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Pain and self-harm: A systematic review

Olivia J. Kirtley [a*], Ronan E. O'Carroll [b] and Rory C. O'Connor [a]

[a] University of Glasgow, Suicidal Behaviour Research Laboratory, Institute of Health and Wellbeing, College of Medical, Veterinary and Life Sciences, University of Glasgow, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow, G12 0XH, United Kingdom

[b] University of Stirling, Division of Psychology, School of Natural Sciences, University of Stirling, Stirling, FK9 4LA, UK.

*Corresponding author:

Dr Olivia J. Kirtley
olivia.kirtley@glasgow.ac.uk
Tel: +44 (0)141 211 3904

Abstract

Background

A growing body of research has explored altered physical pain threshold and tolerance in non-suicidal self-injury (NSSI) and suicidal self-harm. The evidence, however, is inconsistent such that the nature of the relationship is unclear, and whether or not this effect is also present in suicidal self-harm is equivocal.

Methods

A keyword search of three major psychological and medical databases (PsycINFO, Medline and Web of Knowledge) was conducted, yielding 1,873 records. Following duplicate removal and screening, 25 articles were quality assessed, and included in the final systematic review.

Results

There is strong evidence for increased pain tolerance in NSSI, and some evidence for this in suicidal individuals, but notably, there were no prospective studies. The review found a lack of substantive focus on psychological correlates of altered pain tolerance in this population. Several candidate explanatory mechanisms were proposed within the reviewed studies.

Limitations

The current review was a narrative systematic review; methods used to assess pain were considered too heterogeneous to conduct a meta-analysis.

Conclusions

The evidence suggests that there is elevated pain tolerance among those who engage in NSSI. Future prospective research should determine if altered pain tolerance is a cause or a consequence of the behaviour. The identification of psychological correlates of increased pain tolerance is a neglected area of research. It could provide opportunities for treatment/intervention development, if mediating or moderating pathways can be identified. Too few studies have directly investigated candidate explanatory mechanisms to draw definitive conclusions.

Keywords: Self-harm; Suicide; NSSI; Non-suicidal self-injury; Pain

Introduction

Self-harm, defined as "self-injury or self-poisoning irrespective of the apparent purpose of the act" (NICE: National Institute for Health and Care Excellence, 2004, 2011), remains one of the most intriguing behavioural phenomena within psychological medicine. It is a world-wide public health issue and approximately 20,000-30,000 adolescents in the UK receive hospital treatment every year as a result of non-fatal self-harm (Hawton, Rodham & Evans, 2006); a behaviour that appears to go against natural instincts for self-preservation (Tantam & Huband, 2009).

Previous literature has reported self-harm prevalence in the community as ranging from 13.8% in a sample of Scottish adolescents aged 15-16 years old (O'Connor, Rasmussen, Miles & Hawton, 2009) and NSSI prevalence as high as 38% in a sample of American college students (Gratz, Conrad & Roemer, 2002). Generally, self-harm also appears to be more prevalent in females than males (Hawton, Harriss & Rodham, 2010; Nock, Prinstein & Sterba, 2009; O'Connor et al., 2009), although multiple studies have found no significant association between gender and lifetime NSSI (Gratz, 2001; Klonsky, 2011). In adults and adolescents, NSSI and self-harm are prevalent within the general population, but even more so in those who have a psychiatric condition (Hawton, Saunders, Topiwala & Haw, 2013; Jacobson & Gould, 2007; Klonsky, Oltmanns, & Turkheimer, 2003). For adults, NSSI frequently co-occurs with a diagnosis of Borderline Personality Disorder (BPD), however, NSSI has until only very recently been part of the diagnostic criteria for BPD and thus may not be a true reflection of BPD and NSSI co-morbidity (Andover & Gibb, 2010).

A primary function of self-harm appears to be as a method of gaining relief from terrible states of mind; however others have also cited it as a form of self-punishment or as being driven by a wish to die (O'Connor et al., 2009). In addition, Gratz (2003) has reported that those who engage in non-suicidal self-injury (NSSI) feel that it is a method of externalising emotional pain by transforming it into a tangible physical sensation. The exact mechanism or mechanisms that enable self-harm to fulfil these functions however remain, as yet, unclear. (See Klonsky, 2007 for a discussion of this issue). Self-harm appears to overcome the "safety-catch"- the intrinsic mechanism that promotes the avoidance of potentially painful experiences (Tantam & Huband, 2009), which raises the key question of whether those who engage in self-harm may have altered pain threshold and tolerance?

Given the heterogeneous and multiple motives that underpin self-harm (Hawton, Saunders, & O'Connor, 2012), this review set out to include all studies of self-harm irrespective of motivation, as per the NICE guideline definition (2004; 2011), with the specific aim of teasing apart the complex and nuanced relationships that exist between motivations and self-harm behaviour. We also did not restrict the inclusion of studies within this review based upon the types of self-harm behaviours reported by participants, e.g. self-cutting, self-hitting etc. We stress firmly though, that this is not an attempt to homogenise all forms of self-harm into a single category. A key finding of our review, however, was that research in this area has almost exclusively investigated pain threshold and tolerance in NSSI, and thus the data necessitated that our paper focus upon NSSI. Hereafter, we use this term for clarity. In cases where the research pre-dates the introduction of the NSSI term, but where the behaviours described are delineated as being 'non-suicidal' or 'without lethal intent', we have also employed the term NSSI when discussing this research.

Pain

Pain can be defined as the cognitive and affective interpretation of nociception (Tracey, 2008), i.e. a noxious sensory experience (Merksey & Bogduk, 1994). The lowest level of intensity of a stimulus that an individual perceives as painful is their pain threshold, with pain tolerance being the greatest duration or intensity of painful stimuli that one is able to bear (International Association for the Study of Pain, 2012).

Pain and NSSI

A growing body of research has investigated the relationship between pain threshold and tolerance, and NSSI, revealing some interesting, but inconsistent findings. The strength of the evidence for altered threshold and tolerance of physical pain is, therefore, uncertain. Much of the extant research also appears to have been conducted in clinical populations and although there has been a proliferation of studies employing community samples in recent years, whether findings are generalisable across clinical and non-clinical populations is unknown. Several psychological correlates of pain threshold and tolerance have been explored in this population however yet again, the results are sometimes contradictory. As yet, there remains no clear consensus regarding the underlying mechanism for altered pain tolerance in NSSI, nor for how NSSI appears to fulfil an affective regulation function for some individuals. For a discussion of this, see Bresin and

Gordon (2013b) and Kirtley, O'Carroll and O'Connor (2015). Thus, what we actually *know* about the relationship between pain and NSSI is uncertain.

Research aims of this systematic review

Focussing on the areas of ambiguity discussed in the previous sub-section, three key aims for the current systematic review were defined:

1) To evaluate the strengths and limitations of the evidence for/against altered pain threshold and tolerance in NSSI and suicidal self-harm.

2) To identify psychological correlates of altered threshold and tolerance for physical pain.

3) To identify candidate explanatory mechanisms for the phenomenon.

Methods

Search strategy and screening of results

A search of the three key psychological and medical databases was undertaken in March 2014 and updated in September 2015: PsycINFO (1895-September 2015); Medline (1966-September 2015 and Web of Knowledge (1981-September 2015). See Panel 1 and Figure 1 for details.

Inclusion and exclusion criteria

The inclusion criteria were 1) the study must be original, published research, using human participants; 2) the article must be published in the English language; additionally 3) the studies must include a laboratory pain manipulation and a manipulation check, the results of which were analysed as a function of self-harm; and 4) the studies must directly assess self-harm. Studies were included irrespective of the type of self-harm behaviour reported by participants. Studies were excluded if the participants' self-harm was the result of developmental disorder, e.g. Autistic Spectrum Disorder and organic brain dysfunction or dysfunction caused by traumatic brain injury. Studies were not excluded from the review if they had not screened participants for suicidal intent or ideation, as this is an important methodological point to consider when assessing extant research in this area.

Quality assessment

As there is no suitable existing quality assessment tool in this area, a quality assessment framework was designed by the authors based upon O'Connor, Ferguson, Green, O'Carroll & O'Connor (2016), within which studies were evaluated yielding a quality score which was employed to afford greater or lesser "weight" within the review. See Table 1. Initial quality assessment was conducted by the first author, and then each assessment was discussed in detail with all three authors. Disagreements were resolved by discussion until a consensus was reached. Once scored, studies were then ranked from highest to lowest score and divided into quartiles, with higher scores signifying higher quality studies.

Results

The search strategy yielded 25 studies in total, the majority of which (n=15) were cross-sectional (see Table 2) and the remainder were case-control studies (*n*=10); see Table 3). There were no prospective studies and the review yielded only three studies that examined suicidal self-harm. These three studies (Orbach, Mikulincer, King, Cohen & Stein, 1997; Orbach et al., 1996a; 1996b) employed significantly overlapping samples and also included types of self-harm e.g. alcohol intoxication, that were inconsistent with the behaviours generally included under this term. Based upon this, a decision was made to exclude these studies from the review[1]. Consequently, the total number of studies reported upon within this review was 22 (n=15 cross-sectional and n=7 case-control). The heterogeneity of methods employed by the studies precluded meta-analysis, therefore a narrative systematic review is presented here.

Results are separated into findings from cross-sectional studies and findings from case-control studies (as per O'Connor, 2007; McLaughlin, O'Carroll & O'Connor, 2012). They are then further divided into subsections based upon the three aims of the review: strengths and limitations of the evidence, psychological correlates and candidate explanatory mechanisms.

[1] For the interested reader, Orbach et al (1997) found higher pain threshold, tolerance and sensory detection threshold in adolescents who had attempted suicide, relative to health controls. Higher hopelessness was associated with higher pain threshold and greater dissociation with higher sensation threshold. Orbach et al (19961; 1996b) found increased tolerance for electric shock pain in adults who had attempted suicide, compared to healthy controls. Greater hardiness was associated with lower pain ratings in those with a suicide attempt and accidental injury compared to healthy controls (Orbach et al, 1996b).

Cross-sectional studies

Results of quality assessment for cross-sectional studies

Following application of the quality assessment framework, only five studies fell within the top two quartiles, scoring seven or above: Gratz et al., (2011); Hooley, Ho, Slater and Lockshin (2010); Hooley & St Germain (2014); Ludäscher et al., (2009); and St Germain and Hooley (2013). These studies were consequently given more weight within the review, relative to the other cross-sectional studies included. For full details of the quality assessment outcome for each study, see Table 2.

Sample characteristics: Ethnicity, age and gender

Six of the cross-sectional studies reported information regarding participants' ethnicity (Bresin & Gordon, 2013a; Franklin et al., 2012, 2011; Gratz et al., 2011; Russ et al., 1999; Weinberg & Klonsky, 2012). The majority of participants across all samples were White. All cross-sectional studies employed adult samples.

Recent studies increasingly used mixed-gender samples but seven studies recruited exclusively female samples (Kemperman et al., 1997; Ludäscher et al., 2009; Niedtfeld et al., 2010; Russ et al., 1999; 1994; 1992; Schmahl et al., 2004). Given the consistent over-representation of females within self-harm populations (e.g. O'Connor et al., 2009), this was to be expected.

Sample population

Eight of the cross-sectional studies used community samples (predominantly undergraduate students) and 7 recruited participants from psychiatric populations, most commonly patients with a diagnosis of Borderline Personality Disorder (BPD). Only five of the studies employing community samples included some form of assessment of psychiatric symptomatology (Gratz et al., 2011; Hooley et al., 2010; Hooley & St Germain, 2014; St Germain & Hooley, 2013; Weinberg & Klonsky, 2012). All found depression and BPD symptomatology to be elevated in the NSSI groups relative to controls. Dissociative symptoms were also elevated in the NSSI group (Hooley at al., 2010). None, however, found an effect of psychiatric symptomatology upon pain threshold or tolerance.

Type of NSSI

Cutting, severe scratching, skin scraping, and burning were the most common forms of NSSI reported (Bresin & Gordon, 2013a; Franklin et al., 2012; 2011; Gratz et al., 2011; Hooley et al., 2010; Ludäscher et al., 2009; Niedtfeld et al., 2010; Weinberg & Klonsky, 2012). Only Hooley and colleagues (2010) included type of NSSI as a variable within their analyses and found no significant effect of NSSI type upon pain threshold or pain endurance, however subgroups were potentially too small (n=15) to allow reliable analysis.

Recency of NSSI

There were marked differences between studies in terms of how they classified *current* NSSI. Bresin and Gordon (2013a) and Gratz et al. (2011) set inclusion criteria of at least one episode of NSSI within the past year, whereas Ludäscher et al. (2009) and Russ et al. (1999) used criteria of one and three episodes respectively, within the last 6 months. Hooley et al. (2010) and St Germain and Hooley (2013) stipulated participants must have engaged in NSSI within the last month. Two studies used a precursor to the DSM-5 (section three) diagnosis for further study criteria for NSSI of five or more episodes, instead using more than 6 episodes within the last year (Franklin et al., 2012, 2011). Others used lifetime history of self-injury (Kemperman et al., 1997; Niedtfeld et al., 2010; Russ et al., 1994; 1992; Weinberg & Klonsky, 2012) and the remaining 2 studies did not specify. With the exception of Ludäscher et al. (2009)- for which recency of NSSI was their primary dependent variable- no other studies examined the effect of NSSI recency upon pain threshold or tolerance.

Measurement of NSSI

Only half of the cross-sectional studies used a standardised measure to assess NSSI (see Table 2).

Suicidality

One study did not specifically state whether or not participants had a history of previous suicide attempts (Niedtfeld et al., 2010). Hooley et al. (2010), Hooley and St Germain (2014) and St Germain and Hooley (2013) were the only cross-sectional studies to actively

screen and exclude participants from the NSSI groups based on the suicidal intent of their self-harm. The remaining eleven studies all defined self-harm as being without suicidal intent, i.e. NSSI, however they did not report that suicidal intent was one of their exclusion criteria. No standardised measure of suicidal ideation was administered in any of the 15 cross-sectional studies.

Strengths and limitations of the evidence for altered pain threshold and tolerance in NSSI

Most studies measured pain threshold only (n=4), with the remainder measuring both threshold and tolerance (n= 3) and three measuring pain threshold and pain endurance (see Table 2). Other studies assessed pain via self-reported measures of intensity and unpleasantness (n= 3) or intensity and affect (n=1). One study (Weinberg & Klonsky, 2012) asked participants to indicate a point at which the stimulus was painful, but tolerable, which could perhaps be thought of as a midpoint between threshold and tolerance.

Across all of the cross-sectional studies, those who engaged in NSSI exhibited a higher pain threshold than healthy controls. Those with a history of NSSI demonstrated a higher threshold for and endurance of pain than controls (Hooley et al., 2010; Hooley & St Germain, 2014; St Germain & Hooley, 2013), although when Hooley et al. (2010) controlled for psychotropic medications, only pain endurance remained significantly different. Of the four studies that measured pain tolerance, all but one found that the NSSI group exhibited significantly higher pain tolerance than healthy controls (Franklin et al., 2011), however, one study found tolerance to be increased only under conditions of distress (Gratz et al., 2011). Those who engaged in NSSI chose higher (more intense) levels of electric shock stimuli than control participants, although they did not report greater subjective levels of pain (Weinberg & Klonsky, 2012), but conversely, no effect of NSSI was found upon pain intensity pre or post mood induction in the study by Bresin and Gordon (2013a). None of the studies by Russ and colleagues (1999; 1994; 1992) assessed pain threshold or tolerance, but instead recorded participants' self-reported feelings of pain intensity, unpleasantness ("hedonics") and mood. Participants who reported experiencing no pain during NSSI reported significantly lower pain intensity and unpleasantness than controls (Russ et al., 1999; 1992).

Pain induction method, pain threshold and pain tolerance

Several methods were used to induce pain, although irrespective of the wide array of different pain induction methods used, pain threshold and tolerance do not appear to differ noticeably as a function of method. The majority of studies utilised the Cold Pressor Test (CPT), whereby participants submerge their hand, up to the wrist, in thermostatically cooled or ice water (Franklin et al., 2012; 2011; Gratz et al., 2011; Russ et al., 1999; 1994). Temperatures ranged widely, from 0.5° C (Gratz et al., 2011) to 10° C (Russ et al., 1999, 1994, 1992). Other work has used thermal (Bresin & Gordon, 2013a; Kemperman et al., 1997; Ludäscher et al., 2009; Niedtfeld et al., 2010) and laser techniques (Schmahl et al., 2004), which apply heat in timed pulses to the skin. Similarly electric shock stimuli, employed by Weinberg and Klonsky (2012), were also delivered in timed pulses to the skin. Three studies used a pressure algometer (Hooley et al., 2010; Hooley & St Germain, 2014; St Germain & Hooley, 2013), a device for assessing the force or pressure required to reach pain threshold or tolerance (Kinser, Sands & Stone, 2009) and one experiment used a combination of the CPT and the algometer (Gratz et al., 2011) to assess pain threshold and tolerance.

Gender, pain threshold and pain tolerance

There was some evidence that males exhibited a higher pain tolerance than females (Gratz et al., 2011) although other studies did not find this (Franklin et al., 2012, 2011; Hooley et al., 2010; Hooley & St Germain, 2014) Weinberg and Klonsky, 2012). One further study that used a mixed-gender sample (Bresin & Gordon, 2013a) did not investigate gender effects within the analyses and the remainder used only female participants.

NSSI characteristics, pain threshold and pain tolerance

The majority of cross-sectional studies did not explore whether there was a significant association between pain threshold and the length of time participants had been engaging in NSSI. Of those that did, only Hooley et al. (2010) found that individuals who had been engaging in NSSI for longer exhibited a higher pain threshold and this effect did not extend to pain endurance. Ludäscher et al. (2009) examined pain perception in those who had formerly engaged in NSSI, currently engaged in NSSI, and healthy controls, finding that those who currently engaged in NSSI had the highest pain threshold, followed by those who used to engage in NSSI, and healthy controls.

Psychological correlates of altered pain threshold and tolerance

Psychological characteristics

All but two of the cross-sectional studies (Hooley & St Germain, 2014; Schmahl et al., 2004) assessed psychological variables in their research (see Table 2 for details). The focus, however, was predominantly upon hopelessness, depression and dissociative experiences as opposed to broader individual differences such as perfectionism or neuroticism, and there was little to no substantive focus on the relationship between psychological factors, and pain threshold and tolerance. Two studies examined difficulties with emotion regulation (Franklin et al., 2012; Weinberg & Klonsky, 2012), however only Franklin and colleagues (2012) found any significant relationship: both higher pain threshold and tolerance were strongly correlated with high emotion dysregulation and emotion dysregulation was a moderator of the relationship between NSSI and pain tolerance.

Mood

Several studies manipulated participants' affect/stress levels. Using a highly personalised negative mood-induction, whereby participants were asked to describe interpersonal situations during which they felt distressed, Gratz et al., (2011) found that pain tolerance in the NSSI group increased only during distress. Hooley and St Germain (2014) used a positive self-worth manipulation, in which participants were asked to identify 'positive characteristics' from a checklist that they thought may apply to themselves. Following this manipulation, participants in the NSSI group displayed a marked reduction in pain endurance relative to baseline.

Candidate explanatory mechanisms for altered pain threshold and tolerance in NSSI

Findings in relation to potential explanatory mechanisms for elevated pain threshold and tolerance in NSSI are scant. Five studies cite endogenous opioids as candidate mechanisms for increased pain threshold and tolerance in NSSI (Ludäscher et al, 2009; Schmahl et al, 2004; Kemperman et al, 1997; Russ et al, 1992; 1994), however none test this mechanism directly, such as by measuring endogenous opioid levels with blood plasma sampling or by Positron Emission Tomography (PET) imaging.

Endogenous opioids

Ludäscher et al. (2009) discussed three possible explanations for the phenomenon. First, that the differences in pain threshold are the result of differences between subgroups of people with BPD. Second, that pain insensitivity is produced by habituation as a consequence of repeated activation of the endogenous opioid system (EOS) by self-injuring. Thus resulting in pain threshold "normalising" following cessation of NSSI behaviour. Third, that improvement in BPD symptomatology results in the normalisation of pain perception.

Russ et al., (1992) suggested that the dual presence of altered mood and insensitivity to pain is indicative of neural mechanisms such as the release of endogenous opioids. This is further explored in a later study (Russ et al., 1994), using the opioid antagonist naloxone in an attempt to block the analgesia observed during administration of painful stimuli to individuals with BPD who engage in NSSI. No effect was found, however.

The "defective-self" hypothesis

Hooley and colleagues (2010) investigated a *post-hoc* hypothesis that those who engaged in NSSI would feel more deserving of punishment and be more likely to consider themselves to be bad people than controls and that this would be associated with pain tolerance. They reanalysed their pain results as a function of 'self-rating': a brief measure of self-criticism developed by the researchers. The results confirmed their hypothesis, demonstrating that feelings of worthlessness, social ineptitude and guilt were significantly associated with pain endurance and that those with the strongest belief in their lack of worth, also exhibited the highest pain endurance. No association was found between SRS score and pain threshold. Based on this, Hooley et al (2010) proposed the "defective self theory"; that pain endurance is higher in those who injure themselves because they feel as though they deserve the pain and that the elevation in mood observed post-NSSI, is the result of the self-affirmation derived from experiencing pain. Hooley and St Germain (2014) give further weight to this theory by demonstrating that a positive self-worth manipulation could reduce endurance for physical pain in those who have engaged in NSSI; when individuals feel more positively about themselves, elevated pain endurance does not appear to be present.

Case-control studies

Results of quality assessment for case-control studies

Overall, the case-control studies were of higher quality than the cross-sectional studies and the majority scored seven or higher in the quality assessment, see Table 3 for full quality assessment scores for each study.

Sample characteristics: Ethnicity, age and gender

Only two of the case control studies (Franklin et al., 2010; Glenn et al., 2014) reported any information regarding participants' ethnicity, with their sample being predominantly European American.

One study employed an adolescent sample (Glenn et al., 2014). The findings from this study did not appear to deviate from studies that used adult samples.

The three studies including inpatients used predominantly female samples (Bohus et al., 2000; Magerl et al., 2012; Schmahl et al., 2006), as did Franklin and colleagues (2010).

Sample population

One sample was derived from consecutive psychiatric hospital admissions (Bohus et al., 2000), whereas Schmahl et al. (2006) used only those BPD patients who reported partial or complete analgesia during episodes of NSSI. Little information is reported by Magerl et al. (2012) regarding recruitment of BPD patients, however all but two were inpatients at the time of participation. Four recent case-control studies used community samples (Franklin et al., 2010; Glenn et al., 2014; Hamza et al., 2014; McCoy et al., 2010). Of these, two included measures of psychiatric symptomatology (Glenn et al., 2014; Hamza et al., 2014), but only Glenn and colleagues (2014) reported the results: 64.6% of the sample met the criteria for at least one psychiatric disorder, with anxiety, mood disorders, and alcohol and substance use disorders being the most prevalent. There was no effect of psychiatric symptomatology upon pain threshold or endurance.

Type of NSSI

The majority of participants within the community sample studies endorsed cutting and self-hitting as the most common types of NSSI (Franklin et al., 2010; Glenn et al., 2014; Hamza et al., 2014) and within the latter two studies, self-pinching, severe scratching as well as self-hitting were also reported. Little information was given by Bohus et al.

(2000), Magerl et al. (2012) or Schmahl et al. (2006) regarding the type of self-injury that participants engaged in, although cutting and burning are listed among the methods used.

Recency of NSSI

Only Magerl et al. (2012) found an effect of recency of self-injury upon pain, with individuals who had last self-injured more than one year ago, demonstrating pinprick pain thresholds comparable to controls.

Measurement of NSSI

Three case-control studies assessed NSSI by means of self-report (Bohus et al., 2000; Franklin et al., 2010; Magerl et al., 2012) and Franklin et al. (2010) also used the FASM (Lloyd et al., 1997). Bohus et al. (2000) set an inclusion criterion of at least 3 episodes within the last two years and Franklin et al. (2010) used more than 6 episodes in the last year as their inclusion criterion. Magerl et al. (2012) used data from medical notes in addition to self-report and visual inspection of participants' injuries/scars to access lifetime history and recency of last episode. Schmahl et al. (2006) did not specify how recent participants' self-injury was.

Suicidality

Bohus et al. (2000) specifically define the behaviours of participants included within their study as being of non-suicidal intent, although lifetime or current suicidal behaviour is not mentioned in their exclusion criteria. Similarly, the three studies using community samples specify behaviours included as being NSSI, but do not assess whether participants have also engaged in self-harm with the intention of ending their life (Franklin et al., 2010; Glenn et al., 2014; Hamza et al., 2014).

Strengths and limitations of the evidence for altered pain threshold and tolerance in NSSI

There was great variation in pain outcome variables investigated within the case-control studies: three measured both threshold and tolerance (Bohus et al., 2000; Glenn et al., 2014; Hamza et al., 2014) and the other 4 either threshold *or* tolerance only. One study estimated pain tolerance from pain intensity ratings (Magerl et al., 2012). All of the studies

that assessed pain threshold found that the NSSI group demonstrated a significantly higher pain threshold than healthy matched controls. McCoy et al. (2010) found the NSSI group to have a higher pain threshold than controls on the first trial, but did not find a significant difference between groups on the two subsequent threshold trials or between the mean thresholds of the two groups; potentially suggesting that multiple trials result in habituation.

Two studies found significant between-group differences for pain tolerance (higher in NSSI group) (Glenn et al., 2014; Hamza et al., 2014). Bohus and colleagues (2000), however, did not find significant between-group differences for pain tolerance.

Pain induction method, pain threshold and pain tolerance

Methods of inducing pain were heterogeneous. One study used heat stimuli (Schmahl et al., 2006) Two studies used multimodal pain assessment, one employing the CPT for pain threshold and the Tourniquet Pain Test (TPT) for pain tolerance (Bohus et al., 2000) and Magerl et al. (2012) using chemical pain (intradermal capsaicin injection) and mechanical pain (pinprick stimuli). Franklin et al. (2010) and Hamza et al. (2014 used the CPT and Glenn et al. (2014) and McCoy et al., (2010) used the pressure algometer. Despite the heterogeneity of pain induction methods, there appears to be no marked differences in pain outcome as a function of the way in which pain was induced.

Gender, pain threshold and pain tolerance

Females were overrepresented in many of the studies using inpatients samples (e.g. Bohus et al., 2000) and in Franklin et al.'s (2010) community sample, therefore for the most part, any analysis of pain variables as a function of gender were precluded. Glenn et al. (2014) and Hamza et al. (2014) matched cases and controls for gender and therefore did not conduct further analyses based upon gender. McCoy et al. (2010) used a mixed-gender sample, however did not investigate effects of gender within the analyses.

NSSI characteristics, pain threshold and pain tolerance

The two most recent studies investigated the effect of NSSI frequency upon pain endurance and tolerance, but found no effect (Glenn et al., 2014; Hamza et al., 2014). Other work by Magerl and colleagues (2012) investigated the effect of NSSI history and

frequency upon mechanical and chemical pain ratings, finding a positive correlation between recency of NSSI and estimated thresholds for both pain modalities.

Psychological correlates of altered pain threshold and tolerance

Psychological characteristics

Again, there was little substantive focus on the relationship between psychological variables and altered pain threshold or tolerance within the case-control studies. Two studies assessed dissociation (Bohus et al., 2000; Schmahl et al., 2006), but found no significant association between dissociation. See Table 3 for details.

Mood

Bohus et al., (2000) was the only study to find any effect of mood upon pain, with BPD patients who had engaged in NSSI having a higher threshold for pain during self-reported distress than calmness.

Candidate explanatory mechanisms for altered pain threshold and tolerance in NSSI

Few explanations are put forward by the case-control studies for the mechanisms that may underlie altered pain threshold and tolerance in those who engage in NSSI.

Self-punishment and self-criticism

Hamza et al. (2014) compared individuals who engage in NSSI with a motive of self-punishment, to those who engaged in NSSI with alternative motivations (excluding suicide). Individuals who endorse self-punishment as their primary reason for engaging in NSSI exhibited a significantly higher pain tolerance than those who did not use NSSI as a means of self-punishment. The authors suggest that individuals are willing to tolerate more pain because of their high levels of self-criticism, i.e. they believe they are receiving a "just" punishment.

A significant association between high self-criticism and higher pain tolerance was found in the study by Glenn and colleagues (2014), even when controlling for NSSI. They also

suggest that feelings of low self-worth are a key factor in determining pain tolerance in those who engage in NSSI behaviour.

Discussion

This systematic review set out to examine the extant literature regarding the relationship between self-harm and pain threshold and tolerance, with a view to accomplishing three key aims: 1) to evaluate the strengths and limitations of the evidence for/against altered pain threshold and tolerance in NSSI and suicidal self-harm; 2) to identify psychological correlates of altered threshold and tolerance for physical pain; and 3) to identify candidate explanatory mechanisms for the phenomenon. A key finding of the review was that, with the exception of three overlapping studies by Orbach and colleagues (1997; 1996a; 1996b), research had exclusively investigated pain threshold and tolerance in NSSI. Thus, whilst we set out to review all studies of pain and *self-harm* (irrespective of suicidal intent), the data necessitated our review focus solely upon NSSI.

Strengths and limitations of the evidence altered pain threshold and tolerance in those who engage in NSSI

Overall, the evidence suggests that those who engage self-injure without suicidal intent have an increased threshold and tolerance for physical pain. Individuals who engage in NSSI demonstrate higher pain tolerance in response to a wide variety of different pain modalities, including the CPT (Franklin et al., 2012; 2011), pressure algometer (Gratz et al., 2011; Hooley et al., 2010; Hooley & St Germain, 2014), and electrical pain (Weinberg & Klonsky, 2012). This would also suggest that there does not appear to be a significant effect of pain measurement modality upon pain outcome measures within this population. Two studies found no significant differences in pain tolerance at all between control and experimental groups (Bohus et al., 2000; Franklin et al., 2011). The absence of significant between-group differences in pain tolerance reported by Bohus et al. (2000) and Franklin et al. (2011) is perhaps surprising, but the number of participants within the NSSI groups was small in both studies, potentially masking any genuine differences as a result of low statistical power.

Evidence for an association between pain threshold or tolerance and the length of time a person has been engaging in NSSI is mixed. Only two studies found an association

between frequency or length of NSSI history (Hooley et al., 2010; Magerl et al., 2011), however no other studies found such an effect. The conflicting findings regarding length of time individuals had been engaging in NSSI and pain threshold or tolerance may be due to the wide variation in lifetime frequency of NSSI episodes, e.g. Bresin and Gordon (2013a) reported frequency as ranging from 1-1000 lifetime episodes of NSSI and Kemperman et al. (1997) found large variations in age of onset of NSSI. An important, but neglected issue within the literature, is whether pain threshold and tolerance may differ as a function of NSSI repetition. Future studies should investigate potential differences in pain tolerance in individuals with high compared to low volume repetition.

Ludäscher et al. (2009) compared current and former NSSI groups, finding that those who were engaging in NSSI behaviours at the time of the study had the highest pain threshold. Those who no longer self-injured had a lower threshold, but it was still higher than controls. These data may suggest that pain threshold varies depending on the recency of NSSI. There was marked variation in how 'current' participants' NSSI was, ranging from within the last six months (Ludäscher et al., 2009) to lifetime episodes (Kemperman et al., 1997; Niedtfeld et al., 2010; Russ et al., 1994; 1992; Weinberg & Klonsky, 2012) and some studies do not even report this (e.g. Bresin & Gordon, 2013a). The findings from Ludäscher et al., (2009) demonstrate that there may be an important relationship between recency of NSSI and response to behavioural measures of pain threshold. Furthermore, they may be indicative of a temporal aspect to altered pain threshold within this population; potentially it is a short-lived, temporary phenomenon, specific to periods of high distress, as opposed to a stable trait. The results from the study by Gratz and colleagues (2011) would strongly support this; the study found elevated pain tolerance in the NSSI group, relative to controls, only following a distress manipulation. Additionally, Hooley and St Germain (2014) found that pain endurance in NSSI could be modified by administration of a positive self-worth manipulation. It would be useful therefore, for future studies to report information on recency of NSSI, as well as investigating the change in pain threshold and tolerance across an individual's lifetime using a prospective design.

Methods of pain induction

Whilst there do not appear to be differences in the results as a function of how pain was induced, the heterogeneity of the methods employed within this area warrants further mention. Comparison across studies is problematic due to the multitudinous different methods of testing pain threshold and tolerance. For example, the sustained exposure to the

nociceptive stimuli involved in the CPT would undoubtedly produce a distinctly different pain experience to the timed delivery of rapid thermal pulses used in other studies (e.g. Schmahl et al., 2006), potentially raising a question regarding the ecological validity of some pain induction methodologies in this population. Franklin et al. (2012; 2011; 2010) use a temperature of 2°C, citing this temperature as a more effective proxy for NSSI, due to the more acute pain generated by such cold water. Russ et al (1992; 1994), on the other hand, used a temperature of 10°C for their CPT. Regardless of temperature, however, the diffuse nature of CPT pain may still make it a less valid proxy for NSSI than methods which produce a more localised pain. The extreme differences in CPT temperatures employed across the different studies makes comparison of results difficult, and it may be that observed differences in pain tolerance are a function of the individual CPT temperature, as opposed to NSSI. Selecting a CPT temperature that allows individuals to keep their hand immersed in the water long enough to provide meaningful data, whilst also ensuring that this temperature is sufficient to induce pain, is a significant challenge.

A number of recent studies have employed varying forms of pressure algometer (Glenn et al., 2014; Gratz et al., 2011; Hooley & St Germain, 2014). The algometer used by Gratz et al (2011) is self-applied, with the participant gradually pressing the device down onto their hand. The algometer used in Glenn et al (2014) and studies by Hooley and colleagues (Hooley et al., 2010; Hooley & St Germain, 2013; St Germain & Hooley, 2013) is quite different, taking the form of a weighted hinge into which participants insert their finger; the pressure remains constant throughout. Even though these two studies employ the same method of pain induction, the pressure algometer, the experience of pain may be fundamentally different. Results from the handheld pressure algometer may be vulnerable to artefacts resulting from participants' strength and ability to maintain a constant pressure with the device, causing underestimates of participants' pain threshold and tolerance. Whilst participants are in full control of the hinge algometer, it cannot be said that this is self-applied pain. It does, however, remove some of the variability, i.e. participant strength, which occurs with the handheld algometer, but may result in greater response latency as time is the only variable and the pressure remains consistent throughout. Heat and electrical pain methods were also employed in some studies (e.g. Bresin & Gordon, 2013a; Weinberg & Klonsky, 2013). Whilst these methods offer a high degree of stimulus controllability, delivering timed pulses of heat or shock to the skin, they are not self-applied, and in comparison to cold pressor or ischemic pain, have been rated as less unpleasant (Rainville, Feine, Bushnell, & Duncan, 1992). They also correlate only modestly with pressure and ischemic pain (Bhalang, Sigurdsson, Slade & Maixner, 2005).

The inconsistencies between the findings of previous studies could be a function of pain measurement method. There is no 'gold standard' of pain measurement for research within this population; more basic science research focusing upon the methodological aspects of measuring pain in individuals who self-harm is essential, and has thus far been completely neglected.

Russ and colleagues (1992; 1994; 1999) made no behavioural assessment of pain tolerance, such as CPT termination latency, in any of their three studies included within this review, as is the case for Bresin and Gordon (2013a). Franklin et al (2010) also make no assessment of threshold or tolerance, despite participants being administered threshold and tolerance procedures. Task termination latency (time, temperature, pressure or voltage) should be included as a behavioural measure of pain tolerance for all pain modalities.

Additionally, not all studies assessed both threshold and tolerance, with some testing only threshold (e.g. Ludäscher et al., 2009; Niedtfeld et al., 2010; Schmahl et al., 2004) or estimated threshold (Magerl et al., 2012). Weinberg and Klonsky (2012) assessed a midpoint level where the stimulus was painful but tolerable, which raises an interesting point: in using pain tolerance as a proxy for NSSI we are assuming that when an individual self-injures, they are inflicting pain at the maximum level of their tolerance, when this may not in fact be the case. Both threshold and tolerance measures should still be included as standard in future research, but a better proxy for NSSI may be to administer stimuli that are painful but tolerable, as per Weinberg and Klonsky (2012), and to assess pain endurance: the difference between threshold and tolerance. Overall, the relationship between NSSI and increased pain *tolerance* would appear to be stronger compared to the relationship between NSSI and increased pain *threshold*.

Sample and Design Limitations

Sampling and design limitations do impact significantly upon the quality of the evidence for both case-control and cross-sectional studies.

Sample

The clinical studies included within this review all used samples of individuals with BPD, and as such are a distinct group relative to those with other types of psychiatric disorder.

Prevalence estimates for BPD range from 1% (Lenzenweger, 2008) to 5.9% of adults (Grant et al., 2008). Those with BPD experience a range of symptoms, particularly impulsivity, difficulties with emotion regulation and trouble with interpersonal relationships (Leichsenring, Leibing, Kruse, New & Leweke, 2011). Undoubtedly, the overrepresentation of individuals with BPD in the pain and self-harm literature is that, until recently, NSSI existed most prominently as part of the diagnostic criteria for BPD (Andover & Gibb, 2010). Whether or not the altered pain threshold and tolerance that accompanies NSSI is independent of BPD, is uncertain. Furthermore, as only 6 of the 13 studies conducted in non-clinical community samples made any assessment of psychiatric history, these studies also cannot provide a definitive answer to this question. None, however, found a significant effect of psychiatric symptomatology upon pain threshold or tolerance.

A significant proportion of previous research examining pain and NSSI has focused solely upon psychiatric populations - as is the case for much self-harm research (Hawton, Harriss & Rodham, 2010)- and almost exclusively on patients with BPD (e.g. Bohus et al., 2000; Magerl et al., 2012; Russ et al., 1999; 1994; 1992; Schmahl et al., 2006; 2004), however, not all who engage in NSSI meet the diagnostic criteria for BPD (Selby, Bender, Gordon, Nock & Joiner, 2012). Some individuals presenting to hospital following self-harm do not have a psychiatric disorder (Barr, Leitner & Thomas, 2004), although the majority do, exhibiting affective disorders such as depression and anxiety (Haw, Hawton, Houston & Townsend, 2001; Hawton et al., 2013). Future studies should continue to explore altered pain threshold and tolerance within non-clinical samples, and in clinical groups other than those with diagnoses of eating disorder or BPD. Affective disorders such as depression, have been found to alter pain perception in those without a history of self-harm (Dickens, McGowan & Dale, 2003), therefore another highly fruitful line of enquiry is to explore psychiatric disorder as a substantive variable within the relationship between self-harm and pain tolerance.

Females are consistently overrepresented in the samples of studies in this area, and thus we cannot generalise findings regarding altered pain threshold and tolerance in NSSI to males. Some studies have attempted to statistically control for this in their analyses, but with such vast differences in the gender composition of study samples in some cases, such controls may not be meaningful. Additionally, as gender differences in pain threshold and tolerance

are also dependent upon the modality of pain assessment (Racine et al., 2010), this could have significant further implications for the generalisability of study findings.

A key further consideration regarding sample limitations is that none of the studies included a specific measure of suicidal ideation or behaviour. Three cross-sectional studies specifically excluded participants at the recruitment stage if they reported a history of suicidal behaviours (Hooley et al., 2010; Hooley & St Germain, 2014; St Germain & Hooley, 2013). The remaining studies specified that participants had carried out self-harm behaviours 'without lethal intent' (e.g. Bohus et al., 2000), or employed the NSSI definition criteria of '5 or more episodes of self-injury without suicidal intent' (e.g. Franklin et al., 2011; 2012). Crucially though, nothing is known about whether participants may also have experienced suicidal ideation or made suicide attempts *in addition to* their reported NSSI behaviours. Thus, the samples within these studies are potentially NSSI by default only, representing a significant confound across the spectrum of extant research in this area.

Design

In addition to sampling limitations, there are also considerable design limitations, with the majority of the studies reviewed here being cross-sectional (n=15) and only 7 being case-control. The complete absence of prospective studies from the literature means that our knowledge regarding the causal relationship between NSSI and increased pain threshold and tolerance is incomplete. There is an urgent need, therefore, for prospective studies to be conducted.

Psychological and Physiological Correlates of Altered Pain Threshold and Tolerance in NSSI

Around half of the studies included within the review actually make a formal assessment of NSSI using a validated and standardised measure. Whilst the samples used in the studies reviewed herein can be dichotomised almost evenly into those drawn from inpatient clinical populations and those from the community, it is evident that as a group, those who engage in NSSI are far from homogenous and the lack of formal NSSI assessment could potentially mean that important and more nuanced associations between altered pain threshold and tolerance and other characteristics that are present within the population, are being overlooked. It is recommended therefore that future research include

a validated measure of NSSI in order to better ascertain potential correlates of altered pain threshold and tolerance, such as frequency, severity, and method of NSSI.

There are numerous psychological variables that have been reliably associated with suicidal and non-suicidal self-harm (see O'Connor & Nock, 2014 for discussion) and yet these are noticeably absent from the majority of studies within this review. Only the most recent studies (Franklin et al., 2012; Glenn et al., 2014; Hamza et al., 2014; St Germain & Hooley, 2013) devote any substantive focus to the relationship between psychological variables and pain tolerance. A previous study (Schmahl et al., 2006) demonstrated that altered pain threshold and tolerance do not appear to be the result of a physical lack of ability to perceive sensations (painful or otherwise) and the weight of the extant evidence would increasingly point to cognitive-affective mechanisms that underlie this phenomenon. Particularly, emotion dysregulation (Franklin et al., 2012) and self-critical beliefs (Glenn et al., 2014; Hamza et al., 2014; Hooley et al., 2010; Hooley & St Germain, 2014) appear to be lines of investigations that may bear considerable fruit. Based upon these findings, we argue that it is critical that we begin to dedicate more serious attention to exploring psychological variables that may mediate or moderate the relationship between NSSI and increased pain tolerance.

Candidate Explanatory Mechanisms

Ludäscher et al (2009) put forward several potential explanations for the phenomenon of altered pain threshold in individuals who self-injure, including that findings were the result of differences between different subgroups of BPD patients and that improvement in BPD symptoms led to a "normalisation" of pain threshold in their group of individuals who had formerly engaged in NSSI. As several studies have demonstrated altered pain threshold and tolerance in community samples (e.g. Gratz et al, 2011; McCoy et al, 2010; Hooley et al, 2010), the observed differences are unlikely to be the result of either of these explanations. Much more likely is the third explanation they present, that of habituation via endogenous opioid mechanisms of analgesia. Russ and colleagues (1994) were the only group to investigate the potential role of the endogenous opioid system in altered pain threshold and tolerance, but found no significant differences between the naloxone and saline conditions. As a possible explanation for this finding, they argue that the CPT is not sufficient to result in endogenous opioid activity (Bullinger et al, 1984); an idea that is also supported by more recent evidence (Kotlyar et al, 2008; Ring et al, 2007) finding no significant differences in self-reported pain ratings between

naloxone and placebo conditions in samples of healthy and hypertensive adults respectively. This raises two interesting issues: firstly, that no further investigation of the role of endogenous opioids in altered pain threshold or tolerance has been made in this population since Russ et al's (1994) study, even using a different pain modality and secondly, that literature regarding the effects of different painful stimuli used in the laboratory upon endogenous opioid analgesia, even in normative populations, is virtually non-existent (Kirtley et al., 2015). Particularly as there is little correlation between sensitivity to different laboratory-based methods of inducing pain (Nielsen, Staud & Price, 2009), this review strongly recommends that further basic science research be conducted to determine which methods of experimentally inducing pain provide the most reliable elicitation of endogenous opioid activity. Without such knowledge, considerable research energy may be wasted by employing methods that do not produce measurably significant changes in pain outcome variables, e.g. endorphin levels. An endogenous opioid mechanism of analgesia would seem promising and may provide psychobiological explanation for how NSSI fulfils its function of relieving emotional pain and terrible states of mind; with the endogenous opioids released in response to the physical pain of NSSI, also bringing a feeling of relief to the individual (see Bresin & Gordon, 2013b; Kirtley et al., 2015 for discussion).

The results of Schmahl et al (2004) suggest that altered pain threshold in this population is not the result of aberrant sensory-discriminatory perception in this populations, nor is it the result of attentional differences between self-harm and control groups. However, as this research was conducted upon inpatients with BPD, further research using non-clinical participants who engage in NSSI may be required before such explanations can be truly ruled out. The idea that altered pain threshold and tolerance occurs at the level of cognitive-affective processing, rather than sensory-discrimination would seem highly plausible and would be consonant with the work of Melzack and Wall (1965), who first proposed the idea of a cognitive component of pain in their seminal work on gate control theory, in which they contended that emotions and cognitions moderated transmission of impulses from peripheral to central nerves, either opening or closing “the gate” to allow pain to be experienced or not.

The more recent finding of a significant relationship between being highly self-critical and having a higher pain tolerance is particularly suggestive of a cognitive-affective mechanism underlying altered pain tolerance in those who engage in NSSI (Glenn et al.,

2014; Hamza et al., 2014; Hooley et al., 2010; Hooley & St Germain, 2014). Work by Hamza and colleagues (2014) may however suggest that a self-criticism mediated mechanism may only be applicable to certain subgroups of individuals who engage in NSSI, specifically those who self-injure with a motive of self-punishment. The majority of individuals who engage in self-harm endorse a motive of attempting to gain relief from a terrible state of mind (e.g. O'Connor et al., 2009). Therefore it may be interesting for future research to investigate potential differences in whether or not the relationship between self-criticism, self-hate and pain tolerance differs as a function of the motivation for engaging in NSSI.

Gratz and colleagues' (2011) results demonstrating a significant difference in pain tolerance as a function of participants' state of distress, suggests that tolerance may fluctuate with mood; partially supported by Bohus et al (2000), who found that pain tolerance was higher in BPD patients during self-reported distress relative to calmness, but when calm, BPD patients still exhibited higher tolerance than controls. This may indicate that a proportion of variability within pain tolerance is attributable to mood (state) changes, whereas another part is a consistent, more trait-like factor. Hooley and St Germain's (2014) study provides further support for this idea; those participants who had engaged in NSSI evidenced a reduction in pain endurance following a positive self-worth manipulation. Future research should investigate this phenomenon further as these findings may suggest that during a distressed state, elevated pain threshold and tolerance increases an individuals' acquired capability for engaging in NSSI. It is of note, however, that whilst there has been much discussion of pain tolerance as a key component of acquired capability for suicide (Van Orden et al., 2010), the overwhelming majority of studies to directly test the relationship between pain tolerance and self-harm have been conducted in NSSI samples.

Limitations

The findings of the current systematic review must be interpreted within the context of its limitations. We did not conduct a meta-analysis of the studies included within the review, as we felt the studies were too heterogeneous, thus we have presented a narrative review, which may be more vulnerable to bias and subjectivity than a meta-analysis. The quality assessment tool we employed to evaluate the studies, was of our own design, and whilst based upon a published tool (O'Connor et al., 2016), may not be an exhaustive set of criteria for assessing the quality of research in this area. Of note, however, is that no

standardised quality assessment tool for the evaluation of non-trial based research currently exists. All of the studies included within the review were of NSSI, and only three additional studies that were excluded, investigated pain and suicidal self-harm. Significant emphasis is placed upon altered pain tolerance in some contemporary theoretical models of suicide, e.g. the Interpersonal Psychological Theory (IPT, Joiner, 2005); however, given the dearth of evidence directly exploring pain threshold and tolerance in suicidal individuals, this focus lacks a sound evidence base. Furthermore, most of the NSSI studies did not assess whether or not participants also had a history of suicidal behaviours in addition to their NSSI, and therefore these samples may be more heterogeneous than they appear.

Conclusions

In sum, the evidence taken as a whole, indicates that pain threshold and tolerance are elevated in clinical populations of individuals who engage in NSSI (e.g. Ludäscher et al., 2009; Schmahl et al., 2006; 2004) and also in non-clinical populations (Franklin et al., 2011; 2010; Gratz et al., 2011; Hooley et al., 2010; McCoy et al., 2010). The current evidence base is greatly limited by the general dearth of studies in this area as well as the heterogeneity of methods and the narrow populations from which the samples have been selected. Given the high likelihood of a cognitive-affective mechanism underlying altered pain tolerance within this population, inclusion of psychological variables is a critical priority; particularly as there remains no consensus as to why pain threshold and tolerance are altered in individuals who engage in NSSI. Further studies in this area should attempt to establish whether there is a 'gold standard' methodology for measuring pain threshold and tolerance within this population. Future research should further explore pain threshold and tolerance in non-clinical samples of individuals who engage in NSSI as a matter of priority and should also adopt a more integrated approach, attempting to ascertain mediating and moderating pathways to elevated pain threshold and tolerance. There is an urgent need for prospective studies in this area as well as more basic scientific work to robustly establish proof of the existence of altered pain threshold and tolerance in NSSI, as a phenomenon.

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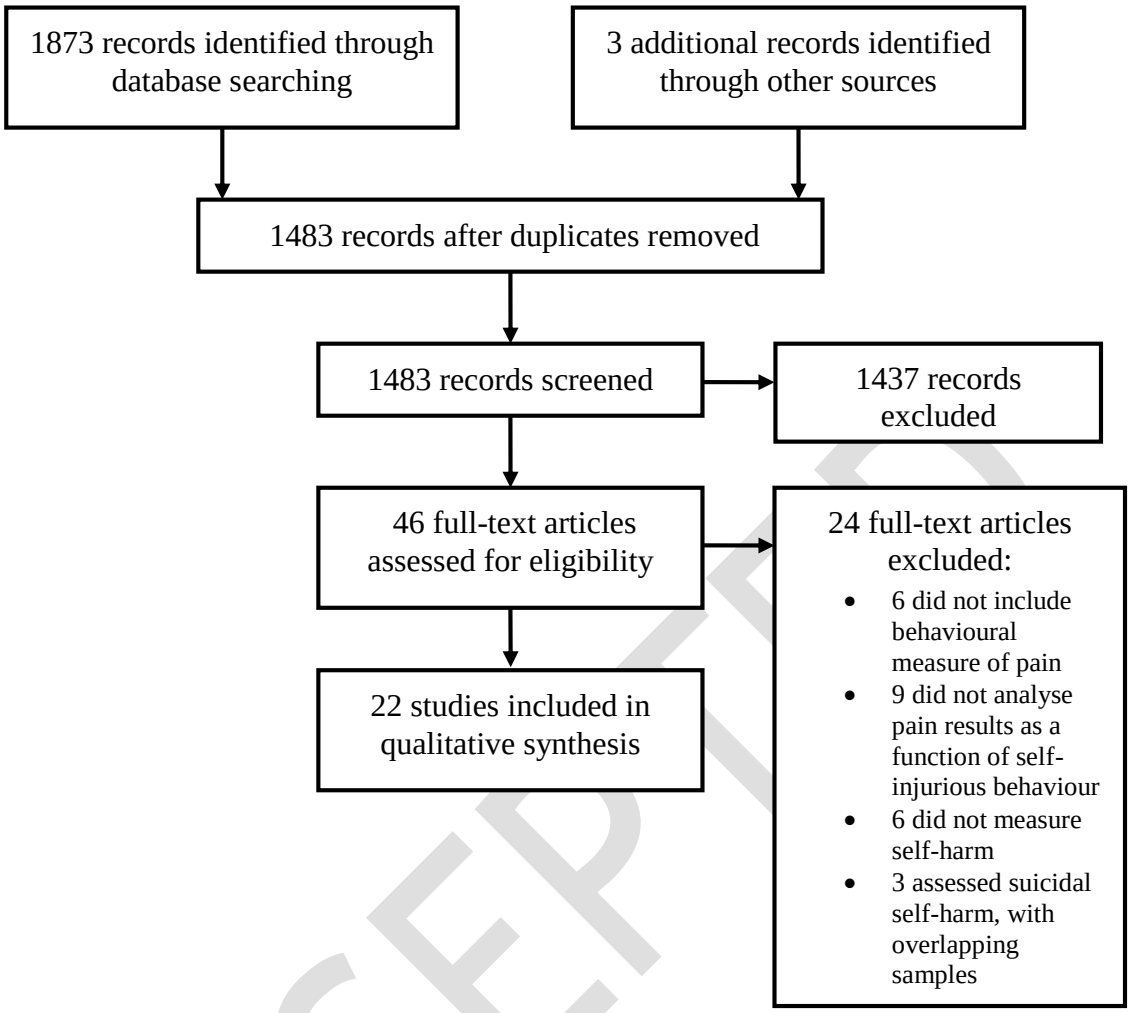

Figure 1. Procedure for identifying, screening and determining the eligibility of studies for inclusion in the review

Panel 1. Search strategy

The following keywords were employed: self injur* AND pain threshold OR pain tolerance OR pain sensitivity OR pain perception; self harm* AND pain threshold OR pain tolerance OR pain sensitivity OR pain perception; NSSI AND pain threshold OR pain tolerance OR pain sensitivity OR pain perception; nonsuicidal self-injur* AND pain threshold OR pain tolerance OR pain sensitivity OR pain perception; suicid* AND pain threshold OR pain tolerance OR pain sensitivity OR pain perception. For Medline, the MeSH terms "self-injurious behaviour" and "suicide" were also employed. This search yielded 1,873 database entries, which were then screened by the first author according to the four-stage Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) process (Moher, Liberati, Tezlaff & Altman, 2009). See Figure 1. The reference sections of all studies meeting the inclusion criteria were then hand-searched to ensure that no relevant articles were missed.

Table 1 Quality assessment framework for assessing studies included within systematic review of pain and self-harm

Criteria	0	1	2
Design	Cross-sectional	Case-control	Prospective
Power	No mention of a power calculation	Power calculation reported, but sufficient power not achieved	Power achieved
Self-Injurious Behaviour Assessment	Non-validated scale; self-report; single question	Hospital admission; items from validated diagnostic/ mood rating scale	Clinical interview; validated scale (e.g. ISAS, SITBI, DSHI)
Suicidal Ideation/Behaviour	Not reported/ not assessed	Mixed group of suicidal and non-suicidal self-harming participants	Homogenous groups of either suicidal OR non-suicidal self-harm
Type of Pain Assessment	-	Self-report only	Behavioural assessment, e.g. maximum time/ temperature/ pressure/ voltage that could be tolerated.
Appropriate choice of comparison group	No case group free from self-harm *E.g. includes those who ideate about self-harm, those who have previously self-harmed or no comparison group.*	One case group with no personal history of self-harm thoughts or behaviours.	-
Confounding variables *Will require some judgement on behalf of the rater as studies will have done this to differing degrees.*	No attempt to control for confounding factors in recruitment or analyses.	Accounts for basic confounding variables either during recruitment or analysis. E.g. age, gender.	Accounts for basic and additional confounding variables either during recruitment or analysis e.g. medication use/substance abuse, comorbid psychiatric conditions

TABLE 2

Cross-Sectional Studies of Pain and NSSI

Study Country Quality assessment (QA) score	Sample	Type of sample	Measures Pain Threshold/Tolerance and Other Physiological	Psychological	Results
Bresin & Gordon (2013a) USA QA score = 4	115 University students. 59 people who had engaged in NSSI (34 females) 56 healthy controls (31 females) Mean age= 19.48 yrs.	Adult college students	Thermal heat stimuli administered via TSA Thermal Sensory Analyzer. Temperature range of 35-50º C, .7s exposure to each temperature. Then second exposure to temperature rated as either 20 or 60 on 1-100 pain intensity scale.	Shortened version of PANAS (Watson, Clark & Tellegen, 1988)	No effect of NSSI on pain intensity ratings at first stimuli exposure. Those in the NSSI group who received the painful stimulus displayed a significantly greater reduction in negative affect than those who received the non-painful stimulus. But following the painful stimulus, the NSSI group did not significantly differ from controls in negative affect.
Franklin, Aaron, Arthur, Shorkey & Prinstein (2012) USA QA score = 6	72 University students (52 females). 25 people who had engaged in NSSI 47 healthy controls Mean age= 19.09 yrs.	Adult college students	CPT at 2º C for maximum of 2 minutes. Self-reported pain intensity, time to reach threshold and tolerance measured.	6 items from DERS (Gratz & Roemer, 2004) FASM (Lloyd, Kelley & Hope, 1997) Subjective Units of Distress Scale.	People who had engaged in NSSI displayed a higher pain threshold and tolerance than controls and lower ratings of pain intensity. Pain tolerance and emotion dysregulation strongly correlated. Both emotion dysregulation and pain threshold significantly moderated the association between NSSI and pain tolerance.
Franklin, Hessel & Prinstein (2011) USA QA score = 6	67 University students (47 females) 16 people who had engaged in NSSI 51 healthy controls. Mean age= 19.25 yrs.	Adult college students	CPT at 2º C for maximum of 2 minutes. Self-reported pain intensity, time to reach threshold and tolerance measured.	FASM (Lloyd, Kelley & Hope, 1997) PPE Scale (Bender et al., 2011) Modified ACS Questionnaire (Van Orden et al., 2008)	Pain tolerance significantly associated with both PPE and ACS score. No significant differences in pain tolerance or pain intensity at threshold between NSSI and control groups. Significant between-group differences in threshold and intensity at tolerance. Tolerance only significant (but modest)

					mediator of association between PPE and ACS.
Gratz et al. (2011) USA QA score = 9	95 University students and community participants. 43 people who had engaged in NSSI (N=30 females). Mean age= 19.3 yrs. 52 healthy controls (N=38 females). Mean age= 20.4 yrs.	Adult college students	CPT at 0.55º C & Algometer. Time to reach pain threshold and tolerance measured.	DSHI (Gratz, 2001) BEST (Pfhol & Blum, 1997) CES-D (Radloff, 1977) PANAS (Watson, Clark & Tellegen, 1988) MTPT-C (Strong et al., 2003)	People who had engaged in NSSI in the distressed group had a significantly higher pain tolerance than those in the neutral group. Males took significantly longer to terminate algometer task.
Hooley, Ho, Slater & Lockshin (2010) USA QA score = 7	Community sample. People with NSSI ideation (N=7); people who had engaged in NSSI (N=31) & Controls (N=29). Overall sample mean age= 22.4 yrs. 53 females.	Adult community sample	Algometer. Time to reach pain threshold and tolerance measured.	NEO-FFI (Costa & McRae, 1992) BHS (Beck, Weissman, Lester & Trexler, 1974) LCB (Craig, Franklin & Andrews, 1984) DES (Bernsetein & Putnam, 1986) SITBI precursor (Nock, Holmberg, Photos & Michel, 2007)	People who had engaged in NSSI had higher pain threshold and tolerance than controls. Significant correlation between number of years of NSSI and pain threshold. NSSI group showed greater external locus of control, neuroticism, openness and negative affect than controls.
Hooley & St Germain (2014) USA QA score = 7	Community sample. People who had engaged in NSSI (N = 50); controls (N= 84). Overall sample mean age = 24.09. 101 females.	Adult community sample	Algometer. Time to reach pain threshold and tolerance measured.	SITBI precursor (Nock, Holmberg, Photos & Michel, 2007) SCID-CV (First et al., 1996) Mood VAS	Individuals in the NSSI group exhibited significantly greater pain endurance than controls. Following positive self-worth manipulation, those in the NSSI group demonstrated reduced pain endurance.
Kemperman et al. (1997) USA QA score = 3	34 female inpatients with BPD. Subdivided into BPD (mean age= 31.5 yrs); BPD-NP	Adult inpatients with BPD	Thermal heat stimuli, delivered via Dolorimeter at 33.7º C, 36.2º C, 46.0º C & 49.5º C. Pain intensity rated on 1-8 categorical scale.	DES (Bernsetein & Putnam, 1986) SPRAS (Sheehan et al., 1988)	Patients in the BPD-P group were better able to distinguish between painful stimuli of similar intensity, relative to patients in the BPD-NP and BPD-C

	(mean age= 28.3 yrs); and BPD-C (mean age= 32.1 yrs). 7 healthy female controls. Mean age= 26.9 yrs			BDI (Steer, Beck & Garrison, 1986)	groups. The BPD-NP group was significantly less likely to describe stimuli as painful.
Ludäscher et al. (2009) Germany QA score = 7	48 female psychiatric inpatients, outpatients and students. People with current NSSI mean age= 28 People with previous NSSI mean age= 30 Controls mean age= 25	Adult inpatients/outpatients with BPD & community controls	Thermal heat stimuli at 32-50º C. Laser stimulation was at 540 mJ.	BSL (Bohus et al., 2007) DSS (Stiglmayer, Shapiro, Stieglitz, Limberger & Bohus, 2001)	BPD patients who were currently engaging in NSSI had lowest pain threshold, followed by BPD patients who had previously engaged in NSSI, and then controls.
Niedtfeld et al. (2010) Germany QA score = 5	20 female outpatients with BPD recruited via adverts on BPD websites. Mean age= 30.50 yrs. 23 healthy female volunteer controls recruited via newspaper advertisements. Mean age= 27.13 yrs	Adult outpatients with BPD & community controls	Thermal heat stimuli. fMRI analysis was conducted during pain testing. Individualized levels of thermal stimuli applied, based on pre-experiment trials.	SCID (First et al., 1995) IPDE (Loranger, 1999) BSL (Bohus et al., 2007) ERQ (Gross & John, 2003)	BPD patients showed significantly higher pain threshold than healthy controls. Amygdala, insula and ACC had significantly higher activation in the BPD group, than in the control group. Decreased amygdala and ACC activation was found in BPD patients, following negative image presentation.
Russ, Campbell, Kakuma, Harrison & Zanine (1999) USA QA score = 5	N= 41 inpatients BPD-P: 22 females with BPD (Mean age= 31.1 yrs); BPD-NP: 19 females with BPD (Mean age= 25.8 yrs). 15 females inpatients with no history of BPD or NSSI (Mean age= 33.3 yrs).20 healthy female volunteers from	Adult inpatients with BPD & community controls	CPT at 10º C (maximum 4 mins). Time to reach pain tolerance measured. EEG activity measured during CPT.	SCID-II (Spitzer et al., 1987) SCID-P (Spitzer at al., 1988) POMS (McNair et al., 1971) BDI (Steer, Beck & Garrison, 1986) Pain intensity scale (1-9)	Significant difference in the number of subjects terminating CPT before maximum time. Pain ratings were significantly lower in BPD-NP than BPD-P and healthy controls. No significant difference in pain rating between the depressed inpatients and the other groups.

	the community. Mean age= 30.1 yrs.				
Russ et al. (1992) USA QA score = 3	11 female inpatients with BPD (BPD-NP). 11 female inpatients with BPD (BPD-P). Mean age for BPD groups= 22.60 yrs. Controls: 6 female volunteer controls. Mean age= 22.2 yrs.	Adult inpatients with BPD & community controls	CPT at 10º C (maximum 4 mins). Pain intensity and unpleasantness were rated on a 1-9 scale.	POMS (McNair et al., 1971) SCID (Spitzer et al., 1987) BDI (Steer, Beck & Garrison, 1986)	Pain ratings -P group and healthy controls. No significant difference in pain ratings between BPD-P and healthy controls. For the BPD-NP group, self-reported ratings of vigor were higher following the CPT, but not in the BPD-P group. Ratings of depression, anger and confusion were also lower following the CPT, but only in the BPD-NP group.
Russ et al. (1994) USA QA score = 3	11 female psychiatric inpatients. BPD-NP (mean age= 21.7 yrs); BPD-P (Mean age= 32.3 yrs)	Adult inpatients with BPD	CPT at 10∘ C. Pain intensity and unpleasantness were rated on a 1-9 scale.	POMS (McNair et al., 1971)	BPD-P experienced more pain following saline but BPD-NP reported more pain following naloxone. Tension and depression decreased in BPD-NP group post-CPT, but not BPD-P. Naloxone did not increase pain intensity ratings.
Schmahl et al. (2004) Germany QA score = 4	10 female BPD patients Mean age= 29 yrs Controls: 14 healthy female volunteers. Mean age= 26 yrs.	Adult inpatients with BPD & community controls	LEP. Laser detection and pain threshold recorded. Rating of pain quality. Pre-LEP quantitative sensory testing for BPD group. EEG during LEP.	SCID-II (First et al., 1996) SCID-I/P (First et al., 1995) DIB-R (Zanarini et al., 1989)	Nociception reduced in BPD group, relative to controls. Laser detection and pain thresholds were significantly higher in the BPD than in the control group. EEG revealed that LEP amplitudes in BPD were either within the normal range, or higher than controls.
St Germain & Hooley (2013) USA QA score = 9	48 individuals reporting direct NSSI (41 female) 37 individuals reporting indirect NSSI (19 female) 63 non-injuring controls Mean age for total sample = 25.4 yrs	Adult community sample	Pressure algometer applied to fingers for maximum of 8 minutes.	MAST (Selzer et al., 1971) DAST (Skinner, 1982) EDEQ (Fairburn & Beglin, 1994) SHI (Sansone, Wiedermen & Sansone, 1998) SNAP: SUICIP SNAP: LSE (both Clark, 1993)	Both NSSI groups demonstrated significantly greater pain endurance than control groups, but the two NSSI groups evidenced comparable pain endurance.

Weinberg & Klonsky (2012) Canada QA score = 6	72 Undergraduate students. Mean age= 20.24 yrs. 39 people who had engaged in NSSI (29 females). 33 healthy controls (17 females).	Adult college students	Electric shocks, increasing from 0v in increments of 0.7v, each administered for 5s. Participants rated pain on 1-10 scale, then following mood manipulation, were randomized to receive either high (painful) or 2v low rated shock.	ISAS (Klonsky & Glenn, 2009) DASS-21 (Henry & Crawford, 2005) BSL-23 (Bohus et al., 2009) MSI-BPD (Zanarini et al., 2003) DERS (Gratz & Roemer, 2004) SAM (Lang, 1980)	The NSSI group selected higher levels of shock than controls, but did not report pain as being more intense. No significant between-group differences in subjective pain ratings at high shock, but at low shock, the NSSI group rated shock as significantly less painful. People who had engaged in NSSI showed greater reduction in NA following high shock. Opposite effect for controls. Higher shock predicted greater decrease in NA, but not associated with subjective pain rating.

Note: ACS= Acquired Capability for Suicide Scale; ASI= Anxiety Sensitivity Inventory; BEST= Borderline Evaluation of Severity Over Time; BDI/BDI-II= Beck Depression Inventory; BHS= Beck Hopelessness Scale; BPD= Borderline Personality Disorder; BPD-C= BPD-Calm; BPD-D= BPD-Distressed; BPD-NP= BPD-No Pain during self-harm; BPD-P= BPD-Pain during self-harm; BSL= Borderline Symptoms List; CES-D= Center for Epidemiologic Studies Depression Scale; CPT= Cold Pressor Test; DASS-21= Depression Anxiety Stress Scale; DAST= Drug Abuse Screening Test; DERS= Difficulties in Emotion Regulation Scale; DES= Dissociative Experiences Scale; DIB-R= Diagnostic Interview for Borderlines Revised; DSHI=Deliberate Self-Harm Inventory; EEG= Electroencephalogram; EDEQ= Eating Disorder Examination Questionnaire; ERQ= Emotion Regulation Questionnaire; FASM= Functional Assessment of Self-Mutilation; ISAS= Inventory of Statements About Self-Injury; IPDE= International Personality Disorder Examination; LCB= Locus of Control of Behavior Scale; LEP= Laser Evoked Potential**;** MAST= Michigan Alcoholism Screening Test; MCMI-I= Millon Clinical Multiaxial Inventory; MSI-BPD= McLean Screening Instrument for Borderline Personality Disorder; MTPT-C= Computerized Mirror-Tracing Persistence Task; NA= Negative Affect; NEO-FFI= Neuroticism Extraversion and Openness- Five Factor Inventory; NSSI= Non-suicidal self-injury; PANAS= Positive and Negative Affect Scale; PPE= Painful and Provocative Events Scale; POMS= Profile of Mood States; SAM= Self-Assessment Manikin; SCID/SCID-P/SCID-I/P = Structured Clinical Interview for Personality Disorders axis I; SCID-II= Structured Clinical Interview for Personality Disorders axis II; SCID-CV= Structure Clinical Interview for Axis I Disorders- Clinician Version; SHI= Self-Harm Inventory; SITBI= Self-Injurious Thoughts and Behaviors Interview; SNAP: Schedule for Non-Adaptive and Adaptive Personality: Low Self-Esteem; LSE= SNAP: SUICIP= Schedule for Non-Adaptive and Adaptive Personality: Suicide Proneness; SPRAS= Sheehan Patient-Rated Anxiety Scale; VAS= Visual Analogue Scale

TABLE 3

Case-Control Studies of Pain and NSSI

Study Country Quality assessment (QA) score	Population Cases	 Controls	Type of sample	Measures Pain Threshold/ Tolerance & Other Physiological	 Psychological	Results
Bohus et al. (2000) Germany QA score = 6	12 female psychiatric inpatients with BPD. Mean age= 29.1 yrs	N= 19 females with no Axis I disorders or BPD. Mean age= 27.3 yrs.	Adult inpatients with BPD	CPT at 10◦ C (maximum 4 mins) & TPT. Pain intensity and unpleasantness assessed for both CPT & TPT. Time to reach pain threshold and tolerance measured for TPT only. HR and SCRF also measured.	5 questions derived from the SDQ-5 (Nijenhuis et al., 1997) and DES (Bernstein & Putnam, 1986), measuring distress, numbness, visual and auditory sensitivity and anesthesia.	BPD-D reported less pain than BPD-C. Onset of TPT pain significantly later in BPD-D than BPD-C. No significant difference between groups in TPT tolerance. No significant difference between BPD-C & BPD-D in unpleasantness & intensity of pain.
Franklin, Hessel, Aaron, Arthur, Heilbron & Prinstein (2010) USA QA score = 8	16 Undergraduates reporting NSSI. Mean age for total sample= 19.73 yrs.	96 Undergraduate students: 24 with high affect dysregulation, but reporting no NSSI (Matched-AD). 33 with low affect dysregulation and no NSSI (Low-AD). 39 healthy controls that received no painful stimuli (No pain).	Adult college students	CPT at 2◦ C for maximum of 2 minutes. Level of distress measured. Startle-alone reactivity measured by administration of 100-dB broadband noises (20 Hz-20 kHz) each of 50ms duration. PPI measured by 85-dB broadband noise of 40ms duration.	SUDS FASM (Lloyd, Kelley & Hope, 1997) Modified 6 item DERS (Gratz & Roemer, 2004)	All groups reported more distress following CPT, apart from no-pain group. Startle-alone reactivity of no-pain group constant, but decreased for all other groups following CPT. PPI increased significantly for NSSI group following CPT, but decreased for other groups.
Glenn, Michel, Franklin, Hooley & Nock (2014) USA QA score = 7	58 adolescents reporting NSSI Mean age for total sample= 17.34 yrs	21 controls with no NSSI history	Adolescent community sample	Pressure algometer applied to fingers for a maximum of 4 minutes.	A-DES II (Armstrong et al., 1997) SITBI (Nock et al., 2007) SRS (Hooley et al., 2010) K-SADS-PL (Kaufman et al., 1997)	Individuals in the NSSI exhibited significantly higher pain tolerance than controls. This was strongly associated with high self-criticism.

Hamza, Willoughby & Armiento (2014) Canada QA score = 7	31 undergraduates reporting NSSI with self-punishment motivation 25 undergraduates reporting NSSI without self-punishment motivation Mean age total sample= 21.52 yrs	26 controls with no NSSI history	Adult college students	Cold pressor test at 1-4◦ C for maximum of 2 minutes	ISAS (Klonsky & Glenn, 2009) TSST (Kirschbaum, Pirke & Hellhammer, 1993) DERS (Gratz & Roemer, 2004) PPES (Bender, Gordon, Bresin & Joiner, 2011) Self-criticism subscale from DEQ (Blatt, D'Afliatti & Quinlan, 1976)	Those who engaged in NSSI with a motive of self-punishment exhibited significantly higher pain tolerance following stress induction than those without a motive of self-punishment. Self-criticism was strongly associated with pain tolerance.
McCoy, Fremouw & McNeil (2010) USA QA score = 9	11 people who had engaged in NSSI from undergraduate population (2 with previous suicide attempt)	33 healthy undergraduate controls. Overall sample mean age= 20.25 yrs.	Adult college students	Algometer. Time to reach pain threshold and tolerance measured. Score on VAS.	Sensation Seeking. DSHI (Gratz, 2001) BDI-II (Beck, Steer & Brown, 1996) BHS (Beck, Weissman, Lester & Trexler, 1974) ASI (Peterson & Reiss, 1993)	Significant difference in threshold and tolerance between groups, but only on first trial. Average pain threshold did not significantly differ between groups. People who had engaged in NSSI had significantly higher pain tolerance than controls and also rated pain as significantly less intense.
Magerl, Burkart, Fernandez, Schmidt & Treade (2012) Germany QA score = 5	22 patients with BPD (20 inpatients; 15 females; mean age= 29 yrs)	22 healthy controls (15 females; mean age= 29 yrs)	Adult inpatients with BPD & community controls	Pinprick stimuli: 7 punctate probes, ranging from 8-512mN, each applied 5 times for 1s. Chemical stimuli: Intradermal capsaicin injection (40µg in 12.5µL). Pain intensity and unpleasantness measured on 0-10 scale. Pain threshold estimated from these.	DIB-R (Zanerini, Frankenburg, Vujanovic, 1989) BPI (Leichsenring, 1997) BfS mood scale (von Zerssen, Koeller & Rey, 1970) SCID-II (First, Spitzer, Gibbon & Williams, 1996)	Higher estimated pain threshold for BPD group than controls. No significant difference in pain intensity ratings, but lower unpleasantness in BPD group. Pain threshold correlated with recency and frequency of NSSI.

Schmahl et al. (2006) Germany QA score = 6	12 female patients with BPD –NP Mean age= 28.67 yrs.	12 healthy female controls. Mean age= 27.67 yrs. 1 with social phobia.	Adult inpatients with BPD & community controls	Thermal heat stimuli ranging from 40-48∘ C in 20x30 second blocks, delivered via thermode. Self-rating of pain on numeric rating scale. fMRI assessment during administration of painful stimuli. Threshold was temperature where 50% of trials perceived as painful.	SCID-I (First et al., 1995) IPDE (Loranger et al., 1999) BDI (Steer, Beck & Garrison, 1986) DSS (Stiglmayer, Shapiro, Stieglitz, Limberger & Bohus, 2001)	BPD group had significantly higher pain threshold than controls. fMRI showed increased activity in DLPFC during pain in BPD, but lower activity in parietal cortex. BPD had neural deactivation in perigenual ACC and the right amygdala, but not controls

Note: A-DES-II= Adolescent Dissociative Experiences Scale; BDI/BDI-II= Beck Depression Inventory; BHS= Beck Hopelessness Scale; BPD= Borderline Personality Disorder; BPD-C= BPD-Calm; BPD-D= BPD-Distressed; BfS= Befindlichkeitsskala mood scale; BPI= Borderline Personality Inventory; BPD-NP= BPD-No Pain during self-harm; CPT= Cold Pressor Test; DEQ= Depressive Experiences Questionnaire; DES= Dissociative Experiences Scale; DERS= Difficulties in Emotion Regulation Scale; DIB-R= Diagnostic Interview for Borderlines Revised; DSS= Dissociative States Scale; FASM= Functional Assessment of Self-Mutilation; fMRI= functional Magnetic Resonance Imaging; HR= Heart Rate; IPDE= International Personality Disorder Examination; ISAS= Inventory of Statements About Self-Injury; K-SADS-PL= Kiddie Schedule for Affective Disorders and Schizophrenia in School-Age Children, Present and Lifetime Version; NSSI= Non-suicidal self-injury; PPES= Painful and Provocative Events Scale; PPI= Prepulse Inhibition; SCRF= Skin Conductance Response Fluctuation; SCID /SCID-P/SCID-I/P = Structured Clinical Interview for Personality Disorders axis I; SCID-II= Structure Clinical Interview for DSM-IV Personality Disorders; SDQ-5= Somatoform Dissociation Questionnaire; SITBI= Self-injurious Thoughts and Behaviours Interview; SRS= Self-Rating Scale; SUDS= Subjective Units of Distress Scale; TPT= Tourniquet Pain Test; TSST= Trier Social Stress Test