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Concerning empathy.

LIST OF CONTENTS

ABSTRACT	7
LIST OF ABBREVIATIONS	8
1 INTRODUCTION	9
1.1 EMPATHY IN GENERAL AND EMPATHY FOR PAIN	9
1.2 PROSOCIAL BEHAVIOUR	13
1.3 STRESS AND ITS EFFECTS ON EMPATHY AND PROSOCIAL BEHAVIOUR	13
1.4 AIM AND CONTEXT OF THE PRESENT MASTER THESIS	17
2 HYPOTHESES	18
3 MATERIALS AND METHODS	19
3.1 PARTICIPANTS	19
3.2 TASKS	20
3.2.1 MONTREAL IMAGING STRESS TASK	20
3.2.2 EMPATHY FOR PAIN PARADIGM	20
3.2.3 PROSOCIAL TASK	21
3.2.4 TEST D2	22
3.3 PROCEDURE	22
3.4 STRESS MEASURES	23
3.5 FMRI DATA ACQUISITION	24
4 DATA ANALYSIS	25
4.1 STRESS MEASURES	25
4.1.1 CORTISOL	25
4.1.2 STRESS AND MOOD RATINGS	25
4.2 BEHAVIOURAL DATA	26
4.2.1 EMPATHY FOR PAIN PARADIGM	26
4.2.2 PROSOCIAL TASK	26

4.2.3 TEST D2	26
4.3 FMRI DATA.....	27
4.3.1 WHOLE BRAIN ANALYSES	27
4.3.2 ROI ANALYSES.....	28
5 RESULTS.....	29
5.1 STRESS MEASURES	29
5.1.1 CORTISOL.....	29
5.1.2 STRESS AND MOOD RATING	29
5.2 BEHAVIOURAL DATA.....	30
5.2.1 EMPATHY FOR PAIN PARADIGM.....	30
5.2.2 PROSOCIAL TASK	31
5.2.3 D2	31
5.3 FMRI DATA.....	32
5.3.1 WHOLE BRAIN ANALYSES	32
5.3.2 ROI ANALYSES	36
6 DISCUSSION.....	37
6.1 STRESS AND MOOD MEASURES.....	37
6.2 EMPATHY FOR PAIN	37
6.3 BEHAVIOURAL DATA.....	42
6.4 GENERAL DISCUSSION	43
7 CONCLUSION	46
8 REFERENCES.....	47
ZUSAMMENFASSUNG	64
CURRICULUM VITAE.....	66

Abstract

So far, effects of stress on empathy have only been assessed on a behavioural level. Therefore, the aim of this master thesis was to assess how acute psychosocial stress impacts the neural underpinnings of empathy, ascertained through an empathy for pain paradigm. We further examined effects of stress on prosocial behaviour, since literature has revealed that it is directly linked to empathy. Therefore empathic reactions of 74 males, randomly assigned to experimental and control group, were tested through the usage of behavioural analyses, as well as functional magnetic resonance imaging (fMRI). Stress was induced by the Montreal Imaging Stress Task (MIST), consisting of mental arithmetic, time pressure and social evaluation. Cortisol, as well as ratings of subjective stress were thereby repeatedly collected from all subjects.

Our study extends existing behavioural evidence of tend-and-befriend patterns in male individuals in consequence to stress. Subjects who were exposed to the psychosocial stressor showed enhanced emotion contagion when empathizing with a person suffering from pain (needle injection in a target hand). Even when they received additional contextual information (target hand is numbed) they activated a great variety of areas of the empathy for pain network, indicating an automatic bottom-up generation of empathic responses in consequence to stress. Enhanced prosocial responses were also found on a behavioural level, whereby participants acted more generous towards others when exposed to the stressor.

This study is the first to show that male tend-and-befriend patterns in consequence to stress can also be found on a neural level.

List of abbreviations

ACC	anterior cingulate cortex
ACTH	adrenocorticotropin hormone
AI	anterior insula
aMCC	anterior medial cingulate cortex
ANOVA	analysis of variance
AUC _G	area under the curve with respect to ground
AUC _I	area under the curve with respect to increase
BSI	Brief Symptom Inventory
CRH	corticotropin-releasing hormone
d2	Test-d2-Aufmerksamkeits-Belastungs-Test
dIPFC	dorsolateral prefrontal cortex
dmPFC	dorsomedial prefrontal cortex
EC	Emotion Contagion Scale
fMRI	functional magnetic resonance imaging
HPA	hypothalamus-pituitary-adrenal
IFG	inferior frontal gyrus
IPC	inferior parietal cortex
IRI	Reactivity Index
l	left
LSAS	Liebowitz Social Anxiety Scale
MIST	Montreal Imaging Stress Task
mPFC	medial prefrontal cortex
MSWS	Multidimensional Self-Concept Scale
OFC	orbifrontal cortex
PS	Perceived Stress Scale
r	right
RMET	Reading the Mind in the Eyes Test
ROI	region of interest
SFG	superior frontal gyrus
SMG	supramarginal gyrus
T	Timepoint
TPJ	temporo-parietal junction

1. Introduction

A mutual understanding of the mental and affective states of oneself and other individuals is essential for human interactions of all kinds (Singer & Lamm, 2009). It enables us to put ourselves in the position of someone else and even to share their representations to a certain extent (Singer & Lamm, 2009). The understanding and sharing of observed emotions can thereby be underpinned by the activation of neural circuits involved in personal experiences of the exact same emotions (shared network hypotheses; e.g. de Vignemont & Singer, 2006; Lamm, Decety, & Singer, 2011). This way we can feel others' emotions "as if they were our own" (de Vignemont & Singer, 2006, p. 435; Singer & Klimecki, 2014).

The ability of perceiving or imaging, understanding and sharing the affective states and experiences of other individuals can be summarized under the term empathy (Singer & Lamm, 2009).

1.1 Empathy in general and empathy for pain

To distinguish between empathy and related concepts, such as mimicry, emotion contagion, sympathy and compassion (for more detail see Singer & Lamm, 2009 or Bernhardt & Singer, 2012), four components to identify empathy were defined (de Vignemont & Singer, 2006)

(i) one is in an affective state; (ii) this state is isomorphic to another person's affective state; (iii) this state is elicited by the observation or imagination of another person's affective state; (iv) one knows that the other person is the source of one's own affective state. (de Vignemont & Singer, 2006, p. 435).

There are two present routes for the generation of empathic reactions (Engen & Singer, 2012). In case of concrete visual stimuli of a specific emotional state of another individual (e.g. suffering in response to pain) they can be initiated by a simple action-perception-observation and simulation of the perceived affective state (Engen & Singer, 2012). On a neural basis this activates brain regions associated with emotion contagion, action observation / anticipation and the bottom-up generation of emotion, such as the anterior insula (AI), anterior cingulate cortex (ACC), midbrain of the brain stem, inferior parietal cortex (IPC), dorsolateral and dorsomedial prefrontal cortex (dlPFC; dmPFC) and inferior frontal gyrus (IFG), pars

opercularis (Engen & Singer, 2012; Lamm, Nusbaum, Meltzoff, & Decety, 2007).

The second, more cognitive route takes its place in case of missing perceptual evidences (Engen & Singer, 2012) or a lack of externally provided sensory information (Lamm et al., 2011). For proper attributions about the affective state of another person, one can avail himself / herself of representations of the potential mental state of the other (Engen & Singer, 2012). This requires the ability of perspective taking and knowledge of the surrounding situation or self- and other-related social information, which in turn yearns for processes of the theory of mind and mentalizing (Engen & Singer, 2012). Associated brain areas are the precuneus (e.g. David et al., 2008), the temporo-parietal junction (TPJ; e.g. Ruby & Decety, 2003; Saxe & Kanwisher, 2003) and the medial prefrontal cortex (mPFC; e.g. Mitchell, Banaji, & Macrae, 2005; van Overwalle & Baetens, 2009). The ability of perspective taking and in further consequence of empathizing with another person is thereby mediated by two important factors, which were also implied in the empathy definition of de Vignemont and Singer (2006): self-awareness and the ability to distinguish between emotional experiences of the self and the other (self/other distinction; Decety & Jackson, 2004; Decety & Lamm, 2006). Without an appropriate self/other distinction, neuroanatomically linked to an activation in the TPJ (e.g. Ruby & Decety, 2003) and supramarginal gyrus (SMG; e.g. Decety & Lamm, 2007), experiencing affective states of another individual could for example lead to “an aversive, self-focused emotional reaction to the apprehension or comprehension of another’s emotional state or condition” (Decety & Lamm, 2009, p. 199) and this in turn can lead to personal distress (Eisenberg & Fabes, 1990; Singer & Lamm, 2009).

The collaboration of the two neuroanatomical distinct routes to empathy – the perception based or basic emotional contagion system and the inference based or advanced cognitive system (Shamay-Tsoory, Aharon-Peretz, & Perry, 2009) – allows us to accurately represent the affective states of other individuals (Engen & Singer, 2012).

One prominent way to examine empathy in scientific settings is through the domain of empathy for pain. The observation of pain in others is one of the latest common accesses for analysing the neural underpinnings of empathy (for a review see Lamm et al., 2011; Singer & Klimecki, 2014), beside studies concentrating on for instance

disgust (e.g. Wicker et al., 2003), taste (Jabbi, Swart, & Keysers, 2007), reward (Mobbs et al., 2009), touch (e.g. Keysers et al., 2004; Lamm, Silani, & Singer, 2015), social exclusion (Masten, Morelli, & Eisenberger, 2011), anxiety (Prehn-Kristensen et al., 2009) or sadness (Harrison, Singer, Rotshtein, Dolan, & Critchley, 2006). It has been found that seeing someone in pain elicits the same neural network involved in the first-hand experience of pain (e.g. Singer & Lamm, 2009). These results were found among couples (Singer et al., 2004), unfamiliar individuals (depicted human facial expressions of pain; Botvinick et al., 2005; Lamm, Batson, & Decety, 2007), as well as in individuals who were only perceiving pictures of several human body parts in pain (e.g. Jackson, Brunet, Meltzoff, & Decety, 2006; Lamm, Nusbaum, et al., 2007). In all cases resonating with such inconvenient experiences of other individuals led to an activation in large parts of the pain matrix (Derbyshire, 2000) associated with nociception and pain processing, similar to the ones involved in experiencing pain oneself (e.g. Singer & Lamm, 2009; Lamm, Nusbaum, et al., 2007, Lamm, Decety, & Singer, 2011).

The core-network of pain empathy is thereby composed of the anterior medial cingulate cortex (aMCC) and bilateral AI, as for instance indicated through a meta-analysis by Lamm et al. (2011). The authors analysed 32 functional magnetic resonance imaging (fMRI) studies which examined pain empathy through cue-based (cues indicating painful electrical stimulation for either the target person or participant him/herself) and picture-based paradigms (depicted human limbs in painful situations), and found that particularly these specific regions, which have been linked to the affective-motivational component of pain (e.g. Lamm, Nusbaum, et al., 2007), were consistently activated across all studies. Further significant brain responses, commonly related to pain empathy were found in posterior ACC, middle and fronto-insular cortex (bilateral IFG, pars opercularis, area 44; ventral frontal operculum), bilateral IPC (SMG, pre- and postcentral gyrus), left thalamus, dorsal mPFC, dorsal premotor cortex, bilateral dlPFC and amygdala (Lamm et al., 2011). Concerning differences between both paradigms picture-based studies recruited stronger activations of areas associated with action understanding, whereas cue-based studies revealed stronger activations in areas associated with theory of mind or mentalizing (Lamm et al., 2011). The AI and aMCC are also the key regions for emotion contagion, which has been considered as automatic response before (Preston & de Waal, 2002; Decety & Lamm, 2006; Singer & Lamm, 2009).

One of the reviewed studies assessed the hemodynamic and behavioural changes of focussing on the affective vs. the sensory consequences of painful (needle injections in human hand) and putatively harmful, but actual non-painful situation (needle injection in anaesthetised hand; Lamm, Nusbaum, et al., 2007). On a behavioural level stimuli depicting painful needle injections were rated significantly higher concerning both, the intensity and unpleasantness evaluations than the non-painful ones, but, although intensity levels of the anaesthetised hand were rated close to zero, unpleasantness ratings were still clearly present (Lamm, Nusbaum, et al., 2007).

Concerning neural changes, the authors found that focussing on the unpleasantness of the depicted situations did not result in significant changes, but attending to the intensity led to a higher personal involvement, as indicated through stronger activations in areas associated with coding first-hand sensory consequences of pain (stronger contribution of sensorimotor representations), action anticipation and understanding (Lamm, Nusbaum, et al., 2007).

The authors found further that observing targets in pain (in contrast to non-painful situations) includes regions associated with affective-motivational aspects of pain such as the bilateral AI, right middle insula, dorsal and ventral aMCC, somatosensory aspects of pain such as regions in the somatosensory cortex (SI, SII, posterior insula) and also areas involved in the anticipation of action consequences, such as the IPC (bilateral SMG, ventral premotor cortex) and IFG, as well as in the thalamus and right medial frontal gyrus (Lamm, Nusbaum, et al., 2007). Further activations were found in cortical, basal ganglia (striatum) and cerebellar motor areas (dorsal lateral premotor areas, putamen, caudate nucleus, cingulate and supplementary motor area; Lamm, Nusbaum, et al., 2007).

Observing targets in putatively harmful situations was associated with signal modulations in medial orbitofrontal cortex (mOFC), aMCC, bilateral superior frontal gyrus (SFG) and the right IFG, pars orbitalis and pars triangularis and revealed less activation in areas of the pain matrix.

Unfortunately this study has only concentrated on participants' perspectives as viewers and did not let them evaluate what they would feel in the target's situation. Such "imagine other" – "imagine self" perspectives can shed light on the distinct differences between these two views and therefore has been included in several other studies (e.g. Jackson et al., 2006; Lamm, Batson, & Decety, 2007).

1.2 Prosocial behaviour

The ability to perceive and share affective states of other individuals has often been associated with prosocial behaviour (see Batson, 2010), which occurs when someone voluntarily and intentionally serves another at a temporary cost to the self (Eisenberg & Miller, 1987). Different to this kind of behaviour, empathy does not necessarily carry other-oriented motivations (Singer & Lamm, 2009) and therefore has to be distinguished from it. Although empirical evidence about a direct link between the two phenomena is still missing (Singer & Lamm, 2009), empathy can be seen as a first necessary step in motivating prosocial behaviour (Hein, Silani, Preuschoff, Batson, & Singer, 2010; Engen & Singer, 2012). In scientific settings prosocial behaviour has often been examined in different variations of decision paradigms, such as the dictator game (Kahneman, Knetsch, & Thaler, 1986) where individuals usually have to split a given amount of money between themselves and other individuals.

1.3 Stress and its effects on empathy and prosocial behaviour

Stress response in general. Individuals are confronted with various stressors of different origins in everyday life. Acute stress leads thereby to a disruption of homeostasis and is followed by an immediate physiological response (Cannon, 1914). The major systems for the reinstatement of the homeostasis are the sympatho-adrenomedullary and hypothalamic-pituitary-adrenal (HPA) axes (Ulrich-Lai & Herman, 2009). Within seconds after perceiving a certain stressor, the sympathetic nervous system stimulates the adrenal medulla to secrete the catecholamines epinephrine (adrenaline) and norepinephrine (noradrenaline) into blood circulation, leading for instance to an increased blood pressure, pulse and heart rate and a widening of respiratory passages (e.g. Ulrich-Lai & Herman, 2009; Nelson, 2011). This sympathetic activation is commonly referred to as fight-or-flight response (Cannon, 1932). Referring to the HPA axes stress exposure triggers the hypothalamus to release corticotropin-releasing hormone (CRH) and several other releasing hormones into the pituitary gland, which in turn releases adrenocorticotropin hormone (ACTH; Ulrich-Lai & Herman, 2009; Pruessner et al., 2010; Nelson, 2011). ACTH acts on the adrenal cortex and initiates a release of glucocorticoid hormones, such as the classic stress hormone cortisol, leading to a

mobilization of energy, allowing to adjust bodily functions in order to manage stress (Ulrich-Lai & Herman, 2009; Pruessner et al., 2010; Nelson, 2011).

Behavioural stress response. Since stress is a state in which individuals are aroused by aversive stimuli (Kim & Diamond, 2002), it is subjectively perceived as unpleasant and uncomfortable (Seyle, 1936) and therefore often accompanied by a worsening of the current mood (e.g. Kudielka, Schommer, Hellhammer, & Kirschbaum, 2003; La Marca et al., 2011). To counteract this disadvantageous state, there are two common behavioural stress response approaches. While the fight-or-flight approach (Cannon, 1914, 1932), which is typically shown by males, leads to a more defensive aggressive and self-centered state (Cannon, 1932), the tend-and-befriend approach (Taylor et al., 2000; Taylor, 2006), which is shown mostly by females, but can also be found in males (see von Dawans, Fischbacher, Kirschbaum, Fehr, & Heinrichs, 2012), leads to protection mechanisms through maintenance of social networks and in turn to the reduction of distress (Taylor et al., 2000; von Dawans et al., 2012).

Inducing stress. For the simulation of physical, social and mental stressors in laboratory settings, several tasks have been developed. Proper stress responses can thereby be elicited through the usage of different triggers for stress induction. Widely used methods are physical challenges (e.g. cold; Deuter et al., 2012), the performance of tasks including cognitive demands (e.g. mental arithmetic; Pruessner, Hellhammer, & Kirschbaum, 1999) and presentations in front of an audience (Kirschbaum, Pirke, & Hellhammer, 1993). The presence of other individuals is thereby important for the generation of a certain type of stressor- the socio-evaluative threat (where task performances could be followed by negative judgements of others; Dickerson & Kemeny, 2004). Thereby the audience does not has to be spatial present, in particular this kind of threat can also be induced when subject's failure, experienced through for instance negative feedback on task performance, is only stated to be communicated to other individuals (Pruessner et al., 1999).

Due to the continual growing number of studies relying on imaging methods, such as fMRI, several stress tasks have been developed and adjusted to the requirements of neuroimaging environments (e.g. Soufer et al., 1998), such as the

Montreal Imaging Stress Task (MIST, Dedovic et al., 2005). This well-established task is based on the Trier Mental Challenge Test (Pruessner et al., 1999) and contains a variety of reliable stress-inducing elements (see Dickerson & Kemeny, 2004), such as mental arithmetic, the experience of failure and also socio-evaluative threat, and therefore is adopted in this study.

Effects of stress on social cognition and emotion. As stress is a popular topic in science, it has been examined frequently (e.g. Dickerson & Kemeny, 2004; Pruessner et al., 2010), but in the last years especially research on distinct influences of stress on social phenomena and its underlying neural mechanisms has become increasingly popular (e.g. Starcke & Brand, 2012). A growing body of studies indicated that stress actually influences empathy and prosocial behaviour (Buchanan & Preston, 2014) on a behavioural level, such as Negd, Mallan, and Lipp (2011) who found that a higher level of anxiety is linked to reduced empathic abilities. A recently published study building on this finding and concentrating on the effects of psychosocial stress on the ability to distinguish self- from other-related representations found further that empathy decreases under acute stress in males, while reverse effects were observed among females (Tomova, von Dawans, Heinrichs, Silani, & Lamm, 2014). Males showed a diminished self-other distinction and displayed more self-related processes when exposed to an acute stressor (Tomova et al., 2014).

Another recent study reported further that, compared with the control group, participants who were exposed to an acute psychological stressor (Trier Social Stress Test; TSST; Kirschbaum et al., 1993), also showed lower pain intensity ratings in an empathy for pain paradigm (by Jackson, Meltzoff, & Decety, 2005; pictures showing hands and feet under painful stimulation vs. non-painful and neutral images), which is a further indicator for a reduction in empathy in consequence to stress (Buruck, Wendsche, Melzer, Strobel, & Dörfel, 2014).

There is also evidence that empathic emotion contagion in individuals who are exposed to physical pain (cold pressure) occurs when they are in presence of a friend, but not a stranger experiencing the same pain, indicated through enhanced pain ratings (Martin et al., 2015). The authors further showed that by reducing social stress, empathic pain responses can also be found in response to strangers suffering from pain (Martin et al., 2015).

Different results were found by a most recent study who examined the effects of stress on emotional and cognitive empathy through pictures showing negative and positive emotional social scenes (Wolf et al., 2015). They reported an enhanced emotional empathy in male participants after an acute psychosocial stressor (TSST; Kirschbaum et al., 1993) in comparison with the control group; no group difference was found concerning cognitive empathy (Wolf et al., 2015).

Relating to prosocial behaviour, various studies reported that stress leads to an increase of acting prosocial in females (e.g. Taylor et al., 2000; Preston, 2013). Recent studies could also find such tend-and-befriend patterns in males (e.g. Takahashi, Ikeda, & Hasegawa, 2007). For instance von Dawans et al. (2012) found that acute psychosocial stress, induced through a public speaking task as socio-evaluative threat, leads to increased prosocial behaviour in men, especially in the paradigms trust, trustworthiness, and sharing. By contrast, Vinkers et al. (2013) found reduced generosity in male subjects in consequence to stress. However, as a most recent study reported that generosity and tend-and-befriend patterns are dependent on timing of stress in relation to decision making, as well as social closeness (Margittai et al., 2015) the findings of Vinkers et al. (2013) are no further surprising, as they asked participants for their willingness of donating money to an impersonal charity organization instead of to a real person. However, building on the other reported studies we expected an increase of generosity and prosocial behaviour in our male sample.

Neural changes of empathy-related brain regions in response to stress have not been examined yet, but several studies focused on the neural underpinnings of several other social processes such as decision making and identified regions sensitive to stress-induced changes (for a review see Starcke & Brand, 2012). In general an increased automatic responding in consequence to stress was reported (Starcke & Brand, 2012; Hermans, Henckens, Joëls, & Fernández, 2014). Since changes in neural activity are strongly dependent on gender (e.g. Lighthall et al., 2012; Wang et al., 2007) and the type of stressor used for induction (see Dedovic, D'Aguiar, & Pruessner, 2009) results concerning the direction (activation / deactivation) of stress effects on the activity of certain brain regions are quite contradictory. Stress in general, in particular induced through the laboratory stress

task MIST (Dedovic et al., 2005), which was also implemented in this study design, led to reduction in limbic system activity, in particular in the hippocampus, hypothalamus, medio-OFC and ACC and to an increase in the left mPFC, the cingulum, occipital cortex, left premotor area, ventral striatum and basal ganglia (Dedovic et al., 2009; Pruessner et al., 2008). While the latter authors found a decrease of the ACC in reaction to stress, others found an increase in this area in consequence to a different stressor (performance of serial subtractions; Soufer et al. 1998; Wang et al., 2005). Further, decreases in areas linked to self-control in consequence to stress have been reported (Maier, Makwana, & Hare, 2015). Concerning gender effects, studies have for instance found increased activity in dorsal striatum, insula (Lighthall et al., 2012), right prefrontal cortex and a decrease in the left OFC (Wang et al., 2007) in men, while woman displayed an activation of the limbic system, including the putamen, ventral striatum and cingulate cortex.

1.4 Aim and context of the present master thesis

The studies mentioned above have taken a first step to increase our knowledge about the influences of stress on social emotions and cognitions, but a lot of research has to be done to strengthen and extend these achievements and reach clarification about inconsistent findings about these phenomena.

Since effects of stress on the neural correlates of empathy have not been examined yet, the aim of this master thesis was to find out how stress influences the neural underpinnings of empathy, using fMRI adopted on male participants.

We therefore conducted a reliable stress task (Dedovic et al., 2005) and observed its influences on the behavioural and hemodynamic changes of empathy, ascertained through a modified version of an empathy for pain paradigm (Lamm, Nusbaum, et al., 2007).

Since research has shown that empathy is widely connected with prosocial behaviour (Batson, 2010), we further conducted a prosocial task at the end of the experiment, without actually measuring changes in cerebral blood flow.

2. Hypotheses

(1) Stress has an impact on the neural correlates of empathy for pain. Literature so far indicated increased automatic responding under stress (Starcke & Brand, 2012; Hermans et al., 2014). Since emotion contagion has been considered as automatic response (Preston & de Waal, 2002; Decety & Lamm, 2006; Singer & Lamm, 2009) we expected an increase in areas associated with emotion contagion in the painful condition *injection* in our stressed participants. Based on the studies of Lamm, Nusbaum, et al. (2007) we further expected that the condition *biopsy* leads to lower activation in areas associated with nociception and pain processing in both groups. Based on findings of decreased self-control under stress (e.g. Maier et al., 2015) we expected lower down-modulation of emotion contagion under stress.

(1.1) On a behavioural level we expected the painful condition of the empathy for pain paradigm to be rated significantly higher than the putatively harmful and non-painful one, as shown in Lamm, Nusbaum, et al. (2007).

(2) Based on the findings of von Dawans et al. (2012) and Margittai et al. (2015) who found that prosocial behaviour of males increases in consequence to stress, we expected that the induced stress in our sample leads to increased prosocial behaviour of individuals in the experimental group compared to the control group, indicated by a larger amount of money left for another person.

3. Materials and Methods

3.1 Participants

Since research revealed gender differences in stress reactivity (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999; Kajantie & Phillips, 2006) only male individuals were recruited for the study. Online screening questionnaires were sent to all individuals advertising interest to participate in the fMRI-study. These included adapted German versions of the perspective taking and empathic concern scale from the Interpersonal Reactivity Index (IRI; Davis, 1983), the Emotion Contagion Scale (EC; Doherty, 1997), the Reading the Mind in the Eyes Test (RMET; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), the Perceived Stress Scale (PS; Cohen, Kamarck, & Mermelstein, 1983), the Liebowitz Social Anxiety Scale (LSAS; Liebowitz, 1987), the Multidimensional Self-Concept Scale (MSWS; Bracken, 1992) and the Brief Symptom Inventory (BSI; Derogatis & Melisaratos, 1983). To guarantee comparable socio-cognitive abilities among potential participants, individuals displaying scores below or above two standard deviations from the group mean in the IRI, EC and RMET were excluded from the study. For additional exclusion criteria, such as prior or current neurological or psychiatric disorders, intake of prescribed medication or factors influencing stress reactivity, as for instance age (e.g. Kudielka, Buske-Kirschbaum, Hellhammer, & Kirschbaum, 2004), chronic alcohol consumption (e.g. McEwen, 2006) or abundant nicotine consumption (e.g. Matta, Fu, Valentine, & Sharp, 1998), further questions were implemented in the screening.

In conclusion 74 healthy male volunteers participated in the study and were equally and randomly assigned to the experimental and control group. Four had to be excluded due to extraordinary high cortisol levels in comparison to the mean of the other participants, and three due to additional reasons (e.g. excessive movement during the experiment). The remaining 67 participants (with 35 in the experimental and 32 in the control group) were aged between 18 and 40 years ($M = 24.78$ years, $SD = 4.26$) and right handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). All had normal or corrected-to-normal vision and were naïve to the goals of the experiment. Written informed consent was obtained from all participants, who received 30 € for their participation.

3.2 Tasks

3.2.1 Montreal Imaging Stress Task

Stress was induced by the computerized MIST (Dedovic et al., 2005; for the user interface see Figure 1) containing mental arithmetic with an induced failure algorithm. In this task mathematical equations had to be solved in varying difficulties and altering time spans, adapted to individual user performances. Subsequent to each calculation the correctness of answers (right / wrong) was displayed on the user interface. Furthermore subjects' performances were continuously compared with the alleged average performance of a reference group. As a further socio-evaluative threat, additionally to the one by Dedovic et al. (2005), subjects were observed through a live camera and received personal and always negative feedback on their performances at the end of each stress task with the requirement to put more effort in solving the given arithmetical problems. This way an intensification of failure experiences and further increase of personal stress levels was expected. The MIST was conducted three times during the whole experiment to maintain the stress levels of the participants.

Prior to the experiment subjects of the stress group were additionally asked to evaluate their mathematical skills to intensify the performance pressure during mental arithmetic.

For the control group the same task was implemented, but without time pressure or socio-evaluative threats.

3.2.2 Empathy for pain paradigm

To elicit activity in brain areas associated with experiencing pain and also when observing pain in others, Lamm, Nusbaum, et al. (2007) provided an empathy for pain task (mentioned in the introduction). The authors assessed how participants' focus on either the sensory or affective consequences of painful situations (stimuli depicting painful needle injections in different parts of a target's hand) affects hemodynamic and behavioural responses (Lamm, Nusbaum, et al., 2007). Therefore subjects had to evaluate either the intensity or the unpleasantness of the surgical procedures from their perspective as observers ("How much does it hurt?" and "How unpleasant is it?"; Lamm, Nusbaum, et al., 2007). Further, the authors

wanted to examine if these hemodynamic and behavioural responses to the aversive and painful stimuli can be modulated by an additional evaluation of seemingly but actual not painful situations (needle injections in anaesthetised hand; Lamm, Nusbaum, et al., 2007). We implemented and slightly modified this paradigm for our study. Our final empathy for pain task was conceptualized as block design consisting of 60 digital colour photographs showing human hands undergoing painful needle injections, seemingly painful and aversive but actually non-painful needle injections (anesthetized hand) and, in extension to Lamm, Nusbaum and colleagues (2007), non-painful haptics with a cotton bud (for stimuli examples see Figure 2). Stimuli were presented in 5 equal blocks consisting of 4 stimuli each, leading to the four different conditions *fixation*, *injection*, *biopsy* and *qtip*, which were presented in randomised order. Prior to each block an instruction screen informed subjects which condition they have to evaluate. Participants had to evaluate only the affective consequences of the depicted situations on a 7-point visual analogue scale with answers varying from “less unpleasant” to “very unpleasant”. The condition *qtip* functioned thereby also as manipulation check. We expected the painful condition *injection* to be rated higher than the other two conditions (as shown in Lamm, Nusbaum, et al., 2007). Additionally to the paradigm of Lamm, Nusbaum, et al. (2007) ratings had to be taken, in equal parts, either for the own perspective (“How unpleasant did *you* feel during the depicted situations?”) or the perspective of the target undergoing always one of the three conditions (“How unpleasant was the situation for *the person* during the depicted situations?”). Hence, participants should differentiate between the unpleasantness felt by the *self* and the *other*. Such “imagine other” – “imagine self” perspectives have been implemented in various studies before, whereas participants were instructed to imagine undergoing the same pain as the target person, but none of them included evaluations about the level of unpleasantness participants themselves perceive while observing such aversive situations.

3.2.3 Prosocial task

Since empathy and prosocial behaviour are connected on a conceptual level (Eisenberg, 2000; Singer & Lamm, 2009; Batson, 2010), a short prosocial task was implemented at the end of the experiment. Participants had to divide 10 € between

themselves and the next subject, whereby they could decide freely how much to keep and give in steps of 50 cents. They received their chosen amount of money and the one the last subject left for them (which was predefined as 2.50 € each to limit cost for the study) together with their payment for participation at the debriefing.

3.2.4 Test d2

In order to reveal possible influencing factors on the performances of participants a test of attention and concentration was conducted. The “Test d2 - Aufmerksamkeits-Belastungs-Test” (test d2 - attentiveness endurance test; d2; Brickenkamp, 2002), was adapted for usage in the fMRI scanner and had to be completed twice during the experiment by all participants. In various trials a row consisting of “d’s” and “p’s” with zero to four lines above and/or below them was shown to participants (for illustration see Figure 3). Their assignment was to click through the rows as fast as possible and mark all the “d’s” with two lines (regardless of whether above, below it or both).

In the interest of completeness it must be mentioned that the whole experiment also contained a further task (egocentricity paradigm) which is of no further interest for this thesis (for expositions see Bühner, 2015).

3.3 Procedure

The study took place at the MR Centre of Excellence, which is part of the general hospital of Vienna and Medical University Campus (Allgemeines Krankenhaus der Stadt Wien – Medizinischer Universitätskampus) and was approved by the ethics committee of the Medical University of Vienna. All participants were instructed to abstain from smoking, drinking alcohol and taking medication 24 hours prior to the experiment. They were further requested to abstain from consuming caffeine on the day of their appearance.

The experiment started with a 15 minutes lasting anatomical scan, followed by a series of different tasks (for a detailed timeline see Figure 4). The egocentricity and the empathy for pain paradigm were presented in randomised order. Prior to each

section of the two paradigms, the stressor (MIST; Dedovic et al., 2005) was conducted. Intermediate a concentration and attention task was implemented twice (see section 3.2.4). At the end of the scanning procedure a prosocial task (see section 3.2.3) was conducted without measurement of active brain regions.

Subsequent saliva samples and ratings about subjectively perceived stress and mood were collected at different time points (see section 3.4 for a detailed description of saliva sampling and rating collection) during the whole experiment.

The procedure was the same for all participants, with the only difference that the stress task (see section 3.2.1) was slightly modified for subjects of the control group.

At the end of the experiment participants received payment for their participation.

3.4 Stress measures

For the analysis of participants' cortisol levels, saliva samples were collected at five different time points during the experiment (see Figure 4 for a more detailed illustration). The first two samples served as baseline and were collected after participant's arrival and before the instruction (T1) and after the instruction (lasting about 20 minutes) and 25 minutes prior to first stressor onset (T2). The third one was taken 20 minutes after the first stressor onset (T3), the fourth 50 minutes after this onset (T4) and the fifth was collected after the debriefing, which took place 70 minutes after the first stressor onset (T5). The last one (T5) was collected to guarantee a returning of participants' cortisol systems to normal levels (recovery phase; Dickerson & Kemeny, 2004).

For the assessment of subjective perceived stress and mood, a rating was implemented at eight different time points throughout the whole experiment (see Figure 4 for a more detailed illustration). The first two ratings were placed contemporaneous with the first two saliva samples: after participant's arrival, before the instruction (T1) and after the instruction (lasting about 20 minutes), 25 minutes prior to first stressor onset (T2). The third one took place exactly before the first stressor onset (T3). Following the first stressor onset the further ratings took place 15 minutes afterwards (T4), 35 minutes afterwards (T5), 45 minutes afterwards (T6), 50 minutes afterwards (T7) and 70 minutes after the first stressor onset and after the debriefing. T3 - T6 were thereby placed immediately after each paradigm.

3.5 fMRI data acquisition

fMRI data acquisition was carried out the same as in Bührer (2015), since the paradigm used and described by Bührer (2015) and the empathy for pain paradigm conducted in this study were part of the same experiment:

MRI data were acquired using a 3 Tesla Siemens Tim Trio MRI system (Siemens Medical, Erlangen, Germany) using a 32-channel head coil for signal reception. Blood oxygen level-dependent (BOLD) sensitive functional imaging was performed using a multi-band accelerated echoplanar imaging (EPI) sequence with the following parameters: echo time (TE)/repetition time (TR) = 33/1800 ms, flip angle 60°, interleaved acquisition, 54 axial slices coplanar the connecting line between anterior and posterior commissure, FOV 192 mm × 192 mm × 108 mm, matrix size 128 × 128, voxel size 2 × 2 × 2 mm, no interslice gap. Structural images were acquired before functional scanning using a magnetization-prepared rapid gradient-echo (MPRAGE) sequence (TE/TR = 4.21/2300 ms, 160 sagittal slices, voxel size = 1.0 × 1.0 × 1.1 mm, field of view = 256 mm). (Bührer, 2015, p. 19)

Stimulus presentation and response collection was performed using Cogent toolbox for Matlab (Cogent 2000, Wellcome Laboratory of Neurobiology, London, UK). Image processing was carried out using statistical parametric mapping (SPM12, Wellcome Department of Imaging Neuroscience, London, UK), implemented in MATLAB 7.8 (Mathworks Inc., Sherborn, MA, USA).

4. Data analysis

Data analysis was carried out using IBM SPSS statistics software (version 22.0). For all computations the significance threshold was set to $p < 0.05$. Partial eta-squared (η_p^2) was used to report effect sizes. In order of a violation of variance homogeneity, indicated through Mauchly test of sphericity, Greenhouse-Geisser corrections were taken in account. In case of multiple comparisons, Bonferroni corrections were computed for main effects and interactions.

4.1 Stress measures

To ascertain successful stress induction, cortisol levels, as well as ratings of subjective perceived stress and mood were analysed.

4.1.1 Cortisol

In order to reveal possible differences in stress reactivity between the two groups a repeated measures analysis of variance (ANOVA) with the within subject factor *time* (T1 – T5) and the between subject factor *group* (experimental vs. control) was conducted for cortisol (reported in nmol/L) taken from participants' saliva samples. Additionally areas under the curve (AUC), one variant for analysing salivary cortisol collected over multiple time points, were calculated for each subject using formulas provided by Pruessner, Kirschbaum, Meinlschmid, & Hellhammer (2003), resulting in an AUC with respect to ground (AUC_G) and an AUC with respect to increase (AUC_I). They represent the increase of cortisol and the total amount of release occurring over time (Pruessner et al., 2003). Differences in AUC_G and AUC_I between both groups were calculated through *t*-tests for independent samples.

4.1.2 Stress and mood ratings

Rating scales of subjectively perceived stress and mood were analysed with, again repeated measures ANOVAs with within subject factor *time* (T1 – T8) and between subject factor *group* (experimental vs. control). Further, and due to violation of normality, Spearman correlations between each time point of stress and mood have been conducted (corr. between T1 stress rating & T1 mood rating, T2 stress rating & T2 mood rating, etc.; reported as stress_1 to stress_8 and mood_1 to mood_8).

4.2 Behavioural data

4.2.1 Empathy for pain paradigm

For the manipulation check concerning the empathy for pain paradigm a repeated measures ANOVA was conducted to assess if the ratings of the three conditions *injection*, *biopsy* and *qtip* differed significantly from each other. We expected the ratings about the stimuli of the painful condition *injection* to be significantly higher than the putatively but actual not harmful condition *biopsy* and the non-painful condition *qtip*.

Differences between self and other rating were examined through a 2x3 repeated measures ANOVA with the between subject factor *group* (experimental vs. control) and the two within subject factors *rating* (injection vs. biopsy vs. qtip) and *condition* (self vs. other).

Further, paired sample *t*-tests were conducted for the assessment of differences between the self and other condition in each rating, separately for each group.

4.2.2 Prosocial Task

Due to distinct results concerning the direction of effects (see von Dawans et al., 2012 and Margittai et al., 2015) and the fact that a great variety of the participants did allocate 50% of the money, a one-tailed non-parametric test (Mann-Whitney U Test) for independent samples was conducted to analyse possible group differences in prosocial behaviour.

4.2.3 Test d2

For analysing data of the d2, a repeated measures ANOVA with the within subject factor *time* (T1 vs. T2) and the between subject factor *group* (experimental vs. control) was conducted.

4.3 fMRI data

4.3.1 Whole brain analyses

fMRI data analyses were again carried out similar as described in Bührer (2015), since both paradigms were part of the same fMRI-experiment.

SPM12 (Statistical Parametric Mapping, <http://www.fil.ion.ucl.ac.uk/spm>) was used for analyzing fMRI data. The first five volumes of each run were discarded to allow for T1 equilibration. The time series for each voxel was then realigned temporally to the acquisition of the first slice in time to correct for differences in slice time acquisition. The image time series were spatially realigned using a sinc interpolation algorithm that estimates rigid body transformations (translations, rotations) by minimizing head-movements between each image and the reference image. Subsequently, each participant's functional image was segmented into gray matter (GM), white matter (WM), and cerebral spinal fluid (CSF) using GM, WM, and CSF tissue probability maps provided to SPM12 and then spatially normalized to the International Consortium for Brain Mapping (ICBM) space templates (European brains) using both, linear and nonlinear transformations. Finally, the images were spatially smoothed using an isotropic 6 mm full-width-at-half-maximum Gaussian kernel. The fMRI time series were analysed using an event-related design approach in the context of the General Linear Model. Measures were analyzed across all images for each condition [...] (Bührer, 2015, p. 28-29).

Single-subject models ("first level analyses") were composed of multiple regressors, modeling the three conditions.

Each effect was modeled on a block design basis as a concatenation of square-wave functions. Each of these square-wave functions was then convolved with a canonical hemodynamic response function, as implemented in SPM12. Head movement effects were accounted for by including the six rigid-body motion parameters (translation and rotation) [...]. (Bührer, 2015, p. 29).

As implicit baseline for computations served the fixation cross. The condition *qtip* served as baseline for computations concerning the two conditions *injection* and *biopsy*.

Contrasts were computed for each subject and contrast images were entered into group statistics (“second-level analyses”), which were calculated through random effects models (implemented in SPM12). For the between-subject design, a flexible factorial model was conducted to compare control with experimental group in the two remaining conditions *injection* and *biopsy*. In order to identify consistent activation a mean [mean(injection+biopsy)] was computed of both groups and conditions. To counteract noisy images / outputs, contrasts of main interest (injection_stress>control and biopsy_stress>control) were masked by this mean.

Significant clusters were anatomically labelled by the SPM Anatomy Toolbox (version 1.7; Eickhoff et al., 2005), used to determine anatomical structures of the MNI-coordinates.

Threshold for whole brain analyses was set to $p < 0.001$. Significant results had a minimal cluster size of $k = 177$ voxels, with $p_{FWE} < 0.05$.

4.3.2 ROI analyses

Relationship between dispositional, behavioural measures and brain activation

Subsequent to the whole-brain analyses, region of interest (ROI) analyses were performed using the Marsbar toolbox ([http:// www. sourceforge.net/projects/ marsbar](http://www.sourceforge.net/projects/marsbar)). ROIs were defined in bilateral anterior insula, rTPJ, aMCC and right IFG, pars opercularis. For the conjunction between ROIs and behavioural data, Pearson correlations were conducted.

5. Results

5.1 Stress measures

Results of the stress measures are displayed in Figure 5 for cortisol analyses, Figure 6 for analyses of stress and Figure 7 for mood ratings.

5.1.1 Cortisol

Analyses of cortisol revealed a significant main effect of time ($F(2.26,146.86) = 13.646$, $p < 0.001$, $\eta_p^2 = 0.174$) and group ($F(1,65) = 4.702$, $p = 0.034$, $\eta_p^2 = 0.067$), as well as a significant interaction time x group ($F(2.26,146.86) = 6.597$, $p = 0.001$, $\eta_p^2 = 0.092$). Bonferroni corrected pairwise comparison showed further significant lower cortisol level in the control compared to the experimental group in T4 (mean diff. \pm SEM = -18.95 ± 5.66 , $p = 0.001$), but no further time points (all p -values ≥ 0.110).

Differences concerning both AUC measures reached significance (AUC_G $t(58.41) = -2.040$, $p = 0.046$; AUC_I $t(55.18) = -2.573$, $p = 0.013$).

5.1.2 Stress and mood rating

Analyses of the stress rating revealed significant main effects of time ($F(4.55,277.72) = 36.762$, $p < 0.001$, $\eta_p^2 = 0.376$), and group ($F(1,61) = 29.697$, $p < 0.001$, $\eta_p^2 = 0.327$), as well as of the interaction time x group ($F(4.55,277.72) = 2.718$, $p = 0.024$, $\eta_p^2 = 0.043$). Bonferroni corrected pairwise comparison revealed further that subjective perceived stress was rated significantly lower in the control compared to the experimental group in all eight time points: T1 (mean diff. \pm SEM = -0.69 ± 0.33 , $p = 0.043$), T2 (mean diff. \pm SEM = -1.08 ± 0.33 , $p = 0.002$), T3 (mean diff. \pm SEM = -0.79 ± 0.37 , $p = 0.034$), T4 (mean diff. \pm SEM = -1.85 ± 0.38 , $p < 0.001$), T5 (mean diff. \pm SEM = -1.50 ± 0.35 , $p < 0.001$), T6 (mean diff. \pm SEM = -1.28 ± 0.35 , $p = 0.001$), T7 (mean diff. \pm SEM = -1.20 ± 0.33 , $p = 0.001$) and T8 (mean diff. \pm SEM = -0.43 ± 0.16 , $p = 0.008$).

Analyses of the mood rating showed a significant main effect of time ($F(4.44, 266.41) = 29.011, p < 0.001, \eta_p^2 = 0.326$), and the interaction time \times group ($F(4.44, 266.41) = 2.742, p = 0.024, \eta_p^2 = 0.044$), but no significant main effect of group ($F(1, 60) = 2.126, p = 0.150, \eta_p^2 = 0.034$). Bonferroni corrected pairwise comparison showed further significant lower mood rating in the experimental compared to the control group in T7 (mean diff. \pm SEM = $-0.87 \pm 0.32, p = 0.008$) and also one on trend level ($p = 0.091$) in T4 (mean diff. \pm SEM = -0.65 ± 0.38). No further significant differences between the mood ratings of the two groups have been found (all p -values ≥ 0.109).

Concerning stress and mood, negative correlations between each respective stress and mood rating were found: stress_1 and mood_1 ($r = -0.307, p = 0.012$), stress_2 and mood_2 ($r = -0.559, p < 0.001$), stress_3 and mood_3 ($r = -0.535, p < 0.001$), stress_4 and mood_4 ($r = -0.679, p < 0.001$), stress_5 and mood_5 ($r = -0.558, p < 0.001$), stress_6 and mood_6 ($r = -0.458, p < 0.001$), stress_7 and mood_7 ($r = -0.547, p < 0.001$), stress_8 and mood_8 ($r = -0.379, p = 0.002$). Further correlations between all time points have not been conducted.

5.2 Behavioural data

5.2.1 Empathy for pain paradigm

The ANOVA for manipulation check revealed a significant difference between all three conditions ($F(2, 132) = 327.243, p < 0.001, \eta_p^2 = 0.832$). Further the painful condition *injection* was rated significantly higher ($p < 0.001$) than the putatively harmful condition *biopsy* (mean difference \pm SEM = 3.991 ± 0.302) and the neutral condition *qtip* (mean difference \pm SEM = 8.288 ± 0.355). Also, *biopsy* was rated significantly higher ($p < 0.001$) than *qtip* (mean difference \pm SEM = 4.297 ± 0.312).

2 \times 3 ANOVA showed significant main effects of condition ($F(1, 65) = 6.502, p = 0.013, \eta_p^2 = 0.091$) and rating ($F(2, 130) = 321.989, p < 0.001, \eta_p^2 = 0.832$), but not of group ($F(1, 65) = 1.469, p = 0.230, \eta_p^2 = 0.022$). Significant interaction effects were found for condition \times rating ($F(2, 130) = 18.759, p < 0.001, \eta_p^2 = 0.224$) and condition \times rating \times group ($F(2, 130) = 3.765, p = 0.026, \eta_p^2 = 0.055$), but not for

rating \times group ($F(2,130) = 0.063$, $p = 0.939$, $\eta_p^2 = 0.001$) and condition \times group ($F(1,65) = 2.661$, $p = 0.108$, $\eta_p^2 = 0.039$).

Bonferroni corrected pairwise comparison revealed only one significant difference between the two groups in the rating *biopsy*, condition *self*, namely a higher *biopsy self* rating in the control compared to the experimental group (mean diff. \pm SEM = 0.80 ± 0.39 , $p = 0.042$).

Further, significant differences between the self and other condition were found in the rating *injection* of the experimental ($t(34) = 5.05$, $p < 0.001$), as well as of the control group ($t(31) = 3.16$, $p = 0.003$), the rating *biopsy* of the control group ($t(31) = -2.54$, $p = 0.016$) and on a trend level in the rating *qtip* of the experimental group ($t(34) = 1.82$, $p = 0.077$), but not for the rating *biopsy* of the experimental ($t(34) = 0.80$, $p = 0.427$) and for *qtip* of the control group ($t(31) = 1.23$, $p = 0.228$). Mean values revealed that the rating for *injection* was in both groups higher in the other condition ($M_{\text{CONTROL}} = 5.91$, $SD = 1.30$, $M_{\text{EXPERIMENTAL}} = 5.67$, $SD = 1.38$) than in the self condition ($M_{\text{CONTROL}} = 4.95$, $SD = 1.58$, $M_{\text{EXPERIMENTAL}} = 4.76$, $SD = 1.53$). Further, it revealed that the control group rated *biopsy* more unpleasant in the condition *self* ($M = 3.88$, $SD = 1.62$) than in the condition *other* ($M = 3.12$, $SD = 1.69$). No further significant differences have been found. Results are displayed in Figure 8.

5.2.2 Prosocial Task

Mann-Whitney U test revealed that the amount of money shared was significantly ($U = 423$, $p = 0.003$, $r = 0.22$) higher in the experimental ($Mdn = 37.91$) than in the control group ($Mdn = 29.27$).

5.2.3 d2

Analyses of the test for concentration and attention revealed a significant main effect of time ($F(1,65) = 10.093$, $p = 0.002$, $\eta_p^2 = 0.134$), but neither of group ($F(1,65) = 0.015$, $p = 0.902$, $\eta_p^2 = 0.000$) nor the interaction time \times group ($F(1,65) = 0.027$, $p = 0.870$, $\eta_p^2 = 0.000$).

5.3 fMRI data

Results of the fMRI analyses are taken from SPM12. All coordinates are presented in MNI standard space.

5.3.1 Whole brain analyses

In order to assess general hemodynamic responses in the empathy for pain paradigm, activations of the mean [mean(injection+biopsy)] were analysed. Consistent activation over both groups and conditions were quite in line with findings of Lamm et al. (2011) and presented in Table 1. Figure 9 illustrates significant activation clusters.

Further activation of the mean was found in the following basal ganglia (MNI x/y/z): bilateral caudate (-10/5/13; 13/5/14), putamen (-18/-3/14; 20/-4/14) and left pallidum (-18/-4/12), as well as in bilateral cerebellum (-8/-76/-24 and 16/-76/-22), right OFC (32/22/14) and rTPJ (58/-42/16).

In order to assess hemodynamic changes in consequence to stress, we contrasted activations of experimental group during the empathy for pain task in the two conditions with the ones of the control group (injection_stress>control, biopsy_stress>control). These contrasts indicated an involvement of areas associated with sensorimotor representations and also first-hand experience of pain, including somatosensory cortex (area 1, area 2, area 3a and 3b of the S1), left posterior insula, bilateral IPC (supramarginal, precentral, postcentral and angular gyrus), left hippocampus, bilateral supplementary motor area, bilateral cerebellum, bilateral superior parietal lobule, as well as in areas associated with emotion contagion, including bilateral AI, aMCC. Activation clusters were further detected in areas associated with self/other distinction, mentalizing and self-awareness, such as the rTPJ, left precuneus, right SFG, as well as with body recognition (left fusiform gyrus). Responses were further found in left insula, left dIPFC, bilateral IFG, pars opercularis and left pars triangularis.

In comparison, the control group showed activations in the aMCC/ dmPFC (6/14/54), right dLPFC (46/44/24), right IFG, lateral OFC (32/22/-16), right precentral gyrus / dorsolateral premotor cortex (42/12/32), bilateral cerebellum (22/-72/-24 and -12/-78/-25), right supplementary motor area (6/14/54) and brain stem (8/-18/2)

in the condition *biopsy* and left somatosensory cortex (area 2; -32/-46/54), left superior parietal lobule (area 7; -20/-60/56), left IPC, SMG (-56/-26/36), left IPC (-28/-54/54), right part of area 18 / occipital cortex (24/-94/-8), left middle occipital gyrus (-34/-78/10) and left inferior temporal gyrus (-52/-66/-10) in the condition *injection*.

Analyses revealed further distinct differences between the painful and putatively painful condition. Figure 10 and 11 illustrate significant activation clusters, Figure 12 especially activations in the empathy for pain network of the contrast stress>control in both conditions.

The contrast *biopsy_stress*>control yielded significant activation (see Table 2) in areas which are part of the pain matrix, such as somatosensory cortex (bilateral area 2, right area 1, bilateral SMG), left AI, left dIPFC, right IPC, postcentral gyrus and areas associated with motor activation (right cerebellum), but considerably fewer as in the condition *injection*. Further activation was found in left insula, bilateral IFG, pars opercularis, left IFG, pars triangularis, rTPJ, right superior frontal and bilateral precentral gyrus.

Table 2. Significant clusters resulting from the contrast *biopsy_stress*>control.

Cluster	Brain region	L/M/R	k	X	Y	Z	t-value
I	temporo-parietal junction	R	192	54	-38	12	6.14
II	inferior frontal gyrus, pars opercularis (area 44)	R	224	58	10	22	5.59
III	precentral gyrus	R	188	32	0	48	5.75
	superior frontal gyrus	R		22	0	58	3.88
IV	precentral gyrus	L	443	-48	2	42	5.59
	inferior frontal gyrus, pars opercularis (area 44)	L		-60	10	24	4.16
V	anterior insula	L	729	-42	18	-2	4.70
	anterior insula, extending to IFG, pars orbitalis	L		-42	18	-12	3.40
	insula	L		-28	24	8	4.62
	dorsolateral prefrontal cortex	L		-46	42	22	4.09
	inferior frontal gyrus, pars triangularis (area 45)	L		-50	36	12	3.86

VI	inferior parietal cortex, supramarginal gyrus (PF, PFt)	L	664	-62	-32	34	4.36
	somatosensory cortex (a 2)	L		-44	-34	40	5.28
				-48	-36	48	4.67
VII	Cerebellum (lobule VI)	R	155	28	-70	-22	4.00
	Cerebellum (lobule VII)	R		18	-82	-20	3.71
VIII	inferior parietal cortex, postcentral gyrus	R	189	48	-34	50	4.93
	somatosensory cortex (a 1)	R		56	-22	48	3.94
	supramarginal gyrus	R		42	-30	40	4.69
	somatosensory cortex (a 2)	R		50	-36	56	3.90

Abbreviations: L/M/R = left/middle/right; a 1 = area 1; a 2 = area 2

In comparison with the non-painful condition *biopsy*, the painful condition *injection* (*injection_stress*>*control*; see Table 3) revealed significant stronger activation in areas coding the first-hand affective-motivational experience of pain, such as the right AI, ACC, and sensorimotor aspects of pain, such as the left hippocampus, S1 (area 3a and 3b), bilateral IPC, postcentral gyrus (area 1 and area 2) and angular gyrus, bilateral SMG, left posterior insula, bilateral superior parietal lobule (area 5, area 7a), left precuneus and bilateral supplementary motor area, left and right cerebellum, as well as in the left fusiform gyrus.

Further activations in the contrast were found in bilateral IFG, pars opercularis (area 44), left precentral gyrus and left insula.

Table 3. *Significant clusters resulting from the contrast *injection_stress*>*control*.*

Cluster	Brain region	L/M/R	k	X	Y	Z	t-value
I	supplementary motor area	L	6207	-8	6	50	6.86
		R		12	4	56	5.54
	anterior cingulate cortex	M		10	14	44	8.00
	inferior frontal gyrus, pars opercularis (area 44)	R		58	10	22	6.34
		L		-50	6	32	5.57
	precentral gyrus	L		-30	-8	52	6.09
	insula	L		-28	22	6	6.03
	anterior insula	R		30	16	-2	5.62

II	primary somatosensory cortex (S1; area 3b)	L	3025	-54	-18	38	7.14
	primary somatosensory cortex (S1; area 3a)	L		-42	-24	38	4.64
	superior parietal lobule (area 7a, a 5)	L		-26	-54	66	6.88
				-20	-50	58	5.22
	postcentral gyrus (area 1)	L		-58	-22	50	4.64
	postcentral gyrus (area 2)	L		-38	-46	62	6.18
				-26	-46	56	6.06
	inferior parietal cortex, supramarginal gyrus (PF, PFop)	L		-20	-62	38	5.38
				-54	-42	50	6.13
	inferior parietal cortex, postcentral gyrus	L		-56	-32	30	4.19
				-62	-38	38	4.67
	precuneus	L		-14	-52	52	5.51
				-10	-78	44	4.49
III	inferior parietal cortex, supramarginal gyrus (PFT)	R	8554	48	-30	38	6.58
	fusiform gyrus	L		-36	-66	-8	6.37
	Cerebellum (lobule VI)	L		-28	-64	-22	5.50
	Cerebellum (lobule VII)	L		-20	-90	-18	5.99
		R		48	-54	-28	5.74
	superior parietal lobule (a 5)	R		20	-56	60	5.80
	inferior parietal cortex, angular gyrus (PGp)	R		48	-74	22	5.63
	primary somatosensory cortex (S1; area 3b)	R		52	-20	40	5.48
	postcentral gyrus (area 1)	R		54	-22	48	5.75
	postcentral gyrus (area 2)	R		26	-42	40	6.21
IV	posterior insula	L	191	-40	-8	14	6.65
	hippocampus	L		-32	-16	-10	5.33
V	inferior parietal cortex, angular gyrus (PGp)	L	177	-42	-80	24	4.59

Abbreviations: L/M/R = left/middle/right; a 5 = area 5

5.3.2 ROI analyses

Correlations between behavioural data and brain activation (injection > baseline and biopsy > baseline) only revealed one significant correlation after Bonferroni correction for multiple comparisons ($p < 0.004$) between *biopsy self* and activation (biopsy > baseline) in the IFG ($r = -0.419$, $p < 0.001$).

6. Discussion

The present master thesis assessed how stress influences empathic reactions to pain in a male sample through the usage of fMRI, hormonal and behavioural analyses. Further, analyses on the impacts on prosocial behaviour were examined. The results will be discussed in this section.

6.1 Stress and mood measures

Covering our expectations, subjects of the experimental group showed a significant higher cortisol level (AUC_G and AUC_I ; Pruessner et al., 2003) and subjective perceived stress rating at all eight time points compared to the ones in the control group. This clearly indicates the success of the stressor and experimental manipulation.

Concerning subjective perceived mood ratings, participants of the experimental group stated worse mood compared to the ones of the control group at the end of the experimental procedure and, on trend level, also subsequent to the first stressor and paradigm.

However, stress and mood ratings did also correlate significantly at each time point, indicating an association between high stress and low mood levels, which is in line with consisting theory (Kudielka et al., 2003; La Marca et al., 2011).

6.2 Empathy for pain

Behavioural measures of the empathy for pain paradigm. Results of the behavioural part of the empathy for pain task indicate that subjects showed an understanding of the task, as they were able to correctly evaluate the affective consequences of the three conditions. *Injection* was rated significantly higher than *biopsy* and *qtip* was rated as least unpleasant.

As in Lamm, Nusbaum, et al. (2007) the depicted numbing of the target's hand resulted in a loss of pain somatosensation, but, as indicated through the still present and increased ratings in the condition *biopsy*, participants still appraised the targets' situations as unpleasant and uncomfortable, which may be due to the present surgical procedure (Lakra & Kujur, 2015).

Concerning the evaluations of the self / other ratings, participants of both groups stated a distinct difference in the painful condition between the self and the other. As both rated the level of unpleasantness lower for the condition *self*, an understanding of the task could be clearly manifested. A further indicator for that is that there was no difference in the self and other rating of the non-painful condition *qtip* in both groups (only on trend level in the experimental group). Participants seemed to understand that this condition is actual not very unpleasant, neither for the self, nor the other person depicted. Experimental and control group did only differ concerning the *biopsy* rating. While stressed participants stated no difference in the unpleasantness level of the putatively harmful condition between the self and other rating, subjects of the control group seemed to evaluate this situation in a different way, as they rated the self condition significantly higher than the other condition. This indicates that participants of the control group correctly evaluated that the situation of a biopsy is actual not very unpleasant for the target person, but stated also that an observation of the situation itself is indeed perceived as unpleasant, as the photographs, so the presumption, still depicted needle injections and surgical procedures with a medical environment, which are generally perceived as unpleasant (e.g. Lakra & Kujur, 2015). So why is there a distinct difference between the two groups in this evaluation? This question cannot be answered sufficiently with this study, but stress may have effected participants' ability of a proper self/other distinction in consequence to the ambiguously painful stimuli. This assumption would be in line with findings of Tomova et al. (2014) who reported diminished self/other distinction in male subjects under stress.

Whole brain analyses. The fact that analyses of consistent activation over both groups and conditions [mean(injection+biopsy)] were quite in line with the findings of Lamm et al. (2011), indicates a proper functioning of the conducted empathy for pain paradigm in our study. Concerning hemodynamic responses, we did find distinct differences between the two conditions and groups.

In the painful condition *injection* subjects of the experimental group clearly showed much stronger activation in the empathy for pain network as compared to the control group. In line with our hypotheses, the experimental group showed significant signal increases in areas associated with emotion contagion (rAI, aMCC) when observing a target person suffering from pain (injection in hand), which could not be found in

the control group. This is also in line with a most recent behavioural study who stated enhanced emotional empathy in stressed participants (Wolf et al., 2015). Further, subjects of the experimental group showed considerably stronger hemodynamic responses in areas coding the sensorimotor aspects of first-hand experiences of pain (left cerebellum, bilateral area 1, 2, 3b and left area 3a of the somatosensory cortex, left posterior insula, left hippocampus, and bilateral supplementary motor area) compared to the control group.

Since emotion contagion has been considered as automatic response (Preston & de Waal, 2002; Decety & Lamm, 2006; Singer & Lamm, 2009), our findings emphasize the role of involvement of bottom-up processes for the generation of emotions in consequence to stress, since subjects of the experimental group showed clear tendencies of automatic neural responses in reaction to the aversive stimuli of a painful needle injection in another one's hand.

The occurred increases in the AI and aMCC in consequence to stress further provide evidence for the findings of recent studies reporting that tend-and-befriend patterns can not only be found in females, but also in males under stress (von Dawans et al., 2012). Different to responses in a fight-or-flight manner (Cannon, 1932), the induced stress triggered a more social approach behaviour in subjects of our experimental group, as indicated through enhanced emotion contagion in the empathy for pain task. Following that, stress might have motivated individuals to behave less egocentric and response in a more other-oriented manner in order to cope with the stressful situations, which matches the concept of the tend-and-befriend approach (Taylor et al., 2000).

Further interesting results were found in the putatively harmful, but actual non-painful condition *biopsy*. In comparison with the painful condition *injection*, the numbing of the target's hand resulted in a loss of activation in areas involved in somatosensation and coding first-hand experiences of pain, apparently indicating a comparatively higher personal involvement during the condition *injection*. Although the extent of this loss strongly differed between the two groups, the general loss in comparison to hemodynamic responses in the injection condition is in conformity with our prospects.

However, literature demonstrated that identical stimuli can lead to different affective reactions depending on stimuli context, stressing the importance of cognitive processes in generation of emotional responses (e.g. Scherer, Schorr, & Johnstone,

2001; Singer et al., 2006). In case of the biopsy condition, stimuli were identical to the ones of the painful condition *injection* (hand pierced by a needle), but additional an external information was provided, informing the subjects that the observed aversive situation is only putatively harmful, but actually not painful, as the depicted hand was numbed, meaning it was not possible for the target person to feel pain during the needle injection. Following that, the additional information would lead to signal decreases in the network coding affect (bilateral AI, aMCC) and somatosensory representations due to processes of cognitive control. This could be clearly shown in the control group who responded with complete a loss of somatosensation and hardly any activation in areas associated with emotion contagion when confronted with stimuli of the biopsy condition. They seemed to understand that the situation is actually not painful for the other person, which is also in line with behavioural results. But how did this modulation proceed? Activation of areas such as the lateral OFC, right dlPFC and dmPFC indicate that a cognitive down-regulation of affective responses has taken place in the control group. As areas in the prefrontal cortex have been linked to emotion regulation (Elliot, Dolan, & Frith, 2000; Kringelbach & Rolls, 2004; Ochsner & Gross, 2005) and cognitive and executive control processes (Lamm, Nusbaum, et al., 2007) the right dlPFC and dmPFC have perhaps contributed in controlling potential affective responses that might have occurred automatically during the observation of the aversive situations in general. Since the lateral OFC is connected to these areas involved in higher-order cognition (e.g. Fuster, 1997; Elliot et al., 2000) it has been suggested that their responses are triggered by conveyed signals of the lateral OFC (Lamm, Nusbaum et al., 2007). Since this area is involved in valence evaluation (Singer et al., 2006) it might have provided information about the actual emotional valence of the observed situation (see also Kringelbach & Rolls, 2004), in this case, information about the fact that the depicted needle injection has no painful effects for the target person, and therefore has conveyed a requirement of affective control.

In contrast to the control group, the experimental group showed indeed distinct signal increases in the empathy for pain network. They displayed a variety of areas involved in coding the first-hand somatosensory aspects of pain, as well as areas involved in emotion contagion, such as the left AI, similar to the ones activated in the injection condition. The additional contextual information did seemingly not lead to distinct changes in activation in the empathy for pain network in the stressed

group. Interestingly, it seems that the experimental group showed indeed an attempt to regulate occurred bottom-up responses, as they displayed activation in areas associated with distinguishing between own and other one's affective experiences (SMG; Silani, Lamm, Ruff, & Singer, 2013), mentalizing (rTPJ; Ruby & Decety, 2003; Saxe & Kanwisher, 2003), and even emotion regulation (left dlPFC; Miller & Cohen, 2001; Knoch, Pascual-Leone, Meyer, Treyer, & Fehr, 2006). But the fact of distinct signal increases in areas of the empathy for pain network indicates that a down-regulation of automatically triggered responses has, in contrast to the control group, not succeeded in the experimental group. This would also be in line with the behavioural results found in the experimental group, showing no significant evaluation difference between the unpleasantness felt by the stressed subjects themselves and the one felt by the target person. As described above a diminished self/other distinction in consequence to stress, which was reported by Tomova et al. (2014), might have concurred this effect. The actual cause of occurred failure of cognitive modulation of automatically triggered affective responses cannot be clarified in this study and therefore has to be examined in detail in future research.

Relationship between behavioural measures and brain activation. We found a negative correlation between ratings for biopsy self and the rIFG, pars opercularis. This region has often been considered for its important role in action anticipation and observation, motor imagery and imitation (e.g. Krams, Rusworth, Deiber, Frackowiak, & Passingham, 1998; Molnar-Szakacs, Iacobini, Koski, & Mazziotta, 2005; Binkofski et al., 2000) especially during observations of pain in others (e.g. Lamm, Nusbaum, et al., 2007). A recent study further emphasizes that the rIFG plays an important role in suppressing the own emotion or perspective when empathizing with another person (Hillis, 2014). Therefore it is of no further surprise that stronger activations in the rIFG are associated with lower unpleasantness ratings in the biopsy self condition and vice versa. Such an effect might have been shown by the control group displaying less activation in the rIFG. The lack of suppression might have led to the higher unpleasantness ratings in the self condition of control participants. But, as we have not assessed how the rIFG actually modulates the unpleasantness ratings in the biopsy self condition, we therefore are not able to make proper assumptions about the occurred effects. This needs to be done in future studies.

6.3 Behavioural data

Prosocial Behaviour. We found distinct differences in prosocial behaviour between the two groups. In line with our hypotheses participants of the experimental group allocated more money to the putatively next participant compared to the control group. This finding is in line with studies reporting increased prosocial behaviour in males under stress (Takahashi et al., 2007; von Dawans et al., 2012; Margittai et al., 2015). It has been argued that social bonding leads to prosocial behaviour more likely (Preston & de Waal, 2002) and that stress can be diminished if individuals are in the presence of supportive behaviour offered by their best friends during a stressful task (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003). Although direct social support was missing in our study design, participants of the experimental group acted more generous as they might have felt a social attachment or bonding to the next participant, who soon had to experience the same stressful situation as themselves. This would further support the notion that men demonstrate tend-and-befriend patterns as coping strategy when confronted with an acute psychosocial stressor, which was also reported by von Dawans et al. (2012).

Test d2 - attentiveness endurance test. Concerning d2, the significant main effect of time indicates an improvement of task performance over time in both, experimental and control group, possible referable to training effects as reported in Brickenkamp (2002). Mean comparison in the d2 showed no significant difference in attention and concentration between the two groups. Hence, no present influence of stress-induced changes in cognitive load on participants' performances throughout the whole experiment was found, indicating that our reported effects were not achieved through fewer cognitive resources due to stress.

6.4 General discussion

This master thesis made a first important step for our knowledge of the impacts of acute stress on empathy for pain, its neural underpinnings and the related concept of prosocial behaviour in a male sample.

As expected, subjects of the experimental group showed a significant higher cortisol level and subjective stress rating as compared to the ones in the control group, indicating the success of the experimental manipulation.

Concerning our presumptions about the behavioural aspects of the empathy for pain paradigm, the resulting significant higher rating of the painful condition in comparison to the putatively and the non-painful one, indicates an affirmation of our hypotheses and also a distinct understanding of the implemented paradigm. Further, we did find a distinct group difference between the ratings of the biopsy condition, as both groups showed a different response pattern concerning the distinction between self and other when confronted with a putatively harmful, but actually non-painful stimuli. We presumed that the lack of differentiation between both views shown by subjects of the experimental group might be referable to a diminished self/other distinction in consequence to stress, which could be shown before in Tomova et al. (2014) but this assumption needs to be confirmed in future studies.

Concerning neural correlates of empathy for pain it is important to note that although the empathy for pain paradigm showed quite the same activations in areas that are also reported in Lamm et al. (2011), our findings concerning neural responses to the aversive stimuli are not quite confirm with the findings of Lamm, Nusbaum, et al. (2007), who reported no significant changes (except for small clusters) in any brain region when participants were instructed to focus on the unpleasantness of pain. In contrast, we did find indeed significant responses during the evaluation of affective consequences of painful situations. In the condition *injection* we found a strong contribution of sensorimotor representations and areas coding the first-hand sensory experiences of pain, even when there was no instruction to focus on the sensory, but on the affective consequences of the depicted situations. Needless to say, we did not control for responses to pain intensity in this study and therefore are not able to affirm this assumption, but the fact that we, after all, did find significant hemodynamic changes in response to evaluations of the unpleasantness of painful situations, suggests a distinct role of affective representations for understanding pain in others, which needs to be examined in more detail in future studies.

Analyses of changes in the neural underpinnings of empathy for pain in response to stress revealed the following: In line with our hypotheses, we found enhanced emotion contagion when empathizing with a target person suffering from a painful needle injection in participants of the experimental group. Since literature has considered emotion contagion as automatic response (e.g. Preston & de Waal, 2002; Singer & Lamm, 2009), this indicates that stress leads to bottom-up processes when empathizing with a person suffering from pain. Further this is in line with the tend-and-befriend concept, stating enhanced social and other-oriented behaviour in order to manage stress (Taylor et al., 2000).

Examinations about the neural correlates in the biopsy condition yielded further interesting effects. In general a great loss of pain somatosensation in comparison to responses concerning *injection* could be clearly manifested in this condition, which confirms another one of our hypotheses. The identical stimuli led, with the additional contextual information about the numbing of the target's hand, to distinct changes in hemodynamic responses in the control, but not the experimental group. While the control group showed no somatosensory responses and in general only slight activation in areas involved in the empathy for pain network, which might be referred to cognitive emotion regulation processes of prefrontal structures (dmPFC, dlPFC, lateral OFC; e.g. Ochsner & Gross, 2005; Lamm, Nusbaum, et al., 2007), the experimental group showed neural responses similar to the ones in the condition *injection*. Although slight neural increases in areas associated with higher-order cognitive processes could be observed, they apparently did not manage to down-regulate bottom-up responses of emotion contagion in order of cognitive control, as indicated through enhanced responses in the empathy for pain network. The finding that automatic affective bottom-up processes could not be controlled in consequence to stress also reflects the lack of differentiation between the unpleasantness felt by the self and other in the behavioural part of the biopsy condition.

Our hypotheses about the effects of stress on prosocial behaviour could also be confirmed, as we did find a significant difference concerning the allocated amount of money between both groups. As reported, the experimental group allocated more money to the putatively next participant, supporting recent findings about enhanced prosocial behaviour in consequence to stress (e.g. von Dawans et al., 2012). Our findings further stress the notion of tend-and-befriend patterns in male subjects.

Our study was the first to ask participants what level of unpleasantness they felt while *observing* the painful and putatively harmful situations. But as we have only regarded these evaluations on a behavioural level there are many opportunities for future research to examine the differences between both, the self and other evaluations, on a neural level. A separation throughout whole brain analyses not only into the conditions, but also in the self and other evaluation of these conditions would be an interesting content and should therefore be a purpose of future studies. Such an approach could further shed light on correlations between brain activation and the behavioural measures found in this study.

Another limitation of this study is that we did not compare our male sample to a female one and can therefore only make statements about the neural correlates of male empathic reactions in consequence to stress. The lack of a direct gender comparison has to be compensated in future research. Since there is no study examining changes in neural underpinnings of empathy in consequence to female stress responses yet this needs to be done in future studies. It is of great interest if the effects of stress on empathic reactions of females that were found in the behavioural studies can also be shown on a neural level.

7. Conclusion

Our study shed new lights on the distinct impacts of stress on empathy for pain and its underlying neural correlates.

First of all we can say that our experimental manipulation was highly successful and the shown effects were not mediated by a lack of concentration or attention of our participants. Secondly our findings are quite in line with existing theory about empathy for pain and its neural underpinnings.

As a result we found interesting impacts of stress on empathy for pain. In the injection condition the experimental group showed a stronger activation in the empathy for pain network compared to the control group. This indicates that stress may provoke an automatic bottom-up generation of empathic responses. It is also an indicator for tend-and-befriend patterns in a male sample, which were shown before in behavioural studies (Takahashi et al., 2007; von Dawans et al., 2012). Stress did also effect hemodynamic responses to the putatively harmful condition *biopsy*. While the control group showed a cognitive down-regulation of empathic responses in the biopsy condition resulting in a great loss of pain somatosenstation and areas associated with emotion contagion, subjects of the experimental group might not have managed to down-regulate automatic affective reactions and showed neural responses similar to the ones in the injection condition, namely a high involvement of areas associated with emotion contagion and somatosensory representations.

The expectation that man under stress behave more prosocial could also be fulfilled which might be a further indicator of male tend-and-befriend patterns in order to cope with stress.

8. References

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Appendix

Table 1. Significant activation resulting from the mean over both groups (control and experimental) and conditions (injection and biopsy).

Brain region	L/M/R	X	Y	X	k	t-value
Anterior insula	R	40	24	-2	225930	8.75
Anterior insula / fronto-insular cortex	L	-32	22	0	225930	10.56
Insula	L	-36	16	8	225930	8.90
Anterior medial cingulate cortex	M	-6	18	46	225930	11.46
Anterior medial cingulate cortex, dorsomedial prefrontal cortex	R	6	14	54	225930	13.12
Dorsolateral prefrontal cortex	R	42	38	16	225930	8.50
Inferior frontal gyrus, pars opercularis	L	-48	6	30	225930	14.92
Inferior frontal gyrus, pars opercularis / operculum (area 44)	R	56	14	24	225930	8.52
inferior frontal gyrus, pars triangularis (area 45)	L	-50	22	30	225930	8.39
inferior frontal gyrus, pars triangularis (area 45)	R	48	28	28	225930	8.77
Superior frontal gyrus	R	-24	0	60	225930	15.44
Inferior parietal cortex, postcentral gyrus	L	-22	-66	34	379180	19.25
Inferior parietal cortex, supramarginal gyrus	L	-54	-26	38	379180	16.82
Postcentral gyrus	L	-40	-48	58	379180	17.64
Superior parietal lobule (area 7)	R	26	-54	58	379180	14.80
Superior parietal lobule (area 7)	L	-26	-56	64	379180	15.78
Middle occipital gyrus	L	-30	-90	-8	379180	19.03
Inferior temporal /occipital gyrus	R	50	-68	-6	379180	17.12
Inferior temporal / occipital gyrus	L	-50	-68	-4	379180	20.06

Precentral gyrus, dorsolateral premotor cortex	R	48	14	36	225930	10,08
Precentral gyrus, dorsolateral premotor cortex	L	-48	6	30	225930	14.92
Fusiform gyrus	L	-28	-62	-8	379180	14.75
Precuneus	L	-18	-62	58	379180	22.52
Postcentral gyrus (area 2)	R	26	-48	50	379180	14.75
Postcentral gyrus (area 2)	L	-30	-46	52	379180	17.73
Supplementary motor area	L	-6	8	54	225930	10.51
Intraparietal sulcus (hlp1)	L	-32	-44	46	379180	15.54

Abbreviations: L/M/R = left/middle/right

Figure 1. MIST user interface (Dedovic et al., 2005)

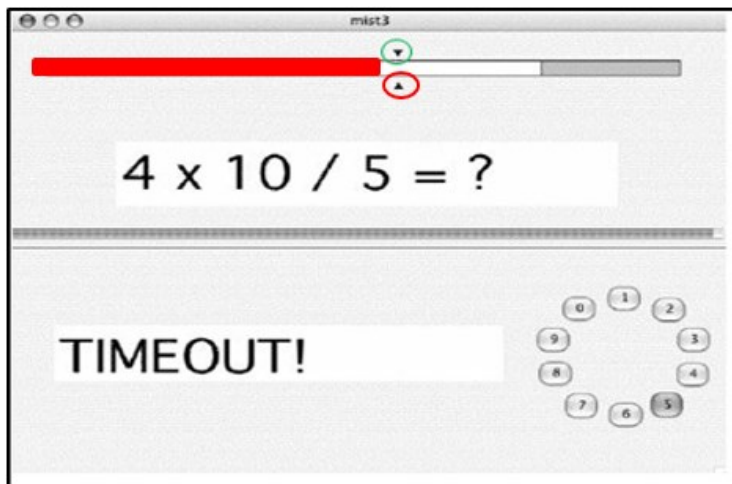


Figure 2. Samples of the stimuli used in the empathy for pain paradigm



Figure 2. Examples of stimuli used for the empathy for pain paradigm. The green background was used to indicate a medical environment. The left image illustrates an example for the condition *injection* and *biopsy*. None of the stimuli used for these conditions showed bleeding, but a distinct compression of the skin caused by the needle. The right image represents the stimuli used for the condition *qtip*, where target hands were touched with a cotton bud.

Figure 3. d2 user interface (Brickenkamp, 2002)

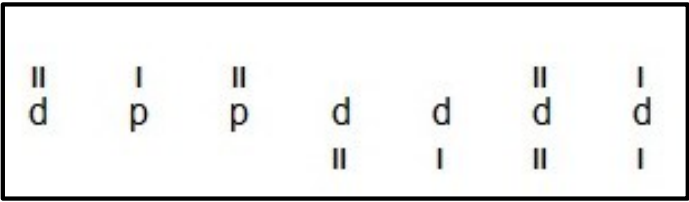


Figure 4. Timeline of the experiment (© by Mag. Livia Tomova). The symbol ① stands for the time points of the ratings, the symbol ▽ for the collection of saliva samples and symbol ! for the d2.

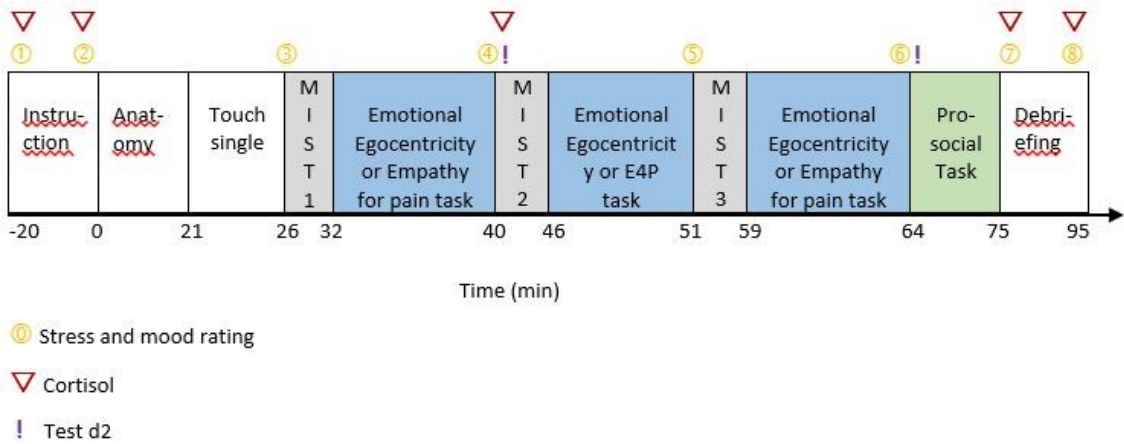


Figure 5. Stress levels of experimental and control group (mean + 1 SD) analysed at five time points by free salivary cortisol. Significant group differences are marked by a *.

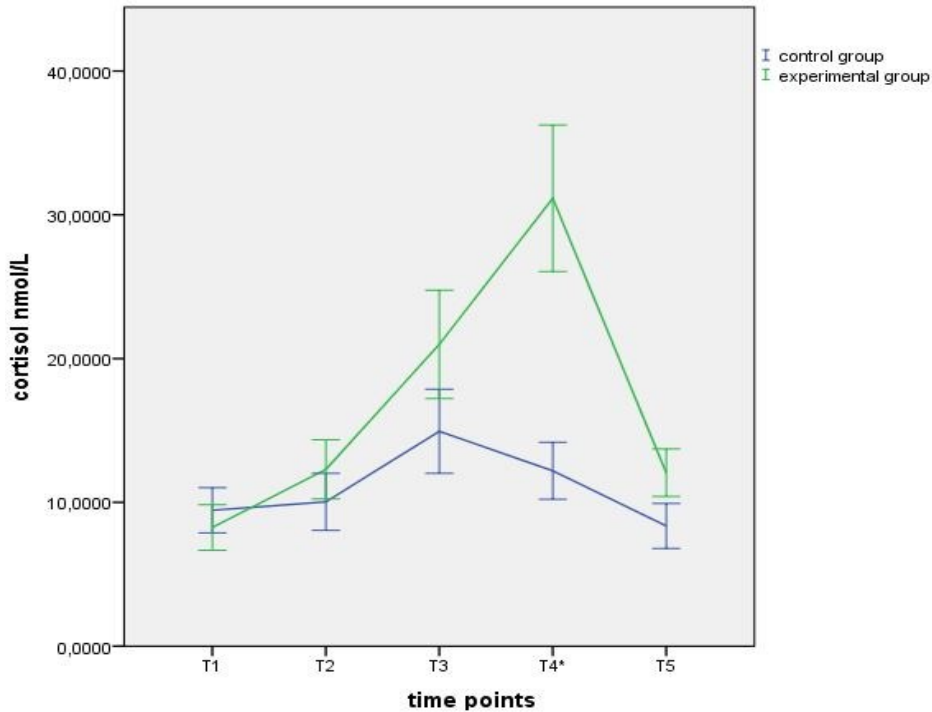


Figure 6. Subjective perceived stress levels (mean + 1 SD) of experimental and control group ascertained at eight time points. The character * indicates significant group differences.

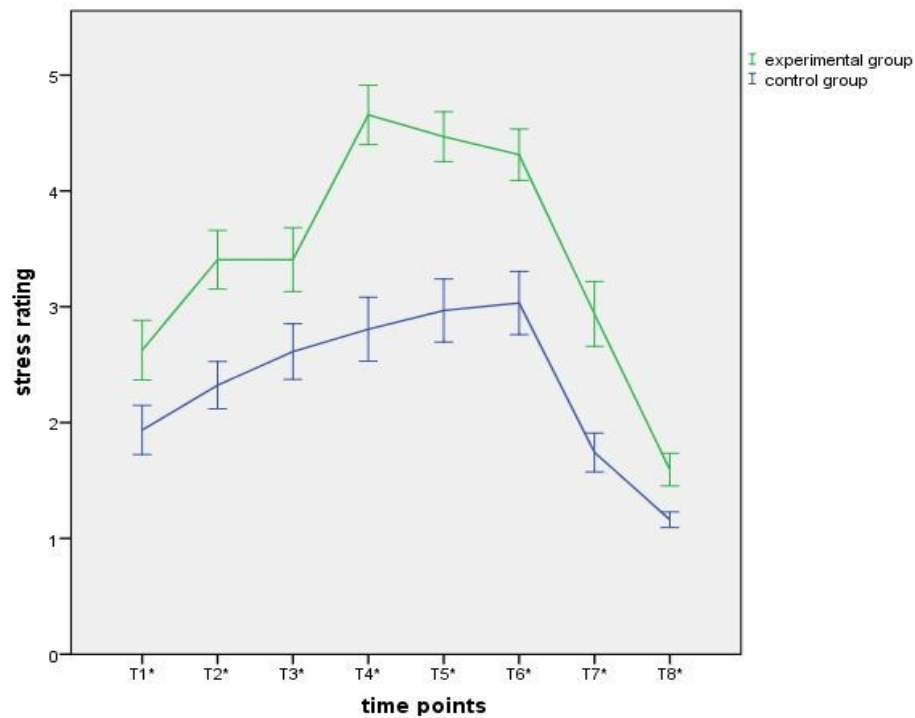


Figure 7. Subjective perceived mood (mean + 1 SD) of experimental and control group ascertained at eight time points. The character * indicates significant group differences.

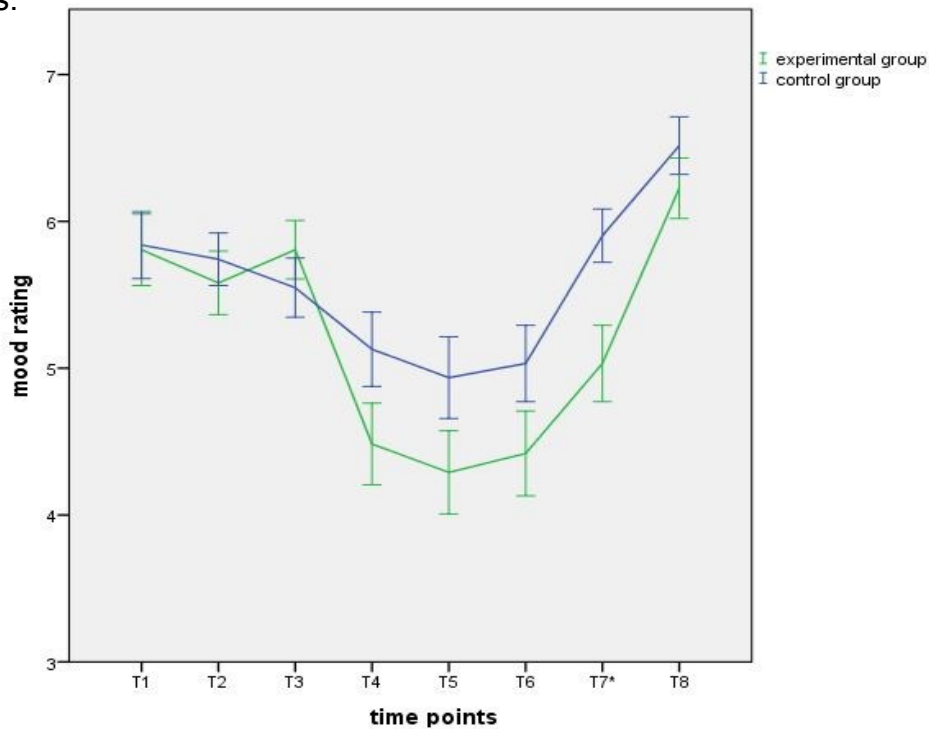


Figure 8. Ratings of the empathy for pain conditions of experimental and control group. Significant group differences are marked by a *.

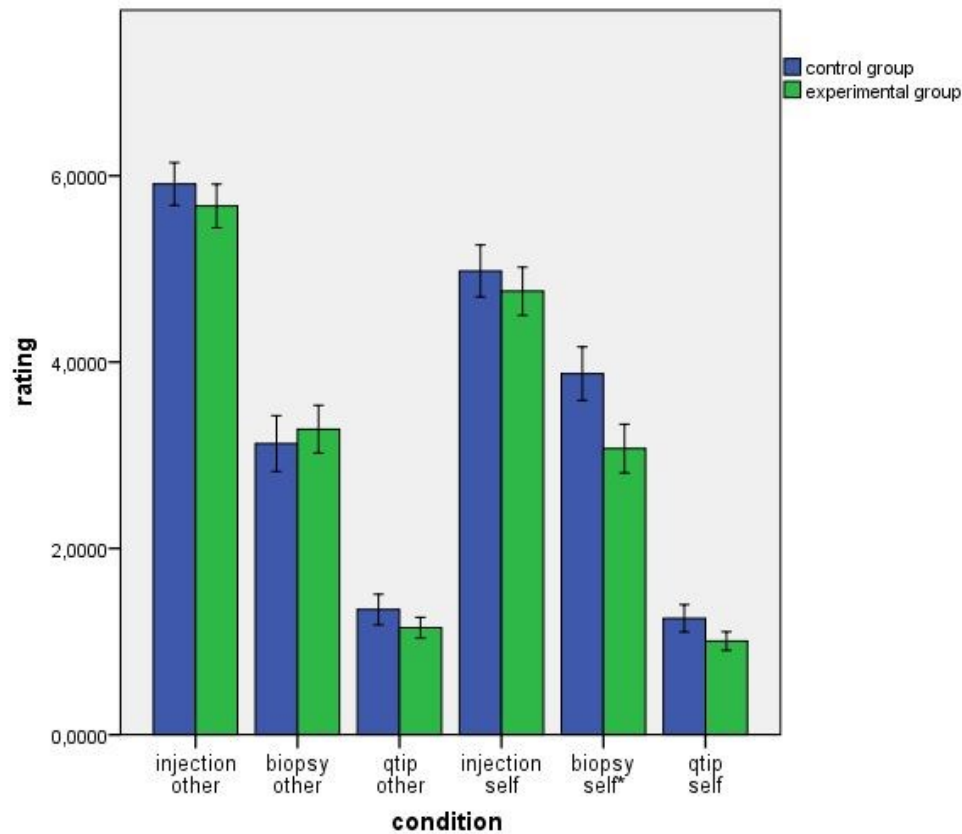


Figure 9. Brain areas activated over both groups and conditions (masking analysis)

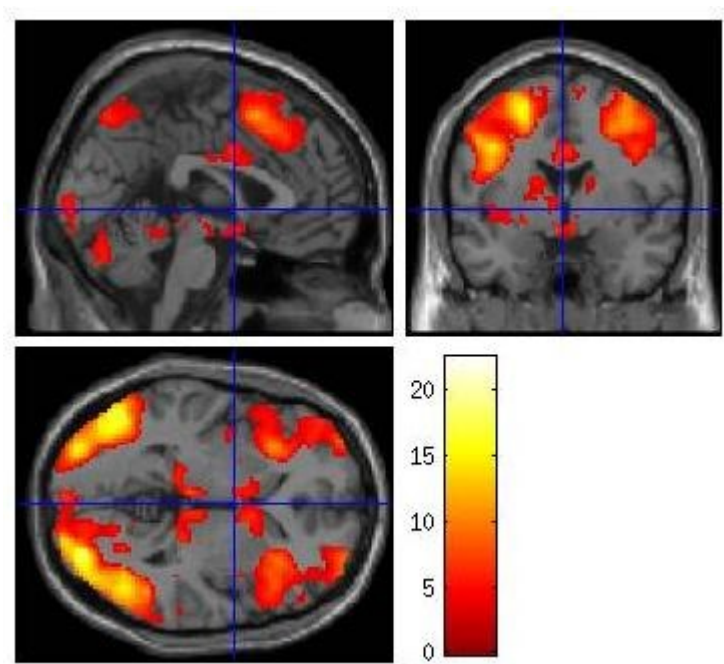


Figure 9. Significant activated brain areas in experimental and control group in the conditions injection and biopsy. Threshold $p = 0.001$, $k = 3$.

Figure 10. Significant clusters of the contrast injection_stress>control

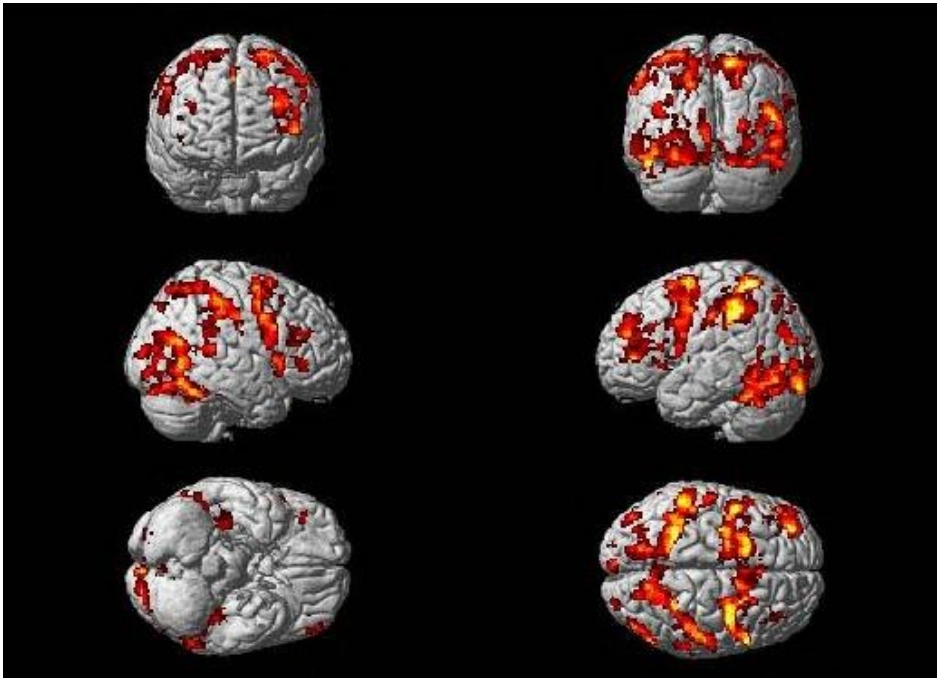


Figure 10. Threshold $p = 0.001$, $k = 5$.

Figure 11. Significant clusters of the contrast biopsy_stress>control

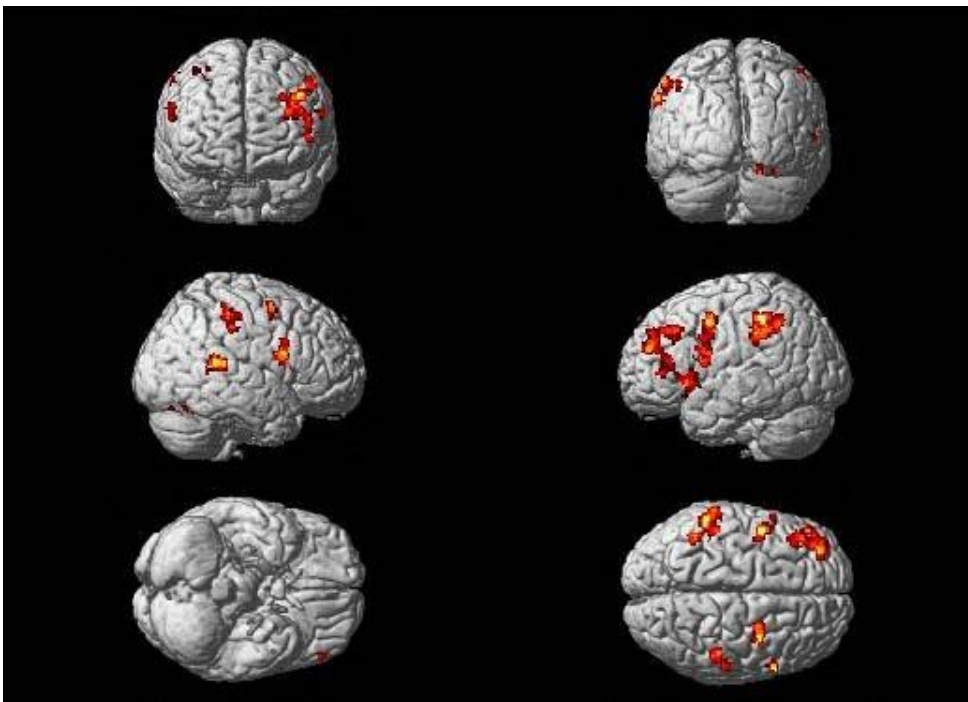


Figure 11. Threshold $p = 0.001$, $k = 8$.

Figure 12. Empathy for pain network of the contrast stress>control in both conditions (injection and biopsy)

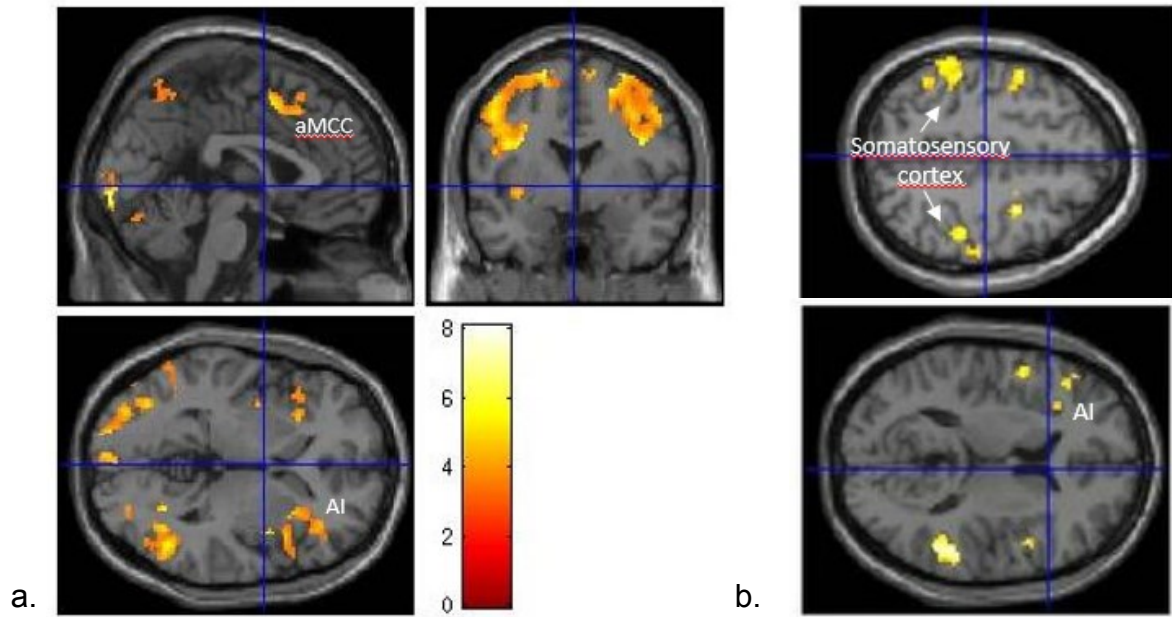


Figure 12. Significant hemodynamic responses in the empathy for pain network in the contrast injection_stress>control with threshold $p = 0.001$, $k = 5$ (a) and biopsy_stress>control with threshold $p = 0.001$, $k = 8$ (b). AI = anterior insula, aMCC = anterior medial cingulate cortex.

Zusammenfassung

Die vorliegende Masterarbeit behandelt die Frage, wie sich Stress auf Empathie und insbesondere auf Schmerzempathie und die damit verbundenen Hirnareale auswirkt. Dabei wurde auch auf ein weiteres Phänomen- das prosoziale Verhalten eingegangen. Einige Studien haben sich bereits mit den Auswirkungen von Stress auf Empathie auf Verhaltensebene beschäftigt. Da diese Effekte jedoch noch nicht auf neuronaler Ebene untersucht wurden, ist dies das Ziel dieser Masterarbeit. Als Methoden dienten dabei die funktionelle Magnetresonanztomographie (fMRT), sowie die Analyse von hormonellen und Verhaltensdaten. Insgesamt wurden 74 männliche Personen getestet, welche randomisiert der Experimental- oder Kontrollgruppe zugewiesen wurden. Die Teilnehmer aus der Experimentalgruppe unterzogen sich dem sogenannten Montreal Imaging Stress Task (MIST), einem Verfahren zur Stressinduktion durch mathematische Aufgaben, Zeitdruck und sozialer Evaluation. Um Unterschiede in Empathie und den zugrundeliegenden Hirnarealen festzustellen, mussten Probanden beider Gruppen eine Reihe von Aufgaben absolvieren, darunter ein Paradigma zu Schmerzempathie und prosozialem Verhalten. Bei ersterer mussten die Probanden Bilder von schmerzhaften Injektionen, sowie schmerzfreien Injektionen in eine betäubte Hand (Biopsie), nach ihren affektiven Konsequenzen („Wie unangenehm ist die abgebildete Situation?“) aus der eigenen und der Perspektive der abgebildeten Person, deren Hand sich der chirurgischen Prozedur unterzog, beurteilen. Die prosoziale Aufgabe beinhaltete das Aufteilen einer gegebenen Geldsumme zwischen sich selbst und dem vermeintlich nachfolgenden Probanden und wurde aufgrund wiederholter Befunde einer Verbindung zwischen Empathie und prosozialem Verhalten mit aufgenommen. Während des gesamten Experiments wurden von den Versuchspersonen mehrfach Speichelproben zur Cortisol-Analyse entnommen und subjektive Einschätzungen zu empfundenem Stress und der Stimmung erfasst. Es konnten, bei nachgewiesener erfolgreicher experimenteller Manipulation, eindeutige Stresseffekte ausgemacht werden. In der schmerzhaften Bedingung (Injektion) wies die Experimentalgruppe im Vergleich zur Kontrollgruppe eindeutig mehr Areale emotionaler Ansteckung, sowie somatosensorischer Repräsentationen auf. Dies deutet auf eine automatische Bottom-Up-Generierung von Emotionen im Schmerzempathie-Paradigma aufgrund von Stress hin. Weiters lässt sich der Effekt gut durch bestehende Theorien bezüglich der *Tend and*

Befriend („Hüten und Befreunden“) -Stressreaktionen erklären, in welcher Individuen erhöhtes soziales Verhalten zur Stressbewältigung aufweisen. Die Einbringung zusätzlicher Information zu den visuellen Stimuli ergab weitere interessante Effekte. Während die Kontrollgruppe wie erwartet eine kognitive Herunterregulierung möglicher automatisch auftretender empathischer Reaktionen in der vermeintlich schmerzhaften Bedingung (Biopsie) zeigte, wiesen Probanden, die dem akuten psychosozialen Stressor ausgesetzt waren, kaum Unterschiede zu den neuronalen Aktivierungen in der schmerzhaften Bedingung (Injektion) auf. Wir vermuteten, dass hier zwar eine Regulierung versucht wurde, was durch aufgetretene Aktivierungen in Prozessen höher kognitiver Ordnung (z.B. *Mentalizing*) angedeutet wurde, diese jedoch nicht gelungen ist, da die Stressprobanden starke Aktivierungen im Schmerzempathie-Netzwerk in Bezug auf die Biopsie-Stimuli zeigten.

Die Erwartung, dass sich männliche Personen unter Stress prosozialer verhalten, konnte ebenfalls bestätigt werden, was vermutlich als weiteres Indiz dafür gesehen werden kann, dass Männer und eben nicht nur Frauen mit einem *Tend and Befriend* („Hüten und Befreunden“) -Muster auf Stress reagieren.

Schlussfolgernd konnte diese Studie bestehende, auf Verhaltensdaten basierende Befunde zu auftretenden *Tend and Befriend* -Mustern in männlichen Individuen mit neuronalen Befunden untermauern.

Curriculum Vitae

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Ausbildung

1997 - 2001 Volksschule Hebbelplatz
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Jan 2015	Stipendium für exzellente Studienleistung im Zeitraum Oktober 2013 bis September 2014 durch das österreichische Bundesministerium für Wissenschaft und Forschung gemäß dem Studienförderungsgesetz (StudFG)

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Englisch	Niveau: Sehr gut in Wort und Schrift
Französisch	Niveau: Schulniveau (6 Jahre)
Latein	Niveau: Basiswissen

Zusatzqualifikationen

Software	Microsoft Office Kenntnisse SPSS Kenntnisse Grundkenntnisse in R Grundkenntnisse in SPM Grundkenntnisse in Matlab
Bildgebende Verfahren	Erste Erfahrung mit: Erhebung und Auswertung von fMRT Daten Erhebung und Auswertung von EEG Daten Erhebung von tDCS Daten (Erhalt der Laborbetrehtigung für tDCS an der Social, Cognitive and Affective Neuroscience Unit der Universität Wien)