people with epilepsy do not fare as well in gaining qualifications as their school age counterparts (Thompson, 2000). One quarter to one half of children with epilepsy have educational difficulties at school (ILAE, 2003d). Epilepsy related variables such as early age of onset, duration, seizure type, nocturnal attacks, high dosage of AEDs and polydrug therapy have been associated with poor educational prognosis. Seizures interfere with how alert the child is and can impair short term memory storage, nocturnal seizures may interfere with consolidation of memory and consequently frequent seizures will impact on the child's ability to learn which may well have implications for educational performance (de Boer et al., 2008). As well as seizure related effects psychosocial aspects of epilepsy have also been implicated. These include teacher parent expectations, misconceptions about the disorder, period of time away from school, low self esteem and increased anxiety as a consequence of a stressful family environment (Thompson, 2000). Fewer PWE graduate from high school in the US (64% of PWE in contrast to the overall national graduation rate of 81.7%) (Fisher et al., 2000).

PWE have been regarded as the most 'difficult chronic health group to place in work' (Chaplin, Wester & Tomson, 1998, p.299). In general underemployment and unemployment are greater for PWE in comparison to the general population and this trend exists world wide (ILAE, 2003a, ILAE, 2003b). A study conducted in the UK by Elwes, Marshall, Beattie & Newman (1991) reported rates of unemployment as high as 46% in people with epilepsy as opposed to 19% in a control group. These disparities have also been reflected in a number of European studies (Bahrs, 1990; Hauser and Hesdorffer, 1990; Reuvekamp et al., 1999). Unemployment rates are especially high for PWE attending a tertiary referral centre and for those who experience at least one complex partial or tonic clonic seizure a year (Hauser & Hesdorffer, 1990; Thorbecke & Fraser, 1997). It seems that PWE are also underemployed and discouraged from reaching their full employment potential because of the perceived limitations of having epilepsy (Chaplin, et al., 1998).

There are multiple interrelated factors that can be attributed to the unemployment and underemployment of people with epilepsy. Factors such as adequate seizure control, stigma, side effects of AEDs, poor self efficacy, social skills deficits, level of education, social isolation, neuropsychological deficits, negative familial attitudes, negative attitudes from teachers, employers and society as a whole have been found to have an impact on unemployment and underemployment in epilepsy (Clarke, et al., 2006; Devinsky et al., 1994; Schultz & Thorbecke, 1985; Seidenberg & Clemmons, 1998; Thorbeck & Fraser, 1997;). Early age of onset has been associated with unemployment in PWE (Chaplin, et al., 1998).



Seizure frequency has been shown to have a strong link with employability where PWE who have frequent seizures are less likely to be employed (Chaplin, et al., 1998; Jacoby et al, 1996; Rätsepp, Õun, Haldre & Kaasik, 2000; Yagi, 1998). Yet PWE in remission are employed at rates which are comparable to the general population (Jacoby, 1995). Seizure type is also a significant factor with those experiencing tonic clonic seizures being less likely to be employed (Jacoby et al., 1996).

Craig and Oxley (1988) argue that it is often common practise to avoid giving a job to a person with epilepsy, this is reflected in the disparity between the number of available jobs for PWE and employers' willingness to knowingly hire them (Hauser & Hedorffer, 1990). Discrimination has also been reflected in a study by Scrambler and Hopkins (1980) where 22% of people with epilepsy lost their jobs after being diagnosed with epilepsy. A recent study by Bautista and Wludyka (2007) found that 40% of a sample of 262 PWE feared discrimination in the workplace because of seizures, this is echoed by the negative attitudes of employers towards employing PWE, (Cooper, 1995).

Stigma is one of the main barriers to employment faced by PWE (Scheid, 2005). Feelings of stigma may impact on self worth and consequently deter people with epilepsy from seeking employment (Clarke et al., 2006). Being employed may also be a significant factor in increasing self worth, as Chaplin (2005) argues 'employment, apart from its economic value to the individual, indicates social acceptance and leads to self-worth' (p.5). Thompson (2000) argues that employment as well as providing financial gain may play an important role in identify and self worth in PWE, it may

also give structure to their day, as often people with refractory epilepsy have no structured daily activity after leaving school.

### ***3.6 Methodological considerations***

PWE are more subject to depression and anxiety so the present thesis excluded participants who had been clinically diagnosed with either condition. AEDs can impact on cognitive functioning, to account for this the number of AEDs that patients are taking have been considered in the analysis of the empirical studies. The longer duration of the epilepsy and the earlier the age of onset of the disorder the more likely the individual is to have accumulated psychosocial difficulties. To take account of this both of these epilepsy-related variables have been considered in the analyses of the thesis. The review on cognitive dysfunction highlights that memory impairments are the most prominent deficit in PWE. Consequently a measure of immediate and delayed recall have been tested on the sample and will be considered in analyses of the data.

It is clear from the literature review in this chapter that PWE have a number of difficulties in relation to social functioning. Along this theme Chapter 5 will review literature that has assessed social cognitive functioning in epilepsy. Advancing knowledge and research in this area may lead to effective treatment interventions which may improve the overall social functioning and degree of integration in of PWE in society.



### ***3.7 Chapter Summary***

This chapter highlights that the impact that epilepsy has on the quality of life of PWE is not simply a consequence of the clinical features of the disorder but a complex interaction of multiple interrelated physical and psychosocial factors. In reviewing the literature in this chapter one recurrent theme was evident: many of the problems that people with epilepsy face are a consequence of other people's attitudes towards them. 'The broad community determines, to a great extent, how disabled an individual will be by his or her seizures disorder' (Morrell, 2002, p.S25). Stereotypes and myths about epilepsy are still prevalent in society and are perpetuated by inaccurate portrayals of epilepsy within the media which only serve to create stigma. Perceived stigma is probably the biggest burden faced by PWE, having consequences for social interaction, the development of relationships and employability. Different individuals may experience the phenomenon to different degrees and past research indicates that seizure severity is the most important epilepsy-related determinant of felt stigma.

PWE are at greater risk of psychopathology, anxiety, depression and suicide than the general public and often the prevalence of psychopathology in epilepsy is under diagnosed and treated. Self esteem, the sense of mastery and self efficacy are all adversely affected in PWE and serve to perpetuate some of the psychosocial difficulties that they experience. Cognitive deficits are commonly reported and memory is the most frequently cited deficit. Recurrent seizures can impact on the ability to learn, to store information and to consolidate memories which may in turn affect educational attainment. There is evidence that PWE underachieve at school in comparison to the general public. Deficits in information processing speed, reaction time, and attentional deficits are also commonly cited cognitive deficits.

Unemployment and under employment in PWE is far more common than in the general population and may not be entirely accounted for by differences in education attainment (Arnston et al, 1986). These factors in turn can adversely affect the PWE's financial status

PWE may have less opportunity for social interaction. They may isolate themselves because of the stigma associated with the condition and for fear of having a seizure in public. They may have reduced opportunities for gaining and retaining employment and have increased feelings of social isolation. Consequently PWE experience difficulties in developing friendships and relationships and this has been reflected in the disparities in marital status compared with the general population. Parental over protectiveness may inhibit the development of important life skills, making the child less autonomous and reducing access to social activities outside the family home.

It is worthy of note that some of the psychosocial difficulties highlighted in this literature review in relation to all PWE may not be wholly representative. The majority of research investigating psychosocial difficulties has been conducted on selected populations of PWE who attend clinics and tertiary referral centres. The impact of epilepsy in these samples may be more pronounced because the severity of the condition in these populations is greater. Therefore it may be that some of the observations set out above cannot be generalised to all PWE.

Despite increasing knowledge about epilepsy it is clear that employers, teachers, family members and society as a whole need to be better educated so as to help reduce misconception, stigma and discrimination thereby enhancing the quality of life of



people with epilepsy. Beyond this, increasing the knowledge that PWE have concerning their condition can improve their ability to manage it and reduce their perceptions of stigma. Engendering positive attitudes and coping strategies and utilising cognitive behavioural techniques in PWE will help combat psychosocial problems and improve quality of life by helping people to adjust and accept their diagnosis. Self help groups and parental support networks may increase social support for the individual and their family and vocational training may help combat issues of employability.

## Chapter 4: Social Cognition

### *Chapter outline*

This chapter will outline what social cognition is and will discuss one important aspect of social cognition namely, theory of mind (ToM). Whilst it is not the purpose of this chapter to provide a comprehensive discussion on theories that have been put forward to account for ToM a brief review of the main theories will be outlined. The chapter will review methods for assessing ToM (in adults) and discuss relevant research in the area of ToM. Much of the research on ToM originated through the study of autism. This research will not be reviewed in detail but reference to research in this area will be made throughout the chapter, where relevant. The neural correlates of ToM will be explored with particular emphasis on the importance of the frontal lobes. A detailed review of relevant lesion studies will follow, as this methodological approach is particularly pertinent to the issues to be addressed in this thesis. A summary of structural and functional imaging studies which have aimed to discover the organic basis of ToM will be included. Whilst a large body of research on theory of mind and social cognition in psychopathology and other neurological disorders now exists, it is not the purpose of this chapter to discuss this research in any depth, though reference to such studies may be made throughout the chapter where appropriate. A detailed discussion of social cognitive deficits in epilepsy will follow in Chapter 5.



#### ***4.1 Social cognition***

Essentially social cognition is concerned with how people process social information and how they use this information in social situations. Social cognitive processing involves the perception and interpretation of social information and the ability to provide an appropriate response to it. Social cognitive neuroscience is a rapidly developing field which is interested in mapping neural structure with function in relation to social cognitive processes. This approach aims to enhance our understanding of the neural correlates that subserve normal social-cognitive abilities.

#### ***4.2 Theory of mind (ToM)***

The ability to comprehend social information and to participate effectively in social interactions is reliant on 'the adequate functioning of a mental mechanism termed theory of mind (ToM)' (Mazza, 2007, p.257). This term was first established by Premack and Woodruff (1978). It is the socio-cognitive ability which normally functioning individuals have and which allows them to effectively infer the thoughts, beliefs and intentions of other people and to appreciate that people's thoughts and behaviour may be based upon beliefs and knowledge that are different from their own. This skill facilitates successful social communication and interaction and the cohesive functioning of individuals in society. ToM skills enable people to interpret their own mental states as well as the mental states of others, consequently one can understand and make predictions about behaviour. ToM is used to understand another person's intention or meaning in social situations where these may not be immediately clear. For example, when someone makes an ironic statement, drops a hint or tells a joke.

The social and communication difficulties experienced in autism, such as the absence of interaction, emotional unresponsiveness, the difficulty in understanding language that is not literal in meaning, impaired social judgement and poor conversational pragmatic skills (Baron-Cohen and Ring, 1994) have all been attributed to ToM impairment. In fact ToM has been proposed to be the core deficit in autism and consequently research in this area has been fundamental for ToM research. The approach typically adopted has involved comparing children with autism and those with normal development in order to develop theories of ToM.

#### ***4.2.1 Theories of theory of mind***

There is general agreement about the definition of what ToM is, but much debate exists as to the theoretical framework that underpins these skills. The alternative theoretical perspectives have conceptually different views concerning the nature of the processes involved in mentalising (another word for ToM) and the neural structures that may be implicated. Some theorists argue that ToM is domain specific while others suggest that it is a domain general skill. Whilst it is the not purpose of this thesis to discuss the different theoretical perspectives in detail or to directly investigate them, it is important to highlight the most prominent theories which have evolved from research in this area. Most disagreement in the field arises as a result of whether ToM is a modular skill or not.

#### ***4.2.2 ToM as a modular skill***

ToM has been most thoroughly explored in the field of developmental psychology



where it has been identified as a fundamental deficit in autistic children who fail to develop the skill. Many developmental psychologists consider ToM to be a modular skill of the central nervous system (Leslie, 1987). Modular theorists argue that mentalising is innate and functionally dissociated from other cognitive skills. The theory regards ToM as a domain specific cognitive module which develops at particular stages in childhood. This view point has arisen largely through the study of autism and Asperger's Syndrome where ToM has been shown to be selectively impaired in comparison to other high level cognitive abilities (Baron-Cohen, 1995; Frith & Frith, 1999; Leslie & Thaiss, 1992). Essentially this theoretical perspective supports the notion that ToM may be a localised skill associated with particular neural structures. If these structures are damaged, ToM functions will be selectively impaired, whilst other cognitive skills will remain largely unaffected. Leslie (1987) and Baron Cohen et al (1985) proposed that this module would enable one to represent objects or states of the world as well as representing states of other people's beliefs about the world. Consequently damage to such a module would seriously impair a person's ability to interact socially. In addition to the idea that ToM was dependent on one specific module, these researchers subsequently proposed that there are a series of modules which mature at different predetermined stages in development (Leslie, 1994; Baron-Cohen, 1995). A number of lesion studies which assess ToM offer support for this theory (Bach, Happé, Fleminger & Powell, 2000; Rowe et al., 2001; Stone et al., 1998).

Peterson & Seigel (1995;1997) found that the ToM skills of deaf children whose parents' could hear did not mature at the same rate as normal children and were similar to the deficits observed in children with autism. This was explained as a consequence

of not receiving the same level of perceptual inputs. Indeed where deaf children were taught to sign by their parents' performance on ToM tasks was not impaired (Peterson & Seigel, 1997). Such studies cast doubt on purely modular accounts of ToM as clearly environmental influences affect the development of such skills. Similarly the impact of nurture on ToM skills has been further highlighted by studies where children who have more opportunities to interact with adults or to engage in pretend play demonstrate enhanced mentalising skills. In addition those children who have more siblings, or older siblings are also advantaged in this respect (Lewis, Freeman, Kyriakidou, Maridaki-Kassotaki & Berridge, 1996; Perner, Ruffman & Leekman, 1994; Ruffman, Perner, Naiton, Parkin & Clements, 1998; Youngblade & Dunn, 1995).

#### ***4.2.3 ToM as a deficit in general theory formation (theory theory)***

Gopnik, Capp and Meltzoff (2000) suggest that people with autism may have a general deficit being unable to formulate theories per se rather than a specific problem with ToM. Like the modular theory, this perspective also proposes that autism is a biologically based disorder. However, Gopnik et al. argue that an innate capacity which supports general theory formation and underpins general inferential abilities exists and that rather than ToM itself being innate, it is this capacity which underpins ToM functioning. Thus ToM is not regarded as a specialised modular cognitive skill but rather a specialised skill which is dependent upon more generalised abilities. The development of ToM occurs as the child constructs a sequence of successive theories about the mind that are updated and modified as a consequence of experience. As Gopnik et al.(2000) suggest 'this system is specifically designed to construct abstract, coherent and revisable causal maps of the world.....innate 'starting-state' theories



about the mind as well as about other particular aspects of the world'(p.51). Meltzoff and Gopnick (1993) purport that children with autism may not have an initial theory (starting-state) representation of other people or if they do it may be different in some way to those present in normal developing children. Whilst autistic children may possess the necessary apparatus to learn, the direction they take in relation to understanding the mind may be fundamentally different and impact on later development (Gopnik et al., 2000). As ToM is not proposed to be a domain specific modular skill but rather a domain general skill it is not believed to be uniquely underpinned by specific neural structures. This theory suggests that damage to the neural structures that support general theory formation or inferential abilities would result in ToM deficits.

#### ***4.2.4 ToM as a simulation skill***

Langdon & Colheart (2001) propose that poor mentalising is a consequence of deficits in perspective taking. They propose that ToM skills involve individuals simulating the reality of another person. This requires the individual to adopt the other person's perspective and to construct possible courses of action based on how they themselves would respond given the other person's circumstances. Thus ToM does not involve inferring the mental states of another person but rather making predictions based on what we ourselves would do if we were in the situation faced by the other. Unlike modularity theory this theory does not make a distinction between manipulating the physical world (visual perspective taking) and manipulating mental states (abstract cognitive processes). Simulation theory does not regard ToM as a domain specific skill uniquely dependant on specific neural structures but rather a domain general skill

dependent on those neural structures that underpin general perspective taking skills. If damaged, these structures would adversely affect ToM performance. The idea of ToM being a domain general skill is also supported by the Gopnik et al's theory formation account of ToM. Making inferences and predictions about the behaviour of others based on our own experience is something that is supported by both the simulation perspective and theory formation account (Gopnik et al., 2000).

#### ***4.2.5 ToM as a skill dependent on executive functioning***

Executive functioning refers to the processes that direct behaviour. Such processes include, among others, planning, decision making, overcoming habitual responses, working memory, set shifting, error correction and the co-ordination and control of action. Damage to the frontal lobes (particularly the dorsolateral PFC) has been associated with disruption to executive functions. Studies have highlighted that autistic children exhibit behavioural and cognitive impairments similar to those found in individuals with frontal lobe damage (Ozonoff Pennington & Rogers, 1991; Ozonoff, Strayder, McMahon & Filloux, 1994; Prior and Hoffman, 1990; Rumsey and Hamburger, 1990; Russell, 1997). Such studies have highlighted that the autistic child's need for routine, familiarity and repetitive behaviour may be a consequence of perseveration or difficulty in shifting attention (Baron-Cohen, 2000). These studies postulate that autism is a consequence of executive dysfunction. Perner and Lang (2000) argue that executive functioning is closely linked to ToM development especially between the ages of three and five. They suggest that ToM is crucial in accomplishing advanced levels of executive control and highlight three important aspects that account for the relationship. They suggest that ToM development enhances



self control, 'the monitoring of actions and the ability to act at will are necessary' (p154) for developing ToM and that conditional reasoning is a common functional component of ToM and executive functioning. The latter proposition will be discussed in more depth in Study 3. This theory does not view ToM as being a specialised skill, dissociated from other higher order cognitive functions and underpinned by specific neural structures. Rather ToM is seen as being fundamentally dependent upon general executive functioning and thus a selective impairment of ToM would not be possible. Lesion studies implicating the involvement of the frontal lobes in ToM processing have provided evidence of dissociation between ToM and executive functioning and consequently contradict this theory (Bach et al., 2000; Bird et al., 2004; Fine et al., 2001; Mazza et al., 2007; Rowe et al., 2001; Stone et al., 1998).

#### ***4.2.6 ToM as a skill dependent on conditional reasoning.***

A number of authors postulate that there is a reciprocal relationship between ToM and conditional reasoning and that both involve reasoning about embedded conditionals (Ermer et al., 2006; Frye, Zelazo &, 1995; Frye, Zelazo, Brooks & Samuels, 1996). Many of these ideas are founded in evolutionary perspectives which suggest that social exchange evolved to enable cooperation and mutual exchange of benefits, which are given conditionally. Evidence to support these ideas come from a number of studies that have shown facilitatory effects when reasoning about conditional rules set within a social context. (Cheng & Holyoak, 1985; 1989; Corcoran & Frith, 2005; Cosmides, 1989; Cosmides & Tooby, 2000; Cosmides & Tooby, 2005; Ermer et al., 2006; Fiddick, Cosmides & Tooby, 2000; Goel et al., 2004; Girgerenzer & Hug, 1992). ToM is particularly important in social exchange as it enables strategic social interaction, which requires the ability to effectively infer the mental states of others. It is therefore

suggested that social exchange is dependent upon ToM (Ermer et al., 2006). These ideas have only briefly outlined here as these will be discussed in detail in Chapter 9 as they are particularly relevant to Study 3

### ***4.3 Assessment of theory of mind***

Researchers have used a variety of assessment techniques to tap into ToM functioning. The most common measures and those which are most relevant to the issues which will be investigated in this thesis will be outlined. The most established and validated measure of ToM has utilised the concept of false belief.

#### ***4.3.1 False belief***

Dennett (1978) argued that the best evidence for an understanding of other people's minds is the ability to attribute a "false belief" to another person. Detection of false belief requires that you can appreciate that another person has misconceived an event as a result of incorrect reasoning. Many subsequent empirical tests of ToM are based on this criterion and assessment of false belief is regarded as the 'litmus test' of ToM functioning. This method is widely used and validated because it establishes whether an individual can attribute beliefs to others that may differ from their own. As Astington (2001) highlights, false belief is 'an unequivocal marker of mentalistic understanding' (p.685).

Typically false belief has been assessed at first order and second order levels of intentionality. Appreciation of first order false belief usually develops by the age of four and by the age of seven, children should be able to pass second order false belief



tasks (Perner & Wimmer, 1985; Wimmer & Perner, 1983; Wellman, Cross & Watson, 2001). Often such tests are developed within the context of ToM stories, which are often accompanied by story boards to aid the participant in following the story. First order stories involve a character having a false belief about the state of the world. The tasks require the individual to understand that another person may not have access to information about the world which they themselves have and as a consequence that the other person's viewpoint is mistaken. Typically first order stories involve a protagonist leaving an object in one location and then leaving a room upon which the object is moved to a new location. Demonstration of intact first order false belief would involve the participant appreciating that the protagonist will look for the object in the old location on re entering the room. To master first order false belief the participant must appreciate that reality and another person's perception of reality can be different (refer to Appendix 7 for an example of a first order false belief task).

Second order stories are more complex and involve one character having a false belief about the belief of another character in a story (refer to Appendix 7 for an example).

The age of developing false belief skills has been shown to be the same across cultures and continents (Avis & Harris, 1991; Wellman et al, 2001; Wellman & Lagattuta, 2000). Generally adults score at ceiling on both first and second order false belief tasks (Stone, Baron-Cohen & Knight, 1998) so designing tests which tap in to ToM in adults can be challenging.

First and second order false belief tasks will be tested and outlined in Study 1.

### ***4.3.2 Deception***

Deception has also been used as another way of testing mentalising ability. As Baron-Cohen (2000) proposes, deception is important in understanding another's mind as it involves trying to make a person believe something that is untrue. It involves being aware that beliefs can be manipulated and people will base these beliefs on knowledge derived from what they have heard or observed (refer to Appendix 7 for an example of a first order and second order deception task.).

Sodian, Taylor, Harris and Perner (1992) found that an understanding of deception starts to develop at around the age of four. Younger children could produce deceptive strategies but did not appreciate their effect. Autistic children have been shown to have deficits in understanding and producing deceptive strategies (Baron-Cohen 1992; Sodian & Frith, 1992; Yirmiya, Solomonica-Levi, & Shulman, 1996).

First and second order deception tasks will be tested and outlined in Study 1.

### ***4.3.3 Pragmatic language and theory of mind***

More advanced tests of ToM involve being able to appreciate non-literal language or figurative speech. An appreciation of the pragmatics of language is needed to understand such things as sarcasm, irony, humour, metaphor and hinting and consequently paradigms tapping these concepts have been used to assess ToM performance. By reference to contextual information, the listener must go beyond the literal meaning of the words that are used and comprehend the intentions of the speaker



and the meaning they are trying to convey. Baron-Cohen (2000) argues that deficits in the appreciation of pragmatic language can occur as a consequence of either impairment in mentalising or as a consequence of weak central coherence (use of context). Deficits in the appreciation of pragmatics have been closely associated with ToM deficits in autism by a number of authors (Baron-Cohen, 1988; Happé, 1993; Tager-Flusberg, 1997).

A number of paradigms have been used in studies to assess these higher order ToM abilities. These include: appreciation of irony (Shamay Tsoory et al. 2003; Shamay-Tsoory et al.,2005a), sarcasm (Shamay –Tsoory et al., 2002; Shamay-Tsoory et al.,2005 a; Shamay-Tsoory et al.,2005 b), hinting (Corcoran, Mercer & Frith, 1995; Corcoran & Frith, 2003), faux pas (Farrant et al.,2005; Schacher, et al., 2006; Shaw et al.,2007; Stone et al.,1998; Shamay-Tsoory et al., 2005 a) humour (Winner et al.,1998), and metaphor (Van Lancker & Kemper, 1987)) to name a few. Two particular paradigms, appreciation of faux pas and hinting will be discussed in more detail.

#### ***4.3.3.1 Hinting***

The understanding of non-literal language has been assessed by the appreciation of hints. The Hinting Task devised by Corcoran et al. (1995), was originally used to assess ToM impairment in schizophrenia. The task involves ten stories which assess the participant's ability to understand the underlying intentions behind a speech act, where someone makes a hint and does not literally mean what they say (refer to Appendix 10 for examples of The Hinting Task).

The Hinting Task will be tested and outlined in more detail in Study 2.

#### ***4.3.4 Faux Pas***

Faux pas tasks involve an appreciation of certain social rules which are generally accepted within a given culture. A violation of such a social rule would be seen as inappropriate social behaviour within that culture. In an attempt to develop a more complex ToM task than just appreciation of false belief, Stone et al. (1998) developed a task involving faux pas. This task involved the appreciation of false belief as well as an understanding of how the 'faux pas' would affect the person in the story. They found that by age 11 most children could pass the faux pas task.

#### ***4.3.5 Reading the Mind in the Eyes task***

Another unconventional ToM task that has proved popular was developed by Baron-Cohen, O'Riorden, Stone, Jones and Plaisted (1997). The Reading the Mind in the Eyes task (RME) involves the participant identifying complex mental states (emotions) by looking at photographs of the eye region only. Participants are provided with four words depicting emotions and are required to select the word corresponding to the emotion expressed by the eyes.



#### ***4.3.6 Testing considerations***

In order to make sure that measures reflect ToM functioning and not other cognitive skills, a number of control measures need to be considered when assessing ToM. Most studies incorporate a measure of general cognitive ability (such as an IQ test) to make sure that apparent deficits in ToM are not a simple consequence of general cognitive dysfunction. To minimize the load on working memory, tasks utilize devices such as pictorial story boards (in ToM stories) or participants are allowed to refer to the relevant text/stimuli throughout testing. As well as questions which assess ToM ability, tasks usually incorporate 'reality' or comprehension questions to ensure that the relevant prose has been understood and to guard against the possibility that poor performance on the task simply reflects memory or comprehension difficulties. In order to achieve this, tasks will typically include some questions requiring general inferential ability (such as making inferences about physical states). These complement the key questions which assess the participant's ability to make inferences about the mental states of others. All these precautions are designed to ensure that the impairments that are observed reflect ToM difficulties as distinct from problems in other cognitive domains.

#### ***4.4 The neural basis for ToM***

ToM is seen to consist of both 'cold cognition' the ability to make inferences about others' cognitive states such as knowledge, desires and beliefs and 'hot cognition' the ability to make inferences about the affective states (the emotions and preferences) of other persons (Brothers & Ring, 1992; Stone, 2000). Stone (2000) argues that due to

the complex nature of ToM inferences, it is doubtful that ToM is located in one brain area and is more likely to involve a distributed neural network with different brain areas supporting different types of ToM processing. In accordance with this idea the rest of this chapter will go on to review the research evidence which has implicated various neural networks/structures in supporting ToM tasks.

#### ***4.4.1 The frontal lobes***

The frontal cortex comprises all tissue lying in front of the central sulcus. The prefrontal cortex (PFC) excludes the motor and premotor areas. Anatomically three distinct functional subdivisions of the PFC have been established, the dorsolateral PFC, the orbitofrontal PFC and the medial PFC.

The dorsolateral PFC includes Brodmann's area 6 and lateral parts of 8-10 and 44-46 (Stone, 2000). Damage to the DLPFC has been associated with deficits in aspects of executive functioning including; inhibition, planning, working memory, flexibility in maintaining or shifting set, temporal organisation, and response selection. In addition aspects of metacognition such as insight, self awareness and moral judgement are also likely to be impaired following DLPFC damage.

Compared to other parts of the PFC, the functional purpose of the medial frontal cortex is less well established. This area lies amid the two hemispheres within the frontal lobes and includes Brodmann's area 12, 32 and the middle areas of 8-10, damage to this area can cause akinesia, lack of will, language impairments and inappropriate behaviour (Stone, 2000).



The orbito frontal cortex consists of 'Brodmann's area 11 and the ventral surface of the frontal lobes that sits above the eyes' (Stone, 2000, p.254.). Damage to this area has been associated with social and emotional disturbances such as socially inappropriate behaviour, a lack of emotion, changes in personality, inappropriate jocularity and self centeredness, rambling and digressive speech and a lack of self insight (Beer, Heerey, Keltner, Scabini & Knight, 2003; Beer, John, Scabini & Knight., 2006; Kringleback & Rolls, 2004; Stone, 2000).

Damage to the orbito frontal and ventromedial (VM) (which includes the orbito frontal and the lower portion of the medial frontal cortex) areas of the PFC have both been associated with impairments in social behaviour (Stone, 2000; Eslinger & Damasio, 1985). Individuals with damage to these areas have problems appreciating the pragmatics of language and they are not always sensitive to subtle social cues when conversing with others, such as when in conversation it is appropriate to let the other person speak (Alexander et al.,1989). They can often make inappropriate remarks such as sexual comments and inappropriate jokes. They are frequently lacking in tact and seem to have little insight into the fact that their behaviour is socially inappropriate. Consequently they often have problems in forming and sustaining friendships and relationships (Stone, 2000). In general, cognitive functioning in these individuals seems to be relatively intact (Mattson and Levin, 1990). The impairments that are observed seem to reflect deficits in social cognition whilst general cognitive functioning remains intact. It seems at least possible that the socially inappropriate behaviour associated with lesions to this area may well also give rise to ToM deficits (Stone, 2000).

Burgess and Alderman (1990) argue that frontal lobe damage causes deficits in information processing and effective self control. Social interaction requires many complex cognitive skills, such as planning, monitoring, testing and acting on feedback, inhibitory control, abstract reasoning, confabulation and insight, to name a few. These cognitive skills can be lacking in frontal patients and lead to impaired or reduced social skills. As Damasio (1994) suggests, damage to the frontal lobes can result in socially inappropriate behaviour and can cause personality changes resulting in a lack of empathetic perspective taking. Empathy, that is the ability to appreciate the emotions of others, is an important aspect of ToM (affective ToM) and has been shown to be impaired in individuals with PFC lesions, particularly where these lesions are in the ventromedial (VM) area (Shamay-Tsoory et al., 2003). Shamay-Tsoory et al. (2005a) suggest that the VM area integrates information concerning the emotional and cognitive aspects of behaviour. Thus damage to the PFC and more specifically to this area may have particular consequences for ToM functioning. 'The prefrontal cortex has been postulated as a putative neural system underlying ToM ability' (Bach et al., 2000 p.177.). Similarly it has been observed that 'attempts to explain the behavioural disturbances following prefrontal damage have emphasized the breakdown of ToM' (Shamay-Tsoory et al., 2005a, p.55.).

#### ***4.4.2. The frontal lobes and theory of mind***

Lesion studies and brain imaging techniques have proved to be effective methods for investigating the neural basis of ToM impairments in adult populations. While there is still considerable debate about the organic basis of ToM abilities recent research suggests that these skills seem to be associated with the anterior regions of the brain



implying frontal lobe involvement in mentalising ability (Rowe, Bullock, Polkey & Morris, 2001; Shamay-Tsoory, Tomer, Berger, Goldsher & Aharon-Peretz, 2005a; Stone, Baron-Cohen, & Knight, 1998; Stuss, Gallup & Alexander, 2001). While lesion studies may shed light on the neural structures underpinning ToM functioning, diagnosing socio-cognitive deficits in those with neurological damage will enable treatment interventions to focus on rehabilitating and retraining mental state inferential abilities.

#### ***4.4.2.1 Lesion studies***

Damage to the frontal lobes can affect high level cognitive functions so it is not surprising that they contribute to mentalising abilities, particularly as past clinical and neuropsychological research has indicated the importance of the frontal cortex in social behaviour. Two classic case studies that illustrate this are the case of Phineas Gage (Harlow, 1993) and EVR (Eslinger & Damasio, 1985). Phineas Gage is a classic example of orbito frontal damage where the medial frontal lobes were penetrated by an iron rod. Gage demonstrated severe affective and emotional personality changes as well as social reasoning deficits after his injury. Similarly after a bilateral orbito-frontal (and VM) lesion (which was caused by an operation to remove a meningioma in the orbitofrontal cortex) Eslinger and Damasio's patient EVR was unable to draw correct inferences about the motives of those around him and thus behaved inappropriately in social situations. Whilst his IQ remained high EVR lost his job and his wife as a consequence of changes to his personality and his general irresponsibility (Kringelbach & Rolls, 2004).

Focusing on those studies that are of particular relevance to this thesis what follows is a detailed review of some of the more influential lesion studies which have assessed ToM abilities. Stone et al. (1998a) assessed ToM performance in five traumatic brain injured patients with bilateral damage to the orbital frontal cortex (OFC), five stroke patients with damage to the left dorsolateral prefrontal cortex (DLPFC) and five healthy volunteers. Participants were tested on a series of ToM tests that were increasingly difficult, first order false belief, second order false belief and a more complex faux pas task. Individual differences in general cognitive impairment and general inferential ability were controlled for as was working memory load. Cognitive functioning was measured using the Mini Mental State Examination and participants all scored within the normal range. The OFC group was impaired on the appreciation of faux pas but not on the first or second order false belief tasks (cold cognition). Nor were they impaired on the general inferential and comprehension questions included in the tasks. The authors suggested that their participants' performance mirrored the way in which they behaved in everyday settings where they often failed to properly read social situations and behaved in socially inappropriate ways. The authors concluded that aspects of 'hot cognition' were impaired in the OFC group while cold cognition remained intact, they may not be able to integrate inferences about mental states with affective information (Stone, 2000). This study is limited in terms of sample size and that a unilateral right frontal group was not included in the design. The methodology employed by this thesis has attempted to address these difficulties by including a RF group and by recruiting larger numbers of people in each experimental group to enable a more thorough comparison across lesion sites.



Rowe et al. (2001) investigated ToM and executive functioning in a group of patients with unilateral frontal lobe damage following frontal lobe excision (15 with right frontal lesions and 16 with left). Thirty-one healthy controls with no history of psychiatric or neurological disease were also tested who were matched for age, education level and IQ. Participants were presented with six first order and six second order false belief stories. The authors included control questions to monitor general story comprehension, memory and general inferential ability. They found impaired performance on both first and second order ToM tasks in both the right and left frontal patients. The normal control group performed well on all aspects of the stories. Patients with left frontal lobe lesions performed poorly on the general inference questions but this was not related to ToM impairment. It was also observed that although both frontal groups showed a range of deficits in executive functioning, the magnitude of these deficits was unrelated to the degree of ToM impairment. Similarly memory, verbal IQ performance, and general inferential ability were also found to be unrelated to ToM impairment. The magnitude of ToM deficits was similar across the different lesion sites in the FL (dorsolateral, medial or orbitofrontal). Rowe et al. suggest that their findings provide strong evidence for the existence of an independent ToM module and that ToM functions are supported by both the right and left frontal lobes. The main criticism with this study is that both frontal lobe groups consisted of participants who had different underlying aetiological conditions e.g. meningioma, epilepsy, aneurysm etc. Consequently ToM performance may be masked by the specific effects of these conditions as opposed to the sites of the surgical lesions incurred. This difficulty will be minimised in the present thesis as all participants with focal lesions have epilepsy. Study 1 assesses first and second order false belief.

Stuss et al. (2001) investigated ToM in patients with acquired brain damage who had a range of different aetiologies. They compared 19 patients with focal frontal lobe damage, 13 patients with non frontal focal lesions and 14 healthy controls, matched for age and education. IQ and depression were included as background measures. There were no significant group differences in depression but there were differences in IQ so this was included as a covariate in the analysis. Participants were presented with deception and visual perspective taking tasks, in which they had to correctly infer the mental state of another person. To investigate whether performance differed according to the specific lesion site, the sample was further sub-divided into a right frontal (RF, N=4), left frontal (LF, N=8), Bi-frontal (BF, N=7), Right Non Frontal (N=5) and Left Non Frontal groups (N= 8). For the purposes of analysis the BF group (which included individuals with lesions in medial areas) were added to each of the right and left FL groups 'to clarify the tendency for frontal laterality effects' (p.280).

A frontal effect in relation to visual perspective taking was found but not in relation to deception. Further analysis revealed that compared to the other groups, participants with BF and RF lesions (combined) were significantly impaired when they were required to make inferences based upon another person's visual perspective. An analysis of the specific effects of lesion site in relation to errors on the deception task revealed that the medial areas of the FL, particularly on the right side were involved in the detection of deception. Study 1 of this thesis will also assess the appreciation of deception. Stuss et al suggest that the frontal lobes and more specifically the right frontal lobe are crucial for ToM processing. They also highlight the importance of the ventromedial area of the FL which they argue may well be important due to its connections with the limbic system and the amygdala (Stuss et al, 2001). Unlike Rowe



et al. (2001), this study did not assess or control for group difficulties in comprehension, general inferential ability or memory. It is worthy of note that Bird et al. (2004) have criticised this study observing that the majority of the BF group had experienced head trauma which is known to cause diffuse damage making it difficult to draw firm conclusions regarding the effects of lesion site.

Shamay-Tsoory et al. (2005a) assessed ToM in 26 patients with well defined lesions in the PFC. Of these, 6 had left FL lesions, 7 had right FL lesions, and 13 had bifrontal lesions (BF). Thirteen participants with posterior lesions were also assessed (9 left, 4 right) as well as 13 controls. There were no differences between the groups in relation to age, education and IQ and participants with lesions had a variety of different underlying aetiologies. A further analysis was conducted in relation to specific FL lesion site, such that 12 participants had orbitofrontal ventromedial (VM) involvement, 7 had dorsolateral involvement (DL) and 7 had a mixture of DL and VM involvement.

Participants were assessed on second order false belief; appreciation of irony and recognition of social faux pas. Participants with FL lesions were impaired on faux pas and irony, when laterality was taken into account the right frontal group performed significantly worse on these two tasks in comparison to people with posterior lesion and controls, however, their performance did not differ from the BF group. In comparison to the other two groups patients with VM lesions exhibited deficits in appreciating irony and faux pas but not second order false belief. These impairments were more profound in people with right VM lesions and the authors concluded that the VM area mediates the affective as opposed to the cognitive aspects of ToM. They suggest that the capacity for understanding cognitive and affective mental states may be dissociated and that damage to the VM PFC only impairs the affective processing of

such states whilst cognitive processing remains intact. They also highlight that understanding the affective states of others requires empathy which patients with VM lesions have been shown to have difficulty with (Eslinger, 1998; Shamay-Tsoory et al, 2003). A positive feature of this study was that participants were allowed to access the stimuli in the tasks as often as they wished. Memory questions were also included thereby controlling for group differences in attention, comprehension difficulties and working memory capacity. However, one potentially confounding factor in this study was that all participants with VM lesions scored at ceiling on the false belief task which suggests that the task was too easy. Thus inferring that the cognitive aspects of ToM are not impaired in these participants may be erroneous given the measures used in the study.

The idea that social cognitive processing systems are dissociated from the affective has also been supported in a study by Blair and Cipolotti (2000). They assessed a patient with right frontal damage (which involved the orbitofrontal cortex) as a consequence of head trauma who had acquired 'sociopathy'. J.S. was assessed on a series of socio-cognitive tasks that involved cognitive and affective social cognition. Performance on tasks involving mental state attributions was intact but performance on tasks that involved an appreciation of the emotions of others was impaired. Blair and Cipolotti argue that 'social cognition is not mediated by a unitary system' (p.1137).

In light of the evidence implicating medial frontal lobe involvement in mentalising ability (from neuroimaging studies), Mazza et al. (2007) assessed nine people with unilateral right and nine with unilateral left ventro medial prefrontal (VMPFC) lesions and compared their performance with a group of patients with schizophrenia (who are



also known to have mentalising difficulties) and a healthy control group. All participants were matched on age, years of education and estimated IQ. One of the paradigms used to assess ToM was very similar to that used in Study 1 of this thesis. Participants were presented with four ToM stories, two assessing first order false belief and two second order false belief. The right VMPFC group was significantly impaired on first order and second order ToM in comparison to the left VMPFC group but their performance did not differ from the schizophrenic sub groups. All patient groups underperformed in comparison to the normal control group. Participants were assessed on the Mach IV Scale (Christie & Geis, 1970) to examine self awareness and social functioning. They were also examined on a Social Situations Task (Blair & Cipollotti, 2000) to determine if participants could judge socially appropriate behaviour in a series of vignettes. The right VMPFC group was impaired in relation to NC and the left VMPFC group on both of these tasks. No correlations were found between ToM performance and tests of executive functioning. Significant correlations existed between social functioning (Mach IV) and first and second order ToM performance and between duration of illness and first order ToM. As expected, negative symptoms of schizophrenia were associated with social cognitive deficits and social dysfunction.

A limitation of Mazza et al's study was that participants with VM PFC involvement were assessed 20-40 days after surgery. It seems likely that not enough time would have passed post surgery to completely rule out the possibility of impaired abilities arising from post operative factors. It is possible that relevant neural structures subserving ToM functions might still be temporarily affected in the PFC group. Whilst it is useful that this study assessed social cognition in relation to social functioning, the use of the Mach IV as an objective assessment measure of social functioning is

questionable. This scale is generally regarded as a personality measure which assesses the ability of people to deceive and manipulate others. Therefore is not an appropriate measure of social competence.

One of the strengths of this study was that participants had unilateral lesions. This contrasts favourably with previous studies that have utilized patients with bifrontal lesions, including a number who had experienced head trauma, which is known to associated with diffuse damage (Shamay-Tsoory et al., 2005a; Stone et al., 1998; Stuss et al., 2001). Mazza et al. (2007) also highlight that these studies lack detail regarding anatomical location of lesion site.

#### ***4.4.3 The right hemisphere and ToM***

Patients with acquired right hemisphere damage demonstrate similar deficits in relation to the social and pragmatic aspects of communication to those seen in people with autism (Surian & Seigal, 2001; Griffen et al., 2006). Such deficits include a difficulty in the production and appreciation of a number of communication forms including humour, irony, metaphor, prosody and the emotional aspects of language (Brownell et al., 2000). These may well reflect impaired ToM ability.

Happé, Brownell & Winner (1999) provide convincing evidence of ToM impairment as a consequence of RH damage. Happé et al. (1999) compared ToM performance using stories and cartoons in 14 people with right hemisphere damage due to stroke, 12 of which had frontal lesions, five people with left hemisphere damage due to stroke, and 19 healthy elderly controls. As well as a mental state inference tasks, physical state



inference tasks were incorporated in to the study so that ToM and general inferential performance could be differentiated from each other. The LH participants were aphasic and so to reduce the verbal demands of the task they received a modified version of the task in which they were required to make a forced choice judgment as opposed to a free response. Happé et al. found that the right hemisphere group were significantly impaired on ToM performance in comparison to the other groups, but did not demonstrate impaired performance on non mental state tasks. They concluded that mental state inferential ability is a separate cognitive skill dissociated from other general higher cognitive functions and inferential abilities and most likely localised to the right hemisphere. People with right hemisphere damage were particularly impaired on second order tasks, a finding which has also been supported by Winner, Brownell, Happé, Blum and Pincus. (1998). Happé et al. also argue that ToM dysfunction may underlie the social communication problems demonstrated by this group. It is important to note that these conclusions need to be considered with caution given the small number of left hemisphere-damaged patients included in the study, and in view of the modifications to the task that were made in order to accommodate the aphasic participants. Happé et al. suggest that future research with people who have clearly defined lesions would help determine which area of the right hemisphere is specific to ToM functioning. This methodological difficulty is overcome in the present thesis which assesses PWE who have focal lesions to the right frontal and temporal lobes contrasting the performance of these individuals with PWE with seizure foci elsewhere.

Griffen et al. (2006) assessed ToM in 11 (non aphasic) people with unilateral right hemisphere damage due to stroke and 20 healthy controls. This study attempted to

overcome the methodological limitations evident in Happé et al's (1999) research by excluding left hemisphere participants and by including both forced choice and free response questions so as to control for the possible effects of expressive language deficits on ToM performance. The emotional salience of tasks were classed as high or lows so that task performance could be differentiated in relation to the emotional content of the measures used. This was particularly relevant to the study as RH damaged patients are known to have difficulty in inferring emotion. RH damaged patients were impaired on second order ToM tasks involving deception but not first order tasks. ToM performance was independent of performance on other cognitive and executive measures and unrelated to the appreciation of humour. Surprisingly recognition of emotion was unimpaired in the RH damaged group. These findings further support those of Happé et al. (1999) and emphasise the importance of the RH in processing cognitive ToM.

#### ***4.4.4. The amygdala, temporal lobes & ToM***

The amygdala is located in the medial temporal lobes in front of the hippocampus and there is general agreement that this structure plays a fundamental role in emotional processing, especially in relation to processing fear (Adolphs, Tranel, Damasio & Damasio, 1995). Whilst it is unlikely that the amygdala is functionally specific to ToM, it is involved in many aspects of emotion and social behaviour and has been associated with ToM deficits especially in relation to affective ToM (Baron-Cohen et al. 1999; Stone et al., 1998a; 1998b). The amygdala has also been strongly linked with eye gaze detection which, Baron-Cohen, Baldwin & Crowson (1997) argue is fundamental to ToM processing. Recognition of affective states would appear to have a



fundamental role in ToM so it is likely that the amygdala is part of a neural network involved in ToM processing (Stone, 2000).

Bilateral damage to the amygdala has been associated with difficulties in identifying facial and vocal emotional expression (Adolphs et al., 1994; Brooks et al., 1998., Scott et al., 1997). Fine et al (2001) found that a patient, B.M. with early left amygdala damage who was later diagnosed with schizophrenia and Asperger's syndrome was impaired on appreciation of second order false belief, appreciation of mental state cartoons and advanced ToM stories involving the appreciation of pragmatic language. B.M. did not exhibit any deficits on tests of executive functioning.

A lesion study by Apperly, Samson, Chiavarino and Humphries (2004) assessed 12 participants on a non linguistic version of a first order false belief task with reduced executive demands. The three participants that demonstrated deficits in false belief reasoning all had lesions in the left temporo-parietal junction (TPJ). This finding supports imaging research which has shown bilateral activation in the TPJ during mentalising tasks (Gallagher et al., 2000; Saxe & Kanwisher, 2003). No participants had right TPJ lesions but the findings of the study suggest that unilateral lesions to the TPJ may be sufficient to interfere with false belief reasoning.

#### ***4.4.5 Structural and functional imaging studies***

Functional and structural imaging studies have also been useful in trying to elucidate the organic basis of ToM abilities. What follows is a brief overview of the most relevant and influential studies which have investigated ToM. A PET study on normal

participants by Goel, Grafman, Sadato & Hallett (1995) found that the left medial frontal lobe (Brodmann areas 8 & 9) and left temporal pole (Brodmann areas 21, 39/19, 38) were activated when participants were engaged in a ToM task. The task involved making mental state attributions regarding the knowledge of objects. Fletcher et al, (1995) also established that an area of the left medial prefrontal cortex (BA 8 & 9) and the posterior cingulate were activated in normal participants during the processing of ToM stories which involved mental state inferences. When using the same test materials people with Asperger's Syndrome activated an adjacent area of the medial PFC (BA 10) which is thought to be involved in general problem solving (Happé et al., 1996). Gallagher et al. (2000) used the same short stories as Fletcher et al. (1995) supplementing these with a set of cartoons which required an appreciation of mental states in order to experience them as humorous. They found that only the right and left medial prefrontal cortex was activated during both verbal and visual mental tasks. Using a similar cartoon paradigm, Brunet, Sarfati, Hardy-Bayle and Decety (2000) assessed eight normal participants. They found activation in the right medial prefrontal cortex (BA 9) and the right inferior prefrontal cortex (BA 47) as well as the left cerebellum and the bilateral temporal lobes. The authors concluded that the right medial prefrontal cortex was implicated in mental state attribution. Involvement of the right PFC in normal participants was also later confirmed in another study using a non verbal ToM task by the same authors (Brunet, Sarfati, Hardy-Bayle & Decety, 2003). Castelli, Frith, Happé and Frith (2000) found that when viewing animations that involved ToM, people with autism and Asperger's syndrome showed less activation in a previously identified mentalising network (comprising the medial prefrontal cortex, superior temporal sulcus at the temporo-parietal junction and the temporal poles) compared to a normal control group.



As noted above, some authors have emphasised the importance of the amygdala to ToM functioning. For example, Baron-Cohen et al (1999) found that individuals with high level autism and deficits in ToM (i.e., on the Reading the Mind in the Eyes Task) did not activate the left amygdala. However this area was activated in normal controls during ToM processing in the same study. They conclude that the amygdala may be especially important in normal ToM functioning. Siegal and Varley (2002) also emphasise the importance of the amygdala and propose that the neural system which underpins ToM includes the amygdala, the temporo-parietal junction (TPJ), the orbital frontal cortex. These authors also maintain that the medial frontal lobes are especially important in supporting ToM functioning. The importance of the TPJ has been demonstrated in a number of neuroimaging studies using different ToM paradigms (Brunet et al., 2000; Fletcher et al., 1995; Gallagher et al., 2000; Goel et al., 1995; Vogeley et al., 2001; Saxe & Kanwisher, 2003). Furthermore, a number of studies have implicated the medial PFC in ToM processing (Baron-Cohen et al., 1994; Brunet et al., 2000; Brunet et al., 2003; Fletcher et al., 1995; Gallagher et al., 2000; Goel et al., 1995; Happé et al., 1996; McCabe et al., 2001; Vogeley et al., 2001; Berthoz et al., 2002; Gallagher et al., 2002; Saxe & Kanwisher, 2003).

Whilst imaging studies have not always shown a consistent pattern of neural circuitry in ToM, evidence suggests that the amygdala, orbito frontal cortex, temporo-parietal junction and especially the medial PFC may support mentalising (Frith & Frith, 2003; Siegal & Varley, 2002). The medial PFC has been found to be activated in most studies (Frith & Frith, 2003) and detailed reviews have concluded that the medial frontal lobes are integral in ToM processing (Amodio & Frith, 2006; Frith & Frith, 2003; Gallagher & Frith, 2003). Evidence of laterality has been mixed with some studies implicating

the left medial PFC (Baron-Cohen et al, 1999; Fletcher et al., 1995; Goel et al., 1995; Gallagher et al., 2000) whilst others implicate the right medial PFC (Baron-Cohen et al., 1994; Brunet et al., 2000; Brunet et al., 2003).

Whilst neuroimaging studies are useful in helping elucidate the neural underpinnings of ToM they cannot conclusively provide evidence that a particular structure is essential for ToM processing. This can only be achieved via lesion studies (Bird et al., 2004). Conducting lesion studies on participants with specific damage to the medial frontal cortex is difficult. As Stone (2000) points out, damage to the medial frontal lobes is uncommon as strokes are more likely to occur in the middle cerebral artery than the anterior cerebral artery which provides the blood supply to the medial frontal lobes. One lesion study by Bird et al. (2004) was able to overcome this and provided a unique opportunity to verify the importance of the medial PFC to ToM functioning. This study found that a patient (G.T.) with extensive damage to the medial frontal regions as a result of a rare form of stroke did not show significant impairment on the ToM tasks previously used in imaging studies which had implicated medial PFC involvement (Berthoz et al., 2002; Fletcher et al., 1995; Gallagher et al., 2000; Happé et al., 1996). Despite the presence of memory impairment and executive (planning) dysfunctions, G.T did not exhibit ToM deficits. Whilst a slight blunt affect was observed, the researchers concluded that this case study provided evidence that the medial PFC was not essential for cognitive ToM. They argue that these findings may be in conflict with the results of neuroimaging studies because the medial PFC may be necessary for acquisition of ToM but not execution of ToM tasks in adulthood. Another possible explanation they put forward is that G.T.'s lesion was not extensive enough to impede all areas of the medial PFC which may underpin ToM functioning.



As well as the medial PFC, the temporo-parietal junction, superior temporal sulcus, temporal pole, amygdala and orbitofrontal cortex have been implicated as a neural circuit for ToM and it could be possible that damage to one part of this neural system such as the medial PFC may not be 'sufficient to destroy its functional integrity' (Bird et al., 2004) (p.925.). Contrary to this proposition, Frith and Amodio (2006) suggest that these other regions may only underpin more general functions and that the medial PFC is critical for mentalising. Nonetheless, Bird et al. (2004) conclude that brain imaging should not be the only method used to establish cognitive neuroanatomy and that the medial PFC may not be crucial in cognitive ToM processing.

#### ***4.5 Methodological limitations***

Baron-Cohen et al (1995) have suggested that ToM may be supported by a network of many neural structures which may represent different aspects of ToM abilities. This may account for the differing results obtained in research studies which could be attributable to variations in task demands. Indeed when trying to compare findings across studies the disparate nature of the ToM paradigms that have been used is one of the main difficulties. Neuroimaging studies alone cannot conclusively demonstrate the neural correlates of ToM, only lesion studies can determine whether a neural structure is essential to ToM processing (Bird et al., 2004; Griffen et al. 2006).

A number of the lesion studies cited in this review did not provide adequate sample sizes (Stone et al., 1998) and some relied on incorporating bifrontal participants in their analysis of laterality to increase statistical power (Stuss et al., 2001; Shamay Tsoory et al., 2005a). Despite evidence that the temporal lobes and especially the amygdala may

be implicated in ToM processing, focal temporal lobe samples were not included in the study designs (Stone et al., 1998; Stuss et al., 2001; Shamay-Tsoory et al., 2005a; Rowe et al., 2001). In order to guarantee a adequate sample of people with clearly defined focal damage, studies had to rely on recruiting participants with a range of different underlying aetiologies, therefore there is no guarantee that the ToM deficits observed are not an artefact of these underlying conditions as opposed to the site of the lesion (Stuss et al., 2001; Rowe et al., 2001).

A number of studies imply that cognitive and affective ToM may be dissociated and sub served by different neural systems (Blair & Cipolotti, 2000; Shamay-Tsoory et al., 2005a) therefore paradigms which include both cognitive and affective components (such as appreciation of faux pas) may make it difficult to differentiate between deficits in hot and cold cognition. In light of this, Studies 1 and 2 of the thesis which assess ToM have only included measures of cognitive ToM. The study design of the thesis attempts to overcome the methodological limitations of past research by conducting a lesion study. Sampled groups of 11 or more have been recruited which include both right and left frontal and temporal lobe participants, all of which have epilepsy. A generalised epilepsy group and a frontal head injured group are also incorporated in the design to help factor out the impact of aetiology on ToM performance.



## **4.6 Chapter Summary**

Social cognitive neuroscience is a growing science which aims to assess performance of tasks of social cognition in relation to underlying neural structures and systems. One area of social cognition which has been the focus of a plethora of research in the last thirty years is ToM, the ability to appreciate the beliefs and intentions of others. ToM has been shown to consist of cognitive and affective components which some authors argue are dissociated from each other.

ToM has been most thoroughly investigated within autism and is regarded as a core feature of the disorder. ToM deficits have also been implicated in a range of neurological and psychopathological disorders and may serve to explain the disruption to social behaviour in some of these clinical groups. It has been theorised that ToM is an innate modular skill which is domain specific and dissociated from other cognitive skills. This theory suggests ToM may well be localised to particular brain structures which if damaged would impair ToM functioning. Other theories suggest that ToM is not a domain specific skill but is underpinned by domain general skills such as inferential abilities (theory theory), general perspective taking (simulation theory) or general executive functioning. Each of these three theories maintains that damage to structures that underlie these domain general skills will cause ToM impairment.

A wide variety of assessment techniques have been used to assess both cognitive and affective ToM ability. The most validated of these measures has been the use of false belief, a measure of cognitive ToM. To ensure that the deficits that are observed are actually attributable to deficiencies in ToM, researchers must make sure that they

control for the effects of other variables such as attention, working memory and comprehension when administering ToM tasks.

The neural correlates of ToM have been investigated via lesion and neuroimaging studies and whilst much debate exists regarding structures that may underpin ToM, most evidence suggests a role for the frontal lobes and most especially the medial PFC. Though lateralising evidence is mixed, some studies suggest an important role for the right hemisphere. Investigating ToM in adult populations with neurological damage may be beneficial in diagnosing socio-cognitive deficits and consequently enabling treatment interventions to enhance ToM abilities and improve social functioning in these populations. Along this theme Chapter 5 will review literature that has assessed social cognitive functioning in epilepsy. As Chapter 3 has highlighted, PWE have difficulties with social functioning. Conducting research into the social cognitive functioning of PWE will advance knowledge in this area and may lead to effective treatment interventions which improve the overall social functioning and integration of people with epilepsy in society.



## Chapter 5: Social Cognition in Epilepsy

### *Chapter outline*

This chapter will provide a detailed critical review of studies that have investigated aspects of social cognition that are particularly pertinent to the focus of the thesis, namely ToM in epilepsy. This research is particularly relevant to Studies 1 and 2 of the thesis. To date there have been seven studies, some of which have also looked at recognition of emotion as well as ToM, though it is not the purpose of the chapter to review research which has assessed emotion recognition in epilepsy per se. One study has investigated emotional intelligence in people with active epilepsy (who have not undergone surgery) and because of its relevance to the area it will be included in the review. The latter part of the chapter will provide a critical review of the methodology used in research to date. Throughout the chapter, the impact of epilepsy related variables in relation to socio-cognitive processing will be considered.

The final part of the chapter will explore why PWE may have social cognitive deficits and will summarise limitations in past research. The chapter will conclude by providing the rationale and aims of the thesis. To the author's knowledge there are no studies which have investigated social conditional reasoning in epilepsy (which is the focus of Study 3) so it was not possible to include a review on these areas.

### ***5.1 Epilepsy and social cognition.***

There is a paucity of research which has investigated social cognition in epilepsy, this is surprising given the abundance of evidence that exists in relation to the difficulties that PWE have with regards to social functioning (outlined in detail in chapter 3).

Impairments in social competence in children, adolescents and adults with epilepsy are also evident (Austin, Smith, Risinger & McNelis, 1994; Caplan et al. 2005; Herman, Black, Chhabria, 1981; Jalava, Sillpanää, Camfield & Camfield, 1997). As Schilbach, Koubeissi, David, Vogeley, and Ritzl (2007) argue, social competence has a considerable effect on quality of life yet the study of social cognition in epilepsy has been largely neglected. A number of studies have shown that quality of life (QoL) scores increase after surgery but often these measures do not adequately assess improvements in social functioning (Kirsch, 2006).

Epilepsy may affect social cognition in many ways that are hard to quantify. Kirsch (2006) suggests that frequent seizures may interfere with the development of interpersonal skills in children or adolescents, such that they may not always be able to participate in situations where they can develop such skills due to ictal and post ictal disruption to functioning. Medication may impact on their ability to respond effectively in interpersonal conversation to subtle social cues. The child's social networks may be reduced due to stigmatisation, lack of self esteem or because parents are more protective over the child and consequently this reduces their exposure to social environments where they may learn the intricate social skills that are necessary to achieve social competence. Children with epilepsy have been shown to under perform on measures of social competence in comparison to children without epilepsy



as indicated by their parents in a number of studies (Dorenbaum et al., 1985; McCusker, et al., 2002; Williams et al., 1996).

Exactly why PWE have social difficulties is not entirely clear but is likely to be a consequence of a number of complex interrelated psychosocial factors that impact on the person with epilepsy (outlined in detail in Chapter 3). These include the impact of stigma, unemployment or underemployment, anxiety and depression, cognitive dysfunction, poor self esteem, social isolation and difficulties in interpersonal relationships

‘Despite many years of speculation, it remains unclear to what extent psychosocial difficulties are related to the fact that patients are living with a chronic and stigmatising condition and to what extent they are related to neuropathology’

(Walpole, Isaac & Reynders, 2008, p. 1470).

Whether social maladjustments can be attributed to social cognitive deficits remains uncertain (Schacher et al., 2006). The main objective of empirical chapters in this thesis is to provide further insight into this problem.

## ***5.2. Temporal Lobe Epilepsy***

### ***5.2.1 Emotional intelligence and emotion recognition.***

***Walpole, Isaac and Reynders (2008)***

Walpole, Isaac and Reynders (2008) investigated emotional intelligence (EI) and emotion recognition in temporal lobe epilepsy (TLE). Sixteen patients with TLE were

compared with 14 healthy controls (HC). People with TLE were only included in the study if they did not have any history of psychiatric illness (excluding anxiety and depression), head injury, hypoxia, personality disorder, neurological condition or autistic spectrum disorder. People with TLE who had undergone surgery for epilepsy were excluded from the study.

Participants were assessed on a range of background measures including the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001), cognitive intelligence as assessed by the Full Scale IQ (FSIQ) score on the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and Quality of Life in Epilepsy 31 (QOLIFE-31; Cramer et al., 1998). Participants were also assessed on emotional intelligence (EI) using the Emotional Quotient Inventory (EQ-I; Bar On, 1997) and identification of emotional expression using Ekman and Friesen (1976) 60 photographs of facial expressions.

This study found that the TLE group were significantly impaired on total EI score but not cognitive intelligence (FSIQ). The TLE group made significantly more errors when identifying emotional expression than the control group. Significant negative correlations were found between EI (total score) and anxiety and depression as measured by the HADS. Higher QoL scores were associated with higher EI in the TLE group, though this relationship was not significant. No significant differences in EI were established between people with LTLE (N=7) and RTLE (N=9) and EI was not significantly associated with duration of illness or number of seizures. The author concludes that the psychosocial problems in TLE may well be associated with low EI which may be a consequence of epilepsy-related disruption to the functions of the medial temporal lobe.



Walpole et al. (2008) conducted their study under the premise that impairments in a study on EI were present in people with VM PFC lesions and lesions to the amygdala or insular cortices, brain areas that have also been implicated in social cognition (Bar On, Tranel, Denburg & Bechara, 2003). Walpole et al. (2008) argue that EI is closely related to social cognition in that it involves being able to discriminate between and monitor 'one's own feelings and those of others' and being able to use 'this information to guide responding' (p. 1470).

This study would have benefited by recruiting a FLE group to establish if EI was impaired in this sample in line with evidence in the literature which implicates the importance of the frontal lobes in social cognition (see Chapter 4). Walpole et al. (2008) do acknowledge the need to study EI in other types of epilepsy to determine if EI impairment is specific to TLE. This study can be criticised for not stating whether people have refractory TLE, where participants were recruited from and what AEDs (and how many) they were taking.

Differences in RTLE and LTLE were not established in this study, though this may or may not have been impeded by the small sample size of each of the groups. It should be noted that a recent study by Gawryluk and McGlone (2007) which investigated PWE who had TL resections did not find any evidence of laterality of EI, although it needs to be emphasised that these participants did not have active epilepsy.

QoL was assessed in the study and was not significantly related to EI although Walpole et al. (2008) does acknowledge that the role of seizure related variables and the impact of epilepsy need to be studied in more depth in relation to EI. If a larger sample was recruited, relationships between these variables may have been more evident.

### ***5.2.2. Theory of mind and emotion recognition.***

#### ***Shaw et al. (2007)***

Shaw et al. (2007) assessed 19 PWE on ToM tasks and emotion recognition before and after anterior temporal lobectomy (excision of the amygdala occurred in all cases as did removal of anterior parts of the hippocampus) for refractory epilepsy. Those with TLE (10 RTLE and 9 LTLE) had amygdala damage as a consequence of gliosis, neuronal loss or focal lesions. Seizures had stopped or there was a marked reduction in seizures post surgery. Testing took place 1-3 months prior to surgery and 4-6 months post-surgery. Patients who underwent surgery were on the same AEDs post surgery. Nineteen healthy controls with no history of neurological or psychiatric disorders were also assessed on the same measures twice, six months apart.

Participants were assessed on a range of background measures including IQ and the Benton Facial Recognition task (Benton, Sivan, Hamsher, Varney & Spreen, 1983). This task entailed matching images of faces of identical people. These images were taken at different angles or levels of illumination. The Hayling and Brixton tests assessed executive functioning (Burgess & Shallice, 1996a, 1996b). The Hayling test assesses the ability to inhibit predominant responses and speed of task initiation and the Brixton test assesses set shifting and rule detection.

The two main experimental measures were recognition of facial expressions and emotions and appreciation of ToM. The Ekman and Friesen (1976) pictures of facial emotion were used and participants had to rate the intensity of one of six basic emotions (sad, happy, surprise, anger, fear, disgust) in two male and female faces who displayed all six emotions. A faux pas test by Stone et al. (1998a) and Happé's Strange



Stories (Happé, 1994) assessed ToM. Happé's Strange Stories depict characters that do not literally mean what they say, participants are required to illustrate that they understand what the character really means and their true motivations. The faux pas test required participants to identify that a faux pas had taken place, why the comment was inappropriate and the affect that the faux pas may have had on the character in the story (how it would have made them feel). A control question was incorporated to assess comprehension.

Verbal and performance IQ was significantly lower in the RTLE (N = 10) and LTLE (N = 9) operative groups in relation to controls. Duration of epilepsy did not differ between these groups. Scores on the Benton Facial Recognition Test and measures of executive functioning did not differ between groups or significantly change as a consequence of surgery in either group.

Shaw et al. (2007) found that there were no significant differences in scores pre or post surgery in Happé's Strange Stories or for detection of faux pas or in either RTLE or LTLE, nor was there a significant change in scores from pre to post surgery in relation to these two groups. When RTLE and LTLE groups were combined there was no significant difference in change scores on either of the ToM measures. Change scores in executive function and ToM tasks were not correlated with each other so changes in executive function were unrelated to changes in ToM performance. Prior to surgery patients with LTLE were impaired in recognising facial expressions depicting fear but improved after surgery which the authors suggest may be accounted for by removing a hyper-excitabile amygdala. . Another explanation they consider is that epileptogenic tissue in the LTLE may inhibit the emotion recognition network prior to surgery which

would account for improvements post surgery, such improvements have occurred in executive processes after anterior temporal lobectomy (Hermann & Sedenberg, 1995; Martin et al., 2000).

Whilst differences in ToM performance pre and post surgery were not evident, the small sample size in the study will have reduced statistical power to detect changes in ToM performance. The ToM tests used in this study may not be sensitive enough to detect change in performance pre and post operatively or differences between right and left TLE in such a small sample. These tests have also not demonstrated functional activation in the amygdala in past research. Past research has shown that bilateral damage is typically found with ToM impairment in adults (Stone et al., 2003), yet participants only had unilateral damage in this study. Memory and learning effects of the tasks may have improved performance after surgery, as the same tests were administered pre and post surgery. Such effects are not controlled for and are hard to quantify, this could be overcome if different tasks were matched in terms of the amount of socio-cognitive processing involved

### *Schilbach et al. (2007)*

Ten right handed females with LTLE were recruited from an epilepsy monitoring unit and an outpatient clinic. Two participants had MTS (mesial temporal sclerosis); there were no detectable structural abnormalities in the other eight. All had a history of complex partial seizures. Ten right handed healthy volunteers with no neurological or psychiatric history were also recruited. All participants included in the study had an MMSE (Mini Mental State Examination) score within the normal range and were



assessed for depression by Beck Depression Inventory (BDI). Two of the epilepsy participants had scores of 16 or above so all further analysis took account of this.

Participants were presented with video scenarios involving virtual reality characters depicting facial expressions. The expressions were either socially relevant and the character was intending to initiate interpersonal relations with either the participant or another virtual character. Alternatively the facial expressions were arbitrary and socially irrelevant. Self involvement in the scenarios was also manipulated such that the characters either looked at the participant or looked away. Participants were required to answer two questions after presentation of each video scenario (there were 100 trials), which evaluated their perception of self involvement and required them to rate how much social interaction was present in each scenario using a four point Likert scale.

The TLE sample group all illustrated the same trend in how they rated social intent despite the different type and number of AEDs that were being taken across the sample. They rated a scenario as more socially relevant if they were more involved in the interaction, this trend was also apparent even if the facial expression was arbitrary. The authors suggest that over reacting to self involvement in social interactions may be a way that people with TLE compensate for their socio cognitive difficulties in interpreting facial expressions and the mental states (intention) of others.

One criticism of this study is that the sample was biased towards females, that the sample was small and that people with LTLE were tested. Another weakness is that the study did not evaluate the impact of epilepsy related variables (age at onset, seizure type or seizure frequency) on social cognition.

*Schacher et al. (2006)*

Schacher et al. (2006) investigated the ability to detect faux pas in 27 people with MTLE of which 16 were investigated prior to surgical resection, and 11 after anterior temporal lobectomy or selective amygdalohippocamectomy (12-18 months after surgery). They also recruited 27 people who had extra mesiotemporal epilepsy but not FLE (extra MTLE) and 12 healthy controls with no history of psychiatric or neurological disorder. PWE were recruited from an in patient epilepsy centre in Switzerland and had refractory epilepsy. MTLE and unilateral seizure onset was determined by EEG and MRI. Testing on PWE and healthy controls took place in hospital, all PWE including post surgical MTLE were being treated with AEDs.

Participants were administered with a shortened version of the faux pas test by Stone et al., (2003). Participants read the story themselves whilst having a copy of the story in front of them to reduce the working memory demands of the task. Participants were asked four questions, three questions assessed inferences about affective and cognitive mental states and one question was a control question to assess that the story had been comprehended correctly. All participants in the study had intact language comprehension as assessed by the Chapman-Cook test (Chapman, 1923) and correct answers on the faux pas comprehension question and IQ were also measured. Participants were required to understand the faux pas correctly, infer the mental state and emotions of another person.

The MTLE (pre and post op) were significantly impaired on faux pas in relation to the extra MTLE group or healthy controls, task performance between these two groups was comparable. No differences between the pre op MTLE and post op MTLE were established. In the MTLE group as a whole (R= 14 and L=13) people with right sided



onset performed significantly worse than those with a left sided onset. There was an interaction between gender and side of onset such that male patients with LMTLE performed better than females with LMTLE and males with RMTLE. Beyond the above noted epilepsy-related differences, faux pas performance was not associated with IQ, age, age at seizure onset or duration of epilepsy. IQ may have mediated faux pas performance in healthy controls as they showed a trend for higher faux pas scores when IQ was a covariate in the analysis, this mediating effect was not apparent when comparing performance in the MTLE and extra MTLE group on faux pas. Schacher et al. (2006) argue that this refutes the idea that a general cognitive deficit impairs ToM performance and supports Frith and Frith (2003) proposal that 'ToM abilities are largely autonomous of other cognitive functions' p. 2144. Impairments in faux pas can not be attributed to language or comprehension as these factors were controlled in the study. The authors suggest that the effect of AEDs is unlikely to account for the observed deficits as the extra MTLE who performed in a similar manner to healthy controls had refractory epilepsy and were receiving AED therapy.

The authors conclude that MTLE plays a role in higher-order aspects of social cognition. They emphasise the role of the amygdala in emotional and socio-cognitive functioning and highlight that this is often impaired in MTLE. MTLE may impact on socio-cognitive skills by disrupting the integration of temporolimbic and frontal systems which have been implicated in social cognitive functioning.

This study would have benefited by recruiting a FLE group to establish if appreciation of faux pas was impaired in this sample in line with evidence in the literature which implicates the importance of the frontal lobes in social cognition (see Chapter 4). This

would also help establish if people with MTLE has a specific deficit in appreciating faux pas.

### ***5.3 The Right Hemisphere***

#### ***5.3.1 ToM and emotion recognition in the right hemisphere***

##### ***Fournier, Claverley, Wagner, Poock and Crossley (2008)***

Fournier et al. (2008) investigated social cognition in two patients, one who underwent a right hemispherectomy (S.M.) and one who underwent a left hemispherectomy (J.H.) to treat intractable epilepsy. Both participants underwent surgery in adolescence and were assessed 30 years after surgery on emotion recognition, formation of social inferences and advanced socio- cognitive judgements. Their performance was compared to normative data collected on the measures.

J.H. (LH) no longer experienced seizures after surgery and was no longer on AED therapy, post surgical recovery was excellent. S.M. (RH) still experienced complex partial seizures after surgery, though these were considerably reduced, and he was still taking AEDs. Both participants experienced hemianopsia and hemiplegia on the contralateral side to surgery.

The two participants were assessed on a variety of background measures to examine IQ, executive functioning, language, construction skills and visual perception. FSIQ scores were comparable and differences in performance on typically RH tasks (attention and visuospatial processing) and LH tasks (verbal working memory, speeded



verbal processing) were as expected. The MMSE Examination was also administered and performance was in the normal range for both participants.

The Awareness of Social Inference Task (TASITS) which assesses ToM judgements, emotion recognition and how people make social inferences in daily life was used to assess social cognition (McDonald, Flanagan, Rollins and Kinch, 2003). What follows is a detailed explanation of the test as this is relevant to further discussion in Chapter 11 (general discussion). This test uses video recordings in which actors engage in scenes of everyday life. The first part of the test (Emotion Evaluation test) requires participants to recognise common emotional expressions in 28 short video vignettes. Happy, sad, disgust, anger, fear, surprise or neutral expressions are demonstrated on 4 separate occasions that are randomly administered. Participants have to choose one of the seven emotions and match them to each of the vignettes.

The second and third part of the TASITS involves identifying whether conversations between individuals are sincere; such that conversations can be understood in terms of their literal meaning or that they are counterfactual, where there are discrepancies in the literal content of the conversation and its context. The counterfactual vignettes involve the participant having to infer the underlying meaning of the conversational exchange. In the second part of the test (Social Inference – Minimal) the participant must detect sincere or sarcastic exchanges in 15 vignettes. To detect sarcasm involves appreciating prosody, body language and facial expressions and participants are asked four questions after each vignette. These questions assess participant's ability to detect what the protagonist was thinking, doing, saying and feeling. Two of the questions probe what the protagonist was intending and feeling, these assess both first and second order levels of ToM.

In the third part of the test (Social – Inference Minimal) 16 short vignettes are administered with similar content to part two of the test, the only difference is that participants are provided with extra information regarding the conversational exchange before and after the video. Participants are expected to comprehend the true nature of the exchange whilst integrating the additional information provided to them so that they can determine the protagonist's intention.

The probe questions asked after the video assess appreciation of deception (lies) and sarcasm. Both participants were also administered the Reading the Mind in the Eyes test (Baron-Cohen et al. 2001).

The participant who underwent RH (S.M.) surgery was impaired in recognising negative emotional expressions and surprise, in appreciation of sarcasm, lies, detecting others intentions and their emotions. The participant who underwent (J.H.) LH surgery was competent in interpersonal situations and was mildly impaired when recognising emotional disgust or anger but performed well on parts two and three of the TASITS.

Fournier et al. (2008) argue that their findings emphasise the importance of the RH in reasoning and social cognition:

‘taken together, the results suggest a strong role of the right hemisphere in social cognition and processing of information related to the understanding of basic emotional expressions, attributions of the beliefs and intentions of others, as well as the meaning of specific types of conversational inferences’ (p. 468).

This study was unique in that it is the first of its kind to establish the long term effects of right and left hemispherectomy on social cognition with reference to ToM. Another strength of the study is that it utilised an ecologically valid measure of ToM and



emotion recognition by using the TASITS. The main criticism is that ToM was not evaluated prior to surgery so the observed impairments cannot be conclusively related to the surgery itself. S.M. who underwent RH surgery was still experiencing seizures and being treated by AEDs at the time of testing which may have accounted for some of the impairments observed.

As MMSE performance was normal and examines general neurocognitive functions the authors argue that the observed socio-cognitive impairments were not specific to any modality (visual, motor or auditory). Attention deficits and general cognitive impairment could account for the impairment in appreciating sarcasm and the intentions of the protagonist observed in S.M. (RH). Fourier et al. (2008) argue that this is unlikely as both the sincere and sarcastic vignettes did not differ greatly in terms of attentional demands. Also J.H. (LH) demonstrated deficits on verbal working memory but showed no difficulty in correctly identifying the true nature of social exchange in the vignettes, her performance on the comprehension questions were comparable to that of healthy controls.

As this research adopted a case study approach this study did not evaluate the impact of epilepsy related variables (AED therapy, duration of epilepsy, seizure type or seizure frequency) on social cognition. Consequently the findings cannot be generalised to the wider epilepsy population.

## ***5.4 Frontal Lobe Epilepsy***

### ***5.4.1 ToM and emotion recognition***

#### ***Farrant et al. (2005)***

Farrant et al. (2005) investigated facial emotion recognition and ToM in 14 people with FLE (8 LFLE, 5 RFLE and 1 Bilateral) and 14 healthy controls. The FLE group were recruited from a specialist epilepsy unit and were being assessed for surgery. Mean age of onset was 11.8 years (SD=8.55). Groups did not differ significantly on age, gender ratio, years of education, premorbid IQ or long term memory. Executive functioning was assessed using the Trail Making Task (Reitan & Wolfson, 1993) to assess sequencing (part A) and mental flexibility (part B). The FLE were significantly slower on the sequencing aspect of this task. The Hayling and Brixton tests (Burgess & Shallice, 1996a, 1996b) were administered and the FLE were significantly slower on the section 1 of the Hayling Test though there were no group differences on response inhibition, though FLE did make more mistakes on the task. The FLE were significantly impaired in relation to controls on a verbal fluency task.

ToM was measured using Happé's Strange Stories (Happé, Malhali & Checkley, 2001; Happé, Brownell & Winner, 1999). The ToM stories all involved human interaction where double bluff, mistakes, white lies or persuasion were evident (with two examples or each of these), participants were asked a question which required them to make an inference about the mental states of people in the story. Faux pas was assessed using a version of Stone et al. (1998) task. Participants were assessed on their ability to make inferences about affective and cognitive mental states and their comprehension of the stories (as a control measure).



Humour was assessed via a cartoon task which required the participant to infer the mental state of a character in six cartoons (ToM) or to acknowledge a physical anomaly or a violation of a social norm (non ToM) in six cartoons. The memory load of the ToM stories, faux pas and humour tasks was reduced as participants had a copy of the story/cartoon in front of them whilst being asked questions. The Reading the Mind in the Eyes Task by Baron-Cohen et al. (2001) was administered where participants had to match correct emotions to the photographs displayed. Recognition of facial emotion was assessed using Ekman and Friesen (1976) pictures of facial emotion depicting the following emotions; sad, happy, surprise, anger, fear, disgust. Twelve pictures were displayed, one male and female picture for each emotion and participants were required to match the correct verbal labels to the emotions displayed.

FLE did not show deficits on the story task or appreciation of faux pas though they did illustrate a trend towards impairment. FLE were impaired in both the mental state and physical state cartoons, on emotion recognition and perception of eye gaze expression. ToM was intact but appreciation of humour and emotional expression was not. Mild impairments were observed except in the appreciation of emotion expression where impairment was substantial. These impairments were in relation to recognising sadness, anger and fear. Verbal second order ToM was intact in the FLE group (as examined in the story task). Age of onset was not correlated with any of the socio-cognitive measures. Executive functions were not correlated with socio-cognitive tasks in the FLE group but verbal fluency was correlated with the eyes task and the non ToM cartoons in the control group.

It is unlikely that the observed deficits in social cognition can be attributed to memory or IQ or deficits in executive functioning in the FLE group. As has been supported in

studies of cognitive dysfunction in FLE the sample in this study exhibited specific as opposed to general deficits in social cognition. This may be because some tests are more sensitive to detecting impairment than others, though it should be noted that a large sample may have detected more impairments across the tasks. Specific areas in the FL may support different aspects of social cognition, consequently deficits in performance may reflect those areas of damage in the brain in the FLE group. This is the main criticism of the study as it did not report any analysis based on whether people had RFLE or LFLE, due to the small sample size of the groups. The exact site of seizure foci could only be established in 9 of the 14 FLE group (6 with medial and 3 with dorsolateral abnormalities), there were no patients with orbitofrontal involvement. Consequently whether different regions of damage within the FL are associated with specific impairments in the social cognition could not be fully explored. The study did not recruit people with MTLE to compare performance on tests of social cognition in relation to FLE.

This study does not provide the reader with any background about seizure frequency, seizure type, duration of epilepsy or AED treatment in the FLE group, all of which could impact on functioning. Analysis has not been considered in light of these epilepsy related variables.

#### ***5.4.2 ToM and pragmatic language***

##### ***Corcoran, Harris and Thompson (cited in Corcoran, 2000) Pilot study***

A small scale pilot study (unpublished) conducted in the Chalfont Centre for Epilepsy in 1999 by Corcoran, Harris and Thompson (cited in Corcoran, 2000) compared the



performance of epilepsy patients on their appreciation of veiled intention in a Hinting Task (Corcoran, Mercer & Frith, 1995), a ToM measure. Five patients with right frontal or right fronto-temporal foci, 3 with left frontal and left fronto-temporal foci, 3 with bilateral frontal foci and 23 normal controls were tested. Despite the small sample size differences were found between the groups on performance of the Hinting Task. The right fronto-temporal group appeared to perform worse than normal controls on the Hinting Task independent of group differences in IQ. This study had a very small sample size and consequently hinting ability was not evaluated in relation to any epilepsy related variables.

This pilot study was prominent in inspiring the current thesis.

### ***5.5 Methodological difficulties of past research***

In critically evaluating their study Farrant et al. (2005) suggest that a larger sample is needed to enable seizure foci in FLE and social cognition to be fully explored. People with FLE need to be compared with other focal epilepsies particularly MTLE to establish if there are specific socio cognitive deficits observed in FLE. Executive impairments have been illustrated in both FLE and TLE, so it is important to determine the nature of socio-cognitive dysfunction in epilepsy. Farrant et al. (2005) also highlight that a larger sample would enable comparison of performance between right and left FLE.

Most of the studies are cross sectional in that they either investigate social cognition post surgery or pre surgery. Consequently these studies cannot differentiate between

social cognitive deficits as a consequence of surgery or the pre-existing epilepsy syndrome (Kirsch, 2006).

One main criticism with all the studies cited in this review is that no single study has compared people with TLE and FLE, so none of the studies can conclusively determine whether socio-cognitive deficits are characteristic of TLE and/or FLE.

Studies that have attempted to investigate the impact of side of seizure onset can all be criticised for having small sample sizes and consequently findings cannot be generalised or the power to detect an effect is greatly reduced. None of the studies reviewed recruited a group of patients with IGE who could act as a clinical control group to help to establish the impact of focal epilepsy on these skills. The added advantage of using an IGE group is that they have active epilepsy, take AEDs and will also be affected by epilepsy related variables such as seizure frequency, seizure type, age of onset and duration. Another major criticism of research in this area is that none of the studies that have investigated social cognition in FLE have recruited a frontal head injured group without epilepsy in order to determine the impact of FLE on socio-cognitive functioning. None of the studies evaluated socio-cognitive performance in relation to social functioning in PWE.

There is a general lack of research investigating social cognition in epilepsy as highlighted in the literature (Schacher et al., 2006; Kirsch, 2006). Research that has been conducted has not utilised designs that can adequately explore socio-cognitive functioning in focal epilepsy. The impact that socio-cognitive skills have in relation to everyday social functioning in PWE needs to be investigated (Walpole et al., 2008; Schacher et al., 2006; Farrant et al., 2005). Such research could provide valuable



insight into the socio-cognitive deficits associated with epilepsy and may ultimately improve social functioning in PWE.

### ***5.6 Rationale for the thesis***

In light of the methodological problems highlighted in previous studies, this thesis aimed to explore socio-cognitive functioning in people with seizure foci in the RF, LF, RT, LT lobes. To overcome previous sample size difficulties the minimum number of people within each group was 11. As well as a healthy control group, this study recruited an IGE and FHI group to establish the impact that focal epilepsy and in particular FLE have on these skills. Social cognition has not been fully explored in FLE (Farrant et al. (2005). Information was also collected on relevant epilepsy related variables (age at onset, AEDs, seizure severity and duration of epilepsy) in relation to the sample. The thesis also aimed to establish the impact that socio-cognitive functioning may have on every day life of PWE by assessing social cognitive performance in relation to perceived impact of epilepsy (Study 4).

Studies 1 and 2 explore two different paradigms that assess ToM skills, appreciation of false belief and deception in ToM stories and understanding veiled intentions in a Hinting Task. Study 3 assesses social conditional reasoning in these groups. Past research has suggested that ToM and social conditional reasoning are related (Corcoran & Frith, 2005; Ermer et al., 2006). Study 4 attempts to draw together the findings of the first three studies and compare task performance in relation to the perceived impact of epilepsy, to establish how these skills may be related to social functioning in real life.

### ***5.7 Aims of the thesis***

- The thesis aims to investigate whether some of the social difficulties that people with epilepsy report may be a consequence of problems with social cognition including ToM.
- The thesis aims to see whether studying social cognition in focal epilepsy can enhance our understanding of the organic basis of social cognitive abilities in the normal population.



*Table 10: A summary of studies which have investigated social cognition, emotional intelligence and emotion recognition in epilepsy*

AUTHORS (S)	FOCUS OF THE INVESTIGATION	FINDINGS	PARTICIPANTS
Walpole, Isaac and Reynnders (2008)	Emotional intelligence in TLE	TLE showed impairments in EI and facial expressions. They had higher levels of psychological distress which was negatively related to EI.	16 TLE (7 Left, 9 Right) 14 HC
Fournier et al. (2008)	Social Cognition 30 years after hemispherectomy for intractable epilepsy.	Assessed emotion recognition, formation of social inferences and advanced socio- cognitive judgements using the TASITS.  The participant who underwent RH surgery was impaired in recognising negative emotional expressions appreciation of sarcasm, lies and detecting others intentions.	1 right-sided hemispherectomy 1 left-sided hemispherectomy
Shaw et al. (2007)	Social Cognition in TLE before and after surgery as tested by facial emotion recognition and ToM tasks.	Social cognition was assessed using ToM stories, appreciation of faux pas and recognition of pictures of facial emotion.  TLE (R or L) were not impaired on ToM tasks pre or post operatively. LTLE improved their performance in being able to recognise fearful facial expressions post surgery.	19 TLE (10 right, 9 Left, pre and post op) 19 HC
Schilbach et al. (2007)	Social cognition in TLE	Animations of dynamic virtual characters displaying socially relevant or irrelevant facial expressions were used. Characters either looked at the participant or looked away so that self involvement was manipulated.  TLE patients rating of the communicative intent of the	10 Females with LTLE (right handed)  10 HC (right handed)

Schacher et al. (2006)	Social Cognition in MTLE before and after surgery	characters was linked to self involvement but HC was not.  Appreciation of faux pas was assessed. MTLE were impaired both pre and post operatively on faux pas in relation to extra mesiotemporal and healthy control groups who's performance was comparable.  Appreciation of faux pas was not associated with IQ, age, age at seizure onset or duration of epilepsy.	27 MTLE (16 pre op and 11 post op)  27 Extra mesio temporal epilepsy (except FLE)  12 HC
Farrant et al. (2005)	Social Cognition in FLE as tested by facial emotion recognition and ToM tasks.	ToM stories and faux pas were used to assess ToM.  FLE were not impaired on the story test and exhibited a mild impairment on faux pas. They were impaired on humour appreciation in both mental state and physical state cartoons and on recognition of facial emotion and perception of eye gaze perception.	14 FLE (8 Left and 5 Right)  14 HC
Corcoran (2000) unpublished	Theory of mind in FLE	A Hinting Task was used to assess ToM. Participants were asked to make inferences based on veiled intentions in the Hinting task.  The right fronto-temporal group appeared to perform worse than normal controls on the Hinting Task independent of group differences in IQ	5 RFT, 3 LFT, 3 Bilateral Frontal  23 HC

HC = health controls; MTL = medial temporal lobe epilepsy; FLE = frontal lobe epilepsy; RFT = right fronto-temporal; LFT = left fronto-temporal.



## **Chapter 6: General Method**

### ***Design***

The study is a cross-section group design exploring a test battery of measures in the following epilepsy experimental groups; people with seizure foci in the right (RF) and left prefrontal (LF) cortex, the right (RT) and left temporal (LT) lobes and a primary generalised epilepsy group (IGE) with no seizure foci. In addition there were two non-epilepsy groups, a group of patients with injury to the pre frontal cortex who did not have epilepsy (FHI) and a normal control group (NC).

Epileptic discharges cause diffuse dysfunction as noted by Engel (1989) ‘large areas of the brain are usually involved in epileptiform dysfunction, even when clinical symptoms appear well localised’ p1. Thus a primary generalised group with no seizure foci were included in the study to control for diffuse effects of epilepsy on these skills. Similarly, to control for the impact of structural brain injury a head injured group has been included.

### ***Participants***

Patients with epilepsy were included in the study if they were between the ages of 18 and 65 years and had been referred to a tertiary referral unit for treatment of their epilepsy. All patients spoke fluent English and were initially approached by letter (refer to appendix 1). They gave written consent to take part in the study after reading a participant information sheet informing them about the study (refer to appendix 2 for consent form and appendix 3 for participant information sheet).

Epilepsy patients were excluded from the study if they had undergone any type of surgery to alleviate the symptoms of epilepsy, had a significant psychiatric history or other neurological condition, or history of alcohol or drug abuse. Patients were also excluded if they were being treated for anxiety or depression at the time of testing and to reduce the effects of post ictal confusion, they were only tested if they have been seizure free for 12 hours. Eleven patients with epilepsy were tested and then later excluded from the study because the results of further diagnostic investigations meant that their epilepsy was not focal in origin (e.g. bilateral) or because their diagnosis was inconclusive.

Suitable epilepsy patients for the study were often candidates for epilepsy surgery and their seizure foci were identified by EEG, MRI, videotelemetry, sodium amytal testing and neuropsychological evaluation. The brain injured patients were recruited from a rehabilitation unit. All of these patients had been involved in road traffic accidents which had resulted in frontal lobe damage. No lateralising information was recorded in the case history of such patients. Patients were included in the study if they had no significant psychiatric history, no history of epilepsy or other neurological condition and no history of alcohol or drug abuse. They also were not included if they were being treated for anxiety or depression at the time of testing. Normal participants were gathered from the various work and social environments of the experimenter.

The demographic characteristics of the sample (N=95) can be seen in Table 1. In order to establish whether the groups differed significantly on any of the background measures, ANOVA was conducted with Experimental Group between participants and Age, Estimated IQ, Medication, Age of Onset, Immediate Story Recall and Duration of



Illness as dependent variables. A chi-square analysis was performed to see if there were any significant differences between the groups for Gender and Education.

These demographic variables were selected and as appropriate taken account of in the analyses as they have been shown to have an impact on neuropsychological performance. Gender and education have been implicated in a number of studies (Heaton, Ryan, Grant & Matthews, 1996., Reitan & Wolfson, 1995., Spreen & Strauss, 1998). In addition to these the influence of age and IQ has also been documented (Leckliter & Matarazzo, 1989). As noted in previous Chapters of this thesis, seizure related variables such as seizure frequency (Mandelbaum & Burack, 1997); age of onset and number and type of AED's (Kent et al., 2006; Meador, Gilliam, Kanner & Pellock, 2001; Upton & Thompson, 1997) have also been highlighted in the literature as potentially affecting cognitive and affective outcomes in PWE.

Chi-squared analysis revealed that there were no significant differences between the groups for gender;  $\chi^2$  (DF=6, N=95) = 12.07;  $p > 0.05$ , though the outcome was close to significance ( $p = 0.06$ ). It is worthy of note that although gender is almost equally distributed across the whole sample (48m, 47f) it is not equally distributed across the experimental groups. This is particularly apparent in the FHI group which is predominantly male (11m, 1f). The gender composition of this group is not unexpected since more males have road traffic accidents than females and such accidents are the most common reason for frontal head injury. Chi-squared analysis revealed that Level of Education differed significantly between the groups,  $\chi^2$  (DF=6, N=95) = 19.88;  $p < 0.005$ . Compared to the other experimental (clinical) groups, NC clearly had a higher percentage (83.3%) of people with A' Levels or above. After NC, IGE had the

highest percentage of people with A' levels or above (45.5%) and the RT group had the lowest percentage (16.7%).

The IQ measured in the sample was comparable with other studies conducted in this area. For example, Farrant et al's (2005) sample of people with FLE had an overall average of score of 96.6. Similarly, Milner (1975) conducted a study of 73 FLE patients and the average IQ as measured by the WAIS was 95 for RF and 108 for LF patients.

There was no significant difference between the groups for mean Age,  $F(6,88) = 1.20$ ,  $p > 0.05$ , or IQ,  $F(6,88) = 1.67$ ,  $p > 0.05$ . There was a significant difference between the groups for Immediate Story Recall:  $F(6,88) = 5.76$ ,  $p < 0.001$ ; post hoc analysis revealed that all groups had poorer recall than NC. All other pairwise comparisons were not significant. There was no significant difference between the epilepsy groups for mean number of anticonvulsants  $F(4,60) = 1.22$ ,  $p > 0.05$ . There was no significant difference between the epilepsy and head injured groups for mean age of onset  $F(5,69) = 0.39$ ,  $p > 0.05$  or duration of illness  $F(5,69) = 0.43$ ,  $p > 0.05$ .



**Table 11: Background variables including age, gender, education, intelligence, age of onset, duration of illness, number of AEDs and immediate story recall by Experimental Group.**

	Normal sample (NC)	Right Frontal (RF)	Left Frontal (LF)	Frontal Head Injury (FHI)	Right Temporal (RT)	Left Temporal (LT)	IGE	P level
Number	18	14	13	12	12	15	11	
Sex M:F ratio	8:10	6:8	7:6	11:1	3:9	8:7	5:6	48m, 47f Ns
Mean Age (years)	29.72 (13.7)	29.9 (11.5)	37.0 (11.9)	28.8 (11.9)	34.2 (10.7)	35.5 (10.7)	36.0 (13.4)	Ns
Education.								*
‘A’ levels or above	83.3%	21.4%	38.5%	25%	16.7%	40.0%	45.5%	p<0.005
Estimated IQ	104.7 (8.5)	96.9 (13.4)	101.2 (11.6)	93.8 (9.7)	95.3 (20.3)	94.9 (10.0)	101.8 (10.9)	Ns
Mean age of onset	n/a	14.7 (12.6)	20.9 (18.1)	16.9 (10.7)	15.9 (10.8)	18.2 (12.4)	15.6 (10.9)	Ns
Mean Duration (years)	n/a	15.6 (8.4)	16.1 (13.5)	13.6 (11.8)	18.3 (11.4)	17.2 (12.0)	20.4 (13.6)	Ns
Mean no of AEDs	n/a	2.4 (0.9)	2.1 (0.8)	N/A	2.2 (1.0)	1.7 (0.7)	2.1 (0.8)	Ns
Immediate Story Recall	30.5 (10.8)	16.3 (8.1)	19.9 (9.4)	15.3 (10.1)	18.3 (9.3)	13.4 (7.7)	18.3 (10.9)	** p<0.001

AED = anti epileptic drugs.

*Table 12: Aetiology of epilepsy by patient group (N=65).*

	Right Frontal RF (N=14)	Left Frontal LF (N=13)	Right Temporal RT (N=12)	Left Temporal LT (N=15)	IGE (N=11)	Total & % of overall sample
Not known	4	3	6	6	5	23 (35.4%)
Tumour (glioma/astrocytoma)	4	4	1			9 (13.8%)
Cyst		1				1 (1.5%)
Cerebrovascular	1	3				4 (6.2%)
Birth trauma/ febrile convulsions	2	1	3	5		10 (15.4%)
Cerebral insult	1	1	2	3		8 (12.3%)
Cortical dygenesis	2					2 (3.1%)
Stressful life event						2 (3.1%)
Juvenile myoclonic epilepsy (JME)					6	6 (9.2%)

\*Cortical dygenesis refers to abnormal development/malformation of the cerebral cortex.

Inspection of Table 2 reveals that for quite a considerable number of patients aetiology was unknown (23). Nine patients had epilepsy as a consequence of tumour (8 FLE and 1 RT). Birth trauma and cerebral insult were the next most common forms of aetiology (18). Six generalised epilepsy patients had juvenile myoclonic epilepsy (JME). Four patients had a cerebrovascular aetiology. Of these two had incidences of infarction, one of an intracerebral haematoma and one an arterial malformation. Two patients (female) had a stressful life event which triggered their seizures, these were reported as sexual abuse in childhood. One other female (RF) patient with a tumour also reported that she had febrile seizures which were triggered by sexual abuse. Her seizures stopped and reoccurred in adulthood. This patient's aetiology was classified under tumour.



**Table 13: Seizure frequency, the number of seizures in the last 12 months by patient group (N=65).**

	Right Frontal RF (N=14)	Left Frontal LF (N=13)	Right Temporal RT (N=12)	Left Temporal LT (N=15)	IGE (N=11)	TOTAL
0-1		1			2	3
2-9		1			1	2
10-99	5	6	4	9	8	31
100+	9	5	8	6		29

Information in relation to current seizure frequency was poor and not always current. This was especially so for those patients who had not attended the clinic for some time. In view of these limitations it was decided to rely on the information given by patients. A similar approach was adopted in the past by Jacoby et al (1996). In an attempt to improve the accuracy of the data, the information was also verified with a family member (or the person living with the PWE).

As can be seen in Table 3 the majority of patients (60) experienced more than nine seizures per month with 31 people having between 10-99 seizures and 29 having over 100 seizures in the last twelve months. This pattern of seizure activity is likely to be due to the fact that all patients were recruited from a tertiary referral unit and have intractable epilepsy. All focal epilepsy patients in the study (all except IGE) were candidates for surgery, so high seizure activity is symptomatic of this population. The RF group had the largest number of patients experiencing over 100 seizures and the LT group had the largest number of people experiencing between 10-99 seizures in the past twelve months.

**Table 14: Seizure type by patient group (N=65).**

	Right Frontal RF (N=14)	Left Frontal LF (N=13)	Right Temporal RT (N=12)	Left Temporal LT (N=15)	IGE (N=11)	TOTAL
Complex partial only	4	3	4	6		17
Simple/complex partial/secondary generalised	10	10	8	9		37
Tonic-clonic only					5	5
Tonic-clonic and other generalised					6	6

The pattern of seizure type by patient group (Table 4) is as expected with focal epilepsy patients (RF,LF, LT and RT) experiencing complex partial seizures in isolation or in conjunction with simple partial seizures or secondary generalised seizures. Patients with IGE experience either tonic clonic seizures in isolation or with other generalised seizures such as absences or myoclonus.



*Table 15: AED use by patient group (N=65).*

	Right Frontal RF (N=14)	Left Frontal LF (N=13)	Right Temporal RT (N=12)	Left Temporal LT (N=15)	IGE (N=11)	TOTAL
Carbamazepine	8	7	6	10	3	32
Clobazam	4	5	1	6	2	18
Gabapentin	2	3		2		7
Lamotrigine	2	5	5	2	3	19
Levetiracetam	1	1	1	2	1	6
Phenobarbitone			1		1	2
Phenytoin	4	5				9
Sodium Valporate	7	1	3	2	5	18
Topiramate	3	3	3	4	4	17
Vigabatrim				1		1
<b>MONOTHERAPY</b>	2	3	4	3	0	12
<b>POLYTHERAPY</b>	12	10	8	12	11	53

Inspection of Table 15 reveals that the majority of patients were being treated with polytherapy (53) with carbamazapine being the most prescribed AED across all patient groups.

*Materials*

All participants were administered with a test battery of measures assessing various aspects of social reasoning and social cognition. This has yielded four separate studies, which address the specific research questions which are the focus of this thesis.

The Quick Test by Ammons & Ammons (1962) was used to measure IQ, (see Appendix 4). This test involves matching a word with an appropriate picture.

Participants match fifty words in each case choosing from among four possible pictures. It is a vocabulary based IQ test which gives a reliable estimate of current general ability (Frith & Corcoran, 1996; Corcoran & Frith, 2005) which converts to a score from the Weschler Adult Intelligence Scale (Frith & Corcoran, 1996; Weschler, 1955). This is a useful test to use with clinical samples because it only takes about 10-15 minutes to administer. The total score on this task is converted into a WAIS full scale IQ equivalent (refer to Appendix 5). This test measures word-knowledge as well as more 'fluid' contextual analysis (Corcoran & Frith, 2005). The Quick Test has been shown to be a valid measure of IQ and a reliable estimate of the WAIS (e.g., Simon, 1995; Doss, Head, Blackburn, Robertson, 1986). It has also been used to measure IQ in a number of studies that have assessed ToM in non clinical populations (Pickup, 2006); schizophrenia (Corcoran & Frith, 1996; Marjoram et al., 2005a; Marjoram et al., 2005b) and in people with right hemisphere damage (Happé et al, 1999).

Immediate Story Recall was assessed using a sub test from the Adult Memory and Information Processing Battery (Coughlan & Hollows, 1985), (refer to Appendix 6). A story is read out to the participant who is asked to recall as much information as possible both immediately and after a delay of 20 minutes. The story is divided into 30 sections, see below. It was considered important to include this measure in the thesis as second order ToM stories (Study 1) and the conditional reasoning task (Study 3) load heavily on narrative memory. This measure has been shown to be a reliable measure of recall ability in studies that have used the same conditional reasoning task used in Study 3 (Corcoran & Frith, 2005) the same ToM stories task used in Study 1 (Frith & Corcoran, 1996) and The Hinting Task used in Study 2 (Corcoran & Frith, 1995).



### ***Immediate Story Recall***

Mr. Peter / William / who died last month / has left two hundred thousand pounds / to a charity that provides / seaside outings / for the children / of refugees. / His younger / brother, / who lives in Canada, / will inherit / his house, / his yacht / and his Rolls Royce car. /

Mr. Williams came from a poor family / but he was determined to do well. / He worked extremely hard / and everyone liked him. / His first job / was as a butcher's boy / but he earned extra money / by doing night work / in a laundry. / When he was thirty / he bought a van / and started a removals business. / However, he eventually made his fortune / selling paintings / and antique clocks.

Score (Max 60)

For every section that the participant recalls correctly they score 2, if they imply some of the content in a section they score 1. For example, in the third section of the first paragraph of the above story, if it was stated that Mr William died but the participant failed to indicate that this occurred last month then they would score 1, whereas if they said that he died last month they would score 2. The maximum score on this test is 60. Immediate story recall is measured by the amount of information that is recalled correctly immediately after the story has been read to the participant.

The remaining materials used for each study will be detailed in the chapters that follow as appropriate.

## **6.4 Procedure**

Written consent was obtained from all participants. Tests were administered in the patient's home environment or in the Walton Centre by the same experimenter.

Participants with epilepsy were tested in the presence of a family member or next of kin. Prior to completing any tests, participants were asked what medication they were on, their educational qualifications and occupation and where relevant, the age of onset and duration of their epilepsy and the level of seizure activity in the past twelve months. Their responses were verified against information in their hospital patient records. Participants with epilepsy were then asked to complete an Impact of Epilepsy Scale before any of the test battery was administered. The experimenter administered the battery of tests in exactly the same order to each participant. Details of the materials used will be outlined in the Chapters that follow as relevant to each study. The tests were administered in the following order, the Quick Test (Ammons & Ammons, 1962), Immediate Story Recall, a sub test from the Adult Memory and Information Processing Battery (Coughlan & Hollows, 1985), the Conditional Reasoning Task (Corcoran & Frith 2005), the Hinting Task (Corcoran et al., 1995) and ToM Stories (after Frith and Corcoran, 1996).

## **6.5 Ethics**

This research received ethical approval from Liverpool John Moores University and the South Sefton Research Ethics Committee.



## **Chapter 7**

### **Study 1: Appreciation of false belief and deception in focal epilepsy.**

Social cognition in epilepsy is under explored (Kirsch, 2006; Schacher et al., 2006) despite the apparent deficits in social functioning experienced by PWE (Austin & de Boer, 1997; Baker et al., 1990; Fisher et al., 2000; Jacoby et al., 1996; Mittan, 1986).

Social cognitive neuroscience is a developing area concerned with establishing whether the brain systems that underpin social behaviour are specific to social cognition, as opposed to more general cognitive functioning (Stone, 2005). Assessing patients with focal epilepsy and thus utilising a lesion study design to investigate social cognition, provides a unique opportunity to investigate whether these processes are dissociated and which underlying structures are essential for socio-cognitive skills, such as theory of mind.

The importance of the frontal lobes in mediating social behaviour has been evident by the deficits in social functioning that are apparent in patients with frontal lobe lesions (Harlow, 1993; Eslinger & Damasio, 1985). Such deficits in social competence may well be a consequence of damage to structures that are integral to ToM.

In an endeavour to clarify the neural structures which underpin ToM and the social cognitive deficits in epilepsy, lesion studies have utilised a range of paradigms which assess both cognitive and affective mentalising ability. The most established measure which assesses cognitive ToM, is the ability to appreciate false belief. This is generally assessed at both first and second order levels of intentionality. So far, the evidence of neural structures that underlie the appreciation of false belief and deception is mixed, although most studies implicate anterior regions of the brain (Rowe et al., 2001; Shamay-Tsoory et al., 2005a; Stone et al., 1998).

First and second order false belief impairments have been found in patients with frontal lobe lesions, independent of executive functioning (Rowe et al., 2001). In contrast, Stone et al. (1998) found that people with bilateral orbitofrontal and left dorsolateral lesions were not impaired on these measures, although the bilateral (OFC) group were impaired on a more complex assessment of ToM, appreciation of faux pas. Second order false belief deficits have also been established in people with right hemisphere damage (Happé et al., 1999; Winner et al., 1998). One detailed case study of a patient who had epilepsy prior to surgery illustrated deficits on both first and second order ToM judgements after right hemispherectomy (Fournier et al., 2008).

Shamay-Tsoory et al. (2005a) found that patients with frontal lesions were not impaired on appreciation of false belief although appreciation of irony and faux pas were lateralised to the right frontal lobe, particularly in patients with right ventromedial lesions. The authors suggest that the findings in relation to false belief may be an artefact of the assessment measure, since all participants with VM lesions scored at ceiling on the tasks. An investigation into ToM in FLE found no second order impairments (Farrant et al., 2005). In contrast Mazza et al., (2007) found impaired first and second order belief reasoning in people with right ventro medial PFC lesions.

Another paradigm which has been assessed in lesion studies is the ability to detect deception. Detection of deception has been lateralised to the right frontal lobe (Stuss et al., 2001) although the effects of story comprehension and memory performance in relation to the tasks that were used were not controlled for in this study. Thus these findings are not entirely conclusive. Griffen et al. (2006) found that RH damaged patients were impaired on second order deception, independent of executive functioning whilst first order deception performance was preserved. A number of



lesion studies have supported the importance of the RH in processing deception (Ganis, Kosslyn, Stose, Thompson, Yurgelun-Todd., 2003; Keenan, Rubio, Racioppi, Johnspon & Barnacz, 2005; Malcolm & Paul, 2005) and the right frontal lobe (Stuss et al.,2001).

Lesion studies and studies investigating ToM in PWE have a number of limitations. They have not always included a right frontal group, so the role of the right frontal lobe in relation to appreciation of false belief at first and second order levels cannot be established (Fournier et al.,2008; Happé et al.,1999; Stone et al., 1998; Winner et al., 1998). Often studies include small sample sizes or rely on incorporating bifrontal participants in their analysis of laterality to increase statistical power (Stuss et al.,2001; Shamay Tsoory et al., 2005a). Comprehension and memory have not always been controlled for during testing to ensure that ToM stories are understood, and that people do not fail them due to problems with retaining information (Stuss et al.,2001). In some instances the results obtained may be an artefact of underlying aetiology as patients with a range of underlying aetiologies have been tested within the same study in order to increase sample sizes (Rowe et al., 2001; Stuss et al.,2001; Shamay Tsoory et al., 2005a). Focal temporal lobe samples have not always been included in study designs (Stone et al., 1998; Stuss et al.,2001; Shamay-Tsoory et al.,2005a; Rowe et al., 2001) despite evidence to suggest temporal lobe involvement in social cognition (Fine et al., 2001; Stone, Baron-Cohen, Calder, Keane & Young, 2003). Another difficulty is that ToM deficits may be hard to differentiate in some studies which have incorporated paradigms that assess both cognitive and affective ToM (such as faux pas) (Stone et al., 1998). This limitation is especially pertinent as evidence suggests that these processes may well be dissociated (Blair & Cipolotti, 2000; Shamay-Tsoory et al., 2005a).

Studies which have investigated ToM in epilepsy have generally been conducted on small samples, and have not included participants with both FLE and TLE in their designs so that laterality or involvement of the frontal and temporal lobes in ToM processes can not be determined (Corcoran et al., 2000; Farrant et al., 2005; Fournier et al., 2008; Schacher et al., 2006; Shaw et al., 2007; Schilbach et al., 2007). None of these studies have included patients with IGE who can act as a clinical control group in order to isolate the impact of focal epilepsy on ToM skills. The IGE group also take AEDs and will be affected by relevant seizure related variables (duration of illness, age of onset, etc).

### ***7.1 Rationale/Aims and Objectives***

The present study aims to overcome some of the methodological limitations of past research and utilises one of the most established and recognised assessments of cognitive ToM, a test of false belief and deception at first and second order levels of intentionality. Epistemic states and especially false belief provide the best evidence of mentalising ability (Astington, 2001; Dennett, 1978). This study aims to assess performance on ToM (appreciation of false belief and deception) in relation to epileptic seizure foci and lesion site in order to establish the organic base of ToM abilities and to enhance our understanding of social cognition in epilepsy. Whilst past lesion studies have mostly focused on assessing ToM in either the frontal or temporal lobes the present study will attempt to establish laterality in task performance by assessing right and left frontal and temporal lobe PWE. The design of the study will also incorporate an IGE group to enable a thorough investigation of the impact that



focal epilepsy has on appreciation of false belief and deception (ToM) and to factor out the cognitive side effects of AED's and seizure related variables on the measures used. As well as assessing the impact of epilepsy per se, any artefact of underlying aetiology will be accounted for in the design by incorporating an IGE group and a FHI group without epilepsy.

Given the existing research evidence which has implicated the importance of the right hemisphere (Fournier et al., 2008; Ganis et al., 2003; Griffin et al., 2006; Happé et al., 1999; Keenan et al., 2005; Malcolm & Paul, 2005; Winner et al., 1998) and particularly the right frontal lobe (Shamay-Tsoory et al., 2005; Stuss et al., 2001) to processing false belief and deception (first and second order) the following prediction is being tested:

***Hypothesis 1:*** It is predicted that relative to the other clinical groups, the RF group will under perform on ToM stories.

In view of the general cognitive deficits that are associated with epilepsy (see section 3.1 for a review):

***Hypothesis 2:*** It is predicted that all clinical groups will perform worse than normal controls on ToM stories.

In order to test these hypotheses Helmert contrasts were performed on the data.

## **7.2 Method**

### **7.2.1 Design**

Experimental group was a between participants independent variable. All participants were assessed on their appreciation of first order and second order deception and false belief in ToM stories (Frith and Corcoran, 1996), which was the dependent variable. IQ was measured using the Quick Test, (Ammons and Ammons, 1962) and immediate story recall was measured using a sub test from the Adult Memory and Information Processing Battery (Coughlan and Hollows, 1985). In light of the findings set out in Table 1, Level of Education and Immediate Story Recall were included as covariates in the analyses conducted in this study.

### **7.2.2 Materials**

**The Theory of Mind Stories (after Frith and Corcoran, 1996; refer to Appendix 7).** Participants were read four short vignettes and given pictorial story boards to help them follow the story. The stories depicted situations involving false belief and deception at first and second order levels of intentionality. For example, the first order false belief story involved appreciating that one of the characters in the story has a false belief, the second order story involved appreciating that one of the characters has a false belief about the mental state of another character in the story.



### ***An example of First Order False Belief***

John has five cigarettes left in his packet. He puts his packet on the table and goes out of the room. Janet comes in and takes one of John's cigarettes and leaves the room.

#### **ToM question:**

When John comes back for his cigarettes, how many does he think he has left? The correct answer here was 5.

#### **Reality question:**

How many cigarettes does John really have left? The correct answer here was 4.

The deception stories involved bluff in the first order and double bluff situations in the second order vignettes. The participant was asked to explain or predict the behaviour of one of the characters in the situations that were described. After each story two questions were presented, one which assessed the participant's understanding of the protagonist's inference or mental state while the other was a reality (control) question which assessed the participants' memory and comprehension of the story. In total there were two first order stories (one false belief and one deception) and two second order stories (one false belief and one deception).

### *An example of Second Order Deception*

Jack has taken the money that Cassy owes him from her purse without asking her.

Cassy has found out and she is angry and looking for Jack. While Jack is trying to hide, he meets Lenny, their little brother. Lenny knows what has happened. Jack promises Lenny lots of sweets if he doesn't help Cassy find him and he tells Lenny that he'll be hiding in the tree-house. Meanwhile, Cassy has looked everywhere for Jack except the shed or the tree-house. She comes across Lenny and asks him: "Do you know if Jack is in the tree-house or the shed?" Cassy suspects that Jack has tried to bribe Lenny so she doesn't trust him. Lenny is smart and he realises that Cassy doesn't trust him. He is looking forward to his sweets.

#### ToM question:

Where will Lenny tell Cassy to look for Jack - in the tree-house or the shed? Why?

The correct response was that Lenny will tell Cassy to look for Jack in the tree-house. He says this because he knows that she doesn't trust him and will expect him not to tell the truth, so she will look for him in the shed.

#### Reality question:

Where is Jack really hiding? The correct response was that he is hiding in the tree-house.

Memory testing was embedded within the ToM stories task as a control. If the answer to a reality/memory question was wrong the answer given to the ToM question was



automatically marked as incorrect. Pictorial story boards were also included to enable the participants to follow the story thereby reducing the working memory load of the task. Participants could score from 0-4 in this test across all stories.

### ***7.2.3 Procedure***

The experimenter read the stories in the same order to each participant. Participants were read the stories in conjunction with the cartoons in the following order, first order false belief, first order deception, second order false belief and then second order deception.

## ***7.3 Results***

### ***7.3.1 ToM Stories***

Levene's test demonstrated that there was inequality of variance across the groups ( $p < 0.01$ ). The F max ratio was calculated and the highest cell variance (RF) was compared with the lowest cell variance across the groups (IGE). 'An F max as great as 10 is acceptable' for homogeneity of variance to be assumed (Tabachnick & Fidell, 2007, p86). In this case  $F_{max} = 6.5$  ( $1.3/0.2$ ) therefore the assumption of equality of variance was not violated. Skewness was problematic in this sample but kurtosis was not;  $Z = 3.27$  and  $Z = 0.74$  respectively, the data was very negatively skewed. To overcome this, the data were transformed and reanalysed to take account of this. Essentially the same trends in the data existed even when the data was transformed so the original analysis is reported here (see reanalysis and interpretation of the data in appendix 8).

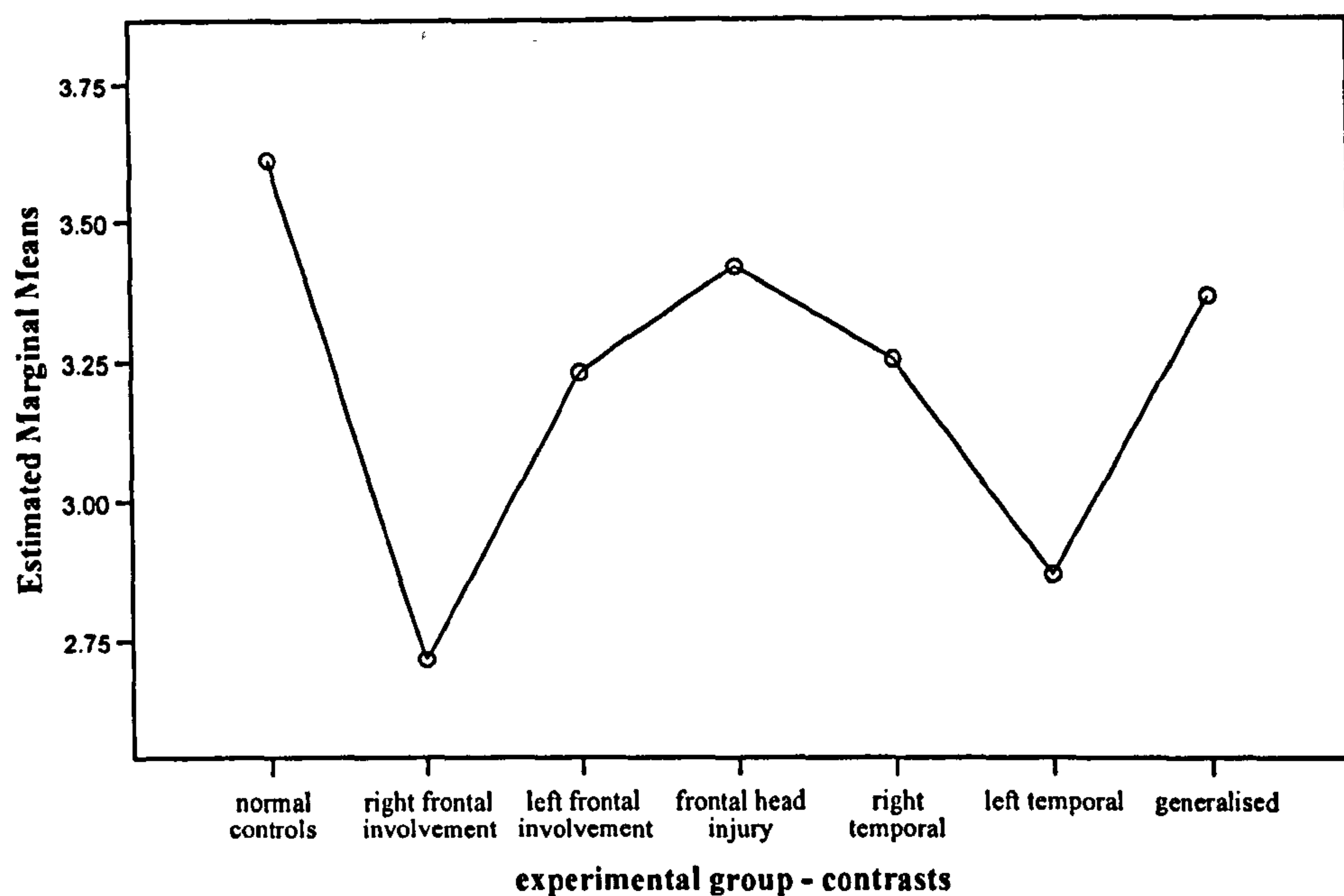
Table 16 illustrates that the NC group produced the best performance on this task and the RF and LT groups performed the worst. ANOVA was conducted with Experimental Group between participants and ToM Story performance as the dependent variable.

*Table 16: Results of ToM Stories for all Experimental Groups (Means and Standard Deviation).*

	Normal sample (NC)	Right Frontal (RF)	Left Frontal (LF)	Frontal Head Injury (FHI)	Right Temporal (RT)	Left Temporal (LT)	IGE
ToM Stories	3.6 (0.6)	2.7 (1.1)	3.2 (0.7)	3.4 (0.7)	3.3 (0.5)	2.9 (0.7)	3.4 (0.5)

The results showed a significant difference between the groups on ToM Stories:  $F(6,88) = 2.78, p < 0.05$ . Multivariate Helmert orthogonal contrasts were conducted to see if the RF group performed significantly worse than all other patient groups combined. The groups were coded and entered into SPSS in the same order as the table above, NC = 1, RF = 2, LF = 3, FHI = 4, RT = 5, LT = 6 and IGE = 7. All patient groups performed significantly worse than NC ( $p < 0.05$ ). The RF performed significantly worse than all other patient groups ( $p < 0.05$ ), (this approached significance in the reanalysed data,  $p = 0.051$ ). All other contrasts were not significant. Refer to Figure 6 to see the trends in the data.





**Figure 6:** *The means of ToM Stories by experimental group.*

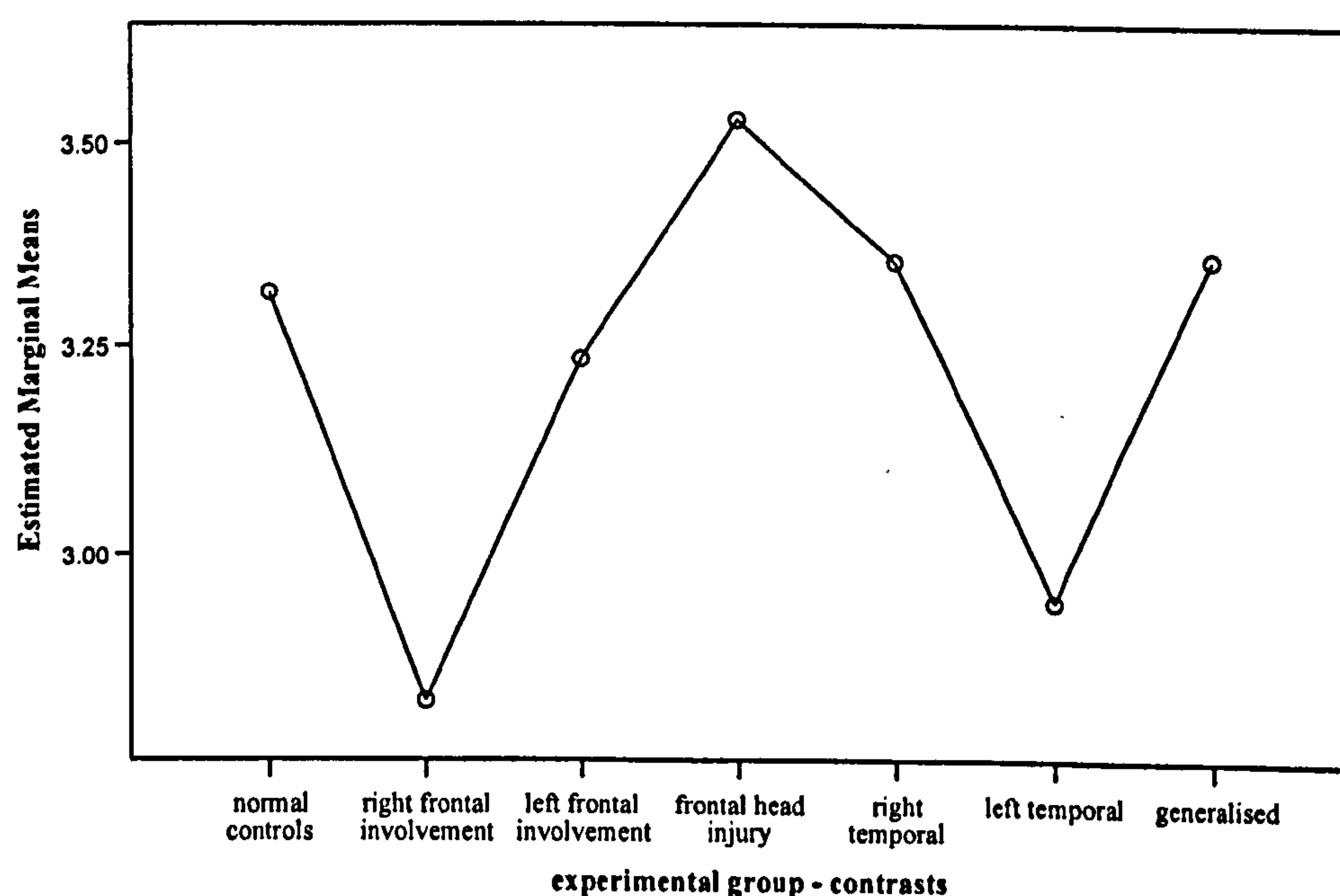
Tukey's post hoc test revealed that the RF group performed significantly worse on ToM Stories in comparison to NC ( $p < 0.05$ ). All other pairwise comparisons were not significant.

### **7.3.1.1 Tom Stories, Immediate Story Recall and Level of Education.**

ANCOVA was conducted in order to test the extent to which poor Immediate Story Recall and Level of Education affected performance on ToM stories in the right frontal group. Experimental group was between participants and ToM story score was a dependent variable. Immediate Story Recall and Level of Education were entered as covariates in the analysis.

### ***The results:***

The effects of Immediate Story Recall (ISR) on ToM Stories was not significant,  $F(1,86) = 2.34$ ,  $p > 0.05$ . However, Level of Education was significant as a covariate,  $F(1,86) = 5.00$ ,  $p < 0.05$ . Following control for group differences in ISR and education, there was no longer a main effect of experimental group on ToM Stories,  $F(6,86) = 1.65$ ,  $p > 0.05$ . Multivariate Helmert orthogonal contrasts revealed NC did not differ significantly compared to combined patient groups ( $p > 0.05$ ), however, the RF group still remained significantly worse than all other patient groups. ( $p < 0.05$ ), this effect was reduced to just below significance ( $p = 0.075$ ) when the data was reanalysed (see appendix 8). All other contrasts were not significant. Refer to Figure 7 to see the trends in the data.



***Figure 7: The means of ToM Stories by experimental group when taking account of immediate story recall and level of education.***



7.3.2 First Order and Second Order ToM Stories

ToM performance was further analysed in relation to performance on first and second order tasks. ANOVA was conducted with Experimental Group between participants and First Order and Second Order ToM story scores respectively as the dependent variables.

Levene’s test demonstrated that there was inequality of variance across the groups ( $p<0.001$ ). The F max ratio could not be calculated because there was no variance in the scores for the NC, FHI, RT, LT and IGE groups. Skewness and kurtosis were very problematic in this sample;  $Z= 18.97$  and  $Z= 47.06$  respectively.

Table 7 illustrates that all groups except the RF and LF performed at ceiling on this task.

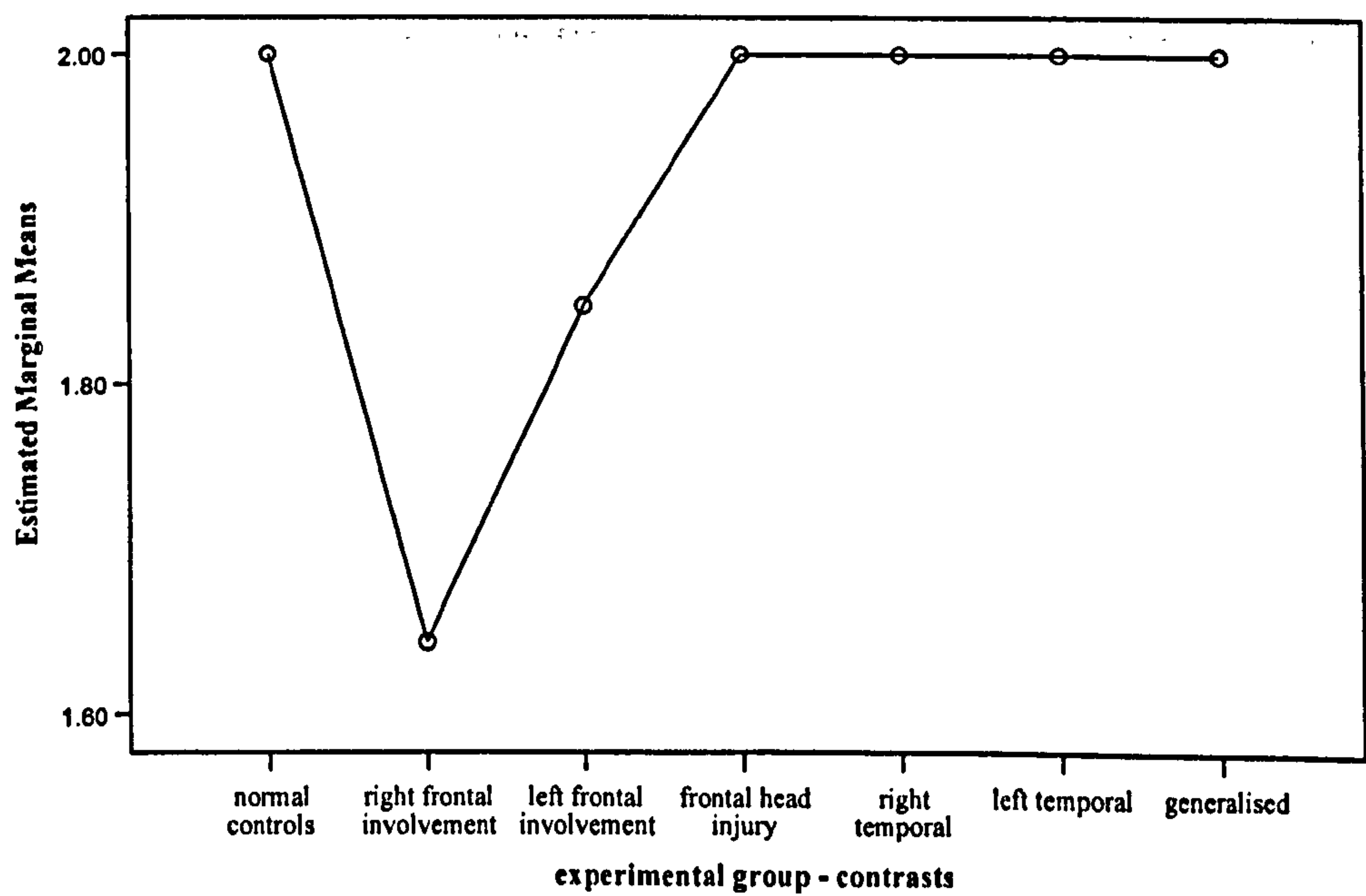
Table 17: Results of First Order ToM Stories (Means and Standard Deviation).

	Normal sample (NC)	Right Frontal (RF)	Left Frontal (LF)	Frontal Head Injury (FHI)	Right Temporal (RT)	Left Temporal (LT)	IGE
First Order ToM	2.0 (0)	1.6 (0.6)	1.8 (0.4)	2.0 (0)	2.0 (0)	2.0 (0)	2.0 (0)

There was a significant difference between the groups on First Order ToM Stories:  $F(6,88) = 3.35, p<0.01$ . Clearly there are ceiling effects in the data with all groups except RF and LF getting all First Order Stories correct. MV Helmert orthogonal contrasts revealed that the RF group performed significantly worse than all other

patient groups ( $p<0.001$ ). All other contrasts were not significant. Refer to Figure 3 to see the trends in the data.

As noted above skewness and kurtosis were very problematic in this sample. In an attempt to overcome this, the data were transformed, see appendix 9. However, as skewness and kurtosis remained problematic non parametric statistics were performed. Essentially the same outcomes were obtained, the Kruskal Wallis test revealed group differences on this measure and one sample t tests revealed that only the RF group performed significantly worse than ceiling.



*Figure 8: The means of First Order ToM Stories by experimental group.*



### **7.3.2.1 First Order Tom Stories, Immediate Story Recall and Level of Education.**

ANCOVA was conducted in order to test the extent that poor Immediate Story Recall and Level of Education affected performance on First Order ToM stories.

Experimental group was between participants and First Order ToM story score was the dependent variable. Immediate Story Recall and Level of Education were included as covariates in the analysis.

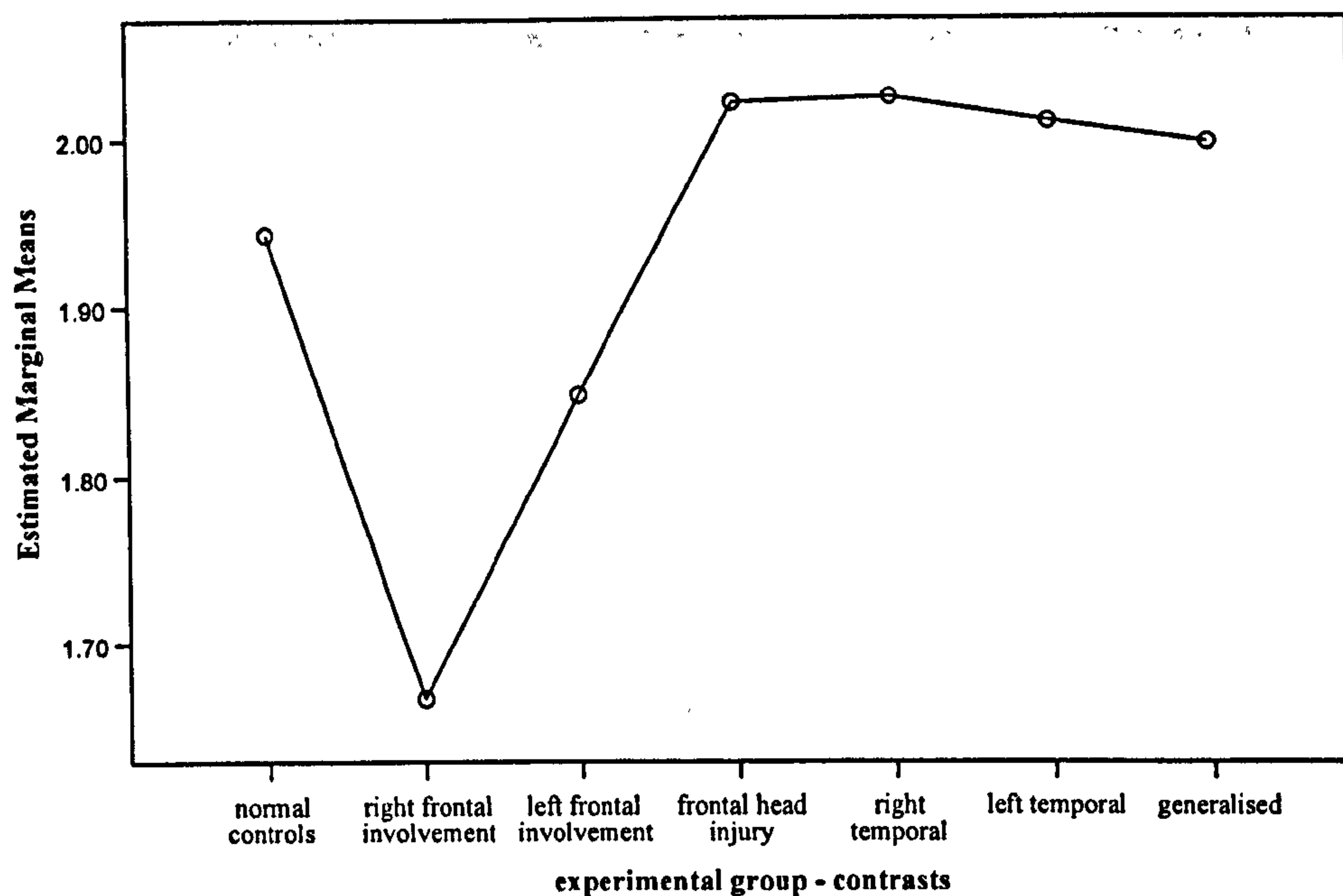
#### ***The results:***

It appears that Immediate Story Recall is not impacting on First Order ToM Stories,  $F(1,86) = 2.34$ ,  $p > 0.05$ , neither is Level of Education  $F(1,86) = 2.02$ ,  $p > 0.05$ .

Following control for group differences in immediate story recall and education, there was a main effect of experimental group,  $F(6,86) = 3.0$ ,  $p < 0.05$ . It is evident that the groups have a specific difficulty in First Order ToM Stories over and above that which is caused by immediate story recall and level of education.

MV Helmert orthogonal contrasts revealed that when taking account of immediate story recall and level of education the RF group performed significantly worse than all other patient groups ( $p < 0.001$ ) and the LF group performed significantly worse than FHI, RT, LT and IGE ( $p < 0.05$ ). All other contrasts were not significant. Refer to Figure 9 to see the trends in the data.

However in view of the extreme deviations from normality and the ceiling effects noted above these outcomes should be treated with caution.



**Figure 9:** *The means of First Order ToM Stories by experimental group when taking account of immediate story recall and level of education.*

### 7.3.3 Second Order ToM Stories

ToM performance was further analysed in relation to performance on second order tasks. ANOVA was conducted with Experimental Group between participants and Second Order ToM story scores as the dependent variable.

Levene's test was not significant ( $p > 0.05$ ) so equality of variance was assumed.

( $p > 0.05$ ). Skewness and kurtosis were not problematic in this sample;  $Z = 1.48$  and  $Z = 1.48$  respectively.

Table 18 illustrates that the NC group produced the best performance on this task and the LT group performed the worst.



Table 18: Results of Second Order ToM Stories (Means and Standard Deviation).

	Normal sample (NC)	Right Frontal (RF)	Left Frontal (LF)	Frontal Head Injury (FHI)	Right Temporal (RT)	Left Temporal (LT)	IGE
Second Order ToM	1.6 (0.6)	1.1 (0.7)	1.4 (0.5)	1.4 (0.7)	1.3 (0.5)	0.9 (0.7)	1.4 (0.5)

There was a significant difference between the groups on Second Order Stories:  $F(6,88) = 2.43, p < 0.05$ . MV Helmert orthogonal contrasts revealed that the NC group performed significantly better than all patient groups ( $p < 0.05$ ) and that the LT performed significantly worse than the IGE group ( $p < 0.05$ ). All other contrasts were not significant, refer to Figure 10 to see the trends in the data.

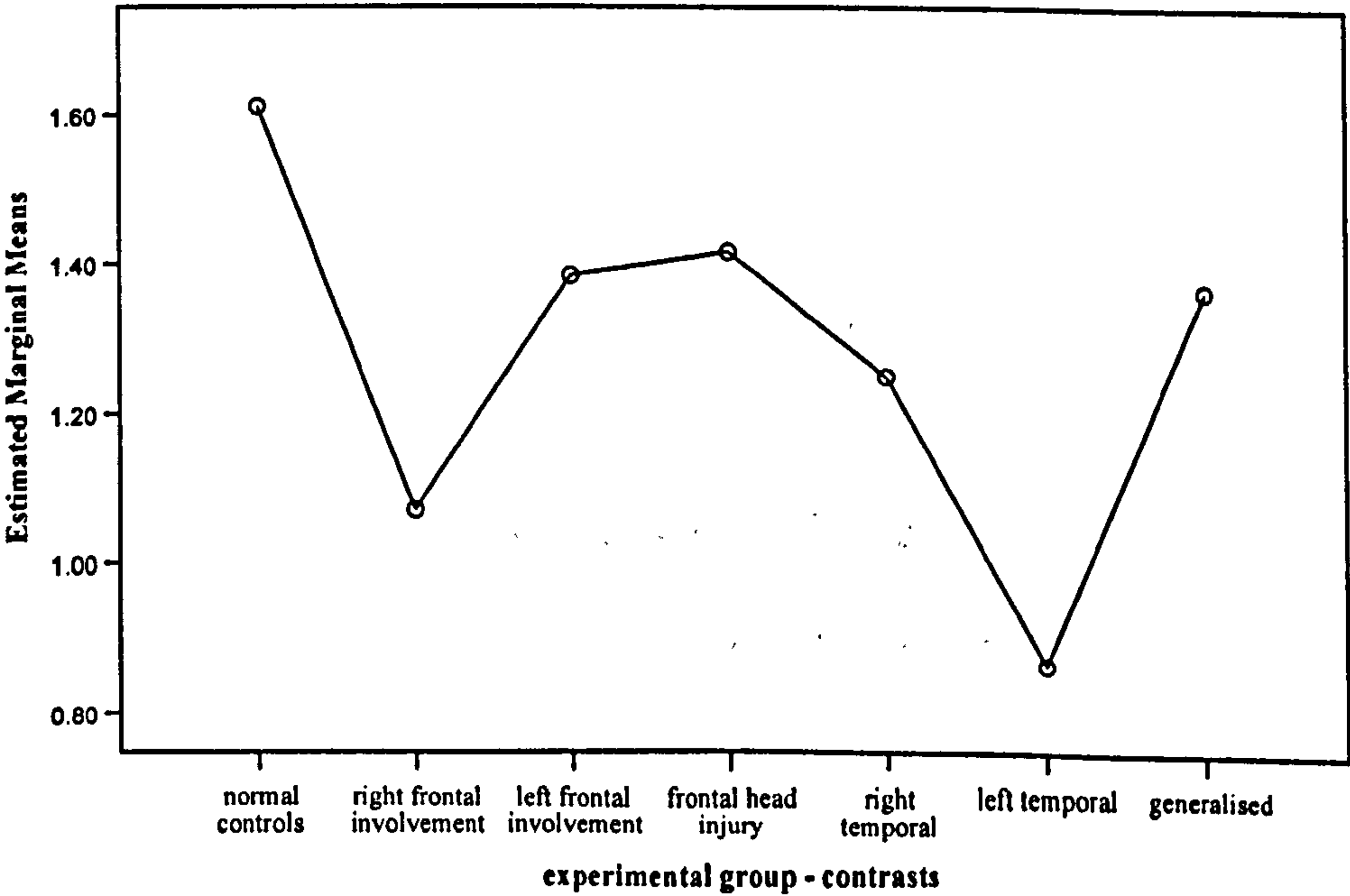


Figure 10: The means of Second Order ToM Stories by experimental group.

Tukey's post hoc tests revealed that the LT group performed significantly worse than NC ( $p < 0.05$ ). All other pairwise comparisons were not significant.

#### **7.3.3.1 Second Order Tom Stories and Immediate Story Recall and Level of Education.**

ANCOVA was conducted in order to test the extent that poor Immediate Story Recall and Level of Education affect performance on Second Order ToM stories.

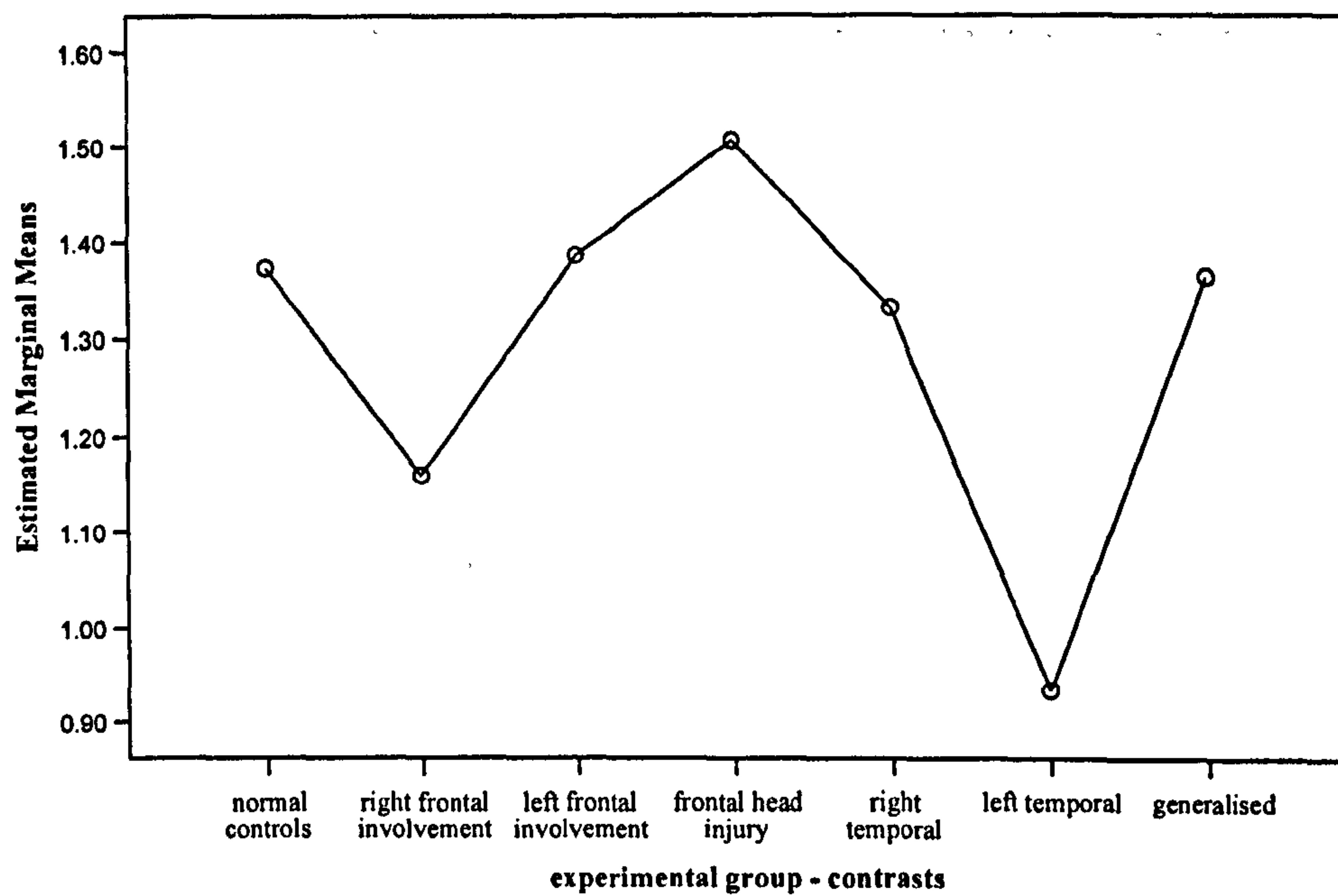
Experimental group was between participants and ToM story score was a dependent variable. Immediate Story Recall and Level of Education were covariates in the analysis.

#### ***The results:***

It appears that Immediate Story Recall is impacting on Second Order ToM Stories,  $F(1,86) = 2.47$   $p < 0.05$ , while Level of Education is not  $F(1,86) = 3.84$   $p > 0.05$  (although the effect approaches significance  $p = 0.053$ ). Following control for group differences in ISR and education, there was no longer a main effect of experimental group on Second Order ToM Stories,  $F(6,86) = 1.32$ ,  $p > 0.05$ .

MV Helmet orthogonal contrasts revealed that after taking account of the impact of Immediate Story Recall and Level of Education NC did not differ significantly compared to combined patient groups ( $p > 0.05$ ) and the LT no longer performed significantly worse than IGE ( $p < 0.05$ ). All other contrasts were not significant, refer to Figure 6 to see the trends in the data. It is evident that the groups do not have a specific difficulty in second order ToM Stories over and above that which is caused by immediate story recall and the impact of level of education.





*Figure 11: The means of Second Order ToM Stories by experimental group when taking account of immediate story recall and level of education.*

## ***7.4 Summary of findings***

It would appear that the RF group are consistently under performing on ToM tasks. On average they perform worse than all the experimental groups on ToM stories and First Order ToM Stories. RF perform worse than all the other patient groups even when the impact of immediate story recall and level of education are accounted for in the analyses. The LT group also appear to be under performing on Second Order ToM tasks though this deficit appears to be mediated by the effects of immediate story recall. These findings will be discussed in more detail in the general discussion in Chapter 11.

Study 2 will follow by assessing another valid paradigm of ToM, appreciation of pragmatic language.



## Chapter 8

### Study 2: Appreciation of hints in focal epilepsy.

There are many difficulties in designing tests to assess ToM skills in adults particularly as many tests are designed to assess mentalising in children, consequently adults tend to score at ceiling on these tasks (Stone et al., 2003). One way that researchers have overcome this problem is to assess the appreciation of pragmatic (non literal) language. A number of paradigms have been established and tested such as appreciation of irony, sarcasm, metaphor, hinting, jokes and faux pas (Corcoran et al., 1995; Corcoran & Frith, 2003; Farrant et al., 2005; Happé, 1994; Schacher, et al., 2006; Shamay –Tsoory et al., 2002; Shamay Tsoory et al. 2003; Shamay-Tsoory et al., 2005a; Shamay-Tsoory et al., 2005b; Shaw et al., 2007; Winner et al., 1998).

The RH appears to play a role in appreciating pragmatic aspects of language such as sarcasm (McDonald, 1999; Shamay-Tsoory et al., 2002) irony (Brownell, Simpson, Bihle, Porter & Gardner, 1990; Shamay-Tsoory et al., 2005a; Winner et al., 1998), indirect requests (Weylman, Brownell, Roman & Gardner, 1989; Stemmer et al., 1994), metaphor (Van Lancker & Kemper, 1987) and appreciation of humour (Birhle et al., 1986; Wapner, Hamby & Gardner, 1981). Those with RH damage have also been shown to be impaired in differentiating between lies and jokes where these involve second order levels of intentionality (Winner et al., 1998). High functioning children with autism exhibit marked deficits in developing pragmatic skills and their ability to successfully appreciate pragmatics has been associated with how good they are at inferring false belief (Surian, Baron-Cohen, Van Der Lely, 1996).

The PFC has been associated with appreciation of irony and sarcasm (Shamay-Tsoory, Tomer & Aharon-Peretz, 2002; McDonald & Pearce, 1996). These studies were not able to determine laterality within the PFC as participants had bilateral PFC lesions. Furthermore, people with lesions outside the PFC were not recruited, so the organic basis of these pragmatic skills could not be confidently localised specifically to the left or right PFC (Shamay-Tsoory, Tomer & Aharon-Petetz, 2005b). To overcome this, Shamay-Tsoory et al. (2005b) assessed the appreciation of sarcasm in people with frontal and non frontal lesions. They found that patients with frontal lobe damage, and especially those with right VMPFC damage were impaired in appreciating of sarcasm. It was also noteworthy that the extent of the lesion was significantly related to task performance. Shamay-Tsoory et al's (2005b) findings support literature which has localised ToM functioning to the right PFC (Stuss et al.,2001; Shamay-Tsorry et al., 2005 a,b).

Other research suggests that areas outside the RH might be associated with ToM functioning. Fine et al. (2001) found that a patient who sustained early left amygdala damage was impaired on Happé's Strange Stories (Happé, 1994), and the appreciation of sarcasm and metaphor. All of these tasks required the comprehension of the underlying intentions in non literal speech (pragmatic language). The impairments were found to be unrelated to executive functioning.

To the author's knowledge there have only been four studies which have assessed ToM in PWE using tests that involve appreciation of non-literal language (Corcoran et al., 2000; Farrant et al.,2005; Schacher, et al., 2006; Shaw et al.,2007) Shaw et al. (2007) assessed a group of people with unilateral RTLE or LTLE before and after an anterior



temporal lobectomy. PWE were assessed on appreciation of faux pas and on Happé's Strange Stories where participants are required to identify what characters really mean in stories where they do not literally mean what they say. No significant deficits were found pre and post surgery, or in relation to laterality in the temporal groups on either task. Farrant et al. (2005) also found that people with FLE were not impaired on these tasks. Alternatively Schacher et al. (2006) found that people with MTLE were impaired on the appreciation of faux pas in relation to a group with extra MTLE. When laterality was analysed within the MTLE group those with right MTLE underperformed in relation to those with left MTLE. Corcoran et al., (unpublished, cited in Corcoran, 2000) found that patients with right frontal or right fronto-temporal foci were impaired on the Hinting Task, compared to people with left frontal and left fronto-temporal foci, bilateral frontal foci and normal controls.

Corcoran and Frith (2003) found that the appreciation of hints (using the same paradigm as this study) was impaired in people with negative signs in schizophrenia. Further analysis revealed that this deficit was mediated by poor narrative memory. The same measure of immediate story recall will be used in this study to take account of the possible effects of narrative memory on the Hinting task performance.

The studies described above may be open to a certain degree of criticism. For example, none of them included people with both (right and left) FLE and TLE within the same design, which meant that a comprehensive comparison of performance across epilepsy groups could not be made. None of the studies recruited a suitable control group (such as an IGE group) that could control for the potentially confounding effects of AEDs or epilepsy related variables across their sample. In Farrant et al. (2005) no analysis was performed in relation to laterality. If laterality was considered, then sample sizes were

very small, such that statistical differences across groups would be hard to detect (Corcoran et al., 2000; Schacher et al., 2006). To summarise, to date the research that has been conducted has not utilised designs that can adequately explore socio-cognitive functioning in focal epilepsy. The present study aimed to overcome these difficulties.

### ***8.1 Rationale/Aims and Objectives***

The present study aimed to use a more advanced measure of ToM to assess the appreciation of non-literal language in the experimental groups. The paradigm used in this study was the Hinting Task, which assesses ‘the ability to understand pragmatic language where intentions are hidden’ and which is said to be ‘an effective way to explore this skill in adult samples’ (Corcoran & Frith, 2003, p.2).

Like Study 1, the present study aims to overcome some of the methodological problems encountered in past studies by attempting to lateralise the appreciation of pragmatic language within the frontal and temporal lobes of PWE whilst using a suitable clinical control group (IGE).

Existing research evidence which has implicated the importance of the right hemisphere to processing pragmatic language (Birhler et al., 1986; Brownell et al., 1990; McDonald, 1999; Shamay-Tsoory et al., 2002; Stemmer et al., 1994; Wapner, Hamby & Gardner, 1981; Weylman, Brownell, Roman & Gardner, 1989; Winner et al., 1998; Van Lancker & Kemper, 1987;) and especially the right frontal lobe (Shamay-Tsoory et al. (2005a, b). People with right fronto-temporal epilepsy have shown impaired



performance on the Hinting Task in a previous study Corcoran (2000). In light of this evidence the following prediction was made;

***Hypothesis 1:*** It is predicted that relative to the other clinical groups, the RF group will under perform on the Hinting Task.

In view of the general cognitive deficits that are associated with epilepsy (see section 3.1 for a review) the following prediction was made:

***Hypothesis 2:*** It is predicted that all clinical groups will perform worse than normal controls on the Hinting Task.

In order to test these hypotheses Helmert contrasts were performed on the data.

## **8.2 Methods**

### **8.2.1 Design**

Experimental group was a between participants independent variable. All participants were assessed on their ability to infer the veiled intentions behind speech acts in a Hinting Task (Corcoran et al., 1995). A measure of performance on this task constituted the dependent variable. IQ was measured using the Quick Test, (Ammons and Ammons, 1962). Immediate story recall was measured using a sub test from the Adult Memory and Information Processing Battery (Coughlan and Hollows, 1985). Level of Education and Immediate Story Recall were covariates in this study.

### **8.2.2 Materials**

**The Hinting Task.** (Corcoran et al., 1995; refer to Appendix 10).

This test consists of 10 short vignettes where a character makes a very strong hint. Each vignette is available for the participant to reread as often as they wish and the task is to infer the hidden meaning and true intention of the character in the story. If the participant makes an appropriate inference the first time around then they score two points. If an appropriate inference is not made, then the experimenter adds an additional more obvious hint and if a correct inference is forthcoming at this stage then the participant scores one point. However, failure to produce a correct inference at this second stage would result in a score of zero on that item of the task. The task has a maximum score of 20 and normal participants tend to score close to ceiling (Corcoran & Frith, 2005).



The Hinting Task was sensitive to ToM deficits in people with different symptoms in schizophrenia (Corcoran et al., 1995; Corcoran and Frith 2003; Corcoran and Frith 2005; Janssen, Krabbendam, Jolles & van Os, 2003; Pickup, 1997; Swarbrick, 2000; Versmissen et al., 2008;), epilepsy (Corcoran, 2000) and in non clinical populations which have investigated schizotypy (Versmissen et al., 2008; Janssen et al., 2003).

Refer to Appendix 10 for all items used on the Hinting Task.

*An example of an item from the Hinting Task*

Melissa goes to the bathroom for a shower. Anne has just had a bath. Melissa notices the bath is dirty so she calls upstairs to Anne: "Couldn't you find the Ajax, Anne?"

QUESTION: What does Melissa really mean when she says this? (score 2)

ADD: Melissa goes on to say:

"You're very lazy sometimes, Anne!"

QUESTION: What does Melissa want Anne to do? (score 1)

The appropriate response here is that Melissa wants Anne to clean the bath.

### **8.2.3. Procedure**

The experimenter read each item of the Hinting Task to the participants in the same order, providing a clue if participants did not get the answer correct the first time round.

### **8.3 Results**

Levene's test demonstrated that there was inequality of variance across the groups ( $p < 0.05$ ). The F max ratio was calculated and the highest cell variance (RF) was compared with the lowest cell variance across the groups (RF). In this case  $f \text{ max} = 3.1$  ( $5.32/1.17$ ) therefore the assumption of equality of variance was not violated. Skewness was problematic in this sample but kurtosis was not;  $Z = 3.47$  and  $Z = 1.07$  respectively. To overcome this the data were transformed and the analysis was repeated. Essentially the same trends were evident in the data following transformation (see reanalysis and interpretation of the data in Appendix 11).

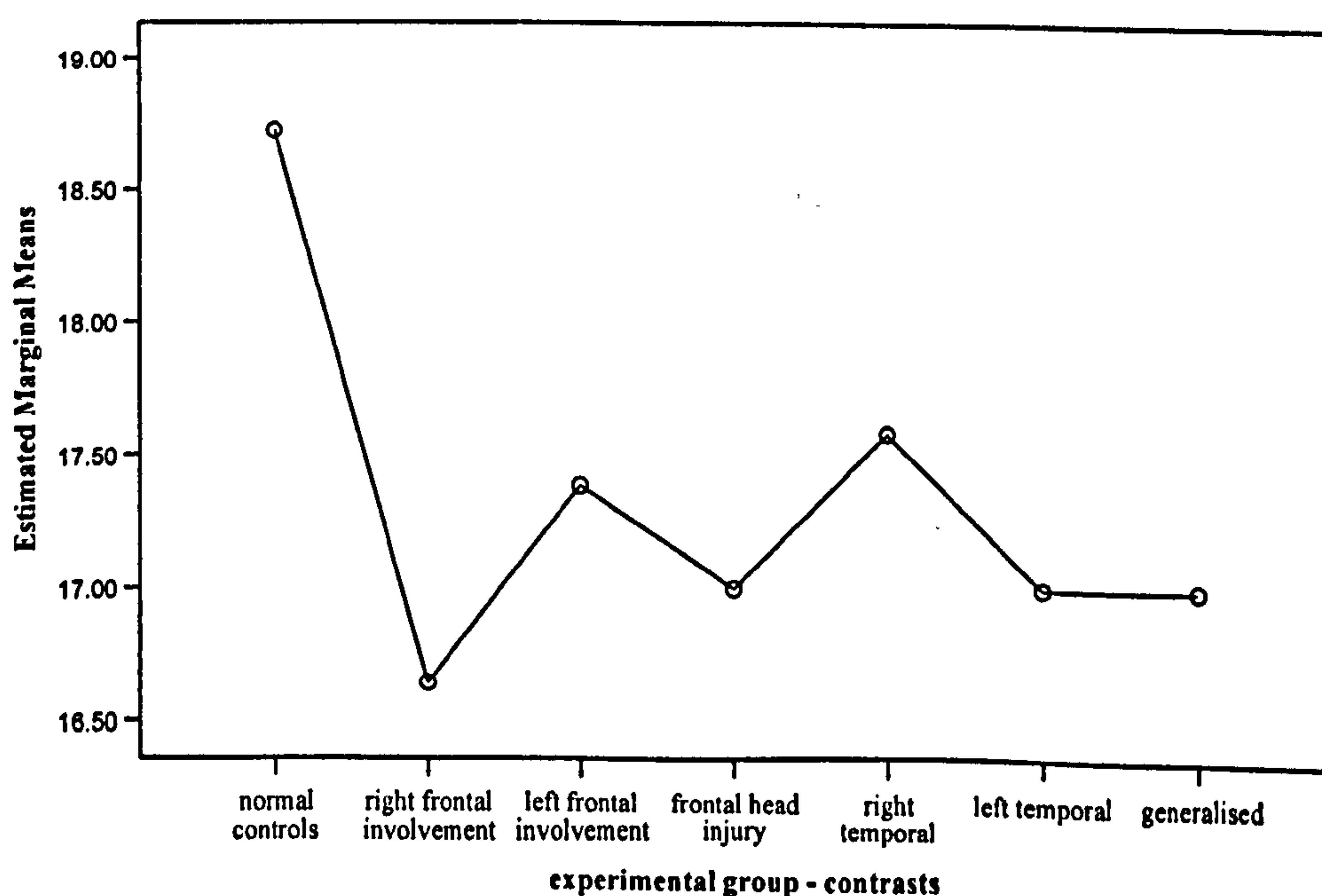
Table 9 illustrates that the NC group produced the best performance on this task and the RF group performed the worst. The maximum score on this test was 20 and in general all groups seem to be performing reasonably well on this task. ANOVA was conducted with Experimental Group between participants and Hints as a dependent variable.



**Table 19: Results of Hints for all Experimental Groups (Means and Standard Deviation).**

	Normal sample (NC)	Right Frontal (RF)	Left Frontal (LF)	Frontal Head Injury (FHI)	Right Temporal (RT)	Left Temporal (LT)	IGE
Hinting Task	18.7 (1.2)	16.6 (2.3)	17.4 (1.8)	17.0 (1.5)	17.5 (1.1)	17.0 (1.3)	17.0 (1.2)

The results showed a significant difference between the groups on Hints,  $F(6,88) = 3.26$ ,  $p < 0.01$ . Multivariate Helmert orthogonal contrasts were run to see if the RF group performed significantly worse than all other patient groups. The contrasts revealed that NC performed significantly better than all other groups ( $p < 0.001$ ). All other contrasts were not significant (refer to Figure 12 to see the trends in the data).



**Figure 12: The means of Hints by experimental group.**

Tukey's post hoc analysis revealed that the RF and LT group were impaired on the Hinting Task in comparison to NC ( $p < 0.01$ ;  $p < 0.05$  respectively). All other pairwise comparisons were not significant. When the data was transformed the FHI and IGE were also impaired in comparison to NC ( $p < 0.05$ ).

### ***8.3.1 Hints, Immediate Story Recall and Level of Education***

ANCOVA was conducted in order to test the extent that poor Immediate Story Recall and Level of Education effect performance on Hints in the right frontal group.

Experimental group was between participants and Hints was a dependent variable.

Immediate Story Recall and Level of Education were covariates in the analysis.

#### ***The results:***

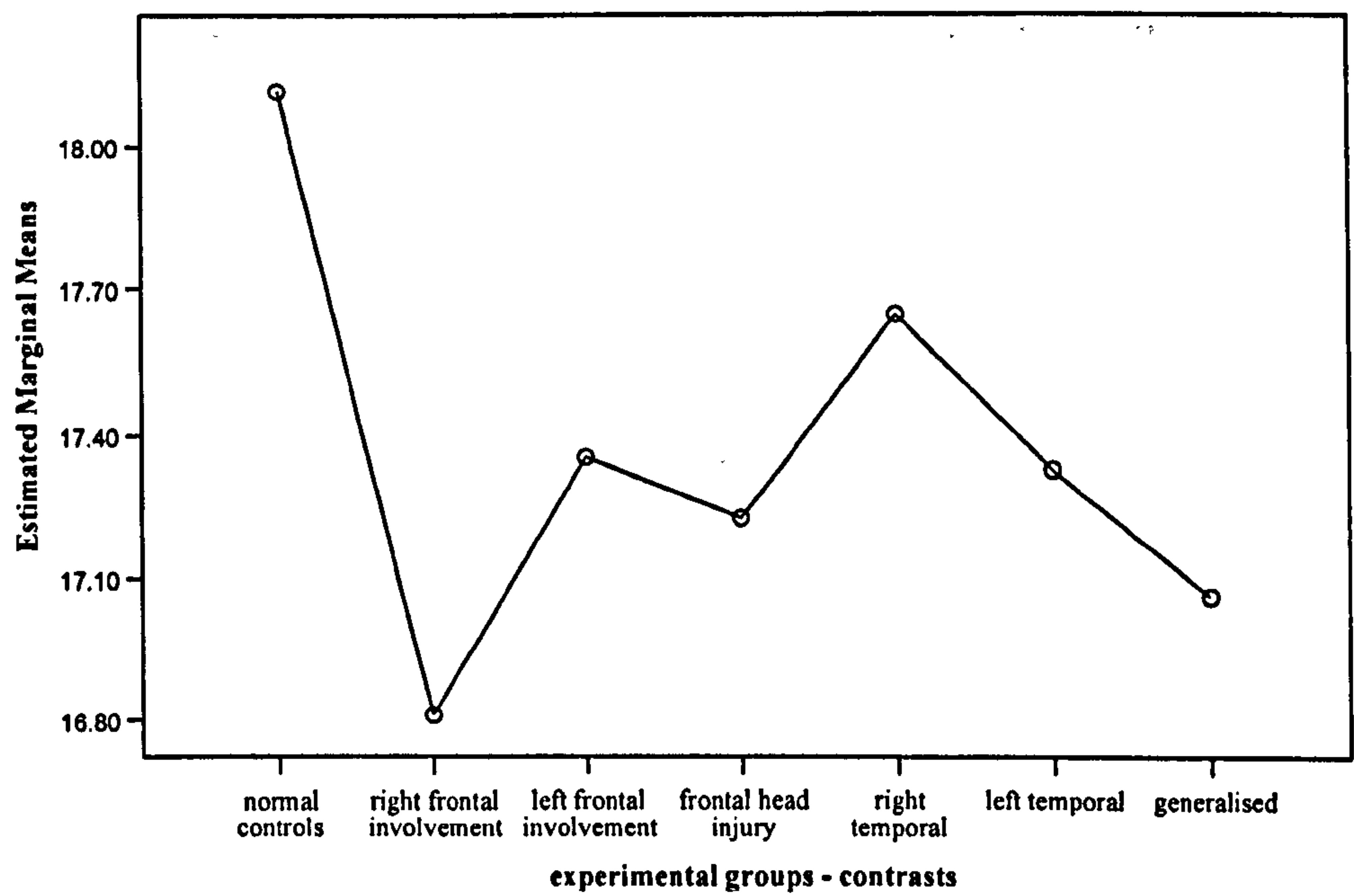
It appears that Immediate Story Recall is having an impact on the Hinting task,  $F(1,86) = 10.67$ ,  $p < 0.005$ , while Level of Education is not  $F(1,86) = 0.00$ ,  $p > 0.05$ .

Following control for group differences in ISR and education, there was no longer a main effect of experimental group on Hints,  $F(6,86) = 1.01$ ,  $p > 0.05$ .

MV Helmert orthogonal contrasts revealed that after taking account of the impact of Immediate Story Recall and Level of Education, NC no longer performed significantly better than all other groups although the difference approached significance ( $p = 0.06$ ).

However, in the analysis with the transformed data the difference did reach significance,  $p < 0.05$ . All other contrasts were not significant, (refer to Figure 13 to see the trends in the data).





**Figure 13: The means of Hints by experimental group taking account of the effect of Immediate Story Recall.**

#### ***8.4 Summary of findings***

On average the RF group perform worse on hints than all the other experimental groups and the NC perform significantly better on the Hinting task than all the other experimental (patient) groups. Both the RF and LT group are significantly impaired on the Hinting task in comparison to NC (as are the FHI and IGE when the data are transformed), though this impairment appears to be mediated by immediate story recall.

These findings will be discussed in more detail in the general discussion in Chapter 11.



## Chapter 9

### Study 3: Social Conditional Reasoning in Epilepsy

Reasoning is ‘a cognitive process of drawing inferences from given information’ (premises or arguments) (Goel & Dolan, 2004, p. B109). Two distinct types of reasoning have long been recognised; inductive and deductive reasoning. Both abilities can be distinguished by how they relate to the premise and the conclusion (Shuren & Grafman, 2002). When people reason deductively they reach a conclusion based only on the information provided within the premise, this information should be sufficient to solve the problem where there is one solution. Conversely, when people reason inductively they draw on other information available to them (personal background knowledge) to facilitate problem solving (Martin, 2006). Inductive reasoning is more likely to be used in everyday life (Evans, 1984) and ToM involves reasoning inductively.

The Wason Selection Task (WST) (Wason, 1966) is the most frequently used test of deductive reasoning (Goel, Shuren, Sheesley & Grafman, 2004). The WST has been used to assess the impact that content has on conditional reasoning ability (Cheng & Holyoak, 1985; 1989; Cosmides, 1989; Fiddick, Cosmides & Tooby, 2000; Goel et al., 2004; Girgerenzer & Hug, 1992). The WST is used in the present study to investigate whether embedding the task in a social familiar context will facilitate conditional reasoning ability. ‘Conditional reasoning involves drawing (deductive) inferences from scenarios in which the occurrence of one event is conditioned on the occurrence of a second event’ (Shuren & Grafman, 2002; p.916.). Typically these conditional rules are presented as ‘if p, then q’. The individual then needs to establish which pieces of

information linking p and q have to be sampled in order to establish whether or not the rule has been violated. In the abstract (traditional) version of the WST (refer to TRAD described in the materials section) participants are read a brief scenario, given a conditional rule to follow and presented with 4 cards. Participants are told that a letter is printed on one side of each of the cards and a number on the other. Only one side of the card is visible and the task involves verifying the rule by turning over one or more of 4 cards that are presented. An example of a rule in the abstract version is 'If there is an A on one side there must be a 9 on the other'. As shown in the example used in the present study (in the material section) participants can see four cards with A, B, 9 and 4 printed on them. The correct answer is to turn over the card with the A and the card with the 4 printed (i.e., P and not Q). This is because it is necessary to confirm the rule to demonstrate that there is a 9 on the opposite side of the 'A card' and that there is not an A on the opposite side of the '4 card'. Generally speaking most people underperform on this version of the task and usually achieve a success rate of between 10-20% (Evans, 2003). Performance on the abstract version provides a baseline measurement of conditional reasoning ability. A common erroneous response is to confirm the rule, rather than to test it by choosing the A and 9 cards (P and Q). This error is referred to as 'matching bias' and is among the most reliable and robust effects in psychological reasoning (Evans, 1998; Evans, 2003).

It has been found that task performance is greatly enhanced by embedding the WST in a socially familiar context where the conditional rules are expressed in terms of behaviours drawn from everyday life. An example of this is the 'social familiar' (SF) version of the task used in the present study in which the conditional rule is expressed as follows: 'If a person was drinking alcohol then that person must be 18 or over'. This



version was originally created by Griggs & Cox (1982) and they found a success rate of up to 75% in a normal sample. Similar success rates have been found in a number of studies which have used thematic (social familiar) versions of the task which involve social exchange (Cheng & Holyoak, 1985; 1989; Cosmides, 1989; Fiddick et al., 2000; Goel et al., 2004; Girgerenzer & Hug, 1992).

Different explanations and theories have been put forward to account for the 'content effect' on the WST. Among these different perspectives and theories a number suggest that a relationship exists between conditional reasoning and ToM. For example, evolutionary perspectives suggest that social exchange evolved because humans and other species who cooperated with each other enjoyed mutual benefits, but that these benefits were given conditionally according to whether or not the actors behaved in the manner expected of them. As an account of the origins and functions of social reasoning ability, this perspective (known as 'social contract theory') has become well established and has been supported by a considerable body of research evidence (Cheng & Holyoak, 1985; 1989; Corcoran & Frith, 2005; Cosmides, 1989; Cosmides & Tooby, 2000; Cosmides & Tooby, 2005; Ermer et al., 2006; Fiddick,; Goel et al., 2004; Girgerenzer & Hug, 1992). According to this theory social exchange is regulated by conditional reasoning and has an adaptive function which is to detect cheaters. Cheaters are people who do not adhere to the rules that constitute the social contract and thereby secure the benefits of an interaction or exchange without fulfilling the requirements upon which the benefit was conditional (Ermer et al., 2006). ToM is particularly important in social exchange as it enables strategic social interaction, which requires the ability to effectively infer the mental states of others. It is therefore apparent that social exchange is dependent upon ToM (Ermer et al., 2006).



Another interesting theory was postulated by Ermer et al., (2006) which suggests that ToM is a specialised ability which has a reciprocal relationship with reasoning about social exchange. 'The logic of social exchange allows the contents of mental states to be inferred and inferring mental states allows social exchange to proceed' (p.201.). They suggest that ToM can be thought of in both broad and narrow terms. Narrow conceptualisations of ToM refer to inferences concerning desires and beliefs, while broad conceptualisations incorporate all social inferential systems that facilitate and utilise mental state inferences and underpin human social interaction. They refer to this broad definition as a Theory of Human Nature (ToHN). Therefore within the context of this broad definition, ToM is necessary to facilitate social exchange.

Frye, Zelazo and Palfai (1995) and Frye, Zelazo, Brooks, and Samuels (1996) suggest that ToM is one aspect of 'the ability to act in accordance with embedded rules' (Fine et al., 2001, p.288). Such embedded rules are used to guide executive functions and therefore mediate ToM processing. Consequently Frye et al. (1995, 1996) argue that ToM is not a modular skill that is domain-specific in nature but is supported by domain-general cognitive functions. Perner and Lang (2000) suggest that there is a relationship between conditional reasoning, ToM and executive functions. They suggest four possible relationships; executive functions depend on ToM, or ToM depends on executive functions, both types of ability require similar embedded conditional rules or are underpinned by the same regions within the brain

Corcoran (2000, 2001) has put forward a model which also proposes the existence of a relationship between social conditional reasoning and ToM. She suggests that ToM is accomplished using analogical reasoning and that effective social reasoning in

conditional contexts underpins the ability to mentalise. Her work has focussed on investigating ToM in people with schizophrenia in an attempt to try and explain the different ToM deficits apparent in this clinical population. Corcoran's model suggests that in order to infer the mental states of others, we initially introspect and retrieve from autobiographical memory any relevant information from our past, which might help to inform and resolve the current problem. In doing this we derive those behaviours that are appropriate to the current context. Once this information has been retrieved it acts as a foundation upon which conditional reasoning takes place. During the reasoning process a suitable solution to the problem is considered in light of any conditional or contextual factors that may be relevant, whilst taking account of how similar or different the current situation is to the past. Therefore both conditional reasoning and autobiographical memory are considered as cognitive subcomponents to ToM ability. In this model, ToM is not considered to be domain specific or modular in nature but reliant on domain general processes. There are similarities between this model and the simulation theory and 'theory' theory account of ToM (outlined in 4.2.3). All these theoretical perspectives suggest that we introspect and refer to our own mental states (experiences) in order to effectively infer the thoughts of others (Gopnick et al., 2000). The role of autobiographical memory in social reasoning ability has also been noted by other authors (Adolphs, Tranel, Bechara, Damasio & Damasio, 1996; Bechara, Damasio, Tranel & Damasio, 1997).

Support for Corcoran's model comes from three studies on people with schizophrenia. In the first study Corcoran and Frith (2003) found that autobiographical memory and ToM (as assessed by the Hinting Task and ToM stories) were significantly correlated, (both ToM paradigms have been used in studies 1 & 2). Corcoran (2003) went on to



find a significant correlation between a task of inductive reasoning (Aha sentences) and the Hinting Task. This relationship was not found in the normal sample and was less apparent in people who were in remission than those with presenting symptoms at the time of testing. In a further study Corcoran and Frith (2005) went on to explore the role of social conditional reasoning in ToM (using the Hinting Task). An abstract measure for the WST was used along with social, non social, familiar and non familiar versions of the task. The same tasks are used in the present study. Social facilitation for conditional reasoning was found to be significantly correlated with ToM performance in people with schizophrenia but not in the normal control group. To explain the facilitation effect, Corcoran and Frith propose that in order to reason in both social and non social contexts we attempt to reason inductively by drawing on past experiences. In non social situations we do not have the same resources and consequently perform poorly on such tasks. While these studies lend support to Corcoran's model of social reasoning in clinical (schizophrenic) populations the applicability of the model to normal persons is open to question.

There is broad agreement that the brain involves general inferential capacities (domain-general). Much debate exists as to whether specific inferential abilities also exist which may be content specific and go beyond the information provided, therefore not solely relying on abstract logic (Ermer et al., 2006). Two lines of evidence which support domain specific inferential abilities have been proposed, ToM reasoning (Bach et al., 2000; Baron-Cohen, 1995; Rowe et al., 2001; Stone et al., 1998) and reasoning in relation to social exchange (Cosmides & Tooby, 2005; Stone Stone, Cosmides, Tooby, Kroll, Knight (2002). There are a number of lines of evidence to support the idea of specialised systems in relation to processing social information. Studies have



illustrated dissociations between reasoning about arbitrary rules (like the abstract version of the WST) as opposed to rules embedded in social content. Dissociations have also been reflected in studies that assess inferential abilities in reasoning about physical states as opposed to mental states. Further support comes from studies involving people with lesions, developmental disorders or neuroimaging which reveal neural dissociations and cross cultural studies which indicate that these skills are universal and develop at particular stages in life (Ermer et al., 2006).

It has been proposed that both hemispheres may contribute differently to reasoning ability. The left hemisphere is more involved in abstract reasoning using logic, whereas the right hemisphere may be more involved in reasoning in familiar contexts, especially social ones, where reference to past experience is important (Shuren & Grafman, 2002). There have been relatively few studies which have investigated the neural basis of reasoning ability. In a series of PET studies by Goel and colleagues activation of the left PFC was found during both deductive tasks (using syllogisms) and inductive tasks. Inductive reasoning also activated the medial PFC (Goel, Gold, Kapur & Houle, 1997; 1998; Goel, Buchel, Frith & Dolan, 2000; Goel & Dolan, 2001). To date their findings have identified two neural networks, a parietal frontal pathway which is activated for arbitrary rules and a temporal-frontal (left) system which is linked to processing familiar social content (Noveck, Goel & Smith, 2004). The left parietal system (BA 6, 7, 44) is predominantly activated when participants reason using materials that are not meaningful to them, (Goel & Dolan, 2003). The left frontal (BA 44, 8, 9) and temporal (BA 21 & 22) regions are recruited when the material has semantic meaning (Goel & Dolan, 2003). Goel & Dolan (2004) also used fMRI to investigate the neural basis of inductive and deductive reasoning. Both tasks activated

the left lateral PFC and bilateral dorsal frontal, parietal and occipital cortices. Inductive reasoning activated the left dorsolateral PFC (BA 8&9) and the deductive reasoning task activated the left inferior frontal gyrus (BA 44). In view of these findings, Goel and Dolan (2003) suggest that both processes may well be dissociated. It is worthy of note that the results of this study replicate the authors' earlier findings in which an inductive reasoning task was found to activate the same area of the medial dorsal PFC (BA 8 & 9) while both types of reasoning activated a fronto-temporal network (Goel, Gold, Kapur & Houle, 1997). More generally, the importance of the left PFC in deductive reasoning has been supported in a number of studies (Acuna et al., 2002; Goel & Dolan, 2001; Knauff et al., 2002).

An fMRI study which utilised a conditional reasoning paradigm was conducted by Canessa et al. (2005). Two versions of the WST were used, an abstract version and one which involved social content. They found that both tasks activated the medial PFC, the left dorsolateral PFC and the parietal cortex, providing further evidence of the importance of the left hemisphere in deductive reasoning. The task involving social content also activated the right PFC and the parietal cortex which the authors conclude is indicative of the involvement of the right hemisphere in reasoning tasks which are framed within a social context.

Precautionary rules are related to potential hazards e.g. 'if you surf in cold water, then you have to wear a wetsuit' (Reis et al., 2007, p.1386.). These rules involve the application of logic except that they do not involve reasoning about social exchange or rely on ToM. Consequently, precautionary rules and social exchange versions of the WST have been used in a number of imaging and lesion studies to assess task



performance in relation to content (Stone et al., 2002; Ermer et al., 2006; Fiddick, Spampinato & Grafman, 2005; Reis et al., 2007).

An imaging study by Ermer et al. (2006) investigated social exchange and precautionary reasoning using the WST in 12 healthy controls. Due to the reciprocal relationship between social exchange and ToM it was expected that the neural correlates of social exchange would mirror those of ToM as the authors suggest that social exchange is dependent on ToM. There was some evidence to support this, the right anterior temporal cortex (BA 20), the left posterior temporal cortex (BA 21) and the posterior cingulate (BA 23) all of which have also been activated in ToM tasks were activated when reasoning about social exchange. Fiddick et al. (2005) used similar paradigms and found that the dorsomedial (BA6/8), bilateral ventrolateral PFC (BA 47), the left angular gyrus (BA 39) and the left orbitofrontal cortex (BA 10) were differentially activated when conducting tasks involving task content relating to social contracts or interchanges. However, this study has been criticised as the social exchange tasks were more complex than the precautionary tasks (Reis et al., 2007). In the first study of its kind Reis et al. (2007) used fMRI to assess social exchange reasoning ability in relation to an objective measure of social competence (emotional intelligence). Emotional Intelligence (EI) was positively related to social exchange reasoning but no relationship was found with reasoning that involved precautionary rules. Social exchange reasoning differentially activated the left frontal and temporal lobes. The authors concluded that EI was mediated by social exchange reasoning, an interesting finding as EI has been positively related to social competence in past research (Brackett, Rivers, Shiffman, Lerner, & Salovey, 2006).



To date there have only been three lesion studies which have investigated the effect of content on reasoning ability (Adolph et al., 1996; Stone et al., 2002; Goel et al., 2004). Adolphs et al. (1996) administered both familiar and unfamiliar versions of the WST to people with DLPFC and VMPFC lesions (damage to the orbito medial area) as well as a healthy control group. When given a traditional version of the task all groups underperformed. When given a familiar version of the task performance was facilitated in the DLPFC group and normal controls but not in the group with VMPFC lesions. The authors' explanation of their findings has similarities with the model proposed by Corcoran (2000; 2001). Adolphs et al (1996) suggest that the task involved analogical reasoning where one must retrieve past experiences in order to solve the current problem. Therefore those with VMPFC lesions either have a difficulty with accessing autobiographical memories or in using the information they retrieve to successfully complete the task. This study can be criticised for not investigating laterality in relation to social conditional reasoning. As the study did not assess a temporal lobe sample, it cannot be concluded that the VMPFC is the only brain region of importance in relation to social conditional reasoning.

Another lesion study was conducted by Stone et al. (2002). They investigated social exchange in a patient (R.M.) with extensive bilateral damage involving the orbito frontal cortex (OFC), temporal pole and amygdala. The patient was presented with a reasoning problem that involved social exchange and was set within the WST. R.M. had previously demonstrated impaired appreciation of faux pas in another study (Stone et al., 1998a). R.M. made significantly more errors on the social contract task in comparison to another control task matched for reasoning difficulty (precautionary reasoning). To ensure that R.M.'s impairments were not just a consequence of

extensive bilateral damage, his performance was compared with two other patients. Both patients also had extensive bilateral damage in regions of the brain that overlapped with the damage present in R.M., namely the OFC and temporal poles. One patient did not have damage to the OFC (B.G.) cortex and the other did not have damage to the right temporal pole (R.B.). Both B.G. and R.B. did not illustrate any deficits on reasoning about precautionary rules or social exchange, nor were their performances significantly different between the tasks. In comparison to R.B., B.G. and NC, R.M. performance was clearly depressed. Therefore the authors concluded that bilateral damage to the amygdala (anterior temporal lobe) and the orbitofrontal cortex could account for the specific deficit observed in R.M. Stone et al. (2002) suggest that bilateral orbitofrontal or amygdala damage alone can cause deficits in ToM (Stone et al., 1998; Stone, 2000) but both structures need to be damaged to impair the detection of cheats. Therefore they argue that reasoning about social exchange is a domain specific skill dissociated from reasoning in other domains. Whilst this is a case study and consequently the findings cannot be readily generalised, this research provides a valuable insight into social exchange reasoning in the normal population.

Goel et al. (2004) conducted a lesion study to investigate the importance of the frontal lobes to conditional (logical) reasoning using the (WST). This study is particularly relevant to the issues addressed by this thesis as some of the same measures were used and because the study investigated social conditional reasoning in people with frontal lesions. Nineteen people with frontal lobe lesions were tested (five right, six left, and eight bilateral) together with 19 healthy controls who were matched for age and education. Three versions of the WST taken from Cheng & Holyoak (1985) which manipulated social context were administered. The versions of the task were graded



according to the extent to which the rules by which the participants had to reason were embedded in a social context. The first version of the task involved a traditional abstract version of the WST (the same task as that used in the present study). The second version involved abstract permission schema 'if one is to take action 'A' then one must first satisfy precondition 'P' (p.785) and the third version used a social familiar version of the WST (same as the SF version in the present study).

Goel et al. (2004) found that normal controls and people with frontal lesions illustrated comparable performance on the traditional version of the task. Social facilitation for conditional reasoning was apparent in normal controls across the second and third versions of the task but this facilitation effect was not present in people with frontal lesions. Further analyses revealed that those with left frontal lesions were the most impaired on the task and that both IQ and memory were significantly correlated with task performance. However, in relation to IQ the LF patients averaged a score of 107.83 on the WAIS-R measure compared to 96.0 for RF patients leading the authors to conclude that the deficits on the task were not due to poor verbal reasoning. Verbal IQ was also higher in LF than RF group with scores of 103.88 and 94.60 respectively.

A possible limitation of Goel et al's (2004) study was that ANOVA was used when analysing the pattern of responses across the different versions of the task. This procedure is questionable given that the data values were limited to zero and one (correct or incorrect) for each version. This essentially nominal data would lend itself more to the chi squared statistical technique. A further criticism of this study is that the majority of participants (15 out of 19) had suffered traumatic open head injuries and one of the remaining frontal patients had a closed head injury. It is worthy of note that

traumatic brain injury can cause diffuse axonal damage (Smith, Meaney & Shull, 2003) so the effect of injury maybe widespread in these patients. The study did not include any tasks to assess familiar but non social content. Consequently the importance of the PFC in social reasoning cannot be conclusively determined. The present study overcomes this limitation by incorporating such a measure. Goel et al's (2004) small sample size led them to combine the bilateral group with both the right and left frontal groups in order to make statistical comparisons in relation to laterality. The present study overcomes this as there is a larger sample of right and left FLE patients which increases statistical power. The inclusion of a right and left temporal group in the present study also helps to determine whether the lack of facilitation for social reasoning is specific to the FL and the left FL in particular.

It is clear that the evidence in relation to the neural basis underlying social conditional reasoning is mixed. Imaging and lesion studies which have investigated the effects of social content on reasoning have emphasised the importance of the frontal lobes (Adolphs et al.,1996; Canessa et al., 2005; Fiddick et al.,2005; Goel et al.,2004; Reis et al.,2007; Stone et al.,2002). There is disagreement in relation to laterality, with some studies emphasising the importance of the left frontal lobe (Fiddick et al.,2005; Goel et al.,2004; Reis et al.,2007) and others the right (Canessa et al.,2005). A role for the temporal lobes has also been suggested in the literature (Ermer et al., 2006; Reis et al., 2007; Stone et al., 2002). Reis et al. (2007) found that the left temporal lobe was differentially activated during a social conditional reasoning task. This finding was supported by Ermer et al., (2006) who used a similar paradigm and found that both the right and left temporal lobes were activated during task performance.



### ***9.1 Rationale/Aims and Objectives***

The current study is the first to assess PWE on thematic versions of the WST. There is also a lack of lesion studies in the research literature investigating social conditional reasoning. This investigation aims to overcome some of the methodological problems encountered in past studies by attempting to lateralise social conditional reasoning within the frontal and temporal lobes of PWE, whilst using a suitable clinical control group (IGE).

The evidence regarding the neural basis of social conditional reasoning is debatable with different studies implicating different areas of the frontal and temporal lobes. In Studies 1 and 2 the RF group underperformed on ToM tasks. In line with this it was expected that the RF group would also under perform on tasks of social exchange as many authors suggest that social conditional reasoning is dependent on ToM (Corcoran, 2000; 2001; Ermer et al., 2006) or that both skills are related to each other (Frye et al., 1995;1996; Perner & Lang, 2000). The right hemisphere has been implicated in reasoning in familiar and social contexts (Shuren & Grafman, 2002) and more specifically the right frontal lobe (Canessa et al., 2005).

In the light of the existing evidence the following two predictions were tested:

***Hypothesis 1 :*** It was expected that the NC group would show facilitation for social conditional reasoning. Therefore their performance would be worst in the Abstract (TRAD) version of the WST and best in the SF (social familiar task).

***Hypothesis 2:*** It was expected that the RF group would not show facilitation for social conditional reasoning.

## **9.2 Methods**

### **9.2.1 Design**

Experimental group was a between participants independent variable. All participants were assessed on a conditional reasoning (CR) task performance on which was the dependent variable. This measure consisted of five versions of the Wason Selection Task (WST) (Wason, 1966) which varied in terms of the contextual information that was provided. In addition to the traditional version of the task (TRAD), the other versions included conditional propositional statements which involved a social and familiar context (SF), a social but unfamiliar context (SU), a non social familiar context (NSF) and finally a non social and unfamiliar context (NSU). The total number of correct responses served as the dependent variable. IQ was measured using the Quick Test, (Ammons and Ammons, 1962). Immediate story recall was measured using a sub test from the Adult Memory and Information Processing Battery (Coughlan and Hollows, 1985). Level of Education and Immediate Story Recall were included as covariates in this study.

For each task version (traditional, social familiar, social unfamiliar, non social familiar and a non social unfamiliar) where possible chi-squared analysis was performed to establish whether the proportion of correct responses differed between the groups.

For each group, Corcoran's Q test was performed to establish whether task version significantly affected the proportion of correct responses.



### **9.2.2 Materials**

**The Conditional Reasoning (CR) Task** (Corcoran & Frith, 2005) refer to appendix 12).

This task incorporates five different thematic versions of the Wason Selection Task (1966) (which differ in social and familiar content) and was designed by Corcoran and Frith (2005). This is a conditional reasoning task where the participant is asked to make appropriate (logically necessary) selections to see if a specified rule has been followed.

The first task is an abstract version (TRAD) and is equivalent to the traditional Wason selection task (although a very brief vignette is given at the beginning of the task in order to set scene). The purpose of this abstract version was to give a baseline indication of conditional reasoning ability.

#### ***Traditional (Abstract version)***

You are a temporary library assistant. You have been asked to check some rules of the coding system used in the library. You are checking the index cards of books to see that books coded with certain letters are sub-coded with particular numbers. You have reached the final four cards. On one side of the card is a letter while on the other side is a number. This is the rule that you are checking:

**IF THERE IS AN 'A' ON ONE SIDE THERE MUST BE A '9' ON THE OTHER.**

You should now show me the card or cards that you would definitely need to turn over to see if the rule has been broken.

<b>B</b>	<b>4</b>
(not P)	(not Q)
<b>A</b>	<b>9</b>
(P)	(Q)

The correct answer to this is: *P* and *not Q* (A and 4).

The remaining four stories differ in content according to whether they involve a social or non social rule and for each of these possibilities a familiar or non familiar context. The social familiar version is included below, see appendix 12.

### *Social Familiar (SF)*

The story is the drinking age rule of Griggs and Cox (1982).

You are a police officer checking up on the under age drinking rule. Your colleague, who was working under cover in a notorious pub the night before, has given you details on cards about four young people who were in the pub last night. On one side of the card is the person's age while on the other side of the card is what that person was drinking. Here is the rule that you must check:

**IF A PERSON WAS DRINKING ALCOHOL THEN THAT PERSON MUST BE 18 OR OVER.**



You should now show me the card or cards that you would definitely need to turn over to see if the rule has been broken.

19	Pepsi
(Q)	(not P)
Alcohol	17
(P)	(not Q)

The correct answer to this is: P and not Q (alcohol and 17).

**9.2.3 Procedure**

The experimenter read each item of the CR task to the participants in the same order. The traditional version was read first followed by a social familiar version, a non social familiar version, a social unfamiliar version and finally a non social unfamiliar version.

**9.3 Results**

For each version of the task participants scored one if they produced the correct answer or zero otherwise. Scores were summed over all versions of the task yielding a maximum possible score of 5. Levene’s test demonstrated that there was inequality of variance across the groups ( $p<0.001$ ). The F max ratio was calculated and the highest cell variance (NC) was compared with the lowest cell variance across the groups (FHI). In this case  $F\ max = 19\ (2.85/0.15)$  therefore the assumption of equality of variance was violated which was accounted for in the choice of post hoc test. Skewness

and kurtosis were problematic in this sample;  $Z= 8.07$  and  $Z= 9.24$  respectively, the data was very positively skewed. To over come this, the data were transformed. The distributions were very negatively skewed and in many cases the modal response was zero. According to Tabachnick and Fidell (2001) for such distributions it is appropriate to take the inverse of the scores by firstly adding one to all scores to remove zeros. The data were reanalysed and with the transformed data (refer to Appendix 13). Skewness was acceptable ( $Z = 1.06$ ) although kurtosis still remained problematic ( $Z=3.46$ ).

Table 20 illustrates that the NC group produced the best performance on this task and the FHI group performed the worst. The trends in the data suggest that none of the groups performed well on this task (the maximum score was 5) and that all patient groups performed very poorly in comparison to NC.

ANOVA was conducted with Experimental Group between participants and the total Conditional Reasoning score as the dependent variable.

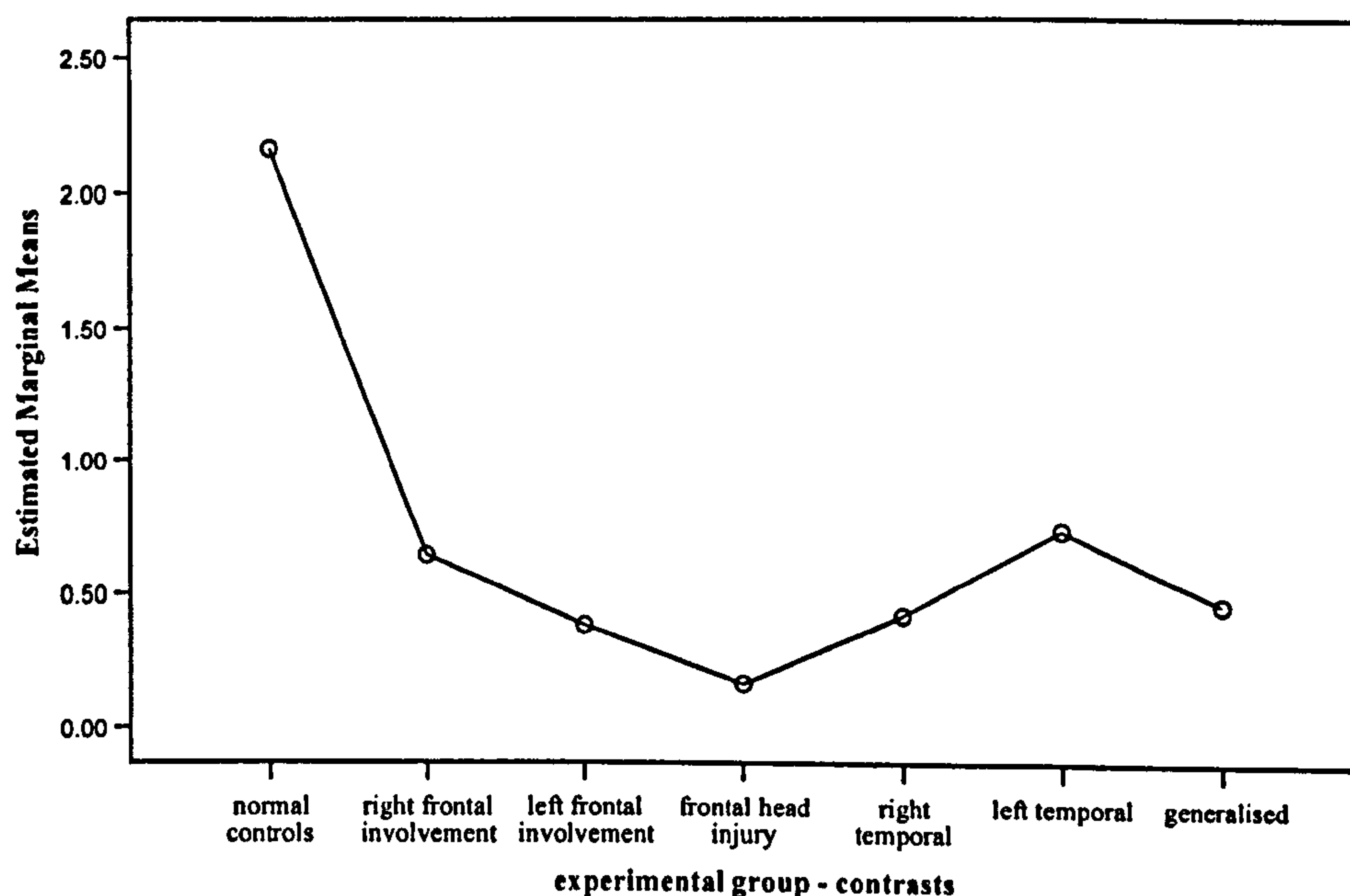
*Table 20: Results of Conditional Reasoning for all Experimental Groups (Means and Standard Deviation).*

	Normal sample (NC)	Right Frontal (RF)	Left Frontal (LF)	Frontal Head Injury (FHI)	Right Temporal (RT)	Left Temporal (RT)	IGE
C R Task	2.2 (1.7)	0.6 (0.6)	0.4 (0.7)	0.2 (0.4)	0.4 (0.5)	0.7 (0.7)	0.5 (0.7)

The results showed a significant difference between the groups on Conditional Reasoning:  $F(6,88) = 8.63, p < 0.001$ . Multivariate Helmert orthogonal contrasts



revealed that all patient groups performed significantly worse than NC ( $p < 0.001$ ). All other contrasts were not significant. Refer to Figure 14 to see the trends in the data. These trends were replicated in the transformed data (refer to Appendix 13).



**Figure 14:** *The means of the CR task by experimental group.*

Since equality of variance was not obtained, Dunnett's C post hoc test was conducted and revealed that the RF, LF, FHI, RT and IGE all performed significantly worse than NC. All other pairwise comparisons were not significant. With the transformed data the LF, FHI, RT, and IGE groups performed significantly worse than NC (refer to appendix 13).

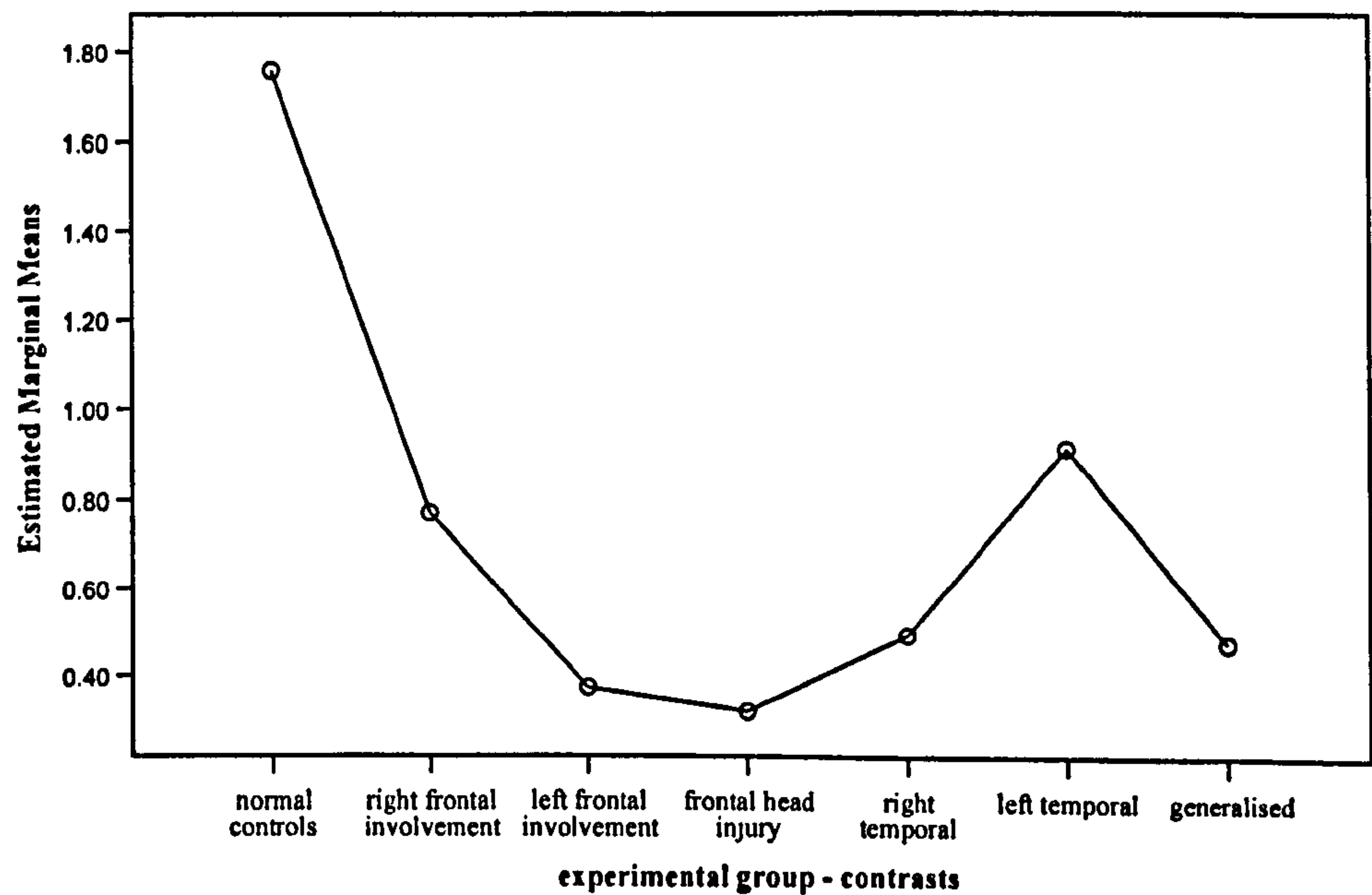
### **9.3.1 Conditional Reasoning, Immediate Story Recall and Level of Education.**

ANCOVA was conducted in order to test the extent that poor Immediate Story Recall and Level of Education affected performance on the conditional reasoning task.

Experimental group was between participants and total CR score was a dependent

variable. Immediate Story Recall and Level of Education were covariates in the analysis.

**The results:**



**Figure 15: The means of CR by experimental group when taking account of immediate story recall and level of education.**

It appears that Immediate Story Recall is impacting on CR,  $F(1,86) = 8.79, p < 0.005$  but Level of Education is not,  $F(1,86) = 0.78, p > 0.05$ . The effect of experimental group on CR, remained significant following inclusion of the covariates,  $F(6,86) = 3.97, p < 0.005$ . Multivariate Helmert orthogonal contrasts revealed that when taking account of immediate story recall and level of education all patient groups still performed significantly worse than NC ( $p < 0.001$ ). All other contrasts were not significant. Refer to Figure 15 to see the trends in the data. It is evident that the groups



have a specific difficulty in CR over and above that which is caused by group differences in immediate story recall and level of education.

The number of correct and incorrect answers for each item of the conditional reasoning task were calculated. As can be seen in Figure 15 all the groups are doing badly on the traditional version of the task. Only performance in the social familiar version could be statistically analysed as the expected cell frequencies were not four or above for any of the other tasks. Chi-square revealed that there were significant differences between the groups for the social familiar version of the task;  $\chi^2$  (DF=6, N=95) = 19.57;  $p < 0.005$ . As can be seen in Table 12, in comparison to the traditional version of the task, the social familiar context did improve reasoning ability across the groups. Reasoning was particularly facilitated in the NC, RF and LT groups. The non social familiar and the non social unfamiliar versions of the task did not facilitate reasoning across the groups. However, the social unfamiliar version did facilitate reasoning but only in the NC group.

**Table 21: Results of the Conditional Reasoning Task for all Experimental Groups (frequency of correct and incorrect answers).**

	Normal sample (NC)	Right Frontal (RF)	Left Frontal (LF)	Frontal Head Injury (FHI)	Right Temporal (RT)	Left Temporal (RT)	IGE	Total
Trad Right	3	1	0	1	0	0	1	6
Wrong	15	13	13	11	12	15	10	89
SF Right	14	6	2	3	3	8	2	38
Wrong	4	8	11	9	9	7	9	57
NSF Right	4	0	0	1	1	1	0	7
Wrong	14	14	13	11	11	14	11	88
NSU Right	5	1	3	1	1	1	1	13
Wrong	13	13	10	11	11	14	10	82
SU Right	13	1	0	0	0	1	1	16
Wrong	5	13	13	12	12	14	10	79

\* SF= Social familiar, NSF = Non social familiar, NSU = Non social unfamiliar, SU = Social Unfamiliar.



For each experimental group Cochran's Q test was used to determine whether the format of each of the tasks significantly facilitated reasoning. The nature of the task did significantly affect reasoning in the NC group:  $Q (DF=4, N=18) = 69.65, p<0.001$ , the RF group:  $Q (DF=4, N=14) = 13.41, p<0.01$  and the LT group:  $Q (DF=4, N=15) = 21.4, p<0.001$ . As Table 12 illustrates it was the social familiar version of the task that facilitated reasoning in NC, RF and LT groups. The social unfamiliar version of the task facilitated reasoning in the NC group. Problem format did not significantly affect reasoning in the LF group  $Q (DF=4, N=13) = 8.89, p>0.05$ , the FHI group  $Q (DF=4, N=12) = 4.36, p>0.05$ ; the RT group  $Q (DF=4, N=12) = 6.00, p>0.05$  or the IGE group  $Q (DF=4, N=11) = 2.22, p>0.05$ .

#### ***9.4 Summary of findings***

None of the experimental groups performed well on the abstract version of the task.

Aggregating the performance over all versions of the task the NC performed significantly better compared to the patient groups. This was still evident even when the effects of level of education and immediate story recall were accounted for. A significant main effect of task was seen across the experimental groups. Social conditional reasoning (SF version) was significantly facilitated in the NC, LT and RF groups. The social unfamiliar (SU) version of the WST also produced facilitation in the NC group but not in any of the patient groups.

Study 4 will lead on to investigate whether performance on the tasks of social cognition used in studies 1, 2 and 3 predict social functioning in PWE.



## **Chapter 10**

### **Study 4: Perceived Impact of Epilepsy on Social Functioning in relation to Social Cognition.**

Epilepsy is one of the most prevalent neurological disorders in the UK with 29,000 people diagnosed each year and as many as half a million people with epilepsy in the UK (Chadwick, 1997). As detailed in Chapter 3, PWE present with a number of difficulties in relation to social functioning. They are at greater risk of psychopathology, anxiety, depression and suicide than the general population and they are also more likely to be socially dysfunctional than those without the condition (Jacoby et al., 1996; ILAE, 2003c; Mensah et al., 2007; Pompili et al., 2005).

PWE have more social problems than the general population (Austin & de Boer, 1997). These difficulties are apparent across different cultures (ILAE/IBE/WHO, 1999; Wiebe et al., 1999). Exactly why PWE experience problems with social functioning remains unclear but is likely to be the result of a series of complex interrelated psychosocial and seizure related factors that impact on the person with epilepsy. Psychosocial difficulties include problems with; interpersonal relationships, unemployment or underemployment, poor self esteem, social isolation, educational underachievement, stigmatisation, cognitive dysfunction and restricted social activities (Austin & de Boer, 1997; Baker et al., 1990; Baxendale & O'Toole, 2007; Corcoran & Thompson, 1992; Collings, 1990; De Souza & Salgado, 2006; Fisher et al, 2000; Grabowska-Grzyb et al., 2006; Jacoby et al., 1996; Jacoby et al., 2006; Mittan, 1986; Morrell, 2002; Suurmeijer et al., 2001; Thompson & Corcoran, 1993; Thompson, 2000).

Impairments in social competence in children, adolescents and adults with epilepsy have been identified in several studies (Austin et al., 1994; Caplan et al. 2005; Dorenbaum et al, 1985; Herman et al., 1981; McCusker, et al, 2002; Jalava et al., 1997; Williams et al., 1996). Despite the impact that social competence has on the quality of life of PWE, the study of social cognition in epilepsy has been largely ignored (Schilbach et al 2007). Studies have shown an improvement in quality of life (QoL) scores after surgery but often these measures do not adequately assess improvements in social functioning (Kirsch, 2006; Mikati, Comair, Ismail, Faour & Rahi, 2004; Rose, Derry, Wiebe & McLachian, 1996). This is particularly important given the continued discontent reported by families of PWE in relation to social functioning after surgery (Mihara et al., 1994). Therefore objective measures of social competence (tests of social cognition) may be useful in identifying deficits in social functioning in PWE. They may also prove to be useful in detecting improvements after surgery.

Research has shown that PWE (TLE and FLE) have impairments in a range of measures of social cognition, these include: recognition of facial expression (Walpole et al., 2008), appreciation of faux pas (Schacher et al., 2006) appreciation of hints (Corcoran, 2000), appreciation of humour and mental state inferences (Farrant et al., 2005). Impaired emotional intelligence has also been reported (Walpole et al., 2008). Lesion studies suggest that ToM is impaired in people with frontal lobe lesions (Mazza et al., 2007; Rowe et al., 2001; Shamay-Tsoory et al., 2005a,b; Stone et al., 1998; Stuss et al., 2001). These studies provide support for the notion that the deficits in social competence apparent in people with FL damage might be due to ToM impairment. ToM deficits have also been found in people with temporal lobe damage (Apperly et al., 2004; Baron-Cohen et al. 1999; Fine et al., 2001; Stone et al., 1998a; 1998b). These



impairments may be particularly relevant to people with FLE and TLE especially since these are the most prevalent forms of focal epilepsy (Farrant et al. 2005; Helmstaedter, 2001; Schacher et al., 2006).

Epilepsy may impact on social cognition in several ways which are difficult to gage. Kirsch (2006) suggests that frequent seizures may interfere with the development of interpersonal skills in childhood and adolescence, such that the disorder and its treatment (medication) may interfere with participation in social activities.

Consequently this may lead to reduced involvement in social networks because of poor self esteem, stigma or parental over protectiveness. This in turn may interfere with the development of important life skills and may in the long term undermine feelings of independence and competence (Austin & de Boer, 1997; Goodyer, 1988; Lothman, Pianta & Clarson, 1990; McCollum, 1981; Scambler & Hopkins, 1986).

This is reflected in children with epilepsy having more social problems than children with other chronic disorders (Aper et al., 1991; Austin et al., 1994; Matthews, Barabas & Ferrari, 1982) as well as impaired social competence in relation to children without the condition (Dorenbaum et al, 1985; McCusker, et al, 2002; Williams et al.,1996).

Despite the prevalence of epilepsy and the social difficulties reported by people with the condition, there is a lack of research investigating social cognitive skills in PWE. It remains uncertain to what degree psychosocial difficulties are related to living with epilepsy or its underlying organic basis, and to what extent these difficulties can be accounted for by social cognitive impairment (Schacher et al., 2006; Walpole et al., 2008).

Thus it is apparent that the impact of epilepsy on quality of life is not just a consequence of the epilepsy related features of the disorder but a complex interaction of multiple interrelated psychosocial factors.

### ***10.1 Rationale/Aims and Objectives***

Farrant et al. (2005) found social cognitive deficits in people with FLE and concluded that the ‘impairments found may translate into everyday difficulties in social situations, an aspect that needs to be explored further (p.513.). To date Farrant et al (2005) and Corcoran (2000) are the only studies which have assessed social cognition in FLE. Both studies included very small sample sizes and did not include a suitable clinical control group or people with TLE to ascertain whether the deficits observed were specific to FLE. Tests of social cognition have been related to measures of social functioning in past research (Frith et al., 1994) yet neither study included an assessment of social functioning to see whether the deficits in social cognition related in anyway to how these individuals function in real life.

In the current study PWE will be asked to complete a questionnaire measure in which they will provide an indication of the extent to which they feel that epilepsy has affected their everyday lives. This is the first study to explore perceived deficits in social functioning in relation to objective measures of social competence in FLE, TLE and IGE. It is hoped that the Impact of Epilepsy scores which measure self perceived social functioning will corroborate the results of the tests of social cognition that have been reported in Studies 1, 2 and 3. If this is the case then the argument that perceived social difficulties in PWE arise from problems with social reasoning will be supported.



**Hypothesis 8:** In view of the deficits in aspects of ToM evident in Studies 1 and 2 it is predicted that the RF group will rate the impact of epilepsy higher than the other epilepsy groups.

**Hypothesis 9:** It is predicted that performance on the tests of social cognition will be inversely related to the quality of perceived social functioning as measured by the Impact of Epilepsy Scale.

To test this hypothesis, scores from the tests of social cognition described in Studies 1 to 3 will be used as predictor variables in a multiple regression analysis to explore whether social cognition performance predicts perceived social functioning.

## ***10.2 Methods***

### ***10.2.1 Design***

Epilepsy experimental group was a between participants independent variable (only patients with epilepsy were included in this study). All participants completed the Impact of Epilepsy Scale which is a self report measure of the perceived impact that the condition has had on a participant's everyday life. This has been used extensively in previous investigations and its reliability and validity have been demonstrated in prior research (Baker, Jacoby & Chadwick., 1996; Baker et al., 1997a; Baker et al., 1999; Baker et al., 2002; Buck, Jacoby, Baker, Ley & Steen, 1999; Jacoby et al., 1993; Jacoby et al., 1996) The score on this measure constituted the dependent variable.

### ***10.2.2 Participants***

A sub group of 40 individuals from the overall sample of 65 patients with epilepsy were included in the study. The use of this measure was adopted during the course of this research after some data had already been collected hence there was not data for the full sample for this study. The demographic details of the sample (N=40) can be seen in Table 22.

ANOVA was conducted with Experimental Group between participants and Age, Estimated IQ, Medication, Age of Onset and Duration of Illness as dependent variables to see if there were any significant differences between the groups on these measures. A chi-square analysis was performed to see if there were any significant differences between the groups in relation to Gender and Education:

**Table 22: Background variables including age, gender, education, intelligence, age of onset, duration of illness, number of AEDs and immediate story recall by Experimental Group (Study 4).**

	Right Frontal	Left Frontal	Right Temporal	Left Temporal	IGE	Overall
Number	6	5	8	13	8	40
Sex M:F ratio	2:4	4:1	2:6	7:6	4:4	18m, 22f
Mean Age (sd)	26.0 (6.8)	43.8 (14.0)	36.6 (8.7)	34.7 (10.7)	40.9 (12.4)	36.2 (11.5)
Education. 'A' levels or above	33.3%	60.0%	25.0%	38.5%	50.0%	40.0%
Mean Estimated IQ	95.7 (13.2)	102.00 (8.4)	91.6 (23.9)	94.0 (9.8)	105.2 (10.8)	97.0 (14.4)
Mean age of onset	16.3 (10.8)	31.2 (24.0)	14.6 (17.8)	17.8 (11.9)	17.1 (12.3)	18.5 (14.1)
Mean Duration	9.6 (7.8)	12.3 (15.5)	22.0 (10.7)	16.9 (12.8)	23.8 (14.0)	17.7 (12.8)
Mean AED's	2.2 (0.8)	2.0 (0.7)	2.5 (1.1)	1.7 (0.6)	1.9 (0.4)	2.0 (0.8)
Mean Immediate Story Recall	14.2 (7.8)	14.6 (7.6)	15.7 (9.4)	12.4 (7.7)	16.0 (9.3)	14.3 (8.1)

AED = anti epileptic drugs.



Chi-square could not be calculated for gender or level of education as the expected cell frequencies were not four or above. Gender was almost equally distributed across the whole sample (18m, 22f) though there were three times more females than males in the RT group, two times more in the RF group and three times more males than females in the LF group. LF had the highest percentage (60.0%) of people with A' Levels or above in relation to the other epilepsy groups and the RT group had the lowest percentage (25.0%).

Levene's test demonstrated that there was equality of variance across the groups on all measures ( $p > 0.05$ ). There was no significant difference between the groups for Age  $F(4,35) = 2.43, p > 0.05$ ; IQ  $F(4,35) = 1.27, p > 0.05$ ; the mean number of Anticonvulsants  $F(4,35) = 1.67, p > 0.05$ ; Mean Age of Onset  $F(4,35) = 1.3, p > 0.05$ ; the Duration of Illness  $F(4,35) = 1.57, p > 0.05$  or Immediate Story Recall:  $F(4,35) = 0.31, p > 0.05$ . However, in view of the small cell sizes, these results need to be treated with caution.

**Table 23: Aetiology of epilepsy by patient group (N=40).**

	Right Frontal RF (N=6)	Left Frontal LF (N=5)	Right Temporal RT (N=8)	Left Temporal LT (N=13)	IGE (N=8)	Total & % of overall sample
Not known	2	1	3	6	4	14 (35%)
Tumour (glioma/astrocytoma)	1		1			2 (5%)
Cyst		1				1 (2.5%)
Cerebrovascular	1	3				4 (10%)
Birth trauma/ febrile convulsions	1		3	5		8 (20%)
Cerebral insult	1		1	2		5 (12.5%)
Stressful life event						2 (5%)
Juvenile myoclonic epilepsy (JME)					4	4 (10%)

Inspection of Table 23 reveals that for quite a considerable number of patients aetiology was unknown (14). Birth trauma and cerebral insult were the next most common forms of aetiology (13). Two patients had epilepsy as a consequence of tumour (1 RF and 1 RT). Five generalised epilepsy patients had JME. Four patients had a cerebrovascular aetiology which included two incidences of infarction, one of an intracerebral haematoma and one involved an arterial malformation. Two patients (female) had a stressful life event which triggered their seizures; these were reported as sexual abuse in childhood. One other female RF patient with a tumour also reported that she had febrile seizures which were triggered by sexual abuse; her seizures stopped and reoccurred in adulthood, this patient's aetiology was classified under tumour.

**Table 24:** Seizure frequency, the number of seizures in the last 12 months by patient group (N=40).

	Right Frontal RF (N=6)	Left Frontal LF (N=5)	Right Temporal RT (N=8)	Left Temporal LT (N=13)	IGE (N=8)	Total
0-1		1			2	3
2-9					1	1
10-99	2	3	3	8	5	20
100+	4	1	5	5		16

As can be seen in Table 24 the majority of patients (36) experienced more than nine seizures per month with 20 people having between 10-99 seizures and 16 having over 100 seizures in the last twelve months. As noted previously, this pattern of seizure activity is likely to be due to the fact that all patients were recruited from a tertiary referral unit and have intractable epilepsy. All focal epilepsy patients in the study (all except the IGE group) were potential candidates for surgery, so high seizure activity is symptomatic of this population. The RT and LT group had the largest number of patients experiencing over 100 seizures and the LT and IGE group had the largest number of people experiencing between 10-99 seizures in the past twelve months.



**Table 25: Seizure type by patient group (N=40).**

	Right Frontal RF (N=6)	Left Frontal LF (N=5)	Right Temporal RT (N=8)	Left Temporal LT (N=13)	IGE (N=8)	Total
Complex partial only	1	1	3	6		11
Simple/complex partial/secondary generalised	5	4	5	7		21
Tonic-clonic only					4	4
Tonic-clonic and other generalised					4	4

The pattern of seizure type by patient group (Table 25) is as expected with focal epilepsy patients (RF, LF, LT and RT) experiencing complex partial seizures in isolation or in conjunction with simple partial seizures or secondary generalised seizures. Patients with IGE experience either tonic clonic seizures in isolation or with other generalised seizures such as absences or myoclonus.

**Table 26: AED use by patient group (N=40).**

	Right Frontal RF (N=6)	Left Frontal LF (N=5)	Right Temporal RT (N=8)	Left Temporal LT (N=13)	IGE (N=8)	Total
Carbamazepine	3	3	4	10	2	22
Clobazam	2	1	1	5	2	11
Gabapentin	1	1				2
Lamotrigine	1	2	4	1	3	11
Levetiracetam	1	1	1	2		5
Phenobarbitone				1		1
Phenytoin	2	1				3
Sodium Valporate	3		2	1	3	9
Topiramate		2	2	3	3	10
Vigabatrim				1		1
<b>MONOTHERAPY</b>	1	1	0	5	0	7
<b>POLYTHERAPY</b>	5	4	8	8	8	33

Inspection of Table 26 reveals that the majority of patients were being treated with polytherapy (33) with carbamazapine being the most prescribed AED across all patient groups (24).

**10.2.3 Materials**

All materials except the Impact of Epilepsy Scale have been outlined in previous chapters.

**Impact of Epilepsy Scale.** (Jacoby et al, 1993), refer to appendix 14.

This is a brief questionnaire consisting of eight questions with responses made using a four point Likert scale. The questions ask the patient to consider how they feel that epilepsy and its treatment has affected their everyday lives The questions ask how the person feels about themselves, their overall health, their social relationships,

employability and social life. The purpose of administering this questionnaire was to ascertain how people with epilepsy perceive their social functioning.

Examples of questionnaire items, the response scale and the scoring protocol are provided below:

We would like to know how much you feel your epilepsy and its treatment affect your everyday life. For each item listed, please tick the response which shows best how you feel.

Does your epilepsy and its treatment affect:

	A lot	Some	A little	Not at all
Score	(4)	(3)	(2)	(1)
Your relationship with close members of your family?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
The way you feel about yourself?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

A maximum score of 4 is given to any items that are ticked ‘A Lot’ and a minimum score of 1 to any items that are ticked as ‘not at all’. The range of scores on this test is therefore 8-32 and a higher score indicates a greater perceived impact on the participant’s everyday life. The internal consistency of the scale reached 0.88 in a



study by Jacoby et al. (1996). Similarly in this study a value for Cronbach's alpha of 0.84 was obtained on for the scale.

#### ***10.2.4 Procedure***

All participants completed the Impact of Epilepsy Scale prior to completing any of the test battery.

#### ***10.3 Results***

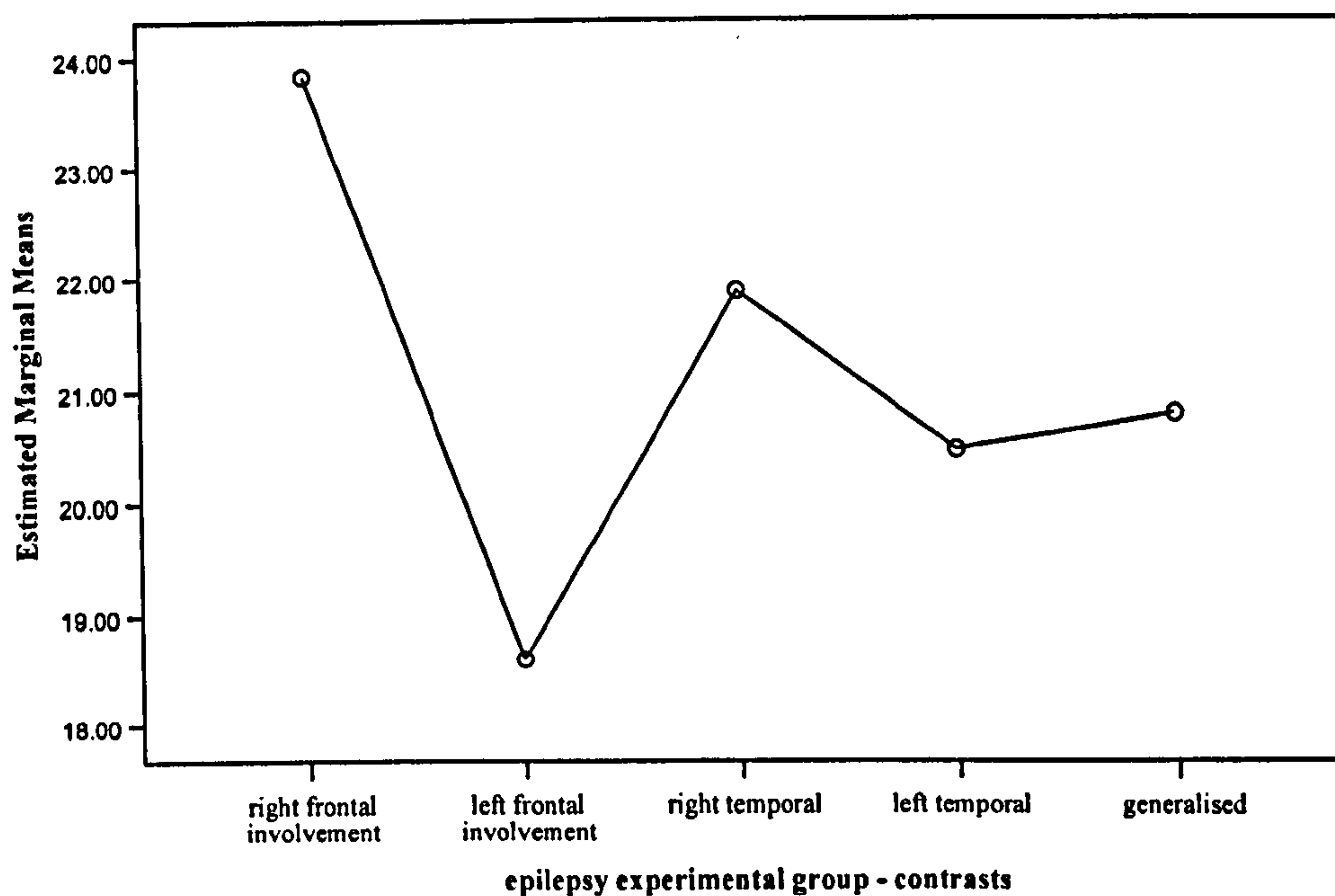
Levene's test demonstrated that there was equality of variance across the groups ( $p>0.05$ ). Skewness and kurtosis were not problematic in this sample;  $Z= 0.11$  and  $Z= -0.86$  respectively.

Table 27 illustrates that the RF group rated the impact of epilepsy the highest and the LF group rated it the lowest. ANOVA was conducted with Epilepsy Experimental Group between participants and Impact of Epilepsy score as the dependent variable.

**Table 27: Results of Impact of Epilepsy Scores for all Epilepsy Experimental Groups**  
*(Means and Standard Deviation).*

	Right Frontal (RF)	Left Frontal (LF)	Right Temporal (RT)	Left Temporal (RT)	IGE	Total
Impact of Epilepsy scores	23.8 (6.4)	18.6 (10.7)	21.9 (3.9)	20.5 (4.8)	20.8 (7.6)	21.1 (6.2)

The results did not show a significant difference between the groups on Impact of Epilepsy score:  $F(4,35) = 0.53, p > 0.05$ . Multivariate Helmert orthogonal contrasts were run to see if the RF group scores were significantly higher than all other patient groups. The results revealed that the RF group did not rate the impact of epilepsy significantly higher than the other patient groups ( $p > 0.05$ ). All other contrasts were not significant; refer to Figure 16 to see the trends in the data. Given the small cell sizes, it is necessary to exercise caution in interpreting these results.



*Figure 16: The means of Impact of Epilepsy scores by epilepsy experimental group.*

Hierarchical multiple regression analysis was performed on the data. The criterion variable was total scores on the Impact of Epilepsy Scale. The predictor variables which were entered in to the model first were Level of Education and Immediate Story Recall. Then total scores on the Hinting Task, ToM Stories, and the total number of correct answers on the Social Familiar Version of the WST, were entered into the model in the second stage.

The first model obtained was not significant,  $F(2,37) = 2.00$ ,  $p > .05$  with a weak relationship  $R = .31$  and a small degree of explained variance  $R\text{-Square} = .10$ . The second (full) model obtained (containing all predictor variables) was also not significant,  $F(5,34) = 1.17$ ,  $p > .05$  with a weak relationship  $R = .38$  and a small degree of explained variance  $R\text{-Square} = .15$ . The social cognition variables added in the



second stage of the hierarchy did not account for statistically significant additional variance. The increment to R-Square was .05,  $F(3,34)=0.66$ ,  $p>.05$ . None of the beta coefficients for the predictors in the full model were statistically significant,  $p>.05$  in all cases.

There were no significant correlations between Impact of Epilepsy score and Hints,  $r = -.23$ ,  $p>0.05$ ; ToM stories  $r = -.10$ ,  $p>0.05$ ; Social familiar (conditional reasoning)  $r = 0.04$ ,  $p>0.05$ ; or Immediate Story Recall:  $r = 0.01$ ,  $p>0.05$ . There was a significant weak and positive correlation between Impact of Epilepsy score and Level of Education,  $r = 0.29$ ,  $p<.05$

#### ***10.4 Summary of findings***

On average the RF group rated the impact of epilepsy on social functioning highest and LF group rated it the lowest. There were no significant differences between the groups on Impact of Epilepsy score and the RF group scores were not significantly higher than the other epilepsy groups. Level of Education, Immediate Story Recall, scores on the Hinting Task, ToM Stories, and social conditional reasoning did not significantly predict the Impact of Epilepsy scores. There was a significant, weak positive correlation between Impact of Epilepsy score and Level of Education, suggesting that the more educated people with epilepsy felt that epilepsy has affected their social functioning to a greater degree compared with less educated PWE.

## Chapter 11 General Discussion

### *11.1 Discussion of findings*

A major outcome from the Studies set out above was that the RF epilepsy group consistently under performed on ToM tasks. In Studies 1 and 2 they illustrated deficits across two different ToM paradigms, appreciation of first and second order false belief and deception and appreciation of non-literal language in the Hinting Task. These findings indicate that impaired ToM may be a particular feature of right frontal lobe pathology. The performance of the RF group on total ToM stories and first order ToM was significantly worse than all other patient groups. Their score was second lowest on the second order ToM stories (after LT) and significantly worse than the NC group. The extent of the RF mentalising deficit is evident in their performance on one of the most basic assessment measures of ToM, first order ToM (Stone, 2000). In fact all of the experimental groups except the LF score at ceiling on this task. Tests involving first order levels of intentionality of false belief and deception are usually passed by the age of 4, in normal children (Perner & Wimmer, 1985; Sodian et al., 1992; Wimmer & Perner, 1983; Wellman et al., 2001). This deficit in first order ToM cannot be attributed to the impact of immediate story recall or level of education, nor is it a consequence of group differences in IQ, number of AEDs, age of onset or duration of epilepsy. The RF group also appears to have difficulty in making inferences based on non-literal language. They were significantly worse on this task than all of the other experimental groups, though further analyses revealed that this deficit was mediated by immediate story recall.



The LT were impaired on second order ToM tasks and appreciation of hints though both of these deficits were mediated by immediate story recall. NC performed significantly better on the Hinting Task than all of the patient groups. When the data were transformed (because of violations of the normality requirement) the IGE and FHI groups were also impaired in relation to NC on this task. The word content of the second order ToM stories is greater than first order stories and this may account for why immediate story recall is mediating this deficit in the LT group. People with MTLE are known to have difficulty retaining information especially as the medial temporal lobe is associated with supporting recall and learning (parahippocampal area). The story recall deficits observed in the LT group may well reflect the fact that left hippocampal damage in MTLE can have more detrimental effects on memory function than right hippocampal damage (Baxendale, 1995; Rausch & Babb, 1993). Frequently people with left hippocampal lesions also exhibit more extra-hippocampal damage and so they are more susceptible cognitive dysfunction (Bonhila et al., 2007). Therefore it could be the additional memory load associated with the task that is affecting the performance of this group in the Hinting Task.

It appears from the analyses in Studies 1 and 2 that the poor narrative memory of people with RF and LT epilepsy can account for their poor performance on the Hinting Task and Second Order ToM Stories. Though, story recall performance does not impact on first order or overall ToM story performance in the RF group. The reason that the RF and LT groups are impaired in immediate story recall may possibly be different to the reasons why the other epilepsy groups do poorly on this measure. However, whilst it is plausible that immediate story recall deficits could be impacting on second order skills in the LT group, even when controlling for the effects of

immediate story recall and level of education Figure 11 clearly indicates that the LT performance is depressed in relation to the other groups, their adjusted means are still the lowest. What is notable in the data is the fact that poor story recall is a characteristic of the epilepsy groups across the board and the deficit looks to be of about the same magnitude across the groups. Yet poor ToM is only clearly seen in the RF and LT groups. This implies either that the story recall deficit has greater impact on ToM performance in these groups or that the RF and LT group have a ToM difficulty over and above the story recall problem.

In the ToM context it is possible that the RF and LT groups rely more on narrative memory than do the other PWE groups. Perhaps an intact ToM module makes minimal demands on narrative memory. With the ToM system impaired perhaps the RF and LT groups rely more on narrative memory so that those with intact memory use this to compensate for the ToM deficit while those with poor narrative memory do not have this option. Hence narrative memory appears to co-vary with ToM functioning in these groups only.

Participants were excluded from the study if they had undergone epilepsy surgery so that this thesis could investigate the impact that focal seizures have on current social cognitive functioning. A FHI control group were used to differentiate the impact that FLE seizures have on functioning in particular. The FHI group were not impaired on ToM performance in Study 1, nor were the IGE group, though once the data were transformed further analyses revealed that they did exhibit deficits on the Hinting Task. This is an interesting finding and implies that focal seizure activity (in the RF and LT group) is particularly detrimental to first and second order ToM task performance but



not to the appreciation of non literal language. The FHI group have acquired their injury and are not incurring any further lesions to the brain, in contrast, the RF and LT experience sub clinical discharges and have ongoing neural disruption due to seizure activity, which may give rise to further lesions in the brain as a consequence.

Propagation of seizure activity may cause neural disruption to systems which underpin social cognitive processes that are important to first and second order tasks. These factors may impact on social cognitive functioning over and above the impact of the site of lesion, particularly in right frontal lobe. Some lesion sites may be contained within extensive neural pathways supporting extensive patterns of interconnectivity, therefore seizure activity originating at these foci may propagate to more diverse regions resulting in greater disruption to the functions that they support. This may be so for the RF group and specifically with regard to the neural systems supporting ToM.

The performance of the RF group on the ToM measures supports a number of lesion studies which have demonstrated the importance of the frontal lobes and especially the right frontal lobe to ToM processing (Mazza et al., 2007; Rowe et al., 2001; Stone et al., 1998a; Stuss et al., 2001; Shamay-Tsoory et al., 2005a). The findings of Study 1 support the importance of the right hemisphere in processing deception (Ganis et al., 2003; Keenan et al., 2005; Malcolm & Paul, 2005) and particularly the right frontal lobe (Stuss et al., 2001).

The findings of Study 1 do not support the overall finding of Stone et al. (1998a) in that all the groups in their study performed well on first and second order false belief. Their study tested patients with bilateral and left dorsolateral PFC damage and they suggest that future research should be done with patients who have unilateral lesions.



They note that one patient (M.R.) in the OFC group whose lesions were mostly unilateral (right side), demonstrated the worst performance on the faux pas test. This provides tentative support for the results obtained in this thesis, which lateralise ToM deficits to the right frontal lobe.

Rowe et al. (2001) found impaired ToM on first and second order tasks in both right and left frontal patients. A specific ToM deficit may be more apparent in the right frontal lobe group in Rowe et al. (2001) study as they did not illustrate deficits in physical inference questions. The left frontal group in their study illustrated deficits on both mental and physical inference state questions so their performance does not adequately establish ToM deficits as being functionally dissociated from general inferential difficulties in this group. Rowe et al. (2001) findings lend support to the performance of the RF in Study 1, though it could be argued that as the present study did not measure general inferential ability, the ToM deficits observed in the RF may or may not be independent of general inferential deficits. Preexisting neurological conditions present in the participants in Rowe et al.'s. (2001) study could have impacted on ToM performance in some way. The present study adequately controlled for this by including a FHI group with no history of epilepsy and an IGE group with no seizure foci.

Stuss et al.'s. (2001) suggestion that a specific module for ToM ability may be partially located in the frontal lobes and may be particularly evident in the right frontal lobe is supported by Studies 1 and 2. Errors on the deception task used in Stuss et al. were correlated with lesion site and demonstrated that the medial areas of the FL, particularly on the right side were involved in the detection of deception, which is

consistent with the findings of the present thesis. Stuss et al. (2001) did not control for comprehension, general inferential ability or memory nor did they administer any other type of cognitive assessment (such as IQ) in order to control for potentially confounding affects of impairment in these areas.

Shamay-Tsoory et al. (2005a) found that frontal lobe patients were impaired on appreciation of faux pas and irony but not second order false belief. The right frontal group performed significantly worse in comparison to those with posterior lesions and controls, and these impairments were more severe in people with right VM lesions. This study supports the findings of Studies 1 and 2 as people with right frontal lobe pathology were impaired on a test of non-literal language appreciation (hinting). The lesion information in the present study was not detailed enough to enable comparison of performance in relation to anatomical site within the frontal lobe. In Shamay-Tsoory et al's study all participants with VM lesions scored at ceiling on the false belief task which suggests that the task was too easy. Similarly in Study 1 all experimental groups except RF and LF scored at ceiling on the first order tasks. This is often a problem when trying to assess cognitive ToM in adults (Stone et al., 1998a).

Mazza et al. (2007) found that a group of people with right orbito VM PFC lesions were impaired on first order and second order ToM in comparison to a left medial PFC group. They also found that all patient groups under performed on ToM in comparison to NC. This supports the RF group's performance on first order tasks in Study 1 and that all patients were impaired on hinting in comparison to NC in study 2. Mazza et al. did not leave sufficient time after surgery before their study (20-40 days) to rule out the confound of suppressed function in the right orbito VM PFC group.



Study 2 supports research which has emphasized the importance of the right hemisphere to deficits in appreciating non-literal language, (Brownell et al., 2000; Surian and Siegal, 2001) and to studies which have specifically emphasized anterior regions of the right hemisphere (Alexander et al., 1989; Happé et al., 1999; McDonald, 1993; Shamay-Tsoory et al., 2005a). The findings of Study 2 also support the importance of the right hemisphere in cognitive ToM, (Griffen et al., 2006) and both first order ToM judgements and appreciation of non-literal language after right hemispherectomy to treat epilepsy (Fournier et al., 2008).

Contrary to the findings of Studies 1 and 2 Shaw et al. (2007) did not find any impairment in ToM stories or appreciation of faux pas in people with right or left TLE. Schacher et al. (2006) argues that 'refractory MTLE may well interfere with certain aspects of social cognition that are reliant on the functional integrity of temporolimbic and frontal networks' (p.2142). It would appear that the left temporal lobe may be particularly important in this respect. Fine et al. (2001) found that a patient with early left amygdala damage was impaired on tasks involving second order false belief and appreciation of pragmatic language, whilst first order belief performance remained unaffected. These findings are replicated in LT patients in Studies 1 and 2 who were not impaired on first order tasks but were impaired on appreciation of hints and were the most impaired group on second order ToM. This is further supported in another lesion study by Apperley et al.(2004) where false belief deficits were apparent in people with lesions in the left temporo-parietal junction (TPJ).

In study 3 none of the experimental groups performed well on the abstract version of the conditional reasoning task. The NC performed significantly better overall on the



tasks than the patient groups, this was still evident even when the effect of level of education and immediate story recall were accounted for. A significant main effect of task was seen across the experimental groups. Statistically significant differences across the different task formats was characterised by superior performance in the social conditional reasoning (SF version) of the task. The NC, LT and RF illustrated facilitation for social conditional reasoning. Superior performance was also established in the NC group for the social unfamiliar (SU) version of the WST.

In Study 3 with 43.3% correct responses NC performed significantly better over all the conditional reasoning tasks compared to the patient groups (10.6% correct). This remained the case when the effects of level of education and immediate story recall were considered. Goel et al. (2004) found that NC success rate was 57.9% in comparison to 33.3% in their lesion sample, so generally the participants in this thesis were not as effective at reasoning across the different versions of the task. None of the experimental groups performed particularly well on the baseline measure of conditional reasoning (TRAD). Three out of eighteen NC managed to provide the correct answer on this version of the task, which equates to a success rate of (16.7%). This is comparable with previous research which suggests that normal participants usually have success rates of between 10-20% (Evans, 2003) and exactly matches the success rate of normal controls in Stone et al. (2002). The rates in the remaining experimental groups were as follows (RF = 7.1%; LF = 0%, FHI = 8.3%; RT=0%; LT= 0%; IGE= 9%). The LF, RT and LT groups did not get any answers correct on this version of the task.

Embedding the task in a social and familiar (SF) context was expected to generate the greatest facilitation effect in reasoning ability. This was the case and a significant effect

of this task was seen across the sample as a whole. Reasoning was especially facilitated in the NC, and the LT and RF groups also demonstrated some benefit. The social unfamiliar (SU) also produced facilitation in the NC group but not in any of the patient groups. In the SF condition the rates of success on the task were as follows:

NC=77.7%; RF=42.8%; LF= 15.4%; FHI = 25%; RT = 25%; LT= 53.3%; IGE=18.2%.

Grigg & Cox (1982) found success rates of 75% in their normal sample; this is comparable to performance in NC in the current study.

The findings of Study 3 are somewhat paradoxical. In Studies 1 and 2 the RF group clearly underperformed on the ToM tasks and the LT were also impaired on these measures (although this deficit was mediated by immediate story recall). It was expected that people with deficits in ToM would also be likely to have deficits in conditional reasoning, since several authors have argued that mentalising is underpinned by the capacity to reason about embedded conditional rules (Corcoran, 2000, 2001; Ermer et al., 2006; Frye et al., 1995; Perner & Lang, 2000). In fact the opposite effect was found. The social context of the tasks facilitated reasoning ability in NC, RF and LT groups, when the context was both social and familiar. As expected and demonstrated in a number of studies the thematic or content version of the task had a pronounced facilitatory affect in the NC group (Cheng & Holyoak, 1985; 1989; Cosmides, 1989; Fiddick et al., 2000; Goel et al., 2004; Girgerenzer & Hug, 1992; Griggs & Cox, 1982). The findings of the present study suggest that conditional reasoning does not underpin ToM ability and lends support to the findings of Fiddick et al.(2000), Goel et al .(2004) and Reis et al. (2007) who demonstrated that it was individuals with LF lesions who under performed on social conditional reasoning tasks. The LF exhibited the worst performance on the SF task in Study 3. The reasoning



ability of LF, FHI, RT and IGE groups was also not significantly facilitated by the social context in which the reasoning task was framed. The site of damage within the FHI group is not established in this sample, so it could be possible that LF damage within the FHI group might explain their lack of facilitation for reasoning in social contexts. This is in line with Goel et al's (2004) emphasis of the importance of the LF lobe in logical reasoning. IGE generally causes global diffuse damage throughout the brain which is not localised to any one region. In relation to IGE performance it is clear that the facilitation effect evident in the RF and LT is over and above the impact of seizure related variables (AEDs, duration illness, age of onset). and seems more specific to focal epilepsy and/or focal lesions.

Taken together the findings of the first three studies would lend support to the idea that there may be a double dissociation between theory of mind and social conditional reasoning ability. LF and RT were impaired on social conditional reasoning whilst RF and LT were impaired on ToM. The evidence seems particularly strong for a double dissociation between RF and LF on these tasks. Obviously further investigation is required to conclusively state that these two tasks are dissociated within the frontal lobes and specifically in people with focal epilepsy. It is worthy of note that this thesis is the largest lesion study to investigate ToM and social conditional reasoning so these findings are potentially important to this field of research

It would be interesting to further explore Corcoran's model by examining the involvement of autobiographical memory in ToM reasoning ability. The current study does not lend support to the involvement of social conditional reasoning in ToM processing. Although if this is the case, the reason that the RF group were particularly



poor at ToM may be because they have deficits in initially retrieving context specific information from autobiographical memory. There is evidence of this deficit in schizophrenia (Corcoran & Frith, 2003). Until the involvement of autobiographical memory in relation ToM is further investigated, Corcoran's model cannot be completely discounted.

Several theorists argue, that in order to solve reasoning problems that are set in social contexts we draw upon past experiences (Adolphs et al., 1996; Bechara et al., 1997; Corcoran 2000, 2001). Therefore if someone has difficulty accessing autobiographical memory their social reasoning abilities will be compromised. One interesting aspect of this idea is that if someone has limited social experiences from which to retrieve relevant information then they will be at a disadvantage in terms of reasoning about social situations. The absence of relevant analogs is likely to adversely affect their capacity for analogical reasoning when faced with a new social dilemma. This possibility is of particular interest in the light of Fine et al's (2001) findings. They found that a patient with early left amygdala damage was impaired on ToM. This patient was very socially isolated in life and this was one explanation put forward to account for the deficits observed. Evidence has suggested that there are environmental influences on developing ToM (Peterson & Siegal, 1995; 1997). This may be particularly relevant to PWE who are known to have limited social opportunities. Kirsch (2006) suggests that frequent seizures may interfere with the development of interpersonal skills in children or adolescents. Consequently due to ictal and post ictal disruption to functioning, PWE may have reduced opportunities to participate in situations where they can develop such skills. Medication may impact on their interpersonal skills and their social networks may be reduced due to stigmatisation,

lack of self esteem or because parents tend to be over protective. Exposure to social environments may be reduced and subsequently their ability to learn the complex social skills that facilitate social competence may be diminished.

The results of Study 4 did not show a significant difference between the epilepsy groups on the Impact of Epilepsy score. Only a subgroup of participants from Studies 1 to 3 was included in Study 4 as this questionnaire was administered part way through recruitment. Therefore this sub sample may not have been representative of the entire target population, though there is no specific evidence to suggest this was the case. The RF group did rate the impact of epilepsy higher than any of the other groups but given the small cell sizes, there may not have been sufficient power to detect significant differences between the groups and so it is necessary to exercise caution in interpreting these findings.

An alternative explanation may relate to impaired insight and self awareness, which is known to be a feature of frontal lobe pathology. Beer, John, Scabini & Knight (2006) found impaired self insight in people with orbitofrontal lesions. They 'lack insight into the inappropriateness of their behaviour' and have a type of social anosagnosia, which can contribute to their lack of social competence (p.872). Anosagnosia is common in people with ventromedial PFC damage and is a disorder which is characterised by lack of insight into one's own limitations and impairments. To date evidence has implicated the OFC and suggested that the medial PFC is critical in ToM processing (Frith & Frith, 2003; Stone et al., 1998a) Therefore the RF group may not recognise that they have difficulties in social situations because they have no insight into these impairments and how they may impact on their daily lives, consequently the ratings on



the Impact of Epilepsy scale may not reflect impairments in ToM experienced in this group. Interestingly a significant negative correlation between impact of epilepsy score and level of education suggesting that the more educated the individual was the more likely they were to realise the social restraints of their condition. In light of this future research should exercise caution when administering self report measures of social functioning, it may be best to give such assessment tools to family members or significant others who may be able to provide a more accurate and objective viewpoint. Frith, Happé and Siddons (1994) correlated caregiver's ratings of social adaption in children with autism in relation to tests of ToM and found significant correlations between the measures.

Administration of self report measures are not without their difficulties in epilepsy. Andelman, Zuckerman-Feldhay, Hoffien, Fried and Neufeld (2004) found that there were differences in self estimated memory ability and memory test performance in epilepsy patients with right hemisphere epileptogenic lesions in comparison to those with left sided lesions. The right sided patients significantly overestimated their memory abilities. The authors suggest that this bias in self awareness may distort their perception of quality of life. Ammerlaan, Hendriks, Colon and Kessels (2008) investigated facial recognition of emotion and measured interpersonal behaviour in epilepsy in nine patients after a unilateral amygdalahippocamctomy and 14 healthy controls. Epilepsy patients were impaired on facial recognition in relation to fear and disgust but these impairments did not reflect self reported difficulties in interpersonal behaviour in real life. The authors argue that this could be an issue with regards to patients not having insight in to their difficulties. These findings concur with a study by Reynders et al. (2005) in which impairments in emotion recognition in people with



TLE did not reflect assessment of social aspects of a quality of life. This is further supported by Schilbach et al. (2007) who criticise quality of life measures for not addressing patient's social role or their limitations, he suggests that epilepsy patients may not be aware of their deficits so therefore will not be able to report them accurately.

## ***11.2 Limitations***

Baron-Cohen (2000) highlights that impairment on ToM tasks is not diagnostic. There could be a number of reasons why someone is underperforming on such tasks. As mentioned in Chapter 4, ToM skills of deaf and blind children may not mature at the same rate as normal children possibly because they are deprived of the same perceptual input (Brown, Hobson, Lee & Stevenson, 1997; Peterson & Seigel, 1995). Peterson and Seigel (1997) found that this deficit was not apparent in deaf children who were taught sign language by their parents. Clearly caution needs to be exercised when assessing such skills in clinical samples, who may have ToM deficits for a number of other reasons relating to their environment or disorder. A good example of the effect that social environments have on ToM is apparent in studies of children. The presence of older siblings has been shown to facilitate performance on false belief tasks, play with older siblings and interacting with older people generally has also been shown to enhance children's ability to mentalise (Ruffman et al. 1998; Lewis et al. 1996; Youngblade & Dunn, 1995). Kirsch (2006) suggests that epilepsy may affect social cognition in a variety of ways, some of which are difficult to measure. Frequent seizures may interfere with the development of interpersonal skills in early life and reduce participation in social activities. PWE may have reduced social networks because of poor self esteem, stigma or parental over protectiveness. Consequently this in turn may interfere with the development of important life skills and have long term consequences on feelings of independence and competence (Austin & de Boer, 1997; Goodyer, 1988; Lothman, Pianta & Clarson, 1990; McCollum, 1981; Scambler & Hopkins, 1986).

Most ToM studies regardless of ToM assessment include additional tasks and/or control measures. Studies assess general cognitive abilities such as IQ, working memory and general inferential skills. In the Studies set out above, to reduce working memory load participants could refer to the stimulus material throughout administration of the tasks, pictorial story boards were also used in the ToM stories task. IQ and narrative memory were also accounted for in analysis of the results. However, it must be conceded that general inferential ability was not assessed in Studies 1 and 2. Therefore it cannot be determined whether the ToM impairments seen in the RF and LT groups are dissociated from deficits in general inferential ability.

Lesion studies that have assessed false-belief have presented with a number of methodological difficulties as tasks are often linguistic in nature and may place inherent demands on executive processes (Apperly et al., 2004). These tasks also rely on a person's ability to inhibit a pre-potent response ( i.e. that they know the real state of the world) (Stone et al., 2003). Problems with inhibition is known to be a feature of frontal lobe pathology, especially in people with orbito frontal and VM damage, areas of the brain which have been implicated in ToM processing. Autistic children (who are known to have ToM difficulty) also have deficits in inhibitory control (Ozonoff, 1997). Deficits in response inhibition as assessed by various forms of the Stroop Task have been evident in FLE (Corcoran & Upton, 1993; Helmstaedter et al., 1998; Helmstaedter et al., 1996). People with left sided lesions may under perform on tasks of a linguistic nature. Social reasoning problems in real life involve being able to inhibit one's knowledge, thoughts or feelings, deficits in being able to do this may account for impairments in social cognition in people with frontal lobe lesions (Apperley et al., 2004). The demand on these executive functions should be accounted



for in determining if a specific ToM deficit is apparent in the population of interest. These factors were not accounted for in Studies 1 and 2 so it is not conclusive that the RF and LT group have ToM deficits that are dissociated from high level cognitive skills.

The exact site of lesion within the frontal and temporal lobes is not analysed in relation to task performance. Whilst seizure foci and lateralisation are clearly established, there was no more detailed information available for the PWE included in this study to further localise the seizure focus. Thus the information obtained for this study was not detailed enough to make generalisations about how important specific anatomical locations were within the frontal and temporal lobes in the processing of the tasks used. This problem has been inherent in a number of lesion studies which have investigated social cognition (Griffen et al., 2006; Happé et al., 1999; Winner et al., 1998). This thesis did not take account of the extent or size of the lesion site in each participant which could have also confounded the findings. Shamay-Tsoory et al. (2005b) assessed appreciation of sarcasm in people with frontal and non frontal lesions. They found that patients with frontal lobe damage, and especially right VMPFC were impaired in appreciation of sarcasm; the extent of the lesion was significantly related to task performance.

The Impact of Epilepsy scale has been used in the past to assess how seizure related variables impact on social functioning and has shown evidence of construct validity. It has never been used before to assess social functioning in relation to social cognitive functioning. It could be possible that the tests of social cognitive functioning used in

this thesis lack ecological validity and do not tap into skills which underpin social competence in real life.

The PWE included in this research were recruited from a tertiary referral centre, therefore the clinical features of their disorder are likely to be more severe than that of an unselected population of PWE. Consequently the sample and their presenting social cognitive deficits and self reported social functioning may well not be representative of the wider epilepsy population, so the findings cannot be readily generalised. This has been highlighted by Aldenkamp, Donselaar, Flamman and Lafarre (2003) who found that self reported psychosocial functioning in an unselected population of PWE was comparable with the general population in relation to educational attainment, marital status and employment. The authors highlight that poor psychosocial functioning in PWE is predominant in a minority of patients with refractory epilepsy and not necessarily prevalent in those with well controlled seizures. Trostle, Hauser & Sharbrough (1989) found that social dysfunction was greater in clinical samples than an unselected population of PWE in the community. Most studies that assess psychological and social functioning in epilepsy are clinically based and so 'patients with chronic disease may well be over represented' in research (Chaplin, Yopez Lasso, Shorvon & Floyd, 1992, p.1414.) Chaplin et al. (1992) found that severe psychosocial problems in epilepsy in an unselected population of 192 PWE were only relevant to a small number of patients. Of the 14 areas of psychosocial functioning that were assessed in only four of these areas did more than 10% of PWE report severe difficulties, these were fear of seizures, fear of stigma in employment, lack of energy and detrimental effects on leisure pursuits. In general psychosocial problems were mild



in this cohort which differs greatly to reported differences in patients with chronic epilepsy.

This difficulty is common in clinical studies where patients who are under treatment are often approached to take part in research. The idea for this thesis was borne out of observations that people who had refractory epilepsy reported problems with social functioning and so in effect whilst the findings may not be entirely generalisable, this does not discount how valuable the findings are in relation to identifying socio-cognitive deficits in people who have severe forms of the condition. This is particularly important since it is these individuals who are more likely to experience problems with social competence and may benefit from treatment intervention.

Neuropsychological studies using PWE with clearly defined seizure foci can provide unique opportunities to investigate if that brain region underpins a particular psychological function. It must be noted that even localised seizures can cause diffuse dysfunction within the brain, particularly in the case of people who experience complex partial seizures with secondary generalisation. Structural imaging has demonstrated diffuse dysfunction throughout the brain in people who have focal epilepsy (McMillan et al., 2004). Diffuse contralateral and ipsilateral propagation of seizure activity is evident in TLE and FLE (Adam, Saint-Hilaire & Richer, 1994; Emerson, Turner Pedley, Walczak, & Forgiione, 1995). Seizure spread is particularly quick in FLE (Williamson, 1992) and because of the connections that the frontal lobe has to other regions of the brain, FLE seizures may impact on many other brain areas (Exner et al., 2002; Helmstaedter, 2001). Epileptogenic tissue in the frontal lobes can diminish general cognitive functioning (Morris & Cowey, 2000) and epileptogenic



tissue may in fact cause disruption to the functions of other cortical tissue (Milner, 1975). Therefore whilst this study used focal epilepsy participants, their seizures may be impacting on other brain regions.

It would also be useful in future studies to measure seizure severity as this may well mediate deficits in social cognition and social functioning in PWE. It is worthy of note that each focal epilepsy group is heterogeneous in nature and there is likely to be a great deal of variability in the amount of damage and underlying pathology within each group. Epilepsy is not 'a unitary disease entity ... seizure onset zone, seizure frequency, seizure duration, and seizure semiology may vary considerably between and within patients' (Jokeit & Schacher, 2004, s.14.). Variability across sample groups is a common problem when conducting lesion studies and in studies that assess functioning in focal epilepsy. Lesion studies involve investigating damaged brains so may not produce the same results as studying healthy brains. Consequently cortical reorganisation, regrowth and compensatory mechanisms may all impact on the psychological functioning of the brain. It is worthy of note that age of onset in the RF was earlier than for any of the other experimental groups. Upton & Thompson (1997) suggest that maturation of the frontal lobes is affected by age at seizure onset such that those with differing ages will be differentially impaired on cognitive tasks because of complex differences in how the frontal lobes develop.

This study took account of the impact of anxiety and depression as both are known to interfere with cognitive functioning. Patients were excluded from the study if they were diagnosed with either condition or taking medication for either disorder. Both anxiety and depression are common in PWE, especially in people with refractory seizures. It may be possible that although patients were not being treated that they may still be

experiencing depression and/or high levels of anxiety. Therefore it is recommended that future epilepsy studies incorporate a measure such as the HADS (Hospital Anxiety and Depression Scale) to account for this.

It is worthy of note that the use of ANCOVA (as used in Studies 1, 2 and 3) to investigate treatment effects is not without criticism. It was established that the experimental groups differed in terms of their level of education and their immediate story recall performance. Whilst ANCOVA was used to control for these differences across the groups, such techniques have been criticised as inappropriate (Miller & Chapman, 2001). This can be especially problematic when 'group membership is determined nonrandomly, as there is typically no thorough basis for determining whether a given pre treatment difference reflects random error or a true group difference' (Miller & Chapman, 2001, p40). This is relevant to the current thesis as the experimental groups were pre existing groups and were not the product of random assignment by the experimenter. Miller and Chapman go on to argue that apparent treatment effects are potentially ambiguous since it is not possible to differentiate between a main effect of treatment and an interaction between pre-treatment differences and the effects of treatment. While ANCOVA continues to be widely used in contexts analogous to those described here the results of studies employing this technique need to be treated with caution.



### ***11.3 Directions for Future Research***

Small sample sizes have reduced the statistical power of findings in many of the studies discussed in the literature review (Farrant et al., 2005; Schilbach et al., 2007; Shaw et al., 2007; Walpole et al., 2008), clearly there is a need for studies with larger sample sizes that will enable comparisons across anatomical lesion sites in the frontal and temporal lobes. None of the epilepsy studies that were reviewed recruited a suitable control group or assessed both right and left frontal and temporal groups. The present thesis, recruited an IGE group, who were also taking AEDs so as to reduce the possibility that the impact of medication might confound the results. Future study designs need to consider these issues. Lesion studies have to date mostly focused on assessing ToM in either patients with frontal or temporal lobe damage but as this study and brain imaging studies have shown, both lobes would appear to be implicated in the processing of ToM. Therefore as in the present thesis future research should incorporate patients with unilateral lesions to both the frontal and temporal lobes.

Often it has been too difficult to compare the findings of studies which employ different ToM paradigms. Harrington, Siegert and McClure (2005) reviewed 30 studies testing ToM in schizophrenia and concluded that ToM deficits are apparent but that comparison of results was difficult due to the fact that a variety of ToM measures were used to test the same construct e.g. irony and picture board stories, deception, false belief, hinting etc. As Baron-Cohen et al. (1995) suggest, ToM may be underpinned by a network of many neural structures which could represent different aspects of ToM abilities and differing task demands. Consequently this may account for the disparity in research findings. Therefore future research should endeavour to administer ToM test



batteries that assess ToM using techniques that are validated and incorporate measures of general inferential ability, executive function and memory. This will help to establish if ToM abilities are domain general or domain specific skills. Immediate story recall mediated some of the ToM deficits observed in Studies 1 and 2 so should be accounted for when assessing ToM in future studies. To enable more fruitful comparison between research findings, future research needs to use similar ToM tasks across different populations or to carefully monitor variations in task demand with corresponding active brain regions.

Studies in future should further explore the effects of brain damage at different stages of development to ToM (Happé et al., 1999). This would differentiate the importance of specific structures in the development of ToM and in online ToM abilities in adulthood. Whilst some studies have attempted to do this (Shaw et al., 2004) there is lack of research in this area.

Inconsistent findings across studies using adult samples may in part be due to the difficulty in finding appropriate measures to assess ToM in adult populations. Tests need to be hard enough to 'generate errors yet simple enough that errors are not merely due to more general processing demands' (Apperley et al., 2004, p.1774.) Future research could endeavour to develop more sophisticated measures. Studies should utilise more ecological valid measures of testing which reflect the complex subtle social cues that are apparent in human social interaction. (Lough, Lough, Kipps, Treise, Watson & Blair, 2006). To date most research which has investigated socio-cognitive functioning specifically in relation to ToM has used vignettes depicting social interactions or photographs illustrating different emotional expressions.

Traditional measures are easy to administer but may not necessarily tap into the complex perceptual processes that occur when we interpret social interactions. Future research should use ecologically valid measures of dynamic social interaction as it occurs in everyday life. It has been asserted that the TASITS (as described in detail in Chapter 5) is a much more ecologically valid measure of emotion recognition and social inference than traditional measures. This test might be incorporated into future research as it may be particularly sensitive in detecting impairments in social functioning. It has been used in one epilepsy study to date (Schilbach et al., 2007) and has been shown to be a valid measure of social cognition in people with head injury in past research (McDonald et al., 2003).

Further support for the relevance of test measures used come from a study by Chaytor, Schmitter-Edgecombe and Burr (2006). They assessed the ecological validity of executive functioning assessment. The sample consisted of people with neurological involvement of which more than 30% were PWE. They report that only 18-20% of the variance of cognitive functioning in daily life in the sample could be explained by traditional neuropsychological evaluation. In a further study, neuropsychological measures high in ecological validity were better able to predict daily cognitive functioning in people with moderate to severe traumatic brain injury than conventional measures (Chaytor, Temkin, Machamer & Dikmen, 2007).

One of the main problems in investigating social cognition in epilepsy is that it is difficult to differentiate between the impact of development, the epileptic foci, AED therapy and surgery, on the social abilities of PWE (Kirsch 2006). A number of studies have shown that quality of life scores increase after surgery but often these measures



do not adequately assess improvements in social functioning (Kirsch, 2006). As Schilbach et al. (2007) argue, social competence has a considerable effect on quality of life yet the study of social cognition in epilepsy has been largely neglected. Future research needs to continue to explore the impact that socio-cognitive dysfunction has on social functioning and quality of life in FLE and TLE. This could be achieved by administering a wide range of measures that utilise different paradigms in social cognition. Future research should include objective ratings of social functioning to see if real life behaviour is related to socio cognitive task performance. Quality of life measures that fully explore the impact of epilepsy on social functioning that are not self report measures but objective measures completed by significant others need to be employed. This may help resolve the difficulty of insight that appears to be apparent in FLE.

Future research which assesses social cognition before and after surgery is needed (Fournier et al., 2008). Surgery may help reduce seizures activity and reduce the amount of AEDs taken which in turn may improve social cognitive performance. Shaw et al. (2007) found improvements in social cognition (facial expression recognition) in people with left TLE after surgery. There is need for longitudinal research which establishes the impact of surgery on social cognition to establish whether epilepsy surgery is beneficial in improving such skills.

Further research should focus on trying to rehabilitate PWE after surgery where they may find themselves in new social situations that they have not previously experienced and may have difficulty adjusting (Bladin, 1992; Wilson, Bladin & Saling, 2004). PWE may have new found independence which can impact on interpersonal relationships,



causing friction and resentment. This may be particularly problematic if parental over protectiveness was a feature before surgery.

Neuroimaging studies alone cannot conclusively demonstrate the neural correlates of ToM, only lesion studies can determine whether a neural structure is essential to ToM processing (Bird et al., 2004; Griffen et al. 2006). 'Studies with lesion patients can supplement neuroimaging studies by revealing whether a particular region is critical for a particular function' (Stone, 2000 p 268). Imaging studies can provide evidence of whether a brain region is involved in ToM processing but not whether the region is essential, alternatively lesion studies can determine if a region is critical for ToM processing (Stone, 2000). Clearly both approaches are complementary and have an important place in furthering our understanding of the neural structures and systems which underpin ToM.

During test administration one RT and two RF female patients disclosed that their seizures and subsequent epilepsy were triggered by sexual abuse in childhood. It has been well established that there is relationship between sexual abuse and non epileptic attack disorder (Alper, Devinsky, Perrine, Vasquez & Luciano, 1993; Reilly, Baker, Rhodes & Salmon, 1999; Dikel, Fennell & Gilmore, 2003). Some evidence exists that there may also be a relationship in epilepsy (Grieg & Betts, 1992; Woods & Gruenthal, 2006), though more research is needed. Participants were not asked specifically about sexual abuse in childhood but chose to disclose this information. Therefore it is possible that other patients within the study were affected by this issue that did not disclose this information. These three participants represent over 5% of the epilepsy

sample tested, therefore this issue is worthy of further investigation. This research would lend itself well to qualitative methodology, such as thematic analysis.

### ***11.4 Implications of findings***

Taken together the findings suggest that impairment in theory of mind may be a particular feature of right frontal lobe pathology and that reasoning about social exchange and ToM may be functionally dissociated. PWE do not appear to have insight into their social functioning difficulties, which may well reflect underlying pathology.

Studies which have used fMRI connectivity analysis highlight the importance of cortical networks in supporting higher order cognitive processes. Connectivity analysis investigates the organic basis of cognition using connectivity maps which are based on the level of synchronicity in areas which are activated during task performance.

Imaging studies which have investigated ToM have found that mentalising is underpinned by cortical networks which involve the amygdala, orbitofrontal cortex, temporoparietal junction and particularly the medial prefrontal cortex (Frith & Frith, 2003; Siegal & Varley, 2002). The findings of Studies 1, 2 and 3 provide strong evidence of the existence of a cortical network which supports different aspects of social reasoning. Studies 1 and 2 suggest that the right frontal and left temporal lobe play an important role in appreciation of false belief, deception and pragmatic language. The findings of Study 3 suggest that the left frontal lobe plays a more important role in reasoning about social exchange. Together these studies support imaging evidence which emphasises the importance of the frontal and temporal lobes in socio cognitive processes. To date there have only been two studies which have used fMRI connectivity analysis to investigate social cognitive functioning (Corden, Critchley, Skuse, & Dolan., 2006; Kim et al., 2004). Future research in this area would



be useful in furthering our understanding of the cortical networks that underpin social cognition.

The findings of lesion studies which have implicated the importance of the frontal lobes and especially the right frontal lobe may provide support for a ToM explanation of the social and communication difficulties experienced by patients with frontal lobe damage (Rowe et al., 2001; Mazza et al., 2007; Stone et al., 1998; Stuss et al., 2001).

As the findings of studies 1 and 2 suggest, ToM deficits may also provide some explanation for the complex psychosocial difficulties apparent in PWE. Such difficulties include the experience of stigma, unemployment or underemployment, anxiety and depression, poor self esteem, social isolation and difficulties in interpersonal relationships (Austin & de Boer, 1997; Collings, 1990; De Souza & Salgado, 2006; Fisher et al, 2000; Grabowska-Grzyb, et al., 2006; Jacoby et al., 2006; Mensah et al., 2007; Morrell, 2002; Suurmeijer et al., 2001.).

Current quality of life measures rely on patients to self report improvements in functioning after surgery which may be problematic as this will rest on how well the patient has insight into their social difficulties. This could pose a particular problem for patients with RH lesions where sense of self may be impaired. (Kirsch, 2006)

Discrepancies between self report and objective measures of social functioning reports by significant others and or carers of social functioning in PWE on quality of life measures have been evident Hays et al. (1995). This evidence and the findings of study 4 imply that self report measures are not reliable so clinicians need to consider alternative ways of measuring social functioning in PWE.

Presurgical neuropsychological evaluation plays a major role in determining potential outcomes and treatment intervention after surgery. Serious consideration needs to be given to the effectiveness of the measures used during these assessments so that they are more ecologically valid and effectively tap into how neuropsychological functioning occurs in real life. This is particularly pertinent in light of recent research which has demonstrated that traditional neuropsychological evaluation of executive functioning only accounts for a small proportion of the variance in cognitive functioning in everyday life (Chaytor et al. 2007; Chaytor et al. 2006). The findings of this thesis and recent research have demonstrated that PWE have difficulties with socio cognitive functioning (Corcoran et al., 2000; Farrant et al., 2005; Fournier et al., 2008; Schacher et al., 2006; Schillbach et al., 2007; Walpole et al., 2008). It is becoming clear that neuropsychological assessment during clinical audit needs to consider assessing socio cognitive functioning in PWE and that such an assessment should be part of the pre and post surgical evaluation of potential surgical candidates. It is recommended that an instrument such as the TASITS which is more ecologically valid and likely to be more sensitive to socio cognitive impairment in real life, should be incorporated with more traditional measures to accurately establish the impairments of social perception in PWE. Such assessments should be complemented by an effective measure of the actual social difficulties that PWE experience in everyday life. A number of authors criticise current measures of social functioning used on PWE, currently these measures do not fully explore the impact that surgery has on interpersonal relationships or social competence (Kirsch, 2006; Schilbach et al., 2007). Therefore development of more appropriate measures is needed.

This study lateralises socio-cognitive dysfunction to the right frontal lobe and left temporal lobe, further study in this area may be able to support the lateralisation of these skills. If this is the case then socio-cognitive assessment may provide clinicians with a useful and inexpensive tool for lateralising the site of seizure foci in patients, particularly where anterior foci are suspected. This may be particularly valuable as there are few neuropsychological tests which can lateralise damage in the prefrontal cortex. The effects of lateralisation or localisation have not been found in studies which assess cognitive functioning in FLE (Helmstaedter et al.,1996; Upton & Thompson, 1996). Tests of social cognition may provide the clinician with an objective measure of deficits in social competence particularly as patients with FLE may lack insight into their impairments.

Patients who are at risk of reduced social competence can be identified and may possibly benefit from treatment intervention. Future investigations should assess the efficacy of such interventions in epilepsy.



### ***11.5 Original contribution to the field of epilepsy***

This thesis constitutes the first attempt to investigate theory of mind and social conditional reasoning in people with focal epilepsy (seizure foci in the RF, LF, RT, LT lobes) in relation to perceived social functioning. To establish the impact that focal epilepsy and in particular FLE had on these skills this research utilised three control groups (NC, IGE, FHI). To date no other research which has investigated social cognition has employed suitable clinical control groups, nor have the effects of FLE and TLE been investigated within the same study to compare differential group effects across these skills. The design of this thesis makes this a completely original piece of work within the field of epilepsy research. Consequently the outcomes of this thesis have the potential to offer valuable insights into the effects of epilepsy on socio-cognitive functioning and may highlight a number of useful clinical implications which will aid the management of the treatment of PWE.

### ***11.6 Clinical application of findings***

Pre surgical assessment for the treatment of epilepsy currently focuses on cognitive sequelae in determining the likelihood of successful surgical outcomes. The findings of this thesis suggest that people with focal epilepsy have impaired social reasoning and may well not have insight into such difficulties. In light of this neuropsychological assessment of PWE should incorporate measures of social reasoning. These tests may provide objective measures of social functioning for the clinician and may indicate PWE who are at risk of psychosocial difficulties. Such people could then be targeted for treatment intervention to improve their functioning within society. Pre and post

surgical assessment will also indicate whether surgical intervention can remediate social reasoning deficits in PWE and thereby improve quality of life. The tests of theory of mind and social conditional reasoning used in this thesis were sensitive to laterality effects and so may prove to be a useful resource in helping clinicians localise the site of seizure foci in patients who are being pre assessed for surgical intervention.

## ***11.7 Conclusions***

The recent development of ToM investigations in individuals with acquired neurological disorders will enhance the understanding of social and communicative deficits and what may be causing behavioural impairments in such clinical populations. It will also contribute to our knowledge of social cognitive functioning in the normal population.

Social cognition is an important but neglected area of study in the field of epilepsy. The study of ToM in epilepsy will lead to a greater understanding of the social cognitive deficits of the epileptic condition. This may in turn lead to more effective psychological interventions to enable the smoother functioning of people with epilepsy in society.



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## **APPENDICES**

- Appendix 1*** Patient Letter
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- Appendix 3*** Participant information sheet
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- Appendix 5*** A table taken from Ammons & Ammons (1962) to convert scores on the Quick Test (QT) into equivalent scores on the Weschler Adult Intelligence Scale (Weschler, 1955).
- Appendix 6*** Immediate Story Recall as measured by a subtest from the Adult Memory and Information Processing Battery (Coughlan & Hollows, 1985)
- Appendix 7*** The Theory of Mind Stories (after Frith & Corcoran, 1996)
- Appendix 8*** The transformed data analysis for Study 1: ANOVA and ANCOVA for performance on ToM stories across the experimental groups.
- Appendix 9*** The transformed data analysis for Study 1. ANOVA, ANCOVA, Kruskal Wallis and one sample t – tests for performance on First Order ToM Stories across the experimental groups
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- Appendix 12*** The Social Conditional Reasoning Task (Corcoran & Frith, 2005)
- Appendix 13*** Transformed data analysis for Study 4. ANOVA and ANCOVA for performance on the Conditional Reasoning Task across the experimental groups
- Appendix 14*** The Impact of Epilepsy Scale (Jacoby et al, 1993)

## APPENDIX 1

### *Patient Letter*

1<sup>st</sup> June 2003

Dear xxxx,

I am a researcher in the Psychology Dept. of Liverpool John Moores University. As part of my research I am exploring the relationship between different types of epilepsy and social cognition. In particular I am interested in a skill called 'theory of mind' which refers to our ability to understand the thoughts, beliefs and intentions of other people when these are not immediately clear like when, for example, someone drops a hint or cracks a joke. We know that certain parts of the brain specialise in tasks such as these and these brain areas can be those which are susceptible to seizure onset.

I have been liasing with Dr. Gus Baker, the Consultant Neuropsychologist at the Walton Centre for Neurology and Neurosurgery and he has identified you as someone who might be willing to help with this research project. Enclosed with this letter you will find an information sheet explaining what this research entails and describing the kind of tasks you would do. I would be very grateful for your help with this research, which is hoped, will benefit people who have epilepsy. This research can be done your home at a time that is convenient with you.

I will be in touch with you by telephone within the next couple of weeks so that we might be able to arrange a convenient date and time for me to visit if you do decide to participate. In the meantime, thank you for your attention to this matter and I look forward to speaking to you shortly.

Yours faithfully,

Jane McCagh.



APPENDIX 2

Consent Form

Title of Project: Social Cognition in epilepsy

Name of Researcher: Jane McCagh

Date of Consent .....

Please tick in the spaces below:

1. I have read and understood the information sheet about this research project. ....
2. I understand that my participation is voluntary and that I may withdraw at  
any time without my medical or legal rights being affected. ....
3. I will allow Jane McCagh to look at my medical records in order to check  
that the study is being carried out correctly. I understand that strict confidentiality will be  
maintained. ....
4. I agree to take part in the above study. ....

.....

Name of patient/                      Date                      Signature  
participant

.....

Name of researcher                      Date                      Signature  
taking consent

## APPENDIX 3

### Participant Information Sheet

#### **Research Study: Social Cognition in Epilepsy**

Researcher: Jane McCagh based at Liverpool John Moores University  
Tel: xxxxxxxxxx

#### **INFORMATION SHEET.**

I am interested in finding out how we understand what other people mean when it is not immediately clear. For example, when someone drops a hint, how are we able to understand what they actually mean?

This is a complex but important social skill that some people with certain conditions can find hard. I want to know why this is. I think that to be able to understand another person's meaning or intention, we need to recollect a similar kind of situation which has arisen in the past and then to compare that to what is going on in the present. It seems that certain areas of the brain are used to accomplish these skills and any disruption to those brain areas might have an impact on the ability to understand other people's thoughts, intentions and beliefs.

I need your help to find out if my ideas are correct by asking you to do some tasks.

I would need to see you for one or two sessions of about an hour long, which we can arrange at your convenience.

First, I will start by asking you to recollect some things from your past- for example things that have happened to you in school. Then I will see how good your memory is by getting you to recall a story. The tasks which follow are problem-solving tasks where you will answer questions about stories. These are quite quick and not very difficult.

Later, or in a second session on a different day if you prefer, you will do some tasks where you must figure out what people mean by things they say or what they intend within social situations. Again, these tasks are quite quick and not very difficult.

You do not have to do these tasks and if you decide not to, it will not affect your treatment in any way, now or in the future. If you do decide to have a go at the tasks, you are free to stop at any time you feel you have had enough.

Anything you tell me during the sessions will be strictly confidential. If you do have a go at these tasks, you must sign a consent form saying that you have agreed to help with the research and that you understand what it involves.

All proposals for research using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by Liverpool John Moores Ethics Committee and the South Sefton Research Ethics Committee .

#### **Please Note:**

**You have the right to withdraw from this study at any time without prejudice to access of services which are already being provided or may subsequently be provided to you.**

## APPENDIX 4

*Form 1 of the Quick Test (Ammons & Ammons, 1962)- words used and correct picture number*

Correct picture	Word
4	belt (easy)
1	dancing (easy)
4	traffic (easy)
4	whistle (easy)
3	fence (easy)
.....	
2	drink (easy)
3	wreck (easy)
1	music (easy)
2	medicine (easy)
4	gun (easy)
.....	
2	pepper ( easy)
3	racing ( easy)
2	salt (easy)
1	woman (easy)
2	sugar (easy)
.....	
3	track (easy)
4	school (6)
1	partner (7)
1	couples (7)
3	rail (7)
.....	
4	respected (8)
3	betting (8)
3	daring (9)
3	stadium (9)
4	pedestrian (10)
.....	
1	graceful (10)
2	fluid (11)
2	solution (11)
4	discipline(11)
.....	
2	crystallised (13)
1	turntable (13)
2	saccharin (14)
4	immature (14)
1	cordiality (15)
.....	



3	velocity (15)	
4	decisive (16)	
3	laceration (16)	
3	foliage (17)	
4	imperative (17)	
.....		
1	intimacy (18)	
2	concoction (18)	
1	conviviality (18+)	
4	hevrons (18+)	
2	condiment (hard)	
.....		
3	cocophony (hard)	
2	miscible (hard)	(ability to mix – associated with fluids/chemisty)
2	imbibe (hard)	(to drink)
1	amicable (hard)	
2	pungent (hard)	

## APPENDIX 4

*Pictures used to match against words in the Quick Test*

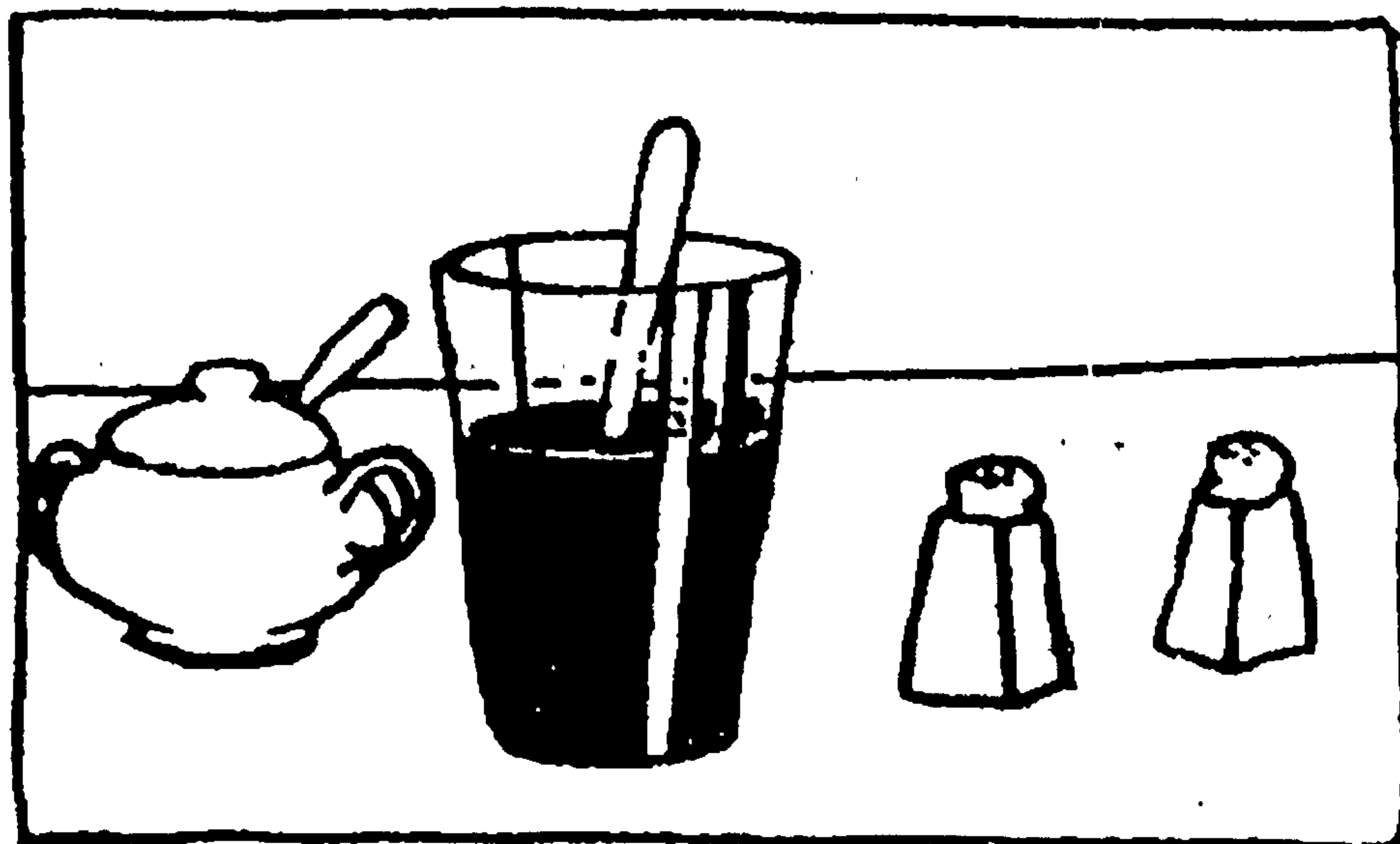
*Picture 1*

①



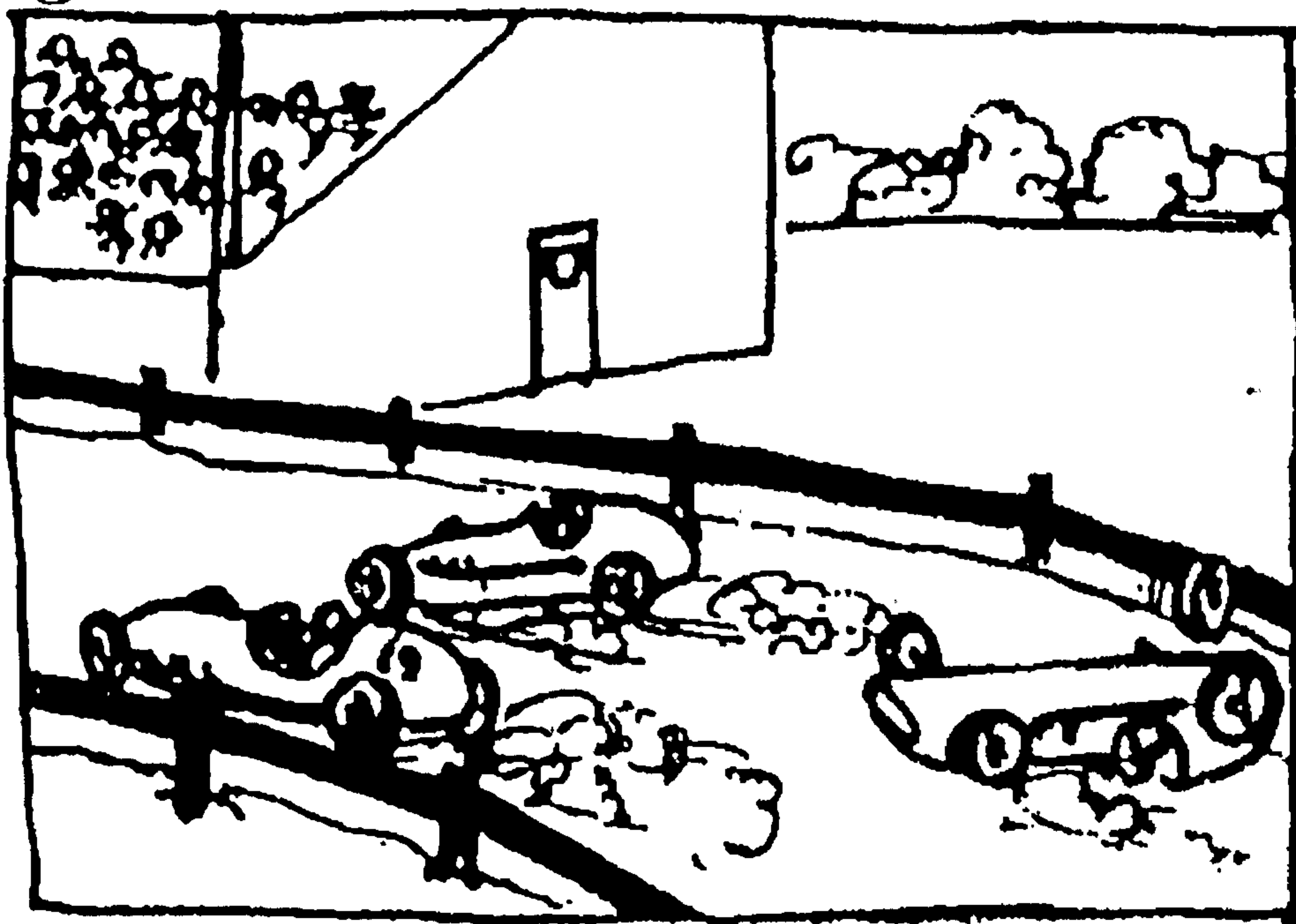
Picture 2

②



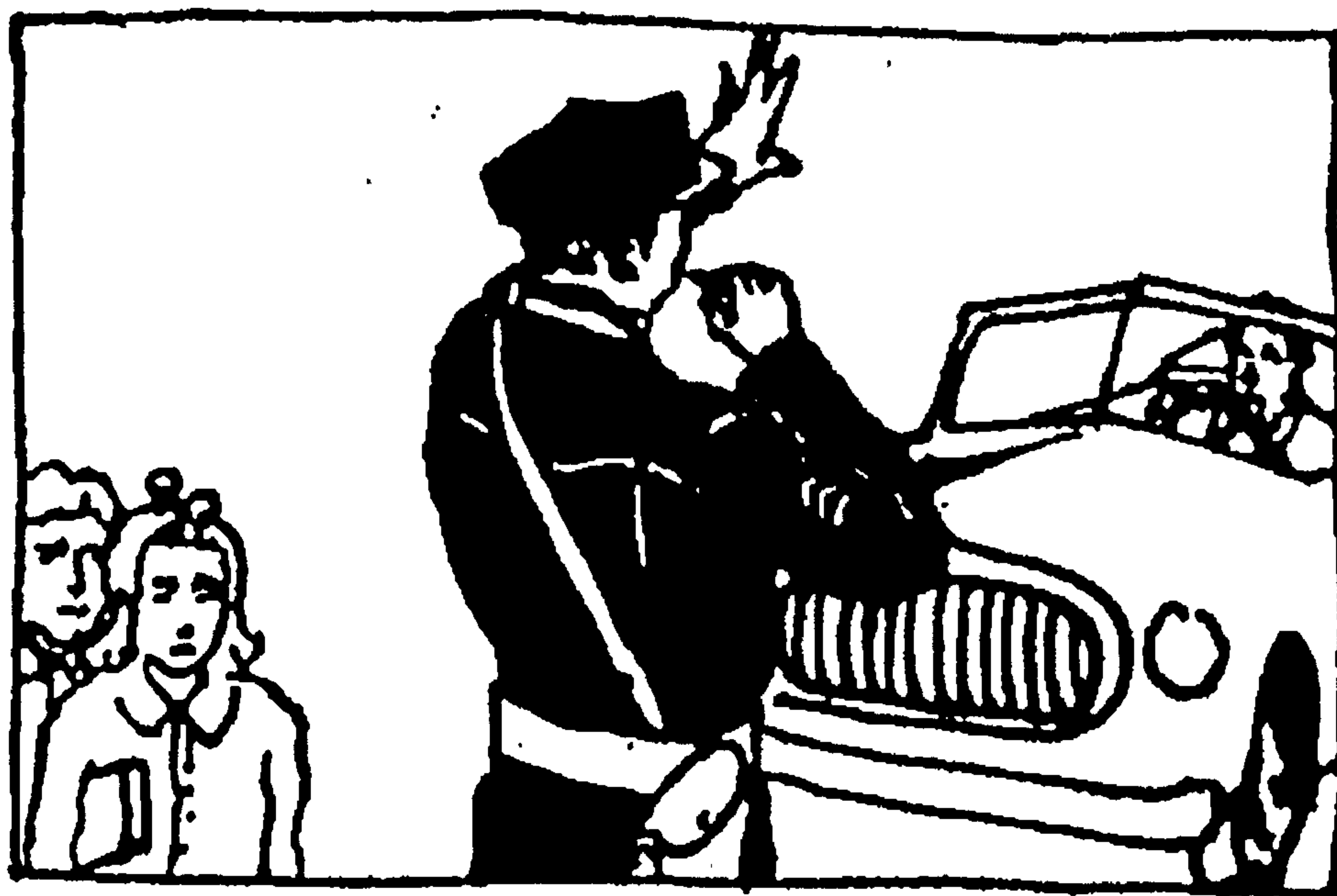
Picture 3

(3)



Picture 4

(4)





APPENDIX 5

Table 28: A table taken from Ammons & Ammons (1962) to convert scores on the Quick Test (QT) into equivalent scores on the Weschler Adult Intelligence Scale (Weschler, 1955).

QT NORMS: Based on the performance of a total sample of 458 white children and adults. The sample was rigorously quota-controlled for age, sex, grade in school and father's, husbands or own occupation. NB: Single Form 1 as highlighted in the table was used in this study.

TABLE 2 IQ AND PERCENTILE NORMS FOR WHITE ADULTS

IQ*	Percentile	Single Forms			Combination Forms			IQ*	Percentile	
		1	2	3	1+2	1+3	2+3		1+2+3	
160								150	160+	
155						100	100	100	149	155
150									148	150
145	99.9					99	99	99	147	145 99.9
140									146	140
135	99		50	50	50	98	98	98	145	135 99.9
130	98		49	49	49	97	97	97	143	130 98
125	95			48	48	95	96	95	142	125 95
120	90		48	46	47	93	94	93	140	120 90
116	85		47	45	46	92	93	91	138	116 85
113	80					91	92	90	136	113 80
110	75		46	44	45	90	91	89	135	110 75
108	70		45	43	44	89	90	88	133	108 70
106										
104	60		44	42	43	86	87	85	129	104 60
102			43			84	85	83	127	102
100	50		42	41	42	83	84	82	125	100 50
98			41	40	41	82	82	81	123	98
96	40		40	39	40	81	81	80	121	96 40
94						79	79	79	118	94
92	30		39	38	39	77	77	77	115	92 30
90	25		38	36	37	74	75	74	111	90 25
87	20		36	34	36	71	72	71	109	87 20
84	15		35	33	35	68	69	68	104	84 15
80	10		32	32	32	63	64	63	96	80 10
75	5		30	30	30	58	59	58	90	75 5
70	2		27	25	28	52	53	52	82	70 2
65	1		25	23	24	47	48	47	77	65 1
60			22	20	21	42	43	42	70	60
55	0.1		21	19	20	39	40	39	66	55 0.1
50			19	17	18	35	36	35	60	50
45			18	16	17	33	34	33	57	45
40			16	14	15	30	31	30	52	40

IQs above 135, below 65 have been estimated from normalized frequency distributions.

## APPENDIX 6

### *Immediate Story Recall as measured by a subtest from the Adult Memory and Information Processing Battery (Coughlan & Hollows, 1985)*

Mr. Peter / William / who died last month (\*)/ has left two hundred thousand pounds / to a charity that provides / seaside outings / for the children / of refugees. / His younger / brother,/ who lives in Canada, / will inherit / his house,/ his yacht / and his Rolls Royce car./

Mr. Williams came from a poor family / but he was determined to do well. / He worked extremely hard / and everyone liked him. / His first job / was as a butcher's boy / but he earned extra money / by doing night work / in a laundry. / When he was thirty / he bought a van / and started a removals business./ However, he eventually made his fortune / selling paintings / and antique clocks.

\* Score 1 if implied

Score (Max 60)

---

## APPENDIX 7

### *The Theory of Mind Stories (after Frith & Corcoran, 1996)*

#### **Instructions**

This task has four stories all about people doing certain things. I'm going to read through them and show you some pictures which describe what is going on in the story. I want you to concentrate carefully on these stories because when I've read each one out, I'll be asking you some questions about them.

Okay. Here's the first story. Listen carefully.

#### **First Order False Belief.**

John has five cigarettes left in his packet. He puts his packet on the table and goes out of the room. Janet comes in and takes one of John's cigarettes and leaves the room.

#### **ToM question:**

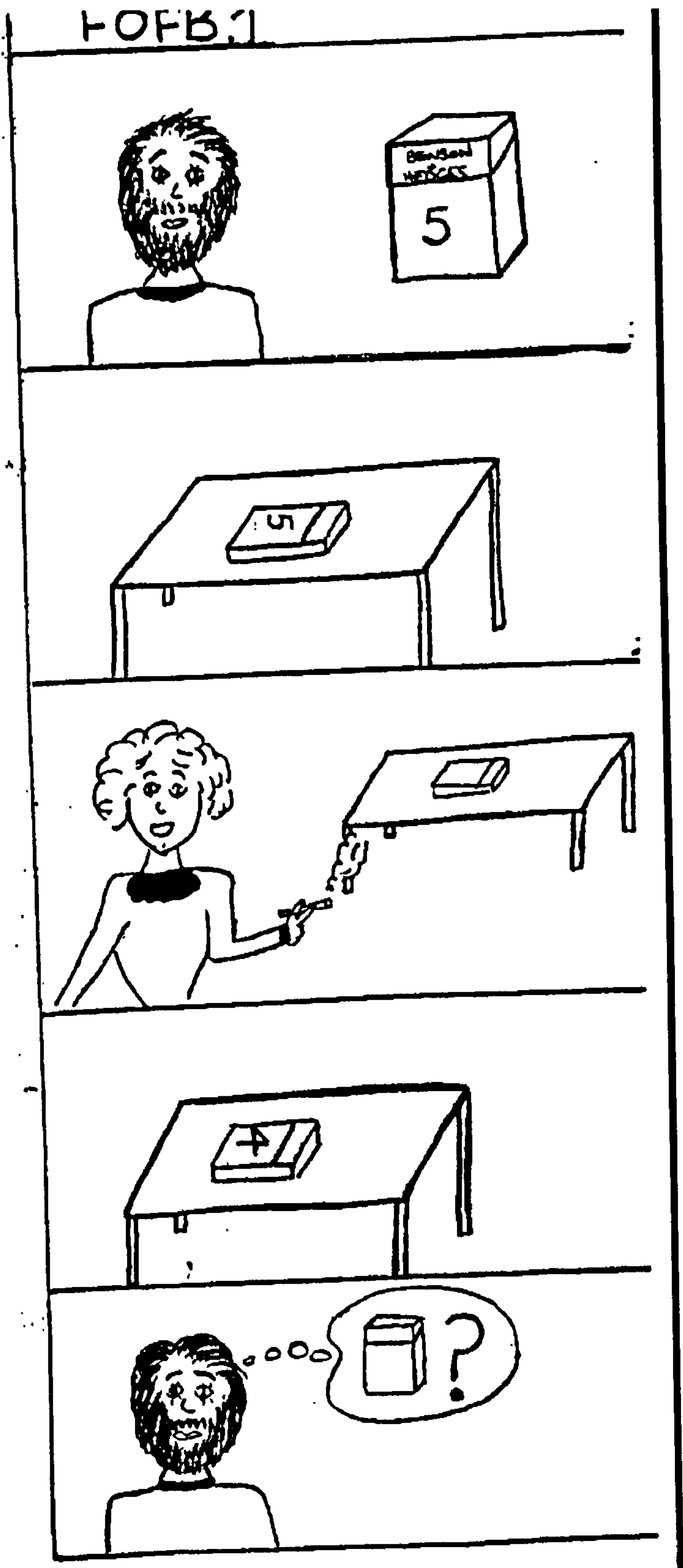
When John comes back for his cigarettes, how many does he think he has left?

#### **Reality question:**

How many cigarettes does John really have left?



First Order False Belief – Story board



**First Order Deception.**

Mary has a box of chocolates which she puts in her drawer for safe-keeping. A few minutes later her greedy brother Bill comes in and asks Mary:

"where are your chocolates, in the top or the bottom drawer?"

Mary doesn't want Bill to find her chocolates.

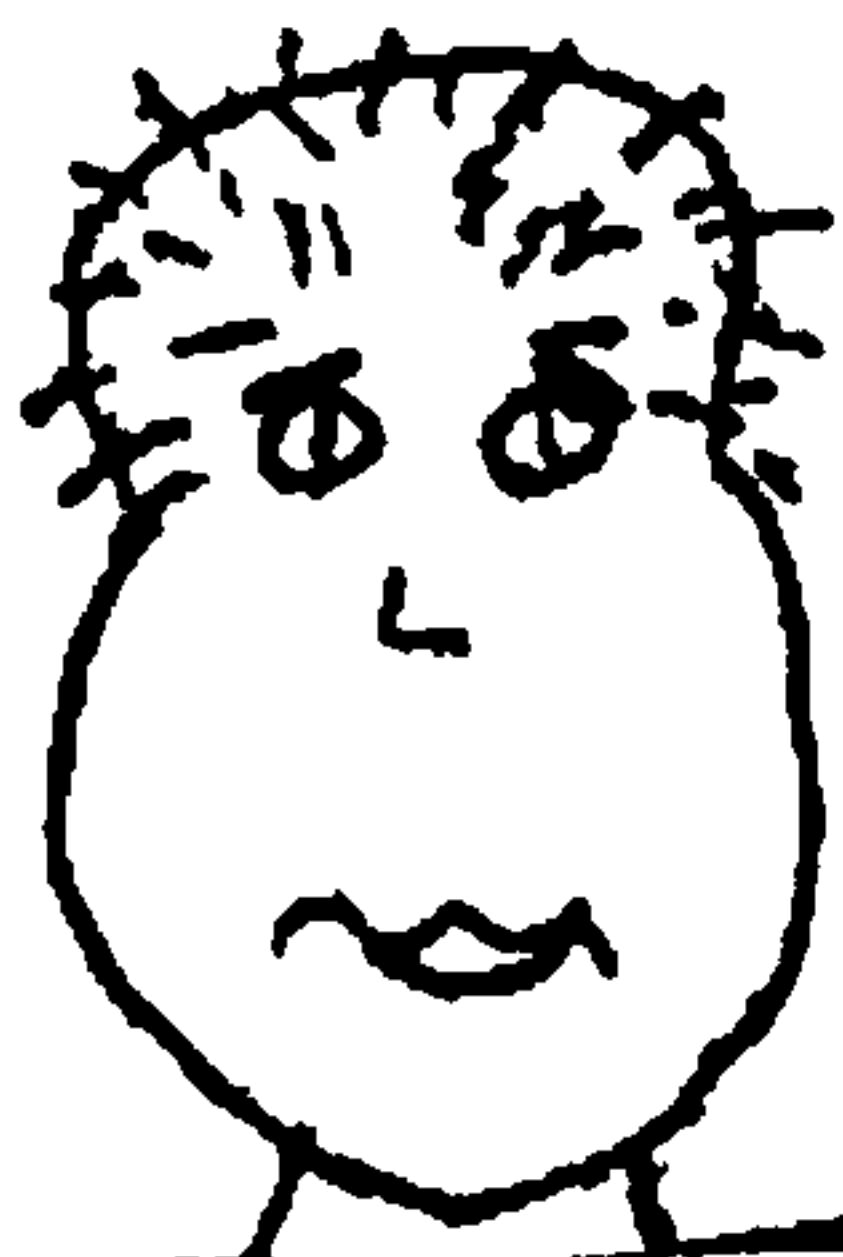
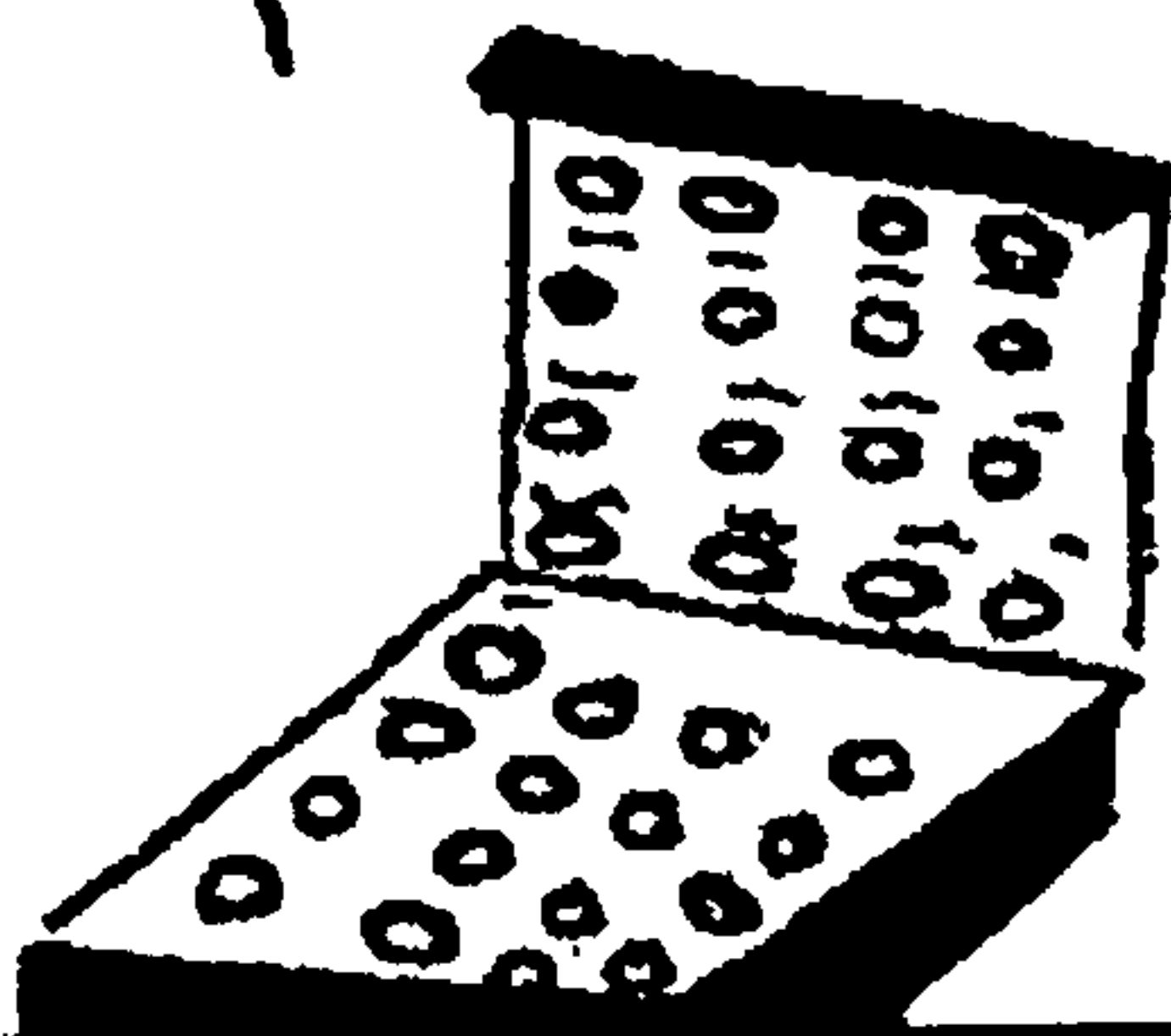
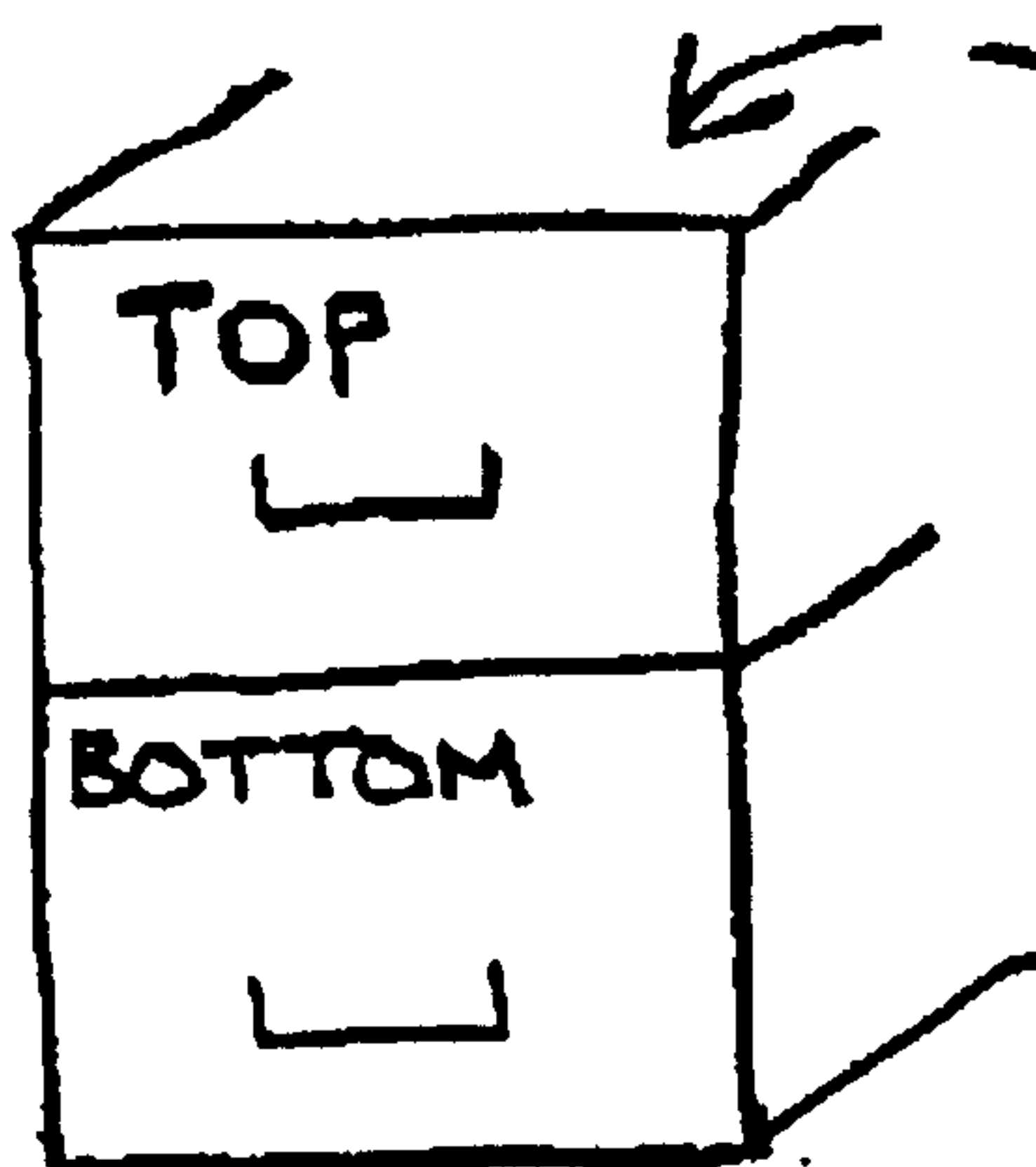
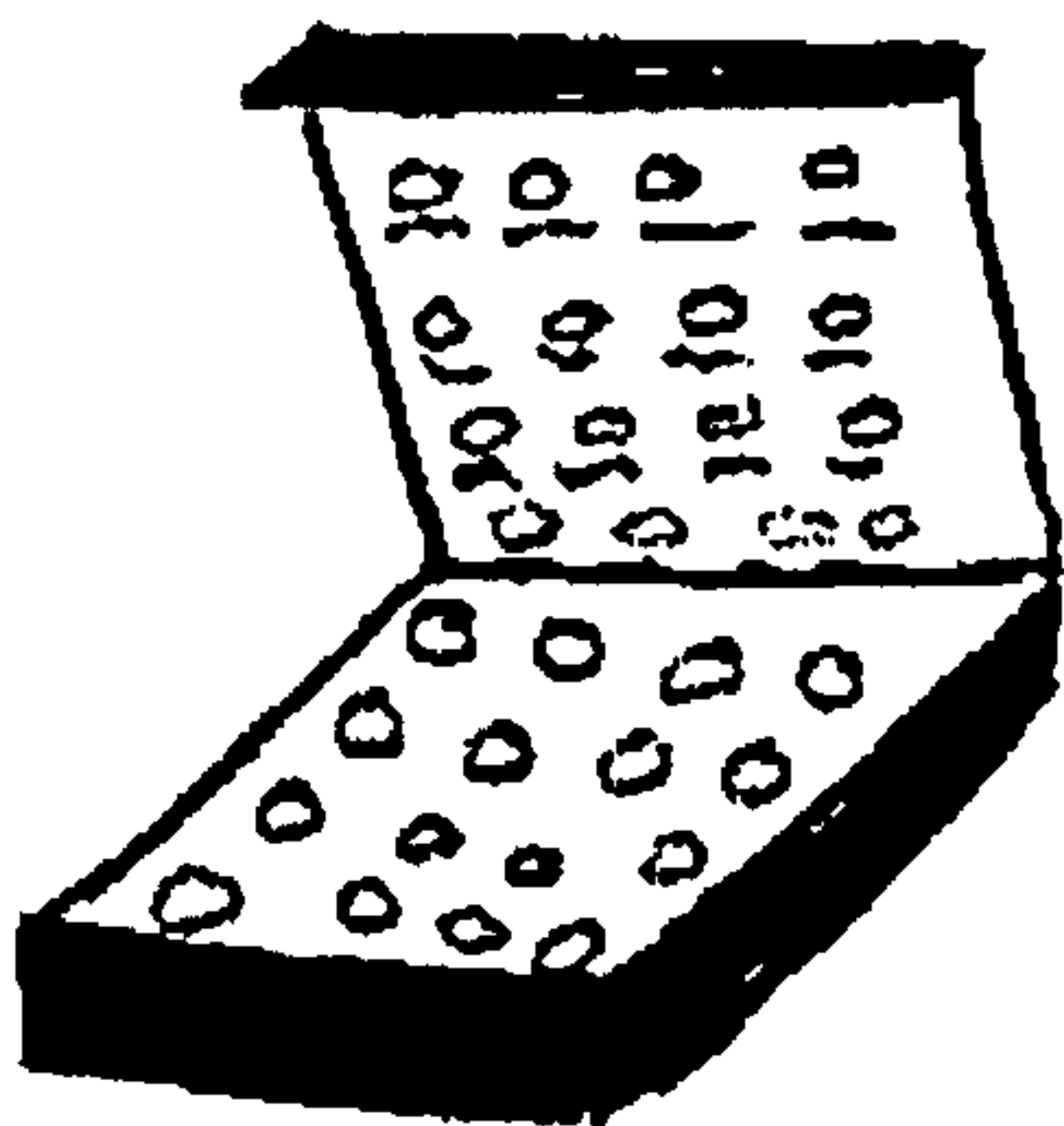
**ToM question:**

In which drawer does Mary say her chocolates are and why?

**Reality question:**

Where are the chocolates really?

F O U L



CHOCOLATES  
?  
yum...  
yum...



? ? ?



### **Second Order False Belief.**

Sally and Ian are at the station because Sally has to catch a train home. Sally lives in Homesville but the train doesn't stop at Homesville station. Sally will have to get off at Neartown and walk. Sally goes to buy a magazine to read on her journey before she buys her ticket. While she is gone, there is an alteration to the timetable and the train is now going to stop at Homesville. The guard tells Ian about this change and Ian sets off to find Sally to tell her. Before Ian finds Sally, the guard finds her and tells her "the train will now stop at Homesville". Ian eventually finds Sally who has just bought her ticket.

#### **ToM question:**

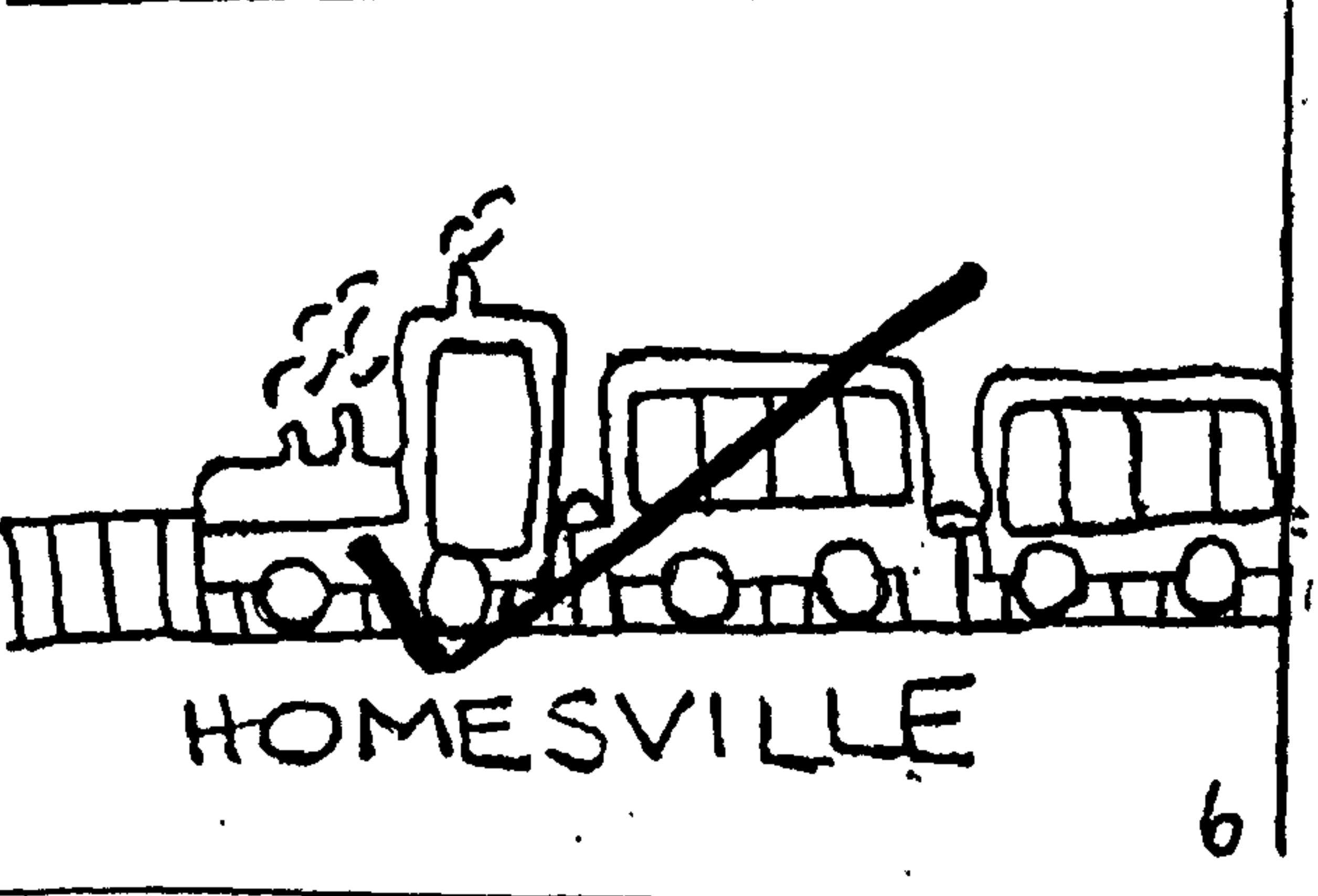
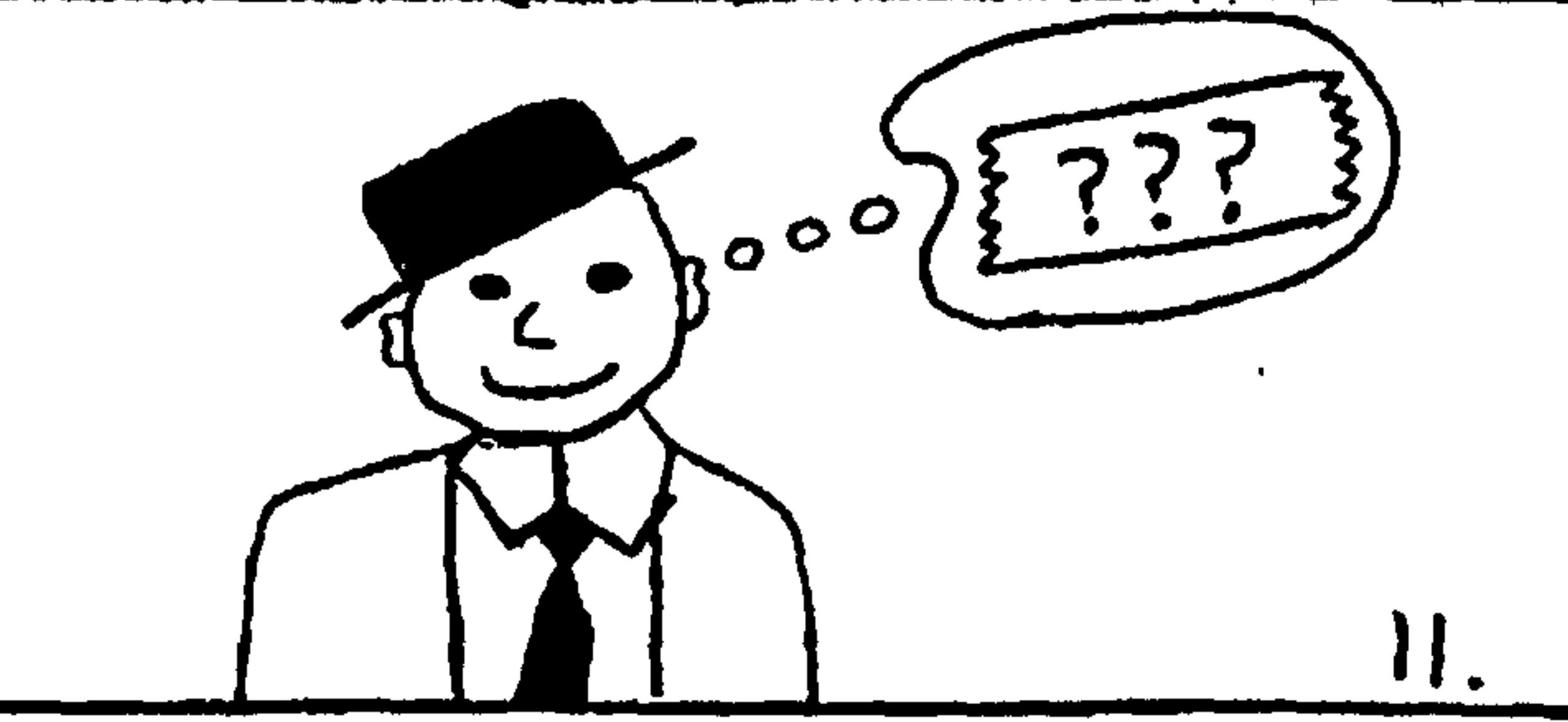
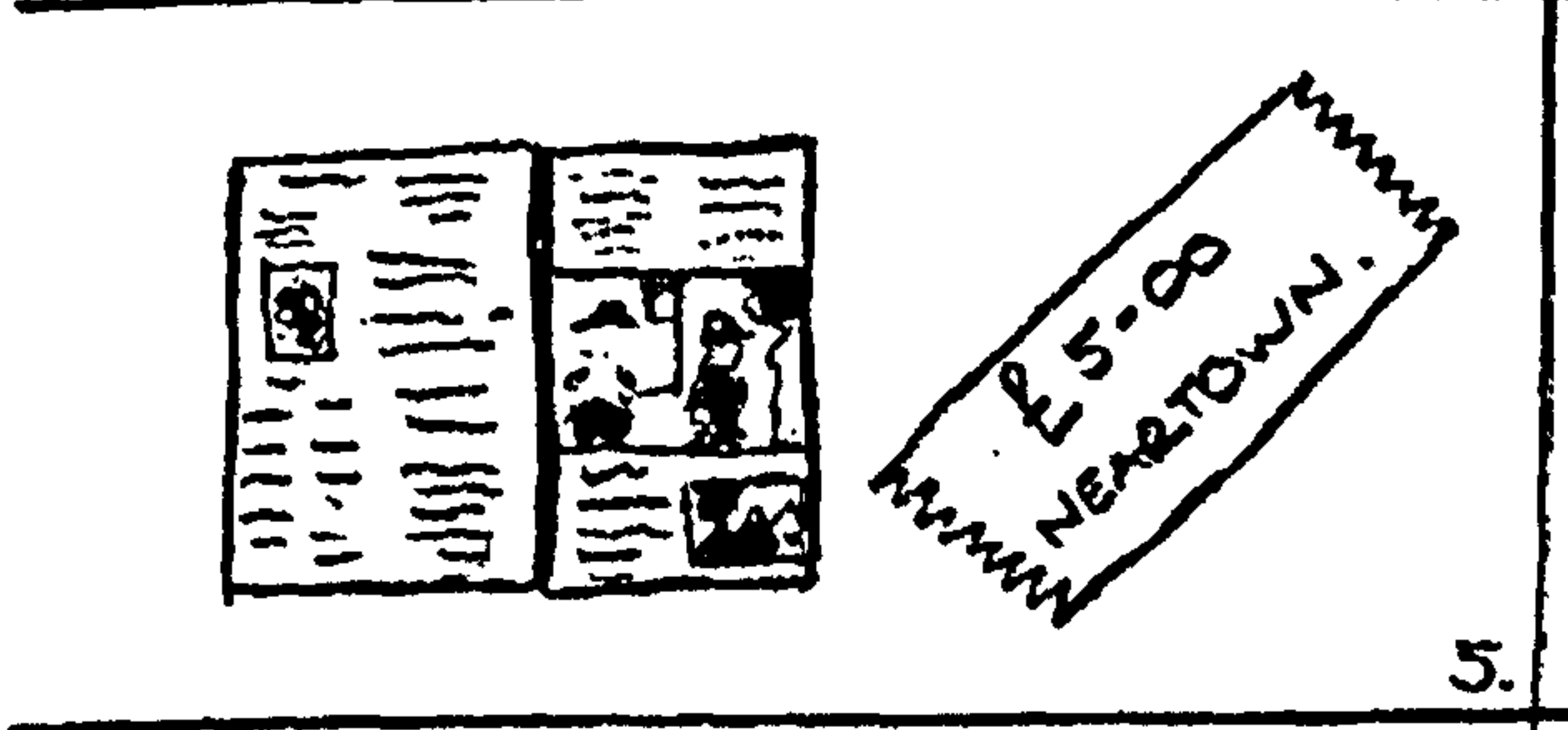
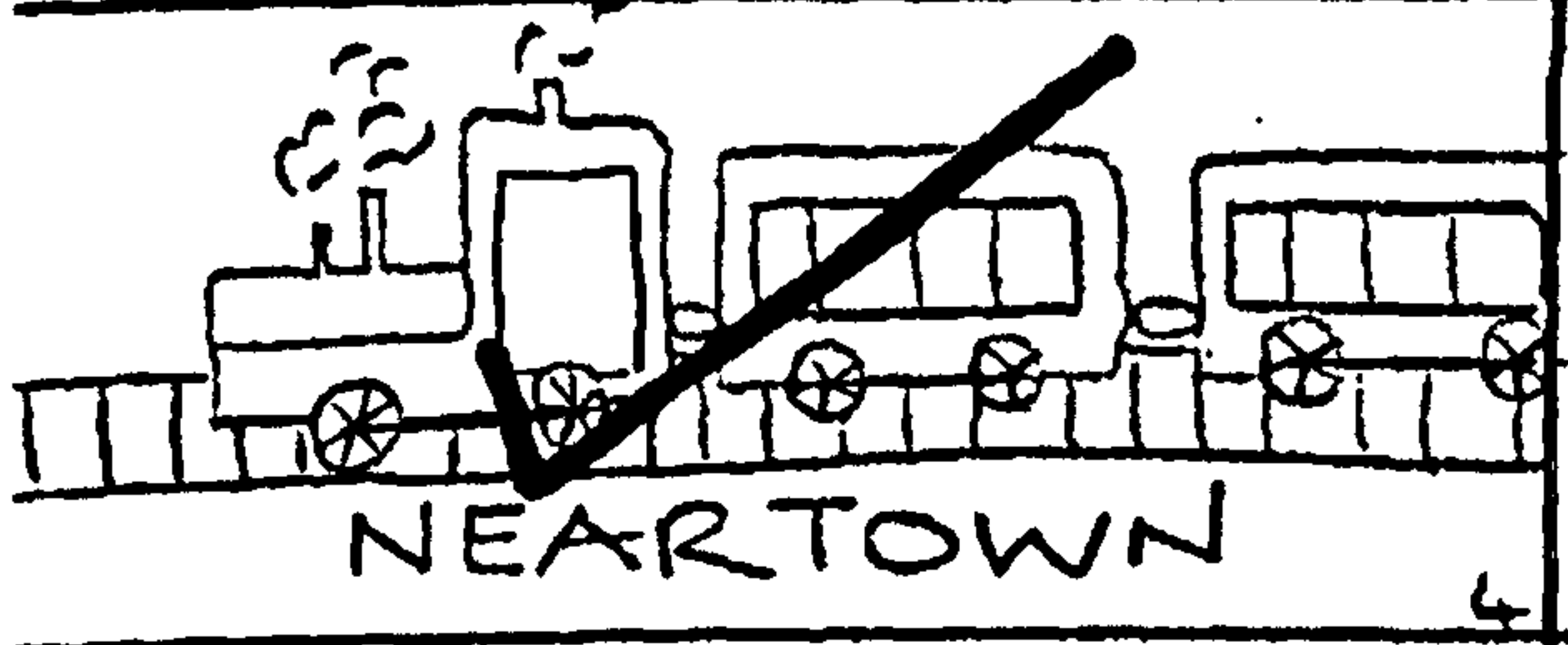
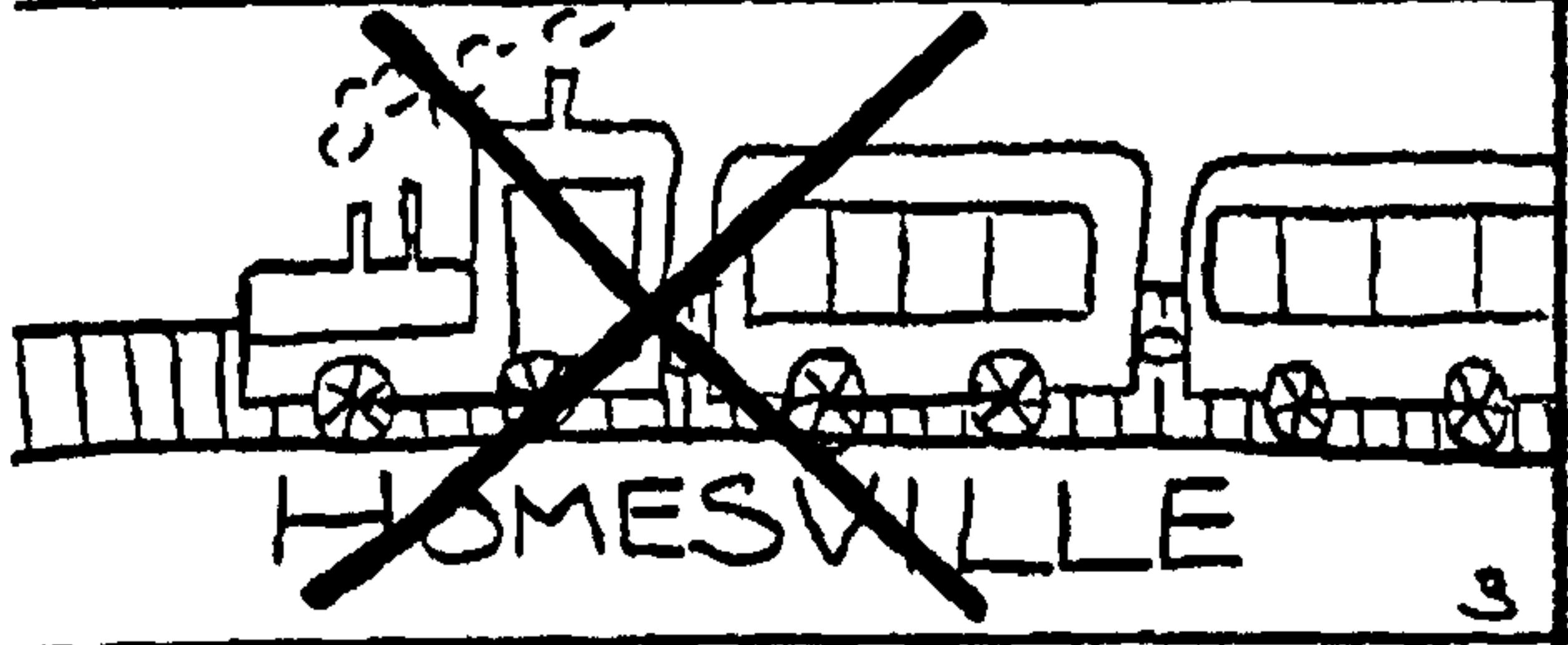
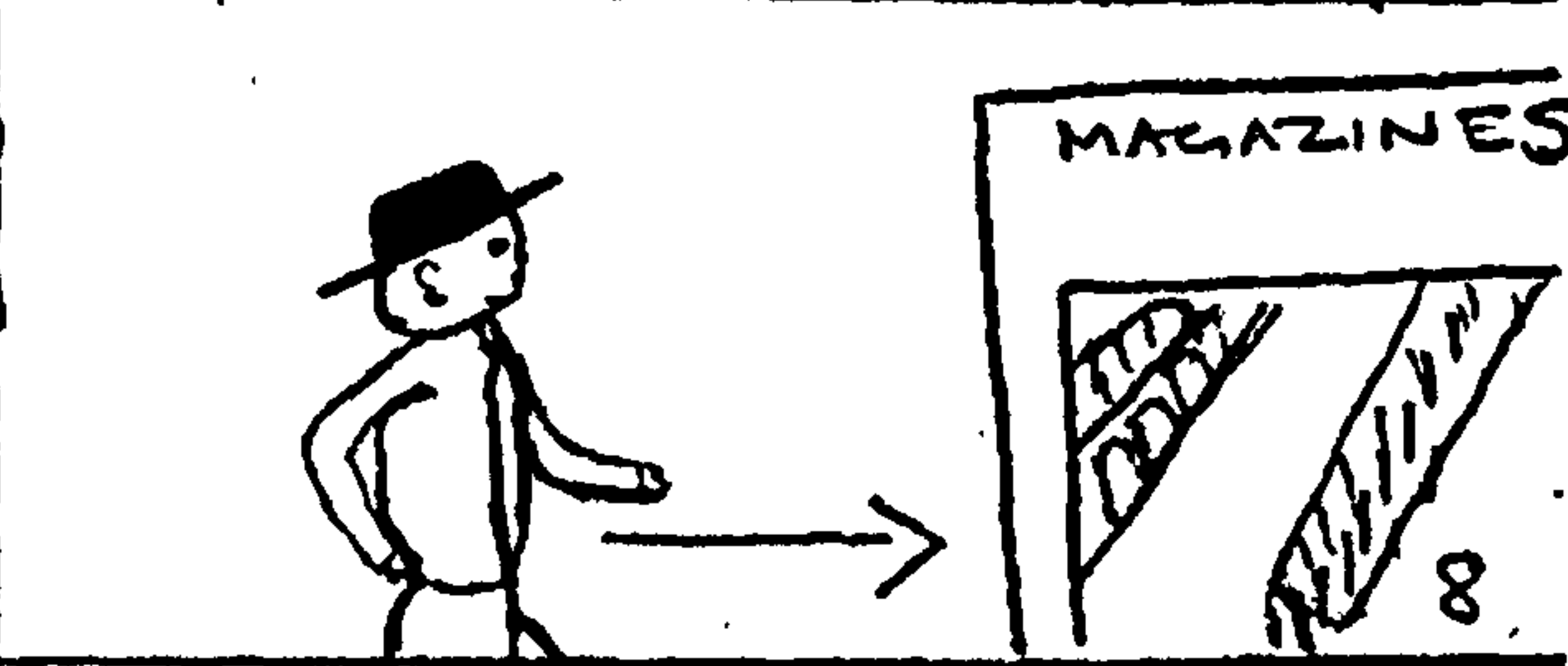
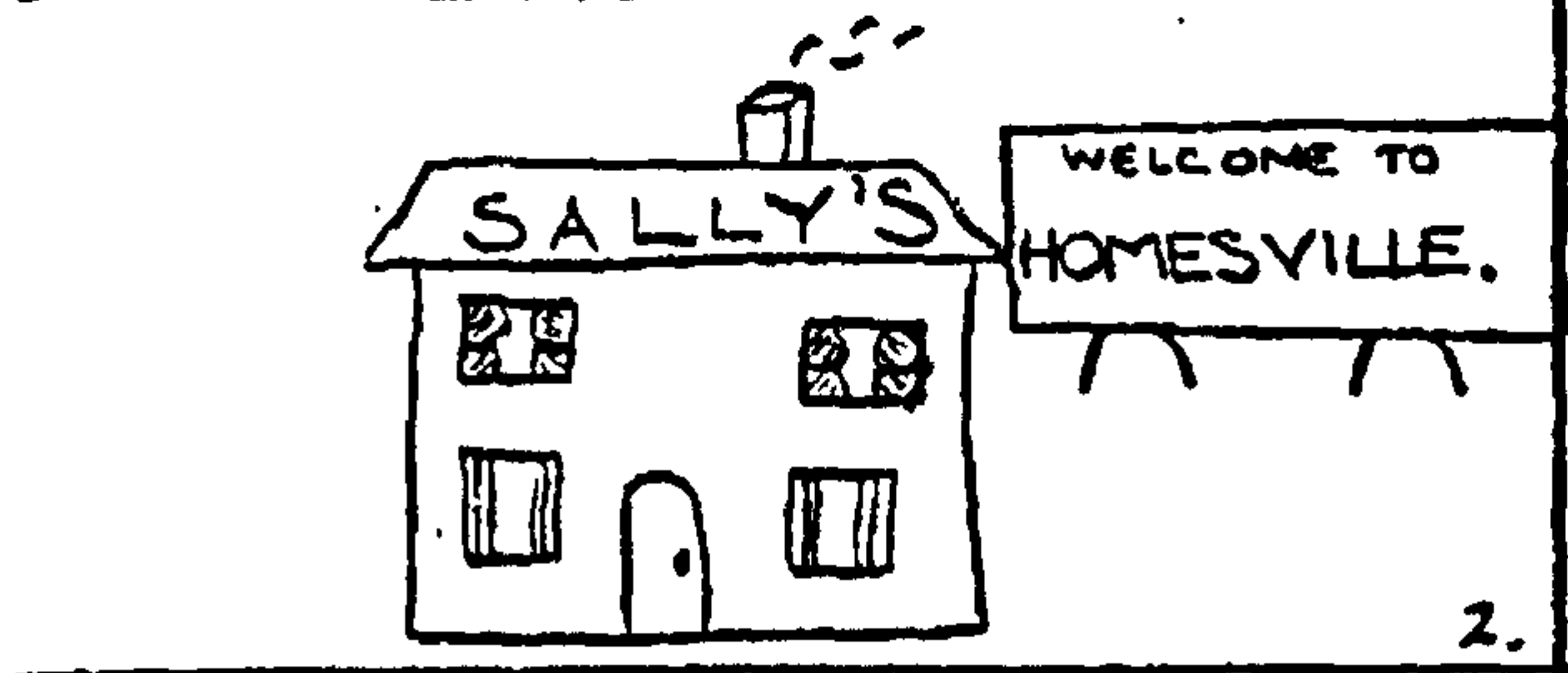
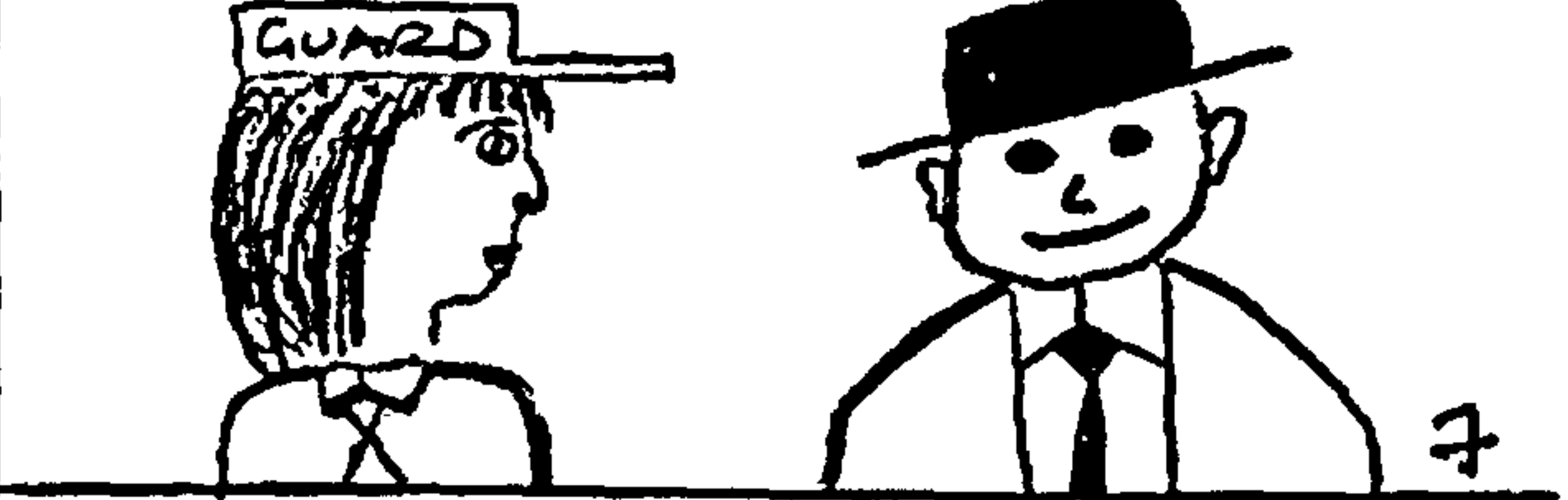
Which station does Ian think that Sally has bought her ticket for?

#### **Reality question:**

Which station has Sally really bought her ticket for?

SOFB1

STATION



### Second Order Deception.

Jack has taken the money that Cassy owes him from her purse without asking her. Cassy has found out and she is angry and looking for Jack. While Jack is trying to hide, he meets Lenny, their little brother. Lenny knows what has happened. Jack promises Lenny lots of sweets if he doesn't help Cassy find him and he tells Lenny that he'll be hiding in the tree-house. Meanwhile, Cassy has looked everywhere for Jack except the shed or the tree-house. She comes across Lenny and asks him:

"Do you know if Jack is in the tree-house or the shed?" Cassy suspects that Jack has tried to bribe Lenny so she doesn't trust him. Lenny is smart and he realises that Cassy doesn't trust him. He is looking forward to his sweets.

#### ToM question:

Where will Lenny tell Cassy to look for Jack - in the tree-house or the shed? Why?

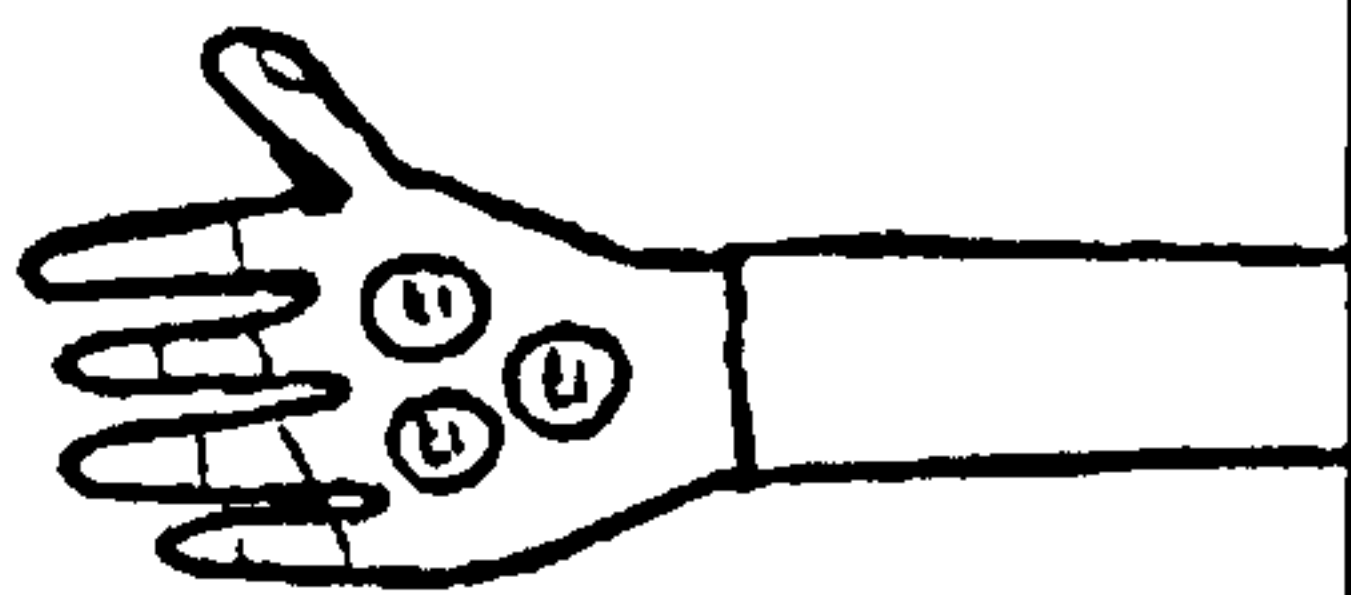
#### Reality question:

Where is Jack really hiding?

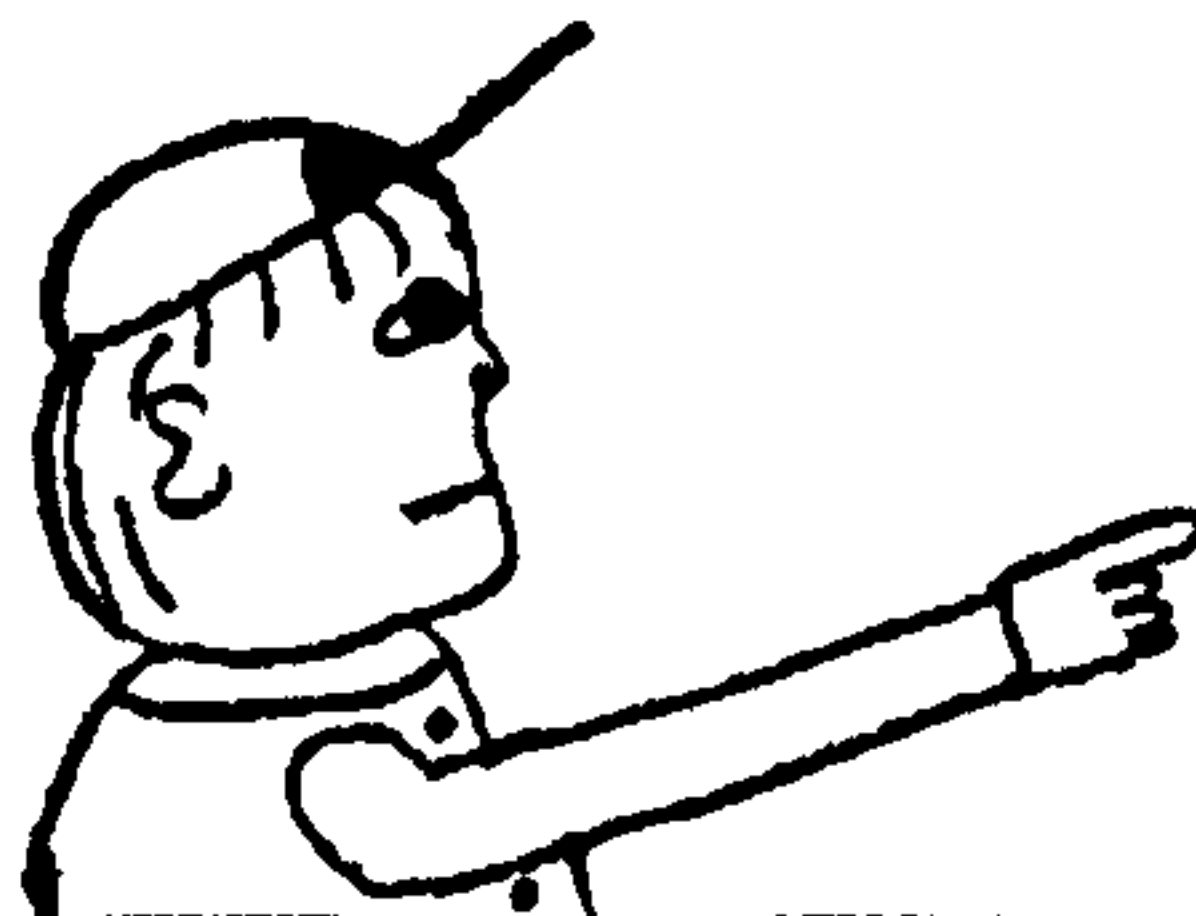


Second Order Deception – Story board

SODI



1

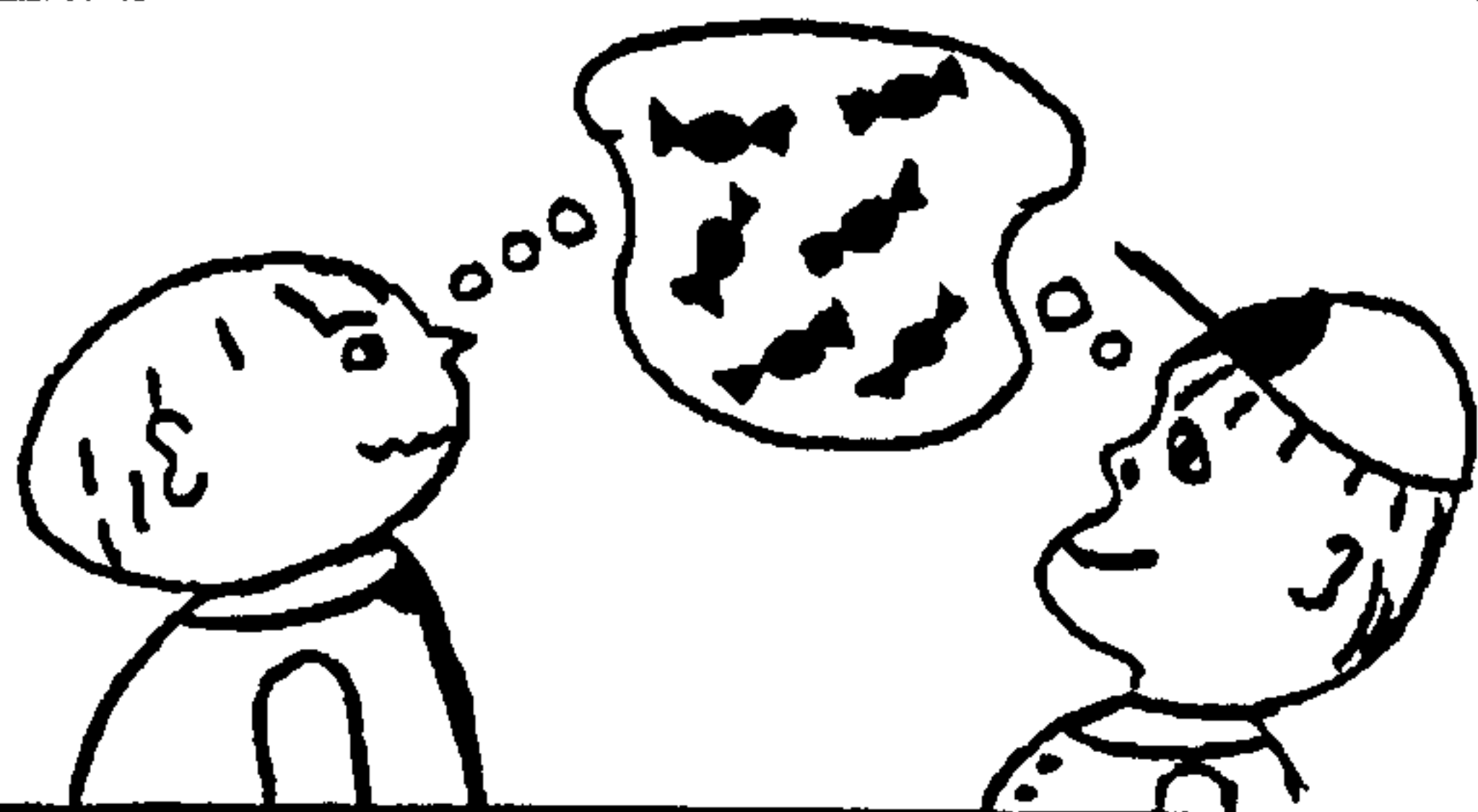


???

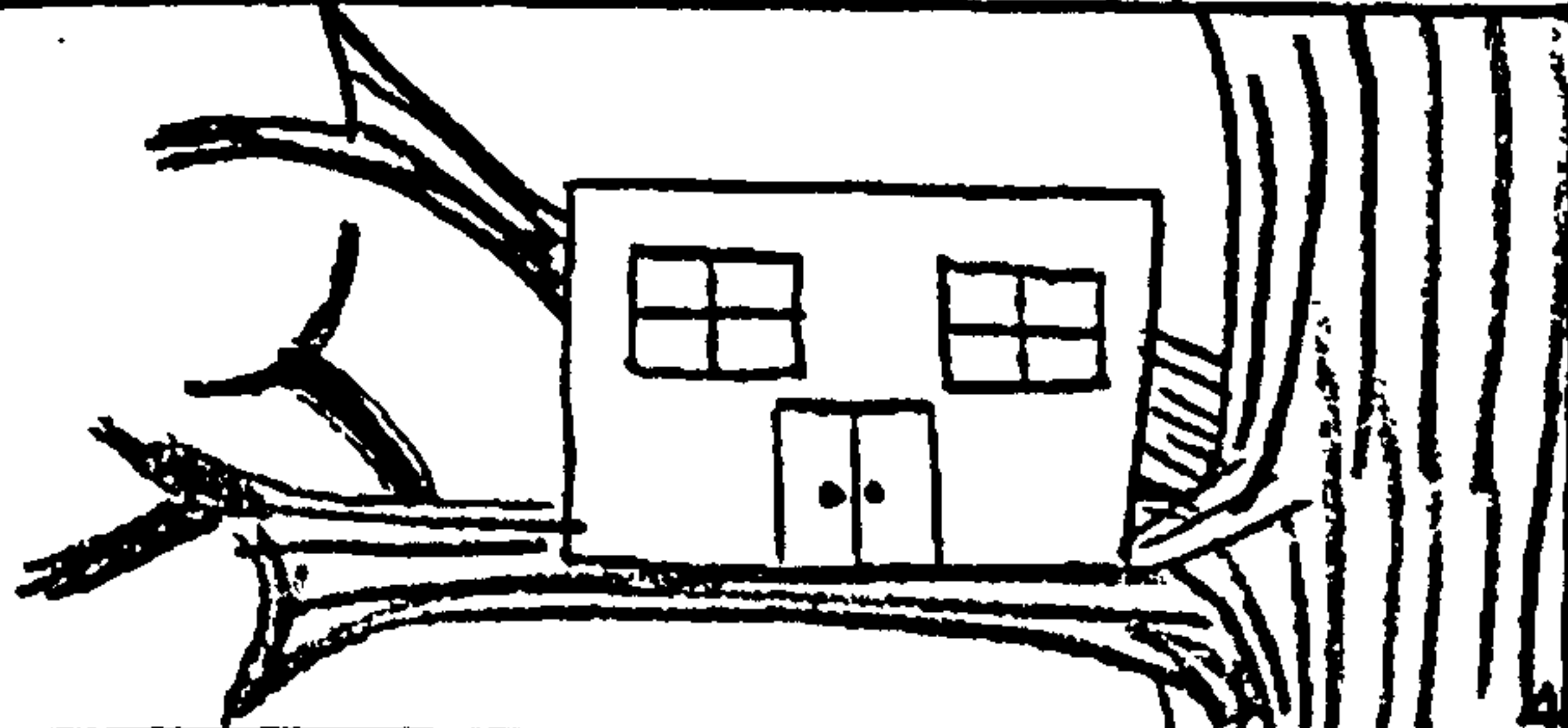
7



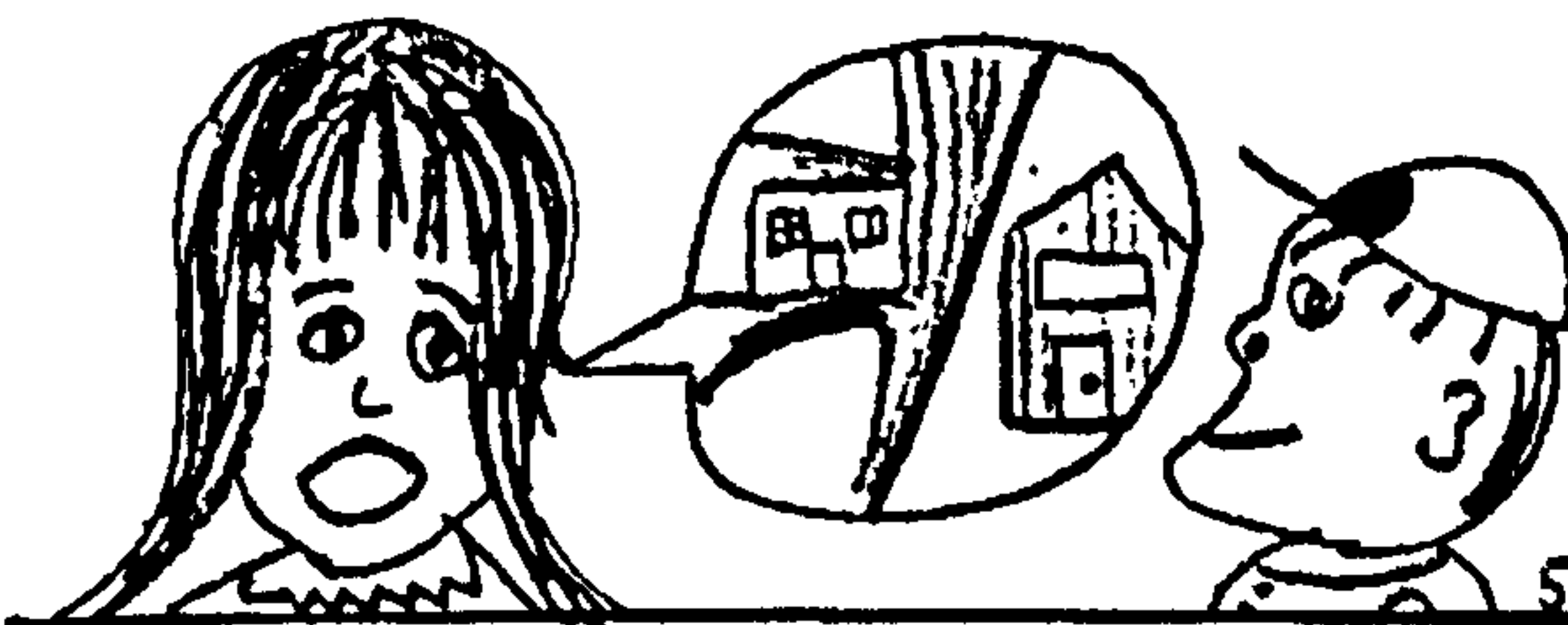
2.



3.



4



5



6

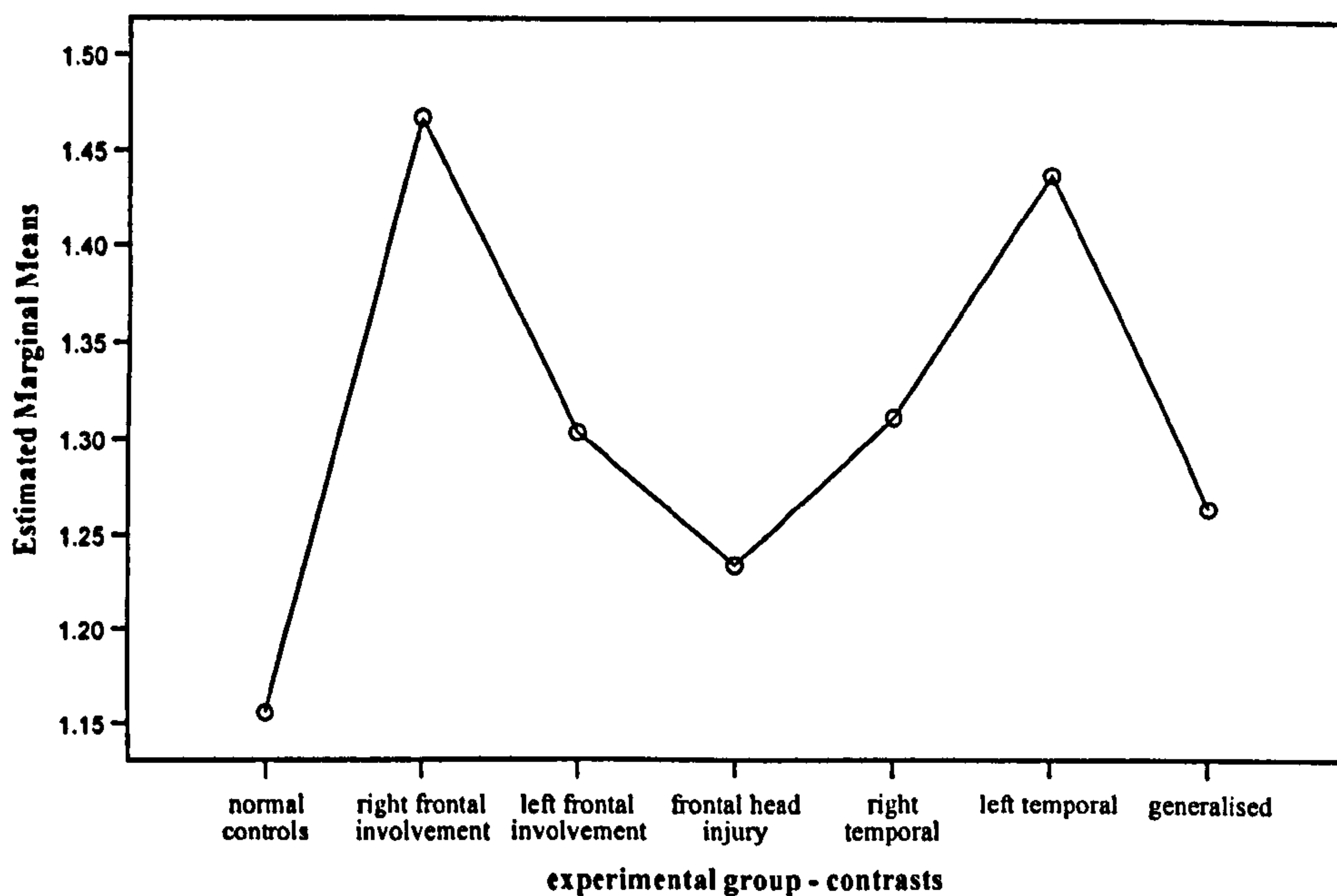
## APPENDIX 8

### *The transformed data analysis for Study 1: ANOVA and ANCOVA for performance on ToM Stories across the experimental groups.*

#### *Results*

Preliminary analyses revealed that data for the ToM stories measure deviated greatly from the normal distribution. The distributions were negatively skewed. According to Tabachnick & Fidell (2001) for such distributions it is appropriate to reflect the scores and then take the square root. To achieve the reflection a constant was created by adding one to the maximum score. Each score was then subtracted from this constant to derive a new score. Then the square root of this new score was calculated to form the reflected variable. Once the data had been transformed skewness was no longer a problem ( $Z=1.57$ ) nor was kurtosis ( $Z=1.3$ ). Levene's test demonstrated that there was equality of variance across the groups ( $p>0.05$ ).

ANOVA was conducted with Experimental Group between participants and transformed ToM Stories as the dependent variable. The results showed a significant difference between the groups on ToM Stories :  $F(6,88) = 2.58$ ,  $p<0.05$ . Multivariate Helmert orthogonal contrasts revealed that all patient groups performed significantly worse than NC ( $p<0.05$ ). The results for the RF group in comparison to all other patient groups approached significance ( $p=0.051$ ). All other contrasts were not significant, refer to Figure 17 to see the trends in the data (note that on the transformed variable, higher scores indicate poorer performance). It is evident that the NC group produced the best performance on this task and the RF group performed the worst.



**Figure 17:** *The means of CR by experimental group (transformed data).*

Tukey's post hoc tests revealed that RF performed significantly worse than NC, ( $p < 0.05$ ). All other pairwise comparisons were not significant.

### ***ToM Stories***

#### **Tom Stories, Immediate Story Recall and Level of Education.**

ANCOVA was conducted in order to test the extent that poor Immediate Story Recall and Level of Education effect performance on ToM stories in the right frontal group.

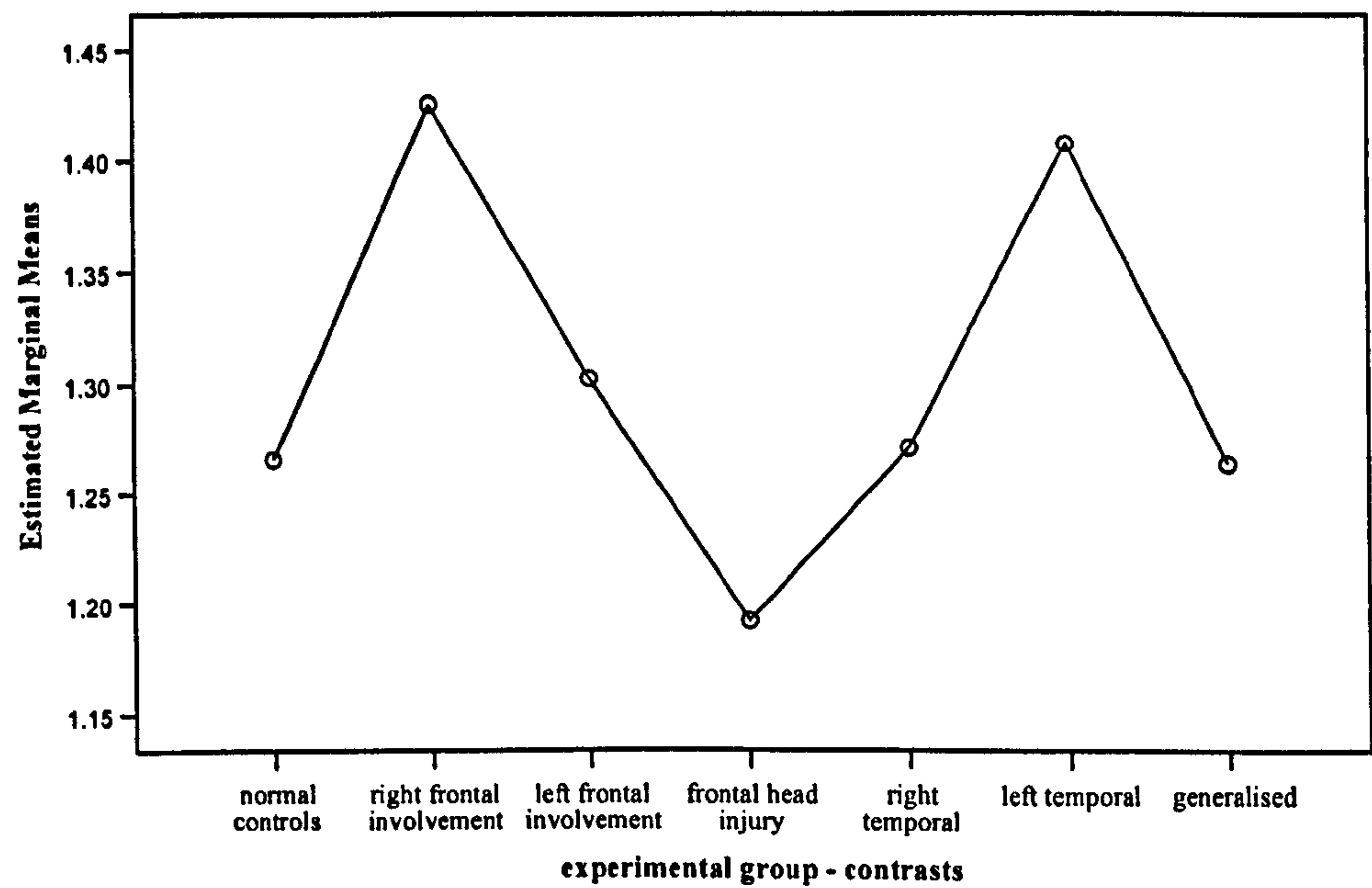
Experimental group was between participants and the transformed ToM story score was a dependent variable. Immediate Story Recall and Level of Education were covariates in the analysis.

#### ***The results:***

The effects of Immediate Story Recall (ISR) on ToM Stories was not significant,  $F(1,86) = 2.52$ ,  $p > 0.05$ . However, Level of Education was significant as a covariate,  $F(1,86) = 4.92$ ,  $p < 0.05$ . Following control for group differences in ISR and education, there was no longer a



main effect of experimental group on ToM Stories,  $F(6,86) = 1.38, p > 0.05$ . Multivariate Helmert orthogonal contrasts revealed NC did not differ significantly compared to combined patient groups ( $p > 0.05$ ). However, the difference between the RF group and the other patient groups approached significance,  $p = 0.075$ . All other contrasts failed to reach significance, refer to Figure 18 to see the trends in the data. Thus to summarise following control for group differences in immediate story recall and education, the RF performed the worse and the NC followed by the FHI group achieved the best performance.



*Figure 18: The means of ToM Stories by experimental group when taking account of immediate story recall and level of education (transformed data).*

## APPENDIX 9

*The transformed data analysis for Study 1: ANOVA, ANCOVA, Kruskal Wallis and Independent Sample T- Test for performance on First Order ToM Stories across the experimental groups.*

### *First Order ToM Stories*

Preliminary analyses revealed that data for the ToM stories measure deviated greatly from the normal distribution. The distributions were very negatively skewed with most participants scoring at ceiling. According to Tabachnick & Fidell (2001) for such distributions it is appropriate to reflect and take the inverse of the scores. The scores were reflected following the same procedure as outlined in Appendix 8. They were inverted (new score = 1/old reflected score). Once the data had been transformed skewness and kurtosis remained a severe problem ( $Z=16.04$ ) and kurtosis ( $Z=10.45$ ). Since the conditions for ANOVA/ANCOVA continue to be not met, analysis of the transformed data would do nothing to improve upon the original analyses reported in Chapter 7. Therefore these analyses were not performed.

Given the problems with normality and equality of variance, the original data were analysed using the Kruskal Wallis procedure.

### *Kruskal Wallis for First Order ToM stories by Experimental Group.*

The Kruskal Wallis test revealed a significant difference between the groups on First Order Tom Stories  $\chi^2$  (DF=6) = 18.00,  $p<0.01$ . Further analyses revealed that, with two exceptions, the RF frontal group performed significant worse than all other groups, Mann-Whitney U values were 90, 60, 60, and 75 for NC, FHI, RT, and LT respectively,  $p<0.05$  in all cases. The exceptions were the RF versus IGE comparison where  $U=55$ ,  $p=0.059$  and the RF-LF comparison where  $U=78$ ,  $p>0.05$ . However, caution should be exercised in interpreting these results as the significance levels are unadjusted for multiple comparisons. At an adjusted alpha level of .008, none of the pairwise comparisons would have been statistically significant.

### ***Independent Samples T-Test for RF and LF***

Given that all participants except RF and LF scored at ceiling it was decided to perform a one sample t test to establish whether these two groups performed significantly worse than ceiling. The RF group did  $t(DF=13) = -2.11$ ,  $p < 0.05$  one tailed, skewness ( $Z = 1.95$ ) and kurtosis (0.49) were not problematic in this sample. However, the LF did not perform significantly worse than ceiling  $T(DF=12) = -1.48$ ,  $p > 0.05$  and skewness was problematic ( $Z = 3.53$ ) but kurtosis was not ( $Z = 2.71$ ) in this sample. These results are consistent with both the original analysis in Chapter 2 and the Kruskal Wallis analysis above. Clearly the RF group is impaired on first order stories, relative to the other groups. Only the LF also performed at less than ceiling.



## APPENDIX 10

### *The Hinting Task (Corcoran, Mercer and Frith, 1995)*

#### Instructions.

I'm going to read out a set of 10 stories involving two people. Each story ends with one of the characters saying something. When I've read the stories out I'm going to ask you some questions about what the character said.

Here's the first story. Listen carefully to it. NB: The word count for each item is included in brackets (less the cues for the experimenter).

#### Hint 1

George arrives in Angela's office after a long and hot journey down the motorway. Angela immediately begins to talk about some business ideas. George interrupts Angela saying:

"My, my! It was a long, hot journey down that motorway!"

QUESTION: What does George really mean when he says this?

ADD: George goes on to say:

"I'm parched!"

QUESTION: What does George want Angela to do?

(64)

#### Hint 2

Melissa goes to the bathroom for a shower. Anne has just had a bath. Melissa notices the bath is dirty so she calls upstairs to Anne:

"Couldn't you find the Ajax, Anne?"

QUESTION: What does Melissa really mean when she says this?

ADD: Melissa goes on to say:

"You're very lazy sometimes, Anne!"

QUESTION: What does Melissa want Anne to do?

(61)

**Hint 3**

Gordon goes to the supermarket with his mum. They arrive at the sweetie aisle. Gordon says:

"Cor! Those treacle toffees look delicious."

QUESTION: What does Gordon really mean when he says this?

ADD: Gordon goes on to say:

"I'm hungry, mum."

QUESTION: What does Gordon want his mum to do?

(47)

**Hint 4**

Paul has to go to an interview and he's running late. While he is cleaning his shoes, he says to his wife, Jane:

"I want to wear that blue shirt but it's very creased."

QUESTION: What does Paul really mean when he says this?

ADD: Paul goes on to say:

"It's in the ironing basket."

QUESTION: What does Paul want Jane to do?

(60)

**Hint 5**

Lucy is broke but she wants to go out in the evening. She knows that David has just been paid. She says to him:

"I'm flat broke! Things are so expensive these days."

QUESTION: What does Lucy really mean when she says this?

ADD: Lucy goes on to say:

"Oh well, I suppose I'll have to miss my night out."

QUESTION: What does Lucy want David to do?

(65)

**Hint 6**

Donald wants to run a project at work but Richard, his boss, has asked someone else to run it. Donald says:

"What a pity. I'm not too busy at the moment."

QUESTION: What does Donald really mean when he says this?

ADD: Donald goes on to say:

"That project is right up my street."

QUESTION: What does Donald want Richard to do?

(59)

**Hint 7**

Rebecca's birthday is approaching. She says to her Dad:

"I love animals, especially dogs."



QUESTION: What does Rebecca really mean when she says this?

ADD: Rebecca goes on to say:

"Will the pet shop be open on my birthday,Dad?"

QUESTION: What does Rebecca want her dad to do?

(45)

**Hint 8**

Betty and Michael moved into their new house a week ago. Betty has been unpacking some ornaments. She says to Michael:

"Have you unpacked those shelves we bought, Michael?"

QUESTION: What does Betty really mean when she says this?

ADD: Betty goes on to say:

"If you want something doing you have to do it yourself!"

QUESTION: What does Betty want Michael to do?

(61)

**Hint 9**

Jessica and Max are playing with a train set. Jessica has the blue train and Max has the red one. Jessica says to Max:

"I don't like this train."

QUESTION: What does Jessica really mean when she says this?

ADD: Jessica goes on to say:

"Red is my favourite colour."

QUESTION: What does Jessica want Max to do?

(55)

**Hint 10**

Patsy is just getting off the train with three heavy cases. John is standing behind her. Patsy says to John:

"Gosh! These cases are a nuisance."

QUESTION: What did Patsy really mean when she said this?

ADD: Patsy goes on to say:

"I don't know if I can manage all three."

QUESTION: What does Patsy want John to do?

(56)

**Mean words in each vignette =  $570/10 = 57$**

## APPENDIX 11

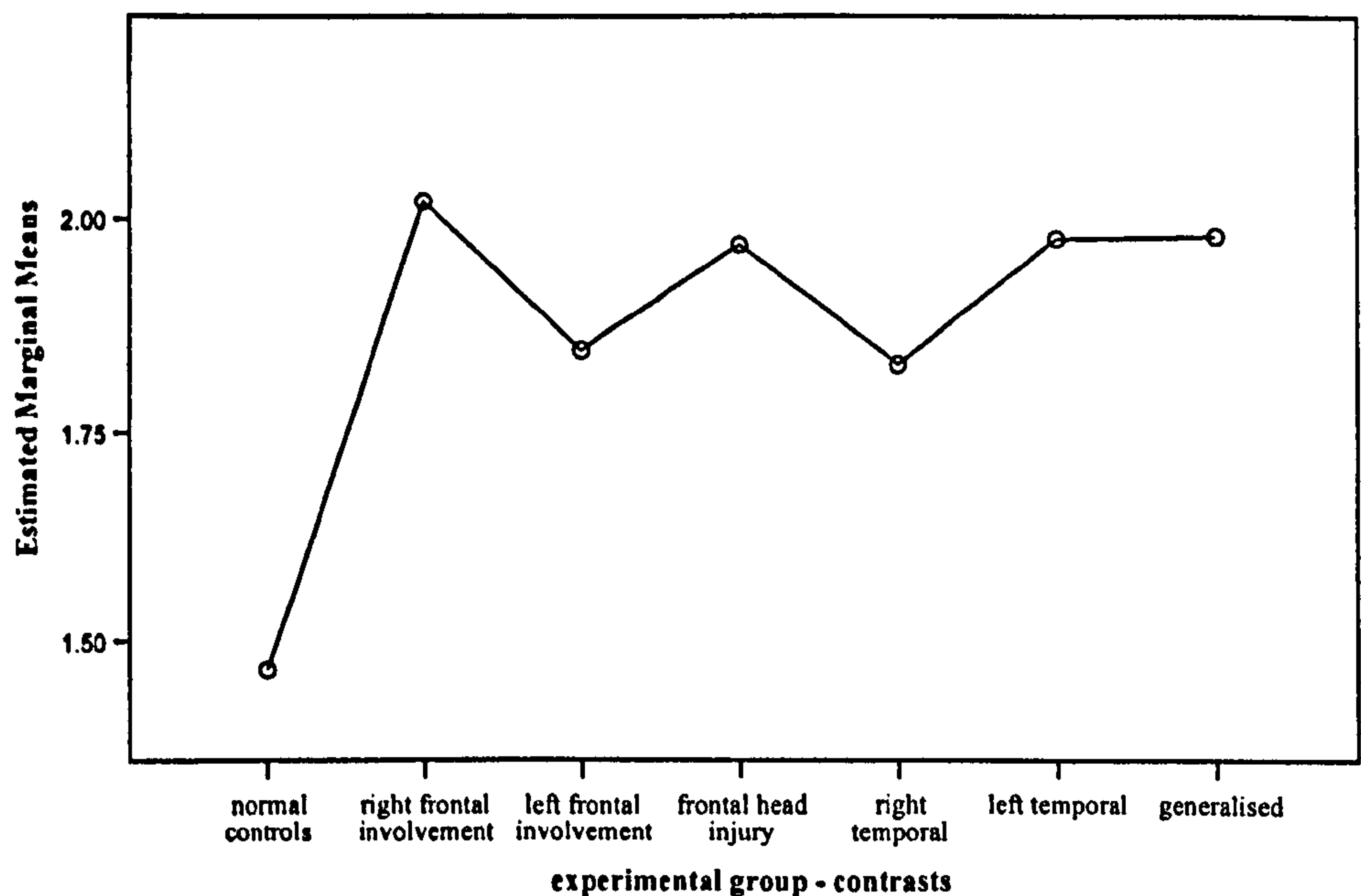
### *Transformed data analysis for Study 2. ANOVA and ANCOVA for performance on the Hinting Task across the experimental groups*

#### *Results*

Preliminary analyses revealed that data for the Hints measure deviated from the normal distribution. The distribution was negatively skewed. According to Tabachnick & Fidell (2001) for such distributions it is appropriate to reflect the scores and then take the square root. To achieve the reflection a constant was created by adding one to the maximum score. Each score was then subtracted from this constant to derive a new score. Then the square root of this new score was calculated to form the transformed variable. Once the data had been transformed skewness was no longer a problem ( $Z=1.1$ ) nor was kurtosis ( $Z=0.39$ ). Levene's test demonstrated that there was equality of variance across the groups ( $p>0.05$ ).

ANOVA was conducted with Experimental Group between participants and Hints as the dependent variable. The results showed a significant difference between the groups on Hints :  $F(6,88) = 4.02$ ,  $p<0.005$ . Multivariate Helmert orthogonal contrasts revealed that all patient groups performed significantly worse than NC ( $p<0.001$ ). All other contrasts were not significant, refer to Figure 19 to see the trends in the data





**Figure 19:** *The means of Hints by experimental group (transformed data).*

Tukey's post hoc analysis revealed that the RF, FHI, LT and IGE groups were impaired on the Hinting Task in comparison to NC ( $p < 0.01$ ;  $p < 0.05$ ;  $p < 0.01$  and  $p < 0.05$  respectively). All other pairwise comparisons were not significant.

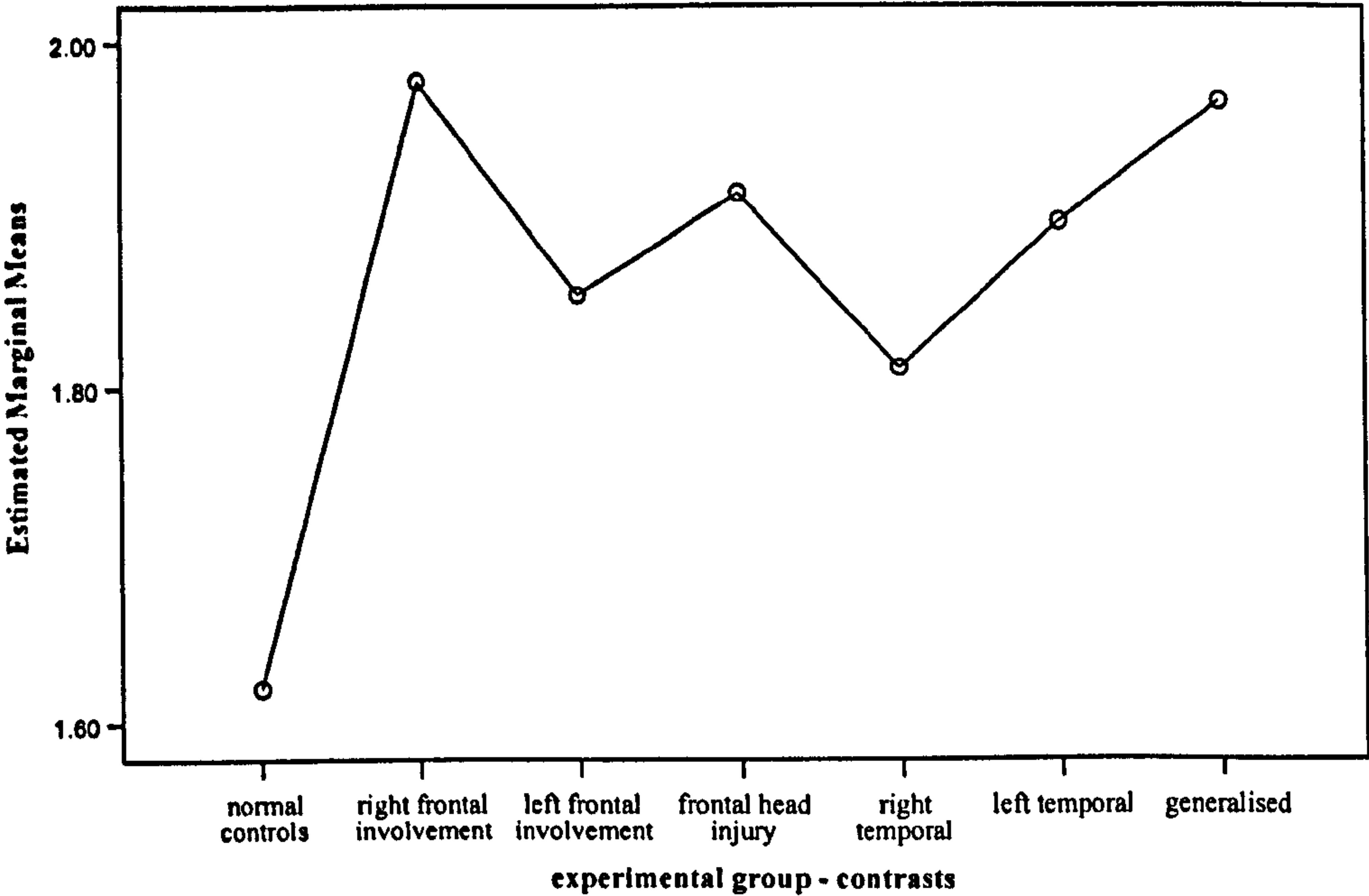
### **Hints, Immediate Story Recall and Level of Education**

ANCOVA was conducted in order to test the extent that poor Immediate Story Recall and Level of Education effect performance on Hints in the right frontal group. Experimental group was between participants and Hints was a dependent variable. Immediate Story Recall and Level of Education were covariates in the analysis.

#### ***The results:***

It appears that Immediate Story Recall is impacting on the Hinting task,  $F(1,86) = 10.06$ ,  $p < 0.005$ , Level of Education is not  $F(1,86) = 0.02$ ,  $p > 0.05$ . Following control for group differences in immediate story recall and education, there was no longer a main effect of experimental group on Hints,  $F(6,86) = 1.25$ ,  $p > 0.05$ . However, MV Helmet orthogonal contrasts revealed that after taking account of the impact of Immediate Story Recall and

Level of Education, NC performed significantly better than all other groups ( $p<0.05$ ). All other contrasts were not significant, refer to Figure 20 to see the trends in the data.



*Figure 20: The means of Hints by experimental group taking account of the effect of Immediate Story Recall (transformed data).*

APPENDIX 12

*The Conditional Reasoning Task (Corcoran & Frith, 2005)*

Instructions.

I'm going to read out five stories to you in which you must imagine yourself in the situations described. In each story you have to try to make sure that certain rules are being followed. When I have read the story out, I will ask you a question about the rule in the story. Here is the first story. Concentrate carefully on this.

Traditional

You are a temporary library assistant. You have been asked to check some rules of the coding system used in the library. You are checking the index cards of books to see that books coded with certain letters are sub-coded with particular numbers. You have reached the final four cards. On one side of the card is a letter while on the other side is a number. This is the rule that you are checking:

**IF THERE IS AN 'A' ON ONE SIDE THERE MUST BE A '9' ON THE OTHER.**

You should now show me the card or cards that you would definitely need to turn over to see if the rule has been broken.

B	4
(not P)	(not Q)
A	9
(P)	(Q)

The correct answer to this is : P and not Q (A and 4).



The remaining four stories differ in content in terms of whether they involve a social rule and/or a familiar rule such that there is a social familiar version, a non social familiar version, a social unfamiliar version and finally a non social unfamiliar version.

**Non Social Familiar.**

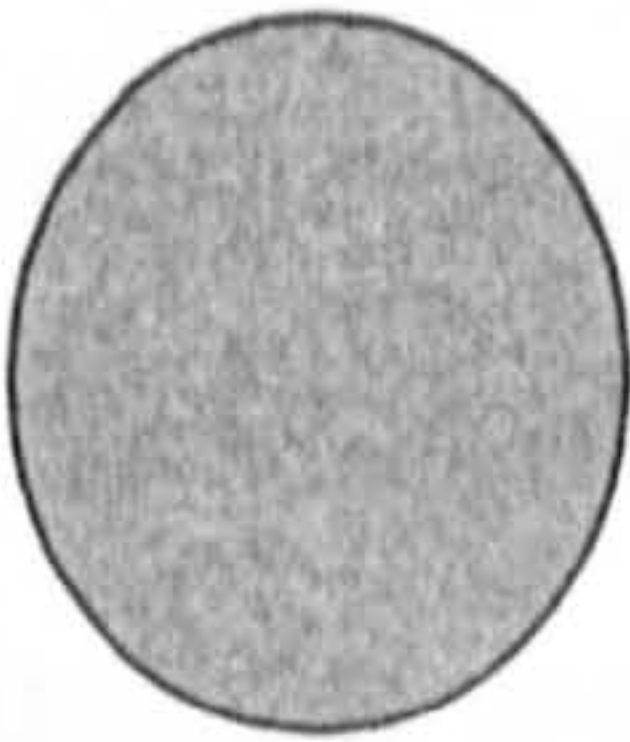
You are a quality controller employed by a company that manufactures and fits hot and cold water taps to sinks. Recently the company have had a number of complaints from customers saying that both of their taps had blue dots on them. You have asked all recent customers to return information cards to you. Here are four cards recently returned to you. On one side is a red or a blue dot while on the other is the word 'hot tap' or 'cold tap'. You have to check that the following rule has been strictly followed. The rule is:

**IF THE TAP IS HOT IT MUST BE MARKED WITH A RED DOT.**

You should now show me the card or cards you would definitely need to turn over to see whether the rule has been broken.

**COLD TAP**

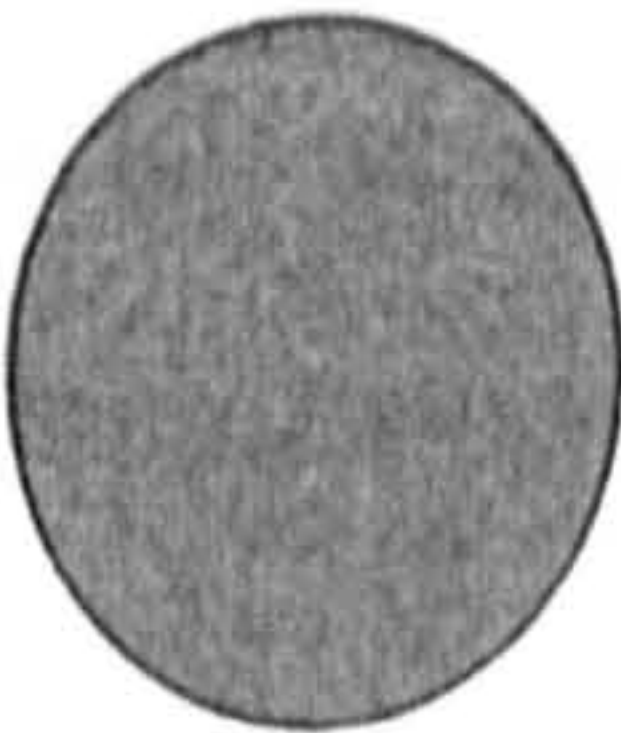
(not p)



(q)

**HOT TAP**

(p)



(not q)

**Social Familiar**

The story is the drinking age rule of Griggs and Cox (1982).

You are a police officer checking up on the under age drinking rule. Your colleague, who was working under cover in a notorious pub the night before, has given you



details on cards about four young people who were in the pub last night. On one side of the card is the person's age while on the other side of the card is what that person was drinking. Here is the rule that you must check:

**IF A PERSON WAS DRINKING ALCOHOL THEN THAT PERSON MUST BE 18 OR OVER.**

You should now show me the card or cards that you would definitely need to turn over to see if the rule has been broken.

20	Pepsi
(Q)	(not P)
Alcohol	17
(P)	(not Q)

The correct answer to this is: P and not Q (alcohol and 17).

**Non Social Unfamiliar.**

You are a tree specialist working in an area where all of the Common Oaks have been hit by a very nasty disease. The English Oaks must be identified since, though they are less susceptible to the disease, they will get it if all of the Common Oaks are not felled and burnt as soon as possible. The two types of tree look very similar and you have had to go around the area marking the trees using orange for a Common Oak and green for an English Oak. The tree surgeons then had to fell all of the Common Oaks in the area and report the details of their work to you. You have now received the cards with the details of the final four Oaks in the area. On one side of the card is an orange or green mark while on the other is whether the tree has been felled or not. The rule you must use is:



**IF THE TREE HAS AN ORANGE MARK ON IT, IT MUST HAVE BEEN FELLED.**

You should now show me the card or cards that you would definitely need to turn over to see if the rule has been broken.

<b>FELLED</b>	<b>NOT FELLED</b>
(q)	(not q)
	
(p)	(not p)

**Social Unfamiliar**

You are a student interested in the rites of passage of the Calculo people which culminates in the Dance of Pride where young men celebrate their manhood in a wild exciting dance provoked by an intoxicating, desirable but rare liquor. Needless to say, young men are very keen to join in the Dance of Pride but, they must not unless they have collected three painted pebbles. These pebbles are earned through acts of bravery. You are checking that this rule is being followed. A colleague who has been living with the Calculo has given you details on four cards about four young men. On one side of the card is whether or not the young man had joined in the Dance of Pride while on the other side is whether he had earned his three painted pebbles. Here is the rule you are checking:

**IF A YOUNG MAN HAS JOINED IN THE DANCE OF PRIDE HE MUST HAVE EARNED THREE PAINTED PEBBLES.**

You should now show me the card or cards you would definitely need to turn over to see if the rule has been broken.



**JOINS DANCE  
OF PRIDE**  
(p)

**DOES NOT JOIN  
DANCE OF PRIDE**  
(not p)

**EARNED 3  
PAINTED PEBBLES**  
(q)

**NOT EARNED 3  
PAINTED PEBBLES**  
(not q)

**Scoring**

The responses to these stories are coded as follows:

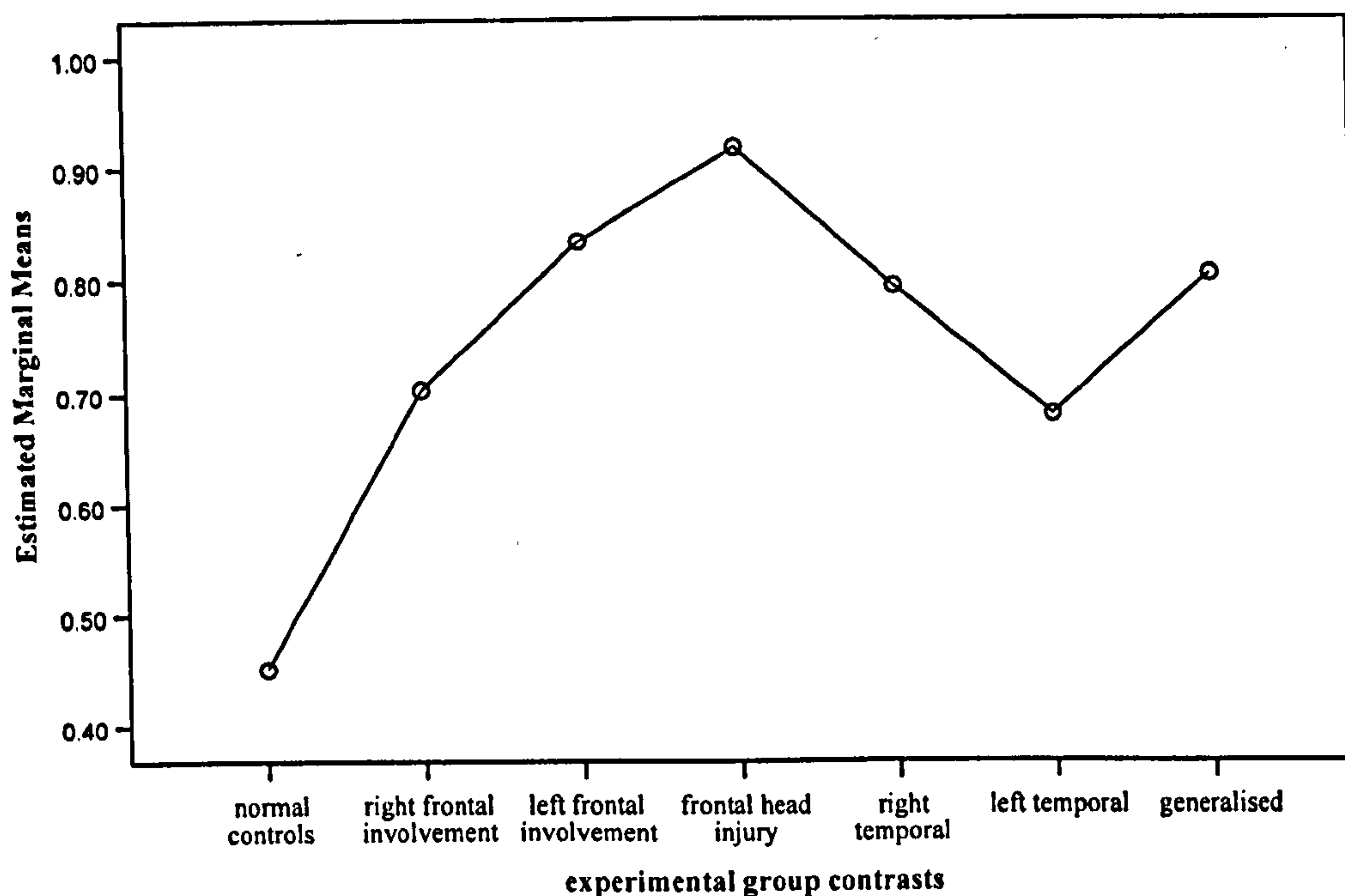
- 1= P & not Q (correct response)
- 2= P&Q
- 3= P only
- 4= All 4 cards
- 5= any other selection

## APPENDIX 13

### *Transformed data analysis for Study 3. ANOVA and ANCOVA for performance on the Conditional Reasoning Task across the experimental groups*

Preliminary analyses revealed that data for the conditional reasoning measure deviated greatly from the normal distribution. The distributions were very positively skewed and in many cases the modal response was zero. According to Tabachnick & Fidell (2001) for such distributions it is appropriate to take the inverse of the scores firstly adding one to all scores to remove zeros. Once the data had been transformed skewness was no longer a problem ( $Z=1.05$ ) but kurtosis still deviated from normality ( $Z=3.46$ ),  $p<0.01$  which is problematic for the size of the sample used in this study according to Tabachnick and Fidell (2007). Levene's test demonstrated that there was equality of variance across the groups ( $p>0.05$ ).

ANOVA was conducted with Experimental Group between participants and Conditional Reasoning score as the dependent variable. The results showed a significant difference between the groups on Conditional Reasoning:  $F(6,88)=4.78$ ,  $p<0.001$ . Multivariate Helmert orthogonal contrasts revealed that all patient groups performed significantly worse than NC ( $p<0.001$ ). All other contrasts were not significant, refer to Figure 21 to see the trends in the data. It is evident that the NC group produced the best performance on this task and the FHI group performed the worst.



**Figure 21:** *The means of CR by experimental group (transformed data).*

Tukey's post hoc tests revealed that LF, FHI, RT and IGE all performed significantly worse than NC, ( $p < 0.005$ ,  $p < 0.001$ ,  $p < 0.05$ ,  $p < 0.05$  respectively). All other pairwise comparisons were not significant.

#### **Conditional Reasoning, Immediate Story Recall and Level of Education.**

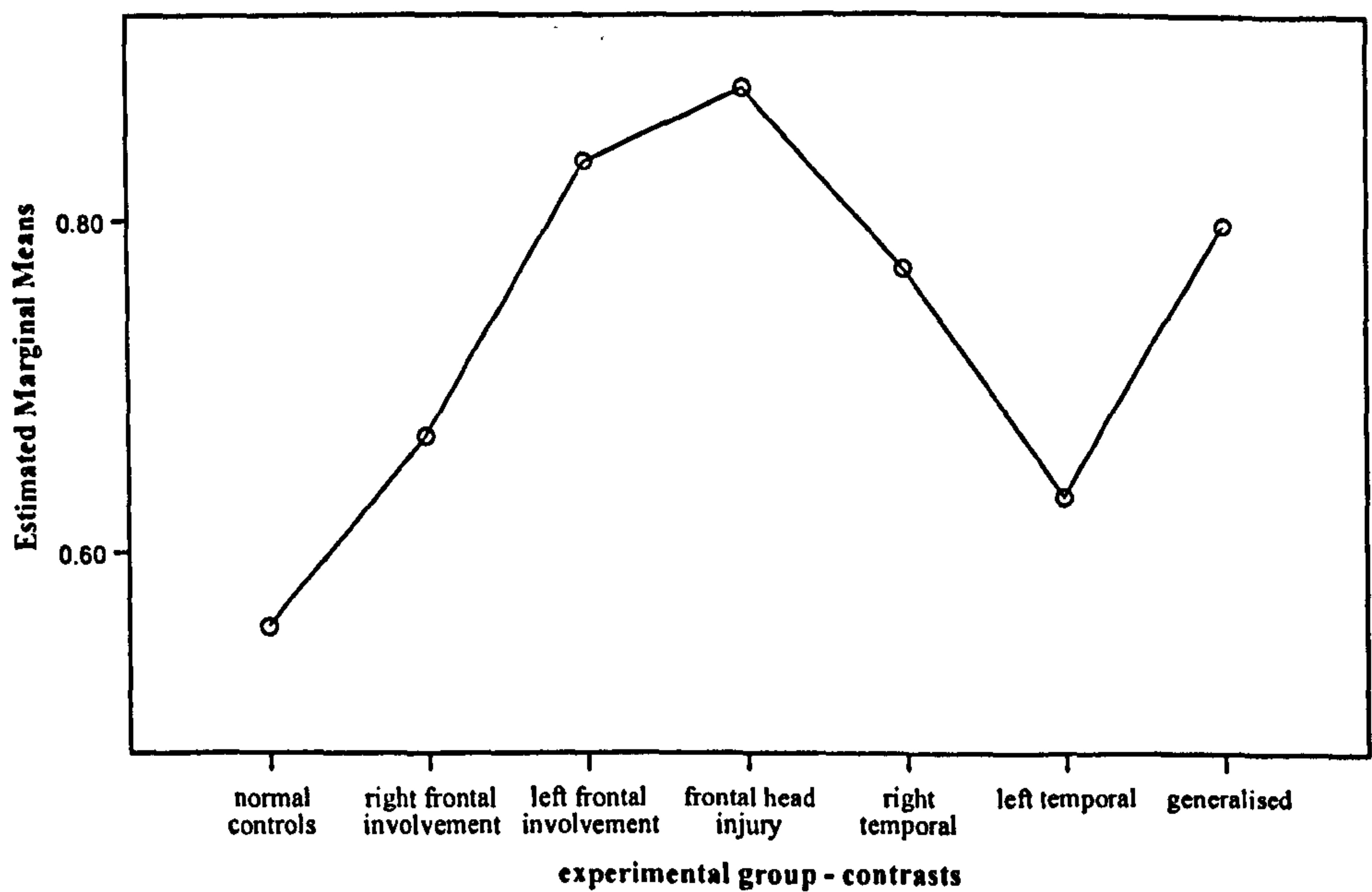
ANCOVA was conducted in order to test the extent that poor Immediate Story Recall and Level of Education effect performance on Conditional reasoning. Experimental group was between participants and total CR score was a dependent variable. Immediate Story Recall and Level of Education were covariates in the analysis.

#### ***The results:***

It appears that Immediate Story Recall is impacting on CR,  $F(1,86) = 5.97$ ,  $p < 0.05$  but Level of Education is not,  $F(1,86) = 0.69$ ,  $p > 0.05$ . There remained a significant effect of experimental group on CR,  $F(6,86) = 2.58$ ,  $p < 0.05$ . Thus it is evident that the groups have a specific difficulty in CR over and above that which is caused by immediate story recall and level of education.



Multivariate Helmert orthogonal contrasts revealed that when taking account of immediate story recall and level of education all patient groups performed significantly worse than NC ( $p<0.05$ ). All other contrasts were not significant, refer to Figure 22 to see the trends in the data. It is evident that even when taking account of immediate story recall and level of education that the NC group produced the best performance on this task and the FHI group performed the worst



*Figure 22: The means of CR by experimental group when taking account of immediate story recall and level of education (transformed data).*

## APPENDIX 14

### *The Impact of Epilepsy Scale (Jacoby et al, 1993)*

We would like to know how much you feel your epilepsy and its treatment affect your everyday life. For each item listed, please tick the response which shows best how you feel.

#### **Does your epilepsy and its treatment affect:**

	A lot	Some	A little	Not at all
Score	(4)	(3)	(2)	(1)
1. Your relationship with close members of your family?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Your social life and social activities?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Whether or not you are able to do paid employment?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Your overall health?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Your relationship with friends?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. The way you feel about yourself?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Your future plans and ambitions?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Your standard of living?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>