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Different psychophysiological and clinical symptoms are linked to affective versus sensory vicarious pain experiences

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Abstract

For some people, seeing pain in others triggers a pain-like experience in themselves: these experiences can either be described in sensory terms and localized to specific body parts (sensory-localized, or S/L) or in affective terms and nonlocalized or whole-body experiences (affective-general, or A/G). In two studies, it is shown that these are linked to different clinical and psychophysiological profiles relative to controls. Study 1 shows that the A/G profile is linked to symptoms of Blood-Injection-Injury Phobia whereas the S/L profile shows some tendency toward eating disorders. Study 2 shows that the A/G profile is linked to poor interoceptive accuracy (for heartbeat detection) whereas the S/L profile is linked to higher heart-rate variability (HRV) when observing pain, which is typically regarded as an index of good autonomic emotion regulation. Neither group showed significant differences in overall heart rate, systolic blood pressure (SBP), or skin conductance response (SCR) when observing pain, and no overall differences in state or trait anxiety. Overall, the research points to different underlying mechanisms linked to different manifestations of vicarious pain response. Affective-General pain responders have strong subjective bodily experiences (likely of central origin given the absence of major differences in autonomic responsiveness) coupled with a worse ability to read objective interoceptive signals. Sensory-localized pain responders have differences in their ability to construct a multi-sensory body schema (as evidenced by prior research on the Rubber Hand Illusion) coupled with enhanced cardiovagal (parasympathetic) reactivity often indicative of better stress adaptation.

KEYWORDS

arousal, autonomic processes, emotion regulation, heart rate variability, interoception, vicarious pain

1 | INTRODUCTION

Seeing someone else in pain may elicit a similar sensation in the observer which is known as vicarious pain perception (Fitzgibbon et al., 2010, 2012). Vicarious pain experiences

have been reported in clinical populations such as patients with a history of traumatic pain or in phantom limb patients (Fitzgibbon et al., 2010; Giummarra & Bradshaw, 2008), but also in the healthy general population. Individuals may report feeling pain on their own body when observing others

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in pain in experimental settings, usually as a response to the presentation of images or videos depicting painful events (Grice-Jackson et al., 2017a; Osborn & Derbyshire, 2010). Grice-Jackson et al. (2017a) identified two subgroups of vicarious pain responders who report different qualities of their vicarious experience. Using a cluster analysis method, they identified a group of sensory-localized vicarious pain responders (S/L) who report feeling a localized pain sensation on their own body when seeing someone else in pain, and a group of affective-general responders (A/G) who report a generalized pain sensation in their entire body. Subsequent research, using a more conservative clustering method, reported a prevalence of 12.3% for S/L and 9.0% for AG (both being more common in women; Botan et al., 2018).

To some extent, one could regard these overt vicarious pain responses as exaggerated versions of a normative (and implicit) tendency to simulate or “mirror” the experiences of others. Seeing others in pain tends to activate a network of regions also involved in physical pain perception report (see Lamm et al., 2011 for a meta-analysis; but see Krishnan et al., 2016, for an alternative view). There is evidence that vicarious pain responders, who consciously report pain-like feelings, do so to a greater extent (Grice-Jackson et al., 2017a; Osborn & Derbyshire, 2010) and have structural and functional differences in these brain regions (Grice-Jackson et al., 2017b). One theory for why these groups engage in greater simulation is that they have problems in self-other control mechanisms (Ward & Banissy, 2015). These have been postulated to act as a brake mechanism that prevents simulation in order to keep one's own feelings and the simulated feelings of others as separate (e.g., Decety & Jackson, 2004), or in terms of a switch metaphor in which participants can flexibly attend to their own feelings or that of others (Bird & Viding, 2014). In this account, vicarious pain responders cannot inhibit their own simulated response to what they see. In effect, the capacity to mirror the sensory experience (pain or touch) of another person on one's own body may reflect a tendency to treat all observed bodies as self-related.

The question as to why (or indeed whether) there are differences between the A/G group and the S/L group is not yet resolved. It may be that the A/G group activates whole-body somatosensory representations and the S/L group does so in a body-part specific manner, and there is preliminary evidence for this (Grice-Jackson et al., 2017b). It may also be the case that these groups differ in terms of autonomic arousal and regulation, such that the A/G phenomenology is more of an interoceptive experience and S/L is more exteroceptive in nature. More generally, there is uncertainty over the extent to which the A/G group is a distinct entity versus an intermediate state between the S/L group and controls. Two patterns have been found in the literature: either that the two responder groups behave similarly to each other but different from nonresponder controls ($S/L = A/G > \text{Controls}$) or that the S/L group differs

from the others ($S/L > A/G = \text{Controls}$). The former pattern, responders being special, is seen on measures such as emotion contagion (Botan et al., 2018) and interoceptive sensibility (Bowling et al., 2019), discussed in more detail below. The latter pattern, S/L responders being special, is found on measures such as EEG mu suppression (Grice-Jackson et al., 2017a), the Rubber Hand Illusion (Botan, Fan, et al., 2018), and a tendency to report vicarious tactile responses to see other people touched (mirror-touch synesthesia; Ward et al., 2018).

Veridical embodied responses such as pain or motor movements lead to suppression of EEG oscillations emanating from sensory-motor cortex in the mu (8–13 Hz) frequency range (Ritter et al., 2009). Mu suppression has also been reported when observing pain and observing actions suggesting that this is a neural signature of simulation of physical bodily sensations in other people (Pineda, 2005). Grice-Jackson et al. (2017a) found that the S/L group showed significantly stronger mu suppression when observing pain relative to the A/G group and controls. The Rubber Hand Illusion is regarded as a distortion of body ownership, such that synchronous tactile signals applied to a seen dummy hand and their own unseen hand results in participants feeling that the dummy hand belongs to them (on questionnaire measures) and that their own hand is shifted in location toward the dummy (a proprioceptive drift measure) (Tsakiris, 2010). Derbyshire et al. (2013) used the RHI paradigm and showed a greater tendency to incorporate the rubber hand in the pain-responders group when compared to controls as recorded by subjective reports (N.B. they did not characterize the pain responders nor divided them into two groups). In a more recent study, Botan, Fan, et al. (2018) showed that only the sensory-localized group of vicarious pain responders had a greater tendency to incorporate the rubber hand in *both* synchronous and asynchronous conditions as recorded by subjective ratings and proprioceptive drifts. This pattern has been rarely reported in the literature but has also been observed in clinical samples with eating disorders (Kaplan et al., 2014; Zopf et al., 2016). This raises the possibility that similar neurocognitive mechanisms (the relative weighting of external and internal cues for body ownership) may be altered in both S/L vicarious pain and eating disorders; that is, acting as a shared vulnerability. In the research below, we examine whether people in the S/L group are more susceptible to symptoms of eating disorders.

Affective feelings are linked to interoceptive (viscerosensory) signaling of changes in the internal state of the body (e.g., heart rate, blood pressure), mediated by the autonomic nervous system. It is possible that both autonomic control and interoceptive signaling might be “tuned” differently in vicarious pain responders, as proposed, for instance, by Giummarra and Fitzgibbon (2015). This could potentially apply to both of the responder groups that we have identified, although it may also apply particularly strongly to the A/G group that reports nonlocalized bodily responses akin to nausea and distress. Physical pain elicits an autonomic arousal response, for example, in the

cardiovascular system, manifest as a shift in sympatho-vagal balance (Koenig et al., 2014). Similar physiological responses occur when simulating the feelings of other people (Levenson & Ruef, 1992). To translate this to individual differences, the most intuitive account would predict that vicarious pain responders would manifest an *exaggerated* sympathetic arousal response to observing pain (i.e., increased heart rate, blood pressure, and skin conductance). However, it is also possible that vicarious pain responders have developed physiological compensatory strategies for these stressors. Two possibilities include greater changes in heart rate variability (HRV) or compensatory wholesale increases in parasympathetic activity. Increased heart rate variability (variability in the interval between successive heartbeats) is often regarded as an adaptive emotion regulation mechanism (Appelhans & Luecken, 2006; Mulcahy et al., 2019; Thayer et al., 2012) whereas decreased heart rate variability has been associated to a poorer adaptability of the autonomic nervous system, cardiac functioning and health outcomes (Koenig et al., 2016; Tracy et al., 2016). However, increased HRV may also be a signature of variant cardiovagal reactivity, for example in blood phobic fainters (Beacher et al., 2009) in whom the inhibition of sympathetic traffic to muscle vascular beds is a putative syncopal mechanism (Donadio et al., 2007). An alternative pattern of compensatory strategy to stressors is to counteract an initial phase of sympathetic arousal with a more substantial activation of the parasympathetic system, such that the sight of pain may produce a *lower* net physiological responsiveness in some people (less skin conductance, drops in heart rate and blood pressure). This can produce feelings of faintness, and is a characteristic of people with Blood-Injection-Injury (BII) phobia (Ritz et al., 2010). In summary, while we hypothesize that there will be differences in autonomic activity in vicarious pain responders the direction of these differences are not straightforward to predict a priori.

In addition to physiological measures linked to interoception, there are various behavioral and self-report measures that are commonly used. Garfinkel, Seth, et al. (2015) proposed three independent dimensions of interoception: *sensibility* (noticing subtle changes in the body recorded with subjective reports), interoceptive *accuracy* (performance on tasks such as heart beat counting), and interoceptive *awareness* (metacognition reported as confidence in the performance on interoceptive tasks). To avoid confusion, we will use the terms and definitions given by Garfinkel, Seth, et al. (2015). These three dimensions of interoception are dissociable; that is, they do not correlate with each other and have been differently associated with bodily self-processing (Garfinkel, Seth, et al., 2015). Vicarious pain responders, both S/L and A/G, have higher interoceptive sensibility as measured with subjective reports (Bowling et al., 2019). However, it is unclear if this also corresponds to higher interoceptive accuracy and/or awareness. Previous research has indicated that high interoceptive accuracy is associated with lower pain thresholds (Pollatos et al., 2012) and that it enhances the

estimated degree of pain (cognitive empathy), as well as arousal and feelings of compassion (affective empathy), in response to painful pictures (Grynberg & Pollatos, 2015). However, the latter study is not related to *shared* self-other pain and, other research suggests that having higher interoceptive accuracy translates into a stronger sense of self (Ainley & Tsakiris, 2013), and less reliance on exteroceptive cues to body ownership such that people with higher interoceptive accuracy are less susceptible to the RHI (Tsakiris et al., 2011). Based on their reasoning, it would be surprising if vicarious pain responders (at least the S/L group) showed higher interoceptive accuracy. There are no predictions with regards to interoceptive awareness but we include this measure for completeness.

In summary, we hypothesize that vicarious pain responders will present a distinctive pattern of clinical vulnerabilities and physiological responsiveness. Specifically, in Study 1, we hypothesize that this may be linked to increased tendencies toward Blood-Injection-Injury Phobia and eating disorders (the latter may be linked specifically to the S/L profile). In Study 2, we hypothesize that there will be an atypical profile of interoception in terms of behavioral measures (interoceptive accuracy) and in terms of physiological responsiveness to stressors (either in terms of overall sympathetic responsiveness or compensatory parasympathetic reactions). We speculate that these might be more apparent in the A/G group because their vicarious pain phenomenology appears more interoceptive in nature.

2 | STUDY 1: CLINICAL PROFILE LINKED TO VICARIOUS PAIN RESPONDERS

This study screened a large sample of undergraduates using the VPQ and additionally incorporated two measures related to clinical disorders that are suitable for administering to a normative sample. This included a set of questions relating to Blood-Injection-Injury Phobia, where we hypothesized that vicarious pain responders would score higher (but we did not have specific predictions about the two subgroups). The second measure related to symptoms of eating disorders, where we predicted a specific association to the S/L profile (based on previous research that the S/L subtype and eating disorders have a similar pattern of differences on the Rubber Hand Illusion).

3 | METHOD

3.1 | Participants

Participants were recruited from the School of Psychology at the University of Sussex and were awarded course credit for research participation. Ethical approval was obtained from

the Science and Technology Research Ethics Committee of the University of Sussex and all participants offered their written informed consent at the beginning of the study.

A total of 395 participants took part. The demographic characteristics are shown in Table 1, together with their profile on the VPQ. Assignment of group was based on k-means cluster analysis as described by Botan, Fan, et al. (2018) on the three variables from the VPQ: mean pain intensity; localized minus generalized responses (L-G); and number of sensory minus affective descriptors (S-A). The three groups were matched on age but not on gender: the two responder groups had fewer men, $\chi^2(2) 6.128, p = .047$, as noted previously for this measure (Grice-Jackson et al., 2017a). As such, gender was taken into account in the analyses (see later).

3.2 | Materials

The three measures consisted of the VPQ, the BII, and the EDE-Q.

The VPQ consists of 16 brief video clips with half depicting injections and half depicting sporting injuries (they are available here for others to use <https://www.youtube.com/channel/UCT8goTgWGRsu14NjVaPCSGw/videos>). None of the videos displayed blood or gore. After each video participants are asked if they felt any pain on their own body. Upon giving an affirmative answer they were then asked to rate the intensity (1–10 scale), where the pain was felt (localized in same location as observed, localized in another location, a nonlocalized general sensation), and asked to choose as many items from a list of pain descriptors (10 sensory such as “tingling,” “burning,” “stinging,” and 10 affective descriptors such as “nauseating,” “gruelling,” “aversive”).

The BII measure consisted of six questions taken from Wani et al. (2014): “Are you phobic of blood, injection, injury, and needle?”, “Do you avoid seeing others’ blood?”, “Do you avoid looking at your own blood?”, “Do you faint at the sight of blood?”, “Do you avoid receiving injections?”, and “Does needle size frighten you?”. These are answered on a Yes/No scale although participants were also given

a “prefer not to answer” response which was rarely used (0.13% of responses). Participants were scored on a 0–6 scale according to the number of affirmative answers, as prior research had indicated reliable loadings on to a single factor (Wani et al., 2014).

The EDE-QS consists of twelve questions that load on to a single factor (Gideon et al., 2016). Example items include: “Have you been deliberately trying to limit the amount of food you eat to influence your weight or shape (whether or not you have succeeded)?” and “Has your weight or shape influenced how you think about (judge) yourself as a person?”. The 0–6 response scale from the original EDE-Q was used (Fairburn & Beglin, 1994). This captures eating habits over a 28-day period, and the scale is coded as 0 (no days), 1 (1–5 days), 2 (6–12 days), 3 (13–15 days), 4 (16–22 days), 5 (23–27 days), and 6 (everyday). (By contrast, the standard EDE-QS asks about the previous 7 days and may be more suited to continual monitoring of symptoms which was not our aim). Participants also had the option of a “prefer not to answer” response which was rarely used (0.27% of responses). The mean response across the 12 items was calculated to give each person a score on the 0–6 scale.

3.3 | Procedure

All three measures were administered online via Qualtrics (Provo, UT) and were completed in a fixed order (VPQ then BII then EDE) with questions administered in a fixed random order. The three measures took no more than 30 min to complete.

4 | RESULTS AND DISCUSSION

Considering the BII measure, a one-way ANOVA contrasting the three groups revealed a main effect of group, $F(2, 393) = 5.673, p = .004$. This is illustrated in Figure 1 and shows that the A/G group are more prone to Blood-Injection-Injury phobia. This measure also showed a significant effect

Group	N	Demographics			Vicarious pain questionnaire		
		Age	F	M	Intensity	L-G	S-A
Nonresponders, control	329	19.42 (1.65)	275	53	0.609 (1.070)	−0.052 (2.671)	0.888 (2.231)
Sensory-localized, S/L	37	19.70 (2.50)	35	2	2.379 (1.278)	2.568 (4.154)	13.946 (5.681)
Affective-General, A/G	29	19.17 (0.89)	28	1	2.177 (1.228)	−2.655 (3.588)	−10.793 (4.403)

TABLE 1 Participant characteristics for Study 1 from an opportunistic sample of Psychology undergraduates (showing mean and S.D.)

Note: The prevalence was estimated as 10.3% S/L and 8.3 A/G in women (F) and 3.6% and 1.8% in men (M); so a weighted population mean (for a 50:50 F:M distribution) is 6.96% for S/L and 5.03% for A/G.

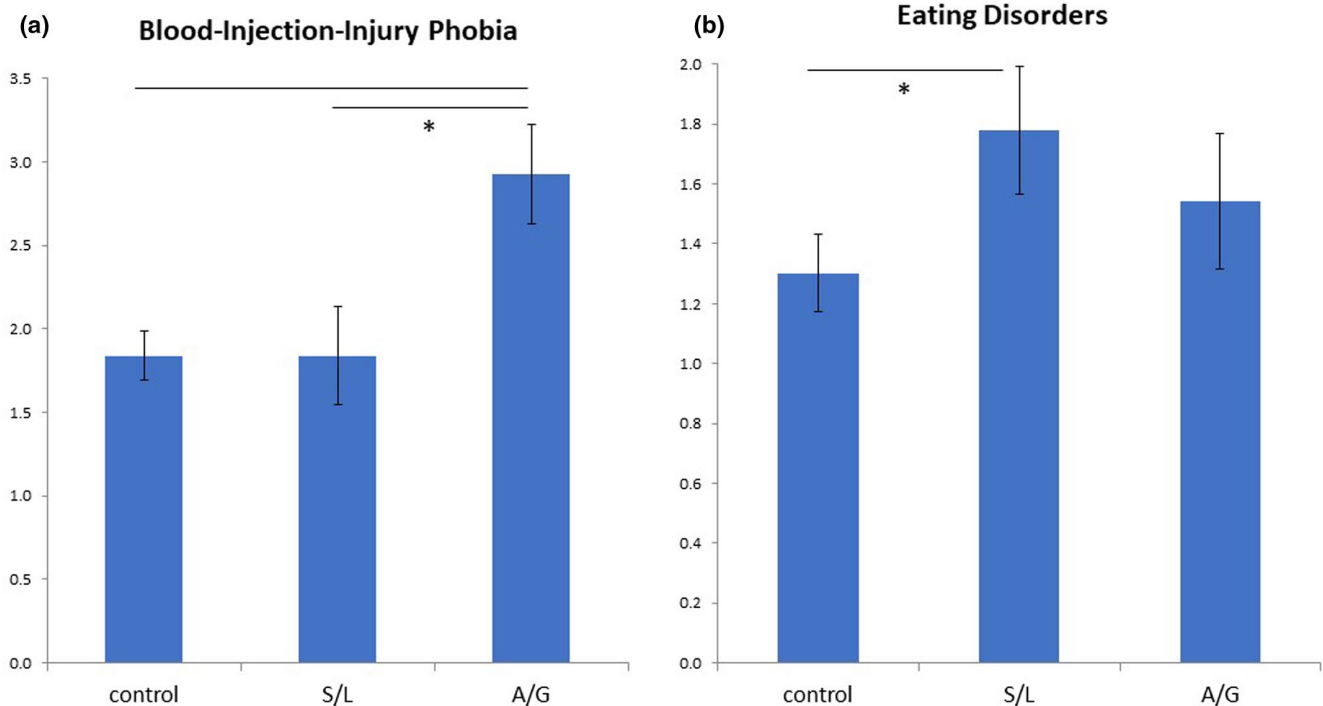


FIGURE 1 Mean level of responding (on 0–6 scales) for the three groups (all participants included) on the BII measure (a) and EQE-QS (b). S/L and A/G refer to sensory/localized responders and affective/general responders, respectively. Error bars show ± 1 SEM

of gender (female mean = 2.039, $SD = 1.290$; male mean = 1.196, $SD = 1.600$; $t(392) = 3.479$, $p = .001$). However, the main effect of group is robust even when only female participants are included (there were too few men in the responder groups to consider them separately): $F(2,393) = 4.716$, $p = .010$. Post-hoc analyses of this female subset, including Cohen's d effect sizes, showed that the A/G group differed significantly from both nonresponders, $t(301) = 3.051$, $p = .002$, $d = 0.61$, and the S/L group, $t(61) = 2.446$, $p = .017$, $d = 0.62$, and that the latter two groups did not differ from each other, $t(311) = 0.259$, $p = .796$, $d = 0.05$. The supplementary data shows the breakdown of responses across the six questions. A similar pattern was observed across items, although there was a generally low level of reports of fainting across all groups and this symptom is not regarded as an essential feature of BII (Page et al., 1997; Wani et al., 2014).

Considering the EDE-QS, the data was heavily skewed to the left: most respondents reported few if any behaviors linked to eating disorders. As such, the data was analyzed nonparametrically. Visual inspection of the data—Figure 1—showed a trend in the predicted direction with the S/L group showing numerically higher scores than the other groups. A Kruskal–Wallis test revealed a significant effect of group for the sample as a whole ($p = .035$). This is driven by a significant difference between the S/L group and controls, Mann–Whitney U, $p = .019$, but no other significant differences (S/L vs. A/G $p = .430$; A/G vs. controls $p = .201$). However, this measure showed a strong effect of gender,

Mann–Whitney U, $p < .001$, and the main effect of group failed to reach significance when considering only women respondents ($p = .157$). A consideration of individual items among women respondents revealed four questions (out of 12) that the S/L group scored significantly higher on relative to controls ($p < .05$), with two of these surviving correction for multiple comparisons using the Benjamini and Hochberg (1995) false-discovery rate (FDR) procedure. These were the items “Has thinking about your weight or shape made it very difficult to concentrate on things you are interested in (such as working, following a conversation, or reading)?” and “Have you tried to control your weight or shape by making yourself sick (vomit) or taking laxatives?”. No items were reliably discriminated between controls and the A/G group.

In summary, this study shows that the trait of consciously experiencing the pain of other people is linked to specific clinical vulnerabilities. People who report Affective-General Vicarious Pain report elevated symptoms relating to Blood-Injection-Injury (BII) phobia. This can have negative health consequences in terms of failure to engage in routine or essential procedures (e.g., dental treatment, inoculations). BII has been linked theoretically to autonomic system dysregulation although empirical evidence is mixed (Ritz et al., 2010). This mechanism may also contribute to A/G vicarious pain insofar as seeing other people in pain can produce autonomic responses that mirror their own personal responses to pain or expectations of pain (via needles, etc.). Importantly, this is not found in the sensory-localized group who report qualitatively different

responses to seeing other people in pain. This is the first empirical evidence to suggest that the A/G group may represent a distinct subtype as opposed to being intermediate between S/L and controls. In contrast, there is some evidence that the S/L group has increased proneness to eating disorders—an association that was initially hypothesized based on a similarity between these two conditions on a measure of body ownership (Rubber Hand Illusion). Here the result was more equivocal—the group difference was not significant when matching for gender (women only) although some items on the scale remained significant even after controlling for both gender and multiple comparisons. The present research provides sufficient motivation to explore this in more detail in future research.

5 | STUDY 2: PSYCHOPHYSIOLOGICAL AND BEHAVIORAL MARKERS OF INTEROCEPTION IN VICARIOUS PAIN RESPONDERS

This study was an experimental study consisting of an assessment of interoceptive accuracy and awareness and, separately, measures of psychophysiological responsiveness (heart rate, blood pressure, skin conductance) to the sight of pain. In addition, we measure state and trait anxiety because anxiety is correlated with interoceptive abilities. This may be a potential confound: that is, differences between our groups may be due to differences in anxiety rather than different vicarious pain profiles. Other research has suggested that anxious vicarious pain responders have less heart-rate variability (HRV) to seeing emotions, suggesting a diminished capacity to engage parasympathetic cardiovagal responses in support of emotion regulation (Nazarewicz et al., 2015). (Note: they didn't use our method for classifying vicarious pain but we assume it overlaps more with our A/G profile). The finding of Study 1 that the A/G profile is linked to Blood-Injection-Injury Phobia would also point to the differential tuning of baroreflex and associated cardiac parasympathetic tone in that group. This may be construed as an over-compensation to a normal arousal response (Ritz et al., 2010). However, evidence for this is mixed: Studies that have measured psychophysiological responses in groups with BII-phobia observing a medical procedure (Page, 2003) or having one performed on themselves (Gerlach et al., 2006) have not necessarily noted drops in BP/HR below the initial baseline.

6 | METHOD

6.1 | Participants

Participants were recruited via email invitation or via an advertisement placed for University of Sussex students. Ethical

approval was obtained from the Science and Technology Research Ethics Committee of the University of Sussex and all participants offered their written informed consent at the beginning of the study.

A total of 72 participants (mean age = 21.57, $SD = 4.30$; 56 women) completed all parts of the study. Each participant had previously completed the VPQ online via Qualtrics Online Survey and was divided into three groups following a cluster analysis conducted on a larger dataset of participants (Aged 18–60 years, mean age = 20.11, $SD = 6.94$; 290 men, 1,004 women). This was based on the dimensions of mean pain intensity, number of sensory minus affective descriptors, and number of localized minus general responses (following Botan, Fan, et al., 2018). There were 30 participants classed as nonresponders (i.e., controls) (mean age = 22.40, $SD = 5.47$, 22 women), 20 participants classed as sensory-localized (S/L) responders (mean age = 21.45, $SD = 3.89$, 14 women) and 22 participants classed as affective-general (A/G) responders (mean age = 20.55, $SD = 2.32$, 20 women). The groups did not differ by age, $F(2,71) = 1.199$, $p = .308$, $\eta^2 = 0.034$, or gender, $\chi^2 = 3.238$, $p = .198$. All participants had a normal Body Mass Index (BMI), based on self-reported height and weight data (where BMI is the weight in kilograms divided by the squared height, in meters). BMI was not a variable of interest but was considered only as a data exclusion criterion (notably being overweight may be linked to lower interoceptive accuracy; Koch & Pollatos, 2014). None were excluded for this reason. Due to technical issues, not all data was recorded from all participants: 2 nonresponders did not complete the interoceptive tracking task, 1 A/G lacked heart rate variability data (HRV), 1 S/L, and 2 A/G lacked blood pressure data, and 1 A/G lacked skin conductance data.

Additional interoception data was recorded, and combined, from a previous unpublished experiment (Grice-Jackson, 2017) using the same methodology from 69 participants which included 57 nonresponders (controls), 11 S/L responders, and 2 A/G responders (classified according to the same cluster analysis as the new participants). Demographics of this sample and the combined samples are shown in Table 2. After merging the two samples, the groups significantly differed in age, $F(2,139) = 5.084$, $p = .007$, but not in gender, $\chi^2 = 5.466$, $p = .243$. Effects of age are therefore considered in the analyses of the interoception task although it is to be noted that differences of around 7 years amongst young healthy adults would not be expected to have a large influence on interoceptive abilities.

The sample size was guided by previous research and limited by the availability of the rarer responder groups. Prior studies on physiological processes in vicarious pain responders have group N 's of 22, 16, and 11 (Nazarewicz et al., 2015) and group N 's of 27 and 23 (Young et al., 2017). Nazarewicz et al. (2015) reported an partial η^2 of 0.15 for group differences in heart rate, corresponding to effect size f of 0.403

TABLE 2 Demographic data for participants completing the interoception task (heartbeat detection) including a second sample (who took only the interoception task), and the merged sample (i.e., those taking the interoception task as part of the psychophysiological battery and those who had only taken the interoception task)

Group	Second sample		Merged sample	
	Age	Gender	Age	Gender
Control	28.98 ± 14.25	29 F, 28 M (<i>N</i> = 57)	26.71 ± 12.34	51 F, 36 M (<i>N</i> = 87)
S/L	22.27 ± 5.76	5 F, 6 M (<i>N</i> = 11)	21.74 ± 4.56	19 F, 12 M (<i>N</i> = 31)
A/G	22.00 ± 4.24	0 F, 2 M (<i>N</i> = 2)	20.67 ± 2.43	20 F, 4 M (<i>N</i> = 24)

where $f = \sqrt{(\eta^2 / (1 - \eta^2))}$, and a group difference of $r = 0.51$ for heart rate variability which is a large effect. A sensitivity analysis using G-power was conducted based on our sample size of $N = 72$, power = 0.8, alpha = 0.05, for a one-way ANOVA (three groups, numerator $df = 2$). This indicated that we would be able to detect a minimum effect size f of 0.374 (i.e., medium-to-large effects).

6.2 | Materials and procedure

Aside from participants who had previously taken the interoceptive tracking task as part of a previous study, all participants were tested in the laboratory with measures given in a fixed order. Specifically, they first completed the physiological measures (40 min including set-up time) and then they completed the STAI (5 min), and finally the interoceptive task (10 min). These are described in turn.

6.2.1 | Psychophysiological responses to observing pain

The task consisted of 32 film clips: 16 videos showed people in physical and 16 control videos showing people performing regular activities (e.g., riding a bicycle, sitting on a sofa, reading the newspaper, etc.). The videos depicting the physical pain were the same as used in the Vicarious Pain Questionnaire (VPQ). Half of them contained images with injections and the other half accidents. All clips lasted for 10 s and their order was randomized. A jittered inter-stimulus interval (ISI) of 5 s, 10 s, or 15 s represented by a grey screen with a fixation cross followed each video. The task was presented on a computer screen placed in front of the participants using Cogent2000 (version 1.32, http://www.vislab.ucl.ac.uk/cogent_2000.php) in Matlab (R2013a, Mathworks). The design of the task can be seen in Figure 2(a). All physiological measures were recorded using Cambridge Electronic Design (CED) hardware and Spike2 physiological recording software (version 7.17) at a sampling rate of 1,000 Hz, interfacing physiological recording with the task in Matlab. Measurement set-up and recording can be seen in Figure 2(b).

Cardiac cycles, for heart rate and heart rate variability measures, were recorded using electroencephalography (ECG, CED1902-11/ECG), with 10 Hz high bandpass filter and 100 Hz low bandpass filter applied (Fedotov, 2016), consisting of three electrodes: two placed under the lower clavicle on the right and left side, respectively, and one (the ground electrode) placed on the back of the participant.

Blood pressure was recorded using photoplethysmographic technology (Finometer PRO; Finapres 2,300, Ohmeda, Eaglewood, CO, USA) using an inflatable finger cuff and infrared plethysmograph attached to the index finger of the participant's left hand. Beat-to-beat values of systolic blood pressure (mmHg) were recorded and smoothed using Spike 2.7.17 channel process function, creating a constant signal of systolic peaks.

Skin conductance was recorded using two finger electrodes (CED2502) placed on the index and middle finger of the participant's right hand (van Dooren & Janssen, 2012).

6.3 | Anxiety questionnaire. State-Trait Anxiety Inventory (STAI)

The State-Trait Anxiety Inventory (STAI) (Spielberger, 1983) is a 40-item self-report scale that assesses both state and trait anxiety. State anxiety items ($N = 20$) assess how participants feel at that precise moment (i.e., “indicate how you feel right now”) and include statements such as: *I am calm, I feel tense, or I am frightened*. Trait anxiety items ($N = 20$) assess the dispositional, or more stable, trait of anxiety proneness (i.e., “indicate how you generally feel”). It contains items such as *I feel nervous and restless or I feel satisfied with myself*. For both state and trait scales, respondents are asked to indicate to what degree the item describes their feelings on a 4-point Likert-type scale ranging from 1 = not at all and 4 = very much so.

6.4 | Interoceptive accuracy and awareness

Interoceptive accuracy was measured using the heartbeat tracking task (Schandry, 1981) containing six trials with

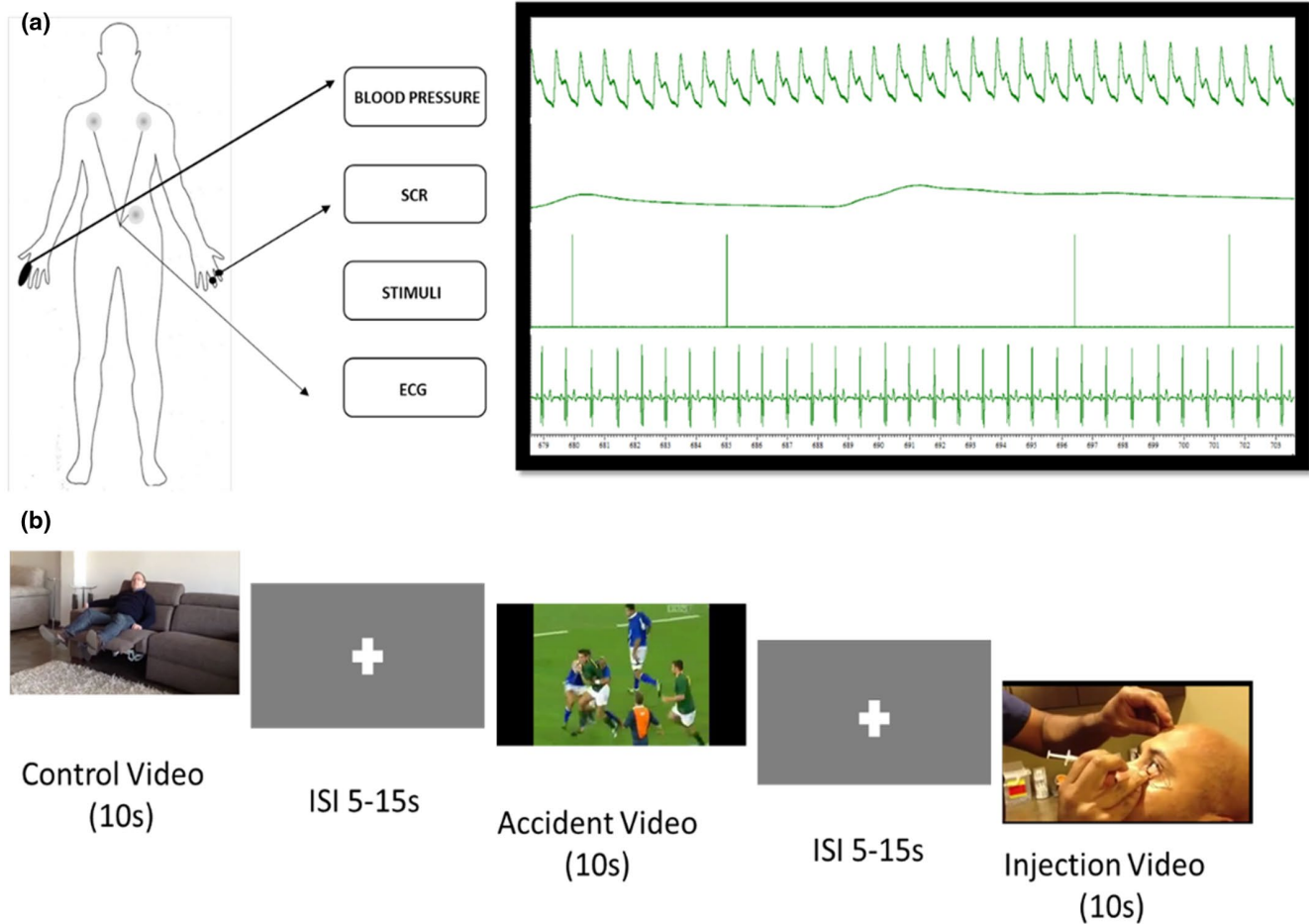


FIGURE 2 (a) Recording set-up and interface; (b) Task set-up

varying interval durations of 25, 30, 35, 40, 45 and 50 s played on a computer in a randomized order. Participants were instructed to silently count, the number of heartbeats perceived in the given interval marked by “start” and “stop” sounds played to them by the program and to report them at the end of each trial. Their reports were recorded after each trial. Participants had their back at the screen and were asked to focus attention on their body and to only count the heartbeats felt without checking their pulse. Their actual heartbeats were measured with a medical grade pulse oximeter (Nonin 8,600) with a soft sensor to minimize the possibility of reporting finger pulse instead of heartbeat.

Confidence judgments were taken at the end of each trial, participants being asked to rate the confidence they had in their reported number of heartbeats. Their response was recorded on a 10 points continuous visual analog scale (VAS) from “total guess/no heartbeat awareness” to “complete confidence/full perception of heartbeat.” The ratings were then correlated with the scores obtained on the heartbeat tracking task (i.e., interoceptive accuracy). A high interoceptive awareness score meant that the person performed well on the task (had high interoceptive accuracy) and reported a high confidence in their ability to detect heartbeats or they

performed poorly on the task and reported low confidence in their judgment.

The interoceptive accuracy score was derived using the following formula: $1 - (n_{\text{beatsreal}} - n_{\text{beatsreported}}) / ((n_{\text{beatsreal}} + n_{\text{beatsreported}}) / 2)$. The resulting scores of each trial were averaged yielding the overall value for each participant (Garfinkel, Seth, et al., 2015). Interoceptive awareness was then calculated using the Pearson correlation between interoceptive accuracy and confidence rating (Garfinkel, Seth, et al., 2015). As the dependent variable for interoceptive awareness was a Pearson's r this was transformed to be normally distributed using the Fisher r -to- z formula for statistical analysis:

$$z' = .5 [\ln(1 + r) - \ln(1 - r)]$$

7 | STATISTICAL DATA ANALYSES

7.1 | Preprocessing

With regards to the psychophysiological measures obtained during the observed pain task, for the heart rate and HRV

analysis, a threshold was applied to isolate R-wave peaks and to extract the number of heartbeats in a given time interval. The heartbeats were extracted for pain videos, control videos, and 3 min resting state period taken at the end of the task. This gave measures of heart rate (HR) (beats per time interval) and heart rate variability (HRV) expressed as the root mean square of successive differences (RMSSD) between normal heartbeats. RMSSD is the primary time-domain measure for short-term variation, it is strongly correlated with high-frequency variations and is an indicator of the vagally mediated (parasympathetic) changes reflected in HRV (Shaffer & Ginsberg, 2017). Both HR and HRV were calculated for injection videos, accident videos, control videos, and resting state. The different kinds of video depicting pain were treated separately given that injections may elicit a strong arousal response. Mean systolic blood pressure levels were then derived by averaging systolic levels over accident videos, injection videos, control videos, and resting state (Garfinkel, Zorab, et al., 2015). The analysis of SCR was performed in Matlab using Ledalab (V3.4.9) software. Adaptive data smoothing was applied, and continuous decomposition analysis was performed with the extraction of continuous phasic and tonic activity. Event-related activation was computed for each type of stimulus events: accidents, injections, and control videos as the sum of SCR-amplitudes of SCRs greater than 0.02 μ S within a time window of 1-4s of stimulus onset. The data were transformed in order to obtain a more normal distribution using the formula $\log_{10}(\text{SCR} + 1)$.

7.2 | Inferential statistics

Analyses of variance (one-way ANOVAs) were used to establish differences between groups on unidimensional measures including the interoceptive accuracy and awareness scores, anxiety scores, and resting state measures of heart rate and heart rate variability.

Mixed models analyses of variance (3×3 mixed ANOVAs) were run for task measures of HR, HRV, blood pressure, and skin conductance. The analyses assessed the interactions between the 3 groups (C, S/L, and A/G) and 3 conditions (control videos, accident videos, and injection videos). When sphericity was not assumed, the most conservative Greenhouse-Geisser correction was reported (Field, 2013).

Variables were treated as continuous and most of them were normally distributed as shown by Shapiro-Wilk tests and Kolmogorov-Smirnov tests. When normality assumptions were violated in more than one group, Kruskal-Wallis H and Mann-Whitney U nonparametric tests were also run, reconfirming the results as shown in supplementary results. These cases included interoceptive accuracy scores and task heart rate data and skin conductance data. All analyses were run in SPSS separately for each measure and test-wise Bonferroni confidence interval adjustment was used for comparisons of

main effects and Hochberg's GT2 or Dunnett's C post hoc tests for different sample sizes were run depending on whether assumption for equal variance or unequal variance were met (Field, 2013).

To consider the role of potential confounding variables a set of hierarchical multiple regression analyses were run. These are reported in detail in the Supplementary Results as they effectively serve to confirm the main findings reported here. They also avoid the need for correction for multiple comparisons given that several variables are taken into consideration within single models. In addition, the eight separate group effects reported in Study 2 (state anxiety, trait anxiety, interoceptive awareness, interoceptive accuracy, heart rate, heart rate variability, systolic blood pressure, and skin conductance) were subjected to FDR correction for multiple comparisons (using the method of Benjamini & Hochberg, 1995).

8 | RESULTS

8.1 | Anxiety results and trait measures correlations

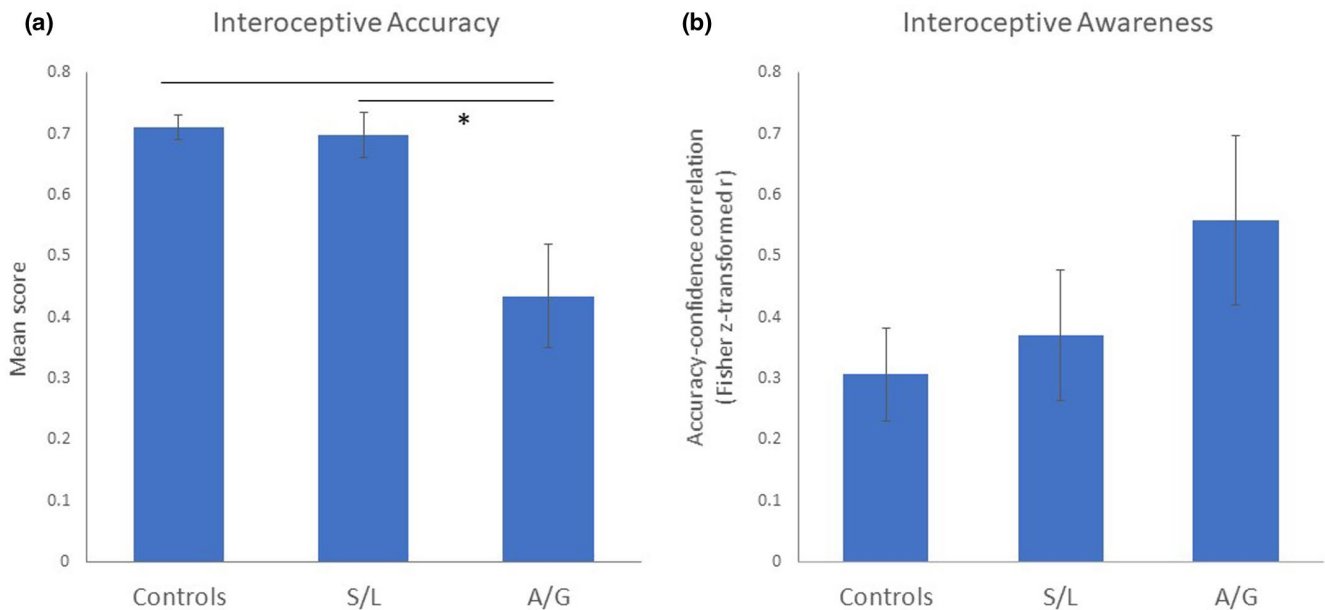
There were no differences between groups in either anxiety state, $F(2, 63) = 0.727, p = .488, \eta^2 = 0.023$, nor trait, $F(2, 63) = 1.494, p = .232, \eta^2 = 0.047$, as previously noted for these groups (Bowling et al., 2019). The mean state anxiety levels for controls, S/L, and A/G were 33.652 ($SD = 8.728$), 32.737 ($SD = 7.030$), and 35.636 ($SD = 8.318$), respectively. The mean trait anxiety levels for controls, S/L, and A/G were 43.261 ($SD = 11.663$), 38.947 ($SD = 7.397$), and 43.591 ($SD = 8.472$), respectively. Anxiety did not correlate with any of the interoceptive or physiological measures. Correlations can be seen in Table 3. A strong inverse correlation was seen between HRV and HR as noted elsewhere (Sacha & Pluta, 2005). As such, we can be confident that any differences that are found between our three groups are not due to being confounded by general state and trait anxiety.

8.2 | Interoceptive accuracy and awareness

Interoceptive accuracy and awareness scores can be seen in Figure 3. There were significant group differences in interoceptive accuracy, $F(2, 137) = 12.960, p < .001, \eta^2 = 0.161$. The A/G group had lower interoceptive accuracy than both controls ($p < .001$, Cohen's $d = 1.115$) and S/L ($p < .001$, Cohen's $d = 0.837$). There were no group differences in interoceptive awareness, $F(2, 139) = 1.268, p = .285, \eta^2 = 0.018$. That is, although the A/G group had worse performance on the task they were just as aware of their performance as the other groups. The interoceptive accuracy results are robust when considering other potentially confounding variables

TABLE 3 Correlations between HR, HRV, anxiety, and interoception

	Interoceptive accuracy	Interoceptive awareness	Anxiety state	Anxiety trait	HR (bpm)	HRV RMSSD
Interoceptive accuracy						
Interoceptive awareness	$r = 0.046$ $p = .706$					
Anxiety state	$r = 0.030$ $p = .817$	$r = -0.065$ $p = .610$				
Anxiety trait	$r = 0.013$ $p = .921$	$r = -0.051$ $p = .690$	$r = 0.599$ $p < .001$			
HR (bpm)	$r = -0.126$ $p = .311$	$r = -0.082$ $p = .510$	$r = 0.111$ $p = .392$	$r = 0.244$ $p = .056$		
HRV RMSSD	$r = 0.189$ $p = .120$	$r = -0.005$ $p = .969$	$r = 0.111$ $p = .388$	$r = -0.032$ $p = .802$	$r = -0.569$ $p < .001$	


FIGURE 3 Interoceptive accuracy (a) and awareness scores (b). Interoceptive accuracy is measured as the absolute difference between actual and reported heart beats (divided by the mean of actual and reported beats) and scaled so that 1 represents a perfect score. Interoceptive awareness is measured as the correlation between confidence and accuracy. Error bars indicate $\pm 1SE$. $*p < .01$

such as age and anxiety (see Supplementary Results for hierarchical mixed models), and remain after correction for unequal sample sizes (Dunnett's c).

9 | PSYCHOPHYSIOLOGICAL RESPONSES TO OBSERVING PAIN

9.1 | Heart rate (HR) and Heart rate variability (HRV)

Results can be seen in Figure 4. For task-related HRV, mixed model 3 x 3 ANOVAs showed a significant effect of group, $F(2,$

68) = 3.230, $p = .046$, $\eta^2 = 0.087$, with S/L group having higher HRV than the control group ($p = .045$, Cohen's $d = 0.695$). There was no effect of condition, $F(2, 136) = 0.759$, $p = .470$, $\eta^2 = 0.011$, nor interaction, $F(4, 136) = 1.223$, $p = .305$, $\eta^2 = 0.035$.

Regarding task-related HR, mixed model 3 x 3 ANOVAs showed a significant effect of condition, $F(2, 109) = 39.859$, $p < .001$, $\eta^2 = 0.377$ (Greenhouse-Geisser corrected), with control videos having lower HR than accident videos ($p < .001$) and injection videos ($p < .001$) and accident videos having lower HR than injection videos ($p < .001$). There was no effect of group, $F(2, 66) = 0.059$, $p = .943$, $\eta^2 = 0.002$, nor interaction, $F(3, 109) = 0.634$, $p = .610$, $\eta^2 = 0.019$ (Greenhouse-Geisser corrected).

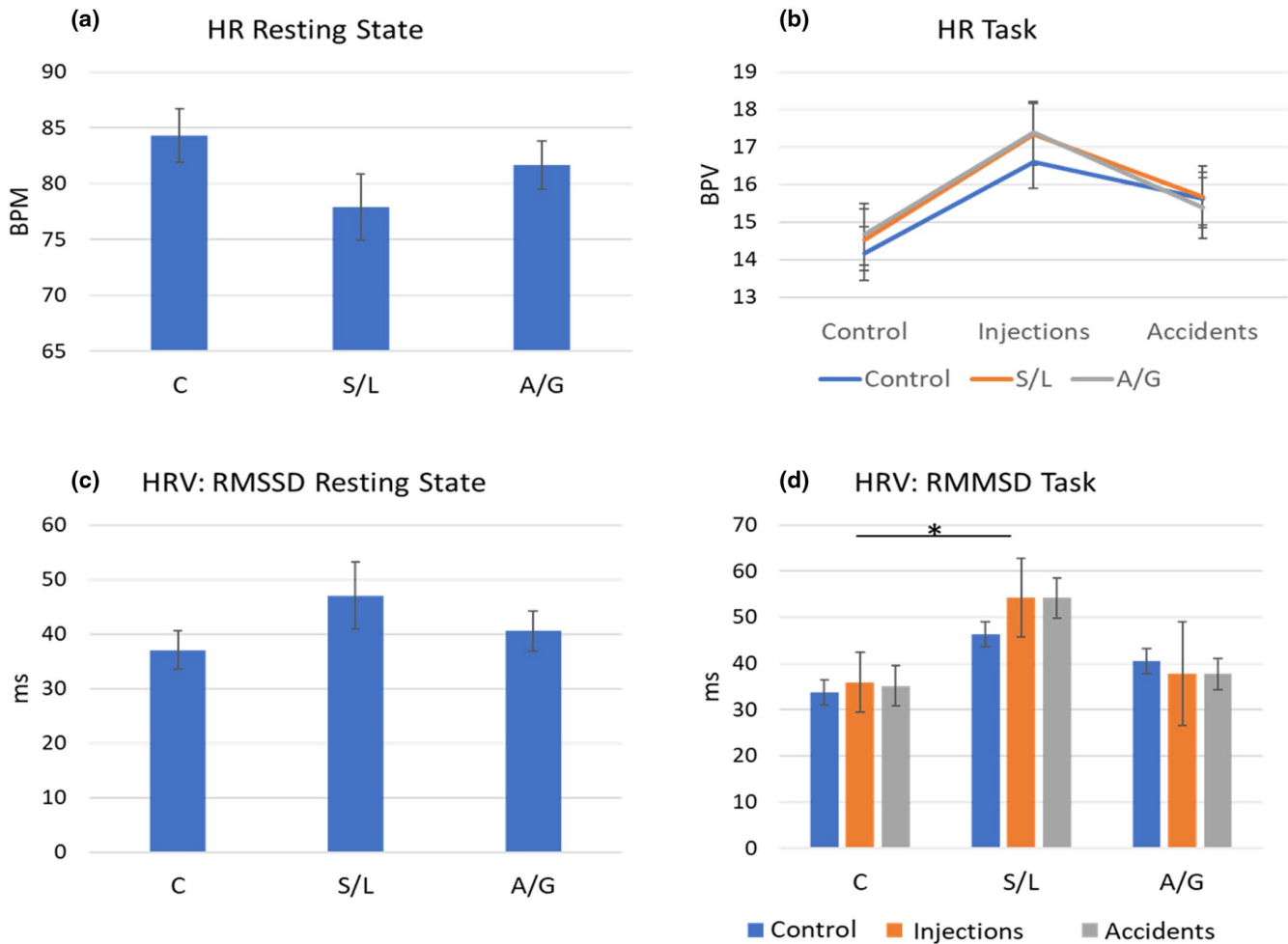


FIGURE 4 Heart Rate (HR) at resting state as beats per minute (BPM) in (a) and during the task as beats per 10s video (BPV) for each pain category and control in (b). Heart rate variability (HRV) as RMSSD (root mean square of the successive differences) expressed in milliseconds (ms) at resting state (c) and during the task in (d). Main effect of group for task HRV with S/L group having higher HRV than controls. Error bars indicate $\pm 1SE$. * $p < .05$

There were no differences between groups in pretask resting state HR, $F(2, 68) = 1.528$, $p = .224$, $\eta^2 = 0.044$, nor HRV, $F(2, 70) = 1.314$, $p = .275$, $\eta^2 = 0.037$.

9.2 | Blood pressure

Results can be seen in Figure 5(a). There was a significant effect of condition in blood pressure, $F(2, 132) = 11.235$, $p < .001$, $\eta^2 = 0.145$, the average blood pressure being higher for injection videos when compared to both control videos ($p < .001$) and accident videos ($p = .002$). There was no effect of group, $F(2, 66) = 1.458$, $p = .240$, $\eta^2 = 0.042$, nor interaction, $F(4, 132) = 1.076$, $p = .371$, $\eta^2 = 0.032$. The A/G group showed a general tendency toward higher blood pressure for all conditions (Cohen's $d = 0.427$, 0.472 , and 0.496 for injections, accidents, and control movies).

9.3 | Skin conductance

Results can be seen in Figure 5(b). There was a significant effect of condition in skin conductance, $F(2, 136) = 13.260$, $p < .001$, $\eta^2 = 0.163$. The average amplitude in skin conductance response was higher for injection videos than control videos ($p < .001$) and accident videos ($p = .001$). There was no effect of group, $F(2, 68) = 0.738$, $p = .482$, $\eta^2 = 0.021$, nor interaction, $F(4, 136) = 0.419$, $p = .795$, $\eta^2 = 0.012$.

9.4 | Multivariate analysis and multiple comparisons

The two significant group effects (lower interoceptive accuracy for A/G group, higher HRV for S/L group when observing pain) remained after hierarchical regression analyses in which other demographic, trait, and physiological variables

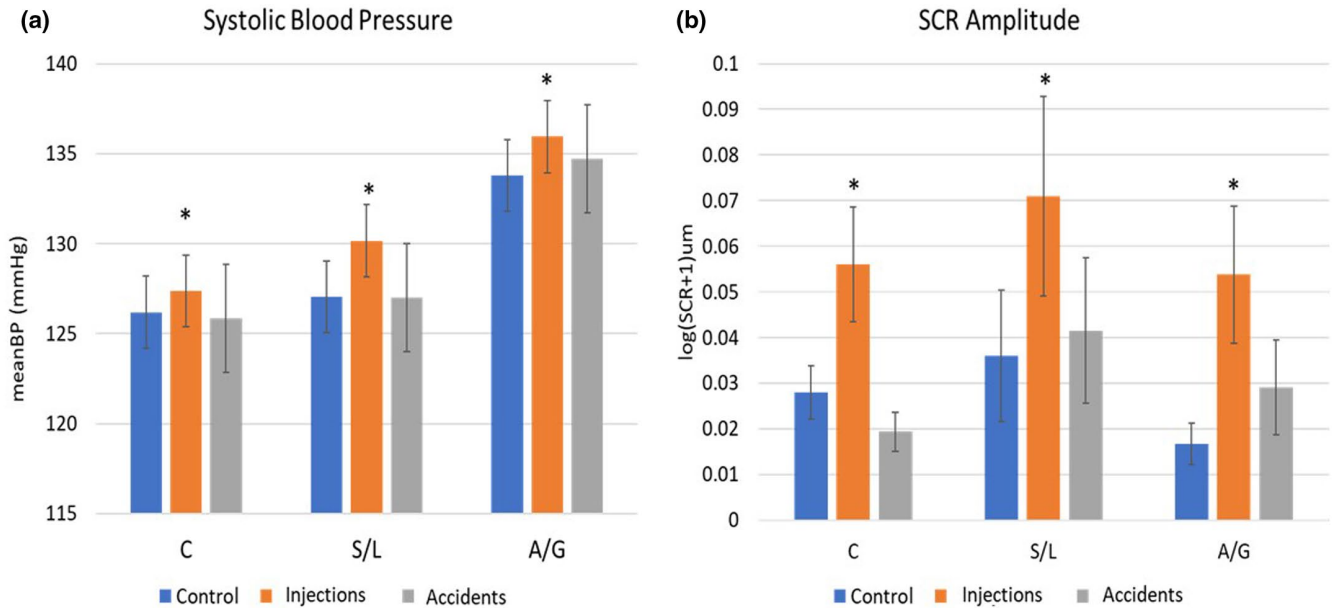


FIGURE 5 Mean systolic blood pressure (a) and skin conductance results (b). There was a main effect of condition for both measures with injection videos showing increased physiological arousal than both accident videos and control videos. Error bars indicate ± 1 SE. * $p < .01$

were entered as possible confounds (see Supplementary Results). In terms of correcting for testing for multiple independent group effects ($N = 8$ analyses), the group effect of interoceptive accuracy survived FDR correction for multiple comparisons but HRV did not.

9.5 | Summary

In summary, this set of studies shows two different group effects that correspond to phenomenological differences in the way that vicarious pain is experienced. Specifically, the A/G responders who report affect-related vicarious pain responses show poor interoceptive accuracy (detection of heartbeat) relative to the S/L responders and control group. This occurs in spite of the fact that both the A/G group and S/L group report higher interoceptive sensibility, and we discuss this dissociation further in the General Discussion. The second main finding is that the S/L group showed higher HRV during the task of observing painful movies. This measure is typically inferred to be a marker of good emotional regulation (Appelhans & Luecken, 2006; Thayer et al., 2012), and therefore may be interpreted as an adaptive response to vicarious pain. In neither responder group did we find an overall increase in physiological arousal to observing pain driven by the sympathetic system (relating to blood pressure, skin conductance, or heart rate) nor a lowering of these indices of arousal that might be elicited by the compensatory overactivity of the parasympathetic system (e.g., as postulated for Blood-Injection-Injury Phobia). That is, the simulation of pain by vicarious pain responders may primarily be driven by

differences in brain activity without concomitant individual differences in the overall level of autonomic responses in the body.

10 | GENERAL DISCUSSION

The broad aim of this study was to determine whether consciously experiencing the pain of others (in vicarious pain responders) is linked to differences in clinical traits (Blood-Injection-Injury [BII] phobia, eating disorder, and general anxiety), and differences in interoceptive processes as measured through both physiology (blood pressure, heart rate, skin conductance) and behavior (interoceptive accuracy and awareness). The theoretical assumption is that vicarious pain responses are indicative of a wider profile of neurocognitive differences in simulation, embodied cognition, and self-other control that are not specific to pain. We considered two different subtypes of vicarious pain responders (affective-general A/G and sensory-localized S/L) that, on other measures such as emotion contagion and fMRI/VBM, appear similar to each other (but different from non-responder controls). The current results suggest that there are key differences between these subtypes and shows, for the first time, that the A/G group has a distinctive cognitive and clinical profile: Affective-general responders show a significantly increased tendency toward BII phobia, whereas sensory-localized responders show a tendency toward eating disorders. The latter finding was only suggestive: it requires further study and therefore is not discussed in detail here. Our results showed that, despite having better interoceptive

sensibility and being more attentive their bodies (Bowling et al., 2019), vicarious responders do not objectively show better perception of their internal sensations (i.e., do not have higher cardiac interoceptive accuracy). In fact, performance on the heartbeat tracking task (known also to be sensitive to other factors such as suggestion) is significantly worse in the A/G group (relative to both S/L and controls). Furthermore, compared to controls, members of the A/G group do not differ significantly in measures of autonomic arousal when observing pain. In contrast, the S/L group manifest higher heart-rate variability (HRV) indicative of enhanced cardio-vagal engagement, a capacity that is usually associated with better health and emotion regulation. Altogether, these results indicate that vicarious pain responses present in these populations are not due to disinhibited arousal. Their autonomic responses are arguably more in keeping with adaptation to, rather than a cause of, the vicarious pain phenotype. These findings are discussed in more detail, considering in turn; anxiety and BII phobia; interoceptive accuracy, awareness, and sensibility; physiological arousal and autonomic measures of emotion regulation.

10.1 | Anxiety and BII phobia

The present research, together with a previous study (Bowling et al., 2019), has shown that vicarious pain responders do not have higher levels of general anxiety as measured by the commonly used STAI measure. However, this finding requires some qualification because BII phobia, which is elevated in the A/G group, is a medically recognized anxiety disorder albeit one that is specific in nature (American Psychiatric Association, 2013). Other researchers, using different measures of anxiety and individual differences in vicarious pain, have reported an anxious vicarious pain responder group that is distinct from nonanxious responders and controls (Nazariwicz et al., 2015; Young et al., 2017). The main measure of anxiety used in these studies (the anxiety subscale of the DASS-21; Henry & Crawford, 2005) focused on bodily symptoms such as dry mouth, breathing, and panic which might be expected to be a greater focus of attention in vicarious pain responders (Bowling et al., 2019). As such, there is a need for further systematic assessments of anxiety that consider different symptom profiles (e.g., physical, cognitive, and social; Taylor et al., 2007) as well as the nature of inducing triggers (general vs. specific).

There is also an extensive literature on psychological factors, such as catastrophizing, that influence how people judge the pain of others (e.g., Sullivan et al., 2006). At present, it is uncertain how these variables map on to being a vicarious pain responder. People who catastrophize may be projecting their own anxieties when seeing others in pain, whereas vicarious pain involves experiencing the pain of other people

on their own bodies. Both examples involve some element of self-other confusion but are at least superficially different.

10.2 | Interoceptive accuracy, awareness, and sensibility

On a heartbeat counting task, the A/G group had lower interoceptive accuracy compared to both controls and S/L responders. All groups had normal interoceptive awareness (i.e., in the case of the A/G group they knew they were bad). This stands in contrast to (trait) interoceptive sensibility, which has previously been shown to be higher in both A/G and S/L groups (Bowling et al., 2019). The results are consistent with previous findings suggesting that interoceptive sensibility and accuracy are dissociable traits (Cali et al., 2015; Garfinkel, Seth, et al., 2015). Trait interoceptive sensibility, as measured by questionnaires such as the MAIA (Mehling et al., 2012), seems to be connected mainly to the attention paid to our bodies and is enhanced in people systematically exposed to or suffering from pain such as chronic pain patients (Valenzuela-Moguillansky et al., 2017). Interoceptive sensibility might not only capture bodily attention and surprise, but may also be related to the propensity for some people to generate realistic embodied sensations (including but not limited to vicarious pain), akin to Damasio's (1999) idea of an "as if" loop. Thus, some individuals may generate false (simulated) bodily sensations (linked to measures of interoceptive sensibility) but need not be grounded in any objective reality (linked to interoceptive accuracy). Interoceptive sensibility, at least as measured by the MAIA, also encompasses the notion of whether bodily sensations are trusted/accepted (i.e., a more mindful or salutogenic approach) or distrusted (linked to anxiety), and vicarious pain responders appear to have normal levels of trust in their bodily experiences (Bowling et al., 2019). A mindful attitude toward the body contributes positively to emotion regulation (Lutz et al., 2013).

There are several possible reasons for lower interoceptive accuracy in the A/G group. Firstly, lower interoceptive accuracy is found in people with higher physical pain thresholds (Grynberg & Pollatos, 2015; Pollatos et al., 2012) but physical pain sensitivity has yet to be explored in vicarious pain responders. Secondly, lower interoceptive accuracy has been linked to a more malleable sense of self (Tsakiris et al., 2011). This fits well with theoretical accounts of vicarious pain (e.g., Ward & Banissy, 2015), but this account makes the prediction that lower interoceptive accuracy would apply to both A/G and S/L groups. It suggests instead that there are dissociable mechanisms relating to self-other processing that is captured by measures of interoceptive accuracy (affecting A/G responders) and rubber hand illusion (affecting S/L responders) that resembles a

neuropsychological double dissociation (albeit at the level of individual differences in the general population). Finally, it is possible that the impairment in interoceptive accuracy observed in the A/G group is context dependent, occurring because the overall experimental setting generates significant external stressors for this group which directs attention away from the body (a form of coping mechanism). There is some evidence that, in conditions of arousal following an experimental stressor, interoceptive accuracy diminishes in female participants (Fairclough & Goodwin, 2007). Further evidence suggests that interoceptive accuracy diminishes under the influence of stressors only if attention ceases to be directed to internal bodily signals and oriented instead toward external stimuli (Schulz et al., 2013).

10.3 | Physiological arousal and autonomic measures of emotion regulation

Emotion regulation, the ability to respond to evocative stimuli in an adaptive manner, critically depends on the adjustment of physiological arousal controlled by the autonomic nervous system (Gross, 1998). Heart Rate Variability (HRV) has been used for decades as an index of emotion regulation: HRV is a measure of the interplay between sympathetic and parasympathetic systems' control over heart rate, thus it indicates the flexibility of the autonomic system which is argued to be crucial for effective emotional self-regulation (Appelhans & Luecken, 2006). Proximally, HRV provides a measure of the baroreceptor-related interplay of parasympathetic activation and deactivation against sympathetic effects on the heart, linked to the affective state in models proposed by polyvagal (Porges, 2001) and neurovisceral integration (Thayer & Lane, 2000) theories.

Previous research indicated that higher resting state HRV is linked to lower levels of distress after watching upsetting videos (Fabes et al., 1993) and better coping in social situations (Fabes et al., 1994). Studies on chronic pain suggest that HRV is diminished in chronic pain patients (Koenig et al., 2016; Terkelsen et al., 2005), the interpretation being that autonomic coping mechanisms to pain are impaired in these patients (i.e., as a predisposing vulnerability). We used this measure as an indicator of emotion regulation in vicarious pain responders (or its lack of). Only the S/L group showed higher HRV during the pain observation task, suggesting that they can implement adaptive coping strategies. This result remained after considering potential confounds (in hierarchical regression analysis) although this needs replication given the larger number of dependent variables considered.

The fact that the A/G group did not show higher HRV needs further investigation. It may be that they have

another coping mechanism or that their tendency toward BII attenuated the effect. There is evidence suggesting that HRV is lower in nonclinical panickers and blood phobics (Friedman & Thayer, 1998) and some evidence of lower HRV in vicarious pain responders with an anxious profile (Young et al., 2017). The physiological responsiveness to the sight of pain (including injections and injuries) in the A/G group was largely unremarkable (there was a non-significant trend toward increased systolic blood pressure across all stimuli). There was no evidence consistent with increased parasympathetic involvement that might, for instance, lead to fainting. Fainting versus phobic responses to Blood-Injection-Injury stimuli may be separable and fainting might be linked specifically to the sight of blood (Page et al., 1997; Wani et al., 2014). Note that none of our stimuli showed blood.

There was no evidence of increased physiological arousal (mediated by the sympathetic system) in either of the two pain responder groups, in terms of skin conductance rates, systolic blood pressure, or heart rate. It is important to note that our stimuli were suitably arousing on all of these physiological measures (main effects of condition driven primarily by observing injections), but there were no additional main effects of group, and no significant group X condition interactions. Caution is needed in interpreting this null result, but our speculation is that vicarious pain is essentially a centrally mediated mechanism (e.g., hyperactivity of the somatosensory and insular cortices driven by differences in self-other control) rather than bottom-up processes (e.g., a disinhibited physiological/visceral response).

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AUTHOR CONTRIBUTIONS

Vanessa Botan: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Validation; Visualization; Writing-original draft. **hugo dyfrig critchley:** Conceptualization; Funding acquisition; Methodology; Resources; Supervision; Writing-review & editing. **Jamie Ward:** Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Supervision; Writing-original draft.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section. Study 2 Interoception_Merged_Data_anon
Study 2 Physiology_Study_Data_Anon
Supplementary Results

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