

## Pain in Psychiatric Conditions

1 Review Article

2 Pain Processing in Psychiatric Conditions: A systematic review

3 Sarah Vaughan<sup>ab</sup>, Helen M. Poole<sup>a</sup>, Mark J. Forshaw<sup>a</sup>, Francis McGlone<sup>a</sup>, Michelle D. Failla<sup>c</sup>,

4 Carissa J. Cascio<sup>c</sup> & David J. Moore<sup>a\*</sup>

5 a: School of Natural Sciences and Psychology, Psychology Department, Liverpool John

6 Moores University., Liverpool, L3 3AF, United Kingdom

7 b: School of Social Sciences, Psychology Department, University of Chester, Chester, CH1

8 4BJ, United Kingdom

9 c: Vanderbilt University Medical Centre, Psychiatry, 2201 West End Ave, Nashville, TN

10 37235, USA.

11

12

13

14 \*Contact details:

15 Dr. David J. Moore,

16 Department of Natural Sciences and Psychology

17 Liverpool John Moores University,

18 Liverpool,

19 L3 3AF

20 United Kingdom

21 email: [D.J.Moore@ljmu.ac.uk](mailto:D.J.Moore@ljmu.ac.uk)

22 tel: +44 (0) 1519046328

23

24 Running Head: Pain in Psychiatric Conditions

25

26

27

28

29

**Abstract**

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

48

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

50

51

**Introduction**

52 Pain is a universal, multidimensional experience with sensory emotional, cognitive and  
53 social components (A. C. d. C. Williams & K. D. Craig, 2016). Understanding pain processing  
54 in psychiatric conditions could provide unique insight into the underlying pathophysiology or  
55 psychiatric disease, especially given the psychobiological overlap with pain processing  
56 pathways (Bird et al., 2010; de la Fuente-Sandoval, Favila, Gómez-Martin, Pellicer, & Graff-  
57 Guerrero, 2010; Fan, Chen, Chen, Decety, & Cheng, 2014; Goesling, Clauw, & Hassett, 2013;  
58 Iannetti & Mouraux, 2010). For example, there is substantial literature on pain perception in  
59 anxiety and depression (for review, see (Thompson, Correll, Gallop, Vancampfort, & Stubbs,  
60 2016) supporting a bidirectional relationship between these conditions and altered pain  
61 behaviours. From this literature, several examples have emerged that highlight the need to  
62 understand pain perception in psychiatric disorders. The co-occurrence of depression or  
63 anxiety and pain have an additive burden on the individual (Bair, Robinson, Katon, &  
64 Kroenke, 2003). Similarly, altered pain behaviours can lead individuals to look for somatic  
65 causes, potentially obscuring or delaying psychiatric diagnoses. There also seems to be  
66 important moderators between depression/anxiety and pain, specifically related to the  
67 exteroceptive or interoceptive nature of the stimuli and attentional resources allocated for  
68 painful stimuli, which provide insight into sensory processing in the disorder (Goesling et al.,  
69 2013; Thompson et al., 2016).

70 Studying pain in psychiatric conditions is likely to provide important insights, yet, there  
71 is a limited understanding beyond the work outside depression and anxiety. This is a missed  
72 opportunity to describe psychiatric conditions in terms of neurobiological alterations  
73 (Lautenbacher & Krieg, 1994). Indeed, a range of psychiatric conditions include core  
74 symptoms or associations with potentially pain-related behaviours, for example self-harm  
75 (Taylor, Hutton, & Wood, 2015). The absence of systematic study of pain responses in these  
76 conditions negates the possibility to understand the contribution of potential sensory changes to

77 these behaviours. Further, pain experience is critical in a number of aspects of environmental  
78 learning, allowing individuals to learn about dangers and threats and distinguish these from  
79 safety cues (Bastian, Jetten, Hornsey, & Leknes, 2014) as well as promoting social bonding  
80 with carers who provide pain relief (Krahé, Springer, Weinman, & Fotopoulou, 2013;  
81 Langford et al., 2010). Altered pain processing may therefore, underlie clinical features of a  
82 range of psychiatric conditions, especially those conditions which have associated threat-  
83 related or social features.

84         A first step in understanding how altered pain processing may contribute to these  
85 psychiatric conditions is to explore processing and responsivity to potentially nociceptive  
86 signals. There is an example of this altered pain responsivity in the diagnostic criteria for  
87 autism spectrum disorder, where the DSM includes “apparent indifference to pain/temperature”  
88 as an example of sensory reactivity (APA, 2013). Understanding whether pain behaviours are  
89 a cause, effect or epiphenomenon of a psychiatric condition would enable better diagnostic  
90 characterization. In the example of autism, more rigorous psychophysical investigation into  
91 these symptoms is likely to improve interventions that aim to reduce their occurrence or  
92 provide environmental adaptations to improve overall participation (Baranek, 2002).  
93 Additionally, while many psychiatric conditions co-occur with depression, first disentangling  
94 processing as a function of individual disorders is crucial to mechanistic-based understanding  
95 (Kendler, 2008; Savitz & Harrison, 2018; Vardeh, Mannion, & Woolf, 2016). As noted in  
96 depression, pain processing was moderated by exteroceptive/interoceptive nature of the stimuli  
97 (Thompson et al., 2016). Given the evidence of altered interoceptive processing in other  
98 psychiatric conditions (Quattrocki & Friston, 2014), understanding pain processing in this  
99 dimension may provide insight into bodily representation and emotional regulation in these  
100 disorders. In this way, understanding pain processing in psychiatric conditioning may also  
101 allow for more mechanism-based treatment.

102 *Aims of the review*

103 Characterization of pain processing may provide understanding into biological  
104 alterations related to psychiatric conditions, as well as, quality of life for these individuals.  
105 Importantly, Lautenbacher and Krieg (1994), published the only review in this area prior to the  
106 development of standardised protocols. Standardised protocols are essential in order to  
107 minimise variability (Backonja et al., 2013), produce reliable and comparable results, and  
108 improve clinical feasibility (Rolke et al., 2006). Recent attempts have been made to generate  
109 standardised psychophysical approaches to understand touch and pain sensitivity in the form of  
110 Quantitative Sensory Testing (QST) batteries i.e. Rolke et al. (2006). Hence, this review will  
111 include studies that have been conducted on psychiatric conditions with experimental pain,  
112 with particular reference to QST. It will also examine factors that have been shown to mediate  
113 the magnitude of pain response including clinical features of the conditions, medication status,  
114 or co-occurring symptoms. Indeed, the impact of clinical symptom management in altering  
115 pain precepts as well as the potential role for pain management strategies in altering clinical  
116 presentation is central in understanding health in these vulnerable groups.

117 This review includes quantification of peripheral afferents associated with pain  
118 processing as well as light touch; non-noxious stimuli like light touch, can sometimes be  
119 experienced as painful (IASP, 2012). This may be particularly relevant to psychiatric  
120 conditions where individuals have reported discomfort or pain to typically non-painful tactile  
121 inputs (Grandin, 1992, 1995). Responses such as these may mimic low-level allodynia,  
122 suggesting that a full assessment of the somatosensory system is necessary for a true  
123 comprehension of pain in psychiatric conditions.

## 124 **Methods**

### 125 **Search Methods**

126 An electronic search strategy was used, according to the Cochrane guidelines (Higgins  
127 & Green, 2011), through author consensus, in the following databases; Medline (1953-

128 Present), PsycINFO (1931-Present), PsycARTICLES (1955-Present), Science Direct (1966-  
129 Present) and Science Citation Index (1989-2014). To gain a list of potentially relevant  
130 publications, DSM-5 psychiatric condition terms were combined with “or”, terms related to  
131 pain/somatosensation and QST were also combined with “or”, and then the two groups of key  
132 words were combined using “and” (Table 1). Subsequently, reference lists from retrieved  
133 papers were scanned for further relevant publications and authors of poster abstracts were  
134 contacted for further information or full text articles.

135 [Table 1 here]

## 136 **Eligibility**

### 137 **Types of Studies**

138 Studies were eligible for inclusion if they 1) were explicitly experimental, 2) utilised  
139 psychophysically appropriate pain or touch sensitivity assessment and 3) included both a  
140 clinical and control group, or adequately compared clinical data values to published norms.

141 Studies were excluded if 1) there was poor quality control of stimuli (i.e. intensity of  
142 stimuli was variable or clear order effects might be present etc.) 2) they utilised poor or non-  
143 comparable pain induction tests, 3) they did not contain a control group or refer to published  
144 norms or 4) were animal studies on pain induction.

145 No publication date restrictions or publication status restrictions were imposed and only  
146 studies published in English were considered. No restrictions were put onto the participants  
147 within studies, other than it was imperative that they were human samples and had a diagnosis  
148 of a condition previously categorized as Axis I or Axis II (APA, 1994). Conditions that have a  
149 neurological or developmental origin i.e. not acquired or environmental, have significant public  
150 health implications, and have not appeared in multiple comprehensive reviews (i.e. anxiety and  
151 depression) were chosen. They included; autism spectrum disorder (ASD), obsessive

152 compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), schizophrenia,  
153 eating disorders (inclusive of anorexia nervosa, bulimia nervosa and binge-eating disorder) and  
154 personality disorder (Borderline personality disorder: BPD/PD).

## 155 **Study Selection and Data Collection**

### 156 **Study Selection**

157 Sourced citations were transferred to Endnote. Eligibility assessment was first  
158 performed on article titles in an un-blinded standardised manner by 2 reviewers (SV and DM).  
159 The first reviewer (SV) checked all titles for relevance, with second reviewer (DM) auditing  
160 10% of the total, with a 97% agreement rate. For those studies where authors disagreed, a third  
161 reviewer (HP) acted as a blinded arbitrator.

162 Eligible abstracts were then assessed for inclusion, under the same process by the first  
163 reviewer (SV). In this instance 10% of the abstracts were divided across three blinded authors  
164 (HP, FMcG, MF) with a fourth (DM) acting as a blinded arbitrator, with 100% agreement rate.  
165 Roles were allocated to ensure that the arbitrator was different for both phases.

### 166 **Data Collection**

167 Information extracted from each study included; 1) Participant characteristics  
168 (including age, gender, condition, diagnosis method, numbers in each group, matching criteria  
169 and psychometric measures), 2) Pain or touch method (including location and test parameters)  
170 and 3) Main data (including all inferential statistics, any subgroup analysis and mean values),  
171 placed into specifically designed extraction tables. Summary sheets were generated to  
172 compare information across conditions.

## 173 **Results**

174 [Figure 1]

### 175 **Results of the search**

176 A final search conducted on 04/02/18, which yielded 2167 potentially relevant records.  
177 The majority of studies have been conducted in the last decade, highlighting the growing  
178 interest of pain across these conditions. Figure 1 flow chart details the records found at each  
179 stage of the screening process. Study characteristics and data will be presented for each  
180 condition in the following sections. Meta-analysis was not possible due to the variability in the  
181 methods utilised and the lack of reported confidence intervals and effect sizes.

## 182 **Autism Spectrum Disorder**

### 183 **Included studies.**

184 Ten studies were included for ASD. These studies included pain responses to thermal,  
185 mechanical, pressure, vibratory and electrical stimuli; therefore, a number of somatosensory  
186 measures were missing. Given the range of available measures, research examining  
187 somatosensory and pain thresholds in ASD is presently limited.

### 188 **Participant characteristics.**

189 Although studies have been conducted using children (n=2) and adolescents (n=2)  
190 samples, the majority (n= 6) were conducted on adults. This bias is understandable given the  
191 nature of the tests administered, which require very precise reports from participants; they may  
192 also be distressing to younger children. Male participants were generally the majority in the  
193 experimental group, and two studies had an all-male sample. This distribution is in line with a  
194 three-time greater prevalence of ASD in males (Baxter et al., 2015).

### 195 **Sensation thresholds.**

196 Six studies examined somatosensory detection thresholds. Three studies examined  
197 thermal detection thresholds, two in adults (Cascio et al., 2008; Fründt et al., 2017) and another  
198 in adolescents (Duerden et al., 2015). All studies adopted a method-of-limits to determine



199 thresholds, with Cascio et al. (2008) and Fründt et al. (2017) having a change rate of 1°C/s and  
200 Duerden et al. (2015) using 0.5°C/s. Results are inconsistent. Cascio et al. (2008) and Fründt  
201 et al. (2017) reported no significant differences, while hyposensitivity was reported by Duerden  
202 et al. (2015). Furthermore, Duerden et al. (2015) report a significant correlation between  
203 autism severity (as measured by ADOS-G scores) and thermal detection thresholds,  
204 specifically to both the social and communication subscales, demonstrating that adolescents  
205 with greater autism severity and lower IQ had higher detection thresholds. However, it is of  
206 note that those studies, which utilised the DFNS standardised battery, report no-significant  
207 differences.

208 Four studies examined vibratory detection thresholds in adults (Blakemore et al., 2006;  
209 Cascio et al., 2008; Fründt et al., 2017) and children (Guclu, Tanidir, Mukaddes, & Unal,  
210 2007). Blakemore et al. (2006) presented two frequencies of vibrotactile stimuli; 200Hz  
211 (stimulating rapidly adapting fibres) and 30Hz (stimulating slowly adapting fibres), in a  
212 method-of-limits. Whereas, Cascio et al. (2008) used a forced-choice paradigm at 33Hz;  
213 participants were asked to indicate in which of two time intervals a stimulus was presented.  
214 Guclu et al. (2007) used sinusoidal displacements at 40 and 250Hz, in a forward-masking  
215 paradigm; a 250Hz stimulus was applied prior to the test stimulus and Fründt et al. (2017) used  
216 the DFNS standardised protocol. Overall results indicate hyper-responsiveness to vibratory  
217 stimuli in adults with ASD, as lower vibrotactile thresholds were achieved (Blakemore et al.,  
218 2006; Cascio et al., 2008). Furthermore, these findings appear to be sensitive to both location  
219 (as differences were reported for the forearm but not the palm (Cascio et al., 2008), and the  
220 frequency at which the stimulus is presented (Blakemore et al., 2006). However, Guclu et al.  
221 (2007) and Fründt et al. (2017) report no significant difference between the vibrotactile  
222 thresholds, and the children with autism had the same detection and masking mechanisms as  
223 the neurotypical children.

224 Finally, Cascio et al. (2008) and Fründt et al. (2017) also examined punctate  
225 mechanical detection thresholds using von Frey hairs. Cascio et al. (2008) reported no  
226 significant group differences, suggesting typical static mechanical functioning in ASD. Whilst  
227 Fründt et al. (2017) reported a greater loss of function for MDT. Their methodologies differed  
228 slightly with the latter using the DFNS standardised protocol and the other utilising a two  
229 ascending and two descending block of trials methodology.

230 Overall, the findings for somatosensory detection thresholds for individuals with ASD  
231 are inconsistent. There are some signs of hyposensitivity in thermal sensations (Duerden et al.,  
232 2015), however, these findings are not reliable with no significant group differences reported  
233 by (Cascio et al., 2008) - these findings are duplicated for mechanical detection. Individuals  
234 with ASD may be hypersensitive to vibrotactile stimuli, though this may be frequency- and/or  
235 location-specific. A wider range of techniques than is presently used could confirm whether  
236 hyposensitivity for one modality may be present at the same time as hypersensitivity for  
237 another, i.e. thermal and mechanical. Additionally, it is not possible to consider somatosensory  
238 detection across the developmental course of ASD as studies in children and adolescents are  
239 limited.

#### 240 **Pain.**

241 Seven studies examined pain thresholds in ASD. Cascio et al. (2008); Duerden et al.  
242 (2015); Fründt et al. (2017) used a method-of-limits to determine thermal pain threshold.  
243 While Duerden et al. and Fründt et al. (2017) reported no group differences, Cascio et al.  
244 (2008) reported hypersensitivity for both heat and cold pain thresholds in the ASD group  
245 compared to healthy controls. Contrary to previous reports that individuals with ASD are  
246 insensitive to pain (Militeri et al., 2000; Minshew & Hobson, 2008), these studies provide  
247 tentative indications that there is typical nociception processing.

248 Four studies investigated pressure pain thresholds; Fan et al. (2014) and Fründt et al.  
249 (2017) in adults, Chen et al. (2017) in adolescents and Riquelme, Hatem, and Montoya (2016)  
250 in children. Ramp rates are reported as  $1\text{kg}/\text{cm}^2\text{ s}$  or  $50\text{ kPa}/\text{cm}^2$  ( $\sim 0.5\text{kg}/\text{cm}^2\text{ s}$ ), or not at all,  
251 and probe sizes are either a non-standard probe size of  $1.52\text{cm}^2$  or the standard  $1\text{cm}^2$ . Non-  
252 standardized probe sizes potentially affects comparison with the general pain research literature  
253 and within study, comparison is difficult to make for similar reasons. With the exception of  
254 Fründt et al. (2017) individuals with ASD are reported to have lower pressure pain thresholds  
255 compared to neurotypical controls (Chen et al., 2017; Fan et al., 2014; Riquelme et al., 2016).  
256 Although, decisive conclusions are problematical due to incomplete methodologies, or the  
257 differing stimuli presentations mentioned, as well as different age groups.

258 Lastly, two studies examined electrocutaneous pain thresholds. Bird et al. (2010) using  
259 square pulse waveform at 100Hz, with a 4ms pulse length and a 1s duration and report no  
260 significant group differences. Whilst Gu et al. (2017) report significantly lower stimulation  
261 levels in the ASD group, using a method-of-levels.

262 Results are inconsistent and reaching conclusions is difficult. The aforementioned  
263 studies do provide tentative insight into the possibility that the sensory abnormalities  
264 mentioned by the DSM can be quantified, but more investigation is required. From the 10  
265 studies, of note is Fründt et al. (2017), who not only utilise the full DFNS QST battery, but also  
266 standardise their scores which extends results from simple group comparisons to clinically  
267 significant sensory losses or gains.

268 [Table 2 here]

## 269 **Attention Deficit Hyperactivity Disorder**

### 270 **Included Studies & Participant Characteristics.**

271           Only one study was identified for ADHD, which selectively covers cold pressor pain  
272 but not sensation (Treister, Eisenberg, Demeter, & Pud, 2015) . Thirty adults with ADHD,  
273 who were prescribed Ritalin and 30 healthy age- and gender-matched controls, took part. The  
274 use of adults is understandable given the nature of the tests administered, which require very  
275 precise reports from participants. However, given that ADHD is most prominent in childhood,  
276 and that adult ADHD has a different phenotype (Mannuzza, Klein, Bessler, Malloy, &  
277 LaPadula, 1993), a study on children is warranted in order to expand insight into pain  
278 processing in this disorder.

279           **Pain.**

280           A cold pressor water bath was set at 1°C, participants submerged their right hand,  
281 providing both threshold (time at which the cold stimulus began to elicit pain) and tolerance  
282 (latency to spontaneous hand removal) over two sessions. Participants were randomised to  
283 complete the task once following administration of Ritalin and once following no medication.  
284 Individuals who had not been administered Ritalin expressed shorter latencies to cold pain,  
285 providing psychophysical evidence of hypersensitivity compared with healthy controls.  
286 Although, both threshold and tolerance were significantly shorter in ADHD participants, no  
287 significant differences were reported for self-reported pain intensities –the intensity of the pain  
288 was similarly felt across the groups regardless of a physiological hypersensitive response.

289           **Schizophrenia**

290           **Included studies.**

291           Eleven studies were included for schizophrenia. Outcomes from these studies were  
292 limited to thermal, pressure and electrical stimuli, thus research examining somatosensory  
293 thresholds in schizophrenia is limited, with pain thresholds receiving more attention.

294           **Participant characteristics.**

295 All studies were conducted with adults and sample ages suggest that somatosensory  
296 assessment has been conducted across the time course of the condition covering early  
297 adulthood, which is a peak for the onset of schizophrenia (Sham, MacLean, & Kendler, 1994).  
298 A previous diagnosis of schizophrenia was accepted and studies did no further testing.

299 **Sensation thresholds.**

300 One study examined somatosensory thresholds, specifically warm detection thresholds  
301 (Jochum et al., 2006) using a method of limits paradigm and a change rate of 0.5°C/s. Patients  
302 with schizophrenia demonstrated hyposensitivity, with significantly higher warmth thresholds  
303 compared to healthy controls.

304 **Pain.**

305 Thermal pain thresholds were examined in six studies. Jochum et al. (2006) and  
306 Boettger, Grossmann, and Bar (2013) obtained warm and cold pain thresholds using a method-  
307 of-limits paradigm, however Boettger et al. (2013) used a temperature change rate of 0.5°C/s.  
308 Higher temperatures were required to achieve a heat (Boettger et al., 2013; Jochum et al.,  
309 2006) and lower to obtain cold (Boettger et al., 2013) pain threshold in patients with  
310 schizophrenia compared to controls.

311 Four studies obtained heat pain thresholds using other methods. Three studies asked  
312 participants to tolerate heat for a duration of 30s (de la Fuente-Sandoval, Favila, Gómez-  
313 Martín, León-Ortiz, & Graff-Guerrero, 2012; de la Fuente-Sandoval et al., 2010) and 120s  
314 (Potvin et al., 2008). The last, Dworkin et al. (1993) obtained thermal pain discrimination  
315 using a signal detection method; 48 stimuli were presented of four different intensities (35.5,  
316 38.5, 46.4 and 48.5°C) and participants verbally rated these as “no-sensation”, “warm”, “hot”  
317 or “painful”. Higher temperatures were required to achieve a heat pain threshold in patients  
318 with schizophrenia compared to controls (de la Fuente-Sandoval et al., 2010). Furthermore,

319 individuals with schizophrenia were shown to be poorer at thermal pain sensory discrimination  
320 and showed no response-bias differences to their matched healthy controls. A significant  
321 correlation was reported for warm-hot stimuli and positive symptoms/affective flattening,  
322 indicating that higher criteria for reporting painfulness were associated with fewer positive  
323 symptoms (Dworkin et al., 1993). Two studies reported non-significant group differences (de  
324 la Fuente-Sandoval et al., 2012; Potvin et al., 2008). These differing results may be the  
325 product of differing methodologies. For example, a shift in response criterion might lead to a  
326 higher intensity required to generate a pain threshold. However, Dworkin et al. (1993)  
327 reported no shift in this criterion. Another explanation is that individuals with schizophrenia  
328 have a higher threshold for thermal pain but a lower endurance, which results in similar pain  
329 tolerance; this would be consistent with a central pain processing explanation for differences  
330 with a change in central sensitization (Kleinböhl et al., 1999). That is to say, that the  
331 magnitude of peripheral input required to induce a pain response (i.e. threshold) might be the  
332 same, but the process of temporal or spatial summation may be magnified. This suggests that,  
333 once pain is perceived, the magnitude of this experience grows to a point of being intolerable  
334 more quickly.

335 . However, there is tentative evidence that, for laboratory-induced thermal stimuli, individuals  
336 may have hyposensitivity towards noxious thermal stimuli. Furthermore, these effects might  
337 relate to threat perception. Tolerance is fundamentally a withdrawal response from a noxious  
338 cue and previous research in the visual domain has suggested that individuals with  
339 schizophrenia withdraw from visually threatening stimuli (Phillips, Senior, & David, 2000).  
340 Potentially the point at which the decision that threat is intolerable may be reduced due to this  
341 symptomology.

342 Two further studies utilised the cold pressor task to investigate thermal pain, with  
343 differing water temperatures. Atik, Konuk, Akay, Ozturk, and Erdogan (2007) used 1°C water  
344 and Potvin et al. (2008) reported water temperature range from 7 to 12°C, with participants

345 rating the pain every 30 seconds, rather than a threshold and tolerance measure. Atik et al.  
346 (2007) report patients to have higher pain tolerance than healthy controls, but pain threshold  
347 did not differ. Furthermore, Potvin et al. report no significant differences between patients and  
348 healthy controls in pain ratings.

349 Three studies investigated electrical pain stimulation. Methods differed across studies,  
350 with Lévesque et al. (2012) applying a TENS square wave pulse. Guieu, Samuélian, and  
351 Coulouvrat (1994) applied five shocks for a 13ms duration, with each train including  
352 increasing and decreasing stimulus intensities at a frequency of 0.16Hz. Kudoh, Ishihara, and  
353 Matsuki (2000) applied transcutaneous pulses at 2000Hz, 250Hz and 5Hz obtaining self-report  
354 pain intensity in response to each stimulus. Levesque et al. report significant group  
355 differences, in which individuals with schizophrenia showed hypersensitivity to electrical  
356 stimuli compared with healthy controls. Additionally, pain thresholds were negatively  
357 correlated to positive symptoms. Kudoh et al. contradict these findings, showing increased  
358 conduction thresholds for individuals with schizophrenia and lower VAS pain rating scores,  
359 suggesting hyposensitivity. Guieu et al. show no significant group differences. Results are  
360 conflicting and the methods employed by each of these studies are contradictory, making it  
361 difficult to identify the validity of each of the findings; or how they might reflect differences in  
362 populations.

363 Lastly, one study investigated pressure pain using an algometer with a 1cm<sup>2</sup> pressure  
364 tip, applied in a static test of 160kPa and then in a method-of-limits (Girard, Plansont,  
365 Bonnabau, & Malauzat, 2011). Pain started significantly earlier for individuals with  
366 schizophrenia, requiring less pressure to achieve a pain rating, suggesting hypersensitivity.

367 A greater range of techniques was employed here, reflected by the age of the studies  
368 included, with many being conducted before guidance on pain research or relevant equipment  
369 had been developed. Results from thermal pain trend toward hyposensitivity, which is

370 tentatively supported by those from thermal sensation. These results are not mirrored in  
371 pressure stimuli, where hypersensitivity is reported, nor in electrocutaneous where results are  
372 inconclusive. There is evidence, as presented above, for different effects in different  
373 modalities, which a wider range of techniques may help, clarify (see Table 3 for detailed  
374 results of each study). Adopting a standardised approach will allow for the replicability of  
375 studies and better result comparisons across studies.

376 [Table 3 here]

### 377 **Personality Disorder**

#### 378 **Included studies.**

379 Ten studies were included all of which focussed on BPD, one of the most common  
380 forms of personality disorder with a weighted prevalence rate of 0.7% of the general  
381 population (Coid, Yang, Tyrer, Roberts, & Ullrich, 2006). Outcomes from these studies were  
382 limited to thermal, mechanical, pressure, electrical stimuli, as well as two-point discrimination.  
383 Thus, with the range of available measures and types of personality disorder, research  
384 examining somatosensory and pain thresholds is presently limited.

#### 385 **Participant characteristics.**

386 One study was conducted using a sample of adolescents, however the majority of  
387 studies were conducted with those in early adulthood (n= 10), which suggests that  
388 somatosensory assessment has been conducted in line with the pattern of onset. Some studies  
389 split the experimental group by personality disorder traits, such as self-injurious behaviour  
390 (Ludäscher et al., 2009) comparing BPD with and without self-injurious behaviour (SIB), and  
391 psychopathic to non-psychopathic prisoners (Fedora & Reddon, 1993).

#### 392 **Sensation thresholds.**



393 Four studies were identified which examined somatosensory thresholds. Ludäscher et  
394 al. (2009) considered thermal sensory thresholds in adults with BPD with and without SIB and  
395 Ludäscher et al. (2014) examined these effects in adolescents. Both studies used a method-of-  
396 limits with a 1<sup>0</sup>C/s change rate. Results from these studies show no significant group  
397 differences. A further experiment conducted by Ludäscher et al. (2009) utilised Infra-red  
398 thulium-YAG-laser. Individuals with SIB require a greater energy intensity for detection  
399 compared to BPD without SIB and healthy controls, although both BPD groups had higher  
400 thresholds than healthy controls. This suggests that SIB may have a role to play in  
401 somatosensation, independent of BPD.

402 One study examined two-point discriminability using a forced-choice paradigm  
403 (Pavony & Lenzenweger, 2014). During the task, a two-point (6mm experimental stimuli or  
404 10mm control stimuli) or one-point (intended for the detection of false alarms) stimulus was  
405 presented. Participants were then asked to indicate how many points were felt with no  
406 significant differences reported between BPD and control participants.

407 Overall results for somatosensory detection thresholds suggest normal functioning in  
408 BPD, with the exception of laser radiant heat stimuli where individuals may have  
409 hyposensitivity (Ludäscher et al., 2009). However, this effect may be specific to individuals  
410 who practice self-injury, and therefore be, at least, partially attributable to the complexity of  
411 the behaviours involved. These findings were not replicated under an alternative method of  
412 producing thermal stimuli within the same study, nor in adolescents (Ludäscher et al., 2014).  
413 Furthermore, results suggest normal tactile discrimination.

#### 414 **Pain.**

415 Ten studies examined pain thresholds in BPD. Thermal pain thresholds were examined  
416 in five studies (Ludäscher et al., 2009; Ludäscher et al., 2014; Schmahl et al., 2006; Schmahl et  
417 al., 2004; Schmahl et al., 2010). Ludäscher et al. (2009) used a method of limits with

418 1<sup>0</sup>C/second change rate, Schmahl et al. (2010) and Ludäscher et al. (2014) used a 1.5°C/s  
419 change rate, with Schmahl et al. (2006) using 2°C/s. Compared to healthy controls, individuals  
420 with BPD required higher temperatures for heat (Ludäscher et al., 2009) and lower  
421 temperatures for a cold pain threshold (Ludäscher et al., 2009; Schmahl et al., 2010),  
422 suggesting hyposensitivity. This was additionally supported by results from the Laser Radiant  
423 Thermal Stimuli Test (parameters previously discussed (Ludäscher et al., 2009; Schmahl et al.,  
424 2004). More specifically, Ludäscher et al. (2009) showed that individuals engaging in SIB had  
425 the highest thresholds, supporting the role of this behaviour in attenuating sensory deficits .  
426 Additionally, SIB symptom severity was negatively correlated with pain ratings, showing that  
427 individuals who have high symptomology rate the stimulus intensity as lower. Ludäscher et al.  
428 (2014) provide further support to these findings, reporting similar hyposensitivity in  
429 adolescents with BPD. Schmahl et al. (2006) also report hyposensitivity in a group of BPD  
430 adults with SIB using their tonic heat methodology. These converging results suggest that for  
431 laboratory-induced thermal stimuli, individuals with BPD may experience hyposensitivity to  
432 noxious thermal stimuli, specifically when engaging in self-injurious behaviour.

433 Three further studies investigated thermal pain through use of a cold pressor (Bohus et  
434 al., 2000; McCown, Galina, Johnson, DeSimone, & Posa, 1993; Pavony & Lenzenweger,  
435 2014). Water temperatures were different across studies; one used 1°C water (Pavony &  
436 Lenzenweger, 2014), with Bohus et al. (2000) using 10°C and McCown et al. (1993) stating an  
437 approximate temperature of 0°C. Procedural methodologies also differed between these  
438 studies. Bohus et al. (2000) asked participants to have their hand submerged for 4 minutes and  
439 to rate the pain intensity every 15 seconds, whereas McCown et al. (1993) and Pavony and  
440 Lenzenweger (2014) obtained threshold, tolerance and endurance. McCown et al. (1993)  
441 reported no significant group differences on baseline tolerance levels, however, Pavony and  
442 Lenzenweger (2014) report that individuals with BPD show significant higher tolerance and  
443 endurance levels, compared with healthy controls. Bohus et al. (2000) reported lower intensity

444 and unpleasantness ratings by individuals with BPD compared to healthy controls.  
445 Specifically, those individuals self-reported as under distress of SIB had the lowest pain  
446 ratings, followed by individuals who felt calmer. This suggests that those individuals who self-  
447 injure perceive pain as less severe or may experience hyposensitivity.

448         One study investigated mechanical pain thresholds using punctate probes (Magerl,  
449 Burkart, Fernandez, Schmidt, & Treede, 2012). BPD threshold estimations are reported as  
450 significantly higher compared to healthy controls. The recency of SIB and pinprick threshold  
451 were significantly correlated. Analysis of the suprathreshold pain measures also revealed  
452 similar self-injurious behaviour-dependent losses of pain sensitivity, occurring in all pain  
453 measures. Overall, patients in the frequent SIB subgroup were significantly less-pain sensitive  
454 than healthy controls and less sensitive than BPD individuals who rarely engaged in SIB,  
455 suggesting hyposensitivity.

456         Two studies reported electrocutaneous thresholds; both utilised constant current  
457 stimulation although methods differed. Fedora and Reddon (1993) applied an ascending series  
458 of stimulation using a Tursky concentric electrode to prisoners. Ludäscher et al. (2007) applied  
459 a continuous stimulation of a pulse with a frequency of 10Hz and 0.5ms duration to the right  
460 index finger, with a 2 ring electrode, to individuals with BPD and healthy controls. Both  
461 studies report significant group differences, in which both prisoners and individuals with BPD  
462 have higher pain thresholds than healthy controls. Additionally, Fedora and Reddon (1993)  
463 show a negative correlation between pain thresholds and the degree of monotony avoidance,  
464 with highest thresholds found in those who are the lowest thrill seekers. In contrast, Ludäscher  
465 et al. (2007) report a positive correlation between pain thresholds and both state and trait  
466 dissociation, as well as aversive arousal; the more avoidant an individual with BPD is, the  
467 higher their pain thresholds. This has important connections with SIB and reinforces the  
468 relationship previously discussed.

469 As can be seen from Table 4 results across both sensation and pain tend towards  
470 hyposensitivity in individuals with BPD. This conclusion is limited due to the varied  
471 methodologies used. Adopting standardised techniques in future studies will allow for the  
472 replicability of studies and better result comparisons, which is the factor vitiating any  
473 statistically significant conclusions. Another important consideration is the characterisation of  
474 stress levels during sensation and pain testing. Evidence suggests that pain sensitivity is  
475 altered by mood induction in BPD (Ludäscher et al., 2007).

476 [Table 4 here]

## 477 **Eating Disorders**

### 478 **Included studies.**

479 Fourteen studies were included for Eating Disorders. Outcomes from these studies  
480 were limited to thermal, mechanical, pressure, vibratory stimuli and two-point discrimination.  
481 Thus, with the range of available measures, research examining somatosensory and pain  
482 thresholds in eating disorders is presently limited, although it is one of the conditions that has  
483 received greater interest.

### 484 **Participant characteristics.**

485 Eating disorders include anorexia nervosa, bulimia nervosa, restrictive anorexia and  
486 binge-purge anorexia (APA, 2013). Twelve studies used an adult sample, with only one study  
487 specifically employing adolescents. Eleven of the 14 studies had an all-female participant  
488 sample. This is in line with increased prevalence in females, or the underreporting of males  
489 with eating disorders (Hackler, Vogel, & Wade, 2010). One study reported the use of both  
490 male and female sample (Bär, Berger, Schwier, Wutzler, & Beissner, 2013).

### 491 **Sensation thresholds.**

492 Two studies examined tactile sensitivity (Faris et al., 1992; Keizer, Smeets, Dijkerman,  
493 van Elburg, & Postma, 2012) via mechanical detection, with the addition of sensory  
494 discrimination to one study. Tactile acuity and size estimation were tested using two-point  
495 discrimination. For tactile acuity, the trial consisted of either one-point (33% of the trials) or  
496 two-point stimuli (66%). Blindfolded participants indicated whether they perceived one single  
497 stimulus or two distinct stimuli. Responses were recorded with a forced-choice one-up two-  
498 down staircase method, with starting distances of 43 and 33mm, for the right underarm and  
499 abdomen, respectively. Participants then estimated the distance of the two points on a  
500 touchpad computer. In a second phase, mechanical detection was measured using calibrated  
501 von Frey hairs, a method mirrored by Faris et al. (1992). Patients with anorexia nervosa had a  
502 higher two-point discrimination threshold, regardless of body site tested, and compared with  
503 healthy controls. Furthermore, distance estimation was larger in this group for both sites; this  
504 effect was largest for the abdomen (Keizer et al., 2012). Rather than a purely sensory effect,  
505 the cognitive processing of somatosensory input may in fact be altered in individuals with  
506 eating disorders, in line with the expression of their condition. A lower threshold for  
507 mechanical detection on the abdomen is reported, but no significant group differences were  
508 found for the arm (Keizer et al., 2012), or the hand (Faris et al., 1992).

509 A third study examined thermal and vibration thresholds (Pauls, Lautenbacher, Strian,  
510 Pirke, & Krieg, 1991) using a method-of-limits. No significant group differences were  
511 reported for patients with anorexia nervosa or bulimia nervosa compared to healthy controls.

512 Overall, the findings for somatosensory detection thresholds are inconsistent. When  
513 considering tactile acuity and mechanical detection individuals with eating disorders were  
514 shown to display both hypo- and hyper-sensitivity, which may be stimulus specific.  
515 Furthermore, there is potential evidence of a psychogenic effect on somatosensation, with the  
516 largest effect reported for the abdomen, an area of cognitive focus for those suffering from an

517 eating disorder. It is not possible to consider somatosensory detection in its entirety, as studies  
518 are limited, impeding comparisons.

519 **Pain.**

520 Thirteen studies examined pain thresholds in eating disorders. Thermal pain thresholds  
521 were examined in eleven of these. Seven studies measured heat pain in a method-of-limits,  
522 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.,  
523 2006; Krieg, Roscher, Strian, Pirke, & Lautenbacher, 1993; Lautenbacher, Pauls, Strian, Pirke,  
524 & Krieg, 1990, 1991; Pauls et al., 1991; Schmahl et al., 2010). Significant increased heat pain  
525 thresholds were observed in eating disorders compared to healthy controls (Bär et al., 2013;  
526 Bär et al., 2006; Lautenbacher et al., 1990, 1991; Pauls et al., 1991). These results were shown  
527 to decrease after weight had been regained (Bär et al., 2006) for both tonic and phasic thermal  
528 stimuli (Lautenbacher et al., 1990). However, Krieg et al. (1993) and Schmahl et al. (2010)  
529 reported no significant group differences. This may be due to the use of recovering anorexics  
530 and may provide tentative support to Bär et al. (2006) in which individuals who had gained  
531 weight and therefore assumed to be in a phase of recovery, showed that threshold levels  
532 decreased. Results from these studies suggest individuals, when in an acute phase, are likely to  
533 experience hyposensitivity.

534 The last four studies that examined heat pain thresholds used radiant heat stimuli,  
535 specifically laser (de Zwaan, Biener, Bach, Wiesnagrotzki, & Stacher, 1996; de Zwaan, Biener,  
536 Schneider, & Stacher, 1996) and thermal latency with a constant stimulus (Papezova,  
537 Yamamotova, & Uher, 2005; Yamamotova, Papezova, & Uher, 2009). Patients with eating  
538 disorders had higher threshold for thermal pain (de Zwaan, Biener, Bach, et al., 1996; de  
539 Zwaan, Biener, Schneider, et al., 1996) compared with healthy controls. Thermal pain  
540 threshold latencies were longer (Yamamotova et al., 2009) in bulimia nervosa than healthy  
541 controls. As well as a general group of individuals with eating disorders (patients with eating

542 disorders; restrictive anorexia, binge-purge anorexia and bulimia nervosa), specifically those  
543 with binge purging symptomatology (Papezova et al., 2005). Providing further evidence of  
544 hyposensitivity in respect of noxious thermal stimuli that may be symptomology related.

545 Five studies investigated pressure pain thresholds (de Zwaan, Biener, Bach, et al., 1996;  
546 de Zwaan, Biener, Schneider, et al., 1996; Faris et al., 1992; Raymond et al., 1995; Raymond et  
547 al., 1999) using a method-of-limits. Individuals with eating disorders, including anorexia, had  
548 higher pressure-pain (de Zwaan, Biener, Bach, et al., 1996; de Zwaan, Biener, Schneider, et al.,  
549 1996; Faris et al., 1992) and detection thresholds (Raymond et al., 1995) compared to healthy  
550 controls. Though no significant difference at suprathreshold tolerance (Raymond et al., 1999).  
551 This may be due to pressure pain threshold being entered as a covariate. There is tentative  
552 evidence for hyposensitivity towards laboratory-induced pressure pain.

553 Results for thermal pain, tactile stimuli, pressure detection and pain suggest that  
554 individuals with eating disorders experience hyposensitivity, which may be specific to acute  
555 phases (see Table 5 for detailed results of each study). However, conclusions are difficult to  
556 make in regards to this. The aforementioned studies do provide tentative insight into the  
557 possibility that the sensory abnormalities can be quantified, but more investigation is required,  
558 specifically as there is a focus on thermal stimuli.

559 [Table 5 here]

## 560 **Discussion**

561 The purpose of this review was to provide an overview of research that investigated  
562 pain processing in a number of psychiatric conditions where this has not been a focus  
563 previously. The most notable global observation is the lack of utilisation of detailed testing  
564 procedures and particularly standardised protocols such as those published by Rolke et al.  
565 (2006). Even when these have been used, small variability in the methods, such as temperature

566 ramp rate, still compromise the ability to compare results and draw definitive conclusions.  
567 Thermal test procedures remain the most widely used form of sensory testing and mechanical  
568 testing remains, for the most part, unused, including; mechanical detection threshold,  
569 mechanical pain sensation, dynamic mechanical allodynia and wind-up ratio. This may be due  
570 to how user-friendly, safe and easily applicable thermal testing is. Furthermore, the absence of  
571 research examining wind-up ratio reduces the possibility of gaining insight into whether there  
572 is a central processing component. Specifically, central sensitization manifests as dynamic  
573 tactile allodynia, secondary punctate or pressure hyperalgesia, and enhanced temporal  
574 summation rather than thermal cutaneous pain, with most clinical pain states involving these  
575 aspects (Woolf, 2011). Therefore, to exclude these from a battery of tests is to exclude the  
576 possibility of understanding alterations in peripheral and central mechanisms that can  
577 contribute to the development and maintenance of pathological states.

578         Additionally, only one paper (Fründt et al., 2017) in the 46 eligible papers, utilised the  
579 DFNS QST battery (Rolke et al., 2006). Utilizing comprehensive psychophysical procedures  
580 across a range of modalities would allow for better across-study comparisons. It would also  
581 allow the development of sensitive indices whilst providing consistency in the approach to  
582 understanding these phenomena across conditions. The DFNS battery in particular provides  
583 this opportunity and is a valuable starting point, as it provides the potential for systematically  
584 comparing the function of small and large sensory afferents, quantification of the full sensory  
585 axis and comparison to known normative values. Although, it must be noted that this  
586 particular battery has been developed through considerable research to identify the most  
587 sensitive indices for neuropathic pain. Without such rigour it is not possible to fully appreciate  
588 the extent of any abnormality, specifically whether it may be systemic or modality specific.

589         Although such a definitive understanding is still not available, results of the reviewed  
590 studies indicate that pain processing may be altered in certain psychiatric groups. When  
591 considering the overarching question of whether changes in pain processing are present in



592 psychiatric conditions, it would appear that for individuals with schizophrenia, BPD and eating  
593 disorders, there is moderate evidence for hyposensitivity to pain and touch. A single study on  
594 ADHD (Treister et al., 2015) suggests that individuals may have a hypersensitivity to pain,  
595 however given the lack of further data, this needs to be considered very carefully. Lastly, for  
596 individuals with ASD the findings are inconsistent, with the possible exception of a  
597 hypersensitivity to vibrotactile stimuli. Furthermore, findings from each of these conditions  
598 suggest that these effects may be more complex, specifically, that effects are specific to a  
599 single site, stimulus intensity or are reliant on some other behaviour.

600 In the case of ASD, the psychophysical methods used to investigate pain sensations  
601 reveal no systematic evidence for hypo- or hyper-sensitivity in this population, and run  
602 contrary to current diagnostic criteria (APA, 2013), as well as clinical and parent reports that  
603 suggest a pain experience to stimuli (Militeri et al., 2000; Moore, 2014; Wing, 1976). While  
604 this may be in large part due to lack of investigation, it highlights the need for systematic  
605 protocols. The most reliable results stem from those studies which have utilised the standard  
606 QST protocol, specifically those by Fründt et al. (2017). This study not only utilised the  
607 methodology it standardised scores based on the published normative values, which means that  
608 a clinically significant hypo- or hyper-sensitivity can be determined. This is not to discount the  
609 other papers who utilised psychophysically robust methods of testing; Cascio et al. (2008);  
610 Duerden et al. (2015); and Fan et al. (2014), however, the utilisation of standard group  
611 comparisons may not be enough to determine true alterations. It is, therefore, clear that more  
612 research is required to understand further the nature of any differences and to reconcile the  
613 differences between *objective* measures and *observations* of behaviour.

614 The hyposensitivity reported in each of the other conditions appears to have different  
615 potential explanations. In eating disorders, changes in both tactile acuity and pressure  
616 detection thresholds appear more pronounced when examined on the abdomen (Keizer et al.,  
617 2012). Specifically, individuals had larger distance estimations and poorer tactile perception,

618 as measured by two-point discrimination, as well as a sensitivity to pressure detection. Both  
619 these tests potentially indicate a cognitive deficit rather than sensitivity, however, those studies  
620 reporting thermal hyposensitivity (Bär et al., 2013; de Zwaan, Biener, Schneider, et al., 1996;  
621 Lautenbacher et al., 1990, 1991; Papezova et al., 2005; Yamamoto et al., 2009), at least for  
622 this modality, suggest a true physiological deficit. Since recovering anorexic patients showed  
623 thresholds returning to healthy control level during weight gain, altered thresholds appear to be  
624 confined to acute phases of the condition, as reported by Bär et al. (2006). Symptom specific  
625 effects are also relevant in considering individuals with BPD. During acute BPD episodes,  
626 self-injury is a common behavioural dysregulation and those individuals under distress of self-  
627 injury required higher temperature for thermal detection and pain thresholds (Ludäscher et al.,  
628 2009; Schmahl et al., 2006), as well as reporting higher mechanical pain thresholds (Magerl et  
629 al., 2012) than those not under distress of self-injury and healthy controls. Therefore, these  
630 sensory deficits might, similarly be, acute phase specific. Unlike eating disorders, where  
631 recovery is possible, there is no evidence that sensory changes return to typical levels once  
632 symptoms reduce, as those who are not under distress of self-injury still have hyposensitivity in  
633 comparison to healthy controls. This symptom effect is similarly present in schizophrenia  
634 (Boettger et al., 2013; Jochum et al., 2006) and those with fewer positive symptoms e.g.  
635 hallucinations and delusions required greater temperatures to report pain (Lévesque et al.,  
636 2012).

637         Given the limited range of studies at present, it is premature to presume specific  
638 mechanisms, which might underlie these psychiatric conditions. Understanding the specific  
639 mechanisms behind these findings will however, be integral in utilizing pain behaviours to  
640 further understand each disorder. Given the role of somatosensory processing and behavioural  
641 differences in each disorder, altered pain behaviours may also be an extension of altered  
642 somatosensory processing or associated with alterations in emotional regulation (Keefe,  
643 Lumley, Anderson, Lynch, & Carson, 2001) or interoceptive abilities (Craig, 2003). Pain and

644 touch have inherent affective and motivational components (Williams & Craig, 2016) as well  
645 as being a signal of problems in homeostatic regulation (Panerai, 2011). As these can all be  
646 seen to be symptoms within psychiatric conditions it is possible therefore, that with the correct  
647 application of individual differences research that pain might help to understand aspects of  
648 these challenges in these conditions. Further, models have proposed pain and touch to be a  
649 critical component of interoceptive abilities (Craig, 2003), suggested to be regulated by lamina  
650 I spinal pathways (Craig, 2002), which are thought to be affected in a range of psychiatric  
651 conditions (Mash et al., 2017; Murphy, Brewer, Catmur, & Bird, 2017). This provides a  
652 potential mechanism for future research to explore, within understanding of susceptibility of  
653 psychiatric conditions.

654         Rather than providing definitive answers to questions related to pain processing in  
655 psychiatric conditions, this review more comprehensively highlights a number of implications  
656 for researchers and clinicians. The first consideration for future research relates to the potential  
657 role of general cognitive and emotional states in these populations. Specifically, as it is already  
658 well established for depression and anxiety that mood is associated with pain responses  
659 (Goesling et al., 2013), it would be prudent for future research into the psychiatric conditions  
660 mentioned above to consider the relationship between mood and pain processing. This is  
661 further in light of the fact that recent evidence has suggested that the relationship between  
662 autism symptoms and pain behaviours was mediated by symptoms of anxiety and depression  
663 (Garcia-Villamizar, Moore, & Garcia-Martinez, 2018). Additionally, difficulties with general  
664 cognitive processing, specifically with executive control; an attentional system, is a hallmark of  
665 many of these psychiatric conditions (Galimberti et al., 2013; Hill, 2004; Niendam et al., 2012)  
666 and there are known links to pain experience (Eccleston & Crombez, 1999; Moore, Keogh, &  
667 Eccleston, 2012). The somatosensory changes observed in eating disorders may also reflect  
668 such a cognitive change. Here an attentional bias towards areas of bodily concern (i.e. the  
669 abdomen) may increase sensitivity at this site. This may also explain why individuals no

670 longer show these hypersensitivities as they recover. More general cognitive processes, may  
671 therefore, mediate responses on these pain assessment measures. Evidence for this in the  
672 context of this review comes from Treister et al. (2015) who found that participants with  
673 ADHD who were currently un-medicated with Ritalin, showed hypersensitivity to pain,  
674 however, when these individuals were given medication these thresholds moved into the  
675 normal range. One potential explanation of these differences might be that clinical groups find  
676 it harder to attend to the task at hand, indeed effects often changed when the ramp rate of  
677 stimuli was also changed, suggesting that attention might be an important factor (Cascio et al.,  
678 2008; Duerden et al., 2015). It may also be the case that treatment with Ritalin helps to  
679 normalize homeostatic set-points across sensory and cognitive systems. For example, previous  
680 studies have suggested that rapid changes in attention, increased motor activity, and enhanced  
681 sensory sensitivity, may all be part of an auto-regulatory attempt to increase stimulation, in  
682 order to maintain homeostasis of brain arousal (Geissler, Romanos, Hegerl, & Hensch, 2014).  
683 Effective treatment (with Ritalin, for example) may obviate the need for such autoregulation,  
684 reducing sensory sensitivity, as well as behavioural and attentional hyperactivity (Geissler et  
685 al., 2014).

686 Medication being taken by these populations therefore, also might directly affect pain  
687 processing. Specifically, it opens up questions regarding any analgesic effects present. Given  
688 the percentage of individuals with a range of psychiatric conditions, who use pharmacological  
689 substances; which are known to act on the serotonergic system (Hurwitz, Blackmore, Hazell,  
690 Williams, & Woolfenden, 2012; Singh, Singh, Kar, & Chan, 2010). As well as many of these  
691 medications having known analgesic effects (Mico, Ardid, Berrocoso, & Eschalier, 2006), it is  
692 important to consider the role of these agents in altering pain processing. Several studies  
693 included in this review explicitly mention the use of non-medicated participants. However,  
694 few mention medication use, therefore, discounting the possibility of investigating this  
695 phenomenon thoroughly. More is needed regarding the management of challenging

696 behaviours, including both those thought to be related to pain (i.e. self-injurious behaviours) as  
697 well as other symptoms, to identify how management of clinical symptoms may alter pain  
698 response and how pain management strategies may help with clinical symptoms.

699         A further consideration is to carefully select appropriate control groups. Comparing  
700 psychiatric or pain patients with healthy controls can result in artificial amplification of QST  
701 differences that are unrelated to clinical state, as they do not represent the general population  
702 who are typically fraught with issues that can affect QST results for e.g. obesity (Coghill &  
703 Yarnitsky, 2015). This can confound significant results, especially considering the number of  
704 additional diagnosed or undiagnosed co-morbidities present in psychiatric conditions (Gillberg  
705 & Fernell, 2014). One potential approach could be to go beyond examining psychiatric  
706 groups' thresholds in relation to healthy controls and compare them with other experimental  
707 groups with specific psychiatric conditions. Several studies within this review considered a  
708 range of conditions or additionally looked at traits within these conditions. This approach  
709 could solve the amplitude issue and provide other areas of interest to be explored.

710         The present research however, is limited by this reliance on condition-based research  
711 and group-level analysis. Current research trends are moving away from such an approach  
712 with The National Institute of Mental Health (NIMH) developing a taxonomy, which proposes  
713 a trans-diagnostic approach to understanding mental health conditions. It might therefore be of  
714 value to examine for the underlying mechanisms which may result in these differences or pain  
715 processing more broadly, as a result of symptoms or traits, rather than conditions (Insel et al.,  
716 2010). There are also large individual differences within the general population with reference  
717 to somatosensory thresholds (Fillingim, 2005) that should be considered when investigating  
718 similar differences in individuals with a diagnosis; variability may be typical regardless of the  
719 diagnosis therefore caution should be adopted to ensure that such variability extends beyond  
720 that which is typically expected. Given these observations, future research may benefit from a  
721 more individualistic approach in examining these. Comparison with published normative

722 values (Magerl et al., 2010) allows for individual profiles to be developed and an  
723 understanding of potential links between individual psychiatric symptoms and somatosensory  
724 differences. As well as an understanding of the number of individuals within each condition  
725 who might be experiencing altered somatosensory interactions with external stimuli (either  
726 hyper- or hypo- sensitivity), including any individuals with typical function.

727 Another feature, which has received only limited indirect attention, is that of the  
728 developmental time course of the somatosensory symptoms in psychiatric conditions. Almost  
729 all studies included in this review examined participants in the age range of 18-30 years with  
730 IQ in the normal range. This is wholly understandable given that the tasks being presented  
731 require very specific responses, as well as being potentially distressing to younger children or  
732 individuals without the capacity to fully understand the procedures. This does, however, limit  
733 the generalisability and utility of these findings. Understanding the experience of pain in  
734 childhood is important, as it could clarify the development of any hyper- or hypo-sensitivity, or  
735 the change from an early atypicality to a potentially more typical somatosensory profile in  
736 adulthood, or the reverse. Further, it is well known that conditions associated with pain have a  
737 progression into old age (Brattberg, Parker, & Thorslund, 1997), and it appears that both  
738 sensory and pain thresholds increase with age (Magerl et al., 2010). It would therefore be  
739 beneficial to further understand the progression of pain sensitivity and response into older  
740 adulthood in individuals with psychiatric conditions.

741 In conclusion, this review highlights the needs for ongoing work that has  
742 methodological rigour. Researchers utilising sound psychophysical methods and carefully  
743 reporting the methods can achieve this. In doing so, research can develop individual profiles,  
744 as well as facilitate comparisons across studies that involve other psychiatric conditions,  
745 physical health conditions and healthy controls. This will provide the more precise results  
746 required to form conclusions that are more definitive. Experimental investigations of pain can  
747 detect or verify altered processing as a symptom and can provide insights into the behavioural

748 consequences (Lautenbacher & Krieg, 1994), which in turn would help to provide the grounds  
749 for accurate interventions to assist in alleviating symptoms. Overall, the findings in the current  
750 review suggest somatosensory hyposensitivity in schizophrenia, eating disorders, and  
751 personality disorders. More investigation that is systematic will correct views based on  
752 inconsistent research, anecdotal and clinical case study views, or support these findings and  
753 potentially lead to better clinical pain management in vulnerable groups.

754

## References

- 755
- 756 APA. (1994). *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR*: American Psychiatric  
757 Association
- 758 APA. (2013). *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-IV-  
759 TR®)*: American Psychiatric Association.
- 760 Atik, L., Konuk, N., Akay, O., Ozturk, D., & Erdogan, A. (2007). Pain perception in patients with bipolar disorder  
761 and schizophrenia. *Acta Neuropsychiatrica*, *19*(5), 284-290. doi:10.1111/j.1601-5215.2007.00193.x
- 762 Backonja, M. M., Attal, N., Baron, R., Bouhassira, D., Drangholt, M., Dyck, P. J., . . . Ziegler, D. (2013). Value of  
763 quantitative sensory testing in neurological and pain disorders: NeuPSIG consensus. *Pain*, *154*(9), 1807-  
764 1819. doi:10.1016/j.pain.2013.05.047
- 765 Bair, M. J., Robinson, R. L., Katon, W., & Kroenke, K. (2003). Depression and pain comorbidity: a literature  
766 review. *Arch Intern Med*, *163*(20), 2433-2445. doi:10.1001/archinte.163.20.2433
- 767 Bär, K. J., Berger, S., Schwier, C., Wutzler, U., & Beissner, F. (2013). Insular dysfunction and descending pain  
768 inhibition in anorexia nervosa. *Acta Psychiatrica Scandinavica*, *127*(4), 269-278. doi:10.1111/j.1600-  
769 0447.2012.01896.x
- 770 Bär, K. J., Boettger, S., Wagner, G., Wilsdorf, C., Gerhard, U. J., Boettger, M. K., . . . Sauer, H. (2006). Changes  
771 of pain perception, autonomic function, and endocrine parameters during treatment of anorectic  
772 adolescents. *Journal of The American Academy of Child and Adolescent Psychiatry*, *45*(9), 1068-1076.  
773 doi:10.1097/01.chi.0000227876.19909.48
- 774 Baranek, G. T. (2002). Efficacy of Sensory and Motor Interventions for Children with Autism. *Journal of Autism  
775 and Developmental Disorders*, *32*(5), 397-422. doi:10.1023/a:1020541906063
- 776 Bastian, B., Jetten, J., Hornsey, M. J., & Leknes, S. (2014). The Positive Consequences of Pain: A  
777 Biopsychosocial Approach. *Personality and Social Psychology Review*, *18*(3), 256-279.  
778 doi:10.1177/1088868314527831
- 779 Baxter, A. J., Brugha, T. S., Erskine, H. E., Scheurer, R. W., Vos, T., & Scott, J. G. (2015). The epidemiology and  
780 global burden of autism spectrum disorders. *Psychological Medicine*, *45*(03), 601-613.  
781 doi:10.1017/S003329171400172X
- 782 Bird, G., Brindley, R., White, S., Frith, U., Silani, G., & Singer, T. (2010). Empathic brain responses in insula are  
783 modulated by levels of alexithymia but not autism. *Brain*, *133*(5), 1515-1525. doi:10.1093/brain/awq060  
784
- 785 Blakemore, S.-J., Tavassoli, T., Calò, S., Thomas, R. M., Catmur, C., Frith, U., & Haggard, P. (2006). Tactile  
786 sensitivity in Asperger syndrome. *Brain and Cognition*, *61*, 5-13. doi:10.1016/j.bandc.2005.12.013



- 787 Boettger, M. K., Grossmann, D., & Bar, K. J. (2013). Increased cold and heat pain thresholds influence the  
788 thermal grill illusion in schizophrenia. *European Journal of Pain*, *17*(2), 200-209. doi:10.1002/j.1532-  
789 2149.2012.00188.x
- 790 Bohus, M., Limberger, M., Ebner, U., Glocker, F. X., Schwarz, B., Wernz, M., & Lieb, K. (2000). Pain perception  
791 during self-reported distress and calmness in patients with borderline personality disorder and self-  
792 mutilating behavior. *PSychiatry Research*, *95*(3), 251-260. doi:10.1016/S0165-1781(00)00179-7
- 793 Brattberg, G., Parker, M. G., & Thorslund, M. (1997). A longitudinal study of pain: reported pain from middle to  
794 old age. *The Clinical Journal of Pain*, *13*(2), 144-149. doi:10.1097/00002508-199706000-00008
- 795 Cascio, C., McGlone, F., Folger, S., Tannan, V., Baranek, G., Pelphey, K. A., & Essick, G. (2008). Tactile  
796 perception in adults with autism: a multidimensional psychophysical study. *Journal of Autism and*  
797 *Developmental Disorders*, *38*(1), 127-137. doi: 10.1007/s10803-007-0370-8
- 798 Chen, C., Hung, A. Y., Fan, Y. T., Tan, S., Hong, H., & Cheng, Y. (2017). Linkage between pain sensitivity and  
799 empathic response in adolescents with autism spectrum conditions and conduct disorder symptoms.  
800 *Autism Research*, *10*(2), 267-275. doi:10.1002/aur.1653
- 801 Coghill, R. C., & Yarnitsky, D. (2015). Healthy and normal? The need for clear reporting and flexible criteria for  
802 defining control participants in quantitative sensory testing studies. *Pain*, *156*(11), 2117-2118.  
803 doi:10.1097/j.pain.0000000000000331
- 804 Coid, J., Yang, M., Tyrer, P., Roberts, A., & Ullrich, S. (2006). Prevalence and correlates of personality disorder  
805 in Great Britain. *The British Journal of Psychiatry*, *188*(5), 423-431. doi:10.1192/bjp.188.5.423
- 806 Craig, A. D. (2002). How do you feel? Interoception: the sense of the physiological condition of the body. *Nature*  
807 *Reviews Neuroscience*, *3*(8), 655-666, doi: 10.1038/nrn894
- 808 Craig, A. D. (2003). Interoception: the sense of the physiological condition of the body. *Current Opinions in*  
809 *Neurobiology*, *13*(4), 500-505. doi. 10.1016/S0959-4388(03)00090-4
- 810 de la Fuente-Sandoval, C., Favila, R., Gómez-Martín, D., León-Ortiz, P., & Graff-Guerrero, A. (2012). Neural  
811 response to experimental heat pain in stable patients with schizophrenia. *Journal of Psychiatric*  
812 *Research*, *46*, 128-134. doi:10.1016/j.jpsychires.2011.09.008
- 813 de la Fuente-Sandoval, C., Favila, R., Gómez-Martin, D., Pellicer, F., & Graff-Guerrero, A. (2010). Functional  
814 magnetic resonance imaging response to experimental pain in drug-free patients with schizophrenia.  
815 *Psychiatry Research: Neuroimaging*, *183*, 99-104. doi:10.1016/j.psychresns.2010.05.003
- 816

- 817 de Zwaan, M., Biener, D., Bach, M., Wiesnagrotzki, S., & Stacher, G. (1996). Pain sensitivity, alexithymia, and  
 818 depression in patients with eating disorders: are they related? *Journal of Psychosomatic Research*, *41*(1),  
 819 65-70. doi.org/10.1016/0022-3999(96)00088-8.
- 820 de Zwaan, M., Biener, D., Schneider, C., & Stacher, G. (1996). Relationship between thresholds to thermally and  
 821 to mechanically induced pain in patients with eating disorders and healthy subjects. *Pain*, *67*(2-3), 511-  
 822 512. doi:10.1016/0304-3959(96)03143-0
- 823 Duerden, E. G., Taylor, M. J., Lee, M., McGrath, P. A., Davis, K. D., & Roberts, S. W. (2015). Decreased  
 824 Sensitivity to Thermal Stimuli in Adolescents With Autism Spectrum Disorder: Relation to  
 825 Symptomatology and Cognitive Ability. *The Journal of Pain*, *16*(5), 463-471.  
 826 doi:10.1016/j.jpain.2015.02.001
- 827 Dworkin, R. H., Clark, W. C., Lipsitz, J. D., Amador, X. F., Kaufmann, C. A., Opler, L. A., . . . Gorman, J. M.  
 828 (1993). Affective deficits and pain insensitivity in schizophrenia. *Motivation and Emotion*, *17*(3), 245-  
 829 276. doi: 10.1007/BF00992222
- 830 Eccleston, C., & Crombez, G. (1999). Pain demands attention: A cognitive–affective model of the interruptive  
 831 function of pain. *Psychological Bulletin*, *125*(3), 356. doi:10.1037//0033-2909.125.3.356
- 832 Fan, Y.-T., Chen, C., Chen, S.-C., Decety, J., & Cheng, Y. (2014). Empathic arousal and social understanding in  
 833 individuals with autism: evidence from fMRI and ERP measurements. *Social Cognitive and Affective*  
 834 *Neuroscience*, *9*(8), 1203-1213. doi:10.1093/scan/nst101
- 835 Faris, P. L., Raymond, N. C., De Zwaan, M., Howard, L. A., Eckert, E. D., & Mitchell, J. E. (1992). Nociceptive,  
 836 but not tactile, thresholds are elevated in bulimia nervosa. *Biological Psychiatry*, *32*(5), 462-466.  
 837 doi.org/10.1016/0006-3223(92)90134-L
- 838 Fedora, O., & Reddon, J. R. (1993). Psychopathic and nonpsychopathic inmates differ from normal controls in  
 839 tolerance levels of electrical stimulation. *Journal of Clinical Psychology*, *49*(3), 326-331.  
 840 doi:10.1002/1097-4679(199305)49:3<326::AID-JCLP2270490304>3.0.CO;2-5
- 841 Fillingim, R. B. (2005). Individual differences in pain responses. *Current Rheumatology Reports*, *7*(5), 342-347.  
 842 doi:10.1007/s11926-005-0018-7
- 843 Fründt, O., Grashorn, W., Schöttle, D., Peiker, I., David, N., Engel, A. K., . . . Bingel, U. (2017). Quantitative  
 844 Sensory Testing in adults with Autism Spectrum Disorders. *Journal of Autism and Developmental*  
 845 *Disorders*, *47*(4), 1183-1192. doi:10.1007/s10803-017-3041-4
- 846 Galimberti, E., Fadda, E., Cavallini, M. C., Martoni, R. M., Erzegovesi, S., & Bellodi, L. (2013). Executive  
 847 functioning in anorexia nervosa patients and their unaffected relatives. *Psychiatry Research*, *208*(3), 238-  
 848 244. doi:10.1016/j.psychres.2012.10.001

- 849 Garcia-Villamisar, D., Moore, D., & Garcia-Martinez, M. (2018). Internalizing Symptoms Mediate the Relation  
 850 Between Acute Pain and Autism in Adults. *Journal of Autism and Developmental Disorders*.  
 851 doi:10.1007/s10803-018-3765-9
- 852 Geissler, J., Romanos, M., Hegerl, U., & Hensch, T. (2014). Hyperactivity and sensation seeking as  
 853 autoregulatory attempts to stabilize brain arousal in ADHD and mania? *Attention Deficit Hyperactivity*  
 854 *Disorders*, 6(3), 159-173. doi:10.1007/s12402-014-0144-z
- 855 Gillberg, C., & Fernell, E. (2014). Autism plus versus autism pure. *Journal of Autism and Developmental*  
 856 *Disorders*, 44(12), 3274-3276. doi:10.1007/s10803-014-2163-1
- 857 Girard, M., Plansont, B., Bonhabau, H., & Malauzat, D. (2011). Experimental Pain Hypersensitivity in  
 858 Schizophrenic Patients. *Clinical Journal of Pain*, 27(9), 790-795. doi:10.1097/AJP.0b013e31821d904c.
- 859 Goesling, J., Clauw, D. J., & Hassett, A. L. (2013). Pain and depression: an integrative review of neurobiological  
 860 and psychological factors. *Current Psychiatry Reports*, 15(12), 421. doi:10.1007/s11920-013-0421-0
- 861 Grandin, T. (1992). An Inside View of Autism. In E. Schopler & G. B. Mesibov (Eds.), *High-Functioning*  
 862 *Individuals with Autism* (pp. 105-126). Boston, MA: Springer US.
- 863 Grandin, T. (1995). *Thinking in Pictures: And Other Reports from My Life with Autism*: Doubleday.
- 864 Gu, X., Zhou, T. J., Anagnostou, E., Soorya, L., Kolevzon, A., Hof, P. R., & Fan, J. (2017). Heightened brain  
 865 response to pain anticipation in high-functioning adults with autism spectrum disorder. *European Journal*  
 866 *of Neuroscience*, n/a-n/a. doi:10.1111/ejn.13598
- 867 Guclu, B., Tanidir, C., Mukaddes, N. M., & Unal, F. (2007). Tactile sensitivity of normal and autistic children.  
 868 *Somatosensory and Motor Research*, 24(1-2), 21-33. doi:10.1080/08990220601179418.
- 869 Guieu, R., Samuélian, J. C., & Coulouvrat, H. (1994). Objective evaluation of pain perception in patients with  
 870 schizophrenia. *The British Journal Of Psychiatry: The Journal of Mental Science*, 164(2), 253-255.  
 871 doi:10.1192/bjp.164.2.253
- 872 Hackler, A. H., Vogel, D. L., & Wade, N. G. (2010). Attitudes Toward Seeking Professional Help for an Eating  
 873 Disorder: The Role of Stigma and Anticipated Outcomes. *Journal of Counseling & Development*, 88(4),  
 874 424-431. doi:10.1002/j.1556-6678.2010.tb00042.x
- 875 Higgins, J., & Green, S. (2011). In *Cochrane Handbook for Systematic Reviews of Interventions* (pp. i-xxi): John  
 876 Wiley & Sons, Ltd.
- 877 Hill, E. L. (2004). Executive dysfunction in autism. *Trends in Cognitive Sciences*, 8(1), 26-32. doi:  
 878 10.1016/j.tics.2003.11.003.

- 879 Hurwitz, R., Blackmore, R., Hazell, P., Williams, K., & Woolfenden, S. (2012). Tricyclic antidepressants for  
 880 autism spectrum disorders (ASD) in children and adolescents. *Cochrane Database of Systematic*  
 881 *Reviews*(3). doi:10.1002/14651858.CD008372.pub2
- 882 Iannetti, G. D., & Mouraux, A. (2010). From the neuromatrix to the pain matrix (and back). *Experimental Brain*  
 883 *Research*, 205(1), 1-12. doi:10.1007/s00221-010-2340-1
- 884 IASP. (2012). IASP Taxonomy. Retrieved from <http://www.iasp-pain.org/Taxonomy>
- 885 Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., . . . Wang, P. (2010). Research Domain  
 886 Criteria (RDoC): Toward a New Classification Framework for Research on Mental Disorders. *American*  
 887 *Journal of Psychiatry*, 167(7), 748-751. doi:10.1176/appi.ajp.2010.09091379
- 888 Jochum, T., Letzsch, A., Greiner, W., Wagner, G., Sauer, H., & Bär, K.-J. (2006). Influence of antipsychotic  
 889 medication on pain perception in schizophrenia. *Psychiatry Research*, 142, 151-156.  
 890 doi:10.1016/j.psychres.2005.09.004
- 891 Keefe, F. J., Lumley, M., Anderson, T., Lynch, T., & Carson, K. L. (2001). Pain and emotion: new research  
 892 directions. *Journal of Clinical Psychology*, 57(4), 587-607. doi. 10.1002/jclp.1030
- 893 Keizer, A., Smeets, M. A. M., Dijkerman, H. C., van Elburg, A., & Postma, A. (2012). Aberrant somatosensory  
 894 perception in Anorexia Nervosa. *Psychiatry Research*, 200, 530-537. doi:10.1016/j.psychres.2012.05.001
- 895 Kendler, K. S. (2008). Explanatory models for psychiatric illness. *The American Journal of Psychiatry*, 165(6),  
 896 695-702. doi:10.1176/appi.ajp.2008.07071061
- 897 Kleinböhl, D., Hölzl, R., Möltner, A., Rommel, C., Weber, C., & Osswald, P. M. (1999). Psychophysical  
 898 measures of sensitization to tonic heat discriminate chronic pain patients. *Pain*, 81(1-2), 35-43.  
 899 doi:10.1016/S0304-3959(98)00266-8
- 900 Krahé, C., Springer, A., Weinman, J. A., & Fotopoulou, A. (2013). The social modulation of pain: others as  
 901 predictive signals of salience - a systematic review. *Frontiers in Human Neuroscience*, 7, 386-386.  
 902 doi:10.3389/fnhum.2013.00386
- 903 Krieg, J.-C., Roscher, S., Strian, F., Pirke, K.-M., & Lautenbacher, S. (1993). Pain sensitivity in recovered  
 904 anorexics, restrained and unrestrained eaters. *Journal of Psychosomatic Research*, 37, 595-601.  
 905 doi:10.1016/0022-3999(93)90054-J
- 906 Kudoh, A., Ishihara, H., & Matsuki, A. (2000). Current Perception Thresholds and Postoperative Pain in  
 907 Schizophrenic Patients. *Regional Anesthesia and Pain Medicine*, 25(5), 475-479.  
 908 doi:10.1053/rapm.2000.7617

- 909 Langford, D. J., Tuttle, A. H., Brown, K., Deschenes, S., Fischer, D. B., Mutso, A., . . . Sternberg, W. F. (2010).  
 910 Social approach to pain in laboratory mice. *Society Neuroscience*, *5*(2), 163-170.  
 911 doi:10.1080/17470910903216609
- 912 Lautenbacher, S., & Krieg, J. C. (1994). Pain perception in psychiatric disorders: A review of the literature.  
 913 *Journal of Psychiatric Research*, *28*(2), 109-122. doi:10.1016/0022-3956(94)90023-X
- 914 Lautenbacher, S., Pauls, A. M., Strian, F., Pirke, K. M., & Krieg, J. C. (1990). Pain perception in patients with  
 915 eating disorders. *Psychosomatic Medicine*, *52*(6), 673-682. doi:10.1097/00006842-199011000-00008
- 916 Lautenbacher, S., Pauls, A. M., Strian, F., Pirke, K. M., & Krieg, J. C. (1991). Pain sensitivity in anorexia nervosa  
 917 and bulimia nervosa. *Biological Psychiatry*, *29*, 1073-1078. doi:10.1016/0006-3223(91)90249-L
- 918 Lévesque, M., Potvin, S., Marchand, S., Stip, E., Grignon, S., Pierre, L., . . . Goffaux, P. (2012). Pain Perception  
 919 in Schizophrenia: Evidence of a Specific Pain Response Profile. *Pain Medicine*, *13*(12), 1571-1579.  
 920 doi:10.1111/j.1526-4637.2012.01505.x
- 921 Ludäscher, P., Bohus, M., Lieb, K., Philipsen, A., Jochims, A., & Schmahl, C. (2007). Elevated pain thresholds  
 922 correlate with dissociation and aversive arousal in patients with borderline personality disorder.  
 923 *Psychiatry Research*, *149*(1-3), 291-296. doi:10.1016/j.psychres.2005.04.009
- 924 Ludäscher, P., Greffrath, W., Schmahl, C., Kleindienst, N., Kraus, A., Baumgartner, U., . . . Bohus, M. (2009). A  
 925 cross-sectional investigation of discontinuation of self-injury and normalizing pain perception in patients  
 926 with borderline personality disorder. *Acta Psychiatrica Scandinavica*, *120*(1), 62-70. doi:10.1111/j.1600-  
 927 0447.2008.01335.x
- 928 Ludäscher, P., Kalckreuth, C., Parzer, P., Kaess, M., Resch, F., Bohus, M., . . . Brunner, R. (2014). Pain  
 929 perception in female adolescents with borderline personality disorder. *European Child and Adolescent*  
 930 *Psychiatry*. doi:10.1007/s00787-014-0585-0
- 931 Magerl, W., Burkart, D., Fernandez, A., Schmidt, L. G., & Treede, R.-D. (2012). Persistent antinociception  
 932 through repeated self-injury in patients with borderline personality disorder. *Pain*, *153*, 575-584.  
 933 doi:10.1016/j.pain.2011.11.021
- 934 Magerl, W., Krumova, E. K., Baron, R., Tölle, T., Treede, R.-D., & Maier, C. (2010). Reference data for  
 935 quantitative sensory testing (QST): refined stratification for age and a novel method for statistical  
 936 comparison of group data. *Pain*, *151*(3), 598-605. doi: 10.1016/j.pain.2010.07.026
- 937 Mannuzza, S., Klein, R. G., Bessler, A., Malloy, P., & LaPadula, M. (1993). Adult outcome of hyperactive boys:  
 938 Educational achievement, occupational rank, and psychiatric status. *Archives of General Psychiatry*,  
 939 *50*(7), 565-576. doi:10.1001/archpsyc.1993.01820190067007

- 940 Mash, L. E., Schauder, K. B., Cochran, C., Park, S., & Cascio, C. J. (2017). Associations between interoceptive  
 941 cognition and age in autism spectrum disorder and typical development. *Journal of Cognitive Education*  
 942 *and Psychology, 16*(1), 23-37. doi. 10.1891/1945-8959.16.1.23
- 943 McCown, W., Galina, H., Johnson, J., DeSimone, P. A., & Posa, J. (1993). Borderline personality disorder and  
 944 laboratory-induced cold pressor pain: Evidence of stress-induced analgesia. *Journal of Psychopathology*  
 945 *and Behavioral Assessment, 15*(2), 87-95. doi:10.1007/BF00960610
- 946 Mico, J. A., Ardid, D., Berrocoso, E., & Eschalier, A. (2006). Antidepressants and pain. *Trends in*  
 947 *Pharmacological Sciences, 27*(7), 348-354. doi:10.1016/j.tips.2006.05.004
- 948 Militerni, R., Bravaccio, C., Falco, C., Puglisi-Allegra, S., Pascucci, T., & Fico, C. (2000). Pain reactivity in  
 949 children with autistic disorder. *The Journal of Headache and Pain, 1*(1), 53-56.  
 950 doi:10.1007/s101940050011
- 951 Minshew, N. J., & Hobson, J. A. (2008). Sensory Sensitivities and Performance on Sensory Perceptual Tasks in  
 952 High-functioning Individuals with Autism. *Journal of Autism and Developmental Disorders, 38*(8),  
 953 1485-1498. doi:10.1007/s10803-007-0528-4
- 954 Moore, D. J. (2014). Acute pain experience in individuals with autism spectrum disorders: A review. *Autism: The*  
 955 *International Journal of Research and Practice.* doi:10.1177/1362361314527839
- 956 Moore, D. J., Keogh, E., & Eccleston, C. (2012). The interruptive effect of pain on attention. *The Quarterly*  
 957 *Journal of Experimental Psychology, 65*(3), 565-586. doi:10.1080/17470218.2011.626865
- 958 Murphy, J., Brewer, R., Catmur, C., & Bird, G. (2017). Interoception and psychopathology: A developmental  
 959 neuroscience perspective. *Developmental Cognitive Neuroscience, 23*, 45-56. doi.  
 960 10.1016/j.dcn.2016.12.006
- 961 Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012). Meta-analytic  
 962 evidence for a superordinate cognitive control network subserving diverse executive functions.  
 963 *Cognitive, Affective & Behavioural Neuroscience, 12*(2), 241-268. doi:10.3758/s13415-011-0083-5
- 964 Panerai, A. E. (2011). Pain emotion and homeostasis. *Neurological Science, 32*(1), 27-29. doi. 10.1007/s10072-  
 965 011-0540-5
- 966 Papezova, H., Yamamotova, A., & Uher, R. (2005). Elevated pain threshold in eating disorders: physiological and  
 967 psychological factors. *Journal of Psychiatric Research, 39*(4), 431-438.  
 968 doi:10.1016/j.jpsychires.2004.10.006
- 969 Pauls, A. M., Lautenbacher, S., Strian, F., Pirke, K. M., & Krieg, J. C. (1991). Assessment of somatosensory  
 970 indicators of polyneuropathy in patients with eating disorders. *European Archives of Psychiatry and*  
 971 *Clinical Neuroscience, 241*(1), 8-12. doi: 10.1007/BF02193748

- 972 Pavony, M. T., & Lenzenweger, M. F. (2014). Somatosensory processing and borderline personality disorder:  
 973 Pain perception and a signal detection analysis of proprioception and exteroceptive sensitivity.  
 974 *Personality Disorders: Theory, Research, and Treatment*, 5(2), 164-171. doi:10.1037/per0000017
- 975 Phillips, M. L., Senior, C., & David, A. S. (2000). Perception of threat in schizophrenics with persecutory  
 976 delusions: an investigation using visual scan paths. *Psychological Medicine*, 30(1), 157-167. doi:  
 977 0.1017/S0033291799001397
- 978 Potvin, S., Stip, E., Tempier, A., Pampoulova, T., Bentaleb, L. A., Lalonde, P., . . . Marchand, S. (2008). Pain  
 979 perception in schizophrenia: No changes in diffuse noxious inhibitory controls (DNIC) but a lack of pain  
 980 sensitization. *Journal of Psychiatric Research*, 42, 1010-1016. doi:10.1016/j.jpsychires.2007.11.001
- 981 Quattrocki, E., & Friston, K. (2014). Autism, oxytocin and interoception. *Neuroscience and Biobehavioral*  
 982 *Reviews*, 47, 410-430. doi:10.1016/j.neubiorev.2014.09.012
- 983 Raymond, N. C., de Zwaan, M., Faris, P. L., Nugent, S. M., Ackard, D. M., Crosby, R. D., & Mitchell, J. E.  
 984 (1995). Pain thresholds in obese binge-eating disorder subjects. *BIOLOGICAL PSYCHIATRY*, 37, 202-  
 985 204. doi:10.1016/0006-3223(94)00244-W
- 986 Raymond, N. C., Faris, P. L., Thuras, P. D., Eiken, B., Howard, L. A., Hofbauer, R. D., & Eckert, E. D. (1999).  
 987 Elevated pain threshold in anorexia nervosa subjects. *Biological Psychiatry*, 45(10), 1389-1392.  
 988 doi:10.1016/S0006-3223(98)00177-2
- 989 Riquelme, I., Hatem, S. M., & Montoya, P. (2016). Abnormal Pressure Pain, Touch Sensitivity, Proprioception,  
 990 and Manual Dexterity in Children with Autism Spectrum Disorders. *Neural Plasticity*, 2016, 9.  
 991 doi:10.1155/2016/1723401
- 992 Rolke, R., Baron, R., Maier, C., Tölle, T. R., Treede, R. D., Beyer, A., . . . Wasserka, B. (2006). Quantitative  
 993 sensory testing in the German Research Network on Neuropathic Pain (DFNS): Standardized protocol  
 994 and reference values. *Pain*, 123(3), 231-243. doi:10.1016/j.pain.2006.01.041
- 995 Savitz, J., & Harrison, N. A. (2018). Interoception and Inflammation in Psychiatric Disorders. *Biological*  
 996 *Psychiatry: Cognitive Neuroscience and Neuroimaging*, 3(6), 514-524. doi: 10.1016/j.bpsc.2017.12.011
- 997 Schmahl, C., Bohus, M., Esposito, F., Treede, R. D., Di Salle, F., Greffrath, W., . . . Seifritz, E. (2006). Neural  
 998 correlates of antinociception in borderline personality disorder. *Archives of General Psychiatry*, 63(6),  
 999 659-667. doi:10.1001/archpsyc.63.6.659
- 1000 Schmahl, C., Greffrath, W., Baumgärtner, U., Schlereth, T., Magerl, W., Philipsen, A., . . . Treede, R. D. (2004).  
 1001 Differential nociceptive deficits in patients with borderline personality disorder and self-injurious  
 1002 behavior: laser-evoked potentials, spatial discrimination of noxious stimuli, and pain ratings. *Pain*, 110,  
 1003 470-479. doi:10.1016/j.pain.2004.04.035

- 1004 Schmahl, C., Meinzer, M., Zeuch, A., Fichter, M., Cebulla, M., Kleindienst, N., . . . Bohus, M. (2010). Pain  
 1005 sensitivity is reduced in borderline personality disorder, but not in posttraumatic stress disorder and  
 1006 bulimia nervosa. *World Journal of Biological Psychiatry, 11*(2), 364-371.  
 1007 doi:10.3109/15622970701849952
- 1008 Sham, P. C., MacLean, C. J., & Kendler, K. S. (1994). A typological model of schizophrenia based on age at  
 1009 onset, sex and familial morbidity. *Acta Psychiatrica Scandinavica, 89*(2), 135-141. doi: 10.1111/j.1600-  
 1010 0447.1994.tb01501.x
- 1011 Singh, S. P., Singh, V., Kar, N., & Chan, K. (2010). Efficacy of antidepressants in treating the negative symptoms  
 1012 of chronic schizophrenia: meta-analysis. *The British Journal of Psychiatry, 197*(3), 174-179.  
 1013 doi:10.1192/bjp.bp.109.067710
- 1014 Taylor, P. J., Hutton, P., & Wood, L. (2015). Are people at risk of psychosis also at risk of suicide and self-harm?  
 1015 A systematic review and meta-analysis. *Psychological Medicine, 45*(5), 911-926.  
 1016 doi:10.1017/s0033291714002074
- 1017 Thompson, T., Correll, C. U., Gallop, K., Vancampfort, D., & Stubbs, B. (2016). Is Pain Perception Altered in  
 1018 People With Depression? A Systematic Review and Meta-Analysis of Experimental Pain Research.  
 1019 *Journal of Pain, 17*(12), 1257-1272. doi:10.1016/j.jpain.2016.08.007
- 1020 Treister, R., Eisenberg, E., Demeter, N., & Pud, D. (2015). Alterations in Pain Response are Partially Reversed by  
 1021 Methylphenidate (Ritalin) in Adults with Attention Deficit Hyperactivity Disorder (ADHD). *Pain  
 1022 Practice: The Official Journal of World Institute of Pain, 15*(1), 4-11. doi:10.1111/papr.12129
- 1023 Vardeh, D., Mannion, R. J., & Woolf, C. J. (2016). Toward a Mechanism-Based Approach to Pain Diagnosis.  
 1024 *Journal of Pain, 17*(9 Suppl), T50-T69. doi:10.1016/j.jpain.2016.03.001
- 1025 Williams, A. C. d. C., & Craig, K. D. (2016). Updating the definition of pain. *PAIN, 157*(11), 2420-2423.  
 1026 doi:10.1097/j.pain.0000000000000613
- 1027 Williams, A. C., & Craig, K. D. (2016). Updating the definition of pain. *Pain, 157*(11), 2420-2423. doi.  
 1028 10.1097/j.pain.0000000000000613
- 1029 Wing, L. (1976). Diagnosis, clinical description and prognosis. In L. Wing (Ed.), *Early childhood autism. 2nd Ed.*  
 1030 Oxford: Pergamon Press.
- 1031 Woolf, C. J. (2011). Central sensitization: Implications for the diagnosis and treatment of pain. *Pain, 152*(3  
 1032 Suppl), S2-15. doi:10.1016/j.pain.2010.09.030
- 1033 Yamamotova, A., Papezova, H., & Uher, R. (2009). Modulation of thermal pain perception by stress and sweet  
 1034 taste in women with bulimia nervosa. *Neuroendocrinology Letters, 30*(2), 237-244.



1035

1036

1037

1038

1039

1040

1041

1042

1043

1044

1045

1046

1047

1048

1049

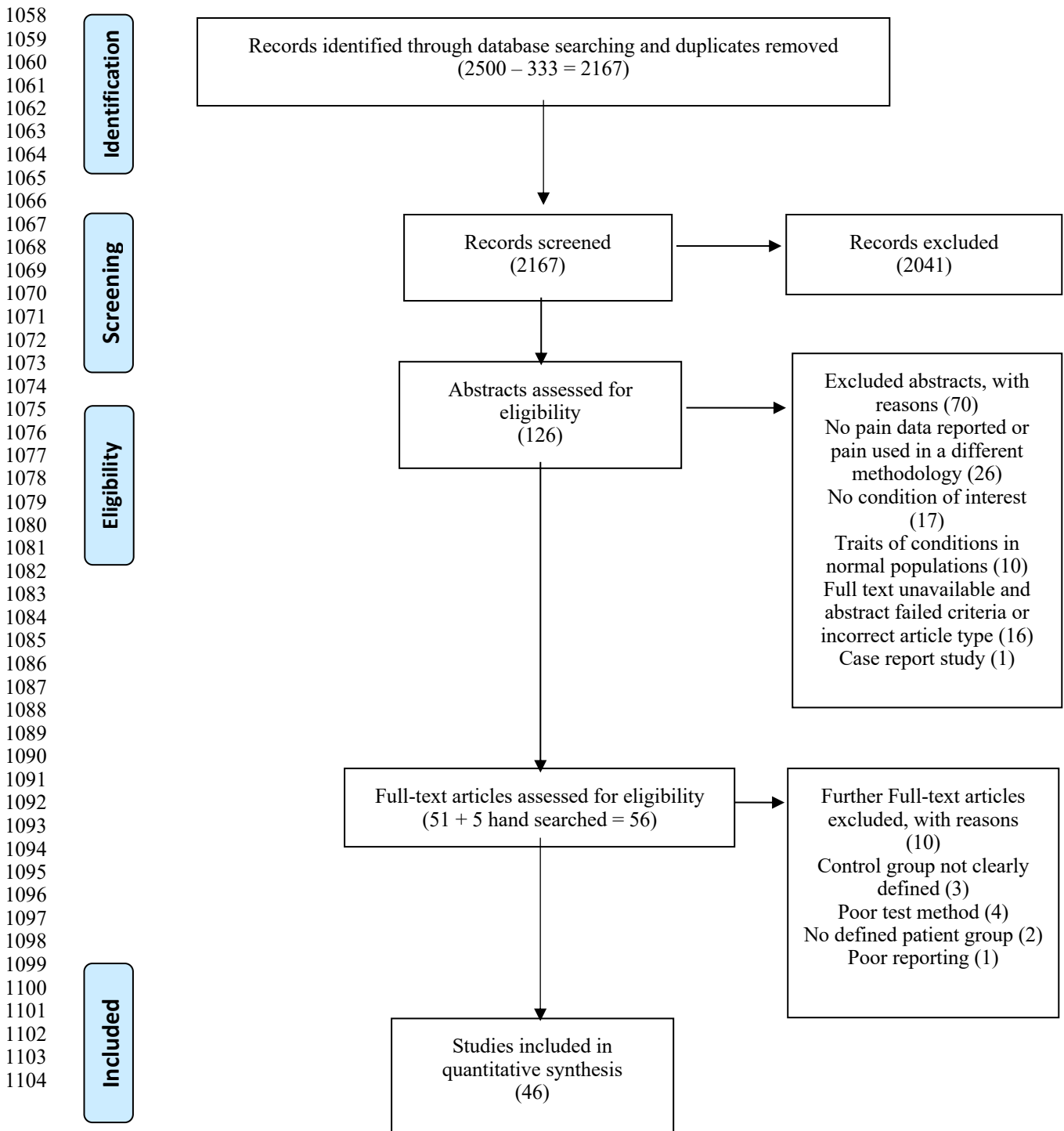
1050

1051

1052

**Figure Legend**

1053  
 1054 Figure 1. Number of identified publications at each phase of the screening process. Adapted  
 1055 from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred  
 1056 Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS  
 1057 Med 6(6): e1000097. doi:10.1371/journal.pmed1000097.



1105  
1106

**Table 1: Electronic search strategy.**

PHASE	TERMS
<p>1. SPECIFIC SEARCH TERMS FOR DSM-5 PSYCHIATRIC CONDITIONS.</p>	<p>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</p>
<p>2. SPECIFIC SEARCH TERMS FOR PAIN/SOMATOSENSATION AND QST.</p>	<p>QST Quantitative Sensory Testing Experimental pain Nociception Nociceptors A<math>\delta</math> 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</p>
<p>3. COMBINATION OF PHASES 1 AND 2.</p>	<p>----</p>
<p>DSM = DIAGNOSTIC STATISTICAL MANUAL QST= QUANTITATIVE SENSORY TESTING</p>	

1107

## Pain in Psychiatric Conditions

1108 **Table 2: Detailed reported results for each study listed by QST test for autism spectrum disorder (ASD).**

Test	Citation	Sample	Control	Matched	Results
<b>CDT</b>	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.
	Fruendt et al. (2017)*	13 ASD	13HC	Age Gender IQ >70	No significant group differences.
<b>WDT</b>	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.
	Fruendt et al. (2017)*	13 ASD	13 HC	AGE Gender IQ >70	No Significant group differences
<b>TSL</b>	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>PHS</b>	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>CPT</b>	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.
	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>HPT</b>	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. 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.

## Pain in Psychiatric Conditions

	Duerdan et al. (2015)*	20 ASD	55 HC	Age Gender	No significant group differences.
	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>MDT</b>	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.
	Fruendt 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.
<b>MPT</b>	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>MPS</b>	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>DMA</b>	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>WUR</b>	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender IQ >70	No significant group differences
<b>VDT</b>	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.
	Guclu et al. (2007)	6 ASD	6 HC	Age Gender	No sig group difference at the unmasked 40Hz, 250Hz unmasked or masked 40Hz.
	Fruendt et al. (2017)*	13 ASD	13 HC	Age Gender	No significant group differences

## Pain in Psychiatric Conditions

				IQ >70	
<b>PPT</b>	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.
<b>ELE</b>	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.
<b>Psychometrics</b>	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.

1109 NOTES: \* indicates standardised DFNS QST protocol used. ASD (Autism Spectrum Disorder), AS (Asperger's) and HC (Healthy Control). CDT (Cold Detection Threshold), WDT (Warm  
1110 Detection Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical Detection Threshold),  
1111 MPT (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection Threshold), PPT (Pressure  
1112 Pain Threshold), and ELE (Electrical Pain Stimulation).

1113 **Table 3: Detailed reported results for each study listed by QST test for Schizophrenia.**

Test	Citation	Sample	Control	Matched	Results
<b>WDT</b>	Jochum et al. (2006)	23 SCH	23 HC	Age Gender Handedness	Significant group differences, Schizophrenic patients indicated perception for warmth later than controls.

## Pain in Psychiatric Conditions

<b>CPT</b>	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.
<b>HPT</b>	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 $\ln\beta$ .
	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.
<b>PPT</b>	Girard et al. (1994)	23 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.
<b>ELE</b>	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)		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.

## Pain in Psychiatric Conditions

		12 SCH			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.
<b>CP</b>	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.
<b>Psychometrics</b>	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.
	Levesque et al. (2012)	12 SCH	11 HC		Pain threshold was negatively correlated with positive symptoms.

1114 NOTES: \* indicates standardised DFNS QST protocol used. SCH (Schizophrenia), BP (Bi-polar) and HC (Healthy Control). CDT (Cold Detection Threshold), WDT (Warm Detection  
1115 Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical Detection Threshold), MP  
1116 (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection Threshold), PPT (Pressure  
1117 Pain Threshold), and ELE (Electrical Pain Stimulation).

1118  
1119  
1120  
1121  
1122  
1123  
1124  
1125  
1126  
1127  
1128  
1129

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

Test	Citation	Sample	Control	Matched	Results
<b>CDT</b>	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.



## Pain in Psychiatric Conditions

<b>WDT</b>	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.
<b>CPT</b>	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.
<b>HPT</b>	**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 $46.7 \pm 0.4^{\circ}\text{C}$ for patients and $44.2 \pm 0.6^{\circ}\text{C}$ 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 20 BN	24 HC	Age Gender	Trend towards BPD having higher thresholds than HC, no significant main effect. 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.
<b>MPS</b>	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.

## Pain in Psychiatric Conditions

<b>ELE</b>	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.
<b>TPD</b>	Pavony & Lenzenweger (2014)*	27 BDP 20 MDD	44 HC		No significant group differences.
<b>CP</b>	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.
<b>Psychometrics</b>	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.

1130 NOTES: \* indicates standardised DFNS QST protocol used. \*\*used both standard and comparable pain induction methods. BPD (Borderline Personality Disorder), PTSD (Post-Traumatic Stress  
1131 Disorder), SIB (Self-Injurious Behaviour), BN (Bulimia Nervosa), MDD (Major Depressive Disorder), OPD (Other Personality Disorder) and HC (Healthy Control). CDT (Cold Detection  
1132 Threshold), WDT (Warm Detection Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical  
1133 Detection Threshold), MPT (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection  
1134 Threshold), PPT (Pressure Pain Threshold), and ELE (Electrical Pain Stimulation).

1135 Table 5: Detailed reported results for each study listed by QST test for eating disorders.

Test	Citation	Sample	Control	Matched	Results
<b>CDT</b>	Pauls et al. (1991)	9 AN 10 BN	10 HC	Gender	No significant group differences.
<b>WDT</b>	Pauls et al. (1991)	9 AN 10 BN	10 HC	Gender	No significant group differences.
<b>HPT</b>	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	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.

## Pain in Psychiatric Conditions

			Coffee Education	
	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.
	Yamamoto 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.
	De Zwaan et al. (1996)	22AN 18BN 32 HC	Gender	Significant group differences for thermal pain thresholds where AN and BN patients had higher thresholds than HC.
<b>PPT</b>	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.

## Pain in Psychiatric Conditions

	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.
<b>VDT</b>	Pauls et al. (1991)	9 AN 10 BN	10 HC	Gender	No significant group differences.
<b>TPD</b>	**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.
<b>Psychometrics</b>	Bar et al. (2013)	19 AN	19 HC	Age Gender Smoking Coffee Education	Significant negative correlation for pain ratings and symptom severity.

1136 NOTES: \* indicates standardised QST protocol used. \*\*used both standard and comparable pain induction. AN (Anorexia Nervosa), BN (Bulimia Nervosa), ED (Eating Disorder), BPD  
 1137 (Borderline Personality Disorder), PTSD (Post-Traumatic Stress Disorder), BED (Binge Eating Disorder), Ob (Obese) and HC (Healthy Control). CDT (Cold Detection Threshold), WDT  
 1138 (Warm Detection Threshold), PHS (Paradoxical Heat Sensations), TSL (Thermal Sensory Limen), CPT (Cold Pain Thresholds), HPT (Heat Pain Threshold), MDT (Mechanical Detection  
 1139 Threshold), MPT (Mechanical Pain Threshold), MPS (Mechanical Pain Sensation), DMA (Dynamic Mechanical Allodynia), WUR (Wind-Up Ratio), VDT (Vibration Detection Threshold),  
 1140 PPT (Pressure Pain Threshold), and ELE (Electrical Pain Stimulation).