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"Self-awareness and social norms: the relation between bodily states and prosocial behaviour"

Candidate: Alessandra Mancini

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Supervisor

Prof. Salvatore Maria Aglioti

Social and Cognitive neuroscience Laboratory

Department of Psychology

Sapienza -University of Rome

Reviewers

Prof. Alessio Avenanti

Centre for studies and researches

in Cognitive Neuroscience

Faculty of Psychology

University of Bologna ‘Alma Mater Studiorum

Prof. Friedemann Pulvermüller

Institute of German and Dutch Studies

Department of Philosophy and Humanities

Freie Universität Berlin

Prof. Patrizia Pantano

Department of Neurology e Psychiatry

Sapienza -University of Rome

Official Referee

Prof. Alessio Avenanti

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Chapter 1

Introduction

Human societies represent a spectacular outlier with respect to all other animal species because they are based on large-scale cooperation among genetically unrelated individuals (Richardson et al., 2003). Cooperation in human societies is mainly based on social norms defined as standards of behaviour that are based on widely shared beliefs on how individual group members ought to behave in a given situation (Ellickson, et al., 2001). Human tendency to stick to social norms such as fairness has been repeatedly investigated using economic games such as the Ultimatum Game (UG), in which self-economic interest is in contrast with social preferences (Camerer and Fehr, 2002). Using this game, pioneer fMRI (Sanfey et al., 2003; Tabibnia et al., 2008) and TMS studies (Knoch et al., 2006; van 't Wout et al., 2005) hint at the existence of a neuronal circuitry comprising the dorsolateral prefrontal cortex, the bilateral anterior insula and the anterior cingulate cortex specifically involved in the perceived fairness of others (Sanfey et al., 2003) (the neural basis of social preferences during economic interactions are reviewed in paragraph 1.1). However, studies on the objective and contextual aspects of fairness highlight the different neural underpinnings of objective social inequality with respect to contextual aspect of fairness (Wright et al., 2011). Moreover, behavioural studies showed that incidental negative emotion influences behavioural responses (Moretti and di Pellegrino, 2010; Harlé and Sanfey, 2007; Andrade and Ariely, 2009) and fairness ratings (Moretti and di Pellegrino, 2010) in the UG (The influence of emotions on fairness related conducts are reviewed in paragraph 1.2). While the above mentioned studies experimentally manipulated the content of the emotions, little is known about whether bodily signals *per se*, such as pain and interoception and can bias fairness related conducts. Of relevance for the present work is the observation that both the attention towards an aversive bodily signal such as pain and towards one own's heartbeat activate a network that strongly overlaps with the one involved in decision making during economic games (Craig 2002, 2009; Critchley et al. 2004; Peyron et al. 2000) (the neural basis of pain and interoception are reviewed in paragraphs 1.3 and 1.4, respectively). Hence, in studies one and two we manipulated respectively the perception of an aversive bodily state (i.e. pain) and the general ability to perceive bodily signals (i.e. interoception) with the aim of testing whether they modulate the economic behaviour of participants playing the UG.

Recent theories proposed that the application of social norms among humans is fostered by social preferences, arguing that people generally prefer to behave prosocially because they derive higher hedonic value from the mutual cooperation outcome (Fehr 2008; Thibaut and Kelley 1959, see paragraph 1.1). In a similar vein the need to belong seems to be deeply rooted in our evolutionary history, being a product of natural selection that have survival benefits (Buss and Schmit, 1993). Indeed, social exclusion for social animals was often literally equal to physical pain or death (MacDonald and Leary, 2005). Being the need for belongingness so important and the threat of social rejection so severe some authors explored the neural underpinnings of social pain, providing evidences suggesting that social pain and physical pain share the same physiological mechanisms (Mac Donald and Leary 2005; Panskepp et al. 1978; Eisenberg et al., 2003). Nevertheless, it is surprising to observe that socially excluded people frequently react to social exclusion in a detached and emotionally indifferent manner (Baumeister et al., 2002; Twenge et al, 2001; Zadro et al., 2004). Consistently with these observations DeWall and Baumeister (2006) showed that laboratory manipulation of social pain caused a broad decrease in physical pain sensitivity. This decrease was mediated by the emotional numbness presented by the excluded participants (the neural basis of social pain are reviewed in paragraph 1.5). However, we are not aware of studies that systematically examined the effect of social pain on the cortical correlates of pain processing. Given the importance of social norms in maintaining social groups' cohesion here we extended the concept of social pain, originally attributed only to social exclusion (Panskepp, 1998; Mac Donald and Leary 2005), to that of an intentional defection of a social norm (i.e. fairness) operated by a peer opponent. The aim of study three was therefore to assess whether and how the fairness of a socio-economic context affect the cortical correlates of pain processing by means of Laser evoked potentials (LEPs) (an introduction to the technique of LEPs can be found in paragraph 1.6).

1.1 The neural basis of social preferences during economic games

Social preferences like altruism, reciprocity and fairness, are undeniably central to human interactions in daily life. However, by definition, choosing to behave prosocially is costly at the personal level. Following Trivers' definition: "*altruistic behaviour can be defined as a behaviour that benefits another organism, not closely related, while being apparently detrimental to the organism performing the behaviour, benefit and detriment being defined in terms of contribution to inclusive fitness.*" Thus, "*under certain conditions natural selection favors altruistic behaviours because, in the long run, they benefit the organism performing them*" (Trivers, 1971).

During economic interactions in the context of one shot anonymous games, pro-sociality could indicate a reflexive behaviour that is highly adapted for repeated interactions (Fehr and Camerer, 2007) and thus can be considered a rational response to changes in economic structures (Samuelson, 2005). Economic games are well structured tasks taken from economic theory, which are routinely employed to test social preferences. The box below reports the description of some of the most used economic games.

Box 1

In an ultimatum game (UG) one player (proposer) plays as the first mover and decides how to divide a given amount of money (e.g. € 10) in an anonymous *one-shot* interaction (Güth et al.,. 1982). In this condition, negotiation effects are ruled out by the absence of repeated plays. The proposer decides how to split the stake with the only constraint that the responder cannot get 0 (e.g. € 8 for him/her, € 2 for the other player). If the responder accepts, each player keeps the allocated amount of money; if he/she rejects the offer, both players receive nothing. According to standard economic models, in order to maximize his/her own payoff the responder should accept any offer. Indeed, although inequitable, the offer is better than nothing. However, in accordance with theories of reciprocity (Rabin, 1993) and inequity aversion (Fehr and Schmidt, 1999), participants systematically reject unfair offers below the 20-30% of the total pot (Nowak, 2000; Camerer, 2003), preferring to gain nothing rather than accept unequal distribution of resources (Fehr and Camerer, 2007).

In a public goods game (PGG) (Ledyard, 1995), players have a token endowment which they can simultaneously invest in any proportion to a private project or a public project. Investment into the public project maximizes the aggregate earnings of the group, but each individual can gain more from investing into the private rather than the public project. In the PGG typically, players begin by investing half their tokens on average (many invest either all or none) (Fishbacher et al., 2001), but when the game is repeated over time, with feedback at the end of each decision period, investments decline until only a small fraction (about 10%) of the players invest anything (Spitzer et al., 2007).

The prisoner's dilemma (PD) game is a special case of a public goods game, with two players and only two actions (cooperate or defect) for each player. When players are also allowed to punish other players at a cost to themselves, many players who invested punish the players who did not invest, which encourages investment and leads players closer to the efficient solution in which everyone invests the whole endowment (Fehr and Gächter, 2002).

Contrasting canonical economic models which posit that material self-interest is the sole motivational force guiding human behaviour, a newborn discipline known as social neuroeconomics used these games as tools to investigate the motivational forces driving the deviation from self-interests, providing evidences in favor of the notion that people generally prefer to behave prosocially because they derive higher hedonic value from the mutual cooperation outcome (Fehr 2008; Thibaut and Kelley 1959).

Several fMRI studies, addressed the hypothesis that pro-social preferences are similar to preferences to other kinds of primary (e.g. food) and secondary (e.g.

money) types of rewards (Cromwell and Shultz 2003). In following with this interpretation, it is widely held that the brain uses a common-reward metric for the processing of both individual and social rewards (Sanfey et al., 2007). In fact, there is evidence that fairness-directed conducts, such as mutual cooperation with a human partner is associated with higher striatal activity as compared to mutual cooperation with a computer partner (Rilling et al., 2002). Likewise, an increased activation of the ventral tegmental and striatal areas were found both when receiving money and in non-costly charitable donations (Moll et al., 2006, Harbaugh et al., 2007). Social preference theories not only suggest that direct cooperation is rewarding, but also imply that people derive satisfaction from implementing justice and maintaining fairness by punishing unfair partners. A positron-emission tomography (PET) study addressed this issue by presenting participants with a version of the PD game with two different punishment opportunities. In one case punishment led to a reduction in the partner's payoff (real punishment condition); in the other case, punishment took place without affecting partner's economic payoff (symbolic condition). Results showed that the dorsal striatum was more activated in the real compared to the symbolic condition (de Quervain et al., 2004). Moreover, Singer and colleagues (2006), studied empathy towards a confederate who had previously played fairly or unfairly with the participant. In this study, participants played a prisoner dilemma game with a fair and an unfair proposer. Later, while in the MRI scanner, participants watched as each partner appeared to receive painful stimuli. While viewing fair partners who appeared to be in pain, men and women both exhibited increased activity in insular and anterior cingulate regions, suggesting an empathic response for pain. This finding suggests that people like and are sympathetic towards those who have previously treated them fairly. Interestingly, authors also found that when men (but not women) watched unfair proposers receiving pain, they showed an increased activity in reward regions, such as the ventral striatum. These latter results provide evidence that the establishment of justice, through punishment of unfair behaviour, may elicit positive feelings. Thus, in the context of economic games, people experience a conflict between two types of reward (namely self and social reward). Using the UG (in which fairness motives are in conflict with economic self-interest), Sanfey et al. (2003) revealed the presence of a neuronal circuitry comprising the dorsolateral prefrontal cortex (DLPFC), the bilateral anterior insula (AI) and the anterior cingulate cortex (ACC) in the contrast between fair and unfair offers (Figure 1.1). Notably, AI activity was significantly greater in response to unfair offers that were later rejected, suggesting an higher amount of negative emotions in response to unfair offers.

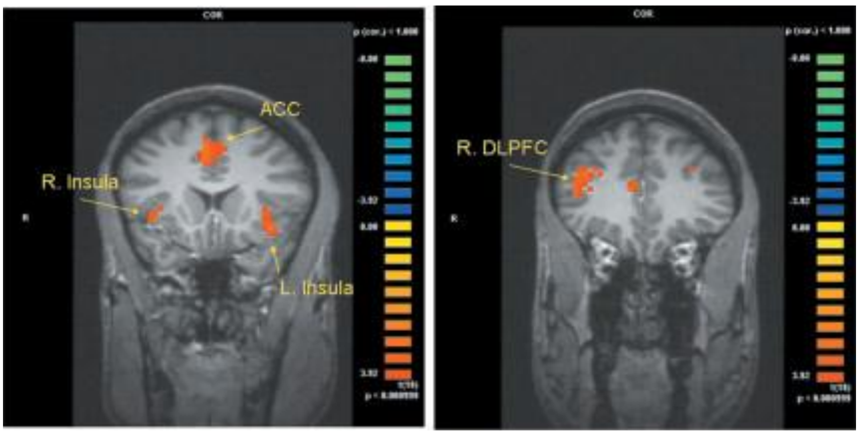

Figure 1.1 Activation related to the presentation of an unfair offer. (**A**) Map of the *t* statistic for the contrast [unfair human offer – fair human offer] showing activation of bilateral anterior insula and

anterior cingulate cortex. Areas in orange showed greater activation following unfair as compared with fair offers (*P* = 0.001). Adapted from Sanfey et al., 2003.

The activation of ACC could reflect its implication in conflict monitoring (Botvinick et al., 2001), while authors interpreted DLPFC activation as an index of cognitive control of the emotional impulse to reject unfair offers. In contrast with this latter interpretation, Knoch and colleagues (2006) found that the disruption of the right, but not the left, DLPFC by low frequency repetitive transcranial magnetic stimulation (TMS) substantially reduced subjects' willingness to reject their partners' unfair offers, which suggests that subjects are less able to resist the economic temptation to accept these offers (i.e the activation seems to represent the cognitive control of the emotional impulse that pushes subjects towards accepting unfair offers). If on the one hand DLPFC is more active when participants deal with unfair offers, on the other hand ventromedial prefrontal cortex (VMPFC) was found to be more activated (when compared to a resting baseline) during the acceptance of unfair offers, possibly reflecting the down-regulation of negative emotions associated to unfair offers (Tabibnia et al., 2008).

1.2 The role of emotions during the Ultimatum Game

Converging evidence on the role played by emotions in the UG come from a study (Wan't Wout et al., 2006) in which 30 healthy undergraduate students played as recipients while their skin conductance responses were measured as an autonomic index of affective state. The results revealed that skin conductance activity was higher for unfair offers and was associated with the rejection of unfair offers.

Interestingly, this pattern was only observed for offers proposed by humans, but not for offers generated by computers. In addition, several behavioural studies demonstrated that incidental negative emotions such as anger (Andrade and Arieli 2009) and sadness (Harlé and Sanfey, 2007) enhanced the rejection rate of unfair offers during the UG. Neuroimaging analyses additionally revealed that receiving unfair offers while in a sad mood (compared to a neutral one) elicited activity in brain areas related to aversive emotional states and somatosensory integration (AI) and to cognitive conflict (ACC) (Harlé et al., 2012). Furthermore, an elegant behavioural study by Moretti and di Pellegrino (2010) showed that induced disgust, as compared to sadness and neutral emotion, specifically enhanced responders' decisions to reject unfair proposals. Importantly, when the partner was not responsible for the fairness violation, such as in a computer-offer condition, the disgust induction failed to affect participants' choices. Given that the AI, plays a role both in signaling disgusting stimuli, and in marking a social interaction as aversive or, more specifically, providing a neural signature for the likelihood of punishing an unfair action at the responder's expense (Montague and Lohrenz, 2007), authors suggested that the conjunction of physical and sociomoral disgust, due to shared representation, results in synergistic effects on fairness related decisions.

1.3 The neural basis of pain

According to current views, pain experience results from a three-dimensional integration of sensory-discriminative (e.g. evaluation of locus, duration and intensity of a noxious stimulus), affective-motivational (e.g. unpleasantness of the noxious stimulus) and cognitive-evaluative (e.g., catastrophizing, context appraisal) axes (Melzack and Casey, 1968; Melzack and Katz, 1994). The sensory-discriminative component subserves the ability to analyze location, intensity and duration of the stimulus, while the affective-emotional component gives rise to the unpleasant character of pain perception. The cognitive axis is involved in attention, anticipation and memory of past experiences (Guilbaud et al., 1994). In addition, the cognitive dimension is able to interact with the other two; for instance, both the intensity and the unpleasantness attributed to a painful stimulus are strongly modulated by the attention allotted to it (Miron et al., 1989).

The most reliable pain-related activity across previous studies is bilateral, and has been located in a broad region comprising the depth of the Sylvian fissure and the parietal and frontal operculi, and therefore extending from the anterior insula to the second somatic (SII) area (primarily contralateral to stimulation but also ipsilateral) and associative parietal cortex (for a review see Peyron, 2000).

Although these regions may be involved in general somatosensory integration (Baron et al., 1999; Craig, 2009; Faurion et al., 1999) in the context of thermal stimuli, their activity dramatically increases when intensity reaches painful ranges (Peyron, 2000). Thus, in the context of thermal pain processing, both the anterior insular and the retro-insular/SII cortices appear functionally implicated in the discrimination of stimulus intensity. However, hemodynamic brain response to pain is modulated by both cognitive (Bushnell et al., 1999) and attentional factors (Peyron et al. 1999). In particular, the *attentional network* disclosed by Peyron and collaborators using fMRI, could be subdivided into a non-specific *arousal* component, involving thalamic and upper brainstem regions, and a *selective attention* and orientating component including prefrontal, posterior parietal and cingulate cortices. In addition, neuroimaging studies have shown that the activity of the dorsal anterior cingulate cortex (dACC) tracks the affective component of pain experience. Subjects who were hypnotized so as to selectively increase the unpleasantness of noxious stimuli (affective component) without altering the intensity (sensory component) showed increased activity in the dACC without changing activity in primary somatosensory cortex (Rainville et al., 1997). Likewise, self-reports of pain unpleasantness correlate specifically with dACC activity (Peyron et al., 2000; Ploghaus et al. 1999; Saewamoto et al., 2000) and those participants with greater pain sensitivity show greater responses to painful stimuli (Coghill et al., 2003).

1.4 The neural basis of interoception

The ability to detect subtle changes in bodily systems, including muscles, skin, joints, and viscera, is referred to as *interoception* (Dunn et al., 2010). Growing evidence suggests that a first order representation of self is proposed within brainstem autoregulatory centers, primary and secondary somatosensory cortices and insula (Critchley et al. 2001; Damasio, 1999). Second-order ‘meta’ representations are proposed to be supported within ventromedial prefrontal and cingulate cortices.

Indeed, empirical evidence implicates anterior cingulate in second order remapping of autonomic responses (Critchley et al. 2001). In particular, it is argued on the basis of neuroanatomical studies (Craig, 2003,) that the Lamina 1 spinothalamocortical pathway is especially dedicated to conveying interoceptive information, converging within the diencephalon with afferent information carried by cranial nerves, including the vagus nerve. This stream of interoceptive information then projects to viscerosensory cortex in mid-insula (Cechetto and Saper, 1987) and onto right anterior insula and orbitofrontal cortices. This neuroanatomical arrangement has been proposed to be evolutionarily specialized in primates, bypassing an obligatory pontine (parabrachial) relay to enable cortical representation of motivationally important visceral and somatosensory information. The map of visceral sensations of autonomic responses is further enriched by other salient sensations including metaboreception, pain, itch, temperature, and sensual touch whereas, parallel specialization of human dorsal cingulate cortex is proposed for expression of motivational drives (Craig, 2003, 2009).

Moreover, it has been argued that representation of the homeostatic condition of the body in the insula and related regions crucially influences cognitive-affective processing (Craig, 2009; Critchley, 2005). Consistently, Critchley et al. (2004), performed functional magnetic resonance imaging (fMRI) during an interoceptive task wherein subjects judged the timing of their own heartbeats. Authors observed enhanced activity in insula, somatomotor and cingulate cortices. Importantly, the right anterior insular/opercular cortex neural activity predicted subjects' accuracy in the heartbeat detection task. Furthermore, local gray matter volume in the same region correlated with both interoceptive accuracy and subjective ratings of visceral awareness. Indices of negative emotional experience correlated with interoceptive accuracy across subjects. These findings support the view that insula is implicated in emotion experience and decision making (e.g., Damasio et al., 2000; Mohr, Biele, and Heekeren, 2010).

1.5 Money, pain and belongingness: behavioural and neural correlates

A growing number of behavioural and neuroscientific studies collected evidences in favor of the notion that money, physical pain and social pain are interrelated (Zhou and Gao, 2008; Baumaister et al., 2008; DeWall and Baumaister 2006, Dewall et al., 2010; MacDonald and Leary, 2005; Rick, Cryder, and Loewenstein, 2008). At the behavioural level, a series of studies tested the hypothesis about a specific relationship among reminders of money, social exclusion, and physical pain (Zhou et al., 2009). In these studies it has been showed that interpersonal rejection and physical pain caused desire for money to increase, while, handling money (compared with handling paper) reduced distress over social exclusion and diminished the physical pain of immersion in hot water. Finally, being reminded of having spent money , intensified both social distress and physical pain (Zhou et al., 2009). Recently we argued that the personal experience of pain changed the balance between self-gain and socially based choices, favoring the emergence of a self-centered perspective aimed at maximizing self-gain during a bilateral version of the UG (Mancini et al. 2011).

Functional MRI (fMRI) studies have shown that the bases of anticipatory monetary loss are similar to those of physical pain (Knutson et al., 2007). Anticipation of a potential monetary loss leads to activation in the insula (Knutson et al., 2001; Paulus and Stein, 2006; Kuhnen et al., 2005), another region associated with anticipation of pain besides ACC (Rainville et al., 2002).

Accumulating evidences suggest that social pain (i.e. social exclusion) and physical pain share the same physiological mechanisms (Mac Donald and Leary 2005; Panskepp et al. 1978). An interesting view by Panksepp (1998) proposed that the evolution prepared animals for increasing social interaction, by adapting existing systems to social events instead of creating entirely new systems to react to social events such as rejection or exclusion. Hence, the pleasure and pain systems became attuned to issues such as social acceptance and rejection.

Striking evidence for this theory comes from a study by Eisenberger, Lieberman, and Williams (2003), who showed that social rejection (ostracism) produced brain responses that resembled responses to physical pain. Being excluded in a ball-tossing game was related to increased activity in several areas also implicated in the affective side of pain processing such as dorsal ACC and insula. This increase was also related to a higher distress, reported after the rejection episode (Eisenberg et al 2003). Recent findings substantively extended these views by demonstrating that social rejection and physical pain are similar not only in that they are both distressing, but they share a common representation in somatosensory brain systems as well. Specifically, areas activated during a pain task dACC, AI but also thalamus and right parietal opercular/insular cortex- SII were overlapping with areas activated during the rejection task (viewing picture of ex-partner vs. loving mother) (Kross et al., 2011). In addition, acetaminophen (Paracetamol) a physical pain suppressant that acts through central (rather than peripheral) neural mechanisms, reduces behavioural and neural responses to social rejection (DeWall et al., 2010).

An important review by MacDonald and Leary (2005) also found support for the link between social and physical pain, showing that social exclusion produced analgesic effects akin to the temporary numbing of physical pain that accompanies a bodily injury. Importantly, a behavioural study by DeWall and Baumaister (2006), investigated the effects of social rejection on the perception of a concurrent painful stimulation. Results revealed that a context of social exclusion caused a broad decrease in pain sensitivity related to the degree of emotional numbness that socially excluded people exhibited. Authors explained this phenomenon hypothesizing that exclusion may produce a biochemical reaction that leads to temporary numbness to physical pain. This physical numbness is also linked to emotional responding, which is demonstrated in the emotional insensitivity presented by the excluded participants (DeWall and Baumeister, 2006).

1.6 Laser Evoked Potentials (LEPs)

Laser stimuli are a source of radiant heat, which can be used to specifically activate Aδ and C nociceptors in the most superficial skin layers without concomitantly activating low-threshold mechano-receptors (Plaghki and Moraux, 2005). Such stimuli elicit a number of transient brain responses (laser-evoked potentials LEPs) in the electroencephalogram (EEG) (Carmon et al., 1976) (Figure 1.2).

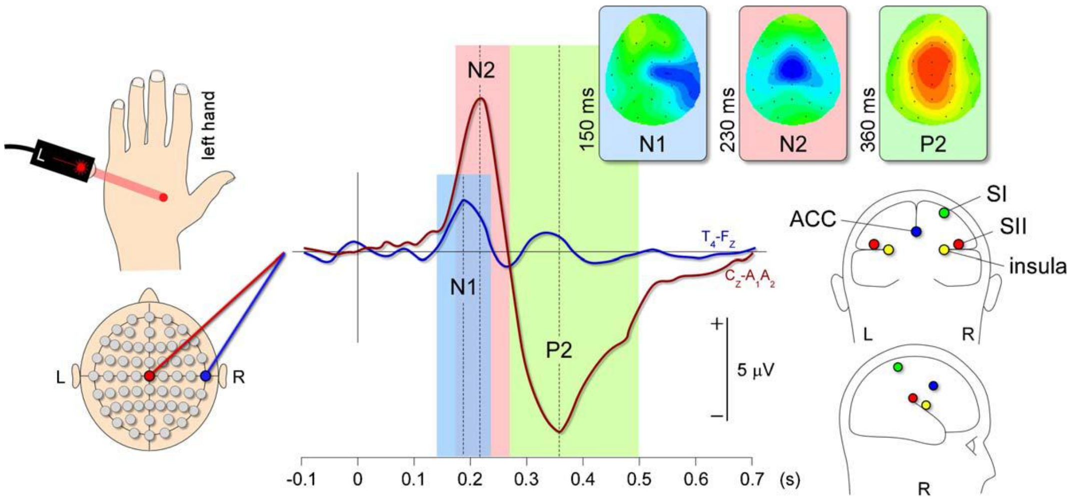

Figure 1.2. The figure illustrates nociceptive ERPs recorded at the scalp vertex electrode (red waveform) and at the contralateral temporoparietal electrode (blue waveform) and evoked by brief nociceptive laser heat stimuli directed to the left hand dorsum. The three successive ERP components are shown in their respective time windows outlined by colored boxes: N1 (blue box), N2 (pink box), and P2 (green box). The time t = 0 corresponds to the onset of the laser stimulus. The upper right part of the figure represents the scalp distribution maps (top view) of nociceptive ERP magnitude at the latency of the N1, N2 and P2 waves respectively. The lower right part of the figure illustrates the localization of the different sources contributing to ERPs obtained from dipole modeling studies and confirmed by direct subdural or deep intracortical recordings (see Garcıa-Larrea et al., 2003). Most of these studies have located sources in the secondary somatosensory (SII) and insular cortex bilaterally, as well in the anterior cingulate cortex (ACC). A smaller number of studies, most of them relying on MEG, have located an additional source in the contralateral primary somatosensory cortex (SI) (Kakigi et al., 2005). Adapted from Legrain et al., 2011.

The most conspicuous response to laser stimulation is a negative–positive biphasic deflection, labeled N2/P2 or N220–P350, recorded over the midline of the scalp. N2 and P2 respectively peak, at about 200–250 and 350–400 ms after hand stimulation, with a maximal amplitude at the vertex (Kunde and Treede, 1993; Miyazaki et al., 1994; Spiegel et al., 1996). Source localization studies suggest that dipoles located in the bilateral parasylvian areas (SII, insula) and the anterior cingulate gyrus (ACG) could explain N2, while P2 would be mainly explained by an ACG dipole (Tarkka and Treede, 1993; Bromm and Chen, 1995; Valeriani et al., 1996).

Moreover, the laser-evoked P2 component can be functionally differentiated in two sub-components (the P2a and P2b waves) that are susceptible to ‘bottom-up’ attentional capture by novel/deviant nociceptive stimuli (Legrain et al., 2009). Importantly, the latency of ACC and MCC activation is compatible with the time window of the laser-evoked P2a, while the parietal topography reflected by the P2b wave may be associated to a major involvement of the PPC (Garcia-Larrea, 2003; Legrain et al., 2009). A cortical response to laser stimuli culminating earlier than the ‘classical’ vertex potential was described by topographic studies (Kunde and Treede, 1993). This response is labeled N1 and it culminates at 160-170 ms, is highly lateralized and has a dipolar distribution on the scalp. There is large agreement that the N1/P1 is generated in the suprasylvian region corresponding to the secondary somatosensory area (SII) contralateral to the stimulated side (Frot et al., 1999; Garcia-Larrea et al., 2003; Vogel et al., 2003). Although a positive relationship between the intensity of laser stimuli, the magnitude of pain sensation and the amplitude of the vertex response has been repeatedly described (Bromm and Treede, 1991; Arendt-Nielsen, 1994), several authors have argued that vertex responses to laser might reflect the attentional, motivational and orienting reactions driven by the stimulus (Lorenz and Garcia-Larrea, 2003; Van Damme et al., 2010; Legrain et al. 2011). On the basis of recent studies these authors argued that i) pain intensity can be dissociated from the magnitude of responses in the cortical correlates of pain, and that (ii) these responses are strongly influenced by the context within which the nociceptive stimuli appear. Indeed, pain perception can be influenced by a number of purely cognitive manipulations such as attentional focusing (Bantick et al., 2002), pain expectation and anticipation (Ploghaus et al., 1999; Porro et al., 2002), and hypnotic suggestion (Valentini et al., 2012). Specifically, cognitive engagement to a focal task goal reduces attentional captures by pain, resulting in a dampening of pain associated with modifications of nociceptive processing in the brain (Bushnell et al. 1985; Seminowicz and Davis 2007; Legrain 2008; Van Damme 2010). However, we are not aware of studies that systematically examined the effect of a social manipulation of the context in which the focal task is performed on the amplitude of the LEPs component.

1.7 The Ultimatum Game

In studies one and two we employed the following modified version of the UG. Modifications to this general procedure are reported in the section dedicated to each study.

Participants were required to play both in the role of proposer and of recipient in a modified version of the *one-shot* Ultimatum Game (UG). Before starting the game, they were told they could see the faces of other participants, located at other two remote Italian Universities, by means of an online network. As in the classical version of the UG (Güth et al., 1982) the proposer's role was to decide how to split an amount of money (here always corresponding to 1 euro), while the recipient's role was to decide whether to accept or reject the proposed allocation. If the recipient rejects an offer, both players would receive nothing, while if he accepts it each player would keep the allocated amount. To rule out the possibility of any negotiation between participants, subjects were ensured that for each match they would be randomly paired with an anonymous partner. Unknown to the participants, the game took place against a PC device, which was programmed using E-Prime software 1.2.

Chapter 2

"Suffering Makes You Egoist: Acute Pain Increases Acceptance Rates and Reduces Fairness during a Bilateral Ultimatum Game"

2.1 Aims and Hypothesis

In this study, we investigate whether the personal experience of pain modulates the economic behaviour of participants playing a bilateral version of the UG. Although pain has been considered as an inherently private experience, recent neuroscientific evidences indicates that the first-hand experience of pain makes individuals more prone to react to the pain of others according to egocentric rather than to other-oriented stances, adopting a less empathic attitude (Valeriani et al. 2008). We employed a bilateral version of the ultimatum game where participants alternatively acted as proposer or responder while receiving on the dorsum of the left hand, laser stimuli that could induce acute pain (Pain condition) or a warm sensation (Heat condition). The procedure allowed us to explore whether being in pain specifically affects the decision of a given individual to accept a given amount of money when playing in the role of responder and the way in which he/she divides a sum of money when playing in the role of proposer. Finding higher acceptance rates of unfair offers and lower offers in the pain with respect to heat condition would support the notion that pain perception may induce a self-centered bias that ultimately inhibit the tendency to implement socially oriented behaviours like altruistic punishment.

2.2 Materials and Methods

Participants

Thirty healthy right-handed subjects (14 female; age range: 18 to 36 years (M = 23.93, SD = 4.56) recruited via an opportunity sample, participated in the study. Subjects were paid a fixed amount of 15 Euros. In addition, they were informed they would effectively receive the money earned during the economic game.

Participants gave their written consent and were naïve as to the purposes of the study. The experimental protocol was approved by the local Ethics Committee at the Fondazione Santa Lucia and the study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

The Ultimatum Game

For the UG version used in this study please refer to paragraph 1.7.

Laser stimulation

Laser stimulation was delivered with an infrared neodymium yttrium aluminium perovskite laser (EL.EN. Group) to the dorsum of the left hand. The laser stimulation allowed us to induce acute painful and warm sensation on the body part selectively stimulated by the laser beam without the concurrent experience of touch. We determined the individual heat and pain threshold according to the method of limits (Yarinsky et al., 1995). The threshold values corresponded to the lowest painful or warm sensation that can be reliably detected in 5 out of 10 trials and were determined before each experimental condition. Moreover, pain and heat thresholds were determined at the beginning of each block. The fluency of the stimuli used in the Pain and Heat Condition was 30% over the painful and warm threshold values; both in the responder (Pain = 14.8 J/cm^2, ±4.0; Heat = 8.7 cm^2 ± 2.9), and in the proposer (Pain = 15.1 cm^2, ±3.6; Heat = 9.2 cm^2± 2.1) role.

Laser pulses were delivered in blocks of 10 trials. To avoid nociceptors fatigue or sensitization, the location of the laser on the skin was slightly shifted after each stimulus. An area of about 8 cm^2 on the radial side of the hand dorsum was stimulated. Moreover, a 5-7 seconds interstimulus interval (ISI) allowed us to minimize central habituation effects. The distance between the laser stimulator and the hand was kept constant (and was about 2 cm).

Experimental Procedure

Subjects were seated in a comfortable armchair and were asked to relax their muscles but to stay alert. In order to avoid that they could explicitly realize we wanted to measure the influence of pain on their social preferences, participants were told that the aim of the study was to assess their subjective pain threshold while they were committed in a distracting game (the UG). Figure 1 schematically represents the procedure. Each subject was preliminarily introduced to the internet-based platform in order to familiarize with the procedure and to visualize the faces of the confederates.

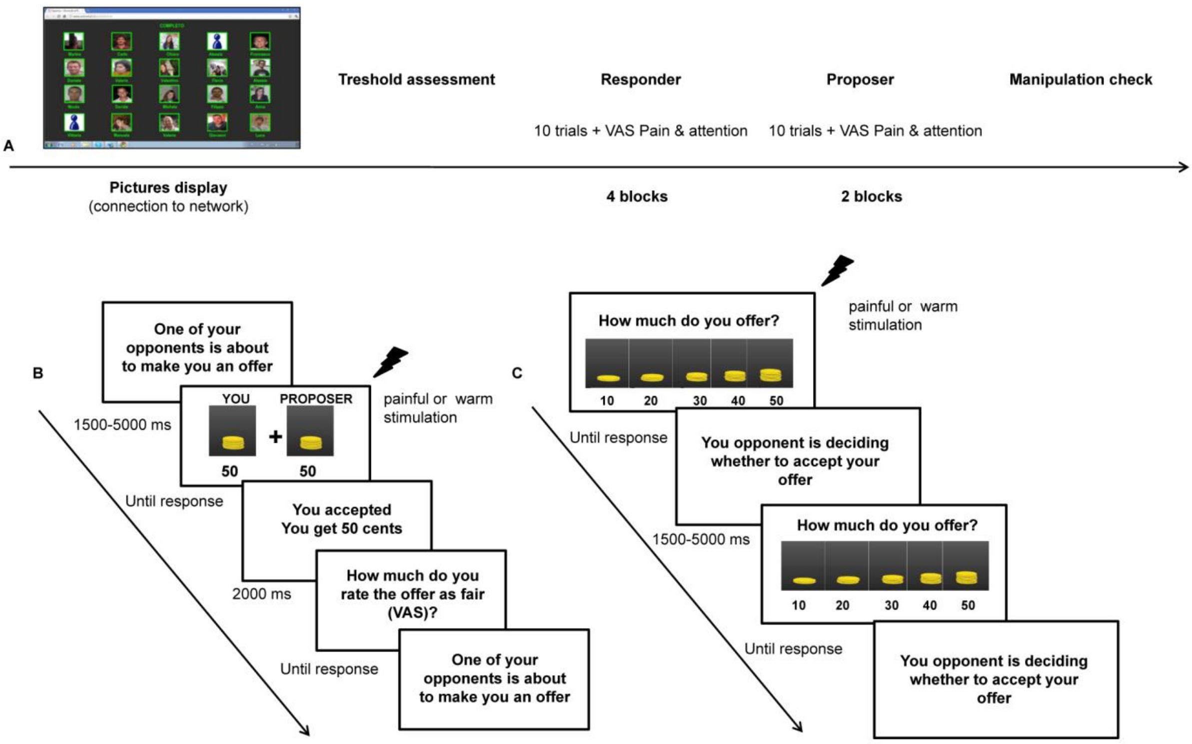

Figure 2.1. Bilateral Ultimatum Game procedure.

Panel A schematically represents the entire procedure. Subjects were introduced to the internet-based platform which displayed the pictures of the confederates. After the determination of the laser threshold, participants played first as responders (four blocks of 10 trials each) and then as proposers (two blocks of 10 trials each). Finally, they were presented with a manipulation check. Panel B: represents the sequence a typical event trial of the responder's blocks. After a variable interval, subjects received the offer contemporaneously to a painful or warm laser stimulation. They could accept or reject the offer by means of a button press. Subsequently, a feedback informed participants how much they received and they could rate the fairness of the offer on a VAS scale ranging from 0 (unfair) to 100 (fair). Panel C represents the sequence of events in a trial of the proposer's blocks. Participants had to decide how to split money (1€), selecting the corresponding offer by clicking with the cursor on the image displayed on the screen. No feedback was provided in order to avoid that the responders' choice influences the subsequent offer.

After the determination of the laser pain and heat thresholds, specific instructions prompted subjects to play the responder or the proposer role (Figure 2.1 A). In the *responder* blocks, subjects were asked to accept of refuse the offer of other confederates, as follows (translated from Italian): “The computer randomly assigned you the role of responder. You may accept or reject the offers that come from your opponents. If you accept, the money will be divided according to the offer, if you reject neither of you will receive nothing". In the *proposer* blocks subjects were instructed to decide how to divide the sum of money, as follows (translated from Italian): "The computer randomly assigned you to the role of proposer. You may decide how to allocate the money. If your opponent accepts the offer, the money will be divided accordingly, if he/she rejects the offer, no money will be given to any of you". In the *responder* blocks subjects accepted or rejected the offer by pressing a button (left to accept, right to reject) with their right hand. At the end of each interaction, a feedback lasting 4 seconds informed participants about how much each player received (for example, "you get € 30 cents" or "you get € 0" if the offer was accepted or rejected, respectively) (Figure 2.1 B).

In the *proposer* blocks, participants had to decide how to split money by clicking on one of five possible offers displayed on the screen (Figure 2.1 C). In these blocks no feedback was provided to avoid any effect of the outcome on the subsequent offer.

Overall, each subject was tested in six experimental blocks. In the first four blocks, participants were assigned to the responder role (*responder* blocks), while in the remaining two blocks they played as proposers (*proposer* blocks). For each subject, the *responder* block was repeated twice, one for Pain and one for Heat Condition. This procedure ensured an adequate amount of iterations. On each block, participants completed 10 trials, for an overall amount of 60 iterations in the whole experiment. The experiment lasted 1 hour. Laser pulses were delivered at the onset of each trial. The order of Heat andPain Condition was counterbalanced across subjects.

Both in the *responder* and in the *proposer* blocks, possible offers ranged from 50 cents to 10 cents, as follows: 50 cents (Fair, *F*), 40 cents (Moderately Fair, *MF*), 30 cents (Moderately Unfair, *MU*), 20 (Unfair, *U*) and 10 cents (Extremely Unfair, EU). Each responder block included 10 offers according to the following: 3 x50 cents, 2 x40 cents,3 x30 cents, 1 x20 cents and 1x10 cents. *Fair* offers were restricted to 50 cents assuming that confederates would not offer more than half of the amount. U and EU offers were limited since are routinely rejected (Camerer, 2003). At the end of the experiment subjects were debriefed about the purpose of the study.

Subjective ratings of offers' fairness and laser stimuli

After each trial, participants were asked to assess the fairness of each offer on a Visual Analogue Scale (VAS) ranging from 0 (unfair) to 100 (fair). The question (translated from Italian) was the following: "on a scale of 0 to 100, where 0 corresponds to unfair and 100 to fair, how would you rate the offer you have just received?". Furthermore, at the end of each block participants were asked to rate the intensity and the unpleasantness of the laser stimulation, along a VAS where 0 corresponded to no pain (intensity or unpleasantness) and 100 the maximum pain that can be imagined. Finally, subjects were instructed to maintain attention to the stimuli and to monitor the interaction. This allowed to check for unwanted fluctuations of attention in the different blocks. Moreover, participants evaluated the attention they addressed to the task and to the stimulation, to assess whether they varied across blocks

Manipulation check

Immediately after the experiment, participants completed a four-items questionnaire investigating their feelings about the experimental task. In particular, they were asked the following questions (translated from Italian): 1) how much did you use a pre-defined strategy during the UG (e.g. you decided a-priori to accept any offer above 30 cents), 2) how much did you feel angry at your opponents, 3) how much did you feel prone to accept,4) did you feel involved in the interaction with your opponents even if you could not see their faces? For item 1 to 3, evaluations along a 5-point Likert scale (ranging from -2 to +2) were required. Separate questions for the Painand Heat conditions were asked. For item 4 a mere “yes” or “no” response was contemplated. Six subjects who declared the lack of involvement in the interaction with the other players or spontaneously expressed scepticism about the real existence of the confederates were excluded from the analysis.

2.3. Results

Data handling

Data analysis was performed on 24 subjects (12 females; age range 18-36 M=23.92, SD=4.75). In the *responder* blocks, we obtained the acceptance rate (%)

for each subject dividing the frequency of the accepted offers for Fair (or Unfair) by the total of number of Fair (or Unfair) items. In the *proposer* blocks, we computed the offer rate (in %) for each subject. In details, the frequency of each offer type (10, 20, 30, 40, 50 cents) was expressed as percentage of the total number of items within each block. Due to unexpected interruption of the experiment caused by technical problems, two subjects could not finish the proposer trials and were excluded from the analysis performed on offer rate.

In the responder blocks, acceptance rates of 40 and 50 offers and of 30, 20 and 10 offers were collapsed in Fair and Unfair categories respectively. This procedure allowed us to compare the same number of trials for each category.

Values of acceptance rate (%) were analyzed by means of a 2X2 repeated-measures ANOVA with Condition (two levels: Pain and Heat) and Fairness of Offer (two levels: *Fair and Unfair*) as main factors. The same analysis was performed on VAS ratings of Fairness and reaction times (RTs).

In the *proposer* blocks a 2X5 repeated-measures ANOVA was performed on offer rate (%) values with Condition (two levels: Pain and Heat) and Fairness of Offer (five levels: *10, 20, 30, 40, 50 cents*) as main factors. A dependent sample t-testwas performed to check for any difference in the RTs of the two conditions. Moreover, we performed standard multiple regression models on subjective ratings of intensity and unpleasantness of the painful laser stimulation (as independent variables) and the acceptance rate of each offer in the responder block and the frequency of each type of offer in the proposer block (as dependent variables). Finally, we performed four separate 2X2 repeated-measures ANOVAs on i) Intensity and ii) Unpleasantness of laser stimulation, iii) attention to stimulation and iv) attention to the task, with Role (two levels, *responder* and *proposer*) and Condition (PainandHeat) as main factors. *Post-hoc* comparisons were performed by means of Newman-Keuls test.

Acceptance rates in the responder blocks

In the *responder* blocks, participants modulated their acceptance rate as a function of Condition as explained by the significance of the main effect ($F_{1,23}=7.20$, $p = 0.013$, $\eta^2_p = 0.23$). Results showed a higher acceptance rate during Pain with respect to Heat (Figure 2.2 A). As expected, the acceptance rate was also higher for *Fair* with respect to *Unfair* offers, as revealed by the significance of the main effect ($F_{1,23}=170.40$, $p<0.000$, $\eta^2_p= 0.88$).

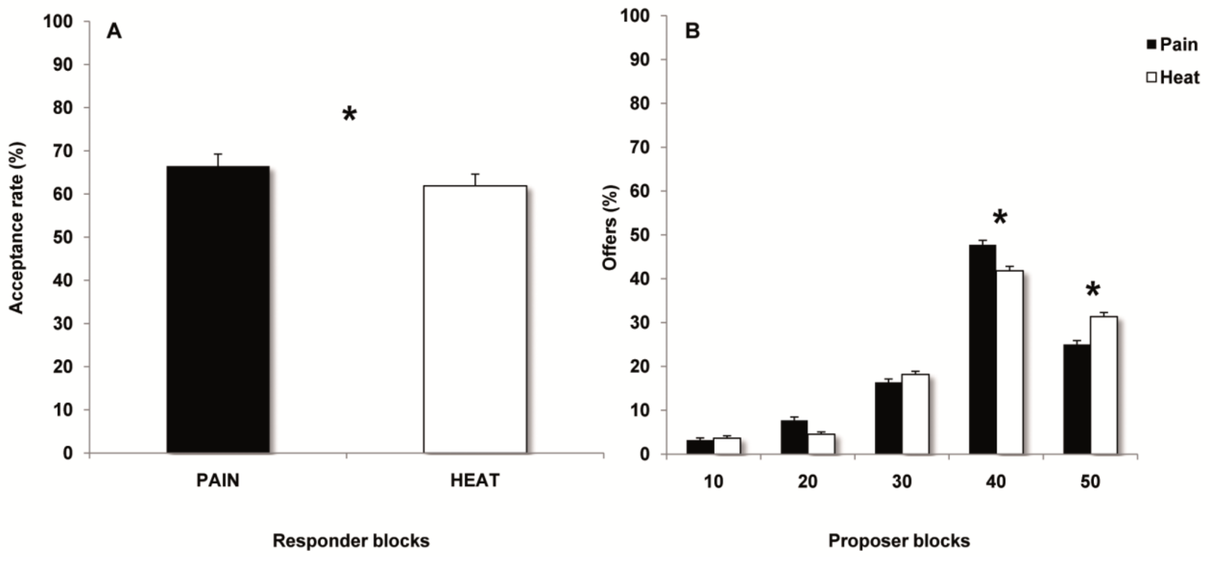

Figure 2.2 Pain induces self-regarding preferences.

Panel A shows the higher acceptance rate observed in the Pain with respect to Heat condition in the responder's blocks. Panel B shows the significant interaction Fairness of Offer × Condition, accounted for by a higher rate of Moderately Fair offers (40 cents) in Pain with respect to Heat Condition and a lower rate of Fair offers (50 cents) in Pain with respect to Heat Condition in the proposer's blocks.

The interaction Condition x Offer was not significant ($F_{1,23}=0.42$, $p=0.52$). Since acceptance of fair offers is usually at ceiling in the UG, this lack of significance may depend on the way in which data were collapsed. Thus, we run an additional ANOVA considering four levels of Fairness of Offer, namely: Fair (50 cents), Moderately Fair (40 cents), Moderately Unfair (30 cents) and Unfair (10-20 cents) as main factors. The results were identical to those obtained running a 2X 2 ANOVA. Indeed, we found significant main effects of Condition ($F_{1,23}=5.35$, $p =.03$, η^2_p = *.19*), and of Fairness of Offer ($F_{3,69}=109.63$, $p<.0000$, η^2_p = *.83*) but no significant Condition x Offer interaction ($F_{3,69}=1.\ 48$, $p=0.23$, *NS*). Importantly, Newman-Keuls*post-hoc* comparisons revealed that participants accepted Fair and Moderately Fair offers at a similar rate ($p= .45$, *NS*) (acceptance rates raw data % are reported in Table1).

	Acceptance Rate Pain (%)				Acceptance Rate Heat (%)			
Subjects	**Unfair**	**Moderately Unfair**	**Moderately Fair**	**Fair**	**Unfair**	**Moderately Unfair**	**Moderately Fair**	**Fair**
1	0	83,33	100	100	0	66,7	100	100
2	0	100	100	100	0	100	100	100
3	0	100	100	100	0	100	100	100
4	25	50	100	100	0	34	100	100
5	0	0	100	100	25	0	75	100
6	0	100	100	100	0	50	100	100
7	0	16,6	100	100	0	33,3	100	100
8	0	50	100	100	25	33,4	100	100
9	0	16,67	75	100	0	0	100	100
10	0	0	100	100	0	0	100	100
11	25	16,67	100	100	25	0	100	100
12	0	66,67	100	100	0	0	75	100
13	25	100	100	100	0	83,34	75	100
14	50	100	100	100	75	100	100	83,34
15	0	100	100	100	0	100	100	100
16	25	83,34	100	100	75	83,34	100	100
17	25	33,34	100	100	0	16,67	75	100
18	0	66,67	75	83,34	25	0	50	100
19	25	0	100	100	0	16,67	100	100
20	25	100	100	100	0	100	100	100
21	0	33,34	100	100	0	50	75	100
22	0	0	100	100	0	0	75	100
23	0	0	100	100	0	16,67	100	83,34
24	0	16,67	75	100	0	33,4	100	83,34
MEAN	**9,37**	**51,39**	**96,9**	**99,3**	**10,41**	**42,39**	**91,66**	**97,91**
SD	**14,39**	**40,5**	**8,44**	**3,4**	**22,01**	**39,3**	**14,11**	**5,63**
SE	**0,16**	**0,26**	**0,12**	**0,07**	**0,19**	**0,26**	**0,15**	**0,09**

The table reports the acceptance rate (%) of Unfair (10–20 cents), Moderately Unfair (30 cents), Moderately Fair (40 cents) and Fair (50 cents) offers presented by each participant in the Pain (left column) and in the Heat (right column) condition.
doi:10.1371/journal.pone.0026008.t001

Table 1. Acceptance rate raw data (%)

Fairness scores.

ANOVA performed on Fairness scores revealed higher scores for *Fair o*ffers with respect to *Unfair* offers, as shown by the main effect of Fairness of Offer ($F_{1,23}$= *129.12, p < 0.000,* η^2_p *=0.85*). Importantly, fairness scores were lower in Pain with respect to Heat condition, as indicated by the main effect of Condition ($F_{1,23}$= *39.98 p < 0.000* η^2_p*=0.63*). Crucially, we found a significant interaction Condition x Fairness of Offer ($F_{1,23}$= *6.99 p=0.014* η^2_p*=0.23*) which was entirely accounted for by lower

VAS scores for Unfair offers during Pain with respect to the Heat condition (*p<0.001*, Newman Keuls*post-hoc*) (Figure 2.3 A).

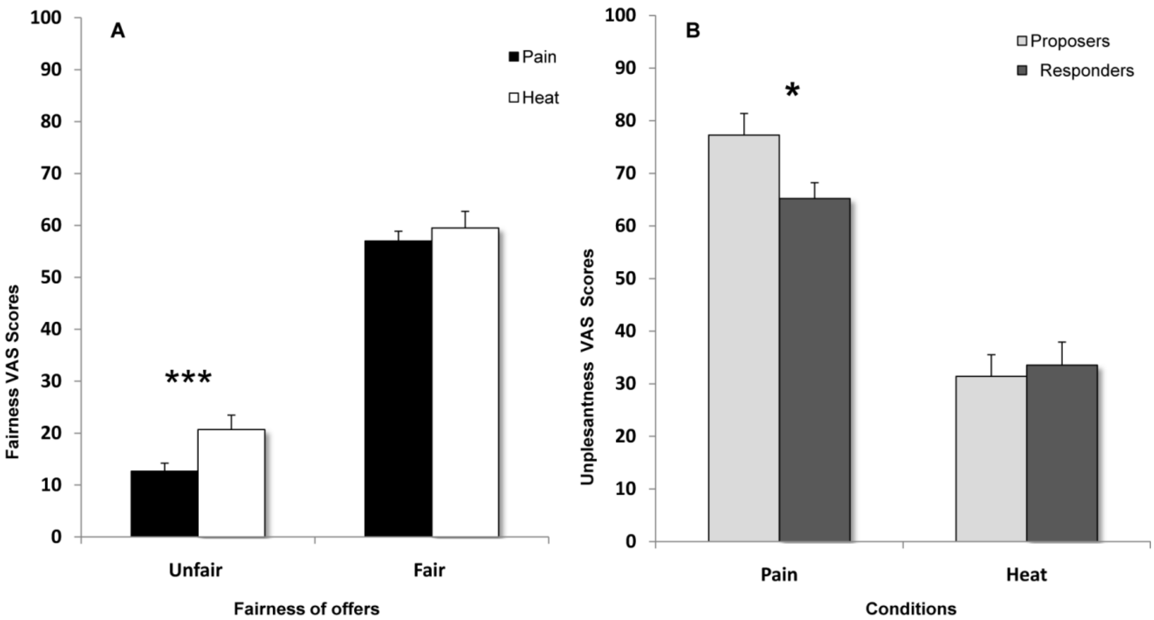

Figure 2.3 Fairness and Pain ratings.

Panel A shows a significant interaction between Fairness of Offer and Condition, revealing that subjects expressed more severe judgments for unfair offers in the Pain Condition with respect to the Heat Condition during the responder's blocks. Panel B shows the significant interaction between Condition and Role, revealing that subjects judged more unpleasant the painful laser stimulation while acting as proposers than as responders.

Reaction Times

ANOVA performed on RTs revealed a main effect of Fairness of Offer ($F_{1,23}= 21.80$, $p<0.001$, $\eta^2_p =0.49$), explained by higher RTs to Unfair offers than to Fair offers ($p<0.001$). The main effect of Condition and its interaction with the Fairness of Offer did not reach the significance (all $ps>0.05$).

Intensity of painful stimulation was predictive of acceptance rates for moderately unfair offers

The only significant regression model was for 30 cents offers (*R = 0.55, Adj* R^2 *= .23, F= 4.51, p <.05*). In particular, for this type of offer the intensity of the painful stimulation was predictive of the acceptance rates (*ß = 0.61*, t_{21} *= 2.92, p< 0.01*). For regression analyses, we computed the Cohen's *f* 2: R^2 / (1 – R^2) as an index of effect size. Cohen's *f* 2 was computed on the AdjR^2 (*f*2 =.29). Both Intensity and Unpleasantness of the warm stimulation were not predictive of subject's acceptance rates in the Heat condition.

Offering behaviour in the proposer blocks

We found a significant main effect of the Fairness of Offer ($F_{4, 84} = 24.5$, $p<0.000$, $\eta^2_p = 0.54$) which was entirely accounted for by higher percentage of *MF* (40 cents) with respect to *F* (50 cents) offers (p< 0.01) and *U* offers (all *Ps <0.001*). Crucially, we found a significant interaction between Fairness of Offer and Condition ($F_{4, 84}=2.9$, $p=0.026$, $\eta^2_p = 0.12$). Specifically, we observed a higher percentages of *MF* (40 cents)offers in Pain with respect to Heat Condition (*p=0.035*) and lower percentages of Fair offers (50 cents) in Pain, with respect to Heat Condition (*p= 0.024*) (Figure 2.2 B). The main effect of Condition did not reach the significance ($F_{1, 21} = 1.0$, $p=0.33$). The regression model performed on proposer blocks was not significant (all *Ps>.05*). Reaction times were not significantly different between conditions (*t= .33, p=.75, NS*).

Intensity and Unpleasantness Ratings. Subjective measures showed a significant effect of Condition both for Intensity ($F_{1,21}= 153.36, p<0.000$) and Unpleasantness scores ($F_{1,21}=73.58, p<0.000$). *Post-hoc* test revealed higher VAS scores for Pain with respect to Heat(all $Ps<0.000$). We did not find a significant effect of Role on laser pain Intensity ($F_{1,21}= 0.08, p=0.78$) or Unpleasantness ($F_{1,21}= 2.04, p=0.17$). Importantly a significant interaction Role x Condition ($F_{1,21}=4.88, p=0.038$) was found only for laser pain Unpleasantness. *Post-hoc* tests showed that in the Pain condition, unpleasantness scores were higher when subjects played as proposers with respect to when they played as responders ($p=0.015$) (Figure 2.3 B). No such difference was found in the HeatCondition ($p=0.64, p>0.05$).

Attention VAS scores. ANOVA performed on subjective ratings of attention to stimulation revealed a significant main effect of Condition ($F_{1,21}=63.54, p<0.000$) showing higher VAS scores during Pain with respect to Heat Condition ($p<0.000$). Neither Role nor its interaction with Condition were significant (all $Ps>0.05$). Subjective ratings of the amount of attention that participants devoted to the UG task revealed a lack of significance both for Condition ($F_{1,21}=2.23, p=.15$) and Role ($F_{1,21}=1.91, p=0.19$) as main factors, as well as for their interaction ($F_{1,21}=1.91, p<.18$).

Manipulation check

Subjects reported higher ratings of anger when they were in the Pain condition with respect to Heat ($t = 3.71$, $p<0.001$) and reported to feel themselves more prone to accept when they were in the Heat condition with respect to Pain condition ($t = -2.12$, $p < 0.04$). Interestingly, such subjective impression contrasts with the actual behaviour of the participants who accepted more offers in the Pain condition. Scores related to the use of an a-priori strategy (e.g. accepting any offer below a given value) were not statistically significant between the two conditions ($t = -.97$, $p=.34$, *NS*).

2.4 Discussion

Recent behavioural studies highlighted the crucial role of incidental negative emotions, as disgust (Moretti and di Pellegrino, 2010), sadness, and anger (Harlé and Sanfey, 2007; Andrade and Ariely, 2009) in exacerbating the human tendency to punish defectors, an index of prosocial behaviour (Güth et al., 1982). Here, using a bilateral iterated version of *one-shot* UG, we demonstrate that first-hand experience of pain strongly modulates the strategic economic interaction in participants playing either the responder or the proposer role. In particular, we show that feeling pain makes an individual less inclined to behave according to the social norms (e.g. punishment of defectors) that regulate most social and economic interactions.

Pain triggers a self-centred perspective when playing the UG as responder

A plausible interpretation of the fact that people generally prefer to behave altruistically is that subjects derive higher hedonic value from the mutual cooperation outcome (Fehr, 2008; Thibaut and Kelley, 1959; Tabibnia et al., 2008). Consistently with this interpretation, it is widely held that the brain uses a common-reward metric for the processing of both individual and social rewards (Sanfey, 2007). Interestingly, there is evidence that fairness-directed conducts, such as mutual cooperation with a human partner (Rilling et al., 2002), donating to a charity (Moll et al., 2006; Harbaugh et al., 2007) altruistic punishment and revenge (de Quervain et al.,2004; Singer et al., 2006) are related to neural activation of the mesolimbic dopaminergic system. We sought to determine whether urgent and unpleasant framing, such as that elicited by an acute painful stimulation, may shift people's preference towardss the individual reward (i.e. monetary gain). Our results show that perceiving pain specifically elicits higher acceptance rates in subjects playing as responders in a bilateral iterated version of *one-shot* UG. No such effect was induced by non-noxious heat stimuli. This result expands previous findings revealing that the personal experience of pain influences social interactions by inducing an egocentric bias and reducing the capacity to react empathically towards others (Valeriani et al., 2008). It is worth noting that the acceptance rates were higher in the Pain condition irrespectively of the fairness of the offer, suggesting that the perception of pain favors the emergence of a maximizing behaviour. Such behaviour allows subjects to make choices aimed at achieving the highest possible gain. Interestingly, this effect is reminiscent of what found in chronic back pain (CBP) patients playing the Iowa Gambling Task (Apkarian et al., 2004), a card game developed to study emotional decision-making (Bechara et al., 1997). Notably, CBP patients tended to choose more frequently cards from the bad decks (those that yielded high immediate gain but larger future losses) with respect to control subjects. Furthermore, the performance of these patients turned out to be associated with the intensity of chronic pain (Apkarian et al., 2004). We showed that the intensity of the painful stimulation is predictive of the higher acceptance rate of moderately unfair offers (MU) (i.e. 30 cents) that correspond to 30% of the total pot. Interestingly this is the percentage at which altruistic punishment starts to occur (Camerer, 2003). Thus, our results raise the possibility that perceiving pain strongly influences the economic interaction, inducing suffering individuals to behave according to selfish motives. It is worth noting that the enhancement of acceptance rate found in the Pain condition cannot be attributed to a decreased moral standard in our participants. On the contrary, participants were more severe, assigning lower scores to unfair offers in the Pain with respect to Heat condition. A similar dissociation between appraisal and actual behaviour was found in a low-frequency repetitive transcranial magnetic stimulation (rTMS) study (Knoch et al., 2006). rTMS inhibition of the right dorsolateral prefrontal cortex reduced the subjects' ability to resist to the selfish temptation to accept intentionally unfair offers, but preserved the ability to judge low offers as unfair (Knoch et al., 2006). Additional evidence for this segregation comes from a clinical study (Moretti et al., 2008) which examines the economic behaviour of patients with focal lesions of ventromedial prefrontal cortex in comparison to that of patients with damage sparing the frontal cortex and of healthy subjects. Confirming previous evidence (Koenigs and Tranel, 2007), the results showed that, when playing the standard version of the UG, patients with lesions to the ventromedial prefrontal cortex rejected unfair offers at higher rate than non-frontal patients and healthy subjects. Importantly, the lesion did not affect the judgment of unfair offers (Moretti et al., 2008).

Pain triggers a self-centred perspective when playing the UG as proposer

The behaviour expressed by subjects acting in the proposer's role has been less explored in literature. To the best of our knowledge there is only one study which explored proposers' preferences and conducts. The study shows that sophisticatedly selfish proposers derived greater pleasure from payoffs patently unbalanced in their favor rather than from fair payoffs (Haselhuhn and Mellers, 2005). Consistently, we observed that when our subjects were playing as proposers their behaviour appeared more strategic and less fair in the Pain than in the Heat condition. In the Pain but not in the Heat condition, participants offered more moderately fair (40 cents) than truly fair amounts (50 cents). This result complements and expands a recent study on the link between pain and money (Zhou et al., 2009) that shows handling money may reduce pain sensitivity and that thinking of having spent money exacerbates physical pain.

The unpleasantness of the laser pain was rated as significantly more unpleasant when subjects played in the proposer than in the responder role. Although further investigation on this effect is needed, it hints at the complex interaction between bodily states and the role during economic interactions.

Participants reported they paid more attention to painful than warm stimuli. Thus, the higher acceptance rate and the decreased level of fairness reported by subjects during Pain conditions of the responder and proposer blocks, could depend on a lower amount of cognitive resources devoted to the UG task in Pain than in Heat conditions. However, the subjective ratings of the amount of attention that participants devoted to the UG task, were comparable in Pain and Heat conditions. Moreover, the analysis performed on Reaction Times both in the Responder' and in the Proposer's role did not show a significant main effect of Condition. Taken together our results suggest that the cognitive resources allotted to the UG task were comparable in Pain and Heat conditions.

Pain modulates interactive behaviour differently from other negative emotions

Most of the research attempting to disentangle the role of negative emotions in the rejection of unfair offers has been conducted inducing the negative emotion before playing the game (Moretti and di Pellegrino, 2010; Harlé and Sanfey, 2007; Andrade and Ariely, 2009). Interestingly, subjects who played the UG in the presence or absence of a disgusting odor showed a higher acceptance in the latter than the former context (Bonini et al., 2011). This effect seems to be gender-selective. Indeed, male participants reported higher disgust and judged the offer as less unfair than females. One plausible explanation for this result posits a spontaneous affective discounting where spontaneous misattribution of the disgust is typically associated to the unfair offer and to the disgusting environmental smell (Bonini et al., 2011).

The manipulation check indicates that our subjects were more angry and less prone to accept in the Pain than in the Heat condition. It is worth noting that in our study painful stimulation and the offers perception were contemporary. In principle, participants might have misattributed the anger they felt for the unfair offer to the painful stimulation that they were receiving. This explanation seems unlikely for at least two reasons. First, the misattribution hypothesis (Srivastava et al., 2009; Bonini et al., 2011) is based on the appraisal theory that suggests specific cognitions are important antecedents of specific emotions and thereby of specific action tendencies (Frijda et al., 1989; Smith and Ellsworth, 1985). Were this the case, our participants should have presented higher fairness ratings for unfair offers in the Pain condition. As a matter of fact, subjects reported lower fairness ratings for the unfair offers in the Pain condition which is exactly the opposite pattern of results. On the contrary, they accepted more in the Pain condition irrespectively of the fairness of the offer.

In conclusion, pain modulates social preferences differently from some negative emotions like induced disgust. This may be surprising because the above negative emotions are underpinned by neural regions, e.g. the insular cortex, that also represent pain (Philips et al., 1997; Derbyshire et al., 1997). Thus, an additional point of interest of our paradigm is that it may be useful for investigating the neural correlates of induced social preferences.

Chapter 3

"Listen to your heart and tune to yourself– a manipulation of interoceptive awareness during the Ultimatum Game

3.1 Aims and Hypothesis

In this study, we aimed to investigate how experimentally induced changes in interoceptive awareness influences the participant's behaviour in an UG. Receiving unfair offers has been connected with changes in various autonomic parameters. Indeed, changes in heart rate were found to be related to the degree of unfairness of an offer and to a higher rejection rate (Osumi and Ohira, 2009). Additionally, interoceptive accuracy has be seen to moderate the relationship between changes in electrodermal activity (EDA) during the reception of unfair offers and the rejection of such offers (Dunn et al., 2012). These results suggest an important link between the interoceptive system and the decision-making task. The influence of interoceptive awareness has been reported in various cognitive or emotional tasks such as attention, decision-making (Werner et al., 2009), emotional intelligence (Schneider et al. 2005), empathy (Schneider et al. 2005), tendency to general anxiety (Stewart et al. 2001). In these tasks interoceptive awareness was generally assessed by comparing (in a between design) good versus bad perceivers, based on a heartbeat tracking task

(Schandry and Weitkunat 1990) or heartbeat detection task (Critchley et al., 2004). Here, we manipulated interoceptive awareness within the same participant by exposing them to various bodily sounds, i.e. one's own heartbeat, another person's heartbeat or footsteps. We employed a bilateral version of the UG (see paragraph 1.7) where participants alternatively acted as proposer or responder while hearing different sounds. We hypothesize that online exposure to one's own heartbeat would increase interoceptive awareness (e.g. Fenigstein and Carver, 1978) and thus heighten appraisal of own emotional responses, producing higher rejection rate of unfair offers when participants are playing as recipients and lower offers when they are playing as proposers.

3.2. Methods

Participants

Thirty healthy participants (18 female; age range: 19 to 39 years (mean = 25.7, SD = 5.0) volunteered in the study. They were informed that the money earned during the economic game corresponded to their actual payoff in the game and were accordingly reimbursed with an amount between 27.4 and 43 euro (mean = 34.7, SD = 3.7). Participants were naïve as to the purposes of the study and gave their written consent. The experimental protocol was approved by the local Ethics Committee at the Fondazione Santa Lucia and the study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Modification to the general procedure used in the present study

In order to prevent participants to decide *a priori* to use a strategy (e.g. always accept anything above 30 cents) and to force them to use a more implicit strategy, they were not provided with explicit quantities of the different offers but with pictures showing the different quantities with two-cents-coins (see Figure 1). Pre-tests in a different sample of n=12 healthy controls showed that if presented to a forced-choice task, participants were reliably able to cluster the different splits into the corresponding categories. For a description of the general procedure please see paragraph 1.7.

The interoceptive manipulation

Participants listened to three sounds corresponding of three conditions, *silicet*: i) their own heartbeat ii) someone else's heartbeat and iii) footsteps. Instructions stressed that participants would listen to sounds while playing but should not pay attention to them. They were told that sounds would be randomly assigned by the PC and among all the possible sounds there was the possibility to listen to the sound of their own heart, and therefore a recording device should be prepared (see below) for this eventuality. No further information was given.

Own heartbeat**:** For the own heartbeat condition, a fetal heart detector (*Angle Sounds*, Doppler Foetal) was attached with an elastic band over the participant's heart. The recorded sound was sent to a sound processing software (Ableton Live 8.2.2, https://www.ableton.com/), which reduced noise using low-pass frequency filters (1.35 kHz) and equaled out volume differences. From there it was played back to the participants headphones.

Someone else's heartbeat**:** The sound of another person's heart that was previously recorded with the same method used in the own heartbeat condition was played to the participant. Importantly the mean heartbeat frequency (at rest) of the two conditions was matched as closely as possible (mean difference= 3.6 beats/minute; STE=0.56).

Footsteps**:** Footstep sounds were matched to correspond to a mean frequency of a typical heartbeat (1.17 Hz). Furthermore we used the Audacity software (version 1.2.6) in order to make the sound a slightly more irregular, making it less comparable to a natural fluctuation in the frequency of the heartbeat sound.

Experimental procedure

Subjects were seated in a comfortable armchair and were asked to relax their muscles but to stay alert. The headphones were mounted, the angle sound Doppler was placed over the participant's heart and a finger pulse transducer (Adinstruments) as well as two electrodes to measure electrodermal skin response (Adinstruments) was attached to the participant's left hand. A cover story was used to avoid participants gaining insight into the experiment's purpose, i.e. participants were told that the aim of the study was to observe spontaneous social interactions during the listening of random sounds.

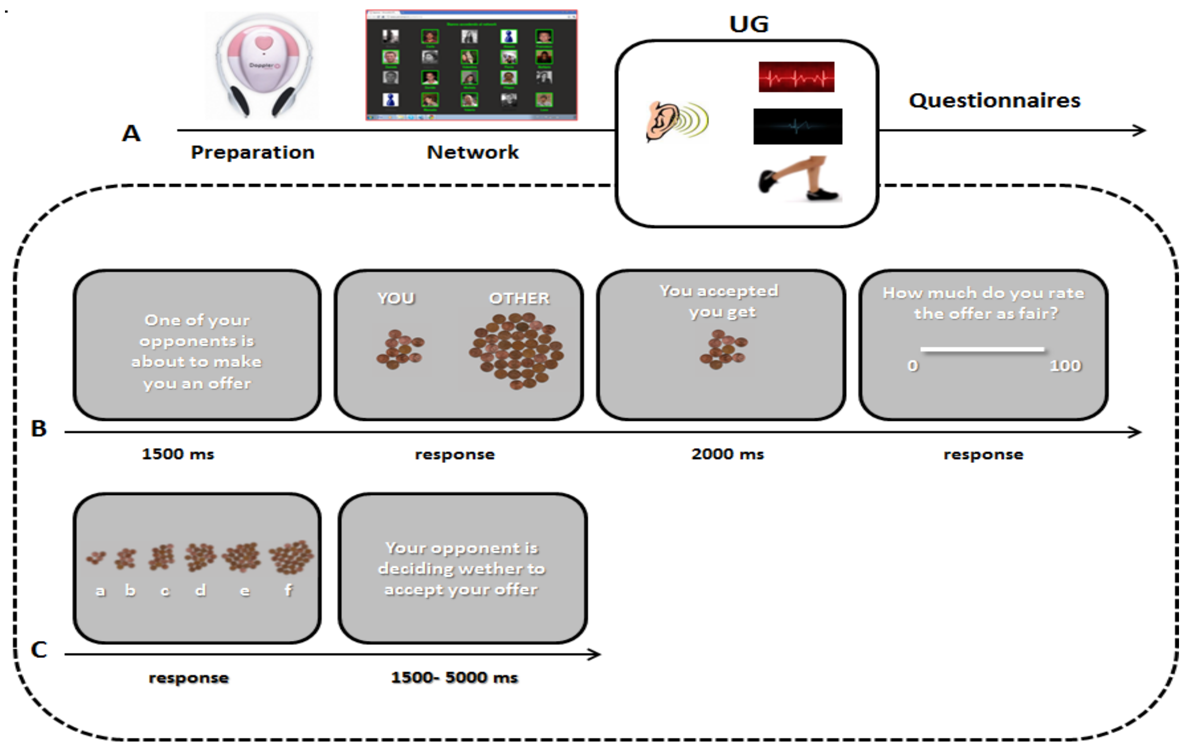

Figure 3.1: Schematic procedure of A) the experimental set-up, B) a trial as recipient and C) a trial as proposer.

First, each subject was introduced to the rules of the Ultimatum game and to the internet-based platform in order to familiarize with the procedure and to visualize the faces of the confederates. Then the participants were told that the game would start. Overall, each subject was tested in six experimental blocks: three in the role of recipient and three in the role of proposer (Figure 3.1 A). For each subject, the recipient block was repeated three times in random order for: Own Heartbeat condition, Other Heartbeat condition and Footsteps condition. On each block, participants completed 24 trials, for an overall amount of 144 iterations in the whole experiment. The order of conditions was counterbalanced across participants.

On the screen specific instructions prompted subjects to play the recipient or the proposer role (Figure 3.1 B). In the recipient blocks, subjects were asked to accept of refuse the offer of other confederates, as follows (translated from Italian): “The computer randomly assigned you the role of responder. You may accept or reject the offers that come from your opponents. If you accept, the money will be divided according to the offer, if you reject neither of you will receive nothing”. In the proposer blocks subjects were instructed to decide how to divide the sum of money, as follows (translated from Italian): “The computer randomly assigned you to the role of proposer. You may decide how to allocate the money. If your opponent accepts the offer, the money will be divided accordingly, if he/she rejects the offer, no money will be given to any of you”.

Every recipient received four offers for each of six splits, that is, 90:10, 80:20, 70:30, 60:40, 50:50, 40:60 eurocents. Recipient could accept or reject the offer by pressing a button (left to accept, right to reject) with their right hand. At the end of each interaction, a feedback lasting 4 seconds informed participants about how much each player received showing the picture of e.g. 30 cents if accepted or, if the offer was rejected, an empty picture). In the proposer blocks, participants had to decide how to split money by choosing one of the six possible offers displayed on the screen (Figure 3.1 C). In these blocks no feedback was provided to avoid any effect of the outcome on the subsequent offer.

At the end of the experiment questionnaires were filled out and the participants were debriefed about the purpose of the study. Over all the experiment lasted about 1 h.

Subjective ratings of offers' fairness

After each trial, participants were asked to assess the fairness of each offer on a Visual Analogue Scale (VAS) ranging from 0 (unfair) to 100 (fair). The question (translated from Italian) was the following: "on a scale of 0 to 100, where 0 corresponds to unfair and 100 to fair, how would you rate the offer you have just received?".

Subjective ratings of attention to the game/sound

After each block, participants evaluated how much attention they have addressed to both the sound and the game (in randomized order) on a VAS scale ranging from 0 (no attention) to 100 (complete attention). This way variation of attention over blocks and condition were assessed.

Manipulation check

At the end of the game we gave the participant a short questionnaire asking about various aspects on how they perceived the interaction during the game. Importantly, the questionnaire included a question on the recognition of their own heartbeat ("Do you think any of the sounds you heard was the sound of your own heart? If yes, in which block(s)?").

Heartbeat counting (interoceptive sensitivity)

Interoceptive sensitivity was measured using the classical "heartbeat tracking paradigm" (Schandry 1981). Participants were asked to focus on their heartbeat and internally count the numbers of heartbeats during 4 different intervals that were presented in random order: 25s, 35s, 45s, 100s. Start and end of the period was presented auditory to the participants. Real heartbeat was recorded using a finger oxymeter (Adinstruments). These two measures were used to calculate a sensitivity index.

3.3 Statistical analysis

A Kolmogorov-Smirnov test showed that most variables of interest were not normally distributed and thus non-parametric statistics were used for acceptance rate, offers made and for the fairness ratings. A Friedman test was performed to test the effect of condition (own HB, footsteps, other HB) on each fairness level of each measure and Wilcoxon tests were used for post-hoc analysis of significant effects of condition. The VAS scale on the attention was analyzed using parametrical measures, as the variables were normally distributed.

2.4. Results

Recognition of own heart sound

A total of 12 out of 30 participants correctly identified the sound of their own-heart. The remaining 18 participants reported that could not identify or misidentified the sound of their own heart. Unfortunately we did not collect confidence levels related to this question that would allow us to have a quantitative measure of recognition. However, experimenter's final subjective debriefing revealed that even within those who correctly discriminated the sound of their own-heart their answer was mostly based on guess or "implicit feeling".

Interoceptive sensitivity

Interoceptive sensitivity was calculated as the mean score of four heartbeat perception intervals (25s, 35s, 45s, 100a= according to the following transformation (see e.g. Schandry 1981): $\frac{1}{4}\sum\frac{(1-recorded\ heartbeats-counted\ heartbeats)}{recorde\ heartbeats}$. This transformation reveals a sensitivity index from 0 (i.e. very low interoceptive sensitivity) to 1 (i.e. very high interoceptive sensitivity). The median value of interoceptive sensitivity was 0.70 (s.d. 0.19). Using a median split method, the group of 27 participants (data of 3 participants were missing due to technical problems with the pluse registration) were split into two groups of high interoceptive sensitivity (GOOD group, mean heart beat perception 0.8 s.d. 0.08, n=13) and low interoceptive sensitivity (BAD group, mean heartbeat perception 0.4 s.d. 0.23 n=12).

The Ultimatum Game

When participants were playing as recipients, the effect of condition (own HB, footsteps, other HB) was analyzed for each possible split both for acceptance rate (see Table 3.1, white background) and for fairness judgments (light gray background). Moreover, it was analyzed for the frequency of each possible offer when participants were playing as proposers (dark gray background).

Acceptance rate	Chi square	P-Value	Post hoc
10:90	0.5	0.78	
20:80	2.9	0.23	
30:70	1.6	0.44	
40:60	1.1	0.58	
50:50	2.0	0.37	
60:40	1.2	0.55	
Fairness judgment			
10:90	1.9	0.39	
20:80	8.9	0.012	Own HB > footsteps (p=0.014) Own HB > Other HB (p=0.016) Other HB = footsteps (p= 0.95)
30:70	1.9	0.39	
40:60	2.5	0.29	
50:50	2.1	0.36	
60:40	3.5	0.17	
Offers made			
10:90	0.9	0.64	
20:80	8.0	0.018	Own HB > footsteps (p=0.014) Own HB > Other HB (p=0.011) Other HB = footsteps (p= 0.64)
30:70	0.9	0.65	
40:60	7.0	0.03	Own HB = footsteps (p=0.30) Own HB < Other HB (p=0.003) Other HB = footsteps (p= 0.20)
50:50	0.1	0.95	
60:40	1.2	0.56	
Sum of money	7.5	0.023	Own HB < footsteps (p=0.014) Own HB < Other HB (p=0.013) Other HB = footsteps (p=0.50)

Table 3.1 shows the results of the Friedman tests as well as for the significant effects of condition the *post-hoc* comparisons.

In the role of recipient

While there was no significant effect of condition on the acceptance rate, unfair offers (20:80 split) were perceived as less fair while listening to one's own heartbeat as compared to both listening to another person's heartbeat as well as when listening to footsteps (see table one, white background). This effect is shown in Figure 3.2 A.

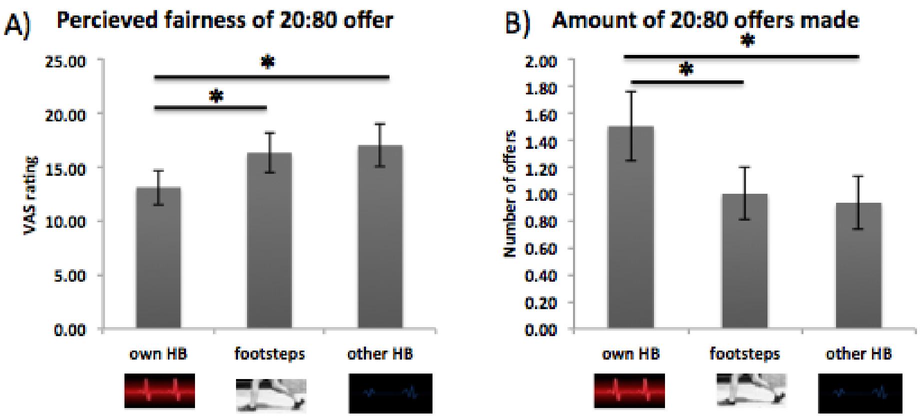

Figure 3.2 A) Perceived fairness of the 20:80 offer as measured by the VAS scale during the three experimental conditions. **B)** 20:80 offers made in the role as proposer.

In the role of proposer

The results of the Friedman test suggest an influence of the experimental condition on both the 20:80 offers, on the 40:60 offers as well as on the sum of money proposed to the other participants during the game (see Table 1, dark gray background).

Influence of trait interoceptive sensitivity

In order to test if the trait interoceptive sensitivity as measured by the heartbeat counting did play a role in explaining the significant effects between conditions, we tested if the difference between conditions (e.g., own HB relative to footsteps) was modulated as a function the sensitivity index by grouping the participants into good versus bad perceivers. Yet, neither of the significant effects (see Table 3.1) differed significantly between the two groups (all ps> 0.05).

Attention to the game and the sound

A 2x3x2 ANOVA with the within factors role (recipient, proposer), condition (own heartbeat, footsteps, other's heartbeat) and object (attention to game/attention to sound) revealed a significant main effect of condition ($F_{(2,28)} = 4.2, p=0.025$) as well as a main effect of object ($F_{(1,29)} = 16.5, p<0.001$) explained by a higher amount of attention being drawn to the game than to the sound and an interaction effect of role and object ($F_{(1,29)} = 10.1, p=0.004$). Post-hoc t-test of the main effect of condition suggest that participants were generally more attentive when hearing their own heartbeat as compared to the footsteps ($t= 2.4, p=0.02$) (see Figure 3.3) and tended to be more attentive as compared to other's heartbeat ($t= 2.5, p=0.02$), while no significant difference was found between footsteps and other's heartbeat conditions ($t= 0.6, p=0.95$) (see Figure 3.3). Post-hoc t-tests of the interaction effect suggest that participants paid more attention to the game and less to the sound when they were in the role of the proposer as compared to when they were in the role of the recipient.

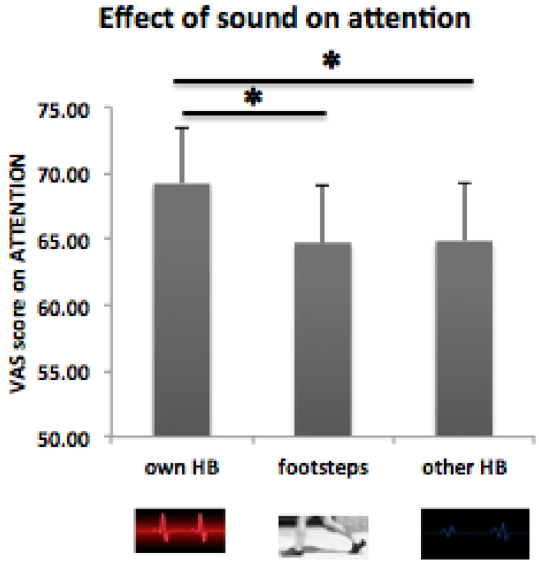

Figure 3.3 Mean attention drawn to the game and the sound over condition.

3.5 Discussion

To the best of our knowledge we explicitly manipulated for the first time interoceptive awareness during the Ultimatum Game (UG), a social economic decision-making task. We demonstrated that providing online interoceptive feedback modulates fairness appraisal and behaviour in the UG. In specific, listening to own-heart sound, compared to other-heart and the sound of footsteps, increased subjective feelings of unfairness in response to unfair offers, and increased the unfair offers resulting in a decreased total amount of money offered when playing in the proposer role. These findings provide first evidence of the influence of interoceptive information in decision-making in socioeconomic exchange scenarios. In addition, we believe we are introducing a new and valuable procedure to manipulate interoceptive awareness online.The UG neatly models the tension between financial self-interest and equity motives (Camerer, 2003). It is of the responders' self-interest to accept any offer for smaller it might be (i.e., to maximize income), however presumable pro-social motives and/or emotional response to inequity may lead to frequent rejection of very unfair offers, a form of punishment behaviour (i.e., altruistic punishment) (Fehr and Gachter, 2002). Recent research identified physiological and neural correlates of this behaviour. In specific, larger EDA responses (Dunn et al., 2012; Moretti et al., 2010; van Wou't et al., 2006), and increased activity in the anterior insular cortex (Sanfey et al., 2003; Harlè et al., 2012), an area involved in integration of emotional and somatosensory information (Craig et al., 2009; Critchley et al., 2009), were found in response to unfair and subsequently rejected offers. Thus, the choice to engage in this costly punishment behaviour is tightly connected to strong feelings of inequity and accompanied by negative emotional reactions. However, how exactly this emotional reaction interacts with decision-making in the UG is still largely unknown. Here we manipulated a key element of emotional experience that is the integration of information about the internal bodily state and the external environment (Damasio, 1994; Craig, 2009).

The influence on perceived fairness of offers

When acting in the role of recipient we found that providing feedback about one's own cardiac responses enhanced the feelings of unfairness with regard to very disadvantageous offers. This shows that increased awareness of bodily responses, i.e. interoceptive states, may play a role in economic decision-making processes by influencing the subjective appraisal of monetary offers. Interestingly, such modulation was true only for offers of 20:80% of the pot, the type of offer frequently reported to have 50% chance of rejection (Camerer, 2003; Nowak et al., 2000). Thus, it is possible that under circumstances of considerably uncertainty the role of bodily reactions might be particularly relevant. In this case, the result was exacerbation of feelings of unfairness probably reflecting enhanced appraisal of one own's emotional reactions to disadvantageous offers previously shown to be related to feelings of anger (Pillutla and Murnighan, 1996).

In our study, enhanced feelings of unfairness were not accompanied by changes in acceptance behaviour, that was equivalent across the three experimental conditions. A similar dissociation between appraisal and acceptance behaviour was previously found in two previous repeated transcranial magnetic stimulation (rTMS) studies (Knoch et al., 2006; Baumgartner et al., 2011). In these studies, rTMS inhibition of the right dorsolateral prefrontal cortex decreased rejection rates while leaving the ability to make fairness judgments intact. The authors conclude that this area, together with the ventral medial prefrontal cortex (Baumgartner et al., 2011; Tabibnia et al., 2008), play a fundamental role in the implementation of fairness-related behaviours. In the present experiment it is not clear if the manipulation was not strong enough to induce also a change in behaviour (i.e. increasing rejection rates), or if participants were able regulate their emotions and act in a self-interest fashion, maybe by using the expression of their enhanced inequity feelings as an alternative (and less costly strategy) to punishment (i.e. rejection). Consistently, it has been shown that recipients who are provided with the possibility of directly displaying their negative emotions to proposers, presented a reduced amount of rejections than those who were constrained to keep their emotions for themselves (Xiao and Houser 2005).

The influence on proposing behaviour

When acting in the role of the proposer, we found that listening to own-heart sound lead participants to offer a lower total amount of money as compared to the other conditions. Interestingly, this effect was explained by the presence of a higher amount of unfair offers (i.e. 20:80) and a lower amount of fair offers (40:60). This behaviour does not seem to be strategic since in the classical game participants usually expect their opponents to reject unfair offers (Frith and Singer, 2008) and as a consequence generally offer an even or almost even split (Camerer, 2003). Two alternative explanations could plausibly underlie this effect: A) the interoceptive feedback could reduce perspective taking by enhancing a self-centered perspective. In line with this a recent study (Tsakiris et al. 2011) showed that participants with high interoceptive sensitivity are more resistant to bodily illusions and self-other confusions. As recent results indicated that enhanced awareness of aversive bodily states (i.e. pain) increased strategic behaviour aimed at maximizing self-gain (Mancini et al. 2011), we suggest that increased general bodily awareness enhances self-centeredness without maximizing self-gain. B) an alternative explanation could be that even if participants take into account their opponents' perspective, they use offering behaviour to give vent to their feelings of inequity which they might previously have felt in the role of the recipient. However, a previous study showed that proposers who once were angry (vs. happy) receivers made fairer offers to their respective partners in a second round of the Ultimatum Game (Andrade and Ariely, 2009). Hence, our findings suggest that enhanced awareness of owns' bodily/interoceptive responses may increase self-centered perspective drives in socioeconomic exchange scenarios.

Implicit manipulation

It is worth noting that these effects seem to be mostly implicit as participants were, by large, unable to discriminate the own-heart from the another person's heart sound. Nonetheless, the modulation of behaviour/appraisal was specific to the own-heart condition. Significant differences were found not only in comparison to the baseline condition (i.e the footsteps sound) but also in comparison to another person's heart sound, a similar sound of a real heart but with different physical characteristics (see discussion below). No differences were either observed between the footsteps and another person's heart condition. Thus, the observed modulation was not due to mere exposure to interoceptive stimuli, that by itself may have a self-focusing effect (Fenigstein and Carver, 1978; Tajadura-Jimenez et al., 2008), but it was specific to real feedback of ongoing visceral responses.

Possible neural correlates

Recent research showed that effortful engagement in different cognitive strategies of emotional regulation (Gross et al., 1998) impacts affective reactions to unfair offers and rejection behaviour (van Wou't et al., 2010; Grecucci et al., 2012). In specific, instructions to down-regulate (reappraise the proposer's intentions as less negative) lead to a decrease in negative affect associated with unfair offers and higher acceptance rates, while instructions to up-regulate (reappraise the proposer's intentions as more negative) lead to enhanced negative affect and increased rejection rates (Grecucci et al., 2012). The posterior insular cortex, an area that processes visceral interoceptive information (Craig et al., 2009; Farb et al., 2012), was found to be particularly responsive to emotional modulation strategies. This brain region was also in evidence in a fMRI study comparing brain activity of experienced Buddhist meditators, presumably more interoceptive sensitive, and control participants while playing the UG (Kirk et al., 2011). Meditators presented higher acceptance rates and activated preferentially the posterior insula during unfair offers, while controls recruited the anterior portion of the insular cortex, an area that has been shown to predict rejection behaviour in the UG (Sanfey et al., 2003). The authors argued that meditators, presumably attending internal body states, were better able to uncouple negative emotional responses from their behaviour. Together with our results, these findings demonstrate that interoceptive representations may partly mediate cognitive reappraisal of economic offers. Increased awareness and appraisal of interoceptive states play a role in financial decision making on the UG, likely by increasing the focus on one's own physiological reactions and promoting a self-centered perspective.

Influence of trait interoceptive sensitivity

Behaviour or fairness appraisal in the UG could not be explained by participants scores in the interoceptive sensitivity task suggesting that the ability to identify one's own cardiac activity at rest does not have a primary or direct role in the modulation we observed. For example, it is very likely that our manipulation enhanced interoceptive awareness even in those participants that in general are not very sensitive to changes in their physiological activity. Thus, other than the general sensitivity or tendency to attend inner bodily signals it is possible that it was the amplified salience of such signals, and consequent reappraisal, that modulated participants' subjective experience. Interestingly, and in line with these findings the only study that has previously explored the role of interoception on the UG did not find a direct relationship between interoceptive awareness, as measured by the counting task, and behaviour (Dunn et al., 2012). Instead, what the authors found was that interoceptive accuracy moderated the relationship between electrodermal responses to unfair offers and rejection behaviour, and only in participants classified as “good interoceptors”. On the other hand, in “bad interoceptors” it was greater heart rate variability (and index of trait emotion regulation ability) that predicted reduced rejection rates. This study demonstrates how individual differences in perceiving bodily signals interact with different strategies of emotional responding. In fact, several studies found the effects of cardiac interoceptive accuracy to be context-dependent or to mediate/or be mediated by other variables (e.g. Boagarts et al., 2005, 2008; Pollatos et al., 2009; Dunn et al., 2012). Thus, individual differences in interoceptive sensitivity may not always provide the most complete description of the role of interoception in cognition. In some cases manipulating interoceptive awareness within-subjects may constitute a more flexible and comprehensive approach to study the interplay between visceral states, cognition and social behaviour.

False feedback theory

An alternative explanation to our results would be that they are not driven by the effect of the real feedback of own-heart but by the false-feedback of interoceptive information in the other-heart condition, in what has been called “Valins effect” (e.g. Valins, 1966; Parkinson and Manstead, 1986; Gray et al., 2007). That is, it could be that altered representation of bodily states due to a mismatch between real and provided heart information were actually the reason for differences across experimental conditions in fairness judgments and in the amount of money offered by participants. However, although equally appealing, this interpretation is not likely to be true. The effects of listening to own-heart were also found when compared with the footsteps condition, a bodily sound that conveys no interoceptive information and therefore should not elicit any, conscious or unconscious, perception of mismatch between real and perceived interoceptive signals (Valins, 1966; Parkinson and Manstead, 1986; Fenigstein and Carver, 1978). Furthermore, the prevalence of perceived mismatch should lead to increased salience of the stimuli which is not congruent with the diminished attention allocated and reduced subjective unfairness ratings found while listening to another person's heart. Higher reported attention to the sound and to the game in the own-heart condition provide further support to the idea that increased interoceptive awareness enhances salience and attention to both internal and externally meaningful stimuli (e.g. Craig et al., 2009; Matthias et al., 2009).

Novel manipulation

While standard interoceptive sensitivity tasks have proven to be useful tools in the study of how individual differences in interoceptive sensitivity correlate with behaviour or personality traits (e.g. Dunn et al., 2012; Matthias et al., 2009; Pollatos et al., 2009; Schneider et al., 2005; Stewart et al., 2001; Werner et al., 2009), several limitations and concerns have been raised (e.g. Khalsa et al., 2009; Ceunen et al, 2012; Jones, 1994; Kapp-Kline and Kline, 2005). Furthermore, such approaches rely on in-between subjects design making them more prone to confounds of other related personality traits . Here, we introduce a novel procedure to manipulate interoceptive awareness in an event-related and fairly implicit way.

It is worth noting that presenting feedback of own-heart sound is substantially different from providing feedback of heart-rate such as an auditory tone or light flash at the occurrence of an heartbeat . The sound of the heart, as translated by means of a doppler device, conveys information such as systolic-diastolic interval, duration and changes in intensity of cardiac tones, that better represent the cardiovascular activity, and thus are likely to provide a more comprehensive feedback on cardiac responses. Future research using this approach should be complemented with further measures such as indices of autonomic activity such as EDA and heart rate (Dunn et al., 2012; Osumi and Ohira, 2009; Vögele et al., 2010), brain activity (Grecucci et al., 2012; Baumgartner et al., 2011; Sanfey et al., 2003) or trait and state anxiety (Hartley and Phelps, 2012; Paulus and Stein, 2006) to help to disentangle the dynamics associated with the feedback of own-heart sound. We foresee that this manipulation might reveal itself as a valuable tool for the study of emotion regulation processes and the interplay between viscero-sensory information and emotional states.

Chapter 4

"Does unfairness hurt? A laser evoked potentials study"

4.1 Aims and Hypothesis

Here, we extended the concept of *social pain*, originally attributed only to social exclusion (Panskepp, 1998; Mac Donald and Leary 2005), to that of an intentional defection of a social norm (i.e. fairness) operated by a peer opponent.

In particular, the first aim of the present study is to investigate whether and how a monetary loss caused by an unfair opponent, who intentionally violates the social norm of fairness, modulates Laser Evoked Potentials as compared to an economic loss in condition of fairness, or to an economic gain. The second aim is to explore whether the effect of the unfair social context is selective for the loss of one's own money or it could be extended to the loss of someone else's money. To these aims, we used the laser-evoked potentials (LEPs) technique.

On the basis of previous observations, which highlighted the similarities in the neural circuits related to physical and social pain, we hypothesize that a personal economic loss that takes place in an unfair social interaction will lead to the reduction of the amplitude of the cortical correlates of pain, compared to an economic loss that take places in a fair social interaction and to an economic gain. This result could be accounted for by a reduced activity of pain related areas due to an emotion regulation process.

4.2 Materials and Methods

Participants

A total of twenty healthy volunteers (8 females; mean age 25.44±5; range 18-35; all right-handed) with normal or corrected-to normal vision, no prior history of neurological, psychiatric or chronic pain disorders and no current psychotropic or analgesic drug use, participated in the study. Four subjects were excluded from the analysis due to distorted EEG pattern. Therefore, EEG data analysis was performed on sixteen participants. The experimental protocol was approved by the local Ethics Committee at the Santa Lucia Foundation and the study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki. Participants gave their written consent before the experiment and were naïve to the purposes of the study. All subjects were paid € 30 for their participation to the study.

Experimental Procedure and Economic Game

Subjects were seated in a comfortable armchair and were asked to stay alert and relax their muscles. Participants were told that the aim of the study was to assess their subjective pain threshold while they were committed in an economic game played against other participants (the opponents) located at other two remote Italian Universities, using an internet-based platform. Prior of the experiment, each subject was preliminarily introduced to the platform in order to familiarize with the procedure and to visualize the pictures of the confederates. Unknown to the participants, the game took place against a PC device, which was programmed using E-Prime software 1.2.

Before starting the economic game, each participant was endowed with an initial amount of 15 euros. In each trial the screen displayed a red traffic light which became green employing a random amount of time between 550 and 1480 ms. The participant had to correctly guess in how many milliseconds this change occurred, by making a choice between two options displayed on the screen (see Figure 4.1). Participants could respond by means of a button press. Importantly, the position of the response button was congruent with the option showed in the screen (e.g. left button for the left option). If they guessed correctly, than 1€ would be added to their initial account and subtracted to their opponent's payoff; conversely, if they performed badly, than 1€ would be subtracted from their account (and added to their opponent's).

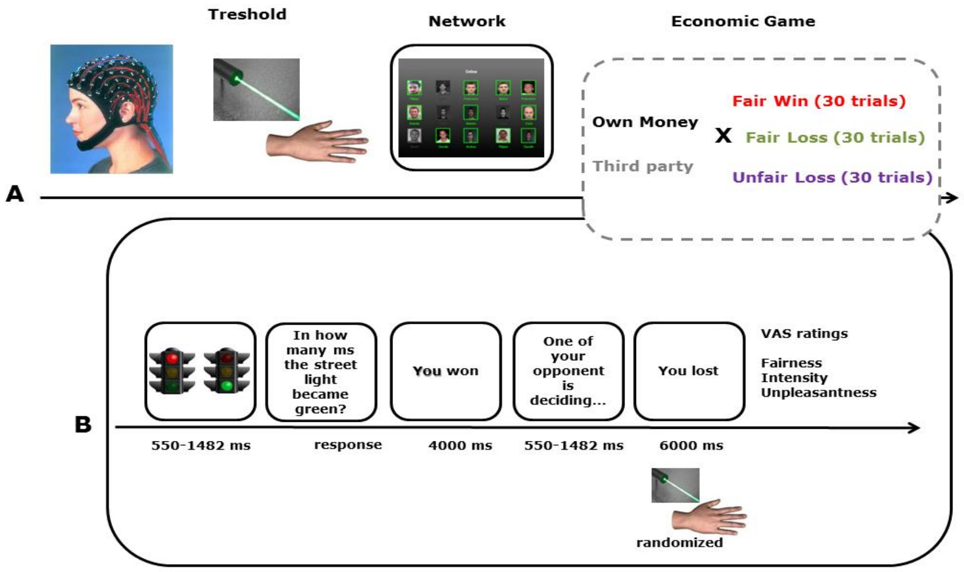

Figure 1. **A)** General procedure. **B)** One trial.

Specific instructions informed participants that the role of the opponent was to decide whether or not reversing the outcome of the participant by making him unfairly lose (when he had actually won) (Unfair Condition) or leaving the actual outcome of the game (Fair Condition) (when he had actually won or lost). To avoid possible reputation effects, subjects were ensured that for each match they would have been randomly paired with a different partner.

At the beginning of each block, specific instructions informed participants whether they were starting to play with their own money (*OM*) or on behalf of a third party (*TP*). On each block, participants completed a total of 30 trials equally distributed in three conditions as the follows: 10 trials in which they fairly win (Fair wins); 10 trials in which they unfairly lose (Unfair Losses); 10 trials in which they fairly lose (Fair Losses). For each manipulation (OM, TP), participants were tested in three experimental blocks (a total of six blocks, 180 iterations)

The order of the manipulation was counterbalanced across subjects. The experiment lasted approximately 3 hours.

Subjective ratings

After each trial, participants were asked to assess the fairness of their opponent behaviour on a Visual Analogue Scale (VAS) ranging from 0 (indicating maximal unfair behaviour) to 100 (maximal fair behaviour). Further, they judged the intensity and the unpleasantness perceived during the laser stimulation, along a VAS where 0 corresponded to no pain (intensity or unpleasantness) and 100 the maximum pain that can be imagined.

Laser stimulation and LEP recordings

During the economic game experiment participants concomitantly received painful laser stimulation delivered using with an infrared neodymium yttrium aluminium perovskite laser (EL.EN.Group) to the dorsum of the right hand. The laser stimulation allowed us to induce acute painful sensation on the body part selectively stimulated by the laser beam with the advantage to avoid the concurrent experience of touch (Bromm and Treede, 1984). Prior of the experiment, we determined the individual pain threshold according to the method of limits (Yarinsky et al., 1995). The threshold values (J/cm2) corresponded to the lowest painful or warm sensation that can be reliably detected in at least 5 out of 10 trials. During the experiment, laser pulses were delivered in blocks of 30 trials. To avoid nociceptors fatigue or sensitization, the location of the laser on the skin was slightly shifted after each stimulus. An area of about 8 cm^2 on the radial side of the hand dorsum was stimulated. Moreover, 7-8 seconds inter-stimulus interval (ISI) allowed us to minimize central habituation effects. The distance between the laser stimulator and the hand was kept constant (and was about 2 cm). A SynAmp amplifiers system and Scan 4.3 software (Neuroscan) was used to record electroencephalographic (EEG) data.

Recordings were obtained using 64 tin electrodes arranged according to the international 10-10 system as follows: Fp1, Fp2, Fpz, AF3, AF4, AF7, AF8, F3, F4, F5, F6, F7, F8, FC1, FC2, FC3, FC4, FC5, FC6, FT7, FT8, Cz, FCz, Fz, Oz, POz, Pz, C3, C4, C5, C6, T7, T8, TP7, TP8, CP1, CP2, CP3, CP4, CP5, CP6, CPz, P3, P4, P5, P6, P7, P8, PO3, PO4, PO7, PO8, O1, O2; the remaining two surface electrodes were positioned for the vertical (VEOG) and horizontal electro-oculographic (HEOG) recording. The reference was at the nose and the ground at AFz. Horizontal electro-oculogram (HEOG) was recorded bipolarly from electrodes placed on the outer canthi of each eye, and vertical electro-oculogram (VEOG) was recorded from an electrode below the right eye.Electrode impedance was kept below 5 KΩ. The EEG signal was amplified and digitized at 1000 Hz.

EEG data analysis.

After EEG recording, an Independent Component Analysis (ICA) algorithm was employed to continuous raw data in order to classify and remove artifactual EEG components. ICA assumes the mutual statistical independence of the non-Gaussian source signal embedded in the linear mixture of brain sources and biological or non-biological artifacts (Hyvärinen et al., 2001) and has been successfully applied to EEG (Jung et al., 2000; Longo et al., 2009) and MEG (Barbati et al., 2004, Mantini et al., 2011) data.

The ICA was computed using the fastica algorithm implemented in Matlab (MathWorks) (http://research.ics.aalto.fi/ica/fastica/). After removal of artifactual IC, EEG signal was band-pass filtered at 1-30 Hz and segmented into epochs time locked to the laser pulses (-200 to 600 ms). EEG epochs were baseline corrected (-200 to 0 ms).

Manipulation check

At the end of the experiment, subjects were asked to judge how much they felt involved in the interaction with the opponents. Subjective scores were provided according to a VAS scale ranging from 0 (absence of any involvement) to 100 (maximal involvement). When the assigned score was higher than 0, they were asked to qualitatively report whether they believed or not to play against a human opponent. Based on VAS scores and qualitative reports subjects were divided into two groups: believers and non-believers.

4.3 Analysis

Based on results of the manipulation check, we divided participants into two groups (see below).

LEPs amplitude

The N1, N2, P2 and the N2P2 were extracted and analyzed as following. The N1 component is defined as the negative deflection (peaking at approximately 160 msec) preceding the N2 wave (Hu et al., 2010) measured at the central electrode controlateral to the stimulated right hand side (left hemisphere, C3) as referenced to

Fz. The N2 was measured at the Cz electrode and was defined as the most negative deflection after the stimulus onset (peaking at about 200 msec). Then, we computed the peak-to-peak amplitude of the N2/P2 consisting of a large biphasic long latency responses (about 200–350 ms following laser hand stimulation), peaking over the vertex region. Its topographic representation was explored by means of Fz, Cz and Pz electrodes. According to Legrain et al. (2009; see also Bastuji et al., 2008) the P2 component shows two overlapping sub-components with different latencies and scalp topographies. The P2a wave peak was measured at Fz, Cz and Pz in the 260-360 msec post-stimulus interval (peaking at about 330 msec at centro-frontal electrodes), while the P2b wave was measured at Fz, Cz and Pz in the 340-440 msec post-stimulus (peaking at about 380 msec at centro-parietal electrodes).

Statistical analysis

LEP amplitude on N1 were analyzed by means of a three-ways mixed design ANOVA with Manipulation (two levels: OM and TP) and Condition (three levels: Fair win, Unfair Loss and Fair Loss) as within subjects factors and Group (two levels: Believers and Non-Believers) as a between subjects factor.

Values of N2/P2, N2 and P2 LEP amplitude were entered in a four-ways repeated measures mixed ANOVA with Electrode (three levels: Cz, Fz, Pz), Manipulations (two levels: OM and TP) and Condition (three levels: Fair win, Unfair Loss and Fair Loss) as within subjects factors and Group (two levels: Believers and

Non-Believers) as a between subjects factor. All *Post-hoc* comparisons were performed using the Newman Keuls test.

Measures of Fairness, Intensity and Unpleasantness of pain perception were entered in separate three-ways mixed ANOVA with Condition (three levels: Fair win, Unfair Loss and Fair Loss) and Manipulation (two Levels: OM and TP) as within subjects factor, and Group (two levels: Believers and Non-Believers) as between subjects factor.

Correlation analysis:

To test any functional relationship between each electrophysiological dependent variable and self-reported pain measures significantly modulated by each given condition (e.g. P2b amplitude observed during 'Unfair Loss' and intensity ratings during this condition in Believers), we computed Pearson's r correlation coefficients. The Bonferroni-corrected p value was .016. This value was obtained correcting the standard p ¼ .05 by the number of comparisons for each condition (Fair Win, Unfair Loss and Fair Loss), each rating type (intensity), separately for each group (Believers and Non-Believers) (i.e., three comparisons).

4.4 Results

Manipulation check

According to the manipulation check question, participants were divided in two groups (Believers: n=8, mean=71.12, sd=12.12; Non-Believers: n=8, mean= 22, sd=18.15 test-t=6.21 $p<0.001$).

Subjective ratings

Fairness. Results of the three-ways mixed ANOVA indicated a significant main effect Condition ($F_{(2,28)}= 36.98, p<0.0001, \eta_p^2=0.72$) accounted by lower scores in the Unfair Loss with respect to Fair Win ($p<0.001$) and Fair Loss ($p<0.001$) conditions. Moreover, results showed a significant effect between conditions of Fair Win and Fair Loss ($p=0.022$) (Figure 4.2 A). No significant interactions were found between Manipulation, Condition and Group ($p>0.05$).

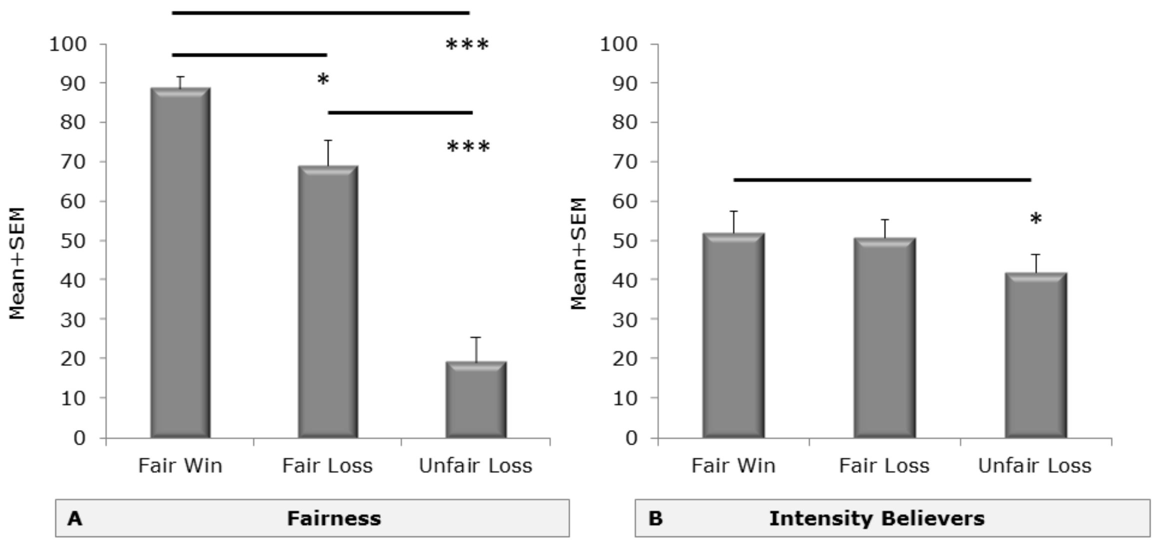

Figure 4.2. **A) Fairness reports.** All participants (n=16) reported lower fairness scores in the Unfair Loss condition with respect to the Fair Win *($p<0.001$)* and to the Fair Loss *($p<0.001$)*. Participants also reported lower scores in the Fair Loss condition with respect to the Fair Win *($p=0.02$).* **B) Intensity reports.** Those who believed to be playing with human participants (n=8) reported lower scores when they experienced an Unfair Loss than a Fair Win *($p=0.0068$)*. These results was present both when participants were playing with their own money, and when they were playing on behalf of somebody else.

Pain Intensity and Unpleasantness. Results of the three-ways mixed ANOVA indicated a significant interaction between Condition and Group *($F_{(2,28)=}$ 4.77, $p= 0.016$, $\eta_p^2=0.25$)* accounted for by lower scores of Intensity in the Believer for the Unfair Loss condition with respect to the Fair Win condition (*$p<0.01$*) (Figure 4.2 B). No other significant effects were found *(all ps>0.05)*.

No significant effects were found for the Unpleasantness scores *(all ps>0.05)*.

Laser evoked potentials

N2/P2 amplitude: Results obtained from the four-ways repeated measures ANOVA showed a significant main effect of Electrode *($F_{(2,28)=}$ 12.40, $p< 0.001$, $\eta_p^2=0.46$*) mainly accounted for by higher amplitude of N2/P2 on Cz with respect to Fz *($p<0.001$)* and Pz *($p<0.001$).* The comparison between Pz and Fz did not reach the significance *($p>0.05$)*. No other main effects were found *($p>0.05$)*. Furthermore, results revealed a significant triple interaction between Manipulation, Condition and Group *($F_{(2,28)=}$ 6.18, $p= 0.0059$, $\eta_p^2=0.30$).* Post-hoc test showed that in the Believers' Group, OM manipulation, the amplitude of the N2/P2 complex, was reduced in the Unfair Loss with respect to Fair Loss *($p=0.05$)*; In addition the Unfair Loss, OM manipulation, is lower with respect to Fair Win *(p=0.046)* and Unfair Loss *(p=0.001)*, TP condition.

Since previous analysis confirmed that N2/P2 is maximally represented on Cz, we performed a separate three-ways mixed ANOVA only on Cz amplitude. Results revealed a triple significant interaction between Manipulation, Condition and Group ($F_{(2,28)}= 4.86$, $p= 0.015$, $\eta_p^2=0.25$) mainly accounted for by lower N2/P2 amplitude in the Unfair Loss, OM manipulation, with respect to Unfair Loss, TP manipulation (see Figure 4.3) .

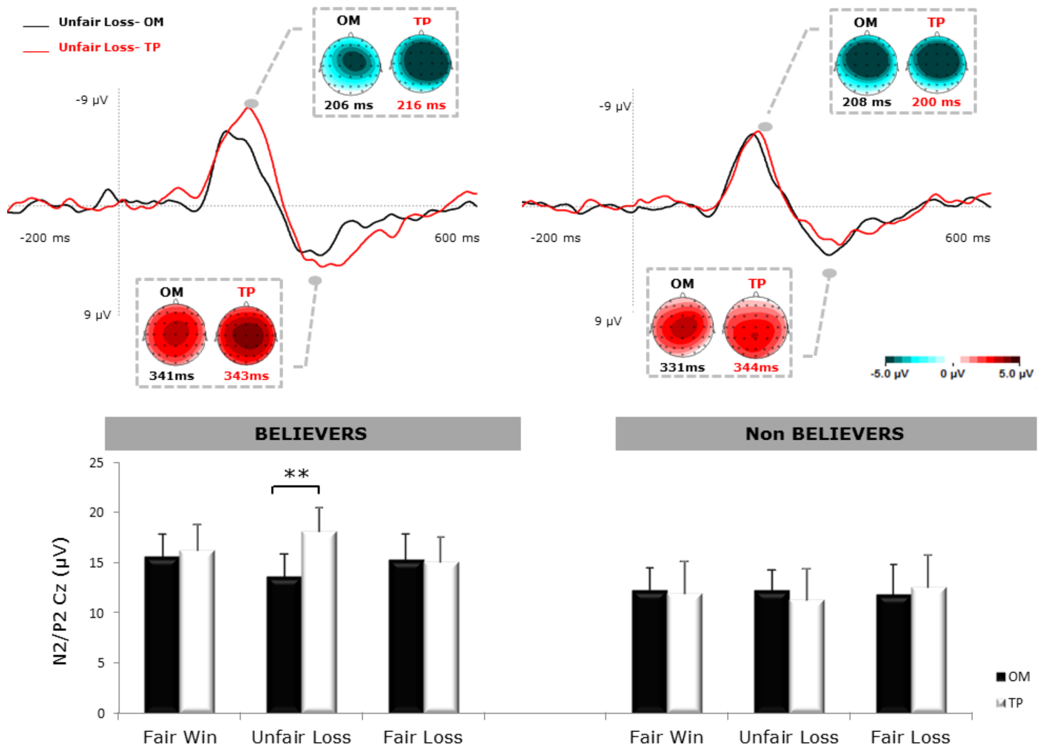

Figure 4.3. The figure shows the N2/P2 amplitudes recorded on Cz electrode in Believers' group (left) and Non-Believers' group (right). **Up:** Average LEP waveforms in the Unfair Loss condition. Waves and topographies of peak amplitude are shown for the OM (black) and TP (red) manipulation. **Down:** N2/P2 amplitudes in the different conditions. Black bars represent the OM manipulation, while white bars represent the TP manipulation.

N2 amplitude: The four-ways mixed ANOVA performed on N2 amplitude showed a main effect electrode *($F_{(2,28)=}$ 15.07, p< 0.001)*. Post-hoc test revealed higher amplitude on Cz with respect to Pz *(p<0.001)* and Fz *(p=0.002)*. In addition, lower N2 amplitude was found for Pz electrode with respect to Fz *(p=0.042)*. No other main effects or interactions were found (p>0.05). Based on these results, we repeated the analysis on Cz and Fz.

The three-ways mixed ANOVA performed on Fz showed a significant interaction between Manipulation, Condition and Group *($F_{2,28}$=4.92, p=0.014)* which was accounted for by lower N2 amplitude, in the OM manipulation, for the Unfair Loss with respect to the Fair Win *(p=0.014)*, Unfair Loss *(p=0.019)* and Fair Loss *(p= 0.02)* in the TP manipulation (Figure 4.4 A). No other main effects and interactions were found *(p>0.05)*.

The same analysis performed on Cz did not reveal any significant main effect or interaction *(all Ps>0.05)*.

P2a amplitude:

The four-ways mixed ANOVA performed on P2a showed a main effect electrode *($F_{(2,28)=}$ 5.22, p= 0.011, η_p^2=0.27)* accounted for by higher amplitude of the P2a on Cz with respect to Fz *(p=0.024)* and Pz *(p=0.0093)*. The comparison between Fz and Pz failed to reach the significance (p>0.05). Furthermore results showed a triple interaction between Manipulation, Condition and Group *($F_{(2,28)=}$ 4.39, p= 0.021,*

$\eta_p^2=0.23$). Post-hoc comparisons revealed that the amplitude of the P2a for the Unfair Loss tended to be reduced in the OM Manipulation, compared with Unfair Loss in the TP manipulation ($p=0.054$). Moreover, when participants were playing in the TP manipulation, the amplitude of the Unfair Loss tended to be higher than that of the Fair Loss ($p=0.057$) (Figure 4.4. B). Importantly, these tendencies were present only in those who believed in the experimental manipulation.

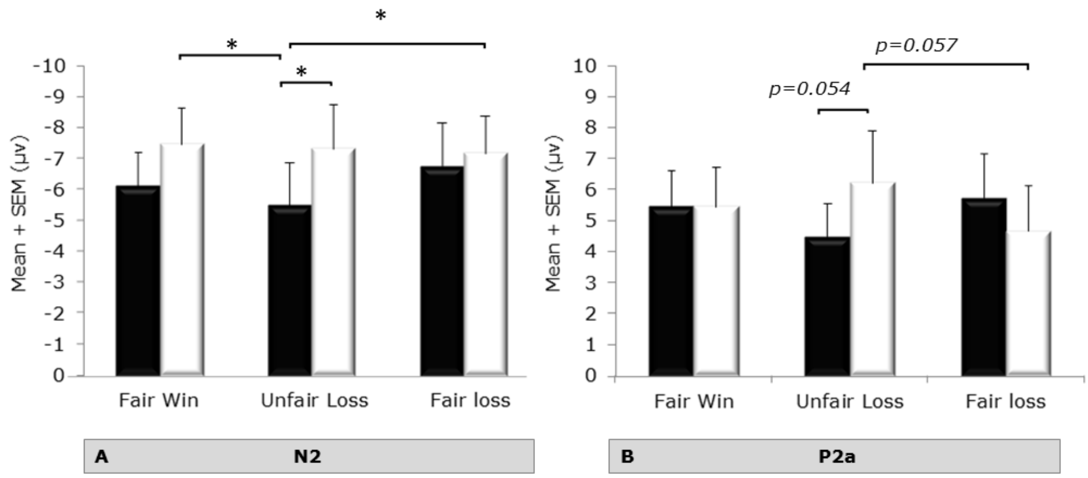

Figure 4.4 The figure represents N2 and P2a amplitudes in Believers' group (n=8). **A)** Mean and Standard errors of the N2 amplitudes recorded on Fz electrode in all the three conditions. **B)** Mean and Standard errors of the P2a amplitudes recorded on Fz, Cz and Pz electrodes in all the three conditions. Black bars represent the OM manipulation and white bars the TP manipulation.

Then, we performed a separate three-ways mixed ANOVA on Cz. Results showed a significant interaction between Manipulation, Condition and Group ($F_{(2,28)}= 4.16$, $p= 0.026$). Post-hoc test revealed that the amplitude of the P2a in the Unfair Loss condition, tended to be reduced in the OM Manipulation, compared with Unfair Loss in the TP ($p=0.06$). Interestingly, we found higher P2a amplitude in the Unfair Loss, TP manipulation, with respect to Fair Win ($p=0.03$).

P2b amplitude: The four-ways mixed ANOVA showed a main effect of electrode *($F_{(2,28)=}$ 8.07, p= 0.0017, η_p^2=0.36)* which was accounted for by lower P2b amplitude in Fz with respect to Cz *(p=0.013)* and to Pz (p=0.0014). The comparison between Cz and Pz did not reach the significance (p>0.05). Moreover a triple interaction between Condition, Manipulation and Group *($F_{(2,28)=}$ 3.55, p= 0.042, η_p^2=0.20)* was found. *Post-hoc* comparisons revealed that only in the Believers' group, the amplitude of the P2b in the Unfair Loss in the OM Manipulation, was reduced as compared to all the others conditions of TP Manipulation (all *ps<0.05*). Moreover, it tended to be reduced as compared to Fair Loss in the OM manipulation (*p=0.07*) (Figure 4.5).

Then, we performed separate three-ways mixed ANOVA for Cz and Pz electrodes. Results on Cz did not show any significant effects or interactions (all Ps>0.05). The same analysis performed on Pz showed only a significant main effect Condition (*$F_{(2,28)=}$ 3.99, p= 0.029, η_p^2=0.22)*. Post-hoc test revealed that the amplitude of Pz in the Unfair Loss was significantly lower than Fair Loss *(p=0.02)*.

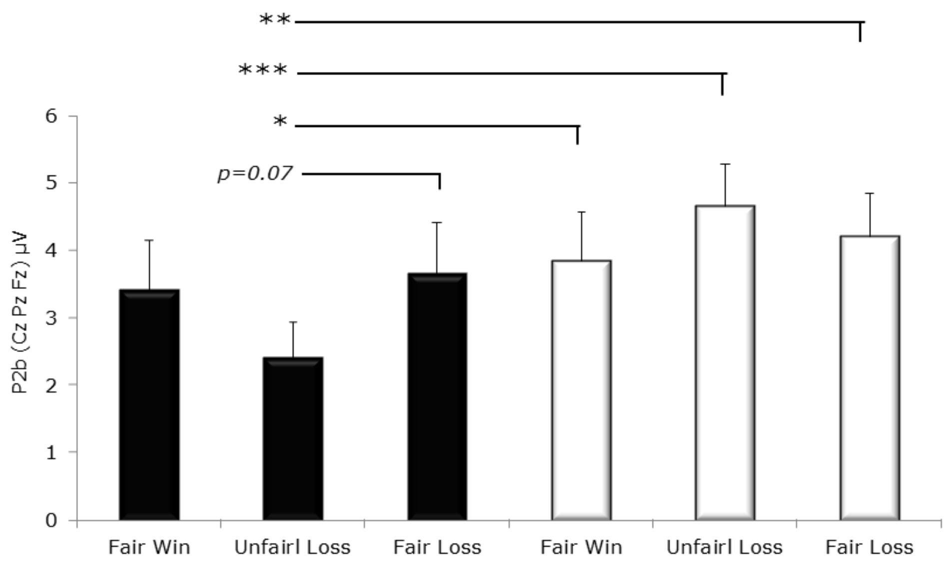

Figure 4.5. The figure represents P2b amplitudes recorded on Fz, Cz and Pz electrodes in the Believers' group (n=8). Black bars represent the OM manipulation and white bars the TP manipulation.

***N1* peak to baseline.** The three-ways repeated ANOVA performed on N1 amplitude did not show any significant effects or interactions *($p>0.05$)*.

Correlations

A strong significant correlation was found in the Believers' group between the amplitude of the P2b component recorded in Pz and the self-reported intensity in the Unfair Loss condition *($r=0.84$, $p=0.008$)*, indicating that those who presented lower P2b amplitude values also reported to perceive less intense pain (Figure 4.6). Importantly, when performing the same correlation in the Non-Believers' group, no significant effects were found *($p_s>0.05$)*. We did not observe any significant correlation between self-reported measures of intensity and the amplitude of the vertex complex N2/P2, or the P2a *($p_s>0.05$)*.

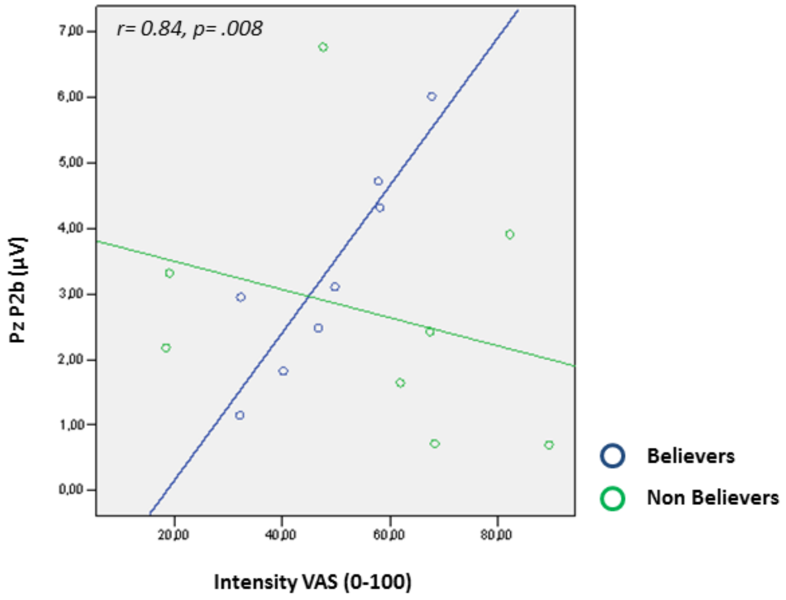

Figure 4.6 The figure represents the correlation between P2b amplitude recorded in Pz (Y axis) and participant's intensity reports (X axis). Blue dots represent Believers' group (n=8), while green dots Non-Believers' group (n=8).

4.5 Methodological considerations

During the data collection we observed that several participants reported to believe they were playing against a computer, whereas some others reported to be very involved in the interaction with their opponents (please see manipulation check). Consequently, we preferred to analyze our data in a between fashion, in order to use those who did not believe in the social nature of our task as a control sample. Thus, the effects found in this study may be potentially reduced by the low-dimensionality of each group.

4.6 Discussion

In this study we provide evidence that the being in an unfairness social context induces a reduction of pain intensity elicited by laser stimulation. Notably, only those who believed in the social nature of our task reported lower intensity scores in the Unfair Loss condition than in the Fair Win condition, irrespectively of the fact that they were playing with their own money or on behalf of a third party. In addition, we found a specific amplitude reduction of laser evoked potentials and topographic changes in condition of unfair loss. The neurobiological implication of these effects are described in details in the next sections.

Behavioural measures

Fairness scores reported in the different conditions indicate that our paradigm was effective in producing different fairness contexts. Fairness ratings show that participants rated the Unfair Loss condition less fair with respect to the other two conditions, independently of the fact that they were losing their own money. Interestingly, however, only those who believed in the social nature of our manipulation reported to experience less intense pain in the Unfair Loss condition with respect to the Fair Win condition. We already highlighted the peculiar relation between pain and money (see introduction) and argued that money can be seen as a pain buffer (Zhou et al., 2009). Of particular relevance for the present study, is the observation that a money loss conditioning can alter perceptual threshold as compared to a neutral conditioning. Indeed, a monetary loss associated with a pure tone decreased sensitivity and increased perceptual threshold of participants performing an auditory task (Laufer and Paz, 2012). Was this the case however participants should have reported decreased intensity scores only when they were losing their own money. Instead the reduction effect showed by our participants was independent of the block (OM or TP) in which they were playing. Recently, Baumaister et al. (2006) showed that a context of social pain (i.e. *the experience of being excluded or devalued by relational partners or groups*, MacDonald and Leary 2005) caused a broad decrease in physical pain sensitivity. Authors argued that this physical numbness was related to the emotional numbness presented by the same subjects in reaction to social exclusion (DeWall and Baumeister 2006). Specifically, they proposed that certain interpersonal events, such as social rejection, activate the body's pain response system (Panskepp, 1998; Eisenberg et al., 2003) and potentially alter how it registers physical pain in order to minimize emotional distress. We believe that the reduction of pain intensity scores presented by the Believers' group in our task is mainly accounted for by an attentional shift towards the game due to the belief that a human opponent is intentionally being unfair. Indeed, those who believed to be playing against a computer did not show any difference in their Intensity reports. Furthermore unpleasantness ratings were equivalent across conditions both in Believers and in Non-Believers. This observation is in line with the notion that social rejected people frequently report emotional states that do not differ significantly from socially accepted and control participants (Gardner et al., 2000; Twenge et al., 2002; Baumeister et al., 2002; Zandro et al., 2004).

LEPs Modulation: vertex components

We found that the amplitude of the entire N2/P2 complex was decreased when participants believed to be losing their own money due to the defection of a human opponent, as compared to the condition in which they lost their money in the context of a fair social interaction (i.e. Fair Loss condition). Moreover, the complex was reduced when participants lost their money after an unfair social interaction as compared to all the conditions in which they were playing on behalf of a third party. Consistently with existing literature, the N2/P2 complex recorded in the present study was maximally represented over the vertex (i.e. Cz). This complex is thought to originate in the ACC (Garcia-Larrea et al., 2003), a region involved in different higher order functions such as attentional shifts and response selection (Paus, 2001; Bantick et al. 2002). Likewise, there are several indications that the processing of nociceptive stimuli is suppressed when selective attention (Corbetta and Shulman 2002; Posner and Petersen, 1990) is strongly focused on a concurrent task goal (Seminowicz and Davis, 2007; Van Damme et al., 2010). In studies where the whole N2/P2 was considered, the vertex complex appeared to be strongly inhibited by distraction as compared to when the stimulus was attended (Garcia-Larrea et al. 1997; Friederich et al. 2001; Siedenberg and Treede, 1996; Yamasaki et al. 2000).

In a similar vein the N2 component had a maximal distribution over the vertex. However, the effects of the social manipulation were observed on the activity of a more frontal electrode (i.e. Fz), suggesting a topographic change. There, a selective reduction of the N2 amplitude was present during trials in which Believers underwent an unfair monetary loss with respect to all the conditions in which they were playing on behalf of a third party. The N2 component has been shown to be susceptible to an attention related reduction (Legrain et al., 2002). In the present study, we cannot exclude that the attention of participants could have been selectively captured by the unfair reduction of their own finances. However, it is worth noting that such effect was found only in the Believers group.

Also the P2a presented lower amplitude in the Unfair loss, OM manipulation with respect to the Unfair Loss, TP manipulation. Moreover, in the TP manipulation, lower amplitudes were observed in the Fair Loss condition with respect to the Unfair Loss condition. This latter finding could indicate that, when participants' payoff is not affected, but participant are responsible for the loss, losing someone else's money is more salient. Similarly, studies which separately analyzed the amplitude of the P2a component, reported a reduction of the magnitude of the vertex positivity when attention was directed to the pain-unrelated task (Yamasaki 1999; Valeriani et al. 2002; Legrain et al., 2005).

In our study participant's selective attention could have been captured by the saliency of the Unfair Loss condition reflecting a threat to the goal of winning as much money as possible (i.e. the main goal of our task). However, this explanation seems unlikely for this goal was shared also by those who believed to be playing against a computer (i.e all participants are really winning or losing money, independently of their belief in the real presence of an opponent).

It is likely that, for the Believers, the unfair behaviour of an opponent is more salient when is directed towardss them than towardss a third party. Indeed, this behaviour could signal a personal threat to belongingness which resulted in a shift of attention away from the painful stimulation and consequently into the vertex components reduction.

LEPs Modulation: P2b

The analysis of the electrodes on the median line, showed a that the P2b component tended to be reduced when participants were losing unfairly their own money as compared to those in which the loss was fair. Moreover, it was reduced as compared to all the trials in which they were playing on behalf of somebody else. This reduction was selective for the believers' group. The P2b has been associated to temporal and parietal cortices generators (Bledowski et al., 2004) and its parietal topography may be associated to a major involvement of the PPC (Legrain et al., 2009b). However, in our study P2b was not clearly distributed on a parietal topography, its amplitude being equal in Cz and Pz. When analyzing Pz amplitude only, all 16 participants presented a reduction of the P2b component during the Unfair Loss condition. This late component usually follows the laser stimulation, and is considered as an equivalent of the cognitive ''P300'' wave (Kanda et al. 1996; Legrain et al. 2002; Legrain et al. 2003; Siedenberg and Treede 1996; Towell and Boyd 1993). The P300 wave, has been extensively studied in auditory, visual and somatosensory modalities and it has been associated to cognitive closure, memory encoding and stimulus access to consciousness (reviews in Hansenne 2000; Picton, 1992; Valentini et al. 2012). Thus, our result may imply a reduced activation of the neural processes related to the detection of the attended stimulus while participants undergo an unfair loss. In line with this interpretation, we found that those participants who presented lower P2b amplitude, recorded on Pz electrode, also reported lower scores of intensity of the painful stimulation. Interestingly, this relation held true only for the participants who perceived the unfair behaviour as intentional, possibly suggesting that a reduction of cognitive appraisal of the painful stimuli occurred just in this group.

LEPs modulation, early components

In our study, N1 amplitudes were not modulated by different conditions. This results is consistent with the observations that reduced attentional load to the incoming laser stimulus could induce a strong reduction of the vertex N2/P2 complex (Siedenberg and Treede, 1996; Garcia-Larrea et al., 1997; Yamasaki et al., 1999), whereas no significant variations of the earlier N1 wave amplitude can be appreciated (see Lorenz and Garcia-Larrea , 2003; Garcia-Larrea et al., 1997, Yamasaki et al., 1999).

4.7 Conclusions

Taken together our results indicate that a social context characterized by the violation of social norms strongly influence both self-reported pain intensity and LEPs. We argue that this reduction was mediated by an attentional shifting process that distracted participants from the painful stimulation in the condition that was more salient for them (i.e. the Unfair Loss condition). It is worth noting that this condition was effective in reducing pain specifically in the participants that believed that the loss took place in a real social environment. Moreover, in these participants the vertex components (i.e. N2, N2/P2 and P2a) were selectively reduced when participants experienced the unfair loss of their own money. Therefore we speculate that for these participants, the saliency of the Unfair Loss could be more emotional than cognitive in nature.

Chapter 5

General Discussion

The cooperative nature of human society is built upon social norms such as fairness. The breaking-off of these norms represents a threat to social cohesion among groups and thus for the individual. The general aim of this project was to explore the relation between fairness norm and bodily states.

We provided evidences that bodily states such as enhanced interoception and pain affect social preferences and economic interactions. Moreover, we showed that an unfair social context modulates pain perception and LEPs. Taken together our results allow two important considerations.

Enhanced interoception and pain differently modulate fairness releated conducts

Some negative emotions like induced disgust (Moretti and di Pellegrino 2010), or sadness (Harlé and Sanfey, 2007) modulate social preferences by enhancing rejecting behaviour which has been connected to the perpetuation of social norms (Guth et al., 1982).

Conversely we showed that bodily signals such as pain and the sound of one's own heart seem to promote a self-centered perspective.

In study one, we demonstrated that first-hand experience of pain strongly modulates the strategic economic interaction in participants playing either the responder or the proposer role. In particular, we showed that feeling pain makes an individual less inclined to behave according to the social norms (e.g. punishment of defectors) that regulate most social and economic interactions.

In study two we manipulated a key element of emotional experience that is the integration of information about the internal bodily state and the external environment (Damasio, 1994; Craig, 2009; Critchley, 2009). We devised a new and valuable procedure to manipulate interoceptive awareness online, to study the influence of interoceptive information in decision-making in socioeconomic exchange scenarios and we showed that providing online interoceptive feedback enhanced subjective feelings of unfairness in response to unfair offers, and increased the amount of unfair offers during a bilateral version of the UG.

However pain and enhanced interoception affected economic behaviour in different ways. Indeed suffering participants presented a behaviour aimed at maximizing their monetary income. This was not the case for participants in study two which presented a general tendency to be focused on their own perspective without trying to maximize self-gains. This difference could be ascribed to the peculiar relation between pain and money.

Experimental evidences suggested the brain basis of monetary losses are similar to those of physical pain (Knutson et al., 2007, Paulus Stein, 2006) and that money acts as a pain buffer. Specifically, handling money (compared with handling paper) reduced distress over social exclusion and diminished the physical pain of immersion in hot water (Zhou et al., 2008). Money is a social resource that provides a broad capability for dealing with problems and securing benefits. Hence the idea of having money should be associated with feelings of strength, efficacy, and confidence, and those feelings should help buffer against social rejection and physical pain. In line with the proposed interpretation, prior work has linked feelings of efficacy to pain tolerance, hardiness, resilience, and interpersonal success (Litt, 1988; McFarlane, Bellissimo and Norman, 1995).

Unfair behaviour shifts attention away from painful stimulation as a function of intentionality

In general, we argued that the salience of the Unfair Loss condition, oriented participants' attention away from the noxious stimulation, resulting in a decrease of both pain sensitivity and LEPs amplitude. In principle, this effect could be accounted for by a higher cognitive load associated with the Unfair Loss condition. Indeed in this condition participants winning expectancies are violated by a subsequent loss. In an EEG study by Legrain et al. (2005), subjects were presented with concomitant visual and nociceptive stimuli. The task was to report the number of items (between one and four) on each visual display. The effect of cognitive engagement was examined by manipulating the cognitive load of the visual task. Higher cognitive load resulted in decreased amplitude of the P2a cortical potential evoked by the concomitant nociceptive stimuli, reflecting attenuated orienting of attention to these stimuli. However, it is worth noting that the P2a amplitude in our study was reduced in believers only, and selectively during the blocks in which participants were playing with their own money. Importantly the amount of cognitive load of the Unfair Loss condition was identical in the two manipulations (OM and TP) and among groups, the only difference being in the appraisal of losing own money due to an intentional unfair behaviour. Recently, Legrain and collaborators (2011) proposed a theoretical framework in which brain responses to nociceptive stimuli could represent a salience detection system for the body. The salience of a given stimulus can derive by the relevance of the stimuli in relation to the subject's cognitive goals and on the effort exerted to achieve these goals (Legrain et al. 2012). Moreover these authors argued that the cortical correlates of pain are strongly influenced by the context within which the nociceptive stimuli appears (Legrain et al., 2011). Therefore, our results highlights that a social context characterized by the violation of social norms strongly influence pain processing. Furthermore, only those who believed to be playing against a human participant reported reduced intensity scores in the Unfair Loss condition, suggesting that the salience of the Unfair Loss condition with respect to the other conditions could be related also to emotional factors connected to the threat to social belongingness signaled by the breaking-off of the social norm of fairness.

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APPENDIX A

Chapter number and title	Original text (not published before)	Submitted: no feedback received	Submitted: revision requested or revision submitted	Accepted/published (specify journal or book)
1.Introduction (partly published)				**PloS ONE (Mancini et al., 2011)**
2. Chapter Two: "Suffering Makes You Egoist: Acute Pain Increases Acceptance Rates and Reduces Fairness during a Bilateral Ultimatum Game"				**PloS ONE (Mancini et al., 2011)**
3.ChapterThree: "Listen to your heart and tune to yourself– a manipulation of interoceptive awareness during the Ultimatum Game"	X In preparation			
4.ChapterFour: "Does unfairness hurt? A laser evoked potentials study"	X In preparation			
5. General Discussion	X			

Other Papers:

Addessi, E., **Mancini, A.**, Crescimbene, L. & Visalberghi, E. (2011). How Social Context, Token Value, and Time Course Affect Token Exchange in Capuchin Monkeys (*Cebus apella*). *International Journal of Primatology*, 32:83–98.

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