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The impact of the social context on the development of secondary hyperalgesia: an experimental study

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Abstract

Social support has been shown to reduce pain ratings and physiological responses to acute pain stimuli. Furthermore, this relationship is moderated by adult attachment styles. However, these effects have not been characterized in experimentally induced symptoms of chronic pain, such as secondary hyperalgesia (SH) which is characterized by an increased sensitivity of the skin surrounding an injury. We aimed to examine whether social support by handholding from a romantic partner can attenuate the development of experimentally induced SH. Thirty-seven women, along with their partners, participated in 2 experimental sessions 1 week apart. In both sessions, SH was induced using an electrical stimulation protocol. In the support condition, the partner was seated across from the participant holding the participant's hand during the electrical stimulation, whereas in the alone condition, the participant went through the stimulation alone. Heart rate variability was measured for both the participant as well as the partner before, during, and after the stimulation. We found that the width of the area of hyperalgesia was significantly smaller in the support condition. Attachment styles did not moderate this effect of social support on the area width. Increasing attachment avoidance was associated with both a smaller width of hyperalgesia and a smaller increase in the sensitivity on the stimulated arm. For the first time, we show that social support can attenuate the development of secondary hyperalgesia and that attachment avoidance may be associated with an attenuated development of secondary hyperalgesia.

Keywords: Secondary hyperalgesia, Central sensitisation, Pain, Social support, Attachment styles, Heart rate variability, Chronic pain

1. Introduction

Despite substantial advances in our understanding of pain, it remains unclear what makes some individuals more vulnerable to develop persistent pain.[6,19,40] The extant research suggests that the mechanisms underlying this process are best conceptualized in a biopsychosocial framework.[25] In this light, pain persistency may emerge from the interaction between not only neurobiological specificities but also their interaction with the rather sparsely studied social context.[6] In clinical populations, social support has been linked to both reduced[13,38,41] and increased pain.[23,31,52] In healthy populations on the other hand, despite some mixed findings,[9,29,46] most of the evidence has suggested that both active social support such as handholding[56] as well as passive or primed social support, such as presence or viewing one's partner photographs, reduces pain intensity and unpleasantness,[9,43,59] pain-related neural activity,[17,21,36,72] and heart rate, skin conductance, and cortisol reactivity in response to experimental pain.[56,57] Social threat, on the other hand, may increase pain intensity—specifically for high pain catastrophizers[54]—as well as pain-related fear learning.[30] Some authors have hypothesized that the presence of social support may serve as a safety signal predicting the relative safety of a given environment, thus reducing the perceived saliency of noxious stimuli.[34,37] However, this effect is not uniform across individuals. Adult attachment styles,[8] which have been linked to chronic pain conditions,[47] have been shown to moderate the effect of social support on pain.[34,36,59] Individuals high on attachment anxiety tend to show hypersensitivity to threats and hypervigilance in threatening situations,[20] whereas individuals high on attachment avoidance tend to downregulate their affectivity in the face of threat and prefer coping alone. Accordingly, anxiously attached individuals have been shown to report lower pain scores in the presence of high vs low empathy partners or affective touch,[59,72] whereas avoidantly attached individuals have been found to report higher pain scores and greater cortical responses to brief heat stimuli in the presence vs the absence of a partner.[35,59]

Despite these data on acute pain, the impact of social support on the development of secondary hyperalgesia (SH), a common symptom of many persistent pain conditions, its interaction with attachment styles, and the role of stress responses in this process remain unexplored. To answer this question, we adopted a mechanistic approach and induced SH in human healthy volunteers (women) using an electrical stimulation protocol, either while their partner was holding their hands (handholding

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Data availability: The authors will make all data available on request.

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condition) or was absent (alone condition). We hypothesized that handholding would reduce the development of SH and that these effects would be moderated by attachment style. Furthermore, social touch has also been shown to increase levels of heart rate and neural synchrony between an individual experiencing pain and their social partner, which is inversely related to the experienced pain intensity.[26,27] We, therefore, explored whether handholding would increase the level of heart rate synchrony during the painful stimulation and whether higher heart rate synchrony would predict lower SH.

2. Methods

2.1. Participants

Thirty-seven romantic couples took part in the experiment (mean ± SD age: 21.5 ± 3.8 years), but only women acted as participants to minimize the confounding effect of sex differences in pain perception.[2] The sample size was estimated based on a power simulation before the start of the study (see supplementary material, available at http://links.lww.com/PAIN/B862). Participants were restricted from participating if any of the following exclusion criteria applied: a history of chronic pain or pain on the day of the experiment, a diagnosis of depression, anxiety, substance use or other psychiatric conditions, injured skin or scars on the forearm, regular use of prescribed or nonprescribed psychotropic medication, pregnancy, or less than 5 hours of sleep the night before the day of the experiment. Participants were asked to refrain from taking any analgesics or other anti-inflammatory medications as well as consuming stimulants such as nicotine or caffeine 12 hours before the start of the experiment. Finally, participants were only included in the experiment if they had been in a relationship for at least 1 year. All couples who volunteered to participate in the study were heterosexual couples, although the inclusion criteria did not limit the recruitment to heterosexual couples. Participants were recruited by the online Experiment Management System (EMS) of the Faculty of Psychology and Educational Sciences, KU Leuven, as well as through advertising posters and social media. An informed consent form was signed by all participants before the start of each experimental session. Participants as well as their partners were compensated with either course credits or financially (1 credit/hr or 10 eur/hr). Ethical approval for the experiment was obtained from the Social and Societal Ethics Committee (SMEC) of KU Leuven (G-2020-2854-R3).

2.2. Procedure

Before attending the experimental sessions, participants answered the experiences in close relationships—Revised (ECR-R) Questionnaire,[24] the Pain Catastrophizing Scale (PCS),[61] and the Revised Dyadic Adjustment Scale (RDAS)[11] (see questionnaires) through an online link. Of the questionnaires that the participants answered, only the ECR-R was analyzed in the current study. The remaining questionnaires were collected as part of a larger project. All participants attended 2 experimental sessions (alone and support conditions) separated by 1 week. The order of the 2 experimental conditions was counterbalanced across participants. On the couple's arrival at the laboratory, the participant and her partner were invited to sit at a table facing each other. The experimenter explained the study protocol, and the participant was invited to read and sign the informed consent form. Afterwards, the experimenter collected the participant's baseline ratings of intensity and unpleasantness for the mechanical pinprick stimuli that were applied on both arms (T0, see following paragraphs for details).

In the *alone condition*, the partner was then invited to sit in an adjacent room. The participant did not have any prior knowledge that the partner would be asked to leave the room in the alone condition. In the *support condition*, the participant and her partner remained in the same room. Heart rate electrodes were placed in a lead II configuration on both the participant and the partner, and the stimulation electrode was placed on the participant's volar forearm. The arm onto which the electrode was placed (dominant vs nondominant) was randomized across participants. The participant's detection threshold was then established using a staircase procedure[65] where a low intensity was presented at first and then was gradually increased (.1 mV step size) until the participant was able to detect the stimulus. The intensity was then lowered again until the participant was unable to detect the stimulus. The threshold was established after 3 such reversals. The baseline heart rate was then recorded for 2 minutes (while the participants remained in a seated position). In the support condition, before performing the painful procedure leading to hyperalgesia, that is, middle frequency stimulation (MFS) on the participant, the partner received the following written explanation in English and Dutch: *"We will now proceed with the stimulation. Your role here is to provide support to your partner. During the stimulation procedure, you will be required to hold both your partner's hands in any way that is most comfortable to you and your partner or in any way that you think will be most supportive to your partner."* Participants and their partners were instructed to stay still, and the handholding was static (rather than stroking). There were no specific instructions given to the partner regarding supporting the participant with verbal support; however, no verbal support was provided by any of the participant's partners. The experimenter informed the participant that her partner would be holding her hands only during the stimulation, and MFS was delivered after handholding started. The intensity of MFS stimulation was calibrated at ×10 the participant's detection threshold. Participants provided a rating for the intensity and unpleasantness for each MFS train (see below). The heart rate was recorded during MFS (stimulation) and up till 2 minutes post-MFS completion (recovery), always in a seated position. Heart rate and electrical stimulation electrodes were subsequently removed. Participants then rated their fear of MFS and perceived support and stress during MFS on a Numerical Rating Scale (NRS) between 0 and 10. Participants were then asked to wait for a period of 20 minutes before pinprick ratings would be collected again at T1. During the waiting period, participants were left free to interact in the support condition but were instructed not to discuss topics that were emotionally arousing or watch emotionally arousing content on their phone. In the alone condition, the participant was asked to refrain from watching arousing content on their phone.

Twenty (T1) and 40 (T2) minutes after the end of MFS, mechanical pinprick intensity and unpleasantness ratings were collected on both the MFS and control arm. The proximal-distal length and the lateral-medial width of increased sensitivity to pinprick stimuli were also measured on the MFS arm at T1 and T2. At the end of the second testing session, each couple was debriefed and compensated. The entire experiment (each session) lasted approximately 75 minutes.

2.3. Mechanical pinprick stimulation

A calibrated 128 mN handheld pinprick stimulator was used to deliver a total of 3 mechanical pinprick stimuli to each arm at each time point (**Fig. 1A**). The pinprick stimulator consisted of a stainless steel flat-tip probe with a cylindrical stainless steel 0.25-

mm diameter flat tip (uniform tip geometry). The probe was mounted on a plastic rod (MRC Systems, Heidelberg, Germany) which moved freely inside a handheld stainless steel tube (**Fig. 1B**). The tube was held perpendicular to the skin by the experimenter and moved down and up with a total duration of ~1 seconds. The exact location of the pinprick stimulus was displaced after each pinprick. The arm onto which pinpricks were first applied (dominant vs nondominant) was randomized across participants.

2.4. Induction of secondary hyperalgesia: middle frequency stimulation

Middle frequency stimulation of the volar forearm skin consisted of 12 trains of electrical pulses that were delivered over the duration of 2 minutes.[14,69] Each train lasted for 1 second and consisted of 2 ms pulses delivered at 42 Hz. There was a 9-second interval between each train of stimulation. The stimuli were delivered using a custom-built electrode[70,71] that consisted of a cathode with 16 blunt stainless steel pins with a diameter of 0.2 mm protruding 1 mm from the base and placed in a circle with a diameter of 10 mm. The anode consisted of a surrounding stainless steel ring with an inner diameter of 22 mm and an outer diameter of 40 mm (**Fig. 1C**). The electrode was controlled by a DS5 Isolated Bipolar Constant Current Stimulator (Digitimer, Welwyn Garden City, United Kingdom). Participants were asked to rate the intensity and unpleasantness of each stimulus train. Intensity was rated on a visually presented NRS from 0 to 100, where 0 represented no sensation at all, 50 marked the transition from non-painful to painful, and 100 represented the most intense pain imaginable. Unpleasantness was rated on an NRS from 0 to 100, where 0 represented not unpleasant at all and 100 represented the most unpleasant pain imaginable.

Pinprick ratings for perceived intensity were collected for each pinprick stimulus on a scale of 0 to 100, where 0 was no sensation at all, 50 marked the transition from nonpainful to painful, and 100 represented the most intense pain imaginable. Unpleasantness ratings were also collected for each of the 3 stimuli on a scale from 0 to 100, where 0 represented not unpleasant at all and 100 represented the most unpleasant pain imaginable.

The area of secondary mechanical hyperalgesia (on the MFS arm) was measured at both post MFS time points (T1 and T2). The area of hyperalgesia was quantified using the 128 mN pinprick stimulator, by stimulating along 4 linear paths arranged vertically (rostral–caudal) and horizontally (lateral–medial) along the stimulated forearm in ~1 cm steps. The stimulation started at the wrist and at the cubital fossa for the vertical axis and at the inner and outer edges of the forearm for the horizontal axis and moved towards the center of the stimulation site until the participant reported a clear change in pinprick intensity. The point at which the change occurred was then marked. The total length was measured along both the vertical (length) as well as the horizontal (width) axes (See **Fig. 1D** for an overview of the timeline of the experiment).

2.5. Support, stress, and fear during middle frequency stimulation

At the end of the MFS, participants reported how supported, stressed, and fearful they felt during MFS on scales ranging from 0 (not supported at all, not stressed at all, and not fearful at all) to 10 (completely supported, most stressed imaginable, and most fear imaginable).

2.6. ECG recording

The ECG recordings were continuously sampled at 2000 Hz using 3 Ag/AgCl electrodes (Kendall/Covidien H66LG ECG Electrodes). One electrode was placed under the left clavicle, another electrode under the right clavicle, and a third electrode was placed under the left ribcage. The signal was amplified and online bandpass filtered (10 Hz-1 kHz) using a Coulbourn LabLinc V Bioamplifier.

2.7. ECG processing

The ECG signals were preprocessed in MATLAB (R2021b).[44] The interbeat interval (IBI) time series was calculated as the difference in milliseconds between successively identified R peaks. The IBI time series was then cleaned using a thresholding procedure: The IBI time series was first median filtered. Each IBI was then compared with the local average of the median filtered IBI time series. Any IBIs that differed from the local average by more than a given threshold were marked as outliers and interpolated using a cubic spline interpolation method.[64] The exact threshold was individually decided for each recording. This procedure was implemented for both the participant and the partner's IBI time series. Heart rate variability (HRV): Once the IBI time series was corrected, it was detrended before calculating the root mean squared of successive differences (RMSSD) between R peaks. Typically, RMSSD tends to reduce under stressful conditions such as pain. HR synchronization: The time series were then interpolated up to 4 Hz using a cubic spline interpolation to obtain an evenly sampled time series,[12] before conducting the synchronization analysis (see statistical analysis).

2.8. Questionnaires

2.8.1. Adult attachment styles

Adult attachment styles were measured using the Experiences in Close Relationships—Revised Questionnaire.[24] The ECR-R is a 36-item questionnaire that yields attachment scores on 2 dimensions: attachment anxiety and attachment avoidance. Scores on both of these dimensions range from 1 (low) to 7 (high). Lower scores indicate greater attachment security, and higher scores indicate greater attachment insecurity.

2.8.2. Dyadic adjustment scale

The RDAS is a 14-item questionnaire used to assess relationship adjustment. Scores on the RDAS range from a minimum of 0 to a maximum of 69, where higher scores indicate greater relationship satisfaction. The mean and SD of the scores in the current sample are summarized in **Table 1**.

2.9. Statistical analysis

Statistical analyses were conducted in R.[55] To account for the clustered nature of the repeated measures data, we fit linear mixed models for all analyses using the lmer function from the lme4 package.[3] We fit a random intercept for each subject, and the fixed factors in all models were sum contrast coded so that the coefficients reflected deviations from the grand mean. This allowed for a clearer interpretation of all main effects and interactions. Significant interactions were followed up using either the emmeans[39] or simple_slopes[28] functions as appropriate. All continuous moderating variables (attachment anxiety

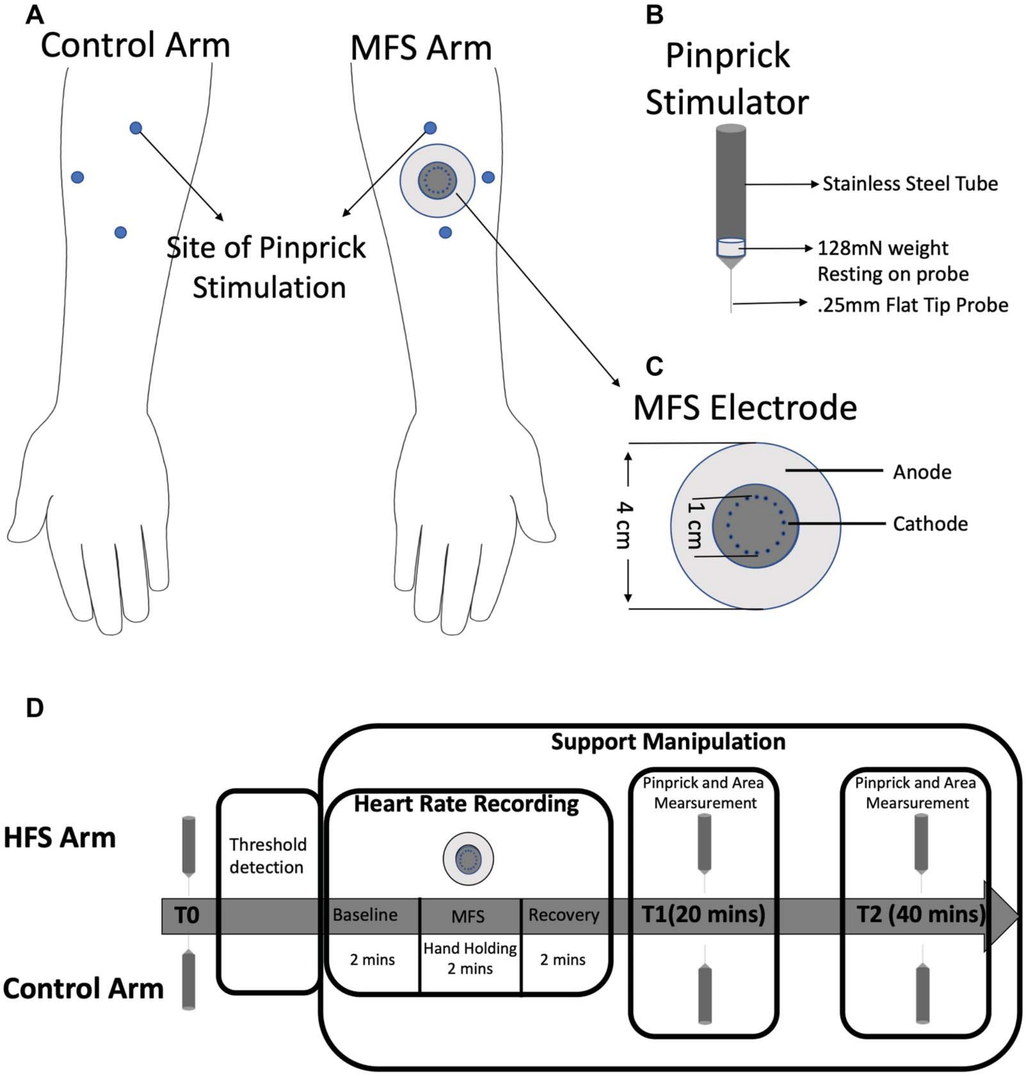

Figure 1. Experimental setup and procedure. (A) Blue dots represent the site of pinprick stimulation and the site of the electrode on the arm represents the location of the MFS stimulation. Three pinpricks were delivered to each arm at each time point at the locations corresponding to the 3 blue dots on each arm. (B) Details of the handheld pinprick stimulator. (C) Details of the electrode used for MFS. (D) Timeline of the experiment. Pinprick sensitivity was assessed at T0 (before), T1(20 mins), and T2 (40 mins) poststimulation. Heart rate was recorded before (2 mins), during (2 mins), and after (2 mins) MFS Stimulation, from both the participant and the partner. The participant and their partner held hands only during the MFS stimulation. The area of hyperalgesia was measured at both T1 and T2.

and attachment avoidance) were mean centered before entering them in the model to avoid collinearity issues.[62] Interactions with continuous moderating variables were followed up with a simple slopes analysis to examine pairwise differences at −1 S.D mean and +1 S.D of the moderating variables. The analyses were conducted as per the preregistered analysis plan (https://osf.io/pfeuc). Any deviations from the preregistered plan, or additional exploratory analyses, have been explicitly reported below. Finally, key nonsignificant findings were followed up with a Bayesian analysis to examine the amount of evidence in favour of the null hypothesis. For these Bayesian models, we used the BayesFactor package in R,[51] with a default Cauchy prior distribution (scale of effect = 0.707). An overview of all statistical models that were used to test each hypothesis can be found in **Table 2** (for a more detailed version of this table, see Supplementary Table 1 in the supplementary material, available at http://links.lww.com/PAIN/B862).

2.10. Support, stress, fear, and middle frequency stimulation ratings (preliminary analyses)

Ratings of support, stress, and fear were analyzed using 2-tailed paired sample t tests. Analyses of subjective ratings of the *MFS stimulation* were conducted separately for intensity and unpleasantness. Ratings for each of the 12 trains were entered into the model with condition (support vs alone) as the fixed factor. A fixed effect for each of the 12 trains of MFS was also added (one factor with 12 levels) to the model to improve the fit. Attachment anxiety and attachment avoidance were added to the models separately as continuous moderators.

2.10.1. Primary outcomes

Separate models were fit for pinprick intensity, pinprick unpleasantness, and area of hyperalgesia. Baseline ratings (T0) for the pinprick ratings were entered into the model as a covariate. The fixed factors in the models were condition (support vs alone),

Table 1

Descriptive statistics for the ECR-R and the RDAS questionnaires collected in the current study.

	Questionnaire data	
	Mean	**SD**
ECR-R		
Anxiety	2.68	0.87
Avoidance	2.15	0.81
RDAS total	43.54	10.92

Scores on the anxiety and avoidance dimensions range from 1 (low) to 7 (high). Lower scores indicate greater attachment security, and higher scores indicate attachment insecurity. Scores on the RDAS range from a minimum of 0 to a maximum of 69, where higher scores indicate greater relationship satisfaction. The criterion score for the RDAS to distinguish between distressed and nondistressed couples is 48.

t (T1 vs T2), and arm (control vs MFS; only for pinprick ratings). Analyses for the area of hyperalgesia were conducted separately for the area length and the area width.

2.10.2. Secondary outcomes

Attachment anxiety and attachment avoidance were both later added to the models (separately) as continuous moderating variables. We decided to deviate from the preregistered plan (which was to fit separate models for the outcomes at T1 and T2) and fit a single model that included T1 as well as T2. This was performed to take a more pragmatic approach because we did not expect any change between T1 and T2. Adding both T1 and T2 in the same model also meant that the model was being fit to a larger data set, thus yielding more robust estimates of our fixed effects. For the analysis of RMSSD scores, we first fit a single model with time (baseline vs stimulation) as well as condition (support vs alone) as predictors. We then fit separate models to assess the effect of attachment anxiety and attachment avoidance on RMSSD scores during MFS (stimulation RMSSD), with the baseline RMSSD scores as a covariate and attachment style and support condition as the fixed factors.

2.11. Deviation from preregistration

For the synchronization analysis, we deviated from the preregistered analysis plan. Instead of assessing phase synchronization at specific frequencies, we opted for a simpler approach that has been used in previous studies with skin conductance traces.[56] This was performed because we did not have any a priori frequencies of interest, and running statistical tests at a large number of frequencies would have significantly inflated the false positive rate. Instead, we computed simple correlations between the participant and their partner's IBI time series at baseline as well as stimulation in both the support condition and the alone condition. We considered the r values from each of these correlations as an index of the extent of synchronization between the participant and their partner. We then fit a linear mixed-effects model to these r values, with condition (support vs alone) and time (baseline vs stimulation) as fixed factors and a random intercept for each participant. Six participant's data from the alone condition and 5 participant's data from the support condition had to be excluded from this analysis because of artifacts caused by the MFS stimulation or due to noise during the recording.

2.12. Exploratory analyses

As a further exploratory step, we fitted separate models to assess whether RMSSD at baseline as well as the amount of change in RMSSD (baseline—stimulation) predicted the absolute increase in pinprick ratings after the stimulation (intensity and unpleasantness) as well as the area of hyperalgesia. Absolute increase in subjective ratings was calculated by a double subtraction $((T1_{mfs}—T0_{mfs})—(T1_{Control}—T0_{Control})$ and likewise for T2 and averaged together to find a single index of the absolute increase in subjective ratings. Similarly for the area length and width, the values were averaged across T1 and T2 to derive a single index of the spread of hyperalgesia along the vertical and the horizontal axis. We also added condition to these models to assess whether change in RMSSD interacted with social support to affect the absolute increase in subjective ratings as well as the area of hyperalgesia. To calculate RMSSD change scores, the RMSSD score during stimulation was subtracted from the RMSSD score at baseline for each subject in each condition.

3. Results

Three participants found the stimulation too painful and asked to stop the stimulation and did not return for the second session. These participants were excluded from all analyses. One participant completed only the first experimental session (alone condition) and did not return for the second session (support condition). In total, complete data sets from 33 participants and data from a single session for 1 participant were entered into the analysis.

3.1. Support, stress, fear, and middle frequency stimulation ratings

3.1.1. Manipulation checks

Our manipulation was successful as indicated by higher ratings of perceived support in the support condition (t (32) = 9.45, $P < 0.001$; mean (SD): support = 8.19(1.23), alone = 3.57(2.86); Cohen d= 2.09) (see supplementary material, Fig. 1, available at http://links.lww.com/PAIN/B862). By contrast, fear and stress were not statistically significantly different in the 2 conditions (fear: [t(32) = 1.82, $P = 0.07$; mean (SD): support = 5.33 (2.66), alone = 5.87(2.21); Cohen d = 0.22] and stress: (t(32) = 0.81, $P = 0.42$; mean (SD): support = 6.37 (2.07), alone = 6.74 (1.92); Cohen d = 0.18) (see supplementary material, Fig. 1).

3.1.2. Middle frequency stimulation ratings

There was a significant main effect of support on the intensity ratings (b = 0.78, SE = 0.29, $P = 0.007$; $\eta_p^2 = 0.009$) indicating that MFS was perceived as less intense in the support condition (**Fig. 2A and 2B**). However, there was no significant main effect of support on unpleasantness ratings (b = 0.42, SE = 0.33, $P = 0.2$; $\eta_p^2 = 0.002$) (**Fig. 2C and 2D**). For descriptive statistics, see **Table 3**.

3.1.3. Moderating effect of attachment styles

For the *MFS intensity ratings*, there was a significant interaction between attachment anxiety and support condition (b = 1.01, SE = 0.37, $P < 0.01$; $\eta_p^2 = 0.01$) such that pain ratings were lower in the support condition at mean (b = −1.89, SE = 0.61, $P = 0.002$; $\eta_p^2 = 0.01$) and +1SD attachment anxiety (b = −3.58, SE = 0.86, $P < 0.001$; $\eta_p^2 = 0.02$) (**Fig. 3A**). There was also a significant main effect of attachment avoidance such that intensity ratings reduced with increasing avoidance scores (b = −6.34, SE = 2.32, $P = 0.01$; $\eta_p^2 = 0.2$) (**Fig. 3B**). For the *MFS*

Table 2

Tabular overview of the statistical models used to test each of the hypotheses.

Overview of statistical analyses	
Hypothesis	**Statistical model**
Effect of social support	
Social support will attenuate subjective ratings of SH	Ratings ~ T0 + condition × arm × time + (1|participant)
Social support will attenuate the area length of SH	Length ~ condition + (1|participant)
Social support will attenuate the area width of SH	Width ~ condition + (1|participant)
Moderation by attachment styles	
Attachment anxiety will moderate the effect of social support on subjective ratings of SH	Ratings ~ T0 + condition × anxiety × arm × time + (1|participant)
Attachment anxiety will moderate the effect of social support on the area length of SH	Length ~ condition × anxiety × time + (1|participant)
Attachment anxiety will moderate the effect of social support on the area width of SH	Width ~ condition × anxiety × time + (1|participant)
Attachment avoidance will moderate the effect of social support on subjective ratings of SH	Ratings ~ T0 + condition × avoidance × arm × time + (1|participant)
Attachment avoidance will moderate the effect of social support on the area length of SH	Length ~ condition × avoidance × time + (1|participant)
Attachment avoidance will moderate the effect of social support on the area width of SH	Width ~ condition × avoidance × time + (1|participant)
RMSSD	
Social support will attenuate the reduction in RMSSD induced by the MFS stimulation (stressor)	RMSSD ~ condition × time + (1|participant)
Attachment anxiety will moderate the effect of social support on the RMSSD scores	RMSSD ~ baseline + condition × anxiety + (1|participant)
Attachment avoidance will moderate the effect of social support on the RMSSD scores	RMSSD ~ baseline + condition*avoidance + (1|participant)
Synchronisation	
Social support and handholding from the partner will both increase the level of synchronization between the participant and their partner	Corr ~ condition × time + (1|participant)

unpleasantness ratings, we again found a significant interaction between attachment anxiety and condition (b = 1.73, SE = 0.42, $P < 0.001$; $\eta_p^2 = 0.02$) such that unpleasantness ratings were lower in the support condition for high attachment anxiety (b = −4.22, SE = 0.97, $P < 0.001$; $\eta_p^2 = 0.03$) (**Fig. 3C**). We also found a main effect of attachment avoidance (b = −8.21, SE = 2.67, $P = 0.004$; $\eta_p^2 = 0.24$), such that unpleasantness ratings reduced with increasing attachment avoidance (**Fig. 3D**). See **Table 1** for descriptive statistics of all questionnaires.

3.2. Primary outcomes

3.2.1. Pinprick stimulation perceived intensity

There was a significant main effect of baseline ratings (b = 0.63, SE = 0.07, $P < 0.001$; $\eta_p^2 = 0.47$), indicating that each participant's ratings at T0 significantly predicted their subsequent ratings at T1 and T2. There was also a significant main effect of arm (b = −9.78, SE = 0.71, $P < 0.001$; $\eta_p^2 = 0.47$) indicating that the ratings at the MFS arm, after stimulation, when controlling for the baseline ratings, were significantly higher than the ratings at the control arm. This result confirmed that we had successfully induced SH at the group level. The expected arm by condition interaction, however, was not significant (b = 0.95, SE= 0.71, $P = 0.18$; $\eta_p^2 = 0.008$), indicating that social support did not have a significant impact on the perceived intensity of the pinprick stimuli (**Fig. 4A**). See **Table 4** for descriptive statistics. To examine extent of evidence in support of the null hypothesis relative to the alternative hypothesis, we conducted a Bayesian analysis, which yielded a BF01 > 10, indicating strong evidence for the null hypothesis.

3.2.2. Pinprick stimulation perceived unpleasantness

Like the findings on intensity ratings, there was a significant main effect of baseline ratings (b = 0.54, SE =0.07, $P < 0.001$; $\eta_p^2 = 0.39$) as well as a main effect of arm (b = −9.02, SE = 0.72, $P < 0.001$; $\eta_p^2 = 0.43$) with subjective ratings of unpleasantness on the MFS arm at both T1 and T2 being significantly increased after MFS stimulation. The arm by condition interaction that we hypothesized was not significant (b = 0.93, SE = 0.72, $P = 0.19$; $\eta_p^2 = 0.008$). The results of this model are plotted in **Figure 4B**. A follow-up Bayesian analysis yielded a BF01 > 10 indicating strong evidence for the null hypothesis.

3.2.3. Area length

There was no significant main effect of condition (b = 0.36, SE = 0.2, $P = 0.07$; $\eta_p^2 = 0.03$), although the mean vertical spread of the area of hyperalgesia in the support condition was smaller than that in the alone condition (**Fig. 4C**). A follow-up Bayesian analysis to examine the amount of evidence in favour of the null hypothesis revealed a BF01 = 5.21 indicating moderate evidence in favour of the null hypothesis. There was a significant main effect of time (b = −0.57, SE = 0.20, $P = 0.005$; $\eta_p^2 = 0.08$) with the vertical spread of hyperalgesia being larger at T2 than at T1.

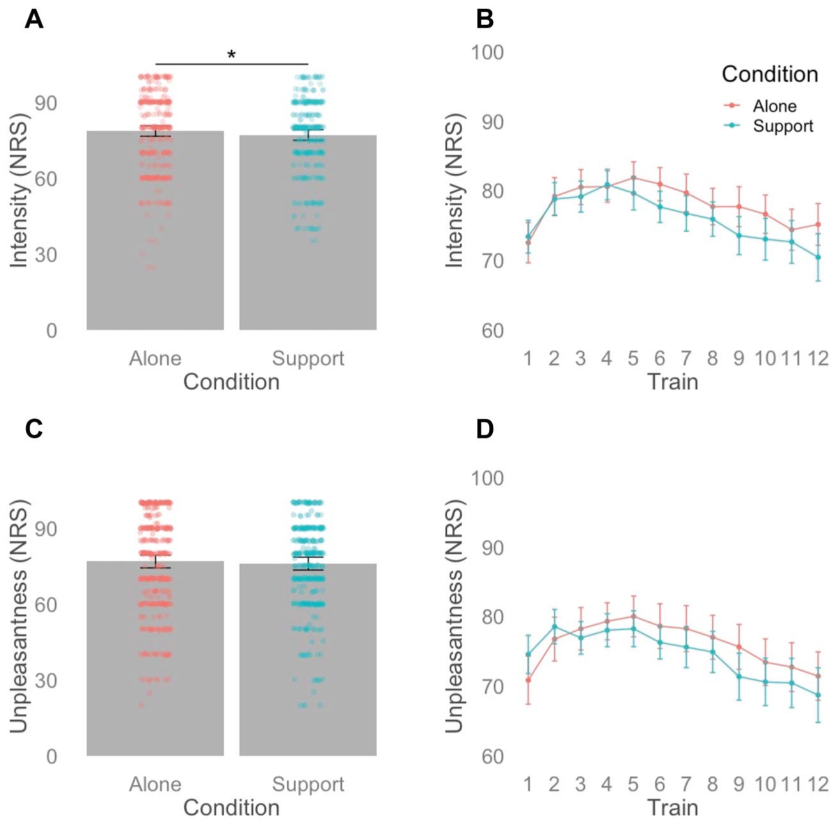

Figure 2. Perceived intensity and unpleasantness of middle frequency stimulation (MFS). (A) Mean perceived intensity of MFS stimulation in the support condition vs the alone condition. The intensity ratings were significantly lower in the support condition. (B) Average intensity ratings for each train of MFS stimulation. (C) Mean perceived unpleasantness of MFS stimulation in the support condition vs the alone condition. There was no significant difference between the 2 conditions. (D) Average unpleasantness ratings for each train of MFS stimulation. Error bars represent standard errors. Statistically significant differences are marked by asterisk.

3.2.4. Area width

There was a significant main effect of condition (b = 0.19, SE = 0.09, $P = 0.04$; $\eta_p^2 = 0.04$) with the mean horizontal spread of the area of hyperalgesia in the support condition being smaller than that in the alone condition (**Fig. 4D**). There was no significant effect of time (b = 0.02, SE = 0.09, $P = 0.82$; $\eta_p^2 = 0.0004$). See **Table 5** for descriptive statistics.

3.3. Secondary outcomes

3.3.1. Moderating effect of attachment styles

3.3.1.1. Pinprick intensity ratings

No significant interactions were observed when attachment anxiety was added to the model. A Bayesian analysis yielded a BF01 > 10 indicating strong evidence in favour of the null hypothesis. By contrast, we observed a significant interaction between attachment avoidance and arm (b = 2.33, SE = 0.92, $P = 0.01$; $\eta_p^2 = 0.03$) (**Fig. 5A**). To follow-up the arm by avoidance interaction, we fit a separate model with only arm and attachment avoidance as the fixed effects of interest and conducted a simple slopes analysis. This analysis revealed that although there was a significant difference in the ratings of both arms, the difference was smaller at +1SD attachment avoidance (b = 15.89, SE = 2.10, $P < 0.001$; Cohen d = 1.06) as compared with mean (b = 19.61, SE = 1.47, $P < 0.001$; Cohen d = 1.87) and −1SD attachment avoidance (b = 23.33, SE = 2.02, $P < 0.001$; Cohen d = 1.61). This difference is evident in both the estimated unstandardized coefficients as well as the respective effect sizes. As can be seen in **Figure 5A**, although there was an increase in the overall ratings at the MFS arm, the difference between the ratings on each arm was smaller at high attachment avoidance. This result indicates that there was a direct effect of attachment avoidance on the subjective intensity ratings of SH but that this effect was independent of the presence of social support. A Bayesian analysis yielded a BF01 > 10 indicating strong evidence in favour of the null hypothesis.

3.3.1.2. Pinprick unpleasantness ratings

When attachment anxiety was added to the model as a continuous moderator, there was no moderating interaction of attachment anxiety with arm and no 3-way interaction between arm, condition, and attachment anxiety (BF01 > 10; strong evidence in favour of the model with no moderating effect of attachment anxiety). However, when attachment avoidance was added as a continuous moderator, we found a significant interaction between attachment avoidance and arm (b = 1.89, SE = 0.94, $P = 0.04$; $\eta_p^2 = 0.02$). As with the intensity ratings, we fit a separate model with only arm and attachment avoidance as the fixed effects of interest and conducted a simple slopes analysis (**Fig. 5B**). There was a significant difference in the unpleasantness ratings between the 2 arms; however, this difference was considerably smaller at +1SD attachment

Table 3

Mean and standard deviation of subjective ratings (intensity and unpleasantness) in response to each train of the middle frequency stimulation.

Train	Intensity				Unpleasantness			
	Alone		Support		Alone		Support	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	72.51	17.11	73.38	13.75	70.86	20.45	74.56	16.02
2	79.18	15.69	78.79	13.58	76.76	18.42	78.55	14.23
3	80.52	14.43	79.15	12.86	78.24	17.54	76.94	13.48
4	80.59	13.14	80.88	12.46	79.32	15.55	78.03	13.45
5	81.85	13.43	79.64	13.73	80.03	17.11	78.24	14.85
6	80.94	13.89	77.67	12.93	78.62	18.73	76.27	13.65
7	79.68	15.72	76.73	14.70	78.26	19.23	75.61	16.96
8	77.71	15.29	75.91	14.22	77.03	18.37	74.91	17.03
9	77.71	16.72	73.55	15.71	75.65	18.82	71.36	19.38
10	76.62	16.06	73.03	17.25	73.44	19.53	70.61	19.60
11	74.38	17.22	72.64	17.62	72.74	20.42	70.45	20.32
12	75.15	17.50	70.42	18.92	71.44	20.28	68.71	21.91
Mean	78.07	15.52	75.98	14.81	76.03	18.70	74.52	16.74

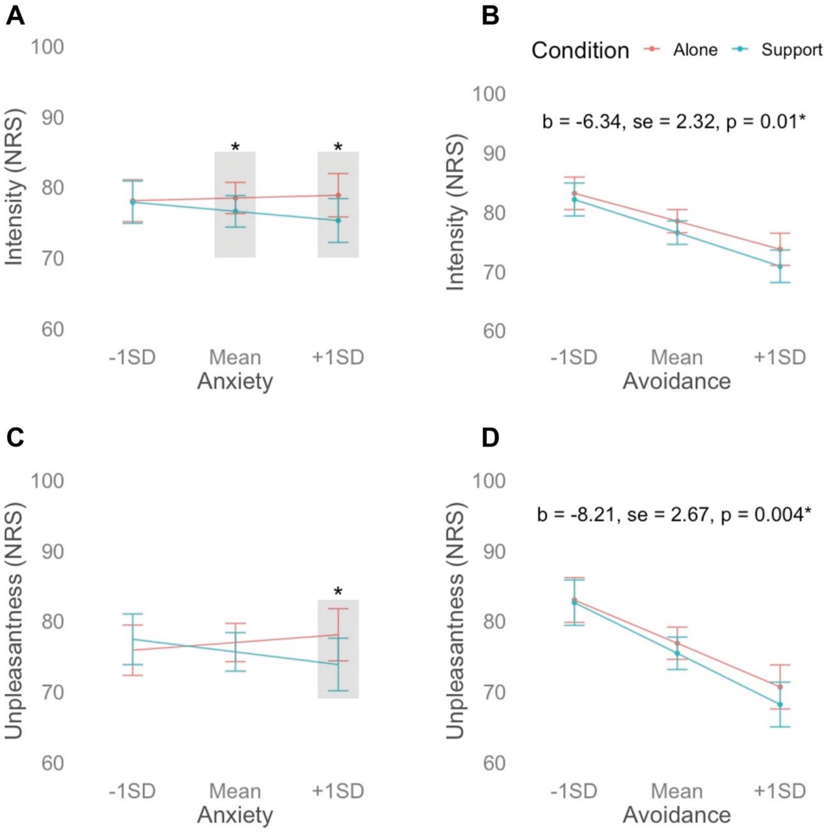

Figure 3. Effect of attachment styles and social support on perceived intensity and unpleasantness of middle frequency stimulation (MFS). (A) Support by attachment anxiety interaction for the perceived intensity of MFS stimulation. (B) Main effect of attachment avoidance on the perceived intensity of MFS. There was no significant interaction of attachment avoidance with support condition. (C) Support by attachment anxiety interaction for the perceived unpleasantness of MFS stimulation. (D) Main effect of attachment avoidance on the MFS unpleasantness ratings. Here again, there was no significant interaction of attachment avoidance with support condition. Error bars represent standard errors. Statistically significant differences are marked by asterisk.

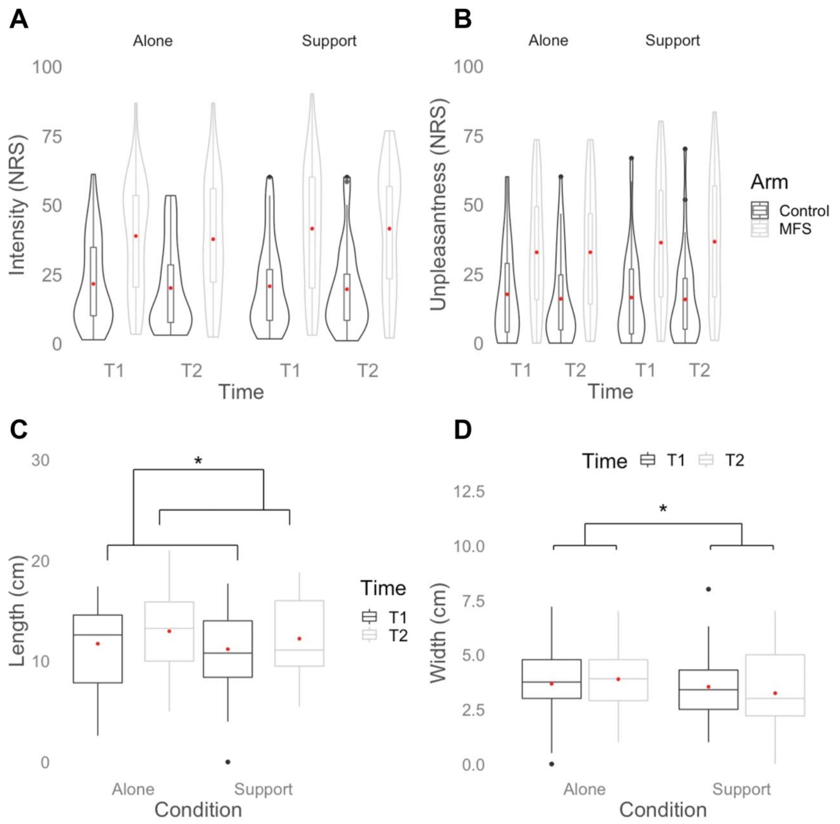

Figure 4. Effect of social support on measures of SH. (A and B) Violin plots of perceived intensity and unpleasantness, respectively, of pinprick stimulation grouped by time (T1 and T2) and arm (middle frequency stimulation vs control). Red dots represent the mean of the distribution, and the box plots represent the interquartile range. Violin plots represent the kernel density of the distribution. There is a significant effect of arm for both intensity and unpleasantness; however, no effect of social support. (C) Boxplots representing the vertical length of the area of hyperalgesia grouped by condition (support vs alone) and time (T1 vs T2). Mean length was significantly larger at T2 compared with T1, but there was no effect of social support. The box represents the interquartile range, the horizontal bar represents the median, and the red dot represents the cell mean. (D) Box plots representing the horizontal width of the area of hyperalgesia grouped by condition (support vs alone) and time (T1 vs T2). Mean width was significantly smaller in the support condition. The box represents the interquartile range, the horizontal bar represents the median, and the red dot represents the cell mean.

avoidance (b = 15.16, SE = 2.14, $P < 0.001$; Cohen d = 0.99) when compared with mean (b = 18.18, SE = 1.50, $P < 0.001$; Cohen d = 1.71) and -1SD attachment avoidance (b = 21.19, SE = 2.06, $P < 0.001$; Cohen d = 1.45). These results indicate that attachment avoidance had a moderating effect on the increase in unpleasantness ratings in response to the electrical conditioning stimulation such that the increase in ratings on the stimulated arm was smaller with increasing attachment avoidance, irrespective of the presence or absence of social support. We conducted a Bayesian analysis to assess the amount of evidence in favour of the null hypothesis (no moderating effect of attachment avoidance on SH). We found that there was strong evidence in favour of the null hypothesis (BF01 > 10).

3.3.1.3. Area length

There was no moderating effect of attachment anxiety (b = 0.02, SE = 0.26, $P = 0.91$; η_p^2= 0.0001; BF01 > 10) or attachment avoidance (b = 0.33, SE = 0.25, $P = 0.2$; η_p^2= 0.02; BF01 > 10) on the area length. The Bayes factor for both

Table 4

Mean and standard deviation of subjective ratings (intensity and unpleasantness) in response to pinprick stimulation at each time point (T0, T1, and T2).

Pinprick ratings

	T0				T1				T2			
	MFS arm		Control arm		MFS arm		Control arm		MFS arm		Control arm	
	Alone	Support	Alone	Support	Alone	Support	Alone	Support	Alone	Support	Alone	Support
						Intensity						
MEAN	22.70	21.86	23.03	22.12	38.75	41.42	21.49	20.64	37.62	41.40	20.00	19.59
SD	15.82	15.25	16.16	16.39	20.71	22.90	15.92	15.95	21.80	22.47	15.84	15.32
						Unpleasantness						
MEAN	18.99	20.01	19.39	19.30	32.74	36.24	17.62	16.42	32.75	36.57	15.97	15.76
SD	15.57	16.67	17.34	18.16	21.44	22.69	16.40	16.22	21.67	23.37	15.98	15.92

Table 5

Mean and standard deviation of the area of secondary hyperalgesia (length and width) in both support conditions.

Area of hyperalgesia				
	Length			
	Alone		Support	
	T1	T2	T1	T2
Mean	11.73	12.97	11.19	12.23
SD	3.99	3.95	4.32	3.95
	Width			
	Alone		Support	
	T1	T2	T1	T2
Mean	3.67	3.88	3.53	3.24
SD	1.55	1.41	1.54	1.96

these effects indicated strong evidence in favour of the null hypothesis.

3.3.1.4. Area width

There was no moderating effect of attachment anxiety (b = −0.07, SE = 0.27, $P = 0.79$; $\eta_p^2 = 0.002$; BF01 > 10), and the Bayes factor indicated that there was strong evidence in favour of the null hypothesis. However, there was a significant main effect of attachment avoidance (b = −0.58, SE = 0.26, $P = 0.03$; $\eta_p^2 = 0.14$). The horizontal spread of the area of hyperalgesia was smaller for individuals with higher attachment avoidance (**Fig. 5C**). There was no significant moderating effect of attachment avoidance (b = −0.04, SE = 0.12, $P = 0.72$; $\eta_p^2 = 0.001$; BF01 = 4.25). The Bayes factor indicated that there was moderate evidence in favour of the null hypothesis.

3.3.2. RMSSD

As expected, RMSSD was lower during MFS compared with baseline (main effect of time b = 2.30, SE = 0.92, $P = 0.01$, $\eta_p^2 = 0.07$). However, the lack of interaction with condition (b = 0.14, SE = 0.92, $P = 0.87$; $\eta_p^2 = 0.0002$), indicated that social support

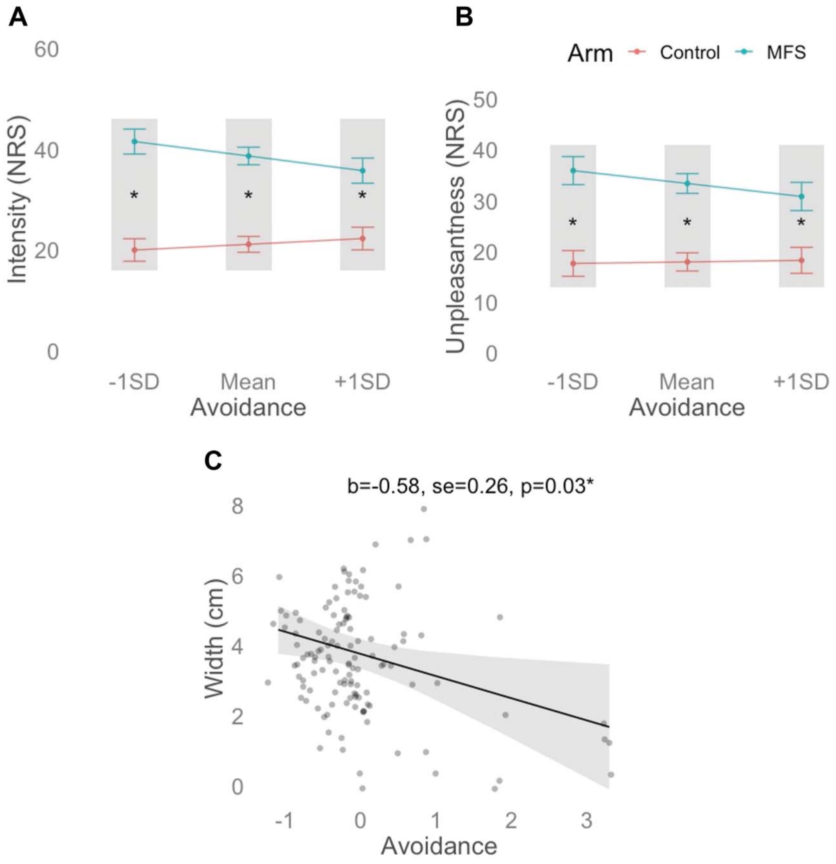

Figure 5. (A and B) Arm by avoidance interaction where the difference in pinprick ratings across the 2 arms reduce with increasing avoidance for intensity and unpleasantness respectively. (C) Main effect of attachment avoidance on the horizontal spread of the area of SH. Shaded area represents 95% CI. Statistical significance is represented by asterisk.

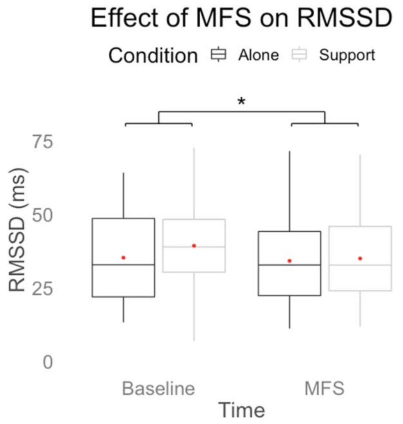

Figure 6. Boxplot representing the effect of electrical stimulation on root mean squared of successive differences. Boxes represent the interquartile range, the horizontal bar represents the median, and the red dot represents the cell means. Statistical significance is depicted by the asterisk.

did not have a significant effect on the reduction of RMSSD. There was also no main effect of condition in the model (b = 0.32, SE = 0.95, $P = 0.73$; $\eta_p^2 = 0.001$) (**Fig. 6**). The separate model including attachment did not show significant interactions between condition and attachment anxiety (b = 1.21, SE = 1.20, $P = 0.32$; $\eta_p^2 = 0.04$) nor with attachment avoidance (b = −0.55, SE = 1.13, $P = 0.62$; $\eta_p^2 = 0.01$). See **Table 6**.

3.3.3. Heart rate synchronization

The results of the analysis showed there was a significant main effect of condition (b = −0.04, SE = 0.01, $P = 0.004$; $\eta_p^2 = 0.08$), such that the level of synchronization was higher in the support condition compared with the alone condition. However, there was no effect of time (b = −0.01, SE = 0.01, $P = 0.29$; $\eta_p^2 = 0.01$) and no significant interaction between support condition and time (b = −0.02, SE = 0.01, $P = 0.09$; $\eta_p^2 = 0.04$), indicating that there was no effect of handholding on the level of synchronization. The results of this analysis are plotted in **Figure 7**. See **Table 7** for descriptive statistics.

3.3.4. Exploratory analysis

Neither the participants' RMSSD scores at baseline nor the change in RMSSD scores from baseline to the MFS stimulation period (baseline—stimulation) predicted any of the measures of hyperalgesia. Although the effect did not reach statistical significance, there was a positive relationship only between the RMSSD change scores and the absolute increase in pinprick intensity ratings (Supplementary Fig. 2; See supplementary materials for further details, available at http://links.lww.com/PAIN/B862).

4. Discussion

This is the first study investigating the development of experimentally induced SH under varying social contexts and its moderation by attachment styles. Our main aim was to examine whether the induction of SH in a supportive context would lead to lesser SH relative to when participants were alone. We, therefore, contrasted a support condition to an alone condition (rather than mere presence). Our choice of handholding by a romantic partner was driven by the fact that it has been shown to most reliably attenuate pain reports in acute pain.[27,4256]

Manipulation checks revealed that participants felt more supported in the support condition compared with the alone condition. The support condition predicted a smaller medial-distal width of SH to pinprick stimuli. Higher avoidance scores were associated with a smaller width of the area of hyperalgesia, as well as a smaller difference in the perceived intensity and unpleasantness of pinprick stimuli between the MFS arm and control arm after stimulation. The MFS procedure was associated with the expected reduction in HRV, but this reduction was not attenuated by social support. Finally, the level of synchronisation between the participant and partner was higher overall in the support condition, although handholding did not have an impact on the level of synchronisation.

4.1. Middle frequency stimulation—the effect of social support and moderation by attachment styles

Pain intensity in response to acute pain stimuli (MFS) was lower in the support condition. This finding replicates the findings of previous studies on handholding.[26,42,56] Furthermore, attachment anxiety moderated the effect of social support on pain ratings (intensity and unpleasantness). In line with our expectations as well as previous findings, higher attachment anxiety predicted lower ratings (intensity and unpleasantness) in the

Table 6

Mean and standard deviation of root mean squared of successive differences scores at baseline and stimulation in each condition.

RMSSD				
	Alone		**Support**	
	Baseline	**Stimulation**	**Baseline**	**Stimulation**
Mean	39.20	34.29	39.42	35.09
SD	21.03	16.18	16.90	14.62

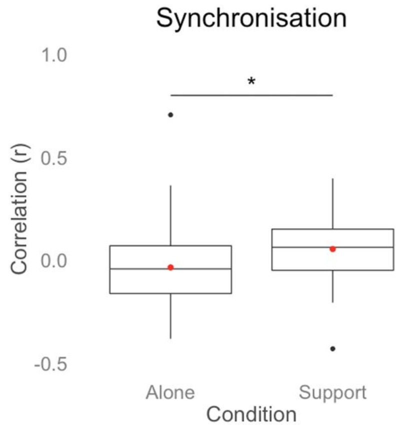

Figure 7. Boxplot representing the effect of social support on heart rate synchronisation. Synchronisation is indexed by the correlation between the participant and the partner's RR interval time series. Boxes represent the interquartile range, the horizontal bar represents the median, and the red dot represents the cell means. Statistical significance is marked by asterisk.

presence of support vs alone.[33,59] Anxiously attached individuals are characterized by hypervigilance to threats[16] and tend to engage in hyperactivating strategies in response to stress, resulting in increased proximity seeking in an effort for social coregulation.[49,50] Thus, they might benefit from the presence of social support and report increased pain in the absence thereof.

High attachment avoidance, on the other hand, predicted lower ratings (intensity and unpleasantness) regardless of social support. This result is somewhat divergent from previous findings. Some studies have found that individuals higher on attachment avoidance reported higher pain ratings (and N2 and P2 local peak amplitudes) in response to pain stimuli in the presence vs absence of a romantic partner.[36,59] However, others have found that higher attachment avoidance predicted lower pain ratings in the presence of a romantic partner but only when they were led to believe that their partner had high empathy for them.[29] Although these findings suggest that the exact relationship between social support and attachment avoidance may be in need of further investigation, the reduction of pain ratings with increasing avoidance is consistent with avoidant individuals' tendency to engage in downregulation or deactivating strategies.[5,49,50]

4.2. Effects of social support on the development of secondary hyperalgesia

Social support was able to modulate the width of the area of hyperalgesia. Although the effect size is small, our findings are in line with studies that have shown that other top–down factors can modulate SH.[22,32,45,58,68] Importantly however, other recent studies that have used similar electrical stimulation protocols have found either modest or no modulation of SH.[4,18,48,66] This apparent difficulty may be due to the intense nature of the electrical stimulation and the large magnitude of SH that these procedures induce (eg, $\eta_p^2 = 0.47$ in the current study). In addition, MFS stimulation induces the largest increase in perceived pinprick intensity compared with other frequencies.[69] These factors in combination may explain the small effect size observed.

Table 7

Mean and Standard Deviation of r values (index of synchronization) at baseline and stimulation in each condition.

Synchronisation	Alone		Support	
	Baseline	Stimulation	Baseline	Stimulation
Mean	−0.08	0.01	0.06	0.04
SD	0.13	0.22	0.13	0.20

Our results suggest that handholding by a romantic partner may have inhibited spinal mechanisms involved in the development of SH, presumably by engaging descending inhibitory pathways.[1,53,67] Krahe et al. (2013) proposed that social support may serve as a predictive safety signal, thereby influencing the salience of the noxious stimulus.[37] However, this possibility needs to be considered with caution here, given that the difference between the fear ratings under the 2 conditions did not reach statistical significance (although the mean was lower in the support condition; $P = 0.07$). There was also no difference in the stress ratings and, likewise, the autonomic response (HRV reduction) to the stimulation between the 2 conditions. If indeed handholding by the partner had served as a safety signal, we might have expected a more unambiguous reduction in fear[60] and perhaps also stress responses (subjective and physiological) in the support condition. It is possible, however, that the intense nature of the stimulation may have undermined the possibility of detecting the effects of social support on autonomic reactivity. For instance, Bourassa et al. (2018) found that social support attenuated blood pressure reactivity during a cold pressor task but not HRV.[7]

It may be that the effect observed is a distraction effect caused by participants engaging in an interaction with their partners after MFS. However, it is not clear that being distracted after the stimulation can affect the development of SH. Most studies that have attempted to modulate SH by attentional effects have focused on the stimulation period.[22,48,65] Any distraction caused by the presence of the partner during the stimulation may have been minimized since providing ratings for the MFS stimulation would have kept participants' attention focused on the stimulation. This, however, remains a possibility that cannot entirely be excluded.

Interestingly, we found no effect of support on subjective ratings to pinprick stimulation. Such a dissociation between the area of SH and subjective ratings was also found by Matre et al. (2006) where a placebo intervention reduced the area of SH but not the intensity ratings.[45] A more recent study using MFS also showed that patients (vs healthy controls) with temporomandibular disorders developed a 76% larger area of SH but showed no difference in the intensity of SH.[15] On the other hand, Torta et al. (2022) found that an observational learning intervention attenuated subjective ratings but not the area.[66] Such dissociations indicate that the 2 measures may be indices of slightly different phenomena or perhaps different aspects of the same phenomenon that are influenced by different variables. For instance, pinprick ratings may be subject to response biases that the area measurement is not.

4.3. The role of attachment styles in the development of hyperalgesia

Increasing attachment avoidance predicted lower SH for both the pinprick ratings as well as the area of SH. This is especially striking given that this effect is consistent across acute pain ratings, pinprick ratings, as well as the area of SH, with a medium-to-large effect size. These findings are again consistent with the tendency of avoidantly attached individuals to engage in deactivating coping strategies[49] and further suggest that this inhibition may occur at a physiological level where endogenous inhibitory mechanisms may readily downregulate spinal mechanisms involved in the development of SH. Although these data seem to suggest that attachment avoidance may be a protective factor in the development of SH, it is important to consider that the pathway through which attachment avoidance may affect chronic pain is not singular. As has been captured by the attachment-diathesis model of chronic pain,[47] insecurely attached individuals may engage in altered help seeking behavior, may be less likely to trust caregivers or physicians, and may be less likely to seek help when needed, leading to worsening of the pain.

The lack of a moderating effect of attachment styles may be related to 2 factors. First, given that participants answered the attachment questionnaire a day before the testing session, we may not have adequately activated their attachment system when answering the questionnaire. In many of the prior studies,[36,59] participants completed the ECR-R after undergoing nociceptive stimulation, which may have activated the attachment system. Second, our sample size was calculated based only on our primary outcome (the effect of social support on SH). We may have thus required a larger sample size to adequately assess an interaction with attachment styles.

4.4. The effect of social support on heart rate variability synchronization

Although we observed increased HRV synchrony in the support condition, this increase was not correlated with any of the measures of SH. An important consideration here is that partner empathy has been shown to play a key role in social touch–induced analgesia[10,63] as well as touch-induced synchrony and the related analgesia.[27] This was not something that we measured in the current study, given that synchrony was not the primary outcome of interest. However, it may be interesting in future studies to examine whether the level of synchrony as well as partner empathy may be associated with outcomes of SH.

5. Conclusion

In conclusion, the current study demonstrates that the development of SH can be influenced by the social context such that SH is lower in a supportive context relative to when participants are alone. We also show that attachment avoidance exerted an inhibitory influence on the development of SH.

Conflict of interest statement

The authors have no conflict of interest to declare.

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