Reactions to social exclusion in psoriasis

Physiological and behavioral reactivity to social exclusion: a functional infrared thermal imaging study in patients with psoriasis

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Abstract

Recent studies show that sympathetic nervous system (SNS) activity can be heavily impacted not only by basic threats to survival, but by threats to social bonds. Herein we explored the behavioral and physiological consequences of social exclusion/inclusion in patients with psoriasis, a disease frequently associated with the experience of being ostracized and deficient emotion regulation skills. We employed a virtual ball-tossing game (Cyberball) to induce the experience of social exclusion/inclusion. We then used a Trust game to measure the effects of this social modulation on trust. During Cyberball, Infrared Thermal Imaging was used to record participants' facial temperature and thus obtain an on-line measure of SNS activation. Behavioral data showed that social exclusion shifted participants' trust toward unfamiliar players who had not previously excluded them. Physiological data indicated that, in control participants, social exclusion triggered higher SNS activation than inclusion. No such effect was found in patients with psoriasis, whose SNS activity was the same during inclusion as it was during exclusion, suggesting that they benefit less from inclusive experiences than control participants. In addition, higher SNS activation in patients during social exclusion was linked to higher monetary investment towards unfamiliar players, but not in controls, a result in keeping with the Social Reconnection Hypothesis, according to which emotions triggered by social rejection can be regulated by investing in new social interactions. We also found that an increase in periorbital temperature is accompanied by a decrease in happiness ratings after experiencing social exclusion during the Cyberball game.

Keywords: social exclusion, social inclusion, trust, emotion regulation, infrared thermal imaging, psoriasis

NEW AND NOTEWORTHY: Previous research on emotional processes in psoriasis has mainly employed self-report measures. Here we used Thermal Imaging to obtain an online measure of the sympathetic nervous system (SNS) activity during social exclusion and tested how this experience influenced subsequent trust. We found that being included was a less positive experience for patients compared to controls and that SNS activity during exclusion had a stronger influence on subsequent trust in patients than in controls.

Introduction

When faced by basic threats, the human body produces a set of physiological responses aimed at increasing survival chances. An encounter with a predator, for example, can trigger the activation of the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis, two systems involved in fight-or-flight responses and the mobilization of energy resources respectively (Eisenberger, 2013). Both systems also affect the immune system by upregulating inflammatory activity, a defense strategy against external agents (Irwin & Cole, 2013).

Importantly, recent research has shown that threats to social connection can have similar effects on human physiology as basic threats to survival do (Eisenberger & Cole, 2012). For example, when socially evaluated during the Trier Social Stress Test (Kirschbaum, Pirke, & Hellhammer, 2008), a test designed to induce social stress, participants showed increased activation in SNS, HPA and inflammatory responding (Bosch, Geus, Carroll, Annebet, & Edwards, 2009; Dickerson, Gable, Irwin, Aziz, & Margaret, 2009). Further, feeling socially disconnected is related to increased proinflammatory cytokine levels and enhanced proinflammatory gene expression (Cole et al., 2007). Also, experiences of social exclusion differentially affect hormonal responses (testosterone and progesterone) in males and females (Radke et al., 2018; Seidel et al., 2013).

Social exclusion is a stressful experience that can cause both retaliatory and prosocial behavioral reactions towards the perpetrators (Will, Crone, Van Lier, & Güroğlu, 2016). Researchers investigated whether chronic social exclusion would lead to exaggerated or blunted behavioral and/or physiological reactions to stressful events. Both possible outcomes are reported in the literature (Iffland, Sansen, Catani, & Neuner, 2014; Newman, 2014; Will, Crone, & Güroğlu, 2015; Will, van Lier, Crone, & Güroğlu, 2016). In particular chronic rejected adolescents compared to control showed similar distress ratings after social exclusion but higher activity in dorsal anterior cingulate cortex (dACC, a brain region involved in exclusion-related distress) while being excluded (Will, van Lier, et al., 2016). Interestingly, when refraining to punish their excluders, chronically rejected adolescents showed higher activity in the dorsal striatum and lateral prefrontal cortex (brain regions implicated in cognitive control). On the contrary, victims of bullying displayed blunted responses (reflecting a sympathetic reduction and not a parasympathetic increase) to social exclusion (Iffland et al., 2014; Newman, 2014).

Psoriasis is a chronic inflammatory skin disease affecting approximately 2% of the population (Icen et al., 2009) characterized by cutaneous inflammation that causes significant psychological distress (Picardi, Abeni, Melchi, Puddu, & Pasquini, 2000) and impaired quality of life (De Arruda & De Moraes, 2001). Given the negative impact of the disease on physical appearance, psoriasis is chronically associated with stigmatization and social exclusion (Fortune, Griffiths, Main, & Richards, 2001; Hrehorów, Salomon, Matusiak, Reich, & Szepietowski, 2012) that can lead to significant social pain (Fortune, Main, O'Sullivan, & Griffiths, 1997). Studies report that the brain structures devoted to the processing of physical pain (i.e. the pain triggered from bodily injury) overlap with those activated by social pain (i.e. the pain triggered by social injury or threat to social connection) such as the dorsal anterior cingulated cortex (dACC) (Eisenberger & Lieberman, 2004; Eisenberger, Lieberman, & Williams, 2003). Further, empathy for social pain (e.g. witnessing social exclusion threats experienced by others) also recruits brain areas involved in processing the somatosensory components of physical pain such as posterior insular cortex and secondary somatosensory cortex (Novembre, Zanon, & Silani, 2015). Crucially, experiencing social pain not only interferes with the regulation of social behaviors (Kouchaki & Wareham, 2015; Twenge, Ciarocco, Baumeister, DeWall, & Bartels, 2007) but also affects the experience of physical pain (Mancini, Betti, Panasiti, Pavone, & Aglioti, 2011, 2014).

One mechanism to attenuate the influence of social pain on other social behaviors is emotion regulation, the process by which individuals explicitly or implicitly influence the emotion-generative process (Gross & Jazaieri, 2014). Deficits in maintaining an equilibrium between cognitive and emotional demands can acutely impair daily life (Clarke & Johnstone, 2013). In fact, emotions can have a great impact on social decisions such as social categorization (Ponsi, Panasiti, Rizza, & Aglioti, 2017; Ponsi, Panasiti, Scandola, & Aglioti, 2015) and social preference (Panasiti, Puzzo, & Chakrabarti, 2015). It has been seen that emotion regulation helps downregulate the effect of social pain on subsequent social decisions (Grecucci, Giorgetta, Wout, Bonini, & Sanfey, 2012), and that the inhibition of brain areas involved in emotion regulation enhances social pain perception (Riva, Romero Lauro, Vergallito, DeWall, & Bushman, 2015).

Importantly, previous findings reported that psoriasis is associated with higher use of emotional suppression compared to controls (Ciuluvica, Amerio, & Fulcheri, 2014; Vari, Velotti, Zavattini, Richetta, & Calvieri, 2013), a primitive emotion regulation strategy that inhibits the expression of the ongoing emotional response (Gross & John, 2003). Conversely, higher use of reappraisal (Ciuluvica et al., 2014), an adaptive strategy consisting in re-thinking a given situation to alter its meaning and emotional impact (Gross & John, 2003), is related to a weaker impact of psoriasis on quality of life (Vari et al., 2013). In psoriasis, emotion regulation is positively related to greater satisfaction with treatment and negatively related to: i) perception of psoriasis' severity and disability; ii) psychopathological symptoms; iii) frequency of missed work/school (Almeida et al., 2017). Since previous research in psoriasis has mainly employed self-report measures, behavioral and physiological evidence regarding emotional processing in these patients is rather scarce. Two studies, however, have been exceptions. They observed that when submitted to cognitively stressful tasks (mental arithmetic and the Stroop Color-Word Naming Test), psoriasis patients show a higher increase in heart rate and diastolic blood pressure than controls (Mastrolonardo, Picardi, Alicino, Bellomo, & Pasquini, 2006), and that this discrepancy is not associated with any difference in stress perception or salivary cortisol levels (Mastrolonardo, Alicino, Zefferino, Pasquini, & Picardi, 2007).

In the present study, we explored how the experience of social exclusion/inclusion in psoriasis patients and healthy controls could differentially engage the SNS and subsequently modulate social behavior. We employed the Cyberball Game (Williams, Cheung, & Choi, 2000) to induce experiences of social exclusion/inclusion and then used the Trust Game (Berg, Dickhaut, &

McCabe, 1995) to measure how participants would trust the players who had previously excluded/included them (familiar) compared to other (unfamiliar) players.

We measured SNS activation during the Cyberball Game by means of functional infrared thermal imaging (fITI), an emerging tool for the study of human emotions that allows for the recording of skin temperature by tracking non-invasively emitted infrared heat (Pavlidis et al., 2007). In other studies, modulation of facial temperature has been detected in a variety of basic and complex affective responses such us fear (Levine, Pavlidis, & Cooper, 2001), joy (Nakanishi & Imai-Matsumura, 2008), guilt (Ioannou et al., 2013), subliminal and supraliminal emotional induction (Kosonogov et al., 2017; Ponsi, Panasiti, Rizza, et al., 2017), social exclusion (Paolini, Alparone, Cardone, van Beest, & Merla, 2016), reputation concerns during moral decisions (Panasiti, Cardone, Pavone, Mancini, & Aglioti, 2016) and empathy (Salazar-López et al., 2015). Here, we focused on the temperature of the periorbital regions that are believed to index SNS activation (Asano, Onogaki, & Muto, 2010; Bergersen, 1993; Levine et al., 2001; Pavlidis, Levine, & Baukol, 2000).

We expected psoriasis patients to show an enhanced SNS activation during social exclusion compared to controls, which would support the idea that chronic exposure to such an experience can sensitize the physiological reaction to it; moreover, we expected patients to be less able to regulate the effect of social exclusion on subsequent trust behavior and thus to show higher need for social reconnection (a quite risky and primitive emotion regulation strategy employed to overcome the pain caused by social rejection; Riva, 2016).

Materials and Methods

Participants

An a priori power analysis performed using G*Power (Faul, Erdfelder, Lang, & Buchner, 2007) indicated that 32 participants would provide a power of 0.80 (α=0.05) to detect a small to moderate effect size (*d* = .42), a typical effect size for social psychological research (Richard, Bond, & Stokes-Zoota, 2003). On this basis, 34 participants were recruited for the study.

17 participants suffering from Psoriasis Vulgaris were recruited from the Department of Dermatology of the University of Campus Bio-Medico in Rome (see Table 1 for demographic information).

All the patients were formally diagnosed with psoriasis by a dermatologist. The severity of the disease was clinically assessed through the PASI (Psoriasis Area and Severity Index (Schmitt & Wozel, 2005) and valued as moderate to severe (mean PASI = 10.84 ranging between 1.80-33.60) (Schmitt & Wozel, 2005). Patients were also administered the Psoriasis Disability Index (PDI (Finlay & Kelly, 1987), a tool for measuring quality of life in psoriasis patients. The mean PDI score was 18.69 (with a range of 4-32 on a scale ranging from 0 to 45); the higher the PDI score, the more severe the impairment of quality of life.

The experiment was part of a wider project aimed at characterizing physiological indexes of the efficacy of a dermatological treatment for psoriasis based on the administration of calcipotriol/betamethasone dipropionate. In order to begin this new dermatological treatment, all participants were asked to interrupt their usual dermatological treatment one month before the experimental session.

The control group consisted of healthy participants who were matched to the clinical group according to age, gender and education (see Table 1). The presence of neurological diseases, psychiatric disorders or dermatological illnesses was considered an exclusion criteria.

Participants were paid 30 euros for their participation in the whole protocol (psychological and dermatological sessions). The study was approved by the independent ethics committee of the Santa Lucia Foundation (Scientific Institute for Research Hospitalization and Health Care) and performed in accordance with the principles of the 1964 Declaration of Helsinki. All the participants signed written informed consent forms.

--Table 1 here---

Procedure

Questionnaires

Prior to the experimental session, participants were evaluated by the administration of two questionnaires: the *Difficulties in Emotion Regulation Scale (*DERS*;* Gratz & Roemer 2004; Sighinolfi et al. 2010), which measures specific patterns of emotional dysregulation, and the *Positive and Negative Affect Schedule (PANAS;* Terracciano et al. 2003), which measures participants' state and trait affect.

Difficulties in Emotion Regulation Scale (DERS) is a self-report questionnaire (Gratz & Roemer, 2004; Sighinolfi et al., 2010) that individuates specific facets of emotion regulation. It is composed of 36 items and 6 subscales: i) Non-acceptance of emotional responses (non-acceptance); ii) Difficulties engaging in goal-directed behavior (goals); iii) Impulse control difficulties (impulse); iv) Lack of emotional awareness (awareness); v) Limited access to emotion regulation strategies (strategies); vi) Lack of emotional clarity (clarity). Each item requires an answer on a Likert scale, from 1 (almost never) to 5 (almost always). The total score is obtained from the sum of the 6 subscales. Higher scores highlight the presence of some difficulties in the emotion regulation.

Positive and Negative affect Schedule (PANAS) (Terracciano et al., 2003). The PANAS is a self-report questionnaire that consists of two 10-item scales to measure both state and trait positive and negative affect. Each item is rated on a Likert scale from 1 *(not at all)* to 5 *(very much).*

Experimental stimuli

The visual stimuli used for the Cyberball Game (Williams et al., 2000; Williams & Jarvis, 2006) were taken from the official Cyberball website (https://cyberball.wikispaces.com/) and modified so that the face stimuli of the other players would be presented in addition to their avatars (see Figure 1a).

The neutral face stimuli employed in the Cyberball game and subsequent Trust Game were taken from two validated face sets (Karolinska Directed Emotional Faces (Lundqvist, Flykt, & Ohman, 1998) and NimStim Face Stimulus Set (Tottenham et al., 2009). The original background color of the face stimuli from NimStim Face Stimulus Set (white) was digitally modified in order to correspond to the face stimuli from the KDEF database. Before performing the study, we validated the selected stimuli by way of an online survey designed to prevent perceptual facial features from creating a positive or negative bias in person perception. The survey was composed of male (N = 23) and female (N = 23) faces and was administered to a sample of 61 Italian participants (28 males; age range 19-32 years, M = 24.35, SD = 3.54). It sought to determine participants' judgments on the following dimensions: attractiveness, likability and trustworthiness. The survey addressed three different questions for each face stimulus on a 5-point scale from 1 (not at all) to 5 (extremely): (a) "How ATTRACTIVE do you judge this person to be?"; (b) "How LIKABLE do you judge this person to be?"; (c) "How TRUSTWORTHY do you judge this person to be?". Accordingly, we selected 8 Caucasian male faces and 8 Caucasian female faces (see Table 2 for descriptive information) with neutral emotional expressions and a straight profile, among the face stimuli whose mean values fell within a half standard deviation of the mean. We also performed a Student's T Test in order to rule out the possibility that the 16 male and female faces chosen could differ in attractiveness, likability or trustworthiness (see Table 2).

--Table 2 here--

We created four different versions of the Cyberball Game and subsequent Trust Game depending on participants' gender (male, female) and experimental condition (social exclusion, social inclusion). As a consequence, 8 different fictional characters (4 male faces and 4 female faces) were employed in the Cyberball Game, while the remaining 8 fictional characters (4 male faces and 4 female faces) were employed in the Trust Game.

Social modulation phase

Participants began the social modulation phase by playing the Cyberball Game with inclusive or exclusive fictional characters (the order of inclusion/exclusion condition was counterbalanced across participants) (see Figure 1A).

--Figure 1 here---

Participants were told that the task had to do with mental visualization ability while playing a computer-based ball tossing game with other players connected via the internet. Since during the games participants could see the picture of the other (fictional) players, we took picture of participants' faces as well and made them believe that those pictures were shown to the other players. Participants were instructed not to pay attention to the actual tossing performance and to mentally visualize their experience instead (e.g., Where were they playing? What was the weather like?) (as in Panasiti et al., 2015). In reality, they were playing with fictional characters whose inclusion/exclusion behavior was pre-programmed (see Figure 1A). Participants were asked to press the left (7) or right key (8) on the keyboard to throw the ball to the player on the left or the right. They then had to wait for the ball to be tossed back to them. The ball-tossing game lasted 30 throws. In the social exclusion condition, participants only got the ball back 3 times. They got it back 12 times in the social inclusion condition. Each phase (social exclusion and inclusion) lasted around one minute and a half.

Each version of the Cyberball Game featured 2 different fictional characters of the same gender that had been selected from 4 of the Caucasian male faces and 4 of the Caucasian female faces validated through the online survey (see Experimental stimuli section).

Participants' face temperature (periorbital regions) was measured during the task by means of fITI.

After each version of the Cyberball Game, participants were presented with four Self-Anchored Scales ranging from 1 to 9 aimed at measuring their current emotional state and corresponding to four different dimensions: [sadness (1) – happiness (9)], [hostility (1) – friendliness (9)], [nervousness (1) – relaxation (9)] and [badness (1) – goodness (9)].

Trust Game

A Trust Game (TG; Berg et al., 1995) (see Figure 1B) was played after each Cyberball session. In this game, the participant (i.e., the investor) was endowed with €10 before starting 12 TG rounds, each composed of two stages (as in Ponsi, Panasiti, Aglioti, & Liuzza, 2017). Stage 1 had the investor decide how much of the €10 to invest in a partner (i.e., the trustee); after the transfer, the money was multiplied by three. In stage 2, the trustee had to decide whether to return half of the sum to the investor or to keep all the money for him or herself. Participants were reminded that one round would be randomly chosen to determine the final compensation for them and the player they were interacting with (implying real monetary consequences for both of them). Importantly, information concerning the outcome of stage 2 was concealed to participants in order to prevent carryover effects across trials that could bias subsequent trusting decisions.

Participants played the TG with 2 familiar players and 2 unfamiliar ones for three rounds each. The familiar players were chosen from those previously encountered in the Cyberball Game, where they behaved in an inclusive or an ostracizing way. The unfamiliar players were new players (though their photos were also selected from those validated through the online survey, see Experimental stimuli section). Unbeknownst to the participants, the game actually took place against a PC device.

Physiological Recordings

Participants were required to avoid the intake of vasoactive substances (e.g., caffeine, nicotine and alcohol) for at least 3 hours prior to the experiment in order to prevent interference with basal sympathetic activity. Once in the experimental room, they waited 30 minutes before starting the experimental task. This procedure allowed their skin temperature to reach a thermal equilibrium (Ioannou, Gallese, & Merla, 2014).

fITI was used to measure face temperature during the Cyberball games (see Figure 4B). This contact-free technique allows for skin temperature to be recorded by tracking changes in temperature with high thermal (<20mK = <0.02°C) resolution. The digital infrared FLIR© camera SC3000 employed for the thermal recording was set at 10 Hz (10 frame/sec) and placed 1 m away from the participant at eye-level in a controlled climate experimental room (23° C ± 1). To avoid motion-related artifacts, participants' heads were kept still by a home-made head-rest.

Data Reduction and Analyses

Thermal data were recorded through the ThermaCAM Researcher Professional 2.8 SR-3 software. The software OTACS V1 (Open Thermal Action Coding System) (Zhou, Tsiamyrtzis, Lindner, Timofeyev, & Pavlidis, 2013) was chosen to extract thermal information offline because it allows for tracking temperature changes in specific regions of interest (ROI) of the face. To ensure a reliable positioning and sizing of the ROIs, we employed the largest possible square that would not touch the eyelids (selection criteria as in Panasiti et al., 2016). We selected left and right periorbital regions as ROIs because the temperature increase of these regions is a reliable measure of SNS activation (Hahn, Whitehead, Albrecht, Lefevre, & Perrett, 2012; Ioannou et al., 2013; Levine et al., 2001; Panasiti et al., 2016; Ioannis Pavlidis, Eberhardt, & Levine, 2002; Ponsi, Panasiti, Rizza, et al., 2017). This increase, to be specific, is caused by an increase in blood flow to the skin as a consequence of heart rate acceleration mediated by the SNS (Ioannou, Morris, et al., 2014). The pixels selected within each ROI were averaged together and constituted the left and right periorbital thermal signal. The extracted data were analyzed separately for each social modulation phase (social exclusion and inclusion) using Brain Vision Analyzer 1.5 (Brain products GmbH, Munich, Germany) software.

To remove eye blink artifacts from the periorbital thermal signal, we filtered thermal data with a 0.10 Butterworth zero phase low-pass filter. Using visual inspection, we identified and removed the remaining physiological and motion artifacts affecting the thermal signal. The thermal data for each participant were constructed by exporting the temperature values in three time bins which included 10 seconds (s) = 100 datapoints each: 0-10 s (beginning), 40-50 s (middle) and 80-90 s (end, i.e. the last 10 seconds available for all participants). The average duration of the thermal signal relative to the social exclusion phase was 109.91s (SD = 9.39), while the average duration of the thermal signal relative to the social inclusion phase was 129.23s (SD = 18.16).

All the statistical analyses were performed with the software STATISTICA 8 (StatSoft, Inc.), with the exception of the moderation analysis which was performed with the software SPSS Statistics v.22.0 (IBM Corp.). In particular, the moderation analysis was computed with the PROCESS macro (Hayes, 2017) for SPSS. Please note that the predictor variable (i.e. periorbital temperature) has been mean centered as suggested for moderation analyses (Aiken & West, 1991).

Results

Questionnaires

Concerning the DERS, the two groups showed a different score only in the sub-scale “Lack of Emotional Clarity” ($t(16) = -2.10$, $p = .0432$, see Table 1), indicating that patients with psoriasis had more difficulty in correctly identifying their own emotions than controls.

Concerning the PANAS, there were no statistically significant differences between the two groups (all ps > 0.05, see Table 1).

Behavioral data

Effect of social modulation on emotional state

Due to technical failures, the ratings of two patients were not recorded correctly, so the analysis was performed on 32 participants (15 patients, 17 controls). A one-way repeated measures ANOVA with group (patient, control) and order (exclusion-inclusion or inclusion-exclusion) as between-subject factors was conducted to compare the effects of social modulation (exclusion, inclusion) on sadness-happiness ratings. It revealed a statistically significant social modulation main effect ($F(1,30) = 5.63$, $p = .024$, , $\eta^2_p = .16$) qualified by a social modulation by group interaction ($F(1,30) = 5.63$, $p = .024$, , $\eta^2_p = .16$). Participants generally felt happier after being included (M = 6.28, SE = .31) than after being excluded (M = 5.425, SE = .35). Newman-Keuls post hoc test on the interaction showed that patients' sadness-happiness ratings were not affected by the social modulation ($M_{exclusion} = 5.73$, $SE_{exclusion} = .52$, $M_{inclusion} = 5.73$, $SE_{inclusion} = .43$, $p = 1.00$), while controls felt significantly more happy after being included (M = 6.82, SE = .40) than excluded (M = 5.12, SE = .49) ($p = .011$) (see Figure 2).

The same analysis conducted on hostility-friendliness ratings revealed a statistically significant main effect of social modulation ($F(1,30) = 9.99$, $p = .003$, , $\eta^2_p = .25$). As expected, participants felt more friendly after being included during the Cyberball game (M = 7.56, SE = .20) than after being excluded (M = 6.36, SE = .37). The social modulation by group interaction did not reach full significance ($F(1,30) = 3.75$, $p = .06$, , $\eta^2_p = .11$).

The same analysis conducted on nervousness-relaxation ratings did not show any significant main effect or interaction (all $p_s > .14$).

The same analysis performed on badness-goodness ratings did not show any significant main effect or interaction (all $p_s > .22$).

--Figure 2 here--

Effect of social modulation on trusting behavior

Due to technical failures, the behavioral responses of one patient were not recorded correctly during the social inclusion modulation phase, so the analysis was performed on 33 participants (16 patients, 17 controls). A repeated measures 2 (social modulation: exclusion, inclusion) by 2 (player: familiar, unfamiliar) mixed ANOVA with group (patient, control) and order (exclusion-inclusion or inclusion-exclusion) as between-subject factors revealed a statistically significant social modulation by player interaction ($F(1,29) = 5.76$, $p = .02$, $\eta^2_p = .165$) on trust behavior (i.e. mean amount of money invested during the TG). Newman-Keuls post hoc test showed that participants trusted the unfamiliar players more after social exclusion (M = 5.83, SE = .36) than after social inclusion (M = 5.01, SE = .27) ($p = .01$) (see Figure 3). The investments into familiar players were not modulated by the social modulation ($M_{exclusion} = 5.40$, $SE_{exclusion} = .33$, $M_{inclusion} = 5.54$, $SE_{inclusion} = .30$, $p = .58$) (see Figure 3).

--Figure 3 here--

Physiological data

Effect of social modulation on periorbital temperature

The analysis on the periorbital regions was performed on 30 participants (15 patients, 15 controls) because 4 participants had to wear glasses, a condition that prevented accurate recordings of this facial area. A repeated measures 3 (Block Phase: Start, Middle, End) by 2 (Periorbital area: Right, Left) by 2 (Social Modulation: Exclusion, Inclusion) mixed ANOVA with Group (Patient, Control) and Block Order (Exclusion-Inclusion or Inclusion-Exclusion) as a between-subject factors revealed statistically significant main effects of Block Phase (F(2,52) = 3.79, p = .029, η^2_p = .13) and Social Modulation (F(1,26) = 15.52, p < .001, η^2_p = .37). Periorbital temperature generally decreased over time (M_{start} = 32.625, SE_{start} = .48, M_{middle} = 32.59, SE_{middle} = .48, M_{end} = 32.56, SE_{end} = .48) and was higher during social exclusion (M = 33.62, SE = .88) than inclusion (M = 31.56, SE = .86). Newman-Keuls test of the Block Phase main effect revealed that periorbital temperature at Start Block Phase was significantly different from the End Block Phase (p = .017), but not from the Middle Block Phase (p = .10), which in turn was also not significantly different from the End Block Phase (p = .24). Moreover, these main effects were qualified by a Social Modulation by Group interaction (F(1,26) = 4.05, p = .05, η^2_p = .13) and by a Social Modulation by Periorbital Area interaction (F(1,26) = 4.28, p = .0485, η^2_p = .14). Newman-Keuls test of the Social Modulation by Group interaction (see Figure 4A) showed that controls' periorbital temperature was higher during social exclusion than social inclusion ($M_{exclusion}$= 33.86, $SE_{exclusion}$= 1.24, $M_{inclusion}$= 30.74, $SE_{inclusion}$= 1.22, p= .002), while patients' periorbital temperature was not affected by the social modulation ($M_{exclusion}$= 33.38, $SE_{exclusion}$= 1.24, $M_{inclusion}$ = 32.37, $SE_{inclusion}$= 1.22, p= .19). Also, patients' periorbital temperature during social inclusion (M = 32.37, SE = 1.22) was higher than controls (M = 30.74, SE = 1.22) (p = .025). Newman-Keuls test of the Social Modulation by Periorbital Area interaction showed that during social exclusion, Left Periorbital Area temperature (M = 32.86, SE = .83) was significantly lower than the Right Periorbital Area one (M = 34.38, SE = .85) (p = .03). The same differential pattern regarding Left (M = 31.74, SE = .85) and Right (M = 31.38, SE = .815) Periorbital Areas is not present during social inclusion (p = .585). Also, Right Periorbital Area temperature is higher during social exclusion (M = 34.38, SE = .85) than social inclusion (M = 31.38, SE = .815) (p < .001). Findings relative to thermal asymmetry in Left and Right Periorbital Areas temperature are often reported in the literature (Abreau et al., 2016; Azharuddin, Bera, Datta, & Dasgupta, 2014; Mapstone, 1968) and are probably due to differing blood supplies related to anatomical differences between the left and right side (Mapstone, 1968).

--Figure 4 here--

Effects of periorbital temperature during social exclusion on trusting behavior

A moderation analysis showed a significant interaction (β = -.68, t = -2.25, SE = .30, p = .0321, R^2 = .14) between the moderator variable group (patients vs controls) and the predictor periorbital temperature during social exclusion (mean centered) on trusting behavior towards unfamiliar players after social exclusion. The periorbital temperature during social exclusion was computed by averaging the temperature bins recorded during the Cyberball game for each participant. In the moderation model, the effect of temperature on trusting behavior is almost significant for patients (β = .445, t = 1.80, SE = .24, p = .081) but not for controls (β = -.237, t = -1.34, SE = .17, p = .19) (see Figure 5).

--Figure 5 here--

This moderation analysis shows that despite the two slopes not being significantly different from zero, they are different from each other, indicating that SNS activation during social exclusion enhances trusting behavior toward unfamiliar players more in patients than in controls.

We also performed the same moderation analysis in which DERS Lack of Emotional Clarity subscale was examined as the moderator of the relation between periorbital temperature (during social exclusion) and trust towards unfamiliar players (after social exclusion). In this moderation model, no significant main (Periorbital temperature during social exclusion: β = -.21, t = -.38, SE = 18.05, p = .50; DERS Lack of Emotional Clarity: β = -.58, t = -.37, SE = 1.57, p = .71) or interaction (Periorbital temperature during social exclusion by DERS Lack of Emotional Clarity: β

= .02, t = .39, SE = .05, p = .70) effects were present.

Correlation between periorbital temperature during social exclusion and sadness-happiness ratings

Since a rise in periorbital temperature signals enhanced emotional arousal but gives no information about emotional valence (that could be either positive or negative), we also tested potential correlations between periorbital temperature during social exclusion and emotional state ratings. We found a significant negative correlation between mean periorbital temperature during social exclusion and sadness-happiness ratings after social exclusion ($r = -.527$, $N = 30$, $p = .003$) (see Figure 6). This finding suggests that, in our study, an increase of periorbital temperature is accompanied by a decrease of happiness ratings after experiencing social exclusion during the Cyberball game.

--Figure 6 here--

Discussion

In this study, we employed fITI to investigate the behavioral and physiological consequences of social exclusion vs inclusion on interpersonal trust in psoriasis patients and healthy controls.

In general, we found that social exclusion shifted participants' trust toward unfamiliar players, who were trusted significantly more after social exclusion than inclusion. On the contrary, trust toward the familiar players (i.e. players who had previously included or excluded participants) was not significantly affected by social modulation, and no difference in trust emerged between patients and controls. A similarly conducted study by Hillebrandt and colleagues investigated the effect of social exclusion/inclusion and reputation (i.e. being a familiar vs unfamiliar player to the participants) on trust (Hillebrandt, Sebastian, & Blakemore, 2011). Differently from our findings, the authors reported that social inclusion enhances trust toward fictional players who had previously included them during the Cyberball Game (Hillebrandt et al., 2011), and that being socially excluded/included had no effect on "strangers" (fictional players not taking part in the Cyberball Game). These differences can probably be explained by differences in the sample (our sample is older: ~50 years old) and in the experimental design (between-subject design vs within-subject design).

Our behavioral findings are in line with the Social Reconnection Hypothesis (Maner, DeWall, Baumeister, & Schaller, 2007), which states that being socially excluded by one's own conspecifics strongly motivates an individual to form social bonds with new interaction partners (in our case the unfamiliar players). Consistently with this theoretical account, Derfler-Rozin and colleagues found that social exclusion induced: (i) enhanced trust, (ii) enhanced trust reciprocation with unknown individuals, and (iii) decreased risk-taking (Derfler-Rozin, Pillutla, & Thau, 2010).

One point of novelty in the present study is that we found an increase in periorbital temperature after social exclusion, suggesting that being excluded by others triggers SNS activation. More specifically, we found that: (i) while periorbital temperature (indexing SNS activation) was higher in social exclusion than inclusion for controls, patients' periorbital temperature did not show such difference; (ii) during social inclusion, patients' periorbital temperature was higher than controls'. These results are in line with recent physiology studies reporting that being ostracized triggers an increase (i) in facial temperature (nose and perioral area) (Paolini et al., 2016) and (ii) in SNS activity (Iffland et al., 2014; Kelly, McDonald, & Rushby, 2012; Newman, 2014).

Periorbital temperature results together with happiness self-reports show that psoriasis patients might not find social inclusion experiences as positive as controls. This is supported by the fact that while controls' SNS seems to be deactivated during the inclusion vs the exclusion block, patients' SNS activity is just as high during exclusion (it is lower in controls), and their reported happiness after inclusion is not higher than that after exclusion (while in controls it is). The reason why patients might have experienced social inclusion as less enjoyable might be in agreement with findings showing that psoriasis patients often develop social avoidance which heavily impacts social activities (Schneider, Heuft, & Hockmann, 2013). Moreover, higher psoriasis severity is associated with higher social anxiety in patients with pre-adult onset psoriasis (Łakuta & Przybyła-Basista, 2017). In particular, the value of physical appearance to one's sense of self-worth seems to be one of the main factors contributing to the development of social anxiety (Łakuta & Przybyła-Basista, 2017). Psoriasis symptoms also seem to be linked to audience and interaction anxiety (Luca et al., 2016). Our results regarding control participants, on the other hand, are in line with previous studies indicating that social exclusion decreases positive mood ratings and increases anger and distress ratings (Radke et al., 2018; Seidel et al., 2013).

Furthermore, we did not find any difference in temperature between the two groups during social exclusion. We did show, however, that the two groups vary in how SNS activation (i.e. periorbital temperature) influences the subsequent trust. In particular, in patients higher SNS activation during social exclusion was related to higher trust on unfamiliar players. Seeking new social connections (in our case, investing in unfamiliar players) after social exclusion is considered a behavioral emotion regulation strategy that has the power to numb the pain caused by social rejection (DeWall, Twenge, Bushman, Im, & Williams, 2010). But this strategy also has some side effects, as it can make people more sensitive to social influences such us obedience, compliance and conformity (Riva, 2016). Thus, the fact that higher SNS activity during social exclusion enhances the need for social reconnection in psoriasis patients highlights the presence of an emotion regulation strategy that is as effective as it is risky.

Importantly, patients and control group only differed on the "Lack of emotional clarity" sub-scale of the DERS questionnaire. This trait measures the extent to which individuals can unambiguously identify their emotional experiences (Lischetzke & Eid, 2017) . The fact that patients have a problem in correctly identifying their emotions might be related to the fact that their happiness self-reports were not different after social exclusion and inclusion. It might also be the reason why we find that they tend to be more influenced by SNS activation during social exclusion than controls. In fact, it is possible that their inability to correctly label SNS activations impedes against the proper use of emotion regulation strategies that could be more adaptive than social reconnection (e.g. positive reappraisal).

Our results indicate that patients with psoriasis might particularly benefit from psychotherapeutic or cognitive behavioral techniques that focus on the identification and disambiguation of different emotional reactions, as well as on “mentalization based treatments” (Krach, 2010) aimed at enhancing their reduced motivation to engage in social interactions.

Limitations and future directions

There are three major limitations in this study that could be addressed in future research. One limitation has to do to with the fact that, for technical reasons, the analysis on the periorbital regions was performed on a subsample of participants (N = 30) in which we managed to record both (left and right) periorbital regions. However, the sample size is in line or even bigger than the one of other thermal imaging studies (Hahn et al., 2012; Panasiti et al., 2016; Paolini et al., 2016; Ioannis Pavlidis et al., 2002; Ponsi, Panasiti, Rizza, et al., 2017). Second, we focused on the different behavioral and physiological patterns induced by social exclusion vs social inclusion, but we did not include a neutral condition to evaluate how social modulations could change participants' baseline behavior. Third, self-report measures of emotion regulation did not correlate with physiological findings, this might have to do with the fact that respect to more implicit physiological measures, self-report ones are more influenced by participants' ability to accurately describe themselves.

Future research should investigate whether the effects we found can be detected also in other clinical populations that suffer from stigmatization (e.g. people with obesity) or emotion regulation problems (e.g. post-traumatic stress disorder). This approach may shed light on the association between behavioral and physiological reactions to social exclusion and different clinical conditions.

Conflict of interest

The authors report no conflict of interest associated with this manuscript.

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Author Contribution

G.P, B.M., V.P., S.M.A., and M.S.P. conceived and designed research; G.P., M.S.P., and B.M. performed experiments; G.P. and M.S.P. analyzed data; G.P. and M.S.P. interpreted results of experiments; G.P. prepared figures; G.P. and M.S.P. drafted manuscript; G.P., B.M., V.P., S.M.A., and M.S.P. edited and revised manuscript; G.P., B.M., V.P., S.M.A., and M.S.P. approved final version of manuscript.

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Table Captions

Table 1. Demographic and clinical characteristics of psoriasis patients and control participants.

Table 2. Descriptive information relative to the selected male and female face stimuli employed in the Cyberball Game and in the Trust Game.

Figure Captions

Figure 1. **(A)** In the social modulation phase, participants were excluded or included by two fictional characters in the Cyberball Game. **(B)** Then participants played a Trust Game (TG) in which they had to decide how much of €10 to invest in familiar and unfamiliar players. The familiar players were those already encountered in the Cyberball Game, while the unfamiliar players were new. All participants took part in both the exclusion and inclusion social modulation phases and played the TG twice. The order of a potential experimental block was the following: (i) Cyberball Game (exclusion), (ii) TG with 2 exclusive familiar participants and 2 unfamiliar participants, (iii) Cyberball Game (inclusion), (iv) TG with 2 inclusive familiar participants and 2 unfamiliar participants.

Figure 2. Social modulation by group interaction on sadness-happiness ratings (F(1,30) = 5.63, p = .024, , η^2_p = .16). SEs are represented by error bars (N = 32 (15 patients, 17 controls), male = 25).

Figure 3. Social modulation by player interaction on trusting behavior (F(1,29) = 5.76, p = .02, η^2_p = .165). SEs are represented by error bars (N = 33 (16 patients, 17 controls), male = 25).

Figure 4. (A) Social modulation by group interaction on mean periorbital temperature (F(1,26) = 4.05, p = .05, η^2_p = .13). SEs are represented by error bars (N = 30 (15 patients, 15 controls), male = 23). **(B)** Infrared thermal image of the face of one participant. The red squares indicate the ROIs' positioning over the left and right periorbital regions.

Figure 5. Linear relationship (β = -.68, t = -2.25, SE = .30, p = .0321, R^2 = .14) between mean investment toward unfamiliar players in the TG after social exclusion and periorbital temperature during social exclusion, moderated by group membership (N = 30, (15 patients, 15 controls), male = 23). The predictor variable (i.e. periorbital temperature) has been mean centered.

Figure 6. Negative correlation between mean periorbital temperature during social exclusion and sadness-happiness ratings (r = -.527, p = .003, N = 30 (15 patients, 15 controls), male = 23).

Tables

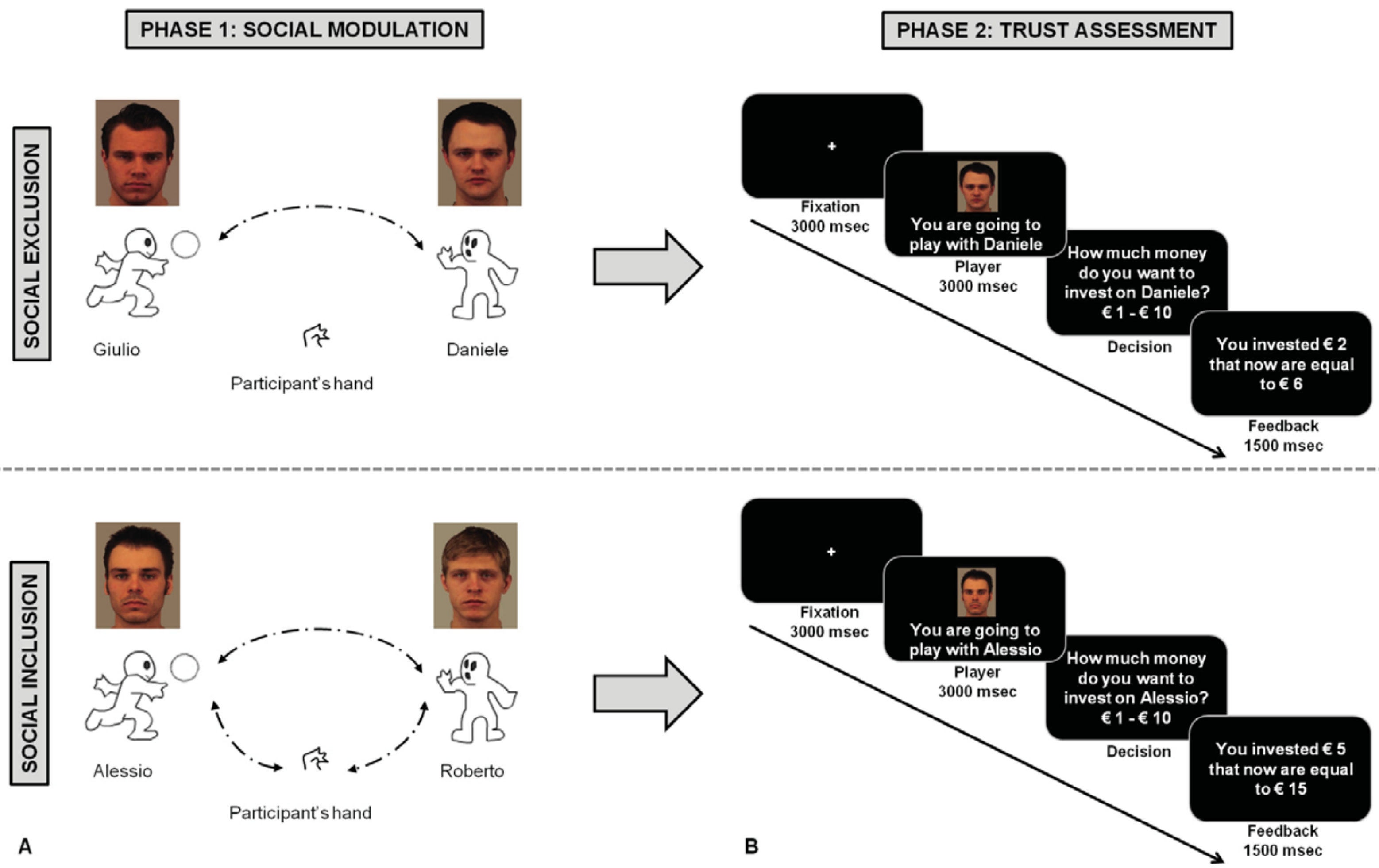
Table 1

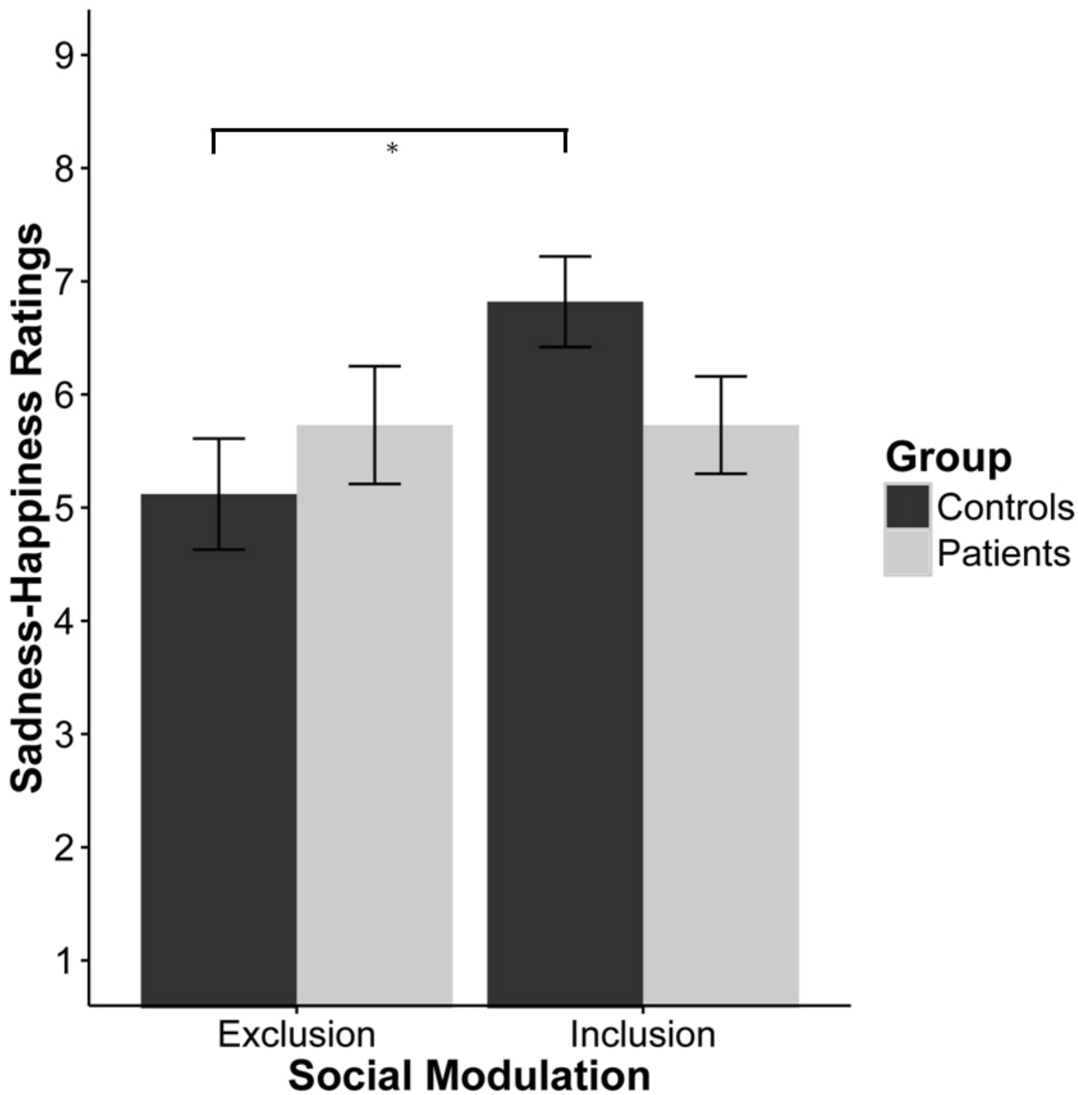
	Psoriasis patients (N = 17) Mean (SD) or (%)	Control participants (N = 17) Mean (SD) or (%)	Student's T df = 16 (P-value)
	Demographic information		
Age	51.82 years (15.44)	51.82 years (15.22)	0.00 (1.00)
Age range	20-74 years	22-74 years	NA
Gender	13 male (76.47%)	13 male (76.47%)	NA
Education	10.82 years (3.32)	12.06 years (3.07)	-1.11 (0.28)
	Clinical information		
DERS	85.76 (18.42)	78.18 (20.15)	-1.05 (0.31)
DERS Nonacceptance of emotional responses	13.06 (4.88)	12.35 (5.69)	0.34 (0.74)
DERS Difficulty in engaging in Goal-directed behavior	11.82 (3.41)	12.76 (4.48)	0.57 (0.58)
DERS Impulse control difficulties	11.94 (5.38)	11.65 (4.17)	-0.19 (0.85)
DERS Lack of emotional awareness	7.53 (2.76)	7.06 (3.30)	-0.45 (0.66)
DERS Limited access to emotion regulation strategies	18.88 (5.72)	15.59 (5.21)	-1.71 (0.11)
Lack of emotional clarity	12.71 (3.24)	10.29 (3.44)	-2.10 (0.04)
PANAS Positive affect (state)	30.18	34.18	1.78 (0.09)
PANAS Positive affect (trait)	32.00	35.00	1.53 (0.145)

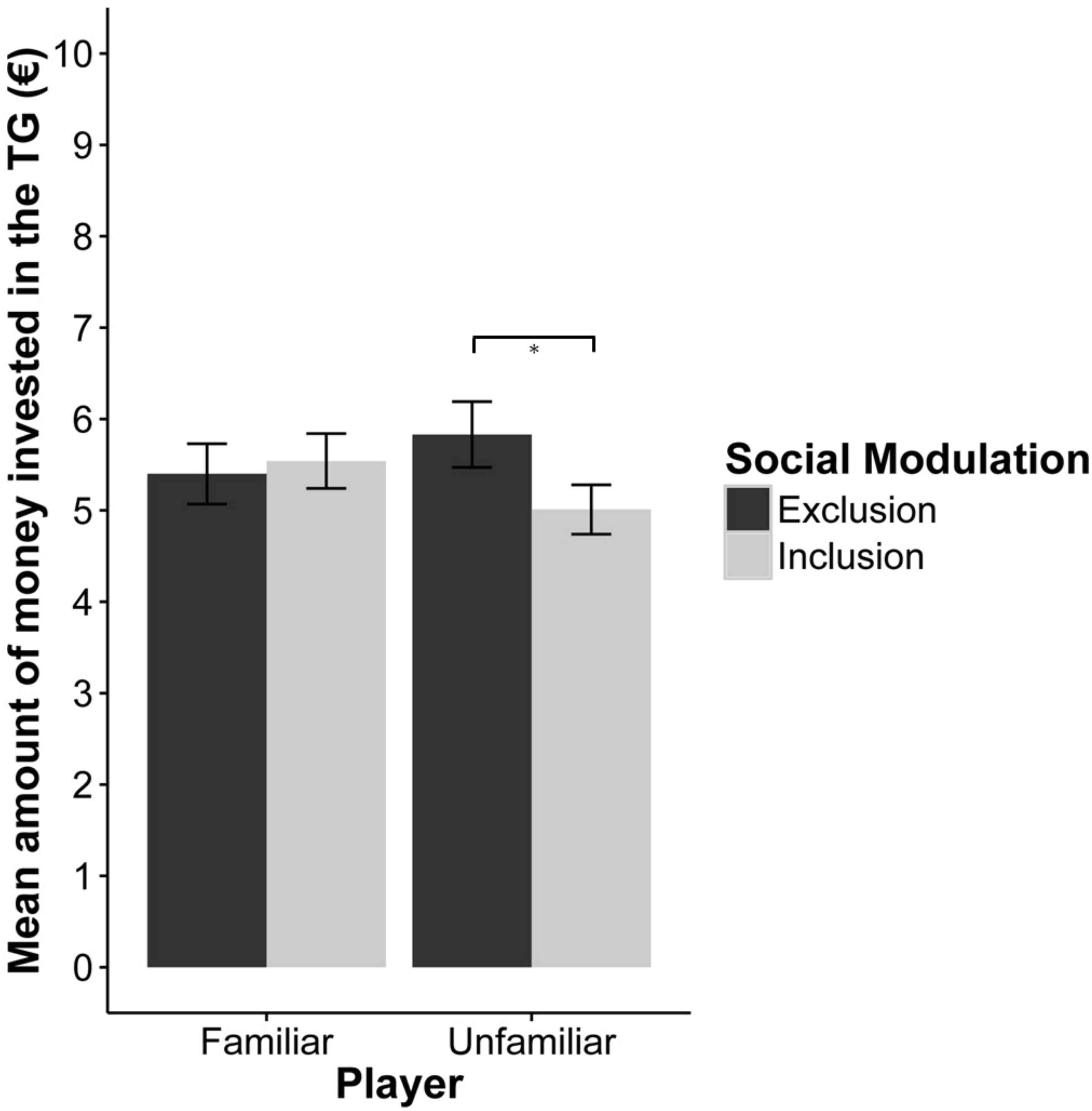
PANAS Negative affect (state)	15.18	13.88	-0.45 (0.66)
PANAS Negative affect (trait)	20.53	17.82	-1.15 (0.27)

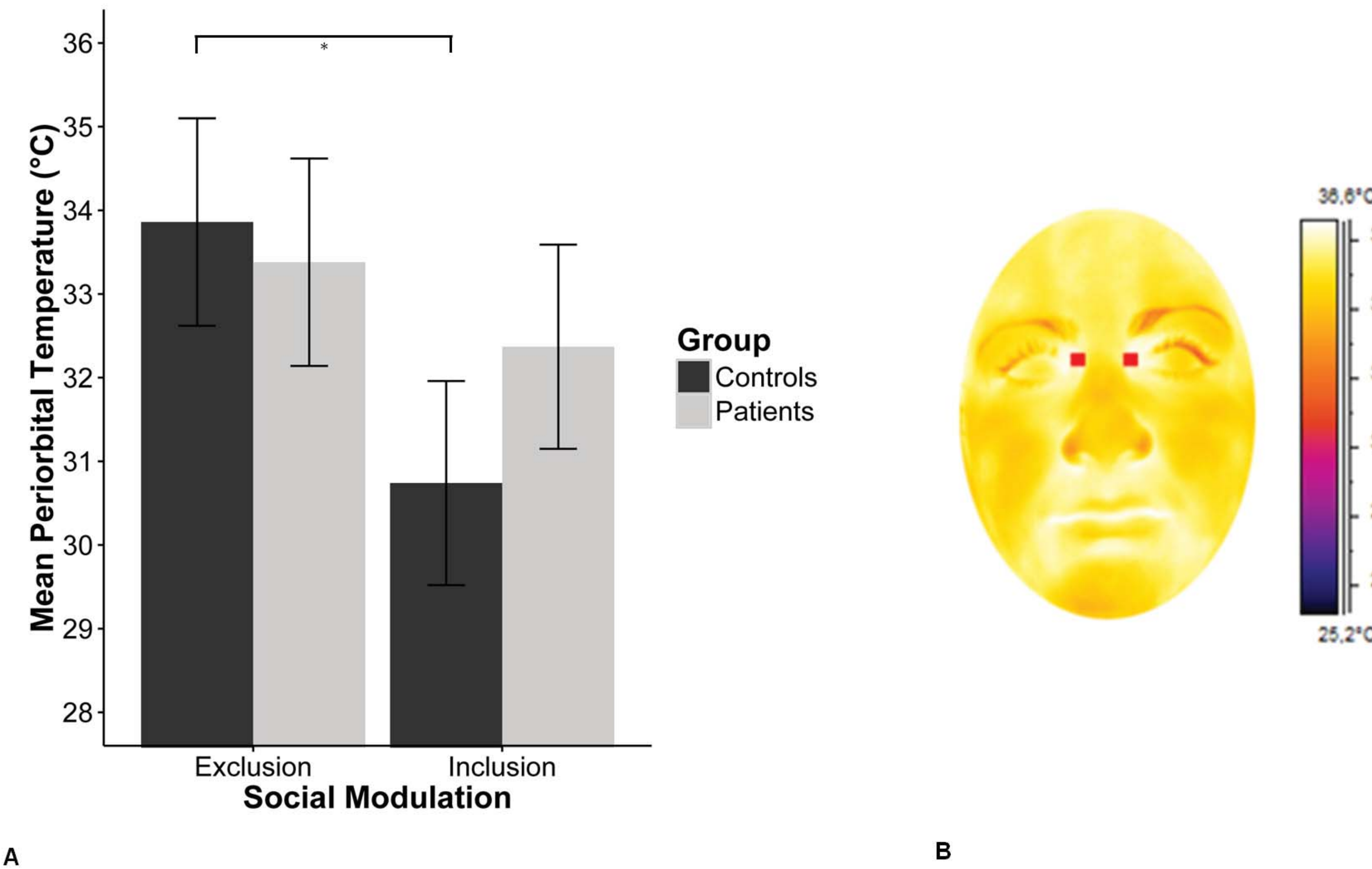
Table 2

	Male faces (N = 8) Mean (SD)	Female faces (N = 8) Mean (SD)	Student's T df = 7 (P-value)
Attractiveness	2.26 (0.38)	2.24 (0.29)	-0.13 (0.90)
Liking	2.43 (0.26)	2.65 (0.21)	1.83 (0.11)
Trustworthiness	2.63 (0.26)	2.90 (0.27)	1.94 (0.09)

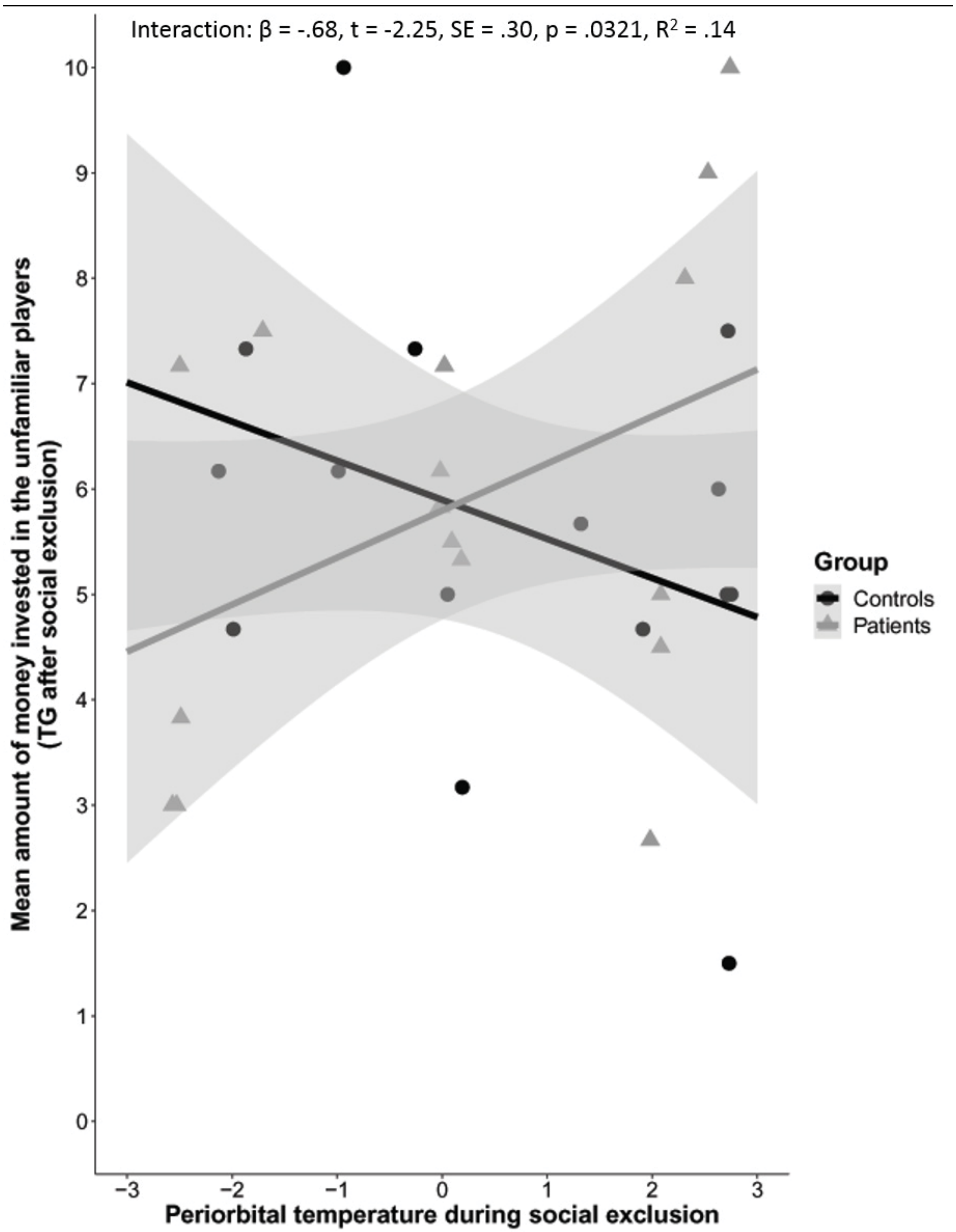

PHASE 1: SOCIAL MODULATION
PHASE 2: TRUST ASSESSMENT
SOCIAL EXCLUSION
Giulio
Daniele
Participant's hand
Fixation
3000 msec
You are going to play with Daniele
Player
3000 msec
How much money do you want to invest on Daniele? € 1 - € 10
Decision
You invested € 2 that now are equal to € 6
Feedback
1500 msec
SOCIAL INCLUSION
Alessio
Roberto
Participant's hand
Fixation
3000 msec
You are going to play with Alessio
Player
3000 msec
How much money do you want to invest on Alessio? € 1 - € 10
Decision
You invested € 5 that now are equal to € 15
Feedback
1500 msec
A
B

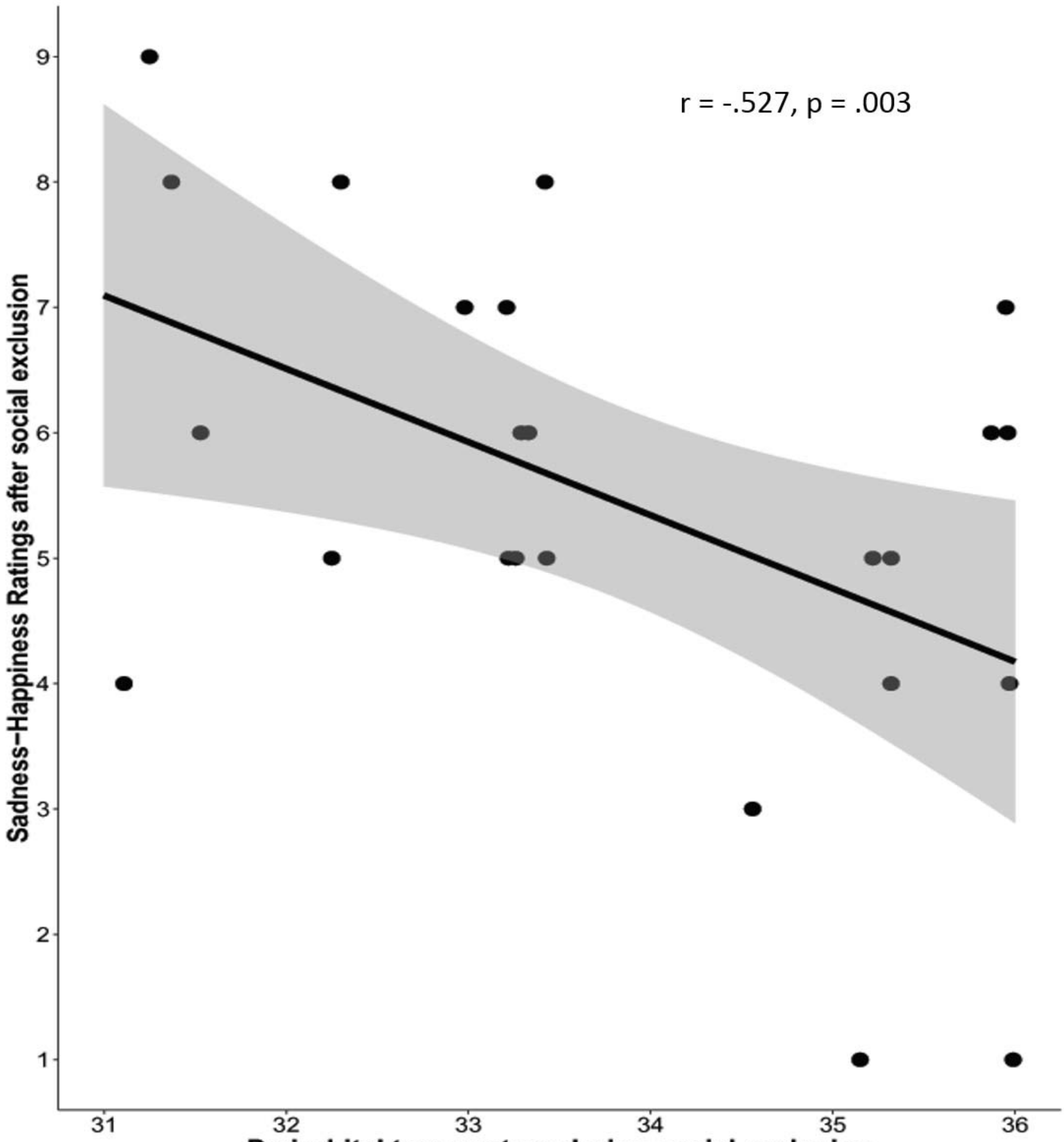

9
8
7
6
5
4
3
2
1
Sadness-Happiness Ratings
*
Exclusion
Inclusion
Social Modulation
Group
Controls
Patients


Mean amount of money invested in the TG (€)
10
9
8
7
6
5
4
3
2
1
0
*
Familiar
Unfamiliar
Player
Social Modulation
Exclusion
Inclusion



36
35
34
33
32
31
30
29
28
*
Mean Periorbital Temperature (°C)
Exclusion
Inclusion
Social Modulation
Group
Controls
Patients
A
36,6°C
36
34
32
30
28
26
25,2°C
B


Interaction: β = -.68, t = -2.25, SE = .30, p = .0321, R2 = .14
Mean amount of money invested in the unfamiliar players
(TG after social exclusion)
Periorbital temperature during social exclusion
Group
Controls
Patients
10
9
8
7
6
5
4
3
2
1
0
−3
−2
−1
0
1
2
3



r = -.527, p = .003
Sadness-Happiness Ratings after social exclusion
9
8
7
6
5
4
3
2
1
31
32
33
34
35
36
Periorbital temperature during social exclusion