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Article

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1   Pain Processing in Psychiatric Conditions: A systematic review

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22   Running Head: Pain in Psychiatric Conditions

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25   Review Article

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Abstract

Objective: Pain is a universal, multidimensional experience with sensory emotional, cognitive and social components, which is fundamental to our environmental learning when functioning typically. Understanding pain processing in psychiatric conditions could provide unique insight into the underlying pathophysiology or psychiatric disease, especially given the psychobiological overlap with pain processing pathways. Studying pain in psychiatric conditions is likely to provide important insights, yet, there is a limited understanding beyond the work outside depression and anxiety. This is a missed opportunity to describe psychiatric conditions in terms of neurobiological alterations. In order to examine the research into the pain experiences of these groups and the extent to which a-typicality is present, a systematic review was conducted. *Methods:* An electronic search strategy was developed and conducted in several databases. *Results:* The current systematic review included 46 studies covering five DSM-5 disorders: autism, attention deficit hyperactivity disorder, schizophrenia, personality disorder and eating disorders, confirming tentative evidence of altered pain and touch processing. Specifically, hyposensitivity is reported in schizophrenia, personality disorder and eating disorder, hypersensitivity in ADHD and mixed results for autism. *Conclusions:* Review of the research highlights a degree of methodological inconsistency in the utilisation of comprehensive protocols; the lack of which fails to allow us to understand whether a-typicality is systemic or modality-specific.

Key words: Psychiatric, DSM-5, Pain, Quantitative Sensory Testing, QST.

Introduction

50

51   Pain is a universal, multidimensional experience with sensory emotional, cognitive and

52 social components (A. C. d. C. Williams & K. D. Craig, 2016). Understanding pain processing

53 in psychiatric conditions could provide unique insight into the underlying pathophysiology or

54 psychiatric disease, especially given the psychobiological overlap with pain processing

55 pathways (Bird et al., 2010; de la Fuente-Sandoval, Favila, Gómez-Martin, Pellicer, & Graff-

56 Guerrero, 2010; Fan, Chen, Chen, Decety, & Cheng, 2014; Goesling, Clauw, & Hassett, 2013;

57 Iannetti & Mouraux, 2010). For example, there is substantial literature on pain perception in

58 anxiety and depression (for review, see (Thompson, Correll, Gallop, Vancampfort, & Stubbs,

59 2016) supporting a bidirectional relationship between these conditions and altered pain

60 behaviours. From this literature, several examples have emerged that highlight the need to

61 understand pain perception in psychiatric disorders. The co-occurrence of depression or

62 anxiety and pain have an additive burden on the individual (Bair, Robinson, Katon, &

63 Kroenke, 2003). Similarly, altered pain behaviours can lead individuals to look for somatic

64 causes, potentially obscuring or delaying psychiatric diagnoses. There also seems to be

65 important moderators between depression/anxiety and pain, specifically related to the

66 exteroceptive or interoceptive nature of the stimuli and attentional resources allocated for

67 painful stimuli, which provide insight into sensory processing in the disorder (Goesling et al.,

68 2013; Thompson et al., 2016).

69   Studying pain in psychiatric conditions is likely to provide important insights, yet, there

70 is a limited understanding beyond the work outside depression and anxiety. This is a missed

71 opportunity to describe psychiatric conditions in terms of neurobiological alterations

72 (Lautenbacher & Krieg, 1994). Indeed, a range of psychiatric conditions include core

73 symptoms or associations with potentially pain-related behaviours, for example self-harm

74 (Taylor, Hutton, & Wood, 2015). The absence of systematic study of pain responses in these

75   conditions negates the possibility to understand the contribution of potential sensory changes to

76   these behaviours. Further, pain experience is critical in a number of aspects of environmental

77   learning, allowing individuals to learn about dangers and threats and distinguish these from

78   safety cues (Bastian, Jetten, Hornsey, & Leknes, 2014) as well as promoting social bonding

79   with carers who provide pain relief (Krahé, Springer, Weinman, & Fotopoulou, 2013;

80   Langford et al., 2010). Altered pain processing may therefore, underlie clinical features of a

81   range of psychiatric conditions, especially those conditions which have associated threat-

82   related or social features.

83   A first step in understanding how altered pain processing may contribute to these

84   psychiatric conditions is to explore processing and responsivity to potentially nociceptive

85   signals. There is an example of this altered pain responsivity in the diagnostic criteria for

86   autism spectrum disorder, where the DSM includes "apparent indifference to pain/temperature"

87   as an example of sensory reactivity (APA, 2013). Understanding whether pain behaviours are

88   a cause, effect or epiphenomenon of a psychiatric condition would enable better diagnostic

89   characterization. In the example of autism, more rigorous psychophysical investigation into

90   these symptoms is likely to improve interventions that aim to reduce their occurrence or

91   provide environmental adaptions to improve overall participation (Baranek, 2002).

92   Additionally, while many psychiatric conditions co-occur with depression, first disentangling

93   processing as a function of individual disorders is crucial to mechanistic-based understanding

94   (Kendler, 2008; Savitz & Harrison, 2018; Vardeh, Mannion, & Woolf, 2016). As noted in

95   depression, pain processing was moderated by exteroceptive/interoceptive nature of the stimuli

96   (Thompson et al., 2016). Given the evidence of altered interoceptive processing in other

97   psychiatric conditions (Quattrocki & Friston, 2014), understanding pain processing in this

98   dimension may provide insight into bodily representation and emotional regulation in these

99   disorders. In this way, understanding pain processing in psychiatric conditioning may also

100   allow for more mechanism-based treatment.

101   *Aims of the review*

102   Characterization of pain processing may provide understanding into biological

103   alterations related to psychiatric conditions, as well as, quality of life for these individuals.

104   Importantly, Lautenbacher and Krieg (1994), published the only review in this area prior to the

105   development of standardised protocols. Standardised protocols are essential in order to

106   minimise variability (Backonja et al., 2013), produce reliable and comparable results, and

107   improve clinical feasibility (Rolke et al., 2006). Recent attempts have been made to generate

108   standardised psychophysical approaches to understand touch and pain sensitivity in the form of

109   Quantitative Sensory Testing (QST) batteries i.e. Rolke et al. (2006).   Hence, this review will

110   include studies that have been conducted on psychiatric conditions with experimental pain,

111   with particular reference to QST. It will also examine factors that have been shown to mediate

112   the magnitude of pain response including clinical features of the conditions, medication status,

113   or co-occurring symptoms. Indeed, the impact of clinical symptom management in altering

114   pain precepts as well as the potential role for pain management strategies in altering clinical

115   presentation is central in understanding health in these vulnerable groups.

116   This review includes quantification of peripheral afferents associated with pain

117   processing as well as light touch; non-noxious stimuli like light touch, can sometimes be

118   experienced as painful (IASP, 2012). This may be particularly relevant to psychiatric

119   conditions where individuals have reported discomfort or pain to typically non-painful tactile

120   inputs (Grandin, 1992, 1995). Responses such as these may mimic low-level allodynia,

121   suggesting that a full assessment of the somatosensory system is necessary for a true

122   comprehension of pain in psychiatric conditions.

123   **Methods**

124   **Search Methods**

5

125   An electronic search strategy was used, according to the Cochrane guidelines (Higgins

126 & Green, 2011), through author consensus, in the following databases; Medline (1953-

127 Present), PsycINFO (1931-Present), PsycARTICLES (1955-Present), Science Direct (1966-

128 Present) and Science Citation Index (1989-2014). To gain a list of potentially relevant

129 publications, DSM-5 psychiatric condition terms were combined with "or", terms related to

130 pain/somatosensation and QST were also combined with "or", and then the two groups of key

131 words were combined using "and" (Table 1). Subsequently, reference lists from retrieved

132 papers were scanned for further relevant publications and authors of poster abstracts were

133 contacted for further information or full text articles.

134   [Table 1 here]

135 **Eligibility**

136   **Types of Studies**

137   Studies were eligible for inclusion if they 1) were explicitly experimental, 2) utilised

138 psychophysically appropriate pain or touch sensitivity assessment and 3) included both a

139 clinical and control group, or adequately compared clinical data values to published norms.

140   Studies were excluded if 1) there was poor quality control of stimuli (i.e. intensity of

141 stimuli was variable or clear order effects might be present etc.) 2) they utilised poor or non-

142 comparable pain induction tests, 3) they did not contain a control group or refer to published

143 norms or 4) were animal studies on pain induction.

144   No publication date restrictions or publication status restrictions were imposed and only

145 studies published in English were considered. No restrictions were put onto the participants

146 within studies, other than it was imperative that they were human samples and had a diagnosis

147 of a condition previously categorized as Axis I or Axis II (APA, 1994). Conditions that have a

148   neurological or developmental origin i.e. not acquired or environmental, have significant public

149   health implications, and have not appeared in multiple comprehensive reviews (i.e. anxiety and

150   depression) were chosen. They included; autism spectrum disorder (ASD), obsessive

151   compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), schizophrenia,

152   eating disorders (inclusive of anorexia nervosa, bulimia nervosa and binge-eating disorder) and

153   personality disorder (Borderline personality disorder: BPD/PD).

154   **Study Selection and Data Collection**

155   **Study Selection**

156   Sourced citations were transferred to Endnote. Eligibility assessment was first

157   performed on article titles in an un-blinded standardised manner by 2 reviewers (SV and DM).

158   The first reviewer (SV) checked all titles for relevance, with second reviewer (DM) auditing

159   10% of the total, with a 97% agreement rate. For those studies where authors disagreed, a third

160   reviewer (HP) acted as a blinded arbitrator.

161   Eligible abstracts were then assessed for inclusion, under the same process by the first

162   reviewer (SV). In this instance 10% of the abstracts were divided across three blinded authors

163   (HP, FMcG, MF) with a fourth (DM) acting as a blinded arbitrator, with 100% agreement rate.

164   Roles were allocated to ensure that the arbitrator was different for both phases.

165   **Data Collection**

166   Information extracted from each study included; 1) Participant characteristics

167   (including age, gender, condition, diagnosis method, numbers in each group, matching criteria

168   and psychometric measures), 2) Pain or touch method (including location and test parameters)

169   and 3) Main data (including all inferential statistics, any subgroup analysis and mean values),

170   placed into specifically designed extraction tables. Summary sheets were generated to

171   compare information across conditions.

Results

[Figure 1]

Results of the search

175   A final search conducted on 04/02/18, which yielded 2167 potentially relevant records.

176   The majority of studies have been conducted in the last decade, highlighting the growing

177   interest of pain across these conditions. Figure 1 flow chart details the records found at each

178   stage of the screening process. Study characteristics and data will be presented for each

179   condition in the following sections. Meta-analysis was not possible due to the variability in the

180   methods utilised and the lack of reported confidence intervals and effect sizes.

Autism Spectrum Disorder

Included studies.

183   Ten studies were included for ASD. These studies included pain responses to thermal,

184   mechanical, pressure, vibratory and electrical stimuli; therefore, a number of somatosensory

185   measures were missing. Given the range of available measures, research examining

186   somatosensory and pain thresholds in ASD is presently limited.

Participant characteristics.

188   Although studies have been conducted using children (n=2) and adolescents (n=2)

189   samples, the majority (n= 6) were conducted on adults. This bias is understandable given the

190   nature of the tests administered, which require very precise reports from participants; they may

191   also be distressing to younger children. Male participants were generally the majority in the

192   experimental group, and two studies had an all-male sample. This distribution is in line with a

193   three-time greater prevalence of ASD in males (Baxter et al., 2015).

194   **Sensation thresholds.**

195   Six studies examined somatosensory detection thresholds. Three studies examined

196   thermal detection thresholds, two in adults (Cascio et al., 2008; Fründt et al., 2017) and another

197   in adolescents (Duerden et al., 2015). All studies adopted a method-of-limits to determine

198   thresholds, with Cascio et al. (2008) and Fründt et al. (2017) having a change rate of 1°C/s and

199   Duerden et al. (2015) using 0.5°C/s. Results are inconsistent. Cascio et al. (2008) and Fründt

200   et al. (2017) reported no significant differences, while hyposensitivity was reported by Duerden

201   et al. (2015). Furthermore, Duerden et al. (2015) report a significant correlation between

202   autism severity (as measured by ADOS-G scores) and thermal detection thresholds,

203   specifically to both the social and communication subscales, demonstrating that adolescents

204   with greater autism severity and lower IQ had higher detection thresholds. However, it is of

205   note that those studies, which utilised the DFNS standardised battery, report no-significant

206   differences.

207   Four studies examined vibratory detection thresholds in adults (Blakemore et al., 2006;

208   Cascio et al., 2008; Fründt et al., 2017) and children (Guclu, Tanidir, Mukaddes, & Unal,

209   2007). Blakemore et al. (2006) presented two frequencies of vibrotactile stimuli; 200Hz

210   (stimulating rapidly adapting fibres) and 30Hz (stimulating slowly adapting fibres), in a

211   method-of-limits. Whereas, Cascio et al. (2008) used a forced-choice paradigm at 33Hz;

212   participants were asked to indicate in which of two time intervals a stimulus was presented.

213   Guclu et al. (2007) used sinusoidal displacements at 40 and 250Hz, in a forward-masking

214   paradigm; a 250Hz stimulus was applied prior to the test stimulus and Fründt et al. (2017) used

215   the DFNS standardised protocol. Overall results indicate hyper-responsiveness to vibratory

216   stimuli in adults with ASD, as lower vibrotactile thresholds were achieved (Blakemore et al.,

217   2006; Cascio et al., 2008). Furthermore, these findings appear to be sensitive to both location

218   (as differences were reported for the forearm but not the palm (Cascio et al., 2008), and the

219   frequency at which the stimulus is presented (Blakemore et al., 2006). However, Guclu et al.

220   (2007) and Fründt et al. (2017) report no significant difference between the vibrotactile

221   thresholds, and the children with autism had the same detection and masking mechanisms as

222   the neurotypical children.

223   Finally, Cascio et al. (2008) and Fründt et al. (2017) also examined punctate

224   mechanical detection thresholds using von Frey hairs. Cascio et al. (2008) reported no

225   significant group differences, suggesting typical static mechanical functioning in ASD. Whilst

226   Fründt et al. (2017) reported a greater loss of function for MDT. Their methodologies differed

227   slightly with the latter using the DFNS standardised protocol and the other utilising a two

228   ascending and two descending block of trials methodology.

229   Overall, the findings for somatosensory detection thresholds for individuals with ASD

230   are inconsistent. There are some signs of hyposensitivity in thermal sensations (Duerden et al.,

231   2015), however, these findings are not reliable with no significant group differences reported

232   by (Cascio et al., 2008) - these findings are duplicated for mechanical detection. Individuals

233   with ASD may be hypersensitive to vibrotactile stimuli, though this may be frequency- and/or

234   location-specific. A wider range of techniques than is presently used could confirm whether

235   hyposensitivity for one modality may be present at the same time as hypersensitivity for

236   another, i.e. thermal and mechanical. Additionally, it is not possible to consider somatosensory

237   detection across the developmental course of ASD as studies in children and adolescents are

238   limited.

239   **Pain.**

240   Seven studies examined pain thresholds in ASD. Cascio et al. (2008); Duerden et al.

241   (2015); Fründt et al. (2017) used a method-of-limits to determine thermal pain threshold.

242   While Duerden et al. and Fründt et al. (2017) reported no group differences, Cascio et al.

243   (2008) reported hypersensitivity for both heat and cold pain thresholds in the ASD group

244   compared to healthy controls. Contrary to previous reports that individuals with ASD are

245   insensitive to pain (Militerni et al., 2000; Minshew & Hobson, 2008), these studies provide

246   tentative indications that there is typical nociception processing.

247   Four studies investigated pressure pain thresholds; Fan et al. (2014) and Fründt et al.

248   (2017) in adults, Chen et al. (2017) in adolescents and Riquelme, Hatem, and Montoya (2016)

249   in children. Ramp rates are reported as $1kg/ cm^2 s$ or $50 kPa/cm^2$ (~ $0.5kg/cm^2 s$), or not at all,

250   and probe sizes are either a non-standard probe size of $1.52cm^2$ or the standard $1cm^2$. Non-

251   standardized probe sizes potentially affects comparison with the general pain research literature

252   and within study, comparison is difficult to make for similar reasons. With the exception of

253   Fründt et al. (2017) individuals with ASD are reported to have lower pressure pain thresholds

254   compared to neurotypical controls (Chen et al., 2017; Fan et al., 2014; Riquelme et al., 2016).

255   Although, decisive conclusions are problematical due to incomplete methodologies, or the

256   differing stimuli presentations mentioned, as well as different age groups.

257   Lastly, two studies examined electrocutaneous pain thresholds. Bird et al. (2010) using

258   square pulse waveform at 100Hz, with a 4ms pulse length and a 1s duration and report no

259   significant group differences. Whilst Gu et al. (2017) report significantly lower stimulation

260   levels in the ASD group, using a method-of-levels.

261   Results are inconsistent and reaching conclusions is difficult. The aforementioned

262   studies do provide tentative insight into the possibility that the sensory abnormalities

263   mentioned by the DSM can be quantified, but more investigation is required. From the 10

264   studies, of note is Fründt et al. (2017), who not only utilise the full DFNS QST battery, but also

265   standardise their scores which extends results from simple group comparisons to clinically

266   significant sensory losses or gains.

267   [Table 2 here]

268   **Attention Deficit Hyperactivity Disorder**

269   **Included Studies & Participant Characteristics.**

270   Only one study was identified for ADHD, which selectively covers cold pressor pain

271   but not sensation (Treister, Eisenberg, Demeter, & Pud, 2015) . Thirty adults with ADHD,

272   who were prescribed Ritalin and 30 healthy age- and gender-matched controls, took part. The

273   use of adults is understandable given the nature of the tests administered, which require very

274   precise reports from participants. However, given that ADHD is most prominent in childhood,

275   and that adult ADHD has a different phenotype (Mannuzza, Klein, Bessler, Malloy, &

276   LaPadula, 1993), a study on children is warranted in order to expand insight into pain

277   processing in this disorder.

278   **Pain.**

279   A cold pressor water bath was set at 1°C, participants submerged their right hand,

280   providing both threshold (time at which the cold stimulus began to elicit pain) and tolerance

281   (latency to spontaneous hand removal) over two sessions. Participants were randomised to

282   complete the task once following administration of Ritalin and once following no medication.

283   Individuals who had not been administered Ritalin expressed shorter latencies to cold pain,

284   providing psychophysical evidence of hypersensitivity compared with healthy controls.

285   Although, both threshold and tolerance were significantly shorter in ADHD participants, no

286   significant differences were reported for self-reported pain intensities –the intensity of the pain

287   was similarly felt across the groups regardless of a physiological hypersensitive response.

288   **Schizophrenia**

289   **Included studies.**

290   Eleven studies were included for schizophrenia. Outcomes from these studies were

291   limited to thermal, pressure and electrical stimuli, thus research examining somatosensory

292   thresholds in schizophrenia is limited, with pain thresholds receiving more attention.

293   **Participant characteristics.**

294   All studies were conducted with adults and sample ages suggest that somatosensory

295   assessment has been conducted across the time course of the condition covering early

296   adulthood, which is a peak for the onset of schizophrenia (Sham, MacLean, & Kendler, 1994).

297   A previous diagnosis of schizophrenia was accepted and studies did no further testing.

298   **Sensation thresholds.**

299   One study examined somatosensory thresholds, specifically warm detection thresholds

300   (Jochum et al., 2006) using a method of limits paradigm and a change rate of 0.5°C/s. Patients

301   with schizophrenia demonstrated hyposensitivity, with significantly higher warmth thresholds

302   compared to healthy controls.

303   **Pain.**

304   Thermal pain thresholds were examined in six studies. Jochum et al. (2006) and

305   Boettger, Grossmann, and Bar (2013) obtained warm and cold pain thresholds using a method-

306   of-limits paradigm, however Boettger et al. (2013) used a temperature change rate of 0.5°C/s.

307   Higher temperatures were required to achieve a heat (Boettger et al., 2013; Jochum et al.,

308   2006) and lower to obtain cold (Boettger et al., 2013) pain threshold in patients with

309   schizophrenia compared to controls.

310   Four studies obtained heat pain thresholds using other methods. Three studies asked

311   participants to tolerate heat for a duration of 30s (de la Fuente-Sandoval, Favila, Gómez-

312   Martín, León-Ortiz, & Graff-Guerrero, 2012; de la Fuente-Sandoval et al., 2010) and 120s

313   (Potvin et al., 2008). The last, Dworkin et al. (1993) obtained thermal pain discrimination

314   using a signal detection method; 48 stimuli were presented of four different intensities (35.5,

315   38.5, 46.4 and 48.5°C) and participants verbally rated these as "no-sensation", "warm", "hot"

316   or "painful". Higher temperatures were required to achieve a heat pain threshold in patients

317   with schizophrenia compared to controls (de la Fuente-Sandoval et al., 2010). Furthermore,

318   individuals with schizophrenia were shown to be poorer at thermal pain sensory discrimination

319   and showed no response-bias differences to their matched healthy controls. A significant

320   correlation was reported for warm-hot stimuli and positive symptoms/affective flattening,

321   indicating that higher criteria for reporting painfulness were associated with fewer positive

322   symptoms (Dworkin et al., 1993). Two studies reported non-significant group differences (de

323   la Fuente-Sandoval et al., 2012; Potvin et al., 2008). These differing results may be the

324   product of differing methodologies. For example, a shift in response criterion might lead to a

325   higher intensity required to generate a pain threshold. However, Dworkin et al. (1993)

326   reported no shift in this criterion. Another explanation is that individuals with schizophrenia

327   have a higher threshold for thermal pain but a lower endurance, which results in similar pain

328   tolerance; this would be consistent with a central pain processing explanation for differences

329   with a change in central sensitization (Kleinböhl et al., 1999). That is to say, that the

330   magnitude of peripheral input required to induce a pain response (i.e. threshold) might be the

331   same, but the process of temporal or spatial summation may be magnified. This suggests that,

332 once pain is perceived, the magnitude of this experience grows to a point of being intolerable

333 more quickly.

334 . However, there is tentative evidence that, for laboratory-induced thermal stimuli, individuals

335 may have hyposensitivity towards noxious thermal stimuli. Furthermore, these effects might

336 relate to threat perception. Tolerance is fundamentally a withdrawal response from a noxious

337 cue and previous research in the visual domain has suggested that individuals with

338 schizophrenia withdraw from visually threatening stimuli (Phillips, Senior, & David, 2000).

339 Potentially the point at which the decision that threat is intolerable may be reduced due to this

340 symptomology.

341   Two further studies utilised the cold pressor task to investigate thermal pain, with

342 differing water temperatures. Atik, Konuk, Akay, Ozturk, and Erdogan (2007) used 1°C water

343 and Potvin et al. (2008) reported water temperature range from 7 to 12°C, with participants

344 rating the pain every 30 seconds, rather than a threshold and tolerance measure. Atik et al.

345 (2007) report patients to have higher pain tolerance than healthy controls, but pain threshold

346 did not differ. Furthermore, Potvin et al. report no significant differences between patients and

347 healthy controls in pain ratings.

348   Three studies investigated electrical pain stimulation. Methods differed across studies,

349 with Lévesque et al. (2012) applying a TENS square wave pulse. Guieu, Samuélian, and

350 Coulouvrat (1994) applied five shocks for a 13ms duration, with each train including

351 increasing and decreasing stimulus intensities at a frequency of 0.16Hz. Kudoh, Ishihara, and

352 Matsuki (2000) applied transcutaneous pulses at 2000Hz, 250Hz and 5Hz obtaining self-report

353 pain intensity in response to each stimulus. Levesque et al. report significant group

354 differences, in which individuals with schizophrenia showed hypersensitivity to electrical

355 stimuli compared with healthy controls. Additionally, pain thresholds were negatively

356   correlated to positive symptoms. Kudoh et al. contradict these findings, showing increased

357   conduction thresholds for individuals with schizophrenia and lower VAS pain rating scores,

358   suggesting hyposensitivity. Guieu et al. show no significant group differences. Results are

359   conflicting and the methods employed by each of these studies are contradictory, making it

360   difficult to identify the validity of each of the findings; or how they might reflect differences in

361   populations.

362   Lastly, one study investigated pressure pain using an algometer with a 1cm² pressure

363   tip, applied in a static test of 160kPa and then in a method-of-limits (Girard, Plansont,

364   Bonnabau, & Malauzat, 2011). Pain started significantly earlier for individuals with

365   schizophrenia, requiring less pressure to achieve a pain rating, suggesting hypersensitivity.

366   A greater range of techniques was employed here, reflected by the age of the studies

367   included, with many being conducted before guidance on pain research or relevant equipment

368   had been developed. Results from thermal pain trend toward hyposensitivity, which is

369   tentatively supported by those from thermal sensation. These results are not mirrored in

370   pressure stimuli, where hypersensitivity is reported, nor in electrocutaneous where results are

371   inconclusive. There is evidence, as presented above, for different effects in different

372   modalities, which a wider range of techniques may help, clarify (see Table 3 for detailed

373   results of each study). Adopting a standardised approach will allow for the replicability of

374   studies and better result comparisons across studies.

375   [Table 3 here]

376   **Personality Disorder**

377   **Included studies.**

378   Ten studies were included all of which focussed on BPD, one of the most common

379   forms of personality disorder with a weighted prevalence rate of 0.7% of the general

380   population (Coid, Yang, Tyrer, Roberts, & Ullrich, 2006). Outcomes from these studies were

381   limited to thermal, mechanical, pressure, electrical stimuli, as well as two-point discrimination.

382   Thus, with the range of available measures and types of personality disorder, research

383   examining somatosensory and pain thresholds is presently limited.

384   **Participant characteristics.**

385   One study was conducted using a sample of adolescents, however the majority of

386   studies were conducted with those in early adulthood (n= 10), which suggests that

387   somatosensory assessment has been conducted in line with the pattern of onset. Some studies

388   split the experimental group by personality disorder traits, such as self-injurious behaviour

389   (Ludäscher et al., 2009) comparing BPD with and without self-injurious behaviour (SIB), and

390   psychopathic to non-psychopathic prisoners (Fedora & Reddon, 1993).

391   **Sensation thresholds.**

392   Four studies were identified which examined somatosensory thresholds. Ludäscher et

393   al. (2009) considered thermal sensory thresholds in adults with BPD with and without SIB and

394   Ludäscher et al. (2014) examined these effects in adolescents. Both studies used a method-of-

395   limits with a 1^0C/s change rate. Results from these studies show no significant group

396   differences. A further experiment conducted by Ludäscher et al. (2009) utilised Infra-red

397   thulium-YAG-laser. Individuals with SIB require a greater energy intensity for detection

398   compared to BPD without SIB and healthy controls, although both BPD groups had higher

399   thresholds than healthy controls. This suggests that SIB may have a role to play in

400   somatosensation, independent of BPD.

401   One study examined two-point discriminability using a forced-choice paradigm

402 (Pavony & Lenzenweger, 2014). During the task, a two-point (6mm experimental stimuli or

403 10mm control stimuli) or one-point (intended for the detection of false alarms) stimulus was

404 presented. Participants were then asked to indicate how many points were felt with no

405 significant differences reported between BPD and control participants.

406   Overall results for somatosensory detection thresholds suggest normal functioning in

407 BPD, with the exception of laser radiant heat stimuli where individuals may have

408 hyposensitivity (Ludäscher et al., 2009). However, this effect may be specific to individuals

409 who practice self-injury, and therefore be, at least, partially attributable to the complexity of

410 the behaviours involved. These findings were not replicated under an alternative method of

411 producing thermal stimuli within the same study, nor in adolescents (Ludäscher et al., 2014).

412 Furthermore, results suggest normal tactile discrimination.

413   **Pain.**

414   Ten studies examined pain thresholds in BPD. Thermal pain thresholds were examined

415 in five studies (Ludäscher et al., 2009; Ludäscher et al., 2014; Schmahl et al., 2006; Schmahl et

416 al., 2004; Schmahl et al., 2010). Ludäscher et al. (2009) used a method of limits with

417 1^0C/second change rate, Schmahl et al. (2010) and Ludäscher et al. (2014) used a 1.5°C/s

418 change rate, with Schmahl et al. (2006) using 2°C/s. Compared to healthy controls, individuals

419 with BPD required higher temperatures for heat (Ludäscher et al., 2009) and lower

420 temperatures for a cold pain threshold (Ludäscher et al., 2009; Schmahl et al., 2010),

421 suggesting hyposensitivity. This was additionally supported by results from the Laser Radiant

422 Thermal Stimuli Test (parameters previously discussed (Ludäscher et al., 2009; Schmahl et al.,

423 2004). More specifically, Ludäscher et al. (2009) showed that individuals engaging in SIB had

424 the highest thresholds, supporting the role of this behaviour in attenuating sensory deficits .

425   Additionally, SIB symptom severity was negatively correlated with pain ratings, showing that

426   individuals who have high symptomology rate the stimulus intensity as lower. Ludäscher et al.

427   (2014) provide further support to these findings, reporting similar hyposensitivity in

428   adolescents with BPD. Schmahl et al. (2006) also report hyposensitivity in a group of BPD

429   adults with SIB using their tonic heat methodology. These converging results suggest that for

430   laboratory-induced thermal stimuli, individuals with BPD may experience hyposensitivity to

431   noxious thermal stimuli, specifically when engaging in self-injurious behaviour.

432   Three further studies investigated thermal pain through use of a cold pressor (Bohus et

433   al., 2000; McCown, Galina, Johnson, DeSimone, & Posa, 1993; Pavony & Lenzenweger,

434   2014). Water temperatures were different across studies; one used 1°C water (Pavony &

435   Lenzenweger, 2014), with Bohus et al. (2000) using 10°C and McCown et al. (1993) stating an

436   approximate temperature of 0°C. Procedural methodologies also differed between these

437   studies. Bohus et al. (2000) asked participants to have their hand submerged for 4 minutes and

438   to rate the pain intensity every 15 seconds, whereas McCown et al. (1993) and Pavony and

439   Lenzenweger (2014) obtained threshold, tolerance and endurance. McCown et al. (1993)

440   reported no significant group differences on baseline tolerance levels, however, Pavony and

441   Lenzenweger (2014) report that individuals with BPD show significant higher tolerance and

442   endurance levels, compared with healthy controls. Bohus et al. (2000) reported lower intensity

443   and unpleasantness ratings by individuals with BPD compared to healthy controls.

444   Specifically, those individuals self-reported as under distress of SIB had the lowest pain

445   ratings, followed by individuals who felt calmer. This suggests that those individuals who self-

446   injure perceive pain as less severe or may experience hyposensitivity.

447   One study investigated mechanical pain thresholds using punctate probes (Magerl,

448   Burkart, Fernandez, Schmidt, & Treede, 2012). BPD threshold estimations are reported as

449   significantly higher compared to healthy controls. The recency of SIB and pinprick threshold

450 were significantly correlated. Analysis of the suprathreshold pain measures also revealed

451 similar self-injurious behaviour-dependent losses of pain sensitivity, occurring in all pain

452 measures. Overall, patients in the frequent SIB subgroup were significantly less-pain sensitive

453 than healthy controls and less sensitive than BPD individuals who rarely engaged in SIB,

454 suggesting hyposensitivity.

455 Two studies reported electrocutaneous thresholds; both utilised constant current

456 stimulation although methods differed. Fedora and Reddon (1993) applied an ascending series

457 of stimulation using a Tursky concentric electrode to prisoners. Ludäscher et al. (2007) applied

458 a continuous stimulation of a pulse with a frequency of 10Hz and 0.5ms duration to the right

459 index finger, with a 2 ring electrode, to individuals with BPD and healthy controls. Both

460 studies report significant group differences, in which both prisoners and individuals with BPD

461 have higher pain thresholds than healthy controls. Additionally, Fedora and Reddon (1993)

462 show a negative correlation between pain thresholds and the degree of monotony avoidance,

463 with highest thresholds found in those who are the lowest thrill seekers. In contrast, Ludäscher

464 et al. (2007) report a positive correlation between pain thresholds and both state and trait

465 dissociation, as well as aversive arousal; the more avoidant an individual with BPD is, the

466 higher their pain thresholds. This has important connections with SIB and reinforces the

467 relationship previously discussed.

468 As can be seen from Table 4 results across both sensation and pain tend towards

469 hyposensitivity in individuals with BPD. This conclusion is limited due to the varied

470 methodologies used. Adopting standardised techniques in future studies will allow for the

471 replicability of studies and better result comparisons, which is the factor vitiating any

472 statistically significant conclusions. Another important consideration is the characterisation of

473 stress levels during sensation and pain testing. Evidence suggests that pain sensitivity is

474 altered by mood induction in BPD (Ludäscher et al., 2007).

475   [Table 4 here]

476   **Eating Disorders**

477   **Included studies.**

478   Fourteen studies were included for Eating Disorders. Outcomes from these studies

479   were limited to thermal, mechanical, pressure, vibratory stimuli and two-point discrimination.

480   Thus, with the range of available measures, research examining somatosensory and pain

481   thresholds in eating disorders is presently limited, although it is one of the conditions that has

482   received greater interest.

483   **Participant characteristics.**

484   Eating disorders include anorexia nervosa, bulimia nervosa, restrictive anorexia and

485   binge-purge anorexia (APA, 2013). Twelve studies used an adult sample, with only one study

486   specifically employing adolescents. Eleven of the 14 studies had an all-female participant

487   sample. This is in line with increased prevalence in females, or the underreporting of males

488   with eating disorders (Hackler, Vogel, & Wade, 2010). One study reported the use of both

489   male and female sample (Bär, Berger, Schwier, Wutzler, & Beissner, 2013).

490   **Sensation thresholds.**

491   Two studies examined tactile sensitivity (Faris et al., 1992; Keizer, Smeets, Dijkerman,

492   van Elburg, & Postma, 2012) via mechanical detection, with the addition of sensory

493   discrimination to one study. Tactile acuity and size estimation were tested using two-point

494   discrimination. For tactile acuity, the trial consisted of either one-point (33% of the trials) or

495   two-point stimuli (66%). Blindfolded participants indicated whether they perceived one single

496   stimulus or two distinct stimuli. Responses were recorded with a forced-choice one-up two-

497   down staircase method, with starting distances of 43 and 33mm, for the right underarm and

498   abdomen, respectively. Participants then estimated the distance of the two points on a

499   touchpad computer. In a second phase, mechanical detection was measured using calibrated

500   von Frey hairs, a method mirrored by Faris et al. (1992). Patients with anorexia nervosa had a

501   higher two-point discrimination threshold, regardless of body site tested, and compared with

502   healthy controls. Furthermore, distance estimation was larger in this group for both sites; this

503   effect was largest for the abdomen (Keizer et al., 2012). Rather than a purely sensory effect,

504   the cognitive processing of somatosensory input may in fact be altered in individuals with

505   eating disorders, in line with the expression of their condition. A lower threshold for

506   mechanical detection on the abdomen is reported, but no significant group differences were

507   found for the arm (Keizer et al., 2012), or the hand (Faris et al., 1992).

508   A third study examined thermal and vibration thresholds (Pauls, Lautenbacher, Strian,

509   Pirke, & Krieg, 1991) using a method-of-limits. No significant group differences were

510   reported for patients with anorexia nervosa or bulimia nervosa compared to healthy controls.

511   Overall, the findings for somatosensory detection thresholds are inconsistent. When

512   considering tactile acuity and mechanical detection individuals with eating disorders were

513   shown to display both hypo- and hyper-sensitivity, which may be stimulus specific.

514   Furthermore, there is potential evidence of a psychogenic effect on somatosensation, with the

515   largest effect reported for the abdomen, an area of cognitive focus for those suffering from an

516   eating disorder. It is not possible to consider somatosensory detection in its entirety, as studies

517   are limited, impeding comparisons.

518   **Pain.**

519   Thirteen studies examined pain thresholds in eating disorders. Thermal pain thresholds

520   were examined in eleven of these. Seven studies measured heat pain in a method-of-limits,

521   with varying temperature change rates 0.5°C/s, 0.7°C/s and 1.5°C/s (Bär et al., 2013; Bär et al.,

522 2006; Krieg, Roscher, Strian, Pirke, & Lautenbacher, 1993; Lautenbacher, Pauls, Strian, Pirke,

523 & Krieg, 1990, 1991; Pauls et al., 1991; Schmahl et al., 2010). Significant increased heat pain

524 thresholds were observed in eating disorders compared to healthy controls (Bär et al., 2013;

525 Bär et al., 2006; Lautenbacher et al., 1990, 1991; Pauls et al., 1991). These results were shown

526 to decrease after weight had been regained (Bär et al., 2006) for both tonic and phasic thermal

527 stimuli (Lautenbacher et al., 1990). However, Krieg et al. (1993) and Schmahl et al. (2010)

528 reported no significant group differences. This may be due to the use of recovering anorexics

529 and may provide tentative support to Bär et al. (2006) in which individuals who had gained

530 weight and therefore assumed to be in a phase of recovery, showed that threshold levels

531 decreased. Results from these studies suggest individuals, when in an acute phase, are likely to

532 experience hyposensitivity.

533 The last four studies that examined heat pain thresholds used radiant heat stimuli,

534 specifically laser (de Zwaan, Biener, Bach, Wiesnagrotzki, & Stacher, 1996; de Zwaan, Biener,

535 Schneider, & Stacher, 1996) and thermal latency with a constant stimulus (Papezova,

536 Yamamotova, & Uher, 2005; Yamamotova, Papezova, & Uher, 2009). Patients with eating

537 disorders had higher threshold for thermal pain (de Zwaan, Biener, Bach, et al., 1996; de

538 Zwaan, Biener, Schneider, et al., 1996) compared with healthy controls. Thermal pain

539 threshold latencies were longer (Yamamotova et al., 2009) in bulimia nervosa than healthy

540 controls. As well as a general group of individuals with eating disorders (patients with eating

541 disorders; restrictive anorexia, binge-purge anorexia and bulimia nervosa), specifically those

542 with binge purging symptomatology (Papezova et al., 2005). Providing further evidence of

543 hyposensitivity in respect of noxious thermal stimuli that may be symptomology related.

544 Five studies investigated pressure pain thresholds (de Zwaan, Biener, Bach, et al., 1996;

545 de Zwaan, Biener, Schneider, et al., 1996; Faris et al., 1992; Raymond et al., 1995; Raymond et

546 al., 1999) using a method-of-limits. Individuals with eating disorders, including anorexia, had

547   higher pressure-pain (de Zwaan, Biener, Bach, et al., 1996; de Zwaan, Biener, Schneider, et al.,

548   1996; Faris et al., 1992) and detection thresholds (Raymond et al., 1995) compared to healthy

549   controls. Though no significant difference at suprathreshold tolerance (Raymond et al., 1999).

550   This may be due to pressure pain threshold being entered as a covariate. There is tentative

551   evidence for hyposensitivity towards laboratory-induced pressure pain.

552   Results for thermal pain, tactile stimuli, pressure detection and pain suggest that

553   individuals with eating disorders experience hyposensitivity, which may be specific to acute

554   phases (see Table 5 for detailed results of each study). However, conclusions are difficult to

555   make in regards to this. The aforementioned studies do provide tentative insight into the

556   possibility that the sensory abnormalities can be quantified, but more investigation is required,

557   specifically as there is a focus on thermal stimuli.

558   [Table 5 here]

559   **Discussion**

560   The purpose of this review was to provide an overview of research that investigated

561   pain processing in a number of psychiatric conditions where this has not been a focus

562   previously. The most notable global observation is the lack of utilisation of detailed testing

563   procedures and particularly standardised protocols such as those published by Rolke et al.

564   (2006). Even when these have been used, small variability in the methods, such as temperature

565   ramp rate, still compromise the ability to compare results and draw definitive conclusions.

566   Thermal test procedures remain the most widely used form of sensory testing and mechanical

567   testing remains, for the most part, unused, including; mechanical detection threshold,

568   mechanical pain sensation, dynamic mechanical allodynia and wind-up ratio. This may be due

569   to how user-friendly, safe and easily applicable thermal testing is. Furthermore, the absence of

570   research examining wind-up ratio reduces the possibility of gaining insight into whether there

571   is a central processing component. Specifically, central sensitization manifests as dynamic

572   tactile allodynia, secondary punctate or pressure hyperalgesia, and enhanced temporal

573   summation rather than thermal cutaneous pain, with most clinical pain states involving these

574   aspects (Woolf, 2011). Therefore, to exclude these from a battery of tests is to exclude the

575   possibility of understanding alterations in peripheral and central mechanisms that can

576   contribute to the development and maintenance of pathological states.

577   Additionally, only one paper (Fründt et al., 2017) in the 46 eligible papers, utilised the

578   DFNS QST battery (Rolke et al., 2006). Utilizing comprehensive psychophysical procedures

579   across a range of modalities would allow for better across-study comparisons. It would also

580   allow the development of sensitive indices whilst providing consistency in the approach to

581   understanding these phenomena across conditions. The DFNS battery in particular provides

582   this opportunity and is a valuable starting point, as it provides the potential for systematically

583   comparing the function of small and large sensory afferents, quantification of the full sensory

584   axis and comparison to known normative values. Although, it must be noted that this

585   particular battery has been developed through considerable research to identify the most

586   sensitive indices for neuropathic pain. Without such rigour it is not possible to fully appreciate

587   the extent of any abnormality, specifically whether it may be systemic or modality specific.

588   Although such a definitive understanding is still not available, results of the reviewed

589   studies indicate that pain processing may be altered in certain psychiatric groups. When

590   considering the overarching question of whether changes in pain processing are present in

591   psychiatric conditions, it would appear that for individuals with schizophrenia, BPD and eating

592   disorders, there is moderate evidence for hyposensitivity to pain and touch. A single study on

593   ADHD (Treister et al., 2015) suggests that individuals may have a hypersensitivity to pain,

594   however given the lack of further data, this needs to be considered very carefully. Lastly, for

595   individuals with ASD the findings are inconsistent, with the possible exception of a

596   hypersensitivity to vibrotactile stimuli. Furthermore, findings from each of these conditions

597   suggest that these effects may be more complex, specifically, that effects are specific to a

598   single site, stimulus intensity or are reliant on some other behaviour.

599   In the case of ASD, the psychophysical methods used to investigate pain sensations

600   reveal no systematic evidence for hypo- or hyper-sensitivity in this population, and run

601   contrary to current diagnostic criteria (APA, 2013), as well as clinical and parent reports that

602   suggest a pain experience to stimuli (Militerni et al., 2000; Moore, 2014; Wing, 1976). While

603   this may be in large part due to lack of investigation, it highlights the need for systematic

604   protocols. The most reliable results stem from those studies which have utilised the standard

605   QST protocol, specifically those by Fründt et al. (2017). This study not only utilised the

606   methodology it standardised scores based on the published normative values, which means that

607   a clinically significant hypo- or hyper-sensitivity can be determined. This is not to discount the

608   other papers who utilised psychophysically robust methods of testing; Cascio et al. (2008);

609   Duerden et al. (2015); and Fan et al. (2014), however, the utilisation of standard group

610   comparisons may not be enough to determine true alterations. It is, therefore, clear that more

611   research is required to understand further the nature of any differences and to reconcile the

612   differences between *objective* measures and *observations* of behaviour.

613   The hyposensitivity reported in each of the other conditions appears to have different

614   potential explanations. In eating disorders, changes in both tactile acuity and pressure

615   detection thresholds appear more pronounced when examined on the abdomen (Keizer et al.,

616   2012). Specifically, individuals had larger distance estimations and poorer tactile perception,

617   as measured by two-point discrimination, as well as a sensitivity to pressure detection. Both

618   these tests potentially indicate a cognitive deficit rather than sensitivity, however, those studies

619   reporting thermal hyposensitivity (Bär et al., 2013; de Zwaan, Biener, Schneider, et al., 1996;

620   Lautenbacher et al., 1990, 1991; Papezova et al., 2005; Yamamotova et al., 2009), at least for

621   this modality, suggest a true physiological deficit. Since recovering anorexic patients showed

622   thresholds returning to healthy control level during weight gain, altered thresholds appear to be

623   confined to acute phases of the condition, as reported by Bär et al. (2006). Symptom specific

624   effects are also relevant in considering individuals with BPD. During acute BPD episodes,

625   self-injury is a common behavioural dysregulation and those individuals under distress of self-

626   injury required higher temperature for thermal detection and pain thresholds (Ludäscher et al.,

627   2009; Schmahl et al., 2006), as well as reporting higher mechanical pain thresholds (Magerl et

628   al., 2012) than those not under distress of self-injury and healthy controls. Therefore, these

629   sensory deficits might, similarly be, acute phase specific. Unlike eating disorders, where

630   recovery is possible, there is no evidence that sensory changes return to typical levels once

631   symptoms reduce, as those who are not under distress of self-injury still have hyposensitivity in

632   comparison to healthy controls. This symptom effect is similarly present in schizophrenia

633   (Boettger et al., 2013; Jochum et al., 2006) and those with fewer positive symptoms e.g.

634   hallucinations and delusions required greater temperatures to report pain (Lévesque et al.,

635   2012).

636   Given the limited range of studies at present, particularly studies that address neural

637   processing of pain, speculation as to mechanisms should be approached with caution.

638   Understanding the specific mechanisms behind these findings will however, be useful in

639   identifying the convergence and divergence of pain processing differences across disorders.

640   An important perspective put forth by Feldman-Barrett (2017) suggests that processing of

641   somatic and emotional processing in the nervous system may share highly similar pathways. In

642   the absence of clear differences in discriminative somatosensory processing, altered pain

643   perception and response are likely to be strongly related to alterations in emotional regulation

644   (Keefe, Lumley, Anderson, Lynch, & Carson, 2001) or interoceptive abilities (Craig, 2003).

645   Pain and touch have inherent affective and motivational components (Williams & Craig, 2016)

646   as well as being a signal of problems in homeostatic regulation (Panerai, 2011). Craig's model

647   (2003) proposes that pain, touch, and interoception represent the sensory component of a

648   unified sensorimotor system that signals the physiological condition of the body and elicits

649   autonomic regulatory, or visceromotor, response. These somatic sensory signals are carried by

650   lamina I spinal pathways (Craig, 2002), which are thought to be affected in a range of

651   psychiatric conditions (Mash et al., 2017; Murphy, Brewer, Catmur, & Bird, 2017). This

652   unified system that integrates somatic sense and the physiological arousal associated with

653   emotions is a promising potential mechanism for susceptibility to psychiatric illness that

654   should be explored in future research.

655   Rather than providing definitive answers to questions related to pain processing in

656   psychiatric conditions, this review more comprehensively highlights a number of implications

657   for researchers and clinicians. The first consideration for future research relates to the potential

658   role of general cognitive and emotional states in these populations. Specifically, as it is already

659   well established for depression and anxiety that mood is associated with pain responses

660   (Goesling et al., 2013), it would be prudent for future research into the psychiatric conditions

661   mentioned above to consider the relationship between mood and pain processing. This is

662   further in light of the fact that recent evidence has suggested that the relationship between

663   autism symptoms and pain behaviours was mediated by symptoms of anxiety and depression

664   (Garcia-Villamisar, Moore, & Garcia-Martinez, 2018). Additionally, difficulties with general

665   cognitive processing, specifically with executive control; an attentional system, is a hallmark of

666   many of these psychiatric conditions (Galimberti et al., 2013; Hill, 2004; Niendam et al., 2012)

667   and there are known links to pain experience (Eccleston & Crombez, 1999; Moore, Keogh, &

668   Eccleston, 2012). The somatosensory changes observed in eating disorders may also reflect

669   such a cognitive change. Here an attentional bias towards areas of bodily concern (i.e. the

670   abdomen) may increase sensitivity at this site. This may also explain why individuals no

671   longer show these hypersensitivities as they recover. More general cognitive processes, may

672   therefore, mediate responses on these pain assessment measures. Evidence for this in the

673   context of this review comes from Treister et al. (2015) who found that participants with

674   ADHD who were currently un-medicated with Ritalin, showed hypersensitivity to pain,

675   however, when these individuals were given medication these thresholds moved into the

676   normal range. One potential explanation of these differences might be that clinical groups find

677   it harder to attend to the task at hand, indeed effects often changed when the ramp rate of

678   stimuli was also changed, suggesting that attention might be an important factor (Cascio et al.,

679   2008; Duerden et al., 2015). It may also be the case that treatment with Ritalin helps to

680   normalize homeostatic set-points across sensory and cognitive systems. For example, previous

681   studies have suggested that rapid changes in attention, increased motor activity, and enhanced

682   sensory sensitivity, may all be part of an auto-regulatory attempt to increase stimulation, in

683   order to maintain homeostasis of brain arousal (Geissler, Romanos, Hegerl, & Hensch, 2014).

684   Effective treatment (with Ritalin, for example) may obviate the need for such autoregulation,

685   reducing sensory sensitivity, as well as behavioural and attentional hyperactivity (Geissler et

686   al., 2014).

687   Medication being taken by these populations therefore, also might directly affect pain

688   processing. Specifically, it opens up questions regarding any analgesic effects present. Given

689   the percentage of individuals with a range of psychiatric conditions, who use pharmacological

690   substances; which are known to act on the serotonergic system (Hurwitz, Blackmore, Hazell,

691   Williams, & Woolfenden, 2012; Singh, Singh, Kar, & Chan, 2010). As well as many of these

692   medications having known analgesic effects (Mico, Ardid, Berrocoso, & Eschalier, 2006), it is

693   important to consider the role of these agents in altering pain processing. Several studies

694   included in this review explicitly mention the use of non-medicated participants. However,

695   few mention medication use, therefore, discounting the possibility of investigating this

696 phenomenon thoroughly. More is needed regarding the management of challenging

697 behaviours, including both those thought to be related to pain (i.e. self-injurious behaviours) as

698 well as other symptoms, to identify how management of clinical symptoms may alter pain

699 response and how pain management strategies may help with clinical symptoms.

700   A further consideration is to carefully select appropriate control groups. Comparing

701 psychiatric or pain patients with healthy controls can result in artificial amplification of QST

702 differences that are unrelated to clinical state, as they do not represent the general population

703 who are typically fraught with issues that can affect QST results for e.g. obesity (Coghill &

704 Yarnitsky, 2015). This can confound significant results, especially considering the number of

705 additional diagnosed or undiagnosed co-morbidities present in psychiatric conditions (Gillberg

706 & Fernell, 2014). One potential approach could be to go beyond examining psychiatric

707 groups' thresholds in relation to healthy controls and compare them with other experimental

708 groups with specific psychiatric conditions. Several studies within this review considered a

709 range of conditions or additionally looked at traits within these conditions. This approach

710 could solve the amplitude issue and provide other areas of interest to be explored.

711   The present research however, is limited by this reliance on condition-based research

712 and group-level analysis. Current research trends are moving away from such an approach

713 with The National Institute of Mental Health (NIMH) developing a taxonomy, which proposes

714 a trans-diagnostic approach to understanding mental health conditions. It might therefore be of

715 value to examine for the underlying mechanisms which may result in these differences or pain

716 processing more broadly, as a result of symptoms or traits, rather than conditions (Insel et al.,

717 2010). There are also large individual differences within the general population with reference

718 to somatosensory thresholds (Fillingim, 2005) that should be considered when investigating

719 similar differences in individuals with a diagnosis; variability may be typical regardless of the

720 diagnosis therefore caution should be adopted to ensure that such variability extends beyond

721 that which is typically expected. Given these observations, future research may benefit from a

722 more individualistic approach in examining these. Comparison with published normative

723 values (Magerl et al., 2010) allows for individual profiles to be developed and an

724 understanding of potential links between individual psychiatric symptoms and somatosensory

725 differences. As well as an understanding of the number of individuals within each condition

726 who might be experiencing altered somatosensory interactions with external stimuli (either

727 hyper- or hypo- sensitivity), including any individuals with typical function.

728   Another feature, which has received only limited indirect attention, is that of the

729 developmental time course of the somatosensory symptoms in psychiatric conditions. Almost

730 all studies included in this review examined participants in the age range of 18-30 years with

731 IQ in the normal range. This is wholly understandable given that the tasks being presented

732 require very specific responses, as well as being potentially distressing to younger children or

733 individuals without the capacity to fully understand the procedures. This does, however, limit

734 the generalisability and utility of these findings. Understanding the experience of pain in

735 childhood is important, as it could clarify the development of any hyper- or hypo-sensitivity, or

736 the change from an early a-typicality to a potentially more typical somatosensory profile in

737 adulthood, or the reverse. Further, it is well known that conditions associated with pain have a

738 progression into old age (Brattberg, Parker, & Thorslund, 1997), and it appears that both

739 sensory and pain thresholds increase with age (Magerl et al., 2010). It would therefore be

740 beneficial to further understand the progression of pain sensitivity and response into older

741 adulthood in individuals with psychiatric conditions.

742   In conclusion, this review highlights the needs for ongoing work that has

743 methodological rigour. Researchers utilising sound psychophysical methods and carefully

744 reporting the methods can achieve this. In doing so, research can develop individual profiles,

745 as well as facilitate comparisons across studies that involve other psychiatric conditions,

746   physical health conditions and healthy controls. This will provide the more precise results

747   required to form conclusions that are more definitive. Experimental investigations of pain can

748   detect or verify altered processing as a symptom and can provide insights into the behavioural

749   consequences (Lautenbacher & Krieg, 1994), which in turn would help to provide the grounds

750   for accurate interventions to assist in alleviating symptoms. Overall, the findings in the current

751   review suggest somatosensory hyposensitivity in schizophrenia, eating disorders, and

752   personality disorders. More investigation that is systematic will correct views based on

753   inconsistent research, anecdotal and clinical case study views, or support these findings and

754   potentially lead to better clinical pain management in vulnerable groups.

755

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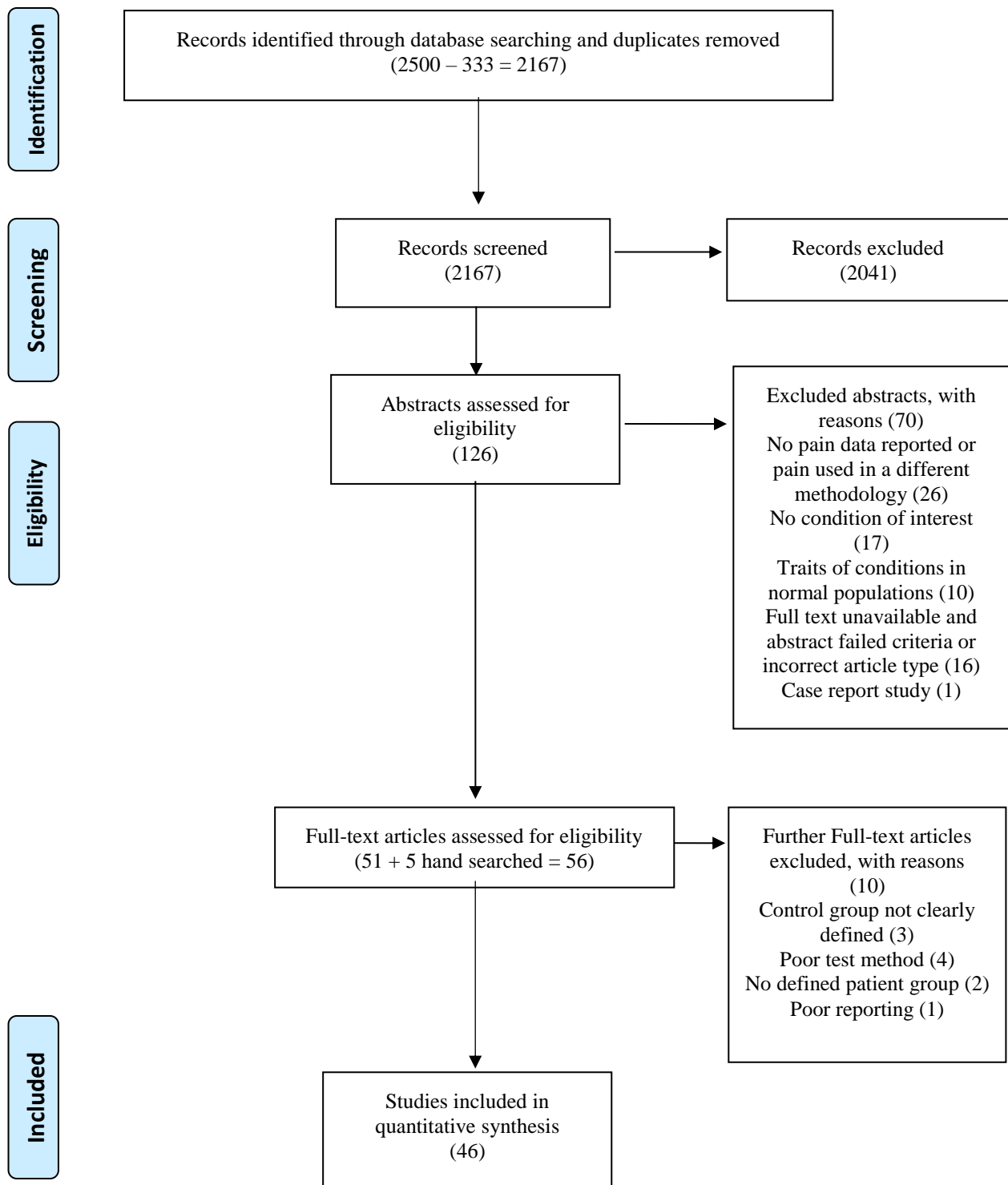
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1055 **Figure Legend**

1056 Figure 1. Number of identified publications at each phase of the screening process. Adapted

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Identification

Records identified through database searching and duplicates removed
(2500 – 333 = 2167)

Screening

Records screened
(2167)

Records excluded
(2041)

Eligibility

Abstracts assessed for
eligibility
(126)

Excluded abstracts, with
reasons (70)
No pain data reported or
pain used in a different
methodology (26)
No condition of interest
(17)
Traits of conditions in
normal populations (10)
Full text unavailable and
abstract failed criteria or
incorrect article type (16)
Case report study (1)

Full-text articles assessed for eligibility
(51 + 5 hand searched = 56)

Further Full-text articles
excluded, with reasons
(10)
Control group not clearly
defined (3)
Poor test method (4)
No defined patient group (2)
Poor reporting (1)

Included

Studies included in
quantitative synthesis
(46)

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1108   **Table 1: Electronic search strategy.**

PHASE		TERMS
1.	SPECIFIC SEARCH TERMS FOR DSM-5 PSYCHIATRIC CONDITIONS.	ASD
		Autism Spectrum Disorder
		Autism
		Asperger's
		ADHD
		Attention Deficit Hyperactivity disorder
		ADD
		Attention Deficit Disorder
		PD
		Personality Disorder
		BPD
		Borderline Personality Disorder
		Schizophrenia
		Anorexia Nervosa
		Bulimia Nervosa
		Binge-eating disorder
		OCD
		Obsessive Compulsive Disorder
		Post-traumatic Stress Disorder
		PTSD
		Depression
		Anxiety
2.	SPECIFIC SEARCH TERMS FOR PAIN/SOMATOSENSATION AND QST.	QST
		Quantitative Sensory Testing
		Experimental pain
		Nociception
		Nociceptors
		Aδ
		A-delta
		C-fibres
		C-fiber
		Thermal pain
		Somatosensation
		Pain thresholds
		Thermal detection
		Tactile detection
		Mechanical pain
		Dynamic mechanical allodynia
		Wind-up ratio
		Vibration detection
		Pressure pain
		Two point discrimination
		Electrocutaneous
		Cold pressor
3. COMBINATION OF PHASES 1 AND 2.		----
DSM = DIAGNOSTIC STATISTICAL MANUAL QST= QUANTITATIVE SENSORY TESTING		

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Table 2: Detailed reported results for each study listed by QST test for autism spectrum disorder (ASD).

Test	Citation	Sample	Control	Matched	Results
CDT	Cascio et al. (2008)*	8 ASD	8 HC	Age Gender	No significant main effects, group differences or interactions.
	Duerdan et al. (2015)*	20 ASD	55 HC	Age Gender	Significant group differences, ASD lower threshold than HC.
	Frundt et al. (2017)*	13 ASD	13HC	Age Gender IQ >70	No significant group differences.
WDT	Cascio et al. (2008)*	8 ASD	8 HC	Age Gender	Showed lower threshold for palm (1.61°C) than forearm (2.91°C) no significant group differences.
	Duerdan et al. (2015)*	20 ASD	55 HC	Age Gender	Significant group differences, ASD increased threshold compared to HC.
	Frudnt et al. (2017)*	13 ASD	13 HC	AGE Gender IQ >70	No Significant group differences
TSL	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
PHS	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
CPT	Cascio et al. (2008)*	8 ASD	8 HC	Age Gender	Main effect of site and group; ASD threshold 16.68°C compared to HC 9.04°.
	Duerdan et al. (2015)*	20 ASD	55 HC	Age Gender	No significant group differences.
	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
HPT	Cascio et al. (2008)*	8 ASD	8 HC	Age Gender	Sig group effect; ASD lower threshold 43.66°C than HC 46.58°C, paired with lower thresholds on the thenar palm than the forearm.

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					Interaction effect reflected ASD had higher thresholds (by 1.86°C, on average) on the second day of testing as compared to the first, HC remained stable.
	Duerdan et al. (2015)*	20 ASD	55 HC	Age Gender	No significant group differences.
	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
MDT	Cascio et al. (2008)*	8 ASD	8 HC	Age Gender	Sig lower on palm than forearm for both groups with a significant increase seen on the second day.
	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	Significant group difference with a greater loss of function for mechanical detection in ASD patients that, nevertheless, did not survive Bonferroni correction
	Riquelme et al. (2016)	27 ASD	30 HC	Age	Significant group*body location*body side interaction. HC had significantly higher thresholds than ASD in the left face and right hand dorsum. Three body locations sig different (face< hand palm< hand dorsum) in HC, whereas only face< hand palm and, face< hand dorsum sig diff in ASD. No sig difference in body side in ASD.
MPT	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
MPS	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
DMA	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
WUR	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
VDT	Blakemore et al. (2006)	32 HF ASD	41 HC	Age IQ	AS hypersensitive to 200Hz compared to HC.
	Cascio et al. (2008)	8 ASD	8 HC	Age Gender	Main effect of site for 33Hz with ASD having 34% lower thresholds than HC on the forearm, decreasing on 2nd day.
		6 ASD	6 HC	Age	No sig group difference at the unmasked 40Hz, 250Hz unmasked or masked 40Hz.

	Guclu et al. (2007)			Gender	
	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
PPT	Fan et al. (2014)*	44 ASD	41 HC	Age Gender IQ	ASD individuals more sensitive than HC.
	Frundt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
	Riquelme et al. (2016)	27 ASD	30 HC	Age	Main group effect, showing lower thresholds in ASD than HC.
	Chen et al. (2017)	37 ASD 26 CDS	34 HC	Age Gender IQ >90	Significant difference between all groups, mean rank from lowest to highest ASD, HC and CDS.
ELE	Bird et al. (2010)*	18 AS	18 HC	Alexithymia Age IQ	Main effect of pain. No group diff. Unpleasantness for low and high pain main effect of pain Sig interaction pain*group. Sig group differences for ratings of low pain self and other. ASD judged unpleasantness of stimulation to be zero compared to controls.
	Gu et al. (2017)	17 ASD	17 HC	Age Gender IQ >80	Significant group differences with ASD lower stimulation levels than HC.
Psychometrics	Duerdan et al. (2015)	20 ASD	55 HC	Age Gender	Significant correlation with Autism severity and WDT as well as CDT. IQ was correlated to WDT, CDT and HPT.
	Guclu et al. (2007)	6 ASD	6 HC	Age Gender	Sig correlation between sensory profile and touch inventory and between the tactile and emotional subsets of the Sensory Profile. Significant correlation between the touch inventory test and the tactile subset of the sensory profile. Those individuals who scored higher, suggesting emotional problems (according to the SP), have more tactile problems (according to the SP) and display more tactile defensiveness behaviours according to the TI.

NOTES: * indicates standardised DFNS QST protocol used. ASD (Autism Spectrum Disorder), AS (Asperger's) and HC (Healthy Control). CDT (Cold Detection Threshold), WDT (Warm Detection Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical Detection Threshold), MPT (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection Threshold), PPT (Pressure Pain Threshold), and ELE (Electrical Pain Stimulation).

1115 **Table 3: Detailed reported results for each study listed by QST test for Schizophrenia.**

Test	Citation	Sample	Control	Matched	Results
WDT	Jochum et al. (2006)	23 SCH	23 HC	Age Gender Handedness	Significant group differences, Schizophrenic patients indicated perception for warmth later than controls.
CPT	Boettger et al. (2013)	18 SCH	18 HC	Age Gender	Significant group differences on both palms, with SCH showing higher thresholds than HC. No significant group differences on VAS scores.
HPT	Boettger et al. (2013)	18 SCH	18 HC	Age Gender	Significant group differences on both palms, with SCH showing higher threshold than HC No significant differences on VAS scores. Significant group differences on thermal grill thresholds, with greater temperature differentials required by SCH group to elicit a painful response. No significant group differences on VAS scores instead the stimulus response curve of TGI pain perception was shifted towards higher stimulus intensities.
	de la Fuente-Sandoval et al. (2010)	12 SCH	13 HC	Age Gender Handedness	SCH reported higher WPT than HC, but no group differences for intensity or unpleasantness ratings.
	de la Fuente-Sandoval et al. (2012)	12 SCH	13 HC	Age Gender Handedness	No group differences for thermal pain tolerance or intensity and unpleasantness ratings
	Dworkin et al. (1993)		19 HC	Age	Sig group differences for thermal d' at lower (warm) and higher (hot-pain), showing SCH poorer at sensory discrimination. No group differences on response bias Inβ.
	Jochum et al. (2006)	13 SCH	23 HC	Age Gender Handedness	Significant group differences with SCH showing higher threshold for heat pain.
	Potvin et al. (2008)	23 SCH	29 HC	Age Gender Ethnicity	No sig group differences for tonic thermal pain but scores were lower in SCH. Windup ratio, time was a positive significant predictor of pain in controls, but not SCH. Diffuse noxious inhibitory control effects in patients and controls, showed a sig effect of time, however, the interaction between time and group did not emerge as significant.
		23 SCH			
PPT	Girard et al. (1994)	35 SCH	35 HC	Age Gender	For the fixed pressure, VAS score was higher in SCH than HC. Step by step pressure and P3 (p is the pressure relating to 3 on the VAS scale) was lower for schizophrenics than HC. Ischemia induction test showed schizophrenics were more sensitive than HC.
ELE	Guieu et al. (1994)	10 SCH	10 HC	Age Gender	Correlation between nociceptive flexion reflex threshold and subjective pain threshold for individuals with SCH. No group differences in Pain threshold.

	Kudoh et al. (2000)	50 SCH	25 HC	Age	Cutaneous thresholds for 2,000 Hz, 250 Hz, and 5 Hz in SCH were significantly higher than HC. No significant differences in conduction thresholds between SCH groups. VAS scores for SCH at 2 and 5 hours post operatively were significantly lower than HC.
	Levesque et al. (2012)	12 SCH	11 HC		Schizophrenic participants had a much lower electrocutaneous pain threshold than healthy control. Reflex threshold trend demonstrates lower withdrawal for SCH though no sig group differences reported. Significant increases in subjective pain sensitization pain ratings as a function of increasing frequency for SCH and HC. Sig group difference with SCH showing less pain sensitization than controls. Withdrawal reflex response/pain sensitivity: Within groups NFR responses increased significantly as a function of increasing stimulation but no sig group differences.
CP	Atik et al (2007)*	27 SCH 30 BP	59 HC	Age Gender Handedness	Cp threshold, tolerance, magnitude and endurance had significant group differences. Post hoc tests revealed that SCH group had higher threshold and lower magnitude than the BP group (who had the lowest), but not to HC. They also had highest tolerance compared to both HC and BP, who again had lowest. They also had the longest endurance times compared to HC, but did not differ to BP.
	Potvin et al (2008)	23 SCH	29 HC	Age Gender Ethnicity	No significant group differences.
Psychometrics	Dworkin et al. (1993)	13 SCH	19 HC	Age	In SCH group sig correlation for lower intensity stimuli and positive symptoms and affective flattening, indicating that higher criteria for reporting painfulness were associated with fewer positive symptoms. Pain threshold was negatively correlated with positive symptoms.
	Levesque et al. (2012)	12 SCH	11 HC		

NOTES: * indicates standardised DFNS QST protocol used. SCH (Schizophrenia), BP (Bi-polar) and HC (Healthy Control). CDT (Cold Detection Threshold), WDT (Warm Detection Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical Detection Threshold), MPT (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection Threshold), PPT (Pressure Pain Threshold), and ELE (Electrical Pain Stimulation).

1131 **Table 4: Detailed reported results for each study listed by QST test for personality disorder.**

Test	Citation	Sample	Control	Matched	Results
CDT	Ludascher et al. (2009)*	24 BPD (13 SIB 11 non-SIB)	24 HC	Gender	No significant group differences.
	Ludascher et al. (2014)*	20 BPD	20 HC	Age Gender	No significant group differences.
WDT	Ludascher et al. (2009)*	24 BPD (13 SIB 11 non-SIB)	24 HC	Gender	No significant group differences.
	Ludascher et al. (2014)*	20 BPD	20 HC	Age Gender	No significant group differences.
CPT	Ludascher et al. (2009)*	24 BPD (13 SIB 11 non-SIB)	24 HC	Gender	Significant group differences, BPD-SIB had highest thresholds. BPD (including BPD-SIB and BPD-non-SIB) were higher than HC. Correlation showed extreme values for CPT were found in the BPD-SIB group. Sig main effect of group for detection thresholds, pain thresholds and intensity ratings for laser radiant heat stimuli. Post-hoc contrasts were sig for detection thresholds, pain thresholds and heat pain ratings. BPD-SIB showed lowest pain sensitivity. BPD (SIB and non-SIB) were lower than HC.
	Ludascher et al. (2014)*	20 BPD	20 HC	Age Gender	Significant effect for group factor, with BPD showing lower CPT temperatures required for pain.
	Schmahl et al. (2010)*	16 BPD 16 PTSD 20 BN	24 HC	Age Gender	High significant group differences for CPT, with BPD having higher threshold than HC. No sig difference between baseline and after stress pain thresholds.
HPT	**Ludascher et al. (2009)	24 BPD (13 SIB 11 non-SIB)	24 HC	Gender	Significant group differences, BPD-SIB had highest thresholds. BPD (including BPD-SIB and BPD-non-SIB) were higher than HC. Correlation showed extreme values for HPT were found in the BPD-SIB group.
	Ludascher et al. (2014)*	20 BPD	20 HC	Age Gender	Significant effect for group factor, with BPD showing highest HPT.
	Schmahl et al. (2006)	12 BPD	12 HC	Age Gender	BPD had lower pain sensitivity to tonic heat than controls. The mean temperature causing perceived pain intensity of NRS 40 was found to be 46.7 ±0.4°C for patients and 44.2 ±0.6°C for controls and a reduced offset of the stimulus-response function in patients, suggesting there was a downward shift of the stimulus-response function in patients by approximately 30 points on the NRS.
	Schmahl et al. (2010)*	16 BPD 16 PTSD	24 HC	Age Gender	Trend towards BPD having higher thresholds than HC, no significant main effect.

		20 BN			Sig interaction group*condition for WPT, indicating an accentuation of possible hypoalgesia in BPD patients under stress.
	Schmahl et al. (2004)	10 BPD	14 HC	Gender	Laser detection and pain thresholds were elevated in BPD patients compared to HC.
MPS	Magerl et al. (2012)	22 BPD	22 HC	Age Gender	BPD pain threshold sig higher than HC for individual threshold estimation. Pain threshold at 50% incidence was 74% higher in BPD than HC. Pain reports in BPD were sig lower at any force. SIB and pinprick threshold sig correlated, suprathreshold and SIB sig group effect, no difference in pain measures and intensity. Pain sent stratified by SIB severity, frequent SIB less sensitive to pain.
ELE	Fedora, & Reddon (1993)	28 BPD	28 HC	Age Gender	BPD groups were significantly higher than HC for pain thresholds. Negative correlation between pain thresholds and degree of monotony avoidance in psychopathic patients, with the highest thresholds recorded in those who were the lowest thrill seekers.
	Ludascher et al. (2007)*	12 BPD	12 HC	Age Gender	No sig group differences for electrical detection thresholds. BPD had sig higher pain threshold than HC.
TPD	Pavony & Lenzenweger (2014)*	27 BDP 20 MDD	44 HC		No significant group differences.
CP	Bohus et al. (2000)	12 BPD	19 HC	Age Gender	HC vs BPD-C and D sig main effect of group on intensity and unpleasantness. Sig effects of time on intensity and unpleasantness ratings.
	McCown et al (1993)*	20 BPD 20 OPD	20 HC	Age Gender	No sig difference between group initial tolerances. Sig group differences, where BPD had longest post immersion voluntary exposure compared to OPD and HC.
	Pavony & Lenzenweger (2014)*	27 BPD 20 MDD	44 HC		No sig group differences for threshold. Sig group differences, BPD had higher tolerance and endurance compared to HC and MDD.
Psychometrics	Ludascher et al. (2009)	24 BPD (13 SIB 11 non-SIB)	24 HC	Gender	Sig positive correlation with pain intensity ratings and symptom severity.
	Ludascher et al. (2007)	12 BPD	12 HC	Age Gender	Pain threshold sig correlated to trait dissociation, state dissociation and aversive arousal in patients but not HC.

NOTES: * indicates standardised DFNS QST protocol used. **used both standard and comparable pain induction methods. BPD (Borderline Personality Disorder), PTSD (Post-Traumatic Stress Disorder), SIB (Self-Injurious Behaviour), BN (Bulimia Nervosa), MDD (Major Depressive Disorder), OPD (Other Personality Disorder) and HC (Healthy Control). CDT (Cold Detection Threshold), WDT (Warm Detection Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical Detection Threshold), MPT (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection Threshold), PPT (Pressure Pain Threshold), and ELE (Electrical Pain Stimulation).

1137 Table 5: Detailed reported results for each study listed by QST test for eating disorders.

Test	Citation	Sample	Control	Matched	Results
CDT	Pauls et al. (1991)	9 AN 10 BN	10 HC	Gender	No significant group differences.
WDT	Pauls et al. (1991)	9 AN 10 BN	10 HC	Gender	No significant group differences.
HPT	Bar et al. (2006)*	14 AN	15 HC	Gender	Sig group main effect, sig group*time interaction for heat pain threshold, where patients had higher thresholds than HC, with results remaining significant even after controlling for skin temperature.
	Bar et al. (2013)*	19 AN	19 HC	Age Gender Smoking Coffee Education	Overall significant group differences for thermal pain on both forearms, with sig diff between patients and HC for WPT on the right and left, with patients averaging 2 degrees higher than HC.
	De Zwaan et al. (1996)	40 ED	32 HC		Patients had significantly higher threshold for thermal pain compared to HC. M threshold for pressure sig related to M threshold to thermally induced pain.
	Krieg et al. (1993)	23 AN	41 HC	Gender	No group differences for warm pain threshold. All groups had clearly lower mean pain thresholds than the patients with acute anorexia nervosa and bulimia nervosa from their previous study. Pain threshold sig correlated to skin temp in recovered anorexics with intermediate recovery outcome.
	Lautenbacher et al. (1990)	10 AN 10 BN	10 HC	Gender	Sig group diff for phasic pain thresholds but not tonic. Warm pain threshold for anorexic and bulimic patients was sig higher under phasic and tonic compared to healthy controls. No other group comparison was sig.
	Lautenbacher et al (1991)	19 AN 20 BN	21 HC	Gender	Sig group differences in pain thresholds, with both Anorectic and bulimic patients having higher warm pain thresholds than HC.
	Papezova et al. (2005)	39 ED	17 HC	Gender	PT detection latencies were highly correlated within subjects. Sig group differences where eating disorders had higher pain thresholds than HC, specifically Bulimia nervosa and binge-purge anorexia, restrictive anorexia did not differ. Sig linear trend with progression from HC to restrictors to bulimics to binge purge.
	Yamamotova et al. (2009)	21 BN	21 HC	Gender BMI	Sig main effect of group, a significant main effect of condition and a significant condition*group interaction. The main effect of group was due to higher pain thresholds in BN than HC on all six measurements.
	Schmahl et al. (2010)	20BN 16BPD 16PTSD	24 HC	Age Gender	No significant group differences
	Pauls et al. (1991)	9 AN 10BN	10 HC	Gender	Significant group differences where both patient groups had higher thresholds, no significant group*site interaction.
		22AN	32 HC	Gender	Significant group differences for thermal pain thresholds where AN and BN patients had higher thresholds than HC.

	De Zwaan et al. (1996)	18BN			
PPT	De Zwaan et al. (1996)*	40 ED	32 HC		Patients had significantly higher threshold for pressure pain compared to HC. M threshold for pressure sig related to M threshold to thermally induced pain.
	Raymond et al. (1999)*	43 AN	65 HC	Gender	AN group had higher baseline PDT than controls, with age acting as the covariate.
	De Zwaan et al. (1996)	22AN 18BN	32 HC	Gender	Mechanical pain thresholds were significantly higher in patients than HC.
	Faris et al. (1992)	27BN	31 HC	Gender	Both pressure detection and pain thresholds were significantly higher in in BN than HC.
	Raymond et al. (1995)	27BED 33 Ob	44 HC	Gender	Significantly higher detection thresholds in patients than HC, but no significant difference for pain threshold.
VDT	Pauls et al. (1991)	9 AN 10 BN	10 HC	Gender	No significant group differences.
TPD	**Keizer et al. (2012)	25 AN	28 HC	Gender Age	For Tactile Estimation there was a sig main group effect, body part effect and a body part*group interaction. Post hoc showed distance estimation for arm and abdomen were larger in patients than controls. Patients had sig higher TPD than controls. There was no sig main group effect for detection and a significant body part*group interaction. Post hoc test showed patients had sig diff PDT for the abdomen but not arm compared to HC. PDT for arm and abdomen diff sig in patients.
Psychometrics	Bar et al. (2013)	19 AN	19 HC	Age Gender Smoking Coffee Education	Significant negative correlation for pain ratings and symptom severity.

NOTES: * indicates standardised QST protocol used. **used both standard and comparable pain induction. AN (Anorexia Nervosa), BN (Bulimia Nervosa), ED (Eating Disorder), BPD (Borderline Personality Disorder), PTSD (Post-Traumatic Stress Disorder), BED (Binge Eating Disorder), Ob (Obese) and HC (Healthy Control). CDT (Cold Detection Threshold), WDT (Warm Detection Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical Detection Threshold), MPT (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection Threshold), PPT (Pressure Pain Threshold), and ELE (Electrical Pain Stimulation).