THE EFFECT OF INTRANASAL OXYTOCIN ON PUPIL DILATION DURING TRUSTWORTHINESS EVALUATION AND FACIAL EXPRESSION RECOGNITION TASKS

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ABSTRACT

THE EFFECT OF INTRANASAL OXYTOCIN ON PUPIL DILATION DURING TRUSTWORTHINESS EVALUATION AND FACIAL EXPRESSION RECOGNITION TASKS

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Our ability to recognize facial expressions and emotions can be modulated by both external and internal factors. One of these internal factors is the neuropeptide "oxytocin". Many studies have highlighted the involvement of oxytocin in recognition of facial expressions and approach-related trusting behaviors. In the current study, we investigated the effects of oxytocin on recognition accuracy and trustworthiness judgements using facial expressions. We used a subset of expressions and images from the Karolinska Directed Emotional Faces (KDEF) as stimuli. We collected pupil diameters with TOBII T120 eye tracker during the experiment to see the effects of oxytocin on physiology. Possible sexual dimorphisms of oxytocin in humans were also of interest to us. Hence we collected data from both male and female participants. The results indicate that intranasal oxytocin resulted in an increase in trusting behavior. In addition, the accuracy of emotion recognition in both male and female participants increased after oxytocin administration. Furthermore, the effect of oxytocin in physiology supported sexual dimorphism: overall, males receiving intranasal oxytocin showed larger pupil diameter changes whereas the reverse situation was observed for females. Independent from the application of intranasal oxytocin/placebo, participants exhibited largest pupil diameters for untrustworthy faces, and smallest pupil diameters for neutral faces. These results suggest that oxytocin has a gender specific crucial role in trusting behavior and emotion recognition in humans. To the best of our knowledge, this is the first study that investigates the relationship between subjective evaluation of trustworthiness and task-evoked pupillary responses, as well as the effect of intranasal oxytocin on trustworthiness evaluation. In addition, this is the first study conducted on both males and females in facial expression recognition collecting pupil diameter changes with oxytocin/placebo manipulation.

Keywords: trustworthiness, facial expression, oxytocin, gender differences, pupillary response

ÖZ

GÜVENİLİRLİĞİN DEĞERLENDİRİLMESİ VE YÜZ İFADELERİNİN TANIMA GÖREVLERİNDE İNTRANAZAL OKSİTOSİNİN GÖZ BEBEĞİ AÇILIMI ÜZERİNDEKİ ETKİSİ

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Duyguları ve yüz ifadelerini tanıma yeteneğimiz hem dış hem de iç faktörler aracılığıyla düzenlenir. Bu iç faktörlerden biri nöropeptid "oksitosin"dir. Birçok çalışma yüz ifadelerin tanınmasında ve yaklaşıma bağlı güven davranışlarında oksitosinin rol aldığını göstermektedir. Bu çalışmada, yüz ifadeleri kullanarak oksitosinin tanıma başarısı ve güvenilirliğin değerlendirilmesi üzerindeki etkilerini araştırdık. Çalışmada Karolinska Directed Emotional Faces (KDEF) veri tabanından seçilen görsel uyaranlar kullanılmıştır. Oksitosinin fizyoloji üzerindeki etkilerini gözlemlemek için, deney sırasında göz bebeği tepkilerini TOBII T120 göz izleme cihazı ile kaydettik. Oksitosinin olası cinsiyetler arası dimorfizme yönelik etkileri de bir başka ilgi konusudur. Bundan dolayı, hem erkek hem de kadın katılımcılardan veri topladık. Sonuçlar intranazal oksitosinin güven davranışında artışa neden olduğunu göstermektedir. Buna ek olarak, okstiosin uygulamasından sonra hem erkek hem de kadın katılımcıların duyguları tanıma başarısı artmıştır. Öte yandan, oksitosinin fizyoloji üzerindeki etkileri cinsiyetler arası dimorfizmi desteklemektedir: İntranazal oksitosin alan erkeklerde tetiklenmiş göz bebeği açılımı gözlemlenirken tam tersi bir durum kadın katılımcılarda gözlemlenmiştir. İntranazal oksitosin ya da plasebo uygulamasından bağımsız, katılımcılar en büyük göz bebeği açılımını güvenilir olmayan yüzlere karşı, en küçük göz bebeği açılımını ise nötr yüzlere karşı göstermiştir. Bu sonuçlar oksitosinin insanlarda güven davranışı ve duygu tanıma görevlerinde cinsiyete özgü önemli bir role sahip olduğunu göstermektedir. Bilgimiz dahilinde, bu çalışma, güvenilirliğin öznel değerlendirilmesi ile görev-uyarımlı göz bebeği tepkisi ilişkisini ve intranazal oksitosinin güvenilirliğin değerlendirilmesi üzerindeki etkisini inceleyen ilk çalışmadır. Buna ek olarak, hem kadın hem de erkeklerde yapılmış, yüz ifadesi tanıma görevlerinde oksitosin/plasebo manipülasyonunun göz bebeği çapı değişiklikleri üzerindeki etkisini inceleyen ilk çalışmadır.

Anahtar kelimeler: güvenilirlik, yüz ifadesi, oksitosin, cinsiyet farklılıkları, göz bebeği tepkisi

To the two pillars of my life: my parents.
Without you, my life would fall apart.

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"You are told a lot about your education, but some beautiful, sacred memory, preserved since childhood, is perhaps the best education of all. If a man carries many such memories into life with him, he is saved for the rest of his days. And even if only one good memory is left in our hearts, it may also be the instrument of our salvation one day."
— Fyodor Dostoyevsky

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CHAPTER 1

INTRODUCTION

Social cognitive neuroscience is an interdisciplinary field that emerged from the union of the classic cognitive neuroscience and social psychology (Adolphs, 2003; Lieberman, 2007). Classical cognitive neuroscience assumes that a description of a prototypical brain is sufficient to gain an understanding of the behavior of all people. However, most of the time, this approach ignores that people usually spend their entire lives in the presence of other people.

By contrast, the social cognitive neuroscience perspective indicates that perception, decision and response should always be considered depending on the social environment, because brains do not exist in isolation (Cacioppo & Berntson, 2004). Therefore, the research approach of social cognitive neuroscience tries to understand the influence of social factors on the behavior, to describe the cognitive processes and the underlying neural and hormonal mechanisms in their social embeddedness (Frith & Singer, 2008). This research is often carried out on several levels: the observation of behavior by using response time measurements and questionnaires in relation to the neural activations or autonomic nervous system responses as measured by skin conductance, heart rate variability, and pupillary responses.

In its early years, social cognitive neuroscience focused mainly on a description of the neural basis of social perception such as biological movement and facial expressions (Adolphs, Tranel, & Damasio, 1998; Ochsner & Lieberman, 2001). This refers to the early stages of information processing, which is used in the course of an analysis of the characteristics and intentions of other individuals. Emotional facial expressions are nonverbal cues of emotions. These external signals inform us about the internal emotional state of an individual which can be extended to intentions. Studies on the expression of emotions by facial features are numerous.

Faces and facial expressions are special stimuli since they are not only markers of personal identity and social status of the individual (for example age, gender or ethnicity) but also they serve as a means of communication where words alone may not be sufficient (Pantic & Rothkrantz, 2004; Ekman, 2003). Indeed, it has long been accepted that the recognition and interpretation of facial information play a major role in the regulation of our social behavior.

The success of any language communication involves properly infer the signals produced by others not only in their verbal activity but also in nonverbal behaviors. The face with more particularly with a specific emotional expression is obviously essential to this understanding. According to Darwin (Darwin, Ekman, & Prodger,

1998), nonverbal communications have been conserved during evolution because they are useful to the survival of the species (vital communication).

Our ability to recognize facial expressions and emotions can be modulated by both external and internal factors. One of these internal factors is a neuropeptide called "oxytocin"[1]. Oxytocin can be defined as a neurohormone because it is synthesized by nerve cells, namely the magnocellular neurons in the supraoptic and paraventricular nuclei of the hypothalamus. The terminations of these neurons join the walls of the blood capillaries of the neurohypophysis allowing oxytocin to be released into the bloodstream and acting as a hormone. Our interest in oxytocin is related to its ability in regulation of social behavior and processing of emotional information.

For over two decades, many psychologists and psychiatrists were interested in oxytocin, making it the hormone whose psychological effects are best known. The most representative research in the area of oxytocin studies has highlighted the involvement of oxytocin in the attachment process (Ditzen et al., 2009; De Dreu, Greer, Van Kleef, Shalvi, & Handgraaf, 2011; Feldman, Weller, Zagoory-Sharon, & Levine, 2007; Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010; Van IJzendoorn, & Bakermans-Kranenburg, 2011), face recognition (Savaskan, Ehrhardt, Schulz, Walter, & Schächinger, 2008; Rimmele, Hediger, Heinrichs, & Klaver, 2009), discrimination and recognition of emotions (Shamay-Tsoory et al., 2009; Van IJzendoorn, & Bakermans-Kranenburg, 2011), the inference of the mental state of others (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007b), the recollection of positive social cues (Guastella, Mitchell, & Mathews, 2008b), trust (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005; Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008; Mikolajczak et al., 2010), generosity (Zak, Stanton, & Ahmadi, 2007) and regulation of intergroup relations (De Dreu et al., 2010). These studies highlight the involvement of the OT in the modulation of social processes, quickly earned oxytocin designations such as "love hormone", "attachment hormone" or "the great facilitator of life" (Lee, Macbeth, Pagani, & Young, 2009).

In the current study, it is aimed to examine whether the evaluation of a visual stimuli with a specific emotional content in a face recognition task triggers pupil dilation, along with the possible effects of oxytocin on the evaluation of the stimuli with emotional content. For further analysis, accuracy of the choice about the emotional content of the stimulus is another variable that is investigated. For faces with neutral expression, trustworthiness ratings, associated pupil dilation and relationship of these

[1] Oxytocin was discovered in 1906 by Sir Henry Dale (Dale, 1906). He named this pituitary secretion in reference to the effect that he had discovered it which is to contract the smooth muscles of the uterus during childbirth. The term oxytocin thus comes from the Greek words "ôkus" and "tokos", meaning literally "fast delivery". In 1954, oxytocin was described by the American biochemist Vincent du Vigneaud as a polypeptide hormone consisting of nine consecutive amino acids (Du Vigneaud, Ressler, Swan, Roberts, & Katsoyannis, 1954).

with oxytocin is also of insterest. Possible sexual dimorphisms of oxytocin in humans are also studied by recruiting participants from both genders.

Remainder of the current thesis comprises of five chapters. In chapter 2, literature review includes introduction about the studies of face and facial expression recognition, oxytocin and pupil dynamics. The subsequent section, chapter 3, covers the participants, the stimuli and preparation of the stimuli, and experimental methodology. Results of the experiments are presented in chapter 4. In the chapter 5, results are interpreted and discussed in a comprehensive manner. At last, chapter 6, presents a concise conclusion.

CHAPTER 2

LITERATURE REVIEW

In this chapter, relevant aspects of the literature in faces, facial expressions of emotions, oxytocin and its effects on social and emotional cognition, pupil size and dynamics are presented. In the first three sections, cognitive aspects and neural correlates of face and emotion perception are reviewed. Then in the fourth part, a brief background on oxytocin and its effects on social cognition and emotion recognition are explained based on previous studies. In the fifth section, all aspects of pupil size and dynamics are discussed including pupillary responses. This part is followed by the presentation of motivation for the initiation of this thesis, research questions and hypotheses.

2.1 Face recognition

Faces must be considered differently from other types of visual stimuli. Indeed, we need to distinguish thousands of faces with very similar characteristics to process this information quickly and to establish links between perceptual representations of a face and social knowledge of the category to which it belongs. This type of stimulus requires an individual level of knowledge, which is rare for other types of visual stimuli.

The neural networks involved in the recognition of facial features are based on multiple neuronal populations which are widely distributed in the brain. The mechanisms involved in the processing of visual information have a hierarchical organization integrating information both sequentially and in parallel with a dynamic framework: both “ascending” or “bottom-up” and “descending” or “top-down”.

Face recognition requires several types of analysis, particularly the detection of a face itself among other visual objects, recognition of the identity of an individual, gender, ethnicity, age, facial expression and gaze direction. It appears that the neural networks involved in the processing of these various components are, at least partly, separated.

The study of face recognition has mainly been discussed by using photographs to easily test this cognitive function in the visual modality. The processing of facial stimuli requires various brain regions such as the visual system, fusiform face area and occipital face area. The description of the organization of the visual system, functional regions involved in face recognition based on data from neuroimaging can be found in Appendix A.

2.2 Definition and classification of emotions

Neurobiologists and psychologists define emotion as a phasic change, concerted and generally adaptive, occurring in multiple biological systems of the individual (including somatic and neural components) in response to a stimulus (Damasio, 1994). An emotional reaction involves changes in multiple physiological systems such as endocrine, visceral, vegetative and muscular systems, including facial muscles.

Emotions can be classified in three categories: background emotions, primary emotions and social emotions. The background emotions consist of the moods or states of the individual and can last several hours, depending on metabolic factors and external stimuli (Damasio, 1999). The most common list of primary emotions (or basic emotions) includes fear, disgust, joy, anger, sadness and surprise. They represent the most common emotions through different cultures (Ekman, 1992). The so-called social emotions are represented by sympathy, embarrassment, shame, guilt, pride, envy, gratitude, admiration, indignation and contempt (Burnett, Bird, Moll, Frith, & Blakemore, 2009).

Whether the emotional concepts have individual characteristics or they are a part of a continuum is a matter of discussion. Some argue for individualized emotional concepts (for example, those that can appoint or express a face) (Ekman, 1992) while others state in favor of a continuum in two-dimensional space, of which, axes are represented by the arousal and emotional valence, or in favor of dependent and transient dynamic assemblies of the context (Russell, 1980).

The research on emotion use several modalities such as visual, auditory, somatosensory to identify the neural correlates between each emotion and to build on theories about emotion recognition. In our study, facial expression recognition through visual stimuli is the main topic of interest.

2.3 Facial expression recognition

The human face is a powerful communication tool. In addition to identity, gender and ethnicity of the person, facial expressions represent clear intentions and emotional state of the person. Facial expressions may reflect the emotional state of an individual or an aspect of social communication in varying proportions (Darwin et al., 1998; Fridlund, 1991). These two components work together to generate the facial expressions, one of them may predominate according to circumstances, individuals and cultures. Hence, identification and definition of the facial movements for transmitting an emotional message became an important aim to understand the intimate mechanisms the recognition of facial expressions in primates and humans.Thanks to modern electrophysiology and brain imaging techniques, the emotions expressed in facial expressions became the source of an extremely rich research axis in the field of psychology and behavioral neuroscience. These studies suggest that the facial musculature -which is controlled by complex neural networks activated automatically

or voluntarily- is highly developed in humans and great apes (Hopf, Muller-Forell, & Hopf, 1992).

In this part, the recognition of emotions through the faces (i.e., facial expressions) and neural systems involved in this function are addressed specifically. The recognition of social messages in humans, especially facial expressions, involves different neural networks depending on the content of the emotional message. It is established that various cortical and subcortical structures such as the amygdala and the insula, react specifically to certain emotional messages.

2.3.1 Mechanisms of recognition of emotions through the faces

The recognition of facial expressions has benefited from many behavioral studies and more recently various neurobiological approaches for decades. In the visual field, facial expressions are a non-verbal communication tool at the origin of numerous scientific works (Adolphs, 2002). In 1872, Darwin argued that this form of emotional expression is innate and universal, in the line with his theory of evolution. Later, intercultural work of Paul Ekman is based on this idea of universality of the emotion recognition from facial expressions (Ekman, 1992; Ekman et al. 1987; Ekman & Friesen, 1971; Izard, 1971; Matsumoto & Ekman, 1989).

The study of facial expressions provided basis for a vast field of theoretical and experimental research. Even today, they are the tool or the preferred paradigm in the field of cognitive studies. Several different mechanisms and neural networks can be involved in recognizing facial expressions.

2.3.1.1 Neural correlates associated to the perception of emotional expressions

It is clear that the emotional processing requires large-scale neural networks ranging from limbic regions to the sensory areas and those associated with high-level cognitive functions (Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012; Schmidt & Trainor, 2001). More specifically, the recognition of emotional expressions is associated with the activity in the orbitofrontal cortex, the superior colliculus, the striate cortex, somatosensory cortex and sensorimotor, the superior temporal gyrus, thalamus and amygdala (Adolphs, 2002). It appears that each of these structures plays a key role in the perception of emotional expressions, according to a time course starting from the initial presentation to the final recognition of the emotion. It is also likely that this network is engaged regardless of the modality in which the emotion is expressed (Kuraoka & Nakamura, 2007). A detailed description of the cortical and subcortical structures involved in recognition of facial expressions can be found in Appendix B.

Subcortical structures including the superior colliculus and the pulvinar nuclei might be specialized in the rapid and automatic processing of visual emotional stimuli, especially their magnocellular attributes. The stimulus would be transmitted through thalamo-amygdala visual pathway. This early processing is specialized in the analysis

of the most salient stimuli, such as aversive facial expressions of fear and anger. Such first processing would be automatic and mandatory.

After a brief analysis of the characteristics of facial expressions provided by the low-level visual structures, cortical regions including the associative visual cortex, build a more detailed perceptual representation and a more precise configuration depending on the facial features. More explicit information on expressions can be built, presumably committing both cortical visual pathways, ventral and dorsal. The superior temporal gyrus develops representations regarding the movements of the lips, gaze direction and facial expressions. The fusiform and posterior temporal gyri, after the first analyses conducted in V1-V2 and V3 areas, build a detailed structural representation of the face around 170 milliseconds after stimulus onset.

Retrograde modulations operate at different levels of visual processing, in other words on different structures and at different times. The activity related to the rapid magnocellular processing could modulate the slower parvocellular activity. Such a retrograde neuromodulation may be partly provided by the amygdala and the prefrontal cortex. Thus, the same visual structures seem to participate in both early perceptual analysis and later stages of recognition. In a natural scene, the context and motivations could modulate every moment of attentional capacity and analysis of visual stimuli.

Cortical motor structures and subcortical areas reinforce these modulations by a simulation process that generates motor programs in response to the detection of facial expressions. The somatosensory and motor cortices involved in the representation of the states of the body defining an emotional state. It would be useful in the construction of the recognition of emotion through simulation, irrespective of whether there is an own emotional reaction to the stimulus.

Thus, recognition of emotion in others is not a monolithic phenomenon. This analysis consists of multiple items of individual strategies depending on experimental task and the context. Some temporal hierarchy seems to influence brain processing of the emotional stimuli. It does not appear that disgust is processed at the same speed as other salient stimuli such fear and even happiness. Evolutionary processes such as survival seem obvious with regard to the processing of aversive and salient stimuli such as fear. The detection of a positive emotion related to the notion of pleasure, also essential to the balance and survival could still be fast.

2.4 The neuropeptide oxytocin

Oxytocin is a small peptide composed of nine amino acids. The term “oxytocin” derives from Greek words “oxys” and “tokos” meaning “fast” and “birth” in reference to its role in the contraction of the uterine muscles during childbirth, as first described by the English scientist Sir Henry Dale in 1906 (Dale, 1906). Its structure was discovered in 1954 by Vincent du Vigneaud and he received the Nobel Prize for Chemistry in 1955 for this precious work (Du Vigneaud et al., 1954).

Oxytocin can be defined as a neurohormone because it is synthesized by nerve cells, namely the magnocellular neurons in the supraoptic and paraventricular nuclei of the hypothalamus (Moos & Richard, 1989). The terminations of these neurons join the walls of the blood capillaries of the pituitary gland allowing oxytocin to be released into the bloodstream and acting as a hormone (Bealer, Armstrong, & Crowley, 2010).

However, oxytocin also acts as a neurotransmitter at the central level. It is indeed transmitted to other structures of the central nervous system via the spinal fluid and by the axon projections of neurons in the paraventricular nucleus of the hypothalamus (Veening, de Jong, & Barendregt, 2010). They send their projections to autonomic centers in the reticular formation, to extra hypothalamic brain areas such as the amygdala, hippocampus, septum, nucleus accumbens, the ventral tegmental area and frontal cortex (Argiolas & Gessa, 1991), as well as to the neurons of the spinal cord and brainstem (Purves et al., 2001).

The release of oxytocin in the central nervous system and neuronal activation, and its release into the bloodstream, are mainly caused by sexual stimuli or stimuli related to reproduction such as coitus, genital stimulation, olfactory stimuli, breastfeeding or parturition. This release also occurs during sexual stimulation or grooming with the offspring and touch contacts (e.g., massage) (Campbell, 2008).

Once released, oxytocin binds to its own receptor. Currently, only one type of specific oxytocin receptor has been found. In humans, oxytocin receptor was isolated and identified by Kimura and colleagues (Kimura, Tanizawa, Mori, Brownstein, & Okayama, 1992). It is a polypeptide of 388 amino acids arranged in typical seven transmembrane domains of the family of receptors coupled to G protein.

Most results concerning the central location of oxytocin receptor are from studies in animals mainly rats and mice. These studies revealed the presence of oxytocin receptors in several brain regions such as the olfactory system, the cortical areas, the limbic system (amygdala and hippocampus) and also in the brain stem (Gimpl, Wiegand, Burger, & Fahrenholz, 2002). Few studies in primates have indicated the presence of receptors for oxytocin also at the orbitofrontal cortex (Boccia, Goursaud, Bachevalier, Anderson, & Pedersen, 2007). In humans, at the peripheral level, oxytocin receptors are mainly found in the digestive tract (Monstein, Grahn, Truedsson, & Ohlsson, 2004), kidneys, heart, thymus and pancreas (Kiss & Mikkelsen, 2005).

Nevertheless, these investigations have also revealed significant variability in the distribution of receptors between different animal species (Insel, Young, & Wang, 1997). Indeed, the rat oxytocin receptor is present in high density in the hypothalamus while no oxytocin receptor has been found in this region in other species like guinea pig, rabbit or hamster (Gimpl & Fahrenholz, 2001). This raises the question of variability or a specific interspecies receptor oxytocin.

For obvious technical reasons, few studies on oxytocin receptors in brain have been conducted in humans. One autopsy study was performed in 12 subjects by Loup, Tribollet, Dubois-Dauphin, Pizzolato and Dreifuss (1989), confirming the presence of oxytocin receptor in the brain. However, again the results showed differences on the location of oxytocin receptor as compared to animal studies. A high rate of oxytocin receptor has been found in the substantia nigra and nucleus basalis of Meynert. Paradoxically, this study revealed the absence of receptor in the hippocampus and amygdala, the entorhinal cortex and around the olfactory bulb (Loup et al. 1989).

Furthermore, there is a difference between the sexes. Indeed, in women, oxytocin receptors are distributed primarily on the smooth muscle walls of the uterus as well as the nipples (Kimura et al., 1992) whereas in men, the OT receptors are found in the cavernous body of the penis and in the epididymis (Vignozzi et al., 2004).

The effects of oxytocin on our behavior and the mechanisms of action are still poorly understood, partly because of obvious methodological difficulties. In contrast to studies in animals that can use many more or less invasive techniques such as central administration of oxytocin and genetic engineering; the same is not possible in humans. Therefore, researchers should use indirect means (i.e., intranasal administration of oxytocin) to evaluate the effect of oxytocin on social behavior. The intranasal administration is explained in detail in Appendix C.

However, the behavioral effects of oxytocin are common to many species. For over two decades, many psychologists and psychiatrists were interested in oxytocin, making it the hormone whose psychological effects are well investigated. The most representative research in the area of oxytocin studies has highlighted the involvement of oxytocin in the attachment process (Ditzen et al., 2009; De Dreu et al, 2011; Feldman et al., 2007; Gordon et al., 2010), face recognition (Savaskan et al., 2008; Rimmele et al., 2009), discrimination and recognition of emotions (Shamay-Tsoory et al., 2009), inference of the mental state of others (Domes et al., 2007b), recollection of positive social cues (Guastella et al., 2008), trust (Kosfeld et al., 2005; Baumgartner et al., 2008; Mikolajczak et al., 2010), generosity (Zak et al., 2007) and regulation of intergroup relations (De Dreu et al., 2010).

These studies highlight the involvement of oxytocin in the modulation of social processes, quickly earned oxytocin designations such as “love hormone”, “attachment hormone” or “the great facilitator of life” (Lee et al., 2009).

2.4.1 The effect of oxytocin on trust behavior

Trust is a concept that everybody understands at some personal level, but it is hard to come out with a specific definition for this concept. In the current study, “trust” is used to explain a subjective “feeling” for determining whether to trust somebody.

Trust in each other is a prerequisite for social affiliation and social approach in humans. Many studies have focused on the link between oxytocin and trust and helped

highlight the crucial role of this hormone in this process. Theodoridou and colleagues (2009) have shown that oxytocin positively modulates the social perception of an unknown individual, so that it looks more attractive and a priori more reliable. Far from being limited to a simple perception, this effect extends to the concrete testimony of trust. An exogenous oxytocin administration increases the trusting behavior (Kosfeld et al., 2005; Baumgartner et al., 2008; Mikolajczak et al., 2010). Although the majority of studies about trust has used tasks involving monetary shares (trust game for example), oxytocin does not only affect the trust behavior of the individual when money is involved, but also when personal and confidential information are involved (Mikolajczak et al., 2010).

In a particularly interesting way, Baumgartner and colleagues (2008) showed that oxytocin increased the capacity of the individual to trust others again (e.g., an individual X) after a betrayal (by an individual Y). It must be emphasized here that in the study of Baumgartner et al. (2008) cited above, the subject interacts with a different partner after a betrayal. Therefore, it is impossible to infer that oxytocin allows restoration of trust in the partner after a betrayal on his part. It would be interesting if future studies would try to determine if this effect can be explained by the memory processes (oxytocin promotes oblivion treason) or motivations (oxytocin increases the motivation to reengage).

Although oxytocin facilitates approach behavior (Taylor et al., 2006), this facilitation is based on the detection of a pathogenic condition (i.e., infectious) in a congener and it is used to modulate the behavior accordingly. The individual will adopt a withdrawal behavior vis-à-vis a potentially contagious partner, but will adopt an approach behavior if it seems healthy interlocutor (Kavaliers & Choleris, 2011).

In addition, oxytocin helps to maintain the social relationship through a circular process: oxytocin promotes pro-social behaviors that increase the rate of oxytocin production. Zak, Kurzban, and Matzner (2005) have shown that when a person A receives a sign of voluntary trust from an individual B (e.g., B entrusts his money to A, which is a sign that he trusts him), his basal rate increases oxytocin and his loyalty to the individual B. This will encourage him to be worthy of the trust received and to reciprocate. A reciprocal system will be set up which consolidates the relationship between two individuals.

Zak et al. (2007) showed that oxytocin increased generosity to a stranger. Individuals in oxytocin group share a sum received from unknown individuals more fairly than the placebo group. Another study (Barraza & Zak, 2009) showed that when the individuals are presented a scene with strong emotional valence (positive or negative), their plasma levels of oxytocin increases and this increase enhances generosity towards an unknown individual.

When oxytocin increases cooperative behavior, it is not indiscriminate. De Dreu et al. (2010) have shown that oxytocin specifically promoted trust and cooperation within the ingroup. However, it does not generate aggressive behavior vis-à-vis the outgroup,

except when the individual feels threatened. Oxytocin may thus favor defensive aggressiveness but not offensive aggressiveness. Meta-analysis of Van IJzendoorn & Bakermans-Kranenburg (2011) confirms this idea: exogenous administration of oxytocin creates a pro-ingroup bias, but does not create de facto anti-outgroup bias.

2.4.2 The effects of oxytocin on social recognition

Social recognition is the ability to recognize a fellow as a familiar individual. It is based on the social memory that allows the individual to adopt appropriate behaviors when it comes into contact with a known congener. This social skill is essential to the formation of social bonds and the survival of the species seem to be partially determined by oxytocin.

In animals, numerous studies (Winslow & Insel, 2004; Neumann, 2008; Lee et al., 2009; Heinrichs, von Dawans, & Domes, 2009) have shown the importance of oxytocin in social recognition. In rodents, social recognition goes through the olfactory pathways. Dluzen and colleagues (Dluzen, Muraoka, Engelmann, & Landgraf, 1998) have shown that injection of oxytocin in the olfactory bulb of a rat before a first encounter with a conspecific improves the ability to recognize it as familiar at a later time. Similarly, other studies show that in mice which have a deficiency of the gene for oxytocin (oxytocin-knockout mouse), repeated presentation of a conspecific does not decrease the time of olfactory exploration. So this is the sign that, in the absence of oxytocin, rodents fail to encode an individual as being a congener familiar (Ferguson, Aldag, Insel, & Young, 2001; Lim, Bielsky, & Young, 2005; Takayanagi et al., 2005). However, when oxytocin is injected in the amygdala of these deficient mice, their ability to discriminate between individuals is restored (Fergusson et al., 2001). It is also remarkable to note that when administering an antagonist of oxytocin for meadow voles, they present a mitigation of the social contacts, which can lead to social isolation (Carter, Grippo, Pournajafi-Nazarloo, Ruscio, & Porges, 2008). These studies therefore suggest that oxytocin plays a crucial role in the socialization process.

In humans, the social recognition is mainly based primarily on visual and auditory signals. Recent studies (Kéri & Benedek, 2009; Perry et al., 2010) show that oxytocin enables the individual to better discriminate the typical human movements (that is to say, a human figure in motion). Compared to a control group, participants who received oxytocin manage to identify with more precision the pictographic stimuli depicting biological motion among a series of neutral stimuli (circles, abstract shapes) (Kéri & Benedek, 2009; Perry et al., 2010). These studies suggest that oxytocin specifically modulates the perception of the individual with respect to socially relevant stimuli and facilitates the recognition of members of our species.

Similarly, oxytocin seems to improve recognition and recall of faces. Administration of oxytocin, both in women and men, allows a better recognition of faces previously presented and this effect can be observed up to 24 hours after the encoding (Savaskan et al., 2008; Guastella et al., 2008b). Besides, it is not related to a general improvement

in memory capacity since the memory improvement seems to be specific to social stimuli (Unkelbach, Guastella, & Forgas, 2008; Rimmele et al., 2009).

2.4.3 The effects of oxytocin on emotion recognition

Besides the fact that oxytocin improves the recognition of faces, it also appears to facilitate the recognition of emotions of others. To interact appropriately with an individual requires being able to accurately recognize their emotions.

The studies suggest that oxytocin facilitates recognition of emotions in various ways. First of all, oxytocin increases the detection of emotional stimuli. The individuals under the intranasal administration of oxytocin better identify the presence of emotional faces shown briefly (less than 60 milliseconds) in a series of neutral faces than individuals under the administration of placebo (Schulze et al., 2011). Moreover, oxytocin increases the fixation on the eye region of the contact, which is particularly adaptive because the eye area is a key region in emotional recognition (Guastella, Mitchell, & Dadds, 2008a).

In line with the above, Domes and colleagues (Domes et al., 2007b) showed that individuals in oxytocin read the emotions in the eyes of their partner better than individuals taking placebo. This effect is even more pronounced in individuals who usually have difficulty in identifying the emotions of others. In people with a high degree of alexithymia (inability to identify and describe emotions in the self), oxytocin intake results in better emotional recognition whereas in subjects with a low score of alexithymia, there is no effect of oxytocin on performance. Alexithymia would therefore be a moderating variable of the effect of oxytocin on the recognition of emotions of others. Furthermore, by enhancing emotional recognition, oxytocin could positively influence interpersonal behaviors of alexthymics and would have a potential therapeutic effect (Luminet, Grynberg, Ruzette, & Mikolajczak, 2011).

Similarly, performance in Reading the Mind in the Eyes Test (which assesses the ability to infer the mental state of others based on eyes) is improved in patients with autistic disorder who received intranasal oxytocin (Guastella et al., 2010). This result is clinically important since autism is characterized by major deficits in emotional recognition (Guastella et al., 2010). Some studies suggest that oxytocin would also act on the recognition of vocal emotions. Hollander and his colleagues (2007) showed that the administration of oxytocin in subjects with autistic disorders improves their ability to identify emotions in prosody.

Although all of the literature agrees on the idea that oxytocin enhances emotional recognition, there are however some discrepancies in the type of emotions for which recognition would be facilitated by oxytocin. According to some researchers, oxytocin would facilitate only the recognition of emotions with positive valence such as happiness (Di Simplicio, Massey-Chase, Cowen, & Harmer, 2008; Marsh, Henry, Pine, & Blair, 2010). For others, this effect would only be valid for the emotions with negative valence, such as fear (Fischer-Shofty, Shamay-Tsoory, Harari, & Levkovitz,

2010; Guastella, Carson, Dadds, Mitchell, & Cox, 2009). Finally, some suggest that oxytocin would have a general action on the recognition and discrimination of emotions, regardless of valence, by increasing the salience of social cues to discriminate (Shamay-Tsoory et al., 2009). The current data do not explain these discrepancies. But in the light of what we have seen above (that is to say, oxytocin specifically enhances the capacity of those who are deficient in emotion recognition), it is likely that contextual and personal differences explain these discrepancies.

In conclusion, oxytocin seems to be involved in a considerable number of processes for the establishment of the social relationship: oxytocin increases the attractiveness and the trust inspired by others while allowing the individual to retain the ability of discernment, promotes social recognition and improves the identification of emotions.

2.4.4 Gender-related effects of oxytocin

The large majority of studies investigating the effects of intranasal oxytocin administration on social cognition and emotion recognition has been conducted in male participants. Therefore, the possible differential effects by gender are not well studied. Moreover, there is not a consistent literature on the gender-related effects of intranasal oxytocin. Some studies suggest that there is no gender difference (Ditzen et al., 2009; Shamay-Tsoory et al., 2009; Savaskan et al. 2008; Theodoridou et al., 2009; Guastella et al., 2009). However, significant gender differences have been reported in more recent studies (Hoge et al., 2014; Lynn, Hoge, Fischer, Barrett, & Simon, 2014; Campbell, Ruffman, Murray, & Glue, 2014; Fischer-Shofty, Levkovitz, & Shamay-Tsoory, 2013; Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010; Kubzansky, Mendes, Appleton, Block, & Adler, 2012).

For instance, Fischer-Shofty et al. (2013) tried to find out the effects of intranasal oxytocin on the accurate perception of male and female participants in social interactions shown in realistic video clips. Researchers reported that male participants receiving intranasal oxytocin more accurately perceive competition interactions while female participants receiving intranasal oxytocin more accurately perceived kinship interactions. Another study conducted by Domes et al. (2010) found that the amygdalar activity of female participants in response to angry faces was not affected by intranasal oxytocin administration whereas the intranasal oxytocin administration led to a decrease in the amygdalar activity of male participants (Domes et al., 2007a).

Thus, in order to better interpret experimental results and to investigate socio-behavioral differences between women and men, the studies on oxytocin should recruit both male and female participants and include gender as a factor in their analysis.

2.5 Pupil size and dynamics

The pupil is the central aperture of the iris which controls the amount of light entering the eye. The size and responsiveness of pupil are regulated by two synergistic-like

pathways that operate on the smooth muscles of the pupil, as first described by Sherrington in 1911 (as cited in Beatty & Lucero-Wagoner, 2000).

The parasympathetic pathway that is mediated from the Edinger-Westphal oculomotor complex in the midbrain controls pupillary sphincter muscle. It is a circular muscle responsible for constriction of the pupil. The sympathetic pathway that is mediated by the hypothalamus controls pupillary dilator muscle. Since the dilator muscle is responsible for dilation, sympathetic excitation results in pupil dilation (Loewenfeld & Lowenstein, 1993).

The physiology of the pupil is complex, but the knowledge of anatomical pathways responsible for pupillary constriction and dilation allow us to evaluate pupillary responses in different tasks.

2.5.1 Primary pupil functions

First of all, the main function of the pupillary movements is to fulfill primarily tasks to prepare the waking organism for optimal viewing conditions. One of these optimal viewing conditions is the reflex of the pupil, namely the pupillary light reflex: In bright light, the pupils get smaller. As the light gets darker, pupils become larger. This size change is particularly important in extreme lighting conditions (i.e., walking at night or on a sunny day). The aim of the pupil size changes is to provide the retina with a reasonable amount of light available, so that the photoreceptors receive neither too many nor too few photons. A second important optical effect of changes in size of the pupil is near reflex which is responsible for the regulation of focus. For instance, when the visual stimuli is located close, unaccommodated pupils get reflexively smaller, reducing the depth of field. Finally, by narrowing pupil diameter optical aberrations can be reduced, which in turn helps the optical system or the visual acuity.

2.5.2 Psychosensory pupillary responses

The psychosensory pupillary response builds a bridge between well-understood pupillary light and near reflexes and not so well understood pupil size changes that occur in cognitive and emotional processes since their neural mechanisms are complex. Stimulation by very intense and/or task-relevant stimuli results in pupil dilation. In addition, even in the absence of external stimuli, cognition, emotions and mental effort are equally capable to modify the pupil size. This reaction shows that the pupil dilation depends on not necessarily physical, but more on task-specific stimulus characteristics. Thus, this type of pupillary response also called as task-evoked pupillary response (TEPR). TEPR is relatively small (from 0.1 millimeters to maximum 0.5 millimeters), compared with the pupil light reflex which can amount to several millimeters. Therefore, these relatively weak psychosensory responses should be correctly evaluated when there are already slightly oscillating pupil movements, due to large spontaneous activity. Depending on the intensity of TEPR, a sympathetic stimulation or a central inhibition of parasympathetic oculomotor nucleus may be in

charge. Finding the origin of the mechanism that initiates the dilation in the pupils is hard.

2.5.3 The relationship between pupil dilation and emotional stimuli

Starting with the precious work of Charles Darwin in 1850 who investigated the effect of emotion and fear in animals, the relationship between cognitive or emotional processes and pupil dilation has been discussed for more than a century (Darwin et al., 1998, Hess, 1975; Steinhauer, 2002). The first description of psychosensory reactions can be dated to 1911, when the neurologist and psychiatrist Oswald Bumke came to the following conclusion:

"Every active intellectual process, every psychological effort, every exertion of attention, every active mental image, regardless of content, particularly every affect just as truly produces pupil enlargement as does every sensory stimulus." (as cited in Hess, 1975)

In the 1960's, these findings were taken up again: In the emotion research, psychologists are interested in whether the pupil diameter could reflect emotions such as sympathy and antipathy. Hess postulated the aversion–constriction hypothesis according to which the pupil constricts when an unpleasant stimulus is presented and dilates when a pleasant stimulus appears (Hess, 1965; Hess & Polt, 1960; Hess, Seltzer, & Shlien, 1965). However, these studies had significant methodological shortcomings, so that their results have been widely questioned (Janisse, 1977). Janisse (1974) examined valence-specific pupillary responses in a methodologically less contestable investigation: The study brought to light that not only positive but also negative emotions lead to pupil dilation. Moreover, it is also reported that highly pleasant or aversive pictures were associated with large pupil dilations (Steinhauer, Boller, Zubin, & Pearlman, 1983; Bradley, Miccoli, Escrig, & Lang, 2008).

Pupil dilation in response to emotional or visual stimuli is mainly controlled by the sympathetic limb of the autonomic nervous system originating in the hypothalamus. The limbic system is reciprocally connected to the visual pathway in the cortex in a complex system and with the help of this system; the pupil dilation can be triggered by the visual recognition pathway. The cortex can also mediate a direct influence on the pupil diameter via its direct projections to the parasympathetic Edinger-Westphal nucleus in the midbrain (Barbur, 2003). Therefore, in principle, a visual target which is semiconsciously recognized in the visual pathway -but not reported by a motor response whose initialization occurs later- is still able to trigger activation in the limbic system, in terms of a pupil dilation response.

It is also widely documented that mental events inhibit the Edinger-Westphal nuclei thus causing the relaxation of the sphincter muscle, contributing to the dilation of the pupil (Smith, Masek, Ichinose, Watanabe, & Stark, 1970; Krenz & Stark, 1985). Visceral, somatic and olfactory sensory information are all relayed to the hypothalamus, converging onto the efferent sympathetic fiber system. It has been

known for centuries, that they elicit a pupillary dilation (Loewenfeld & Lowenstein, 1993; Kahneman, 1973; Hess, 1975; Beatty, 1982; Steinhauer, 2002).

2.5.4 The effect of intranasal oxytocin on pupillary responses

To the best of our knowledge, there are only two studies that specifically recorded the pupil response during the evaluation of emotional expressions under the administration of intranasal oxytocin (Leknes et al., 2012; Prehn et al., 2013). Their data indicate that a single dose of intranasal oxytocin enhanced evaluative processing of others' positive and negative facial expression represented as both explicit and implicit visual stimuli. The researchers reported that the administration of oxytocin results in an increase in stimulus-induced pupil dilation, consistent with the prosocial effects of oxytocin such as enhancement of attention towards socially relevant stimuli (Leknes et al., 2012). This result is interpreted as a mechanism that human affiliation is increased by the administration of oxytocin since pupil dilation is generally related to increased attractiveness and approach behavior (Leknes et al, 2012).

2.6 Motivation, Research Questions and Hypotheses

Studies suggest that intranasal administration of oxytocin improves the skill to recognize emotions since it is involved in the processing of socially relevant stimuli. Moreover, recent studies report that intranasal administration of oxytocin results in higher pupil diameter changes in response to emotional stimuli which may reflect the affective state of the individual. In the current study, it is aimed to examine whether the simple appearance and evaluation of a visual stimuli with a specific emotional content triggers pupil dilation in a face recognition task. Possible effects of oxytocin is evaluated specifically for two aspects of the facial stimuli: 1. Trustworthiness of the face when the facial expression is neutral 2. Recognition of the emotional facial expressions. Possible sexual dimorphisms of oxytocin intake in humans are investigated by recruiting male and female subjects. Dependent variables that are investigated are subjective ratings and pupil diameter.

The research questions and hypotheses are as follows:

Trustworthiness evaluation related research questions and hypotheses

Research Question 1: Is there a relationship between intranasal oxytocin intake and trustworthiness judgments?

Hypothesis 1: Since oxytocin increases the attractiveness and the trust inspired by others, participants receiving oxytocin will rate neutral faces as more trustworthy than participants receiving placebo.

Research Question 2: Is there a relationship between subjective trustworthiness evaluation and pupil size?

Hypothesis 2: Since pupillary changes reflect the arousing state and attention of the individual, faces rated as trustworthy will differ in terms of initiation of pupillary responses. Thus, trustworthy and untrustworthy faces will elicit larger pupil diameters compared to faces rated as neutral.

Research Question 3: Will the general effect of oxytocin on pupils, which is increased pupil diameter, hold during trustworthiness judgements?

Hypothesis 3: Participants receiving oxytocin will show larger pupil diameters compared to participants receiving placebo while judging trustworthiness.

Facial expression recognition related research questions and hypotheses

Research Question 4: Is there a relationship between intranasal oxytocin intake and accuracy of facial expression recognition?

Hypothesis 4: Since the oxytocin improves the ability to recognize facial expressions, participants receiving oxytocin will recognize emotions expressed by faces more accurately compared to participants receiving placebo.

Research Question 5: Is there a relationship between facial expression judgement and pupil size?

Hypothesis 5: Since pupillary changes reflect the arousing state and attention of the individual, faces expressing different emotions will differ in terms of pupillary responses. Moreover, faces expressing six basic emotions will elicit bigger pupil diameters compared to neutral faces.

Research Question 6: Will the general effect of oxytocin on pupils, which is increased pupil diameter, hold during recognition of facial expressions?

Hypothesis 6: Since oxytocin has an effect on sympathetic activation leading to pupil dilation, participants receiving oxytocin will show larger pupil diameter changes compared to participants receiving placebo during recognition of facial expressions.

Gender related research question and hypothesis

Research Question 7: Does intranasal oxytocin intake affect males and females differently?

Hypothesis 7: Since it is reported that intranasal oxytocin affects the physiological responses of female and male subject differently (i.e., it is related to sympathetic arousal in males but parasympathetic activation in females), intranasal oxytocin may affect both genders differently due to differential endogenous hormone levels.

CHAPTER 3

METHOD

In this chapter, scale-based and computer-task-based materials, experimental stimuli generation and preprocessing steps, participants and experimental design are covered. There were two phases in the experiment. In the first phase, participants rated the trustworthiness whereas in the second phase they indicated the name of the facial emotional expression. Detailed information about these steps can be found below.

3.1. Materials

3.1.1. Scale-Based Materials

Two different scale-based materials are used in the present study: Beck Depression Inventory (BDI) and Positive and Negative Affect Schedule (PANAS). The detailed explanation of each material can be found below.

Beck Depression Inventory

In order to detect whether the participants are depressed, the Beck Depression Inventory (BDI) was used. The BDI was initially developed by Dr. Aaron T. Beck in 1961 (Beck, 1961). It is mainly used to measure the severity of depression in humans. It is composed of 21 questions with multiple-choice answers. The questions focus on items related to symptoms of depression including hopelessness, irritability, physical symptoms and cognitions. For each item of the BID, four levels ranging from non-severe (scored 0) to severe (scored 3) are specified. Thus, the lowest score and the highest score to be gained in the inventory are 0 and 63, respectively. Higher scores indicate more severe symptoms of depression whereas lower scores indicate no sign or least severe symptoms of depression.

Adaptation and validation of the BDI in the Turkish population were done by Hisli (1988) and Sahin and Sahin (1992). Based on results of studies in the Turkish population, participants who got 17 or lower points are accepted as non-depressed and included in the study. The answer sheet of the inventory used in the study can be found in Appendix D.

Positive and Negative Affect Scale (PANAS)

To assess their mood and to obtain a measure of their emotional state, participants were asked to complete the Positive and Negative Affect Schedule (PANAS) at the time in the beginning, middle and end of the experiment. The PANAS is the most commonly used standardized test to assess the affect or mood. The scale developed by Watson,

Clark, & Tellegen (1988) is composed of two sets of positive and negative affect with 10-items. Positive affect (PA) reflects the degree of alertness and activeness of a person while negative affect (NA) reflects the amount of fear, anger and guilt that a person experiences. Adaptation and validation of the PANAS in the Turkish population were done by Gençöz (2000).

As a measure of their current mood state, participants were asked to evaluate the degree of the emotion they experienced by rating each emotion word (e.g. upset, alert) on a 5-point Likert type scale ranging from 1=very slightly/not at all to 5=extremely. The scoring of the scale is made separately for positive and negative affect evaluation. Items 1, 3, 5, 9, 10, 12, 14, 16, 17 and 19 are summed for the positive affect score whereas remainder items are summed for the negative affect score. In each set of affect, scores can range from 10 to 50, and higher scores indicate higher levels of positive/negative affect. If the positive score of the participant is greater than her/his negative score, s/he is considered to be in positive mood whereas for the reverse situation, s/he is considered to be in negative mood. The answer sheet of the scale used in the study can be found in Appendix E.

3.1.2. Computer-Task-Based Materials

Stimulus materials are taken from the set of pictures of the Karolinska Directed Emotional Faces (KDEF) collection (Lundqvist, Flykt, & Öhman, 1998). The database is one of the most elaborate sets used in the research field of perception, attention, memory and emotion. The set contains two sets of images of 70 individuals (35 females and 35 males) with an age range of 20-30, each displaying 7 different emotional expressions (neutral, happy, angry, afraid, disgusted, sad, and surprised), and each expression being photographed from 5 different angles. Participants all wearing gray t-shirt have no beards, mustaches, earrings, eyeglasses or visible. Detailed information about the database can be found in the study of Lundqvist et al. (1998).

Frontal head-shot photographs of 33 males and 33 females with neutral expressions and a direct gaze were used for the trustworthiness evaluation task. For the emotional recognition task, frontal head-shot photographs of 5 males and 5 females with each emotional expression (neutral, happy, angry, afraid, disgusted, sad, and surprised) and a direct gaze were used. Examples of stimuli used in the study can be found in Figure 3.1.

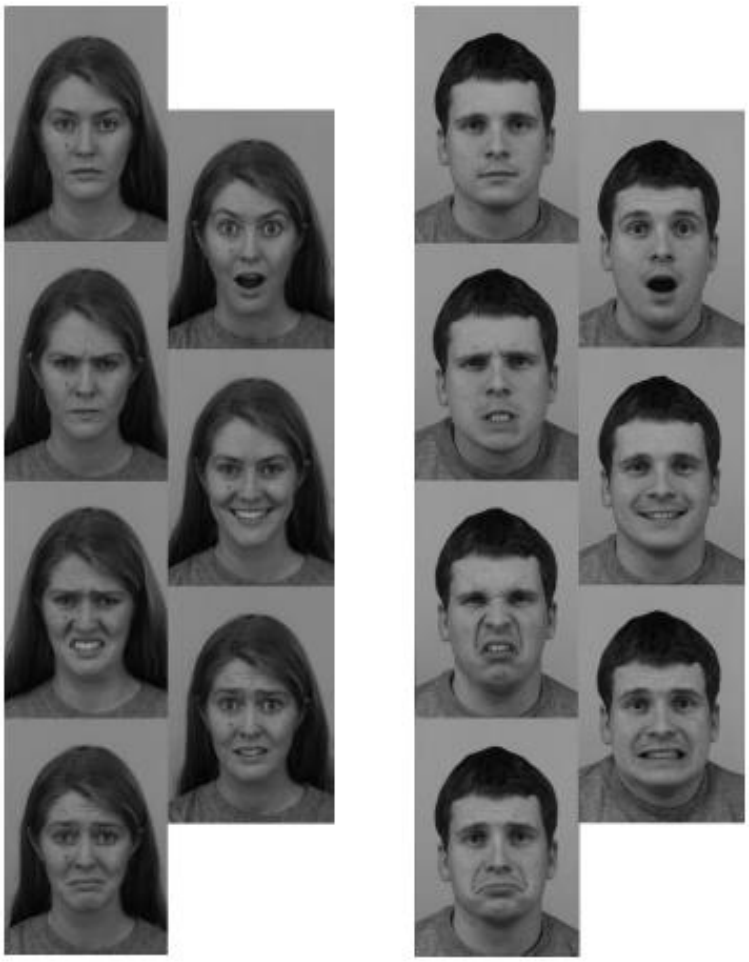

Figure 3.1 Sample stimuli from KDEF

3.2. Stimuli Creation

Since the pupils' responsiveness to brightness, color and illumination of visual stimuli changes, these features of the images should be standardized. Therefore, in order to reduce the variations among stimuli, pre-processing was applied to the database by using the methods of Hepsomalı (2013). Pre-processing includes converting images from three colored (RGB) to gray scale, face size rescaling. Pre-processing was accomplished by using Adobe Photoshop CS4.

3.2.1. Converting from RGB to Gray scale

Three coloured (RGB) images are converted into gray scale. Conversion of the gray scale is done in order to reduce the effect of illumination changes on pupillary responses.

3.2.2. Face Size Rescaling

In order to control the head size differences, four extreme points on the each face are selected: uppermost, lowermost, leftmost and rightmost. After the completion of the selection, these points are used to find the vertical and horizontal axes for faces. In order to find the width of the face left and right extremes are subtracted. Likewise, lower and upper extremes are subtracted to find the length of the face. Since the average width and length of the faces are 313 and 450 pixels, respectively, all images are rescaled in order to keep a constant aspect ratio of 1.43.

3.2.3. Intensity Adjustment

In order to normalize brightness of the stimuli, mean intensity values of all images were computed and outliers were set to the values that are similar to mean intensity values. After adjustment, mean intensity of the entire image set was 105.13 and standard deviation was 10.45.

3.3. Experimental Design

The aim of the experiment is to find possible effects of intranasal oxytocin on fixation durations, pupillary responses, trustworthiness rating, and emotional recognition in a subset of KDEF databases.

3.3.1. Participants

48 right handed participants (24 male, 24 female) between ages of 21-26 (M = 23.5, S.D = 1.60) were recruited for participation in this study. The participants were randomly assigned to control and experimental groups. In the control group, saline solution was administered as placebo. The average ages of male and female participants were 23.6 (S.D. = 0.95) and 23.6 (S.D. = 1.03) respectively. In the experimental group, oxytocin was administered. The average ages of male and female participants were 23.4 (S.D. = 1.04) and 23.75 (S.D. = 0.93), respectively. All participants were blind to aim of the study, free of psychoactive and endocrinologically relevant medication (including oral contraceptives), had normal or corrected to normal vision, and did not report a history of neurological or endocrine disease. Female participants were in the luteal phase of the cycle during at the time of experiment, based on reported number of days since the last menses. All participants provided written informed consent to the study procedures, which were previously approved by the METU Ethics Committee (see Appendix F).

Exclusion criteria

Since BDI scores of participants were 17 or lower points, none of the participants were considered as outliers in terms of depressive status. Since PANAS scores indicated positive and negative affect scores were acceptable (for positive affect: all higher than

20, for the negative affect: all below 20), none of the participants were considered as outliers in terms of mood (see section 4.1).

3.3.2. Apparatus

Tobii Studio (TS) 3.1.3 software and Tobii Eye Tracking System (TETS) T120 were used to present stimuli and record data, respectively. All stimuli were presented by TS with 1280x1024 pixels resolution and pupillary responses were collected by TETS on a 17" TFT monitor under the control of Windows 7 based desktop computer in Human Computer Interaction (HCI) Laboratory in Middle East Technical University Computer Centre, with data rate of 60 Hz, tracking distance of 50-80 cm.

3.3.3. Procedure

On the experimental days, participants were instructed to abstain from smoking, caffeine, and analgesic medication. Subsequently, participants were familiarized with the experimental procedures, the administration of the neuropeptide or placebo, and the stimuli. For female participants in both control and experimental group, in order to rule out possible interactions of exogenous oxytocin with fluctuations of gonadal steroids over the menstrual cycle, all sessions were conducted in the mid-luteal phase as assessed by participants self-report.

In the experiment, participants were seated in HCI Laboratory. After a brief explanation of the experimental procedure, written consent (see Appendix G) and demographic information (see Appendix H) were taken from the participants before they filled in the BDI and the PANAS for mood assessment. Completion of admission procedure generally took 10 minutes.

Mood was measured at three time points during each session: 1) before the nasal spray administration; 2) immediately before the experimental protocol; and 3) immediately after the experimental protocol. Participants rated their current level of feelings using PANAS.

An overview of the study design is presented in Figure 3.2. There were two periods in the experiment: treatment and experiment periods. There were two groups which are control and experimental groups. Three male and one female participants in the control group participated with placebo (0.9% saline; six puffs alternating between the left and the right nostril) whereas remaining three male and one female participants in the experimental group participate in one session with 24IU oxytocin (Syntocinon, Novartis; six puffs alternating as above). A previous study (Prehn et al., 2013) focused on the effect of intranasally administered oxytocin on pupil dilation and emotion perception during a face recognition task. Following a standardized protocol of administration of intranasal oxytocin, we choose to administer the same dose. Participants were not aware of the contents of the spray they received, and self-administered oxytocin or placebo under the supervision of the study coordinator (G.S.) 45 minutes before the start of the experiment period. Before the experimental protocol,

participants were seated alone in HCI laboratory and asked to refrain from any type of social interaction.

Before the initiation of the experiment, 9-dot calibration of TETS was applied and participants were asked to fill the PANAS. In the experiment period, there were four experiments: gender classification, trustworthiness evaluation, facial expression recognition and gender classification.

In the **first experiment**, participants were shown 20 images (10 male and 10 female faces with neutral expression) on the center of gray background (R: 106 G: 106 B: 106) with 15º horizontal visual angle. The instructions were presented on the computer screen, aided with verbal explanations by the experimenter. They were asked to classify the gender of the faces they saw on the computer screen. Each stimulus was presented for 4 seconds. The order of presentation of the stimuli was pseudorandomized (Appendix I). Between faces, a fixation cross was presented for 2 seconds. Each stimulus was followed by the presentation of gender classification question which was presented until the participant made a response. Responses were entered directly using specific keys assigned to female and male choices on the computer's keyboard. Fixation durations and pupil diameters were collected throughout the experiment, but among these, only data during stimulus presentation was used for analysis.

In the **second experiment**, participants were shown 66 images (33 male and 33 female faces with neutral expression) on the center of gray background (R: 106 G: 106 B: 106) with 15º horizontal visual angle. The instructions were presented on the computer screen, aided with verbal explanations by the experimenter. The instructions explained how the task should be performed and stressed that the participant should respond with his/her very first impression regarding trustworthiness. In order to prevent emotional judgments influencing trustworthiness, "neutral" faces were presented. The experimenter explained the meaning of "trustworthiness" using the example of visiting an unknown town and having to decide whom to ask for an address based on how much confidence their faces suggest[2]. Ratings were made along a 1 to 9 scale (1: not at all trustworthy; 9: very trustworthy). Each stimulus was presented for 4 seconds. The order of presentation of the stimuli was pseudorandomized (Appendix I). Between faces, a fixation cross was presented for 2 seconds. Each stimulus was followed by the presentation of trustworthiness scale which was presented until the participant made a response. Responses were entered directly using specific keys corresponding to trustworthiness ratings on the computer's keyboard. Fixation durations and pupil diameters were collected throughout the experiment, but among these, only data during stimulus presentation was used for analysis.

[2] "Daha önce bulunmadığınız bir kenttesiniz ve bir adrese gitmek istiyorsunuz. Ekranda yüzünü gördüğünüz kişiye elinizdeki bu adrese nasıl gideceğinizi sorar mıydınız? Seçiminizi 1'den (kesinlikle sormam) 9'a kadar (kesinlikle sorarım) rakamlara basarak yapabilirsiniz."

In the **third experiment**, participants viewed 70 faces displaying a range of emotional expressions (5 male and 5 female with 7 different emotional expression) on a computer screen. They were asked to evaluate the emotional expression of the faces they see on the computer screen. After each stimulus, participants made an emotional categorization of the visual stimulus. Each stimulus was presented for 4 seconds. The order of presentation of the stimuli was pseudorandomized according to the following rules: no more than two consecutive images of the same expression, no more than two consecutive images of the same person (Appendix I). Between faces, a fixation cross was presented for 2 seconds. Each stimulus was followed by the presentation of emotional categorization which was presented until the participant made a response. Participants were asked to designate the facial expression of emotion according to a numerical setting. They had to press 1-happy, 2-sad, 3-angry, 4-disgust, 5-surprise, 6-fear or 7-neutral in order to name the facial expression of emotion on the screen. Fixation durations and pupil diameters were collected throughout the experiment, but among these, only data during stimulus presentation was used for analysis.

The **fourth experiment** was exactly the same as the first experiment. It was conducted to observe whether there was a difference in physiology of pupil dilation between the beginning and the end of the experiment due to metabolism of oxytocin.

After the completion of the experiments, the participants were asked to fill PANAS and given a debriefing form that explains the aims and possible results of the experiment (Appendix J).

3.3.4. Analysis

Kolmogorov-Smirnov tests were performed in order to check the normality assumption of the data. Since p-values were all above 0.05, it was concluded that the data showed a normal distribution. The results of repeated measures of analysis of variances (ANOVAs) for pupil diameter changes revealed that although there was no main effect of condition and gender, there was a highly significant interaction effect during trustworthiness evaluation and facial expression recognition tasks, ($p < 0.0001$ and $p = 0.001$, respectively).

Previous studies investigating the effect of intranasal oxytocin on pupillary responses were done in only male subjects (Prehn et al., 2013; Leknes et al., 2012). Hence we did not have background information regarding the female population. Furthermore, physiological responses of the sympathetic and parasympathetic systems of the females were reported to differ from males, as we discussed in section 2.4.4. Due to these reasons, we expected differential responses in females. Therefore, the data of male and female participants were separately analyzed. The results can be seen in the following section.

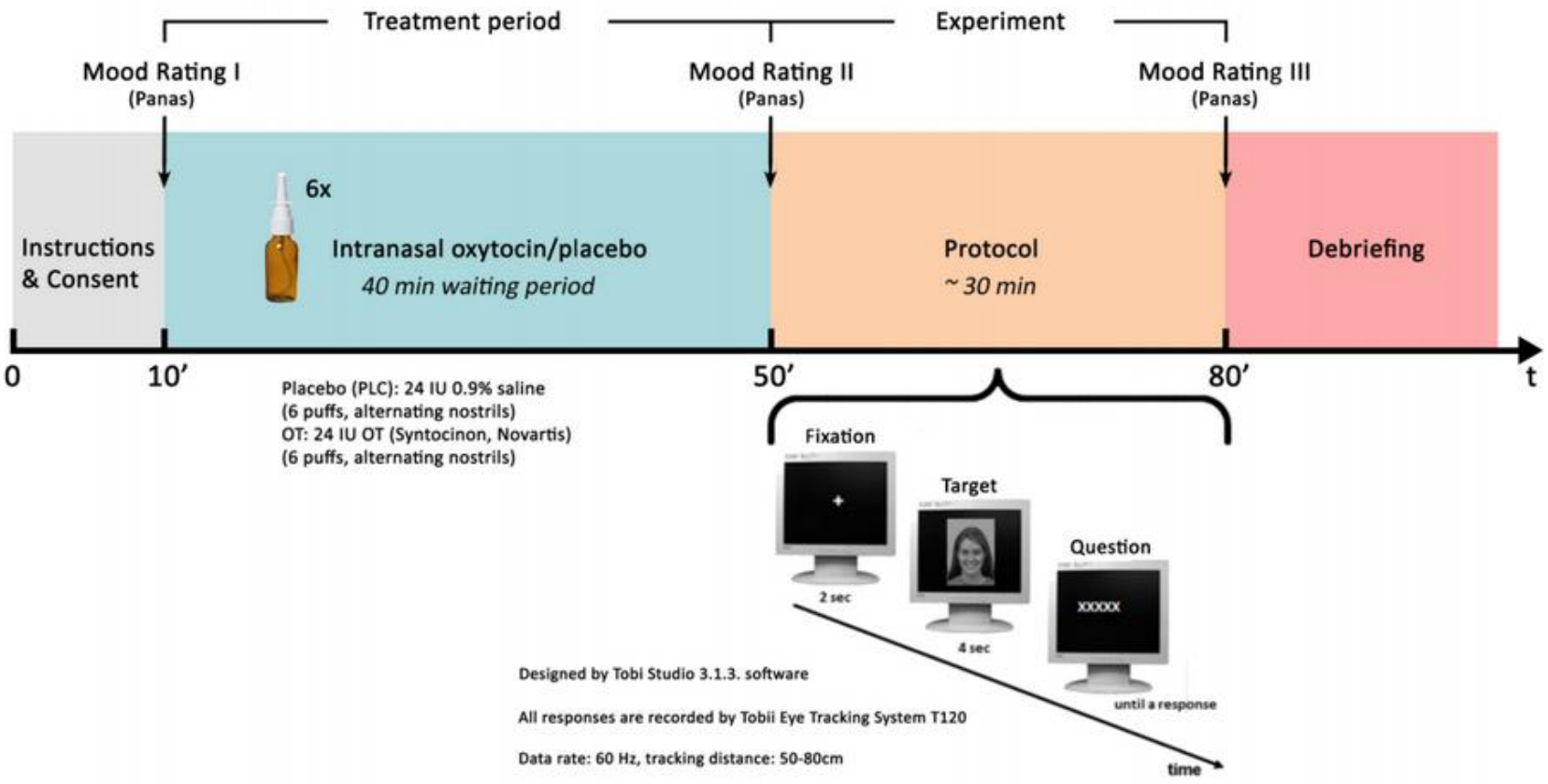

Figure 3.2 Overview of the study design.

CHAPTER 4

RESULTS

4.1. Mood assessment

For each gender group, a mixed-design ANOVA with time-point in which the participants were asked to fill PANAS (beginning, middle, end) as a within-subjects factor and the application of substance (oxytocin, placebo) as between-subjects factor was conducted to examine the effect of oxytocin administration and time-points on positive and negative affect scores.

For the male participants' positive affect scores, there was a significant main effect of time-points in which PANAS was filled ($F (2, 44) = 3.284$, $p = 0.047$, $\eta^2 = 0.13$). However, the statistical analysis revealed nonsignificant effect of oxytocin administration ($F (1, 22) = 0.484$, $p = 0.494$, $\eta^2 = 0.022$). The predicted interaction among time-point and oxytocin administration was not significant ($F (2, 44) = 0.156$, $p = 0.856$, $\eta^2 = 0.007$). In terms of time-point main effect, the positive affect scores of male participants tended to rise throughout the experimental procedure (at time-point(1) M = 43.83, S.E. = 0.29, at time point(2) M = 43.96, S.E. = 0.29, at time-point(3) M = 44.46, S.E. = 0.27).

For the male participants' negative affect scores, there was a significant main effect of time-points in which PANAS was filled ($F (2, 44) = 3.85$, $p = 0.029$, $\eta^2 = 0.149$). However, the statistical analysis revealed nonsignificant effect of oxytocin administration ($F (1, 22) = 0.085$, $p = 0.773$, $\eta^2 = 0.004$). The predicted interaction among time-point and oxytocin administration was not significant ($F (2, 44) = 0.55$, $p = 0.581$, $\eta^2 = 0.024$). In terms of time-point main effect, the negative affect scores of male participants tended to decrease throughout the experimental procedure (at time-point(1) M = 11.33, S.E. = 0.16, at time-point(2) M = 11, S.E. = 0.14, at time-point(3) M = 10.83, S.E. = 0.13).

For the female participants' positive affect scores, there was nonsignificant main effect of time-points in which PANAS was filled ($F (2, 44) = 2.106$, $p = 0.134$, $\eta^2 = 0.087$). Further, the statistical analysis revealed nonsignificant effect of oxytocin administration ($F (1, 22) = 2.093$, $p = 0.162$, $\eta^2 = 0.087$). Also, the predicted interaction among time-point and oxytocin administration was not significant ($F (2, 44) = 0.702$, $p = 0.501$, $\eta^2 = 0.031$).

For the female participants' negative affect scores, there was nonsignificant main effect of time-points in which PANAS was filled ($F (2, 44) = 0.855$, $p = 0.432$, $\eta^2 = 0.037$). Further, the statistical analysis revealed nonsignificant effect of oxytocin administration ($F (1, 22) = 1.005$, $p = 0.327$, $\eta^2 = 0.044$). Also, the predicted interaction

among time-point and oxytocin administration was not significant ($F(2, 44) = 0.115$, $p = 0.892$, $\eta^2 = 0.005$).

Since all participants' BDI score is lower than 17, all participants were considered as non-depressed and none of their data was excluded based on BDI score.

4.2. Task-related pupillary responses in gender classification tasks

For each gender in different conditions (oxytocin or placebo), a paired-samples t-test was conducted to compare the pupil diameter changes in gender classification tasks.

For the male participants receiving oxytocin, there was a significant difference in the the pupil diameter changes in the first ($M = 0.342$, $S.D. = 0.119$) and second ($M = 0.3$, $S.D. = 0.102$) gender classification tasks; $t(10) = 3.847$, $p = 0.003$. For the male participants receiving placebo, there was not a significant difference in the the pupil diameter changes in the first ($M = 0.268$, $S.D. = 0.05$) and second ($M = 0.25$, $S.D. = 0.045$) gender classification tasks; $t(6) = 0.869$, $p = 0.418$.

For the female participants receiving oxytocin, there was not a significant difference in the the pupil diameter changes in the first ($M = 0.358$, $S.D. = 0.097$) and second ($M = 0.328$, $S.D. = 0.084$) gender classification tasks; $t(10) = 1.149$, $p = 0.277$. For the female participants receiving placebo, there was a significant difference in the the pupil diameter changes in the first ($M = 0.3$, $S.D. = 0.053$) and second ($M = 0.252$, $S.D. = 0.034$) gender classification tasks; $t(10) = 2.574$, $p = 0.028$.

This variability introduced due to timing of the task in the experimental session needs to be inspected later.

4.3. Trustworthiness evaluation

4.3.1 Behavioral data

4.3.1.1 Trustworthiness ratings of male participants

An independent samples t-test between the male participants in oxytocin and placebo groups revealed that the male participants receiving oxytocin ($M = 5.69$, $S.E. = 0.07$) rated neutral facial expressions more trustworthy than the male participants receiving placebo ($M = 4.74$, $S.E. = 0.098$), $t(22) = 7.798$, $p < 0.0001$.

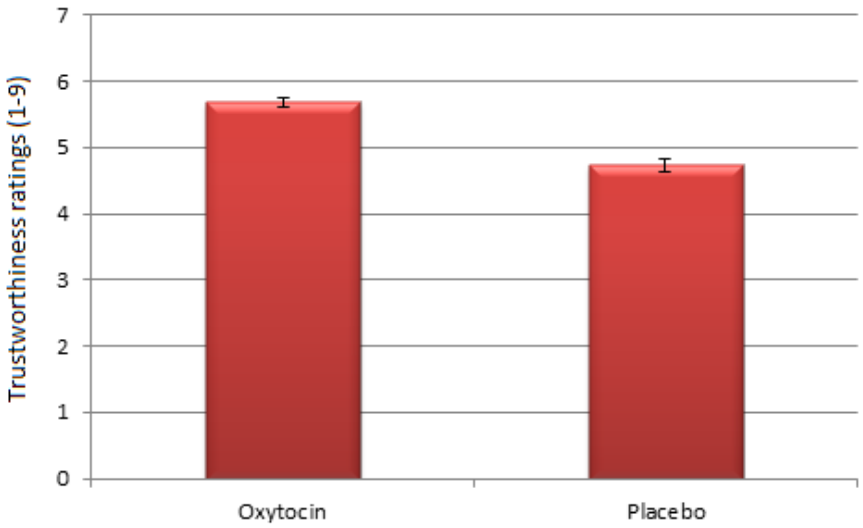

Figure 4.1 Trustworthiness ratings of neutral faces in both oxytocin and placebo groups (male participants). (Error bars represent standard error)

An ANOVA revealed significant main effect of the gender of the face stimuli (i.e., whether a male or female face was presented) ($F(1, 11) = 38.765$, $p < 0.0001$, $\eta^2 = 0.731$). In terms of gender main effect, the male participants rated female faces ($M = 5.86$, S.E. = 0.082) more trustworthy compared to male faces ($M = 4.58$, S.E. = 0.091).

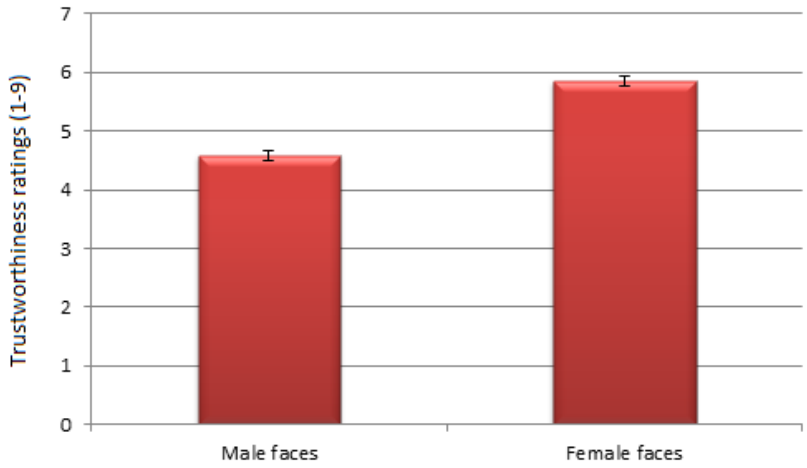

Figure 4.2 Trustworthiness ratings of female and male faces with neutral expression (male participants). (Error bars represent standard error)

4.3.1.2 Trustworthiness ratings of female participants

An independent samples t-test between the female participants in oxytocin and placebo groups revealed that the female participants receiving oxytocin ($M = 5.62$, S.E. =

0.027) rated neutral facial expressions more trustworthy than the female participants receiving placebo (M = 4.70, S.E. = 0.052), t(22) = 15.710, p < 0.0001.

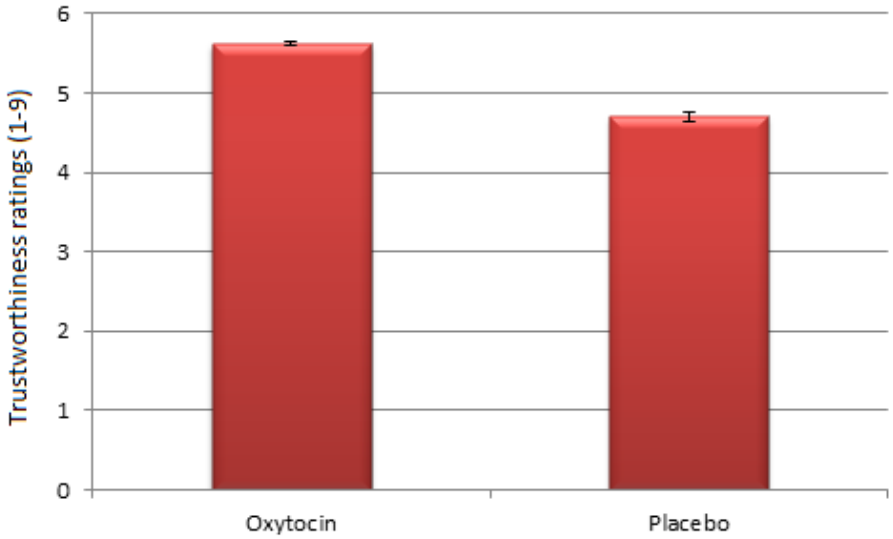

Figure 4.3 Trustworthiness ratings of neutral faces in both oxytocin and placebo groups (female participants). (Error bars represent standard error)

An ANOVA revealed significant main effect of the gender of the face stimuli (i.e., whether a male or female face was presented) ($F(1, 11) = 18.231$, $p < 0.0001$, $\eta^2 = 0.853$). In terms of gender main effect, the female participants rated male faces (M = 5.52, S.E. = 0.041) more trustworthy compared to female faces (M = 4.81, S.E. = 0.033).

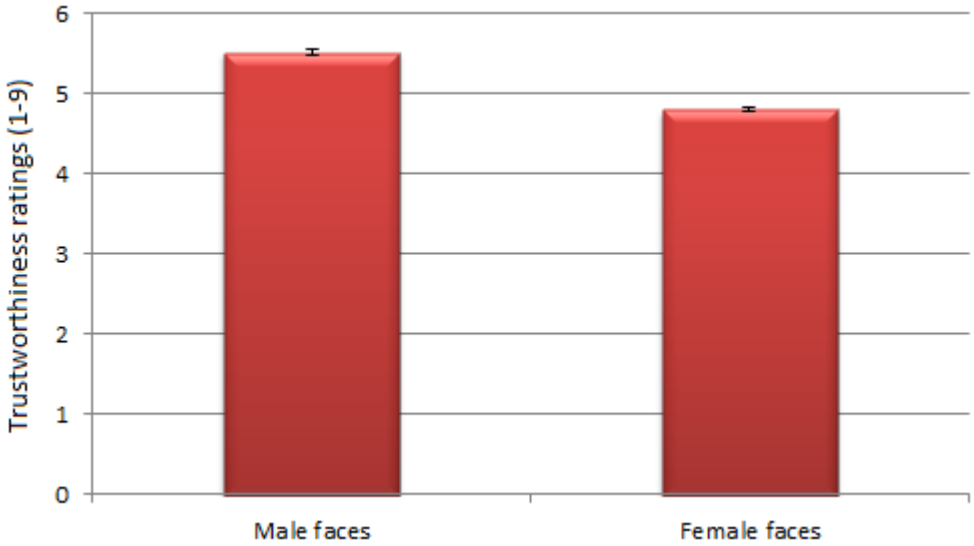

Figure 4.4 Trustworthiness ratings of female and male faces with neutral expression (female participants). (Error bars represent standard error)

4.3.2 Physiological data

Pupillary Responses

Data were preprocessed by linear interpolation in order to fill in the gaps that resulted from eye blinking or head movements. When more than 30% of the data of a participant had to be corrected, pupillary response is assumed to be unreliable and the pupil data of that trial has to be discarded. In this study, none of the participants' data was discarded in terms of excessive correction. Pupil responses during the 4-second stimulus presentation section of the trials were extracted. In other words, only passive viewing sections of the experiment was taken into consideration, disregarding fixation and judgment sections. At the end of the extraction, 240 data points (60 Hz x 4 seconds) were obtained for each image. For each trial, the initial pupil diameter was subtracted from each of the following samples so the initial pupil diameter was set to zero in all of the stimulus onsets. Then, only the peak values of pupil diameter were used in analysis below. This way, changes from the stimulus onsets (i.e. baselines) are normalized between different trials.

4.3.2.1 Comparison of responses of left and right eyes in terms of pupil diameter changes of male participants

A 2 (condition: oxytocin, placebo) x 3 (eye location: left eye, right eye, averaged) ANOVA was applied to assess whether the response of eyes differed significantly. There was no main effect of eye ($F(2,484) = 1.068$, $p = 0.43$) and no interaction effect of condition and eye ($F(2,484) = 0.864$, $p = 0.39$); that is, pupil dilation was not affected by eye location. Moreover, since healthy people have equal pupils (isocoria), a correlation must be observed between left and right pupil sizes. Correlation analysis revealed a statistically significant correlation ($r = 0.916$, $p < 0.0001$) between left and right pupil sizes and thus data from left and right pupils were averaged for each subject in order to use in further analysis.

4.3.2.2 Task-related pupillary responses of male participants

A 2 (condition: oxytocin, placebo) x 3 (trustworthiness evaluation: untrustworthy, trustworthy, neutral) ANOVA on pupil diameter changes was performed in order to find whether there is an effect of oxytocin and/or trustworthiness evaluation on pupil diameter changes. First, the trials based on subjective evaluation of trustworthiness in both oxytocin and placebo conditions were listed. Then based on subjective evaluation, untrustworthy trials which got 1, 2 or 3; neutral trials which got 4, 5 or 6 and trustworthy trials which got 7, 8 or 9 as rating scores were grouped together. The statistical analysis was conducted on average data from these grouped trials.

In male subjects, the analysis showed that the application of oxytocin has a marginally significant effect on pupil dilation ($F(1,11) = 4.709$, $p = 0.053$) and there is a highly statistically significant effect of subjective trustworthiness evaluation ($F(1,22) = 42.777$, $p < 0.0001$). Moreover, there is also a statistically significant interaction effect

of oxytocin application and subjective trustworthiness evaluation ($F(1,22) = 3.914$, $p = 0.035$).

In terms of condition main effect, the participants receiving oxytocin ($M = 0.419$, S.E. = 0.033) showed larger pupil diameter changes than the participants receiving placebo ($M = 0.341$, S.E. = 0.01).

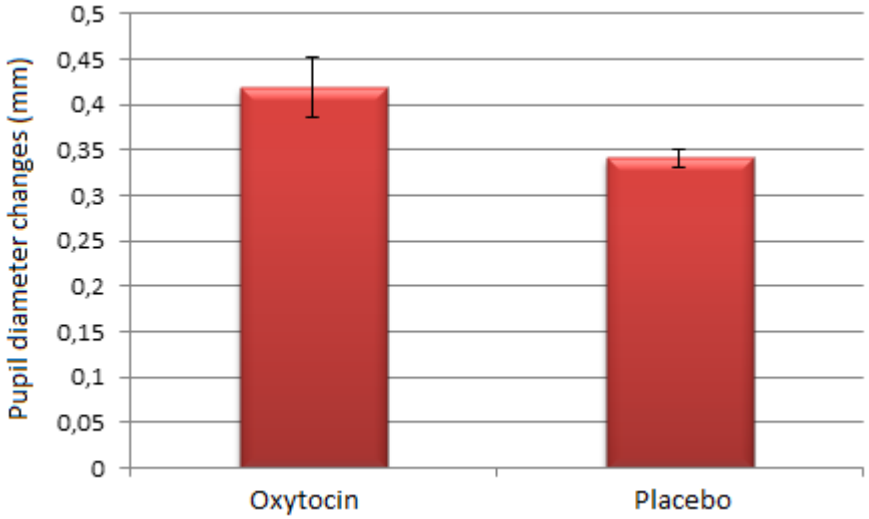

Figure 4.5 Pupil diameter changes during trustworthiness evaluation in oxytocin and placebo groups (male participants). (Error bars represent standard error)

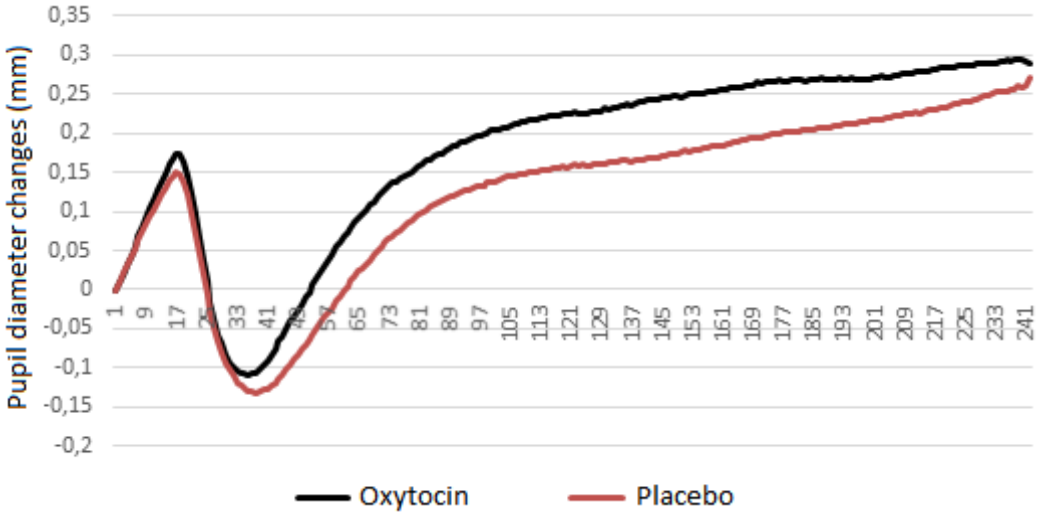

Figure 4.6 Pupil diameter changes of male participants during trustworthiness evaluation in oxytocin and placebo groups. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

In terms of trustworthiness evaluation main effect, untrustworthy faces (M = 0.455, S.E. = 0.017) resulted in larger pupil diameter changes than trustworthy faces (M = 0.389, S.E. = 0.016) and neutral faces (M = 0.297, S.E. = 0.023).

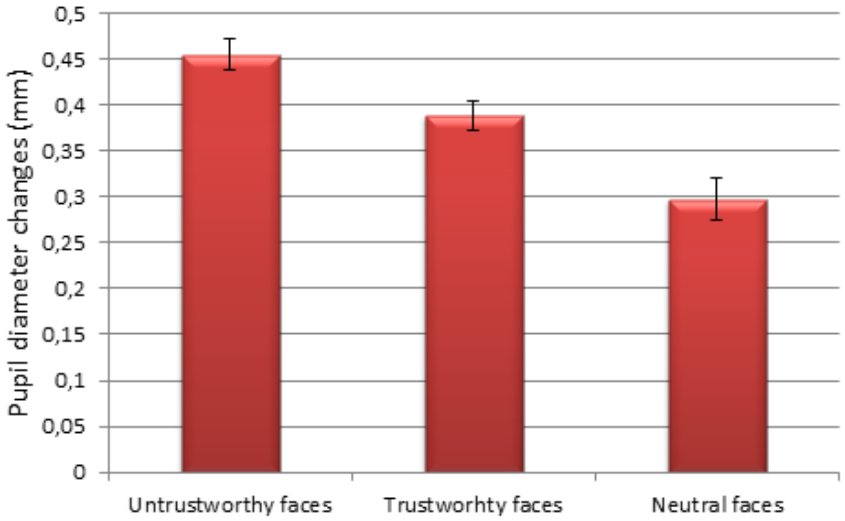

Figure 4.7 Pupil diameter changes in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation (male participants). (Error bars represent standard error)

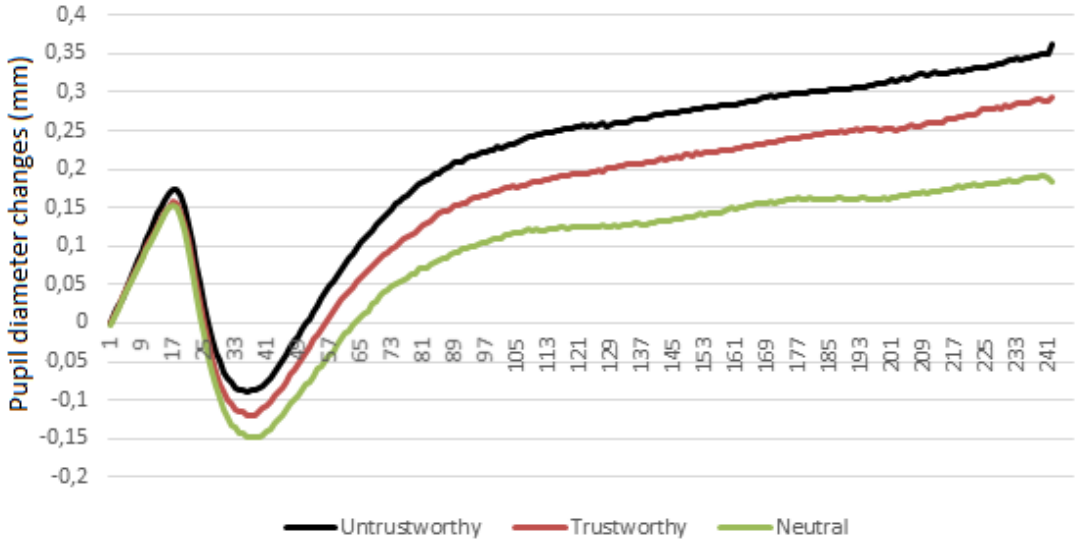

Figure 4.8 Pupil diameter changes of male participants in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

In terms of interaction effect of condition and trustworthiness evaluation, the effect of application of oxytocin is most prominently seen in response to untrustworthy faces.

There is a statistically significant difference in pupil diameter changes of the participants receiving oxytocin (M = .516, S.E. = .034) and the participant receiving placebo (M = .394, S.E. = .012) in response to untrustworthy faces.

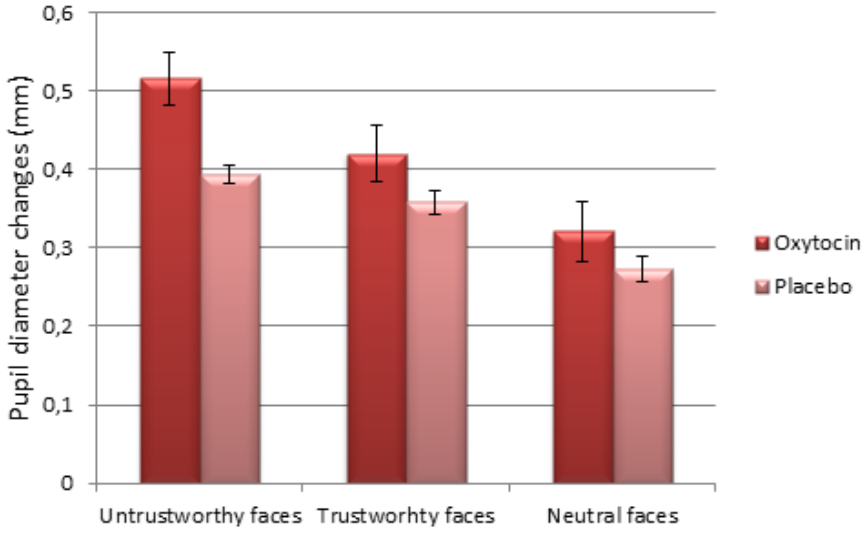

Figure 4.9 Pupil diameter changes in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation in both oxytocin and placebo groups (male participants). (Error bars represent standard error)

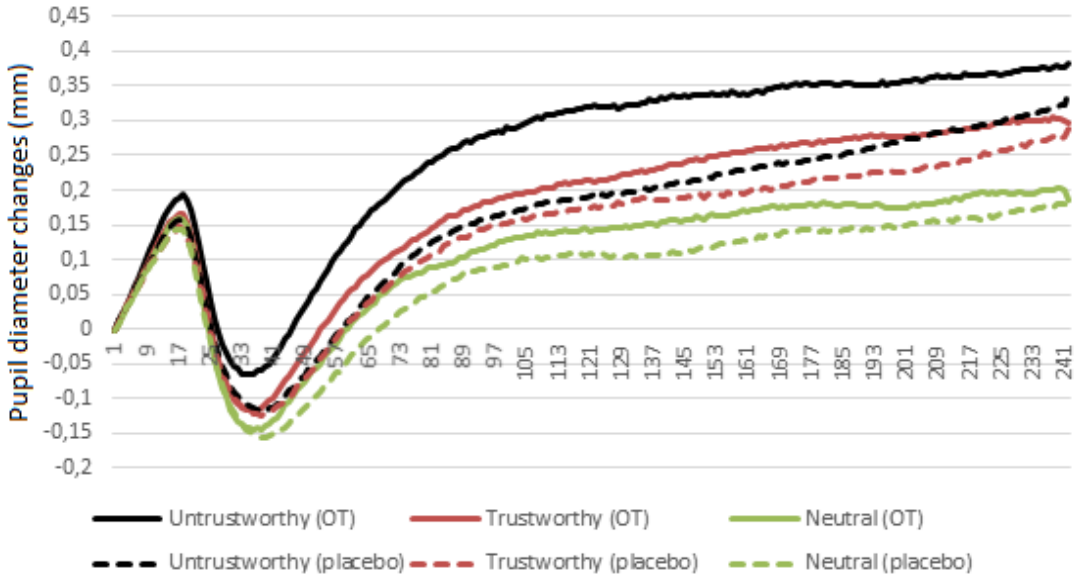

Figure 4.10 Pupil diameter changes of male participants in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation in both oxytocin and placebo groups. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

Table 4.1 Pupil diameter changes during trustworthiness evaluation (male participants).

	Oxytocin group			Placebo group		
	Untrustworthy	Trustworthy	Neutral	Untrustworthy	Trustworthy	Neutral
Mean	0.516	0.420	0.321	0.394	0.358	0.273
Std. Error	0.034	0.036	0.038	0.012	0.015	0.016

4.3.2.3 Comparison of responses of left and right eyes in terms of pupil diameter changes of female participants

A 2 (condition: oxytocin, placebo) x 3 (eye location: left eye, right eye, averaged) ANOVA was applied to assess whether the response of eyes differed significantly. There was no main effect of eye ($F(2,484) = 0.967$, $p = 0.561$) and no interaction effect of condition and eye ($F(2,484) = 0.943$, $p = 0.42$); that is, pupil dilation was not affected by eye location. Moreover, since healthy people have equal pupils (isocoria), a correlation must be observed between left and right pupil sizes. Correlation analysis revealed a statistically significant correlation ($r = 0.923$, $p < 0.0001$) between left and right pupil sizes and thus data from left and right pupils were averaged for each subject in order to use in further analysis.

4.3.2.4 Task-related pupillary responses of female participants

A 2 (condition: oxytocin, placebo) x 3 (trustworthiness evaluation: untrustworthy, trustworthy, neutral) ANOVA on pupil diameter changes was performed in order to find whether there is an effect of oxytocin and/or trustworthiness evaluation on pupil diameter changes. First, the trials based on subjective evaluation of trustworthiness in both oxytocin and placebo conditions were listed. Then based on subjective evaluation, untrustworthy trials which got 1, 2 or 3; neutral trials which got 4, 5 or 6 and trustworthy trials which got 7, 8 or 9 as rating scores were grouped together. The statistical analysis was conducted on averages of the grouped trials.

In female subjects, analysis showed that application of oxytocin has a highly significant effect on pupil diameter changes ($F(1,11) = 30.060$, $p < 0.0001$) and there is a highly statistically significant effect of subjective trustworthiness evaluation ($F(1,22) = 90.995$, $p < 0.0001$). However, there is no interaction effect of oxytocin application and subjective trustworthiness evaluation ($F(1,22) = 1.963$, $p = 0.164$).

In terms of condition main effect, the participants receiving placebo ($M = 0.478$, S.E. $= 0.026$) showed larger pupil diameter changes than the participants receiving oxytocin ($M = 0.349$, S.E. $= 0.008$).

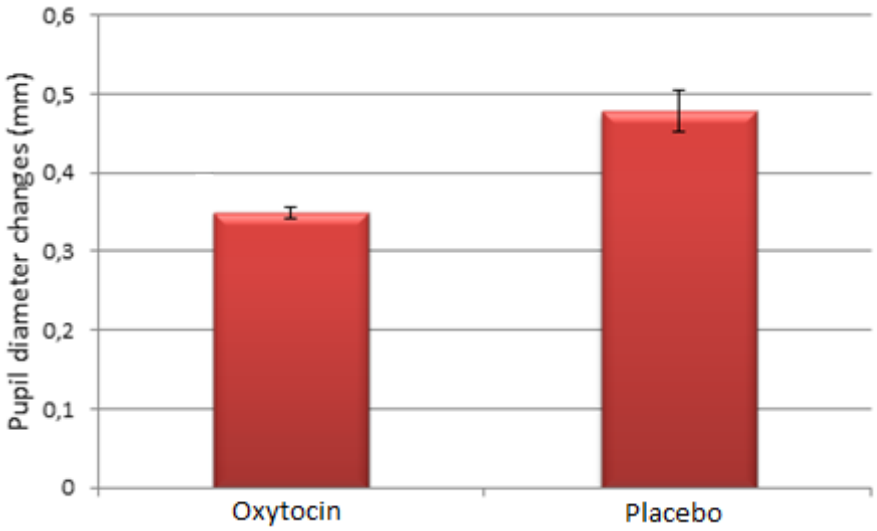

Figure 4.11 Pupil diameter changes during trustworthiness evaluation in oxytocin and placebo groups (female participants). (Error bars represent standard error)

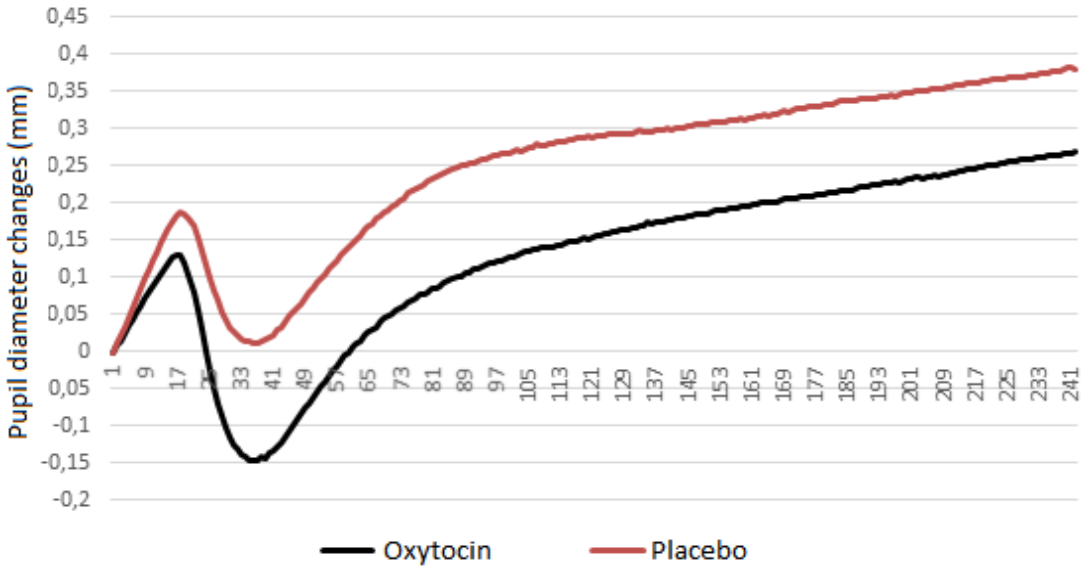

Figure 4.12 Pupil diameter changes of female participants during trustworthiness evaluation in oxytocin and placebo groups. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

In terms of trustworthiness evaluation main effect, untrustworthy faces (M = 0.538, S.E. = 0.019) resulted in larger pupil diameter changes than trustworthy faces (M = 0.414, S.E. = 0.019) and neutral faces (M = 0.288, S.E. = 0.017).

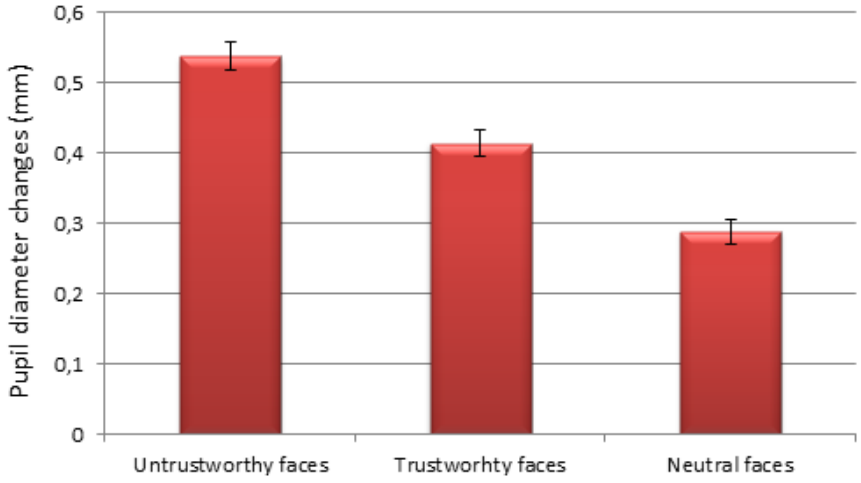

Figure 4.13 Pupil diameter changes in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation (female participants). (Error bars represent standard error)

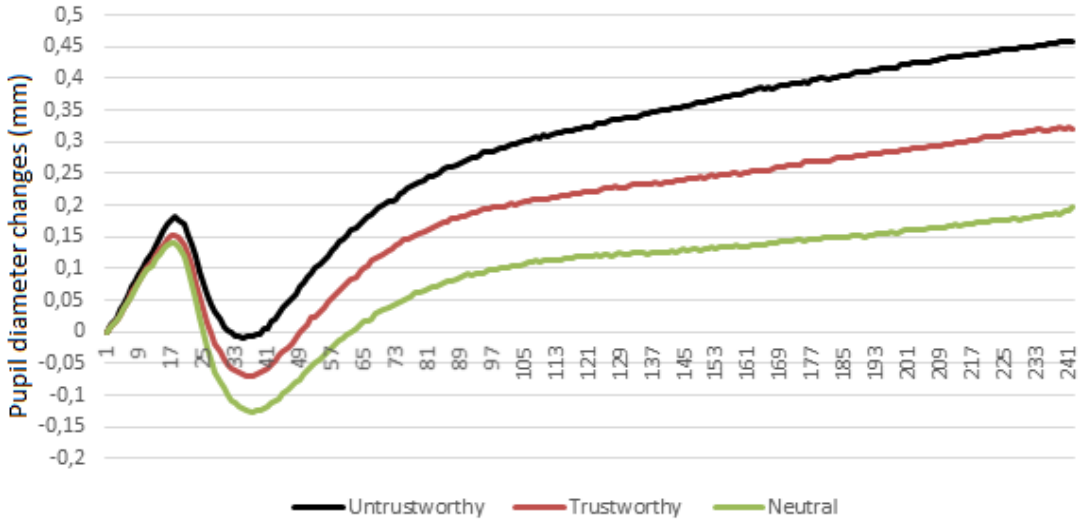

Figure 4.14 Pupil diameter changes of female participants in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

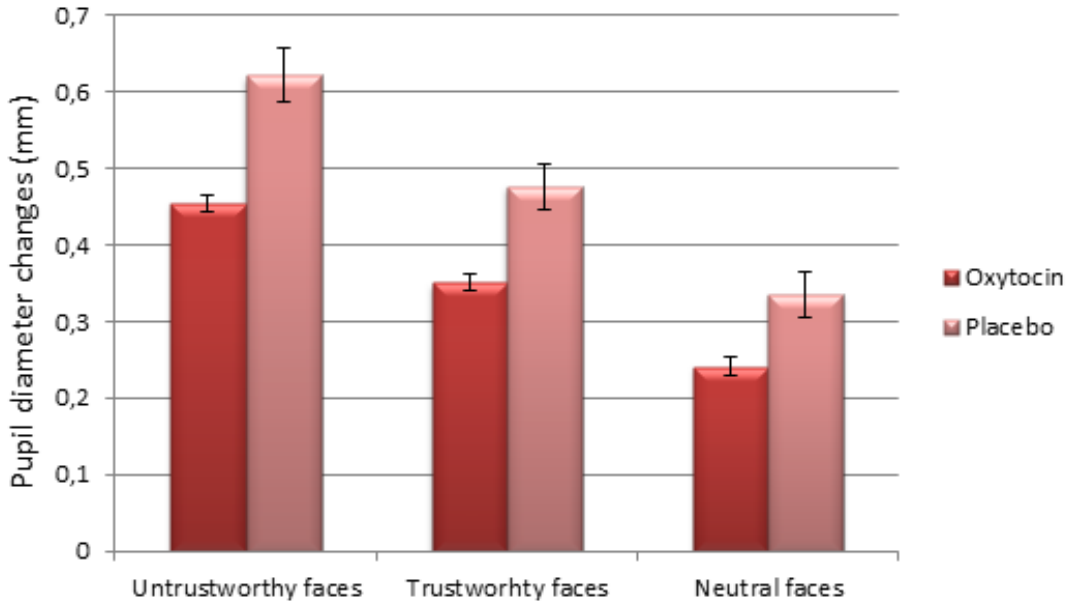

Figure 4.15 Pupil diameter changes in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation in both oxytocin and placebo groups (female participants). (Error bars represent standard error)

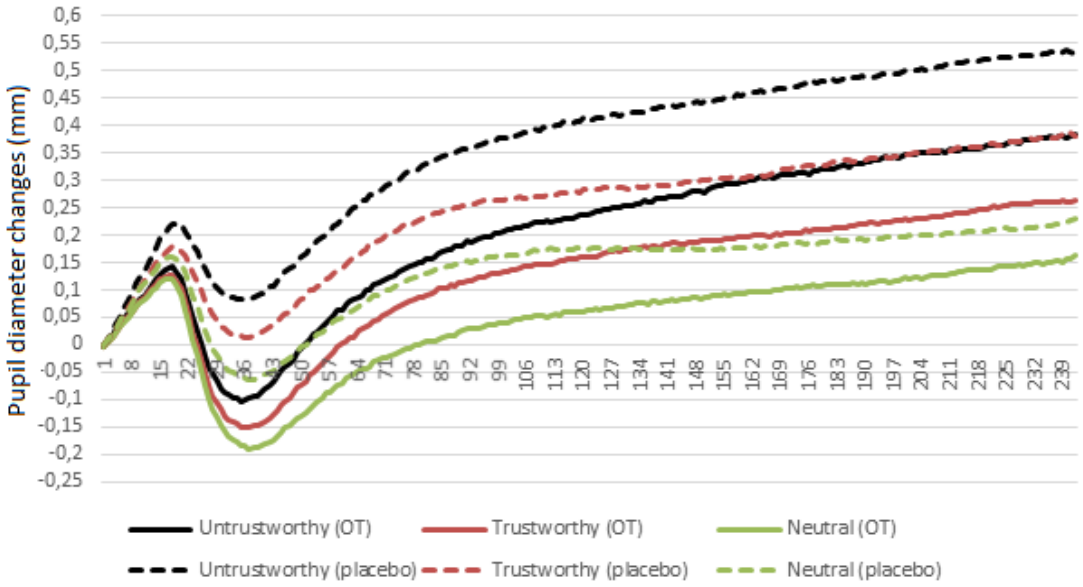

Figure 4.16 Pupil diameter changes of female participants in response to untrustworthy, trustworthy and neutral faces during trustworthiness evaluation in both oxytocin and placebo groups. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

Table 4.2 Pupil diameter changes during trustworthiness evaluation (female participants).

	Oxytocin group			Placebo group		
	Untrustworthy	Trustworthy	Neutral	Untrustworthy	Trustworthy	Neutral
Mean	0.455	0.351	0.241	0.622	0.477	0.335
Std. Error	0.011	0.011	0.012	0.036	0.030	0.031

4.4 Facial expression recognition

4.4.1 Behavioral data

4.4.1.1 Accuracy of male participants

A 2 (condition: oxytocin, placebo) x 7 (emotional expression: afraid, angry, disgust, happy, neutral, sad, surprised) ANOVA was conducted to assess whether there is an effect of oxytocin on the accuracy of emotional classification of facial expressions and whether there is a difference in the responses to each emotional expression. The ANOVA revealed statistically significant main effect of oxytocin ($F(1,22) = 5.289$, $p = 0.031$) and main effect of emotional expression ($F(6,132) = 20.502$, $p < 0.0001$). However, there is no interaction effect between condition and emotional expression ($F(6,132) = 1.62$, $p < 0.126$).

In male subjects, in terms of condition main effect, the participants receiving oxytocin ($M = 94.17$, S.E. = 0.95) identified emotional expressions more accurately than the participants receiving placebo ($M = 91.07$, S.E. = 0.95).

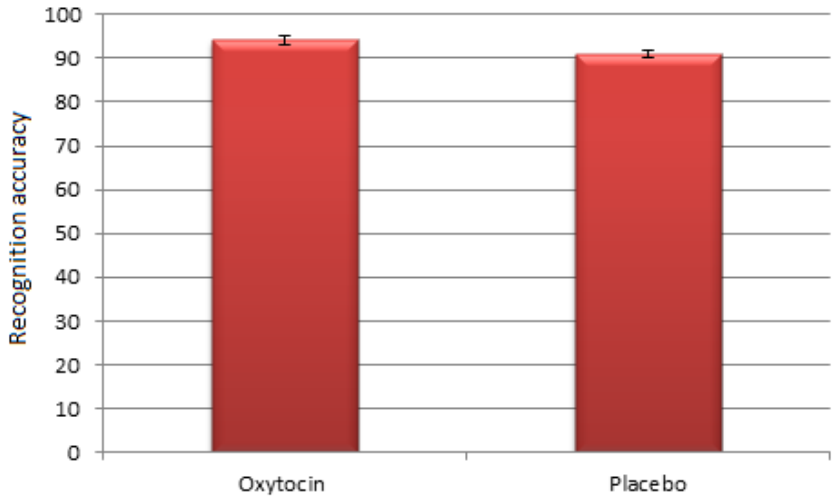

Figure 4.17 The accuracy of facial expression recognition in both oxytocin and placebo groups (male participants). (Error bars represent standard error)

Pairwise comparisons between emotional expressions showed that the accuracy of male participants was significantly lower in response to afraid faces (M = 87.5, S.E. = 1.57) compared to faces expressing disgust (M = 95.42, S.E. = 1.22) and neutral faces (M = 97.08, S.E. = 0.97), with p = 0.003 and p = 0.001, respectively. The accuracy of male participants was significantly higher in response to happy faces (M = 99.17, S.E. = 0.52) compared to afraid (M = 87.5, S.E. = 1.57) and angry faces (M = 92.5, S.E. = 1.27), p < 0.0001. The accuracy of male participants was significantly lower in response to faces expressing sadness (M = 89.17, S.E. = 1.04) compared to faces expressing disgust (M = 95.42, S.E. = 1.22), happy faces (M = 99.17, S.E. = 0.52) and neutral faces (M = 97.08, S.E. = 0.97), with p = 0.011, p < 0.0001 and p < 0.0001, respectively. At last, the accuracy of male participants was significantly lower in response to surprised faces (M = 87.5, S.E. = 1.37) compared to faces expressing disgust (M = 95.42, S.E. = 1.22), happy faces (M = 99.17, S.E. = 0.52) and neutral faces (M = 97.08, S.E. = 0.97), with p = 0.006, p < 0.0001 and p < 0.0001, respectively.

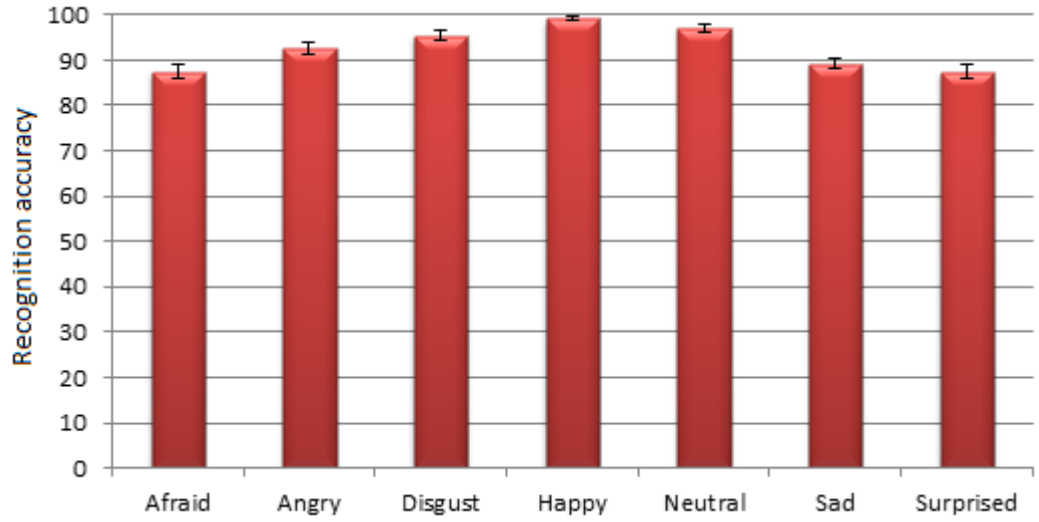

Figure 4.18 The accuracy of facial expression recognition (male participants). (Error bars represent standard error)

Table 4.3 Recognition accuracy of emotions
(male participants).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	87.5	92.5	95.42	99.17	97.08	89.17	87.5
Std. Error	1.57	1.27	1.22	0.56	0.96	1.04	1.37

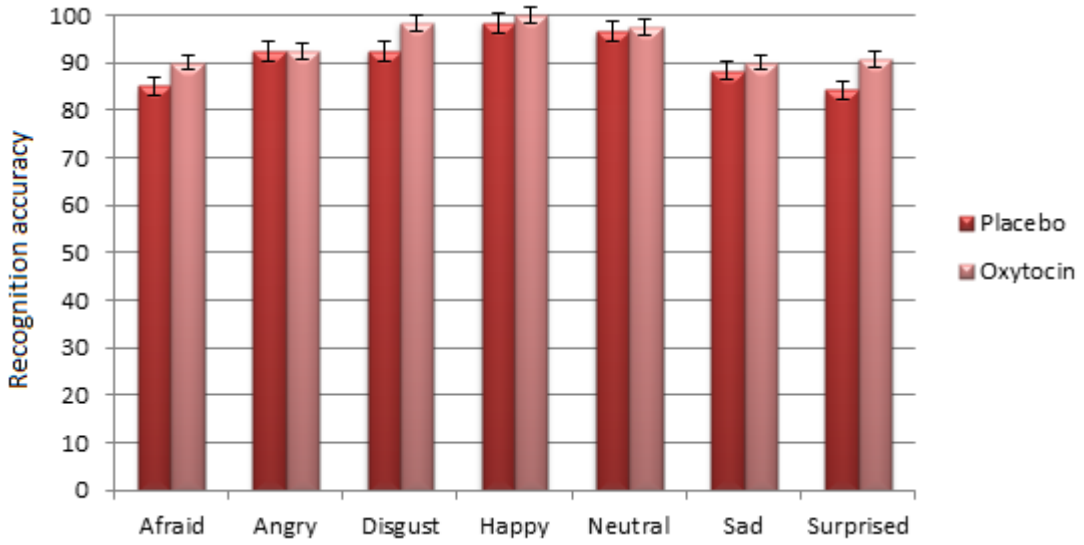

Figure 4.19 The accuracy of facial expression recognition in both oxytocin and placebo groups (male participants). (Error bars represent standard error)

Table 4.4 Recognition accuracy of emotions
(male participants in the placebo group).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	85	92.5	92.5	98.33	96.67	88.33	84.17
Std. Error	2.22	1.79	1.73	0.80	1.37	1.47	1.93

Table 4.5 Recognition accuracy of emotions
(male participants in the oxytocin group).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	90	92.5	98.33	100	97.5	90	90.83
Std. Error	2.22	1.79	1.73	0.80	1.37	1.47	1.93

4.4.1.2 Accuracy of female participants

A 2 (condition: oxytocin, placebo) x 7 (emotional expression: afraid, angry, disgust, happy, neutral, sad, surprised) ANOVA was conducted to assess whether there is an effect of oxytocin on the accuracy of emotional classification of facial expressions and whether there is a difference in the responses to each emotional expression. The ANOVA revealed statistically significant main effect of oxytocin ($F(1,22) = 33.796$, $p < 0.0001$) and main effect of emotional expression ($F(6,132) = 8.746$, $p < 0.0001$). In addition, there is an interaction effect between condition and emotional expression ($F(6,132) = 2.188$, $p < 0.048$).

In female subjects, in terms of condition main effect, the participants receiving oxytocin (M = 95, S.E. = 0.68) identified emotional expressions more accurately than the participants receiving placebo (M = 89.4, S.E. = 0.68).

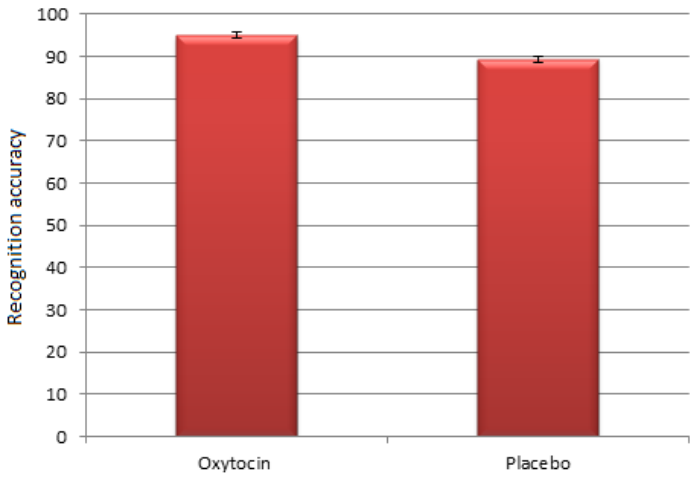

Figure 4.20 The accuracy of facial expression recognition in both oxytocin and placebo groups (female participants). (Error bars represent standard error)

Pairwise comparisons between emotional expressions showed that the accuracy of female participants was significantly higher in response to happy faces (M = 97.92, S.E. = 0.82) compared to faces expressing fear (M = 88.75, S.E. = 1.58), $p = 0.001$. The accuracy of female participants was significantly lower in response to faces expressing disgust (M = 87.92, S.E. = 1.3) compared to happy (M = 97.92, S.E. = 0.82) and neutral faces (M = 95, S.E. = 1.05), with $p < 0.0001$ and $p = 0.005$, respectively. The accuracy of female participants was significantly lower in response to faces expressing sadness (M = 90.42, S.E. = 1.54) compared to happy faces (M = 97.92, S.E. = 0.82), $p = 0.004$. At last, the accuracy of female participants was significantly lower in response to surprised faces (M = 91.25, S.E. = 1.03) compared to happy faces (M = 97.9,2 S.E. = 0.82), $p < 0.0001$.

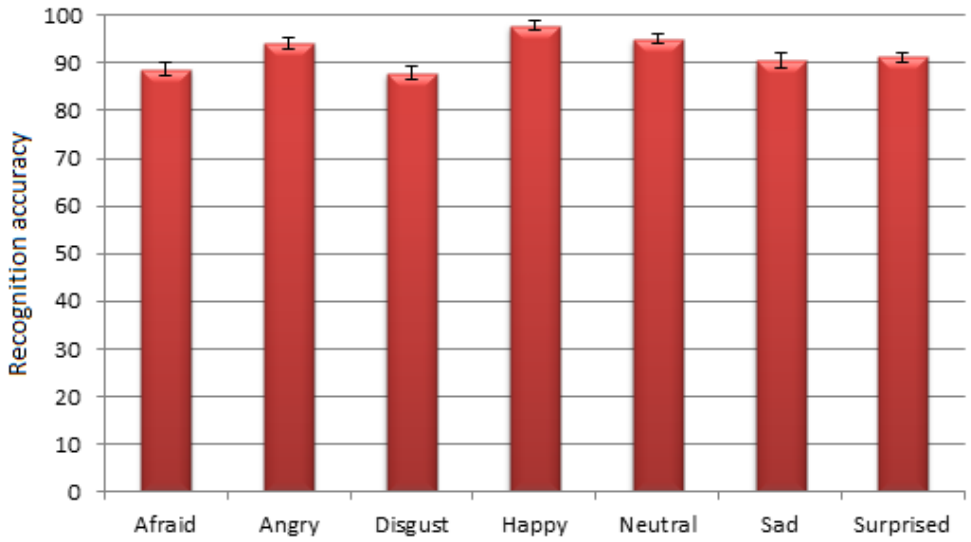

Figure 4.21 The accuracy of facial expression recognition (female participants). (Error bars represent standard error)

Table 4.6 Recognition accuracy of emotions (female participants).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	88.75	94.17	87.92	97.92	95	90.42	91.25
Std. Error	1.58	1.1	1.3	0.82	1.05	1.54	1.03

In terms of interaction effect of condition and emotional expression, the effect of application of oxytocin is most prominently seen in response to faces expressing disgust and surprise. There is a statistically significant difference in the recognition accuracy of these in emotions in the participants in oxytocin and placebo groups. The female participants receiving oxytocin (M = 92.5, S.E. = 1.84) recognized faces expressing disgust with higher accuracy compared to the female participants receiving placebo (M = 83.33, S.E. = 1.84). Furthermore, the female participants receiving oxytocin (M = 96.67, S.E. = 1.45) recognized surprised faces with higher accuracy compared to the female participants receiving placebo (M = 85.83, S.E. = 1.45).

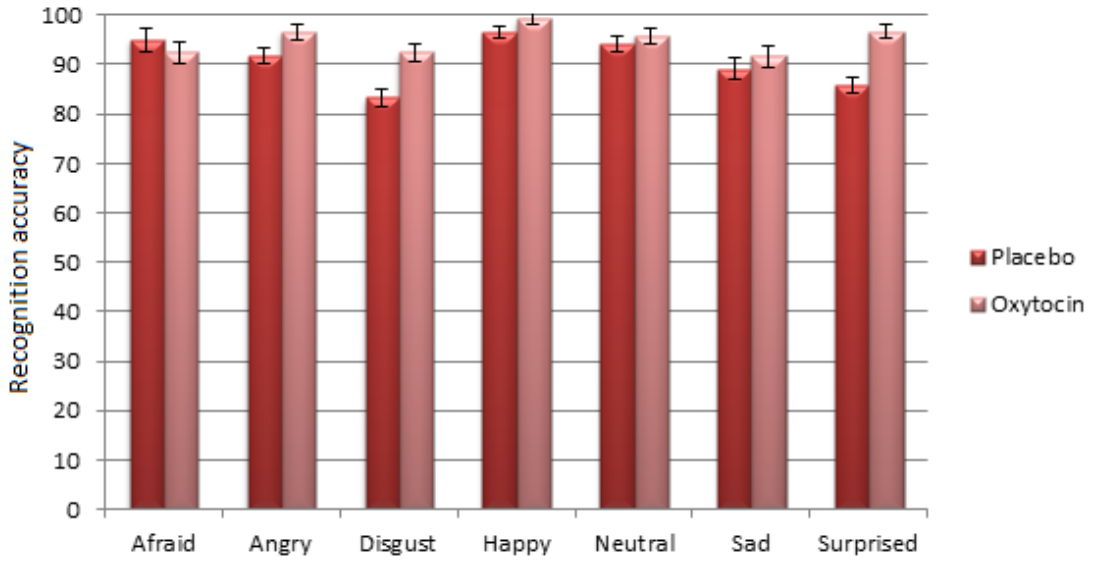

Figure 4.22 The accuracy of facial expression recognition in both oxytocin and placebo groups (female participants). (Error bars represent standard error)

Table 4.7 Recognition accuracy of emotions
(female participants in the placebo group).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	95	91.67	83.33	96.67	94.17	89.17	85.83
Std. Error	2.24	1.55	1.84	1.17	1.49	2.18	1.46

Table 4.8 Recognition accuracy of emotions
(female participants in the oxytocin group).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	92.5	96.67	92.5	99.17	95.83	91.67	96.67
Std. Error	2.24	1.55	1.84	1.17	1.49	2.18	1.46

4.4.2 Physiological data

Pupillary Responses

Data were preprocessed by linear interpolation in order to fill in the gaps that resulted from eye blinking or head movements. When more than 30% of the data of a participant had to be corrected, pupillary response is assumed to be unreliable and the pupil data of that trial has to be discarded. In this study, none of the participants' data was discarded in terms of excessive correction. Pupil responses during the 4-second stimulus presentation section of the trials were extracted. In other words, only passive

viewing sections of the experiment was taken into consideration, disregarding fixation and judgment sections. At the end of the extraction, 240 data points (60 Hz x 4 seconds) were obtained for each image. For each trial, the initial pupil diameter was subtracted from each of the following samples so the initial pupil diameter was set to zero in all of the stimulus onsets. Then, only the peak values of pupil diameter were used in analysis below. This way, changes from the stimulus onsets (i.e. baselines) are normalized between different trials.

4.4.2.1 Comparison of responses of left and right eyes in terms of pupil diameter changes of male participants

A 2 (condition: oxytocin, placebo) x 3 (eye location: left eye, right eye, averaged) ANOVA was applied to assess whether the response of eyes differed significantly. There was no main effect of eye ($F(2,484) = 2.003$, $p = 0.62$) and no interaction effect of condition and eye ($F(2,484) = 1.201$, $p = 0.42$); that is, pupil dilation was not affected by eye location. Moreover, since healthy people have equal pupils (isocoria), a correlation must be observed between left and right pupil sizes. Correlation analysis revealed a statistically significant correlation ($r = 0.924$, $p < 0.0001$) between left and right pupil sizes and thus data from left and right pupils were averaged for each subject in order to use in further analysis.

4.4.2.2 Task-related pupillary responses of male participants

A 2 (condition: control, experimental) x 7 (emotional expression: afraid, angry, disgust, happy, neutral, sad, surprised) ANOVA on pupil diameter was performed for male participants in order to find whether there is an effect of oxytocin and/or emotional expression of the face presented on pupil dilation.

In male subjects, analysis showed that there is no effect of the application of oxytocin ($F(1,11) = 2.406$, $p = 0.149$) and no interaction effect of condition and emotional expression ($F(6,66) = 0.828$, $p = 0.553$). On the contrary, there is a significant effect of emotional expression of the face presented to the participant ($F(6,66) = 2.726$, $p = 0.02$).

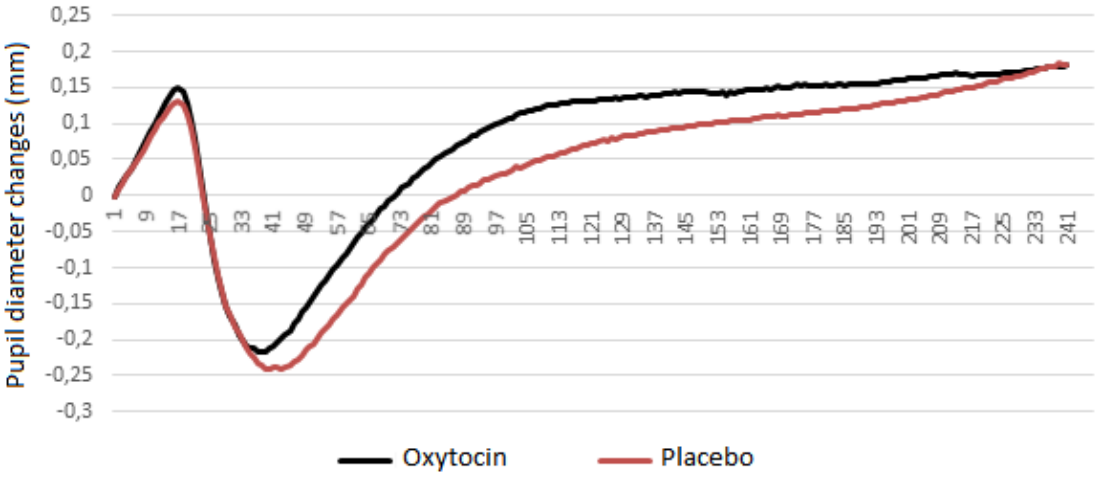

Figure 4.23 Pupil diameter changes of male participants during facial expression recognition task in oxytocin and placebo groups. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

In terms of emotional expression main effect, the pairwise comparisons revealed that the difference between pupil dilation in response to happy (M = 0.252, S.E. = 0.012) and sad faces (M = 0.300, S.E. = 0.015) is statistically significant (p = 0.05).

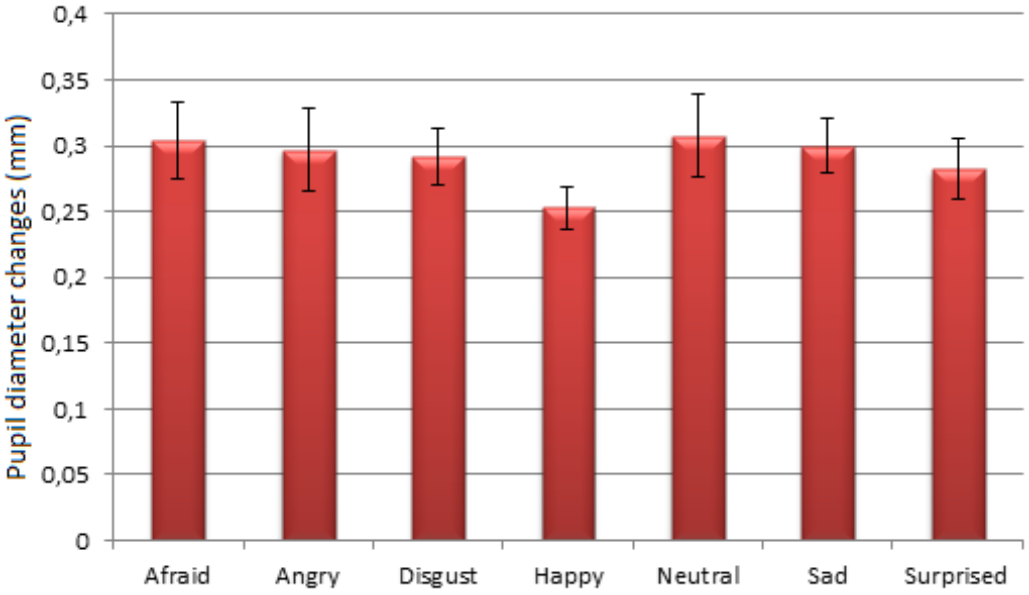

Figure 4.24 Pupil diameter changes during facial expression recognition task (male participants). (Error bars represent standard error)

Table 4.9 Pupil diameter changes in oxytocin group (male participants).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	0.318	0.317	0.318	0.273	0.355	0.312	0.304
Std. Error	0.042	0.038	0.027	0.022	0.037	0.025	0.034

Table 4.10 Pupil diameter changes in placebo group (male participants).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	0.29	0.276	0.265	0.232	0.260	0.288	0.26
Std. Error	0.017	0.025	0.016	0.011	0.025	0.016	0.012

4.4.2.3 Comparison of responses of left and right eyes in terms of pupil diameter changes of female participants

A 2 (condition: oxytocin, placebo) x 3 (eye location: left eye, right eye, averaged) ANOVA was applied to assess whether the response of eyes differed significantly. There was no main effect of eye ($F(2,484) = 1.421$, $p = 0.65$) and no interaction effect of condition and eye ($F(2,484) = 0.946$, $p = 0.43$); that is, pupil dilation was not affected by eye location. Moreover, since healthy people have equal pupils (isocoria), a correlation must be observed between left and right pupil sizes. Correlation analysis revealed a statistically significant correlation ($r = 0.936$, $p < 0.0001$) between left and right pupil sizes and thus data from left and right pupils were averaged for each subject in order to use in further analysis.

4.4.2.4 Task-related pupillary responses of female participants

A 2 (condition: control, experimental) x 7 (emotional expression: afraid, angry, disgust, happy, neutral, sad, surprised) ANOVA on pupil diameter was performed for female participants in order to find whether there is an effect of oxytocin and/or emotional expression of the face presented on pupil dilation.

In female subjects, analysis showed that there is a main effect of the application of oxytocin ($F(1,11) = 31.563$, $p < 0.0001$). However, there is no main effect of emotional expression of the face presented to the participant ($F(6,66) = 1.476$, $p = 0.2$) and no interaction effect of condition and emotional expression ($F(6,66) = 0.293$, $p = 0.938$).

In terms of condition main effect, the female participants receiving oxytocin ($M = 0.254$, S.E. = 0.017) showed smaller pupil diameter changes compared to the female participants receiving placebo ($M = 0.331$, S.E. = 0.022).

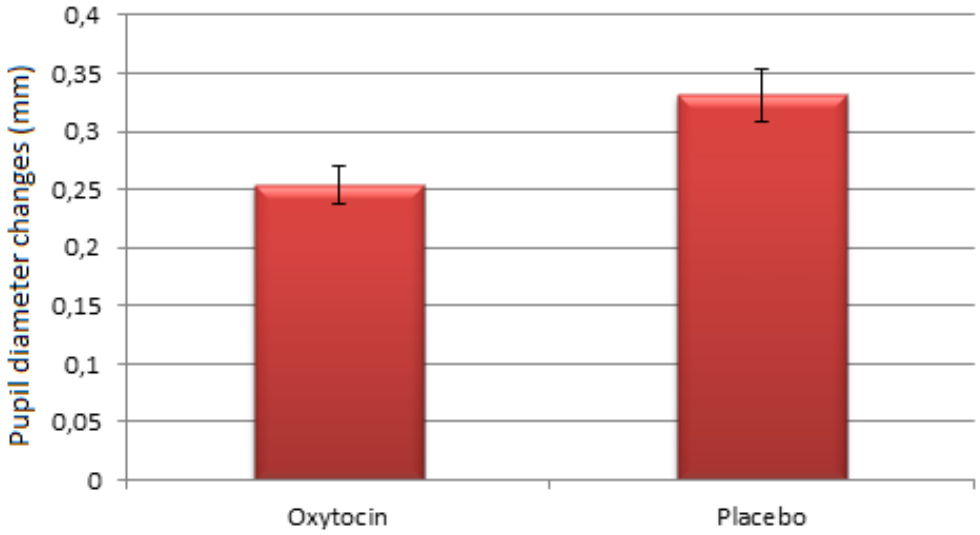

Figure 4.25 Pupil diameter changes in both oxytocin and placebo groups (female participants). (Error bars represent standard error)

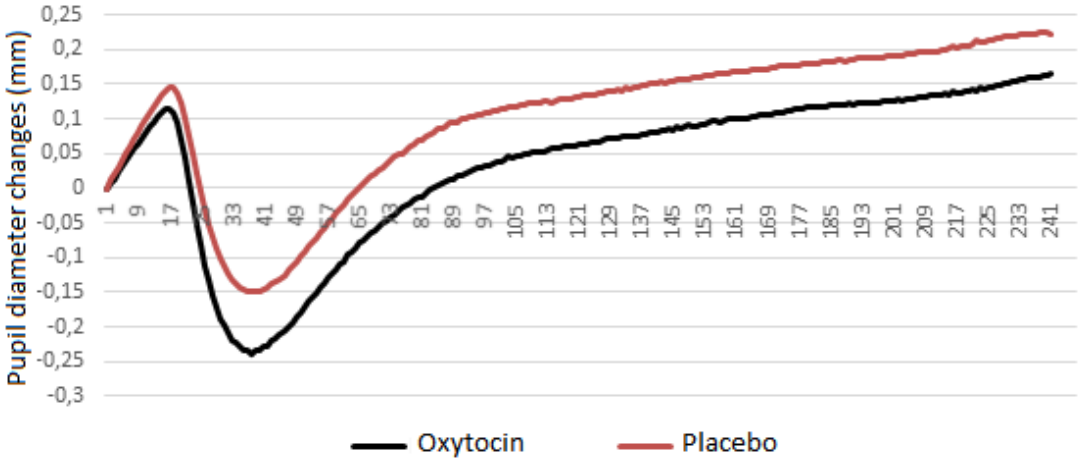

Figure 4.26 Pupil diameter changes of female participants in both oxytocin and placebo groups. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

Table 4.11 Pupil diameter changes during emotion recognition task (female participants in oxytocin group).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	0.242	0.256	0.274	0.240	0.268	0.267	0.231
Std. Error	0.014	0.016	0.021	0.013	0.026	0.012	0.016

Table 4.12 Pupil diameter changes during emotion recognition task (female participants in placebo group).

	Afraid	Angry	Disgust	Happy	Neutral	Sad	Surprised
Mean	0.336	0.341	0.349	0.321	0.314	0.351	0.304
Std. Error	0.022	0.018	0.019	0.019	0.021	0.03	0.027

4.5 Difference between task-related pupillary responses in response to neutral faces

Since the faces with neutral expression were used in both phases of the experiment, a 2 (condition: oxytocin, placebo) x 2 (task: trustworthiness, emotional recognition) ANOVA was applied in order to assess any possible effect of task requirements on pupil dilation. In this test, data from both genders are merged. In terms of condition, we found no statistically significant effect of oxytocin ($F(1,11) = 3.225$, $p = 0.064$) and no significant interaction effect of condition and experimental task ($F(2,22) = 1.941$, $p = 0.143$). However, in terms of task type, there was a significant effect of task on pupil dilation ($F(1,11) = 7.871$, $p = 0.012$). The pupil diameter change in response to neutral faces in trustworthiness task ($M = 0.397$, S.E. = 0.033) is higher than the change in the emotional recognition task ($M = 0.301$, S.E. = 0.019).

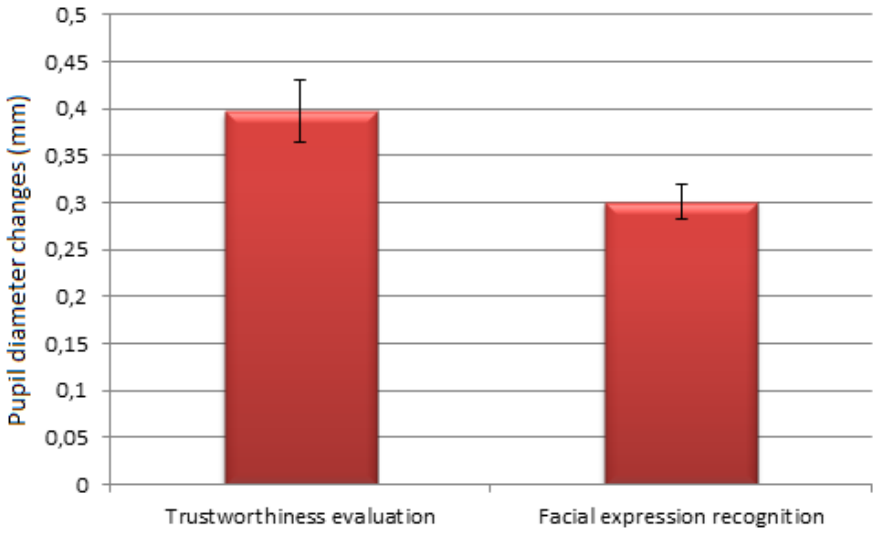

Figure 4.27 Pupil diameter change in response to neutral faces during both trustworthiness and emotion recognition tasks. (Error bars represent standard error)

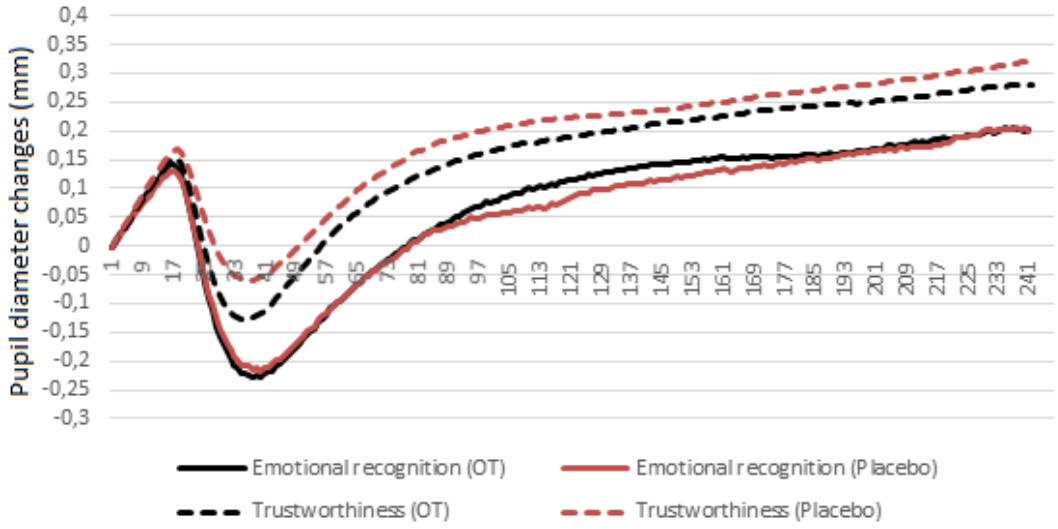

Figure 4.28 Pupil diameter changes in response to neutral faces during both trustworthiness and emotion recognition tasks in both oxytocin and placebo groups. (x axis: each data point corresponds to 1/60 seconds, y axis: pupil diameter difference from baseline in mm)

	Trustworthiness evaluation		Facial expression recognition	
	Behavioral data Trustworthiness ratings	Physiological data Pupil dilation	Behavioral data Recognition accuracy	Physiological data Pupil dilation
Male	OT > PLC (p<0.0001) Female > Male (p<0.0001)	OT > PLC (p=0.053) Untrustworthy > Trustworthy > Neutral (p < 0.0001) UN in OT > UN in PLC (p=0.035)	OT > PLC (p=0.031) Afraid < Disgust (p=0.003), Neutral (p=0.001) Happy > Afraid , Angry (p<0.0001) Sad < Disgust (p=0.011), Happy, Neutral (p<0.0001) Surprised < Disgust (p=0.006), Happy, Neutral (p<0.0001)	Not significant effect of OT (p=0.149) Happy < Sad (p=0.02)
Female	OT > PLC (p<0.0001) Male > Female (p<0.0001)	PLC > OT (p < 0.0001) Untrustworthy > Trustworthy > Neutral (p < 0.0001)	OT > PLC (p<0.0001) Happy > Afraid (p=0.001) Disgust < Happy (p<0.0001), Neutral (p=0.005) Sad < Happy (p=0.004) Surprised < Happy (p<0.0001) Disgust in OT > Disgust in PLC (p=0.048) Surprised in OT > Surprised in PLC (p=0.048)	PLC > OT (p < 0.0001) Not significant effect of emotion (p=0.2)
Task dependency	Pupil dilation in response to same neutral faces is higher in trustworthiness task compared to facial expression recognition task. (p=0.012)			

Table 4.13 Summary table for the results (OT: oxytocin, PLC: placebo)

CHAPTER 5

DISCUSSION

The aim of this thesis was to investigate how oxytocin manipulates the accuracy of emotion recognition and trustworthiness ratings of the face pictures. Aside from these behavioral measures, oxytocin also manipulates physiological responses, such as pupil dilation. Hence, a secondary aim in this study was to investigate possible effects of oxytocin on the pupil dilation triggered by facial expression recognition and trustworthiness evaluation.

Since possible sexual dimorphisms of oxytocin in humans were also subject of interest, data from both genders are analyzed precisely to examine differences. Behavioral data (trustworthiness ratings and accuracy of emotion recognition) and pupillary responses (pupil diameter) were recorded on both phases of the experiment while judging trustworthiness and recognizing facial expressions. In line with the aims of the study and literature review presented on Chapter 2, there were seven hypotheses (see section 2.7).

At the end of the experiment, **hypotheses 1, 2, 4** were confirmed, **hypothesis 3, 5 and 6** were supported in male but not female participants. Hypotheses 7, which indicated gender differences based on oxytocin intake are expected, is supported as seen from these. For convenience, these hypotheses are listed below, and an overview showing all results is presented in Table 5.1 (for male participants) and Table 5.2 (for female participants).

Table 5.1 Results of hypotheses for male participants

Hypothesis	Significance	Finding
H1, Trustworthiness ratings: OT>PLC	$p<0.0001$	Confirmation
H2, Pupil dilation: U, T > N	$p<0.0001$	Novel finding (UT>T>N)
H3, Pupil dilation during trustworthiness evaluation: OT>PLC	$p=0.053$	Novel finding
H4, Accuracy of emotion recognition: OT>PLC	$p=0.031$	Confirmation
H5, Pupil dilation: ALL>N	$p=0.02$	Confirmation (H>S)
H6, Pupil dilation: OT>PLC	Not significant	Rejection

Table 5.2 Results of hypotheses for female participants

Hypothesis	Significance	Finding
H1, Trustworthiness ratings: OT>PLC	p<0.0001	Confirmation
H2, Pupil dilation: U, T > N	p<0.0001	Novel finding (UT>T>N)
H3, Pupil dilation during trustworthiness evaluation: OT>PLC	p<0.0001	Novel finding (PLC>OT)
H4, Accuracy of emotion recognition: OT>PLC	p<0.0001	Confirmation
H5, Pupil dilation: ALL>N	p=0.2	Rejection
H6, Pupil dilation: OT>PLC	p<0.0001	Novel finding (PLC>OT)

Trustworthiness evaluation task

In the current thesis, while evaluating trustworthiness for neutral faces, the participants receiving oxytocin made more trustworthy ratings compared to the participants receiving placebo. This result verifies **hypothesis 1**, and it is consistent with the literature since it has been reported by many studies that intranasal administration of oxytocin results in trust and approach-related behaviors (Theodoridou et al., 2009; Kosfeld et al., 2005; Baumgartner et al., 2008; Mikolajczak, 2010). Theodoridou et al. (2009) investigated the effect of intranasal oxytocin on judgments of facial trustworthiness and attractiveness. They found that the ratings of trustworthiness and attractiveness of male and female target stimuli in raters of both sexes increased upon OT administration compared to the ratings of control group. Although in that study, the evaluation of trustworthiness is done in the context of attractiveness and our study is more associated with social judgements of trustworthiness, our results replicate that study.

Bar et al. (2006) conducted a study in order to determine the minimum exposure time needed to decide whether someone was threatening or not. The results showed that thirty-nine milliseconds was enough to forge a strong impression on threat detection. Todorov and his team (2006) have also obtained similar results when it came to determining whether a person was trustworthy or not. Researchers explained that the detection of reliability of a person is an automatic process, essential to our survival (Willis and Todorov, 2006). Functional magnetic resonance imaging studies also tend to confirm that. Researchers have shown that the detection reliability was linked to the activity of the amygdala, the central control our emotions, especially fear (Winston et al., 2002). It was found that the more a face was perceived as untrustworthy, the more the amygdala response was prominant (Winston et al., 2002). Therefore, it can be concluded that our first impressions would be formed in a "primary" judgment. In other words, it is very likely that our ability to infer traits from the face just depends on our ability to recognize emotions. This seems logical, because for a long time, research has shown that we are able to easily detect the emotions expressed by the faces, especially fear and anger (Blair et al., 1999; Todorov et al., 2006).

In addition, although the experiments described herein were conducted on neutral faces, not reflecting a priori any particular emotional state, the subjects still detected some emotions. Thus, Oosterhof and Todorov (2009) suggested that a neutral face can actually have some traits tending to express specific emotions, according to the orientation of the mouth, or the thickness of the eyebrows. They also present a theory that recognition of emotional expressions and evaluation of trustworthiness from faces share a common perceptual basis (Oosterhof and Todorov, 2009). In the light of these studies, we tried to conduct a study to see whether this theory would be confirmed by examining pupillary responses. Since researchers suggest that evaluation of trustworthiness is based on a dimension polarized by emotional valence, we used the results of studies on the effect of emotional valence on pupil dilation. For example, Bradley et al. (2008) found that pupil dilation was significantly affected by picture emotionality. When participants viewed emotional pictures compared to neutral pictures, there was a significant increase in pupil dilation. From another point of view, it is known that pupil dilation is observed due to approach-related behavior (Wiseman and Watt, 2010). Thus, we also expect that pupil dilation would be higher in response to trustworthy faces since trust behavior is an example of approach-related behavior. On the other hand, due to activation of avoidance mechanism by untrustworthy evaluation, greater pupil dilation might be observed in response to untrustworthy faces. Since there is no research investigating the relationship between pupil dilation and trustworthiness, it was hard to precisely determine expectations. Based on the studies investigating the effect of emotionality on pupillary responses, we mainly hypothesized (**the hypothesis 2**) that pupil diameter changes in response to both trustworthy and untrustworthy faces would be higher than pupil diameter changes in response to neutral faces. It is found that pupil diameter changes in response to untrustworthy faces are the largest, and the smallest pupil diameter changes is found in response to neutral faces, verifying **the hypothesis 2**. To the best of our knowledge, this is a novel finding, which complements the literature in emotionality, trustworthiness and pupil dilation response.

Higher pupil dilations for untrustworthy faces might be linked to arousal as a part of survival mechanisms. Many of our movements and our actions are a legacy that has been built through our evolution. These reflex reactions have been acquired over thousands of years and humans have learned to develop in particular in relation to its survival. These instinctive responses are now stored in one specific spot in the brain called the limbic system. It's like a survival kit that comes to every human being from birth. These reactions appear faced with a danger or threat. One of the most prominent reactions is called fight-or-flight response.

Fight-or-flight response is a reaction that most importantly appear when faced with a danger or threat (Cannon, 1932). This response mainly controls the activation of sympathetic nervous system. The primary role of this system is to activate physiological changes such as increase in heart rate and dilation of pupil. In fact, this response is the alarm signal composed of activities of many hormones. These hormones are mainly epinephrine, norepinephrine and cortisol, produced by adrenal

gland to let organism adapt a behaviour against the situation that is threat to its survival (Weiss, 1945; Fujiwara, Cherrington, Neal, & McGuinness, 1996). It is also known that cortisol is released in response to stress in everyday life. The recent studies show that cortisol and oxytocin oppose each other. When a person is faced with a stressful condition, firstly secretion of cortisol begins. However, to control homeostasis and keep the organism balanced, release of oxytocin also increases (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003).

The release of these regulatory hormones allows the organism to cope with "predators" which can be a wild beast or some unknown animal producing dangerous signals. In our study, the dangerous signals can be seen as facial features of a person rated as untrustworthy. Therefore it can be argued that seeing an untrustworthy face and thinking about asking her/him for an address in an unknown town is enough to produce a fight-or-flight response.

In our study, the male participants receiving intranasal oxytocin showed larger pupil diameter changes compared to the male participants receiving intranasal oxytocin during trustworthiness evaluation. In the literature, there are two studies investigating the effect of intranasal oxytocin on pupillary responses of male participants during facial expression recognition tasks (Leknes et al., 2012; Prehn et al., 2013). The results of these studies suggest that oxytocin has an effect on pupil dilation in male participants. On the other hand, the female participants in oxytocin group showed smaller pupil diameter changes compared to the female participants in the placebo group during trustworthiness evaluation. Since there is no study investigating the effect of intranasal oxytocin on pupillary responses of female participants, this is the first study suggesting that oxytocin has a gender related effect on pupillary responses.

Facial expression recognition task

Participants receiving oxytocin recognized emotions expressed by faces more accurately compared to the participants receiving placebo. This result verifies **hypothesis 4**, and it is consistent with the literature since it has been reported by many studies that intranasal administration of oxytocin improves the ability to recognize facial expressions (Guastella et al., 2009, 2010; Domes et al., 2007b; Di Simplico et al., 2009).

In this study, faces expressing all six basic emotions and faces with a neutral expression are used as stimuli. Previous studies on pupil dilation showed that when people view pleasant and attention-requiring (arousing) pictures compared to neutral pictures, an increase in pupil size is observed (Hess and Polt, 1960). Further research on this area revealed that not only pleasant pictures with a positive emotional characteristic but also unpleasant pictures with high arousal result in larger pupil size (Bradley et al., 2008). However, the studies cited above did not use any facial expression as visual stimuli, so that their results do not represent the mechanisms modulated by processing of facial stimuli. Nevertheless, the study of Hepsomalı

(2013) showed that pupil diameter changes was found larger in response to highly arousing facial stimuli (angry and surprised faces) compared to neutral faces.

In the literature, there is no study investigating pupil size during processing of emotions expressed by faces in a facial expression recognition task. Although Schrammel et al. (2009) investigated the influence of facial expression on attention allocation and physiological arousal by measuring pupil size, the subjects were presented virtual characters instead of real facial stimuli and were not asked to identify emotion. Nevertheless, the result indicated no effect of emotion on pupil dilation. Another study by Kret et al. (2013) used whole body stimuli while measuring physiological responses in a facial expression recognition task. In the experiment, the subjects viewed emotionally congruent and incongruent face-body pairs while pupil size were recorded. The results showed that observing an angry person evoked greater pupil dilation than fearful or happy person while there was no difference between fear and happiness. There are also other studies that try to investigate the effect of emotional processing on pupillary responses of different subject groups (infants, older people, and patient groups) in various experimental tasks. All these studies suggest that there is no consensus differential effects of emotions expressed by faces on pupillary responses. Thus based on the literature on the effects of general emotion processing on pupil dilation, we expected larger pupil diameters in response to all emotional expressions compared to neutral faces (**hypothesis 5**). However, this hypothesis was only confirmed partially in male participants (i.e., the male participants showed significantly larger pupil diameter changes in response to happy faces compared to sad faces) while it is not supported by the pupillary responses of female participants.

This result indicates that although attention demand of happy and sad faces in terms of emotional polarity (i.e., positive-negative valence) seems similar, there might be differences in arousal states of individuals in response to these two emotional expressions since there is a significant difference between pupillary responses. Furthermore, this difference is not observed in the female participants. Since the studies investigating pupillary responses in response to visual stimuli (Janisse, 1974; Bradley et al., 2008) did not use facial stimuli with emotional expressions, their result might not reflect the specific situation in processing of facial expressions. In addition, all six basic emotions and neutral expression were used in that study. A lack of difference in response to different emotions may also reflect limitations in larger stimuli group.

In our study, the male participants receiving intranasal oxytocin showed larger pupil diameter changes compared to the male participants receiving intranasal oxytocin during facial expression recognition task, replicating the literature (Leknes et al., 2012; Prehn et al., 2013). On the contrary, the female participants in oxytocin group showed smaller pupil diameter changes compared to the female participants in the placebo group during facial expression recognition task. Since there is no study investigating the effect of intranasal oxytocin on pupillary responses of female participants, this is

the first study suggesting that oxytocin has a gender related effect on pupillary responses. This gender-related finding is discussed below.

Gender-related findings

Possible sexual dimorphisms of oxytocin in humans were of interest as hypothesized in **hypothesis 7**. In the current study, in male participants, the intranasal administration of oxytocin resulted in larger pupil diameters in line with previous studies (Leknes et al., 2012; Prehn et al., 2013). On the contrary, the intranasal administration of oxytocin resulted in smaller pupil diameters in female participants. Since there is no study in the literature which investigated pupil responses in female participants, it is hard to justify this finding.

In previous studies, it is reported that intranasal oxytocin intake affects the physiological responses of female and male subject differently. (i.e., it is related to sympathetic arousal in males but parasympathetic activation in females) (Hoge et al., 2014; Lynn et al., 2014; Domes et al., 2010; Lischke et al. 2012). Therefore, this result confirms **the hypothesis 7:** the intranasal oxytocin affected both genders differently.

The effect of task context on pupillary responses

It is crucial to note that during trustworthiness evaluation and facial expression recognition, arousal levels of participants are observed to be different. In other words, in the trustworthiness task compared to facial expression recognition, the participants receiving oxytocin/placebo showed larger pupil diameter changes suggesting that the pupil size is affected by not only visual stimuli but also by the context of the experimental task.

One of the reason behind context-dependent pupillary changes might be explained in terms of evolutionary approaches. Task-evoked pupillary responses are a reliable index of cognitive demands and information-processing loads. The larger pupil diameter changes are found in response to increased cognitive processing demands during different experimental tasks such as a digit span recall task (Granholm, Asarnow, Sarkin, & Dykes, 1996; Cabestrero, Crespo, & Quirós, 2009) and lexical translation task (Hyönä, Tommola, & Alaja, 1995). In our study, we mainly used two different experimental tasks: trustworthiness evaluation and facial expression recognition. In everyday life, since we are exposed to emotions expressed by faces, people tend to get used to recognize facial expressions in order to develop an appropriate reaction. However, although trustworthiness evaluation is evolutionary significant, this cognitive evaluation seems out of favour in modern times. Therefore, trustworthiness evaluation which requires more cognitive demands results in larger pupil diameter changes.

Limitations and future work

Although this study aims to control many variables, there are still some limitations concerning selected stimuli and data analyses. First of all, visual stimuli are selected from an optimized and well-studied database (KDEF), but the subjects participated in the study might not be familiar with this type of faces. Secondly, the data analysis is done by extracting only peak pupil diameter from the entire pupil time series during passive viewing.

While selecting subjects, different questionnaires such as Toronto Alexithymia Scale (Bagby, Parker, & Taylor, 1994) may also be used to control for psychopathological symptoms in identification and recognition of emotions to guarantee that the subjects are capable in processing facial stimuli.

In addition, regression slope, polynomial functions or mean square error may be used to analyze pupil diameters to conduct a more detailed analysis of pupillary responses. Finally, fixation patterns and durations can be evaluated in sub-regions of the face to investigate possible effects of intranasal oxytocin on eye gaze and fixation patterns.

CHAPTER 6

CONCLUSION

In this thesis, we investigated the possible effects of intranasal oxytocin administration on trustworthiness evaluation, facial expression recognition and task-evoked pupillary responses. In addition, sexually dimorphic effects of intranasal oxytocin intake on males and females are also our subject of interest. For these purposes, we conducted an eye-tracking study and recorded pupillary responses as well as behavioral data.

During **trustworthiness evaluation**, we presented only neutral facial expressions as stimuli. The participants in oxytocin group rated neutral faces as more trustworthy compared to the participants in placebo group, replicating the literature (Theodoridou et al., 2009). Moreover, the participants rated the faces of the opposite sex as more trustworthy in both oxytocin and placebo group, suggesting that trustworthiness evaluation seems to be driven by evolutionary forces (i.e., selection of partner of opposite sex) which may dominate other possible effects.

In terms of pupil dilation, regardless of whether participants received oxytocin or placebo, and regardless of gender, largest pupil diameters were observed during subjective evaluations in which participants classified faces as untrustworthy compared to trustworthy and neutral. In addition, pupil diameters were also larger during subjective evaluations in which participants classified faces as trustworthy compared to neutral. Furthermore, the male participants in oxytocin group showed larger pupil diameter changes compared to the male participants in placebo group, replicating the literature (Leknes et al., 2012; Prehn et al., 2013). On the contrary, the administration of intranasal oxytocin resulted in smaller pupil diameter changes in the female participants, exhibiting a gender related physiological difference which needs to be investigated in the future.

During **facial expression recognition**, we presented all six basic emotions as stimuli. This is a strength of our study because in the literature, most studies investigate only a subset of facial expressions (such as pleasant or unpleasant). In this task, the participants in oxytocin group recognized emotional facial expressions more accurately than the participants in placebo group, replicating the literature (Shamay-Tsoory et al., 2009; Van Ijzendoorn & Bakermans-Kranenburg, 2011, Shahrestani, Kemp, & Guastella, 2013). There was no difference in males in terms of recognition accuracy for individual emotions. However, for females, the effect of intranasal oxytocin was most prominently seen in response to faces expressing disgust and surprise. In terms of pupillary responses, it is observed that the male participants in oxytocin group showed larger pupil diameter changes compared to the male participants in placebo group, replicating the literature. On the contrary, in line with the results reported for the trustworthiness task above, the administration of intranasal

oxytocin resulted in smaller pupil diameter changes in the female participants. Such sexual dimorpihsms of oxytocin intake should definitely be investigated further.

Our experiment design allowed for comparison of task dependent responses. We found that for neutral face pictures, in the trustworthiness task, the participants showed larger pupil diameter changes compared to facial expression recognition task. This suggests that the pupil size is not only affected by visual stimuli but it is also dependent on the context of the experimental task. When lined up with the suggestions of previous studies (Granholm et al.2007; Cabestrero et al., 2009; Hyönä et al., 1995), our finding is complements the literature.

To summarize, it can be said that the application of intranasal oxytocin resulted in an increase in the trusting behavior and in accuracy of emotion recognition in both male and female participants. Males receiving intranasal oxytocin showed larger pupil diameter changes whereas the reverse situation was observed in females, suggesting possible sexually dimorphic effects of oxytocin, probably related to endogenous hormone levels and/or physiological differences across genders. After independent of application of intranasal oxytocin/placebo, the pupil diameter changes of the participants during trustworthiness evaluation were found as follows: in response to untrustworthy faces > trustworthy faces > neutral faces.

These results verify our current knowledge regarding oxytocin's crucial role in trusting behavior, social cognition and emotion recognition in humans.

To the best of our knowledge, this is the first study that investigates the relationship between subjective evaluation of trustworthiness and task-evoked pupillary responses, the effect of intranasal oxytocin on trustworthiness evaluation and facial expression recognition in both males and females along with physiological responses such as pupil diameter changes. Furthermore, the effect of intranasal oxytocin on pupillary responses is examined in females for the first time. Our finding on trustworthiness is a significant contribution to the literature which might open new research questions regarding the pivotal role of oxytocin in pro-social behavior.

REFERENCES

Adolphs, R. (2002). Recognizing emotion from facial expressions: psychological and neurological mechanisms. *Behavioral and cognitive neuroscience reviews, 1*(1), 21-62.

Adolphs, R. (2003). Cognitive neuroscience of human social behaviour. *Nature Reviews Neuroscience, 4*(3), 165-178.

Adolphs, R., Damasio, H., Tranel, D., Cooper, G., & Damasio, A. R. (2000). A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. *The Journal of Neuroscience, 20*(7), 2683-2690.

Adolphs, R., Gosselin, F., Buchanan, T. W., Tranel, D., Schyns, P., & Damasio, A. R. (2005). A mechanism for impaired fear recognition after amygdala damage. *Nature, 433*(7021), 68-72.

Adolphs, R., Russell, J. A., & Tranel, D. (1999). A role for the human amygdala in recognizing emotional arousal from unpleasant stimuli. *Psychological Science, 10*(2), 167-171.

Adolphs, R., Tranel, D., & Damasio, A. R. (1998). The human amygdala in social judgment. *Nature, 393*(6684), 470-474.

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature, 372*(6507), 669-672.

Allison, T., Puce, A., Spencer, D. D., & McCarthy, G. (1999). Electrophysiological studies of human face perception. I: Potentials generated in occipitotemporal cortex by face and non-face stimuli. *Cerebral cortex, 9*(5), 415-430.

Amaral, D. G. (2003). The amygdala, social behavior, and danger detection. *Annals of the New York Academy of Sciences, 1000*(1), 337-347.

Anderson, A. K., & Phelps, E. A. (2001). Lesions of the human amygdala impair enhanced perception of emotionally salient events. *Nature, 411*(6835), 305-309.

Argiolas, A., & Gessa, G. L. (1991). Central functions of oxytocin. *Neuroscience & Biobehavioral Reviews, 15*(2), 217-231.

Bagby, R. M., Parker, J. D., & Taylor, G. J. (1994). The twenty-item Toronto Alexithymia Scale—I. Item selection and cross-validation of the factor structure. *Journal of psychosomatic research, 38*(1), 23-32.

Bar, M., Neta, M., & Linz, H. (2006). Very first impressions. *Emotion, 6*(2), 269.

Barakat, N. S., Omar, S. A., & Ahmed, A. A. E. (2006). Carbamazepine uptake into rat brain following intra-olfactory transport. *Journal of pharmacy and pharmacology, 58*(1), 63-72.

Barbur, J. L. (2003). Learning from the pupil-studies of basic mechanisms and clinical applications. In L. M. Chalupa & J. S. Werner (Eds.), *The visual neurosciences* (Vol. 1, pp. 641-656). Cambridge (MA): MIT Press.

Barraza, J. A., & Zak, P. J. (2009). Empathy toward strangers triggers oxytocin release and subsequent generosity. *Annals of the New York Academy of Sciences, 1167*(1), 182-189.

Baumgartner, T., Heinrichs, M., Vonlanthen, A., Fischbacher, U., & Fehr, E. (2008). Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. *Neuron, 58*(4), 639-650.

Bealer, S. L., Armstrong, W. E., & Crowley, W. R. (2010). Oxytocin release in magnocellular nuclei: neurochemical mediators and functional significance during gestation. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 299*(2), R452-R458.

Beatty, J. (1982). Task-evoked pupillary responses, processing load, and the structure of processing resources. *Psychological bulletin, 91*(2), 276.

Beatty, J., & Lucero-Wagoner, B. (2000). The pupillary system. *Handbook of psychophysiology, 2*, 142-162.

Beck, A. T. (1961). An inventory for measuring depression. *Archieves of General Psychology, 4*, 561-571.

Blair, R. J. R. (1995). A cognitive developmental approach to morality: Investigating the psychopath. *Cognition, 57*(1), 1-29.

Blair, R. J. R., Morris, J. S., Frith, C. D., Perrett, D. I., & Dolan, R. J. (1999). Dissociable neural responses to facial expressions of sadness and anger. *Brain, 122*(5), 883-893.

Boccia, M. L., Goursaud, A. P. S., Bachevalier, J., Anderson, K. D., & Pedersen, C. A. (2007). Peripherally administered non-peptide oxytocin antagonist, L368, 899®, accumulates in limbic brain areas: a new pharmacological tool for the

study of social motivation in non-human primates. *Hormones and behavior, 52*(3), 344-351.

Bouvier, S. E., & Engel, S. A. (2006). Behavioral deficits and cortical damage loci in cerebral achromatopsia. *Cerebral Cortex, 16*(2), 183-191.

Bradley, M. M., Miccoli, L., Escrig, M. A., & Lang, P. J. (2008). The pupil as a measure of emotional arousal and autonomic activation. *Psychophysiology, 45*(4), 602-607.

Breiter, H. C., Etcoff, N. L., Whalen, P. J., Kennedy, W. A., Rauch, S. L., Buckner, R. L., Strauss, M. M., Hyman, S. E., & Rosen, B. R. (1996). Response and habituation of the human amygdala during visual processing of facial expression. *Neuron, 17*(5), 875-887.

Burnett, S., Bird, G., Moll, J., Frith, C., & Blakemore, S. J. (2009). Development during adolescence of the neural processing of social emotion. *Journal of Cognitive Neuroscience, 21*(9), 1736-1750.

Cabestrero, R., Crespo, A., & Quirós, P. (2009). Pupillary dilation as an index of task demands. *Perceptual and motor skills, 109*(3), 664-678.

Cacioppo, J. T., & Berntson, G. G. (Eds.). (2004). *Essays in social neuroscience.* Cambridge, MA: MIT Press.

Calder, A. J., Keane, J., Lawrence, A. D., & Manes, F. (2004). Impaired recognition of anger following damage to the ventral striatum. *Brain, 127*(9), 1958-1969.

Calder, A. J., Keane, J., Manes, F., Antoun, N., & Young, A. W. (2000). Impaired recognition and experience of disgust following brain injury. *Nature neuroscience, 3*(11), 1077-1078.

Campbell, A. (2008). Attachment, aggression and affiliation: the role of oxytocin in female social behavior. *Biological psychology, 77*(1), 1-10.

Campbell, A., Ruffman, T., Murray, J. E., & Glue, P. (2014). Oxytocin improves emotion recognition for older males. *Neurobiology of aging, 35*(10), 2246-2248.

Cancelliere, A. E., & Kertesz, A. (1990). Lesion localization in acquired deficits of emotional expression and comprehension. *Brain and cognition, 13*(2), 133-147.

Cannon, W. B. (1932). *The wisdom of the body.* New York: Norton.

Carter, C. S., Grippo, A. J., Pournajafi-Nazarloo, H., Ruscio, M. G., & Porges, S. W. (2008). Oxytocin, vasopressin and sociality. *Progress in brain research, 170*, 331-336.

Dale, H. H. (1906). On some physiological actions of ergot. *The Journal of physiology, 34*(3), 163-206.

Damasio, A.R. (1994). *Descartes' Error: Emotion, Reason, and the Human Brain.* Grosset/Putnam, New York.

Damasio, A.R., (1999). *The Feeling of What Happens: Body and Emotion in the Making of Consciousness.* Harcourt Brace & Co., New York.

Darwin, C., Ekman, P., & Prodger, P. (1998). *The expression of the emotions in man and animals.* Oxford University Press, USA.

De Dreu, C. K., Greer, L. L., Handgraaf, M. J., Shalvi, S., Van Kleef, G. A., Baas, M., Ten Velden, F. S., Van Dijk, E., & Feith, S. W. W. (2010). The neuropeptide oxytocin regulates parochial altruism in intergroup conflict among humans. *Science, 328*(5984), 1408-1411.

De Dreu, C. K., Greer, L. L., Van Kleef, G. A., Shalvi, S., & Handgraaf, M. J. (2011). Oxytocin promotes human ethnocentrism. *Proceedings of the National Academy of Sciences, 108*(4), 1262-1266.

De Renzi, E., Perani, D., Carlesimo, G. A., Silveri, M. C., & Fazio, F. (1994). Prosopagnosia can be associated with damage confined to the right hemisphere—an MRI and PET study and a review of the literature. *Neuropsychologia, 32*(8), 893-902.

Di Simplicio, M., Massey-Chase, R., Cowen, P. J., & Harmer, C. J. (2008). Oxytocin enhances processing of positive versus negative emotional information in healthy male volunteers. *Journal of Psychopharmacology, 23*(3), 241-248.

Ditzen, B., Schaer, M., Gabriel, B., Bodenmann, G., Ehlert, U., & Heinrichs, M. (2009). Intranasal oxytocin increases positive communication and reduces cortisol levels during couple conflict. *Biological psychiatry, 65*(9), 728-731.

Dluzen, D. E., Muraoka, S., Engelmann, M., & Landgraf, R. (1998). The effects of infusion of arginine vasopressin, oxytocin, or their antagonists into the olfactory bulb upon social recognition responses in male rats. *Peptides, 19*(6), 999-1005.

Dolan, R. J., Fletcher, P., Morris, J., Kapur, N., Deakin, J. F. W., & Frith, C. D. (1996). Neural activation during covert processing of positive emotional facial expressions. *Neuroimage, 4*(3), 194-200.

Domes, G., Heinrichs, M., Gläscher, J., Büchel, C., Braus, D. F., & Herpertz, S. C. (2007a). Oxytocin attenuates amygdala responses to emotional faces regardless of valence. *Biological psychiatry*, *62*(10), 1187-1190.

Domes, G., Heinrichs, M., Michel, A., Berger, C., & Herpertz, S. C. (2007b). Oxytocin improves "mind-reading" in humans. *Biological psychiatry*, *61*(6), 731-733.

Domes, G., Lischke, A., Berger, C., Grossmann, A., Hauenstein, K., Heinrichs, M., & Herpertz, S. C. (2010). Effects of intranasal oxytocin on emotional face processing in women. *Psychoneuroendocrinology*, *35*(1), 83-93.

Du Vigneaud, V., Ressler, C., Swan, J. M., Roberts, C. W., & Katsoyannis, P. G. (1954). The synthesis of oxytocin. *Journal of the American Chemical Society*, *76*(12): 3115–3118.

Eblen, F., & Graybiel, A. M. (1995). Highly restricted origin of prefrontal cortical inputs to striosomes in the macaque monkey. *The Journal of neuroscience*, *15*(9), 5999-6013.

Ekman, P. (1992). An argument for basic emotions. *Cognition & emotion*, *6*(3-4), 169-200.

Ekman, P. (2003). Darwin, deception, and facial expression. *Annals of the New York Academy of Sciences*, *1000*(1), 205-221.

Ekman, P., & Friesen, W. V. (1971). Constants across cultures in the face and emotion. *Journal of personality and social psychology*, *17*(2), 124.

Ekman, P., Friesen, W. V., O'Sullivan, M., Chan, A., Diacoyanni-Tarlatzis, I., Heider, K., Krause, R., LeCompte, W. A., Pitcairn, T., Ricci-Bitti, P. E., Scherer, K., Tomita, M., & Tzavaras, A. (1987). Universals and cultural differences in the judgments of facial expressions of emotion. *Journal of personality and social psychology*, *53*(4), 712-717.

Everitt, B. J., Parkinson, J. A., Olmstead, M. C., Arroyo, M., Robledo, P., & Robbins, T. W. (1999). Associative processes in addiction and reward the role of amygdala-ventral striatal subsystems. *Annals of the New York Academy of Sciences*, *877*(1), 412-438.

Faber, W. M. (1937). The nasal mucosa and the subarachnoid space. *American Journal of Anatomy*, *62*(1), 121-148.

Feldman, R., Weller, A., Zagoory-Sharon, O., & Levine, A. (2007). Evidence for a neuroendocrinological foundation of human affiliation plasma oxytocin levels

across pregnancy and the postpartum period predict mother-infant bonding. *Psychological Science, 18*(11), 965-970.

Ferguson, J. N., Aldag, J. M., Insel, T. R., & Young, L. J. (2001). Oxytocin in the medial amygdala is essential for social recognition in the mouse. *The Journal of Neuroscience, 21*(20), 8278-8285.

Fischer-Shofty, M., Levkovitz, Y., & Shamay-Tsoory, S. G. (2013). Oxytocin facilitates accurate perception of competition in men and kinship in women. *Social cognitive and affective neuroscience*, 8(3): 313-317.

Fischer-Shofty, M., Shamay-Tsoory, S. G., Harari, H., & Levkovitz, Y. (2010). The effect of intranasal administration of oxytocin on fear recognition. *Neuropsychologia, 48*(1), 179-184.

Fridlund, A. J. (1991). Evolution and facial action in reflex, social motive, and paralanguage. *Biological psychology, 32*(1), 3-100.

Frith, C. D., & Singer, T. (2008). The role of social cognition in decision making. *Philosophical Transactions of the Royal Society of London B: Biological Sciences, 363*(1511), 3875-3886.

Fujiwara, T., Cherrington, A. D., Neal, D. N., & McGuinness, O. P. (1996). Role of cortisol in the metabolic response to stress hormone infusion in the conscious dog. *Metabolism, 45*(5), 571-578.

Gainotti, G., Barbier, A., & Marra, C. (2003). Slowly progressive defect in recognition of familiar people in a patient with right anterior temporal atrophy. *Brain, 126*(4), 792-803.

Gallese, V., Keysers, C., & Rizzolatti, G. (2004). A unifying view of the basis of social cognition. *Trends in cognitive sciences, 8*(9), 396-403.

Gauthier, I., Skudlarski, P., Gore, J. C., & Anderson, A. W. (2000). Expertise for cars and birds recruits brain areas involved in face recognition. *Nature neuroscience, 3*(2), 191-197.

Gençöz, T. (2000). Pozitif ve Negatif Duygu Ölçeği: Geçerlilik ve güvenilirlik çalışması. *Türk Psikoloji Dergisi, 15,* 9-26.

Gimpl, G., & Fahrenholz, F. (2001). The oxytocin receptor system: structure, function, and regulation. *Physiological reviews, 81*(2), 629-683.

Gimpl, G., Wiegand, V., Burger, K., & Fahrenholz, F. (2002). Cholesterol and steroid hormones: modulators of oxytocin receptor function. *Progress in brain research, 139*, 43-55.

Gizurarson, S., Bechgaard, E., & Hjortkjær, R. K. (2006). Two intranasal administration techniques give two different pharmacokinetic results. *Scandinavian Journal of Laboratory Animal Sciences, 33*(1), 35-38.

Gizurarson, S., Gudbrandsson, F. K., Jónsson, H., & Bechgaard, E. (1999). Intranasal administration of diazepam aiming at the treatment of acute seizures: clinical trials in healthy volunteers. *Biological & pharmaceutical bulletin, 22*(4), 425-427.

Gordon, I., Zagoory-Sharon, O., Leckman, J. F., & Feldman, R. (2010). Oxytocin and the development of parenting in humans. *Biological psychiatry, 68*(4), 377-382.

Gorno-Tempini, M. L., Pradelli, S., Serafini, M., Pagnoni, G., Baraldi, P., Porro, C., Nicoletti, R., Umità, C., & Nichelli, P. (2001). Explicit and incidental facial expression processing: an fMRI study. *Neuroimage, 14*(2), 465-473.

Granholm, E., Asarnow, R. F., Sarkin, A. J., & Dykes, K. L. (1996). Pupillary responses index cognitive resource limitations. *Psychophysiology, 33*(4), 457-461.

Guastella, A. J., Carson, D. S., Dadds, M. R., Mitchell, P. B., & Cox, R. E. (2009). Does oxytocin influence the early detection of angry and happy faces?. *Psychoneuroendocrinology, 34*(2), 220-225.

Guastella, A. J., Einfeld, S. L., Gray, K. M., Rinehart, N. J., Tonge, B. J., Lambert, T. J., & Hickie, I. B. (2010). Intranasal oxytocin improves emotion recognition for youth with autism spectrum disorders. *Biological psychiatry, 67*(7), 692-694.

Guastella, A. J., Mitchell, P. B., & Dadds, M. R. (2008a). Oxytocin increases gaze to the eye region of human faces. *Biological psychiatry, 63*(1), 3-5.

Guastella, A. J., Mitchell, P. B., & Mathews, F. (2008b). Oxytocin enhances the encoding of positive social memories in humans. *Biological psychiatry, 64*(3), 256-258.

Halgren, E., Dale, A. M., Sereno, M. I., Tootell, R. B., Marinkovic, K., & Rosen, B. R. (1999). Location of human face-selective cortex with respect to retinotopic areas. *Human brain mapping, 7*(1), 29-37.

Han, J. S., McMahan, R. W., Holland, P., & Gallagher, M. (1997). The role of an amygdalo-nigrostriatal pathway in associative learning. *The Journal of neuroscience, 17*(10), 3913-3919.

Hanson, L. R., & Frey II, W. H. (2008). Intranasal delivery bypasses the blood-brain barrier to target therapeutic agents to the central nervous system and treat neurodegenerative disease. *BMC neuroscience, 9*(Suppl 3), S5.

Harmer, C. J., Thilo, K. V., Rothwell, J. C., & Goodwin, G. M. (2001). Transcranial magnetic stimulation of medial–frontal cortex impairs the processing of angry facial expressions. *Nature neuroscience, 4*(1), 17-18.

Haxby, J. V., Hoffman, E. A., & Gobbini, M. I. (2000). The distributed human neural system for face perception. *Trends in cognitive sciences, 4*(6), 223-233.

Haxby, J. V., Ungerleider, L. G., Clark, V. P., Schouten, J. L., Hoffman, E. A., & Martin, A. (1999). The effect of face inversion on activity in human neural systems for face and object perception. *Neuron, 22*(1), 189-199.

Heinrichs, M., Baumgartner, T., Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biological psychiatry, 54*(12), 1389-1398.

Heinrichs, M., von Dawans, B., & Domes, G. (2009). Oxytocin, vasopressin, and human social behavior. *Frontiers in neuroendocrinology, 30*(4), 548-557.

Hepsomalı, P. (2013). The role of symmetry and facial expressions of emotions in evaluation of attractiveness and perceived symmetry: an eye tracking study. MS Thesis Submitted to Graduate School of Informatics of METU.

Hess, E. H. (1965). Attitude and pupil size. *Scientific American, 212*(4), 46-54.

Hess, E. H. (1975). *The tell-tale eye: How your eyes reveal hidden thoughts and emotions.* Van Nostrand Reinhold.

Hess, E. H., & Polt, J. M. (1960). Pupil size as related to interest value of visual stimuli. *Science, 132*(3423), 349-350.

Hess, E. H., Seltzer, A. L., & Shlien, J. M. (1965). Pupil response of hetero-and homosexual males to pictures of men and women: A pilot study. *Journal of Abnormal Psychology, 70*(3), 165.

Hisli, N. (1988). Beck Depresyon Envanteri'nin geçerliliği üzerine bir çalışma. *Psikoloji Dergisi, 6*(22); 118-122.

Hoge, E. A., Anderson, E., Lawson, E. A., Bui, E., Fischer, L. E., Khadge, S. D., Barrett, L. F., & Simon, N. M. (2014). Gender moderates the effect of oxytocin on social judgments. *Human Psychopharmacology: Clinical and Experimental, 29*(3), 299-304.

Holl, A. (1980). Selektivdarstellung der Riechsinneszellen des Zwergwelses Ictalurus nebulosus mit Procionfarbstoffen/Selective Staining by Procion Dyes of Olfactory Sensory Neurons in the Catfish Ictalurus nebulosus. *Zeitschrift für Naturforschung C, 35*(5-6), 526-528.

Hollander, E., Bartz, J., Chaplin, W., Phillips, A., Sumner, J., Soorya, L., Anagnostou, E., & Wasserman, S. (2007). Oxytocin increases retention of social cognition in autism. *Biological psychiatry, 61*(4), 498-503.

Hopf, H. C., Muller-Forell, W., & Hopf, N. J. (1992). Localization of emotional and volitional facial paresis. *Neurology, 42*(10), 1918-1918.

Hornak, J., Bramham, J., Rolls, E. T., Morris, R. G., O'Doherty, J., Bullock, P. R., & Polkey, C. E. (2003). Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. *Brain, 126*(7), 1691-1712.

Hyönä, J., Tommola, J., & Alaja, A. M. (1995). Pupil dilation as a measure of processing load in simultaneous interpretation and other language tasks. *The Quarterly Journal of Experimental Psychology, 48*(3), 598-612.

Janisse, M. P. (1974). Pupil size, affect and exposure frequency. *Social Behavior and personality, 2*(2), 125-146.

Janisse, M. P. (1977). *Pupillometry: The psychology of the pupillary response*. Halsted Press.

Joubert, S., Felician, O., Barbeau, E., Ranjeva, J. P., Christophe, M., Didic, M., Poncet, M., & Ceccaldi, M. (2006). The right temporal lobe variant of frontotemporal dementia. *Journal of neurology, 253*(11), 1447-1458.

Joubert, S., Felician, O., Barbeau, E., Sontheimer, A., Barton, J. J., Ceccaldi, M., & Poncet, M. (2003). Impaired configurational processing in a case of progressive prosopagnosia associated with predominant right temporal lobe atrophy. *Brain, 126*(11), 2537-2550.

Iidaka, T., Omori, M., Murata, T., Kosaka, H., Yonekura, Y., Okada, T., & Sadato, N. (2001). Neural interaction of the amygdala with the prefrontal and temporal cortices in the processing of facial expressions as revealed by fMRI. *Journal of Cognitive Neuroscience, 13*(8), 1035-1047.

Illum, L. (2004). Is nose-to-brain transport of drugs in man a reality?. *Journal of Pharmacy and Pharmacology, 56*(1), 3-17.

Illum, L., Jørgensen, H., Bisgaard, H., Krogsgaard, O., & Rossing, N. (1987). Bioadhesive microspheres as a potential nasal drug delivery system. *International journal of pharmaceutics, 39*(3), 189-199.

Insel, T. R., Young, L., & Wang, Z. (1997). Central oxytocin and reproductive behaviours. *Reviews of reproduction, 2*(1), 28-37.

Ishai, A. (2008). Let's face it: It's a cortical network. *Neuroimage, 40(2),* 415-419.

Ishai, A., Haxby, J. V., & Ungerleider, L. G. (2002). Visual imagery of famous faces: effects of memory and attention revealed by fMRI. *Neuroimage, 17*(4), 1729-1741.

Izard, C. E. (1971). *The face of emotion.* New York: Appleton-Century-Crofts.

Kahneman, D. (1973). *Attention and effort.* Englewood Cliffs, NJ: Prentice-Hall.

Kampe, K. K., Frith, C. D., Dolan, R. J., & Frith, U. (2001). Psychology: Reward value of attractiveness and gaze. *Nature, 413*(6856), 589-589.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. *The Journal of Neuroscience, 17*(11), 4302-4311.

Kavaliers, M., & Choleris, E. (2011). Sociality, pathogen avoidance, and the neuropeptides oxytocin and arginine vasopressin. *Psychological science, 22*(11), 1367-1374.

Kéri, S., & Benedek, G. (2009). Oxytocin enhances the perception of biological motion in humans. *Cognitive, Affective, & Behavioral Neuroscience, 9*(3), 237-241.

Kimura, T., Tanizawa, O., Mori, K., Brownstein, M. J., & Okayama, H. (1992). Structure and expression of a human oxytocin receptor. *Nature, 356*(6369), 526-529.

Kiss, A., & Mikkelsen, J. D. (2005). Oxytocin--anatomy and functional assignments: a minireview. *Endocrine regulations, 39*(3), 97-105.

Kosfeld, M., Heinrichs, M., Zak, P. J., Fischbacher, U., & Fehr, E. (2005). Oxytocin increases trust in humans. *Nature, 435*(7042), 673-676.

Krenz, W. C., & Stark, L. (1985). Systems model for pupil size effect. *Biological cybernetics, 51*(6), 391-397.

Kret, M. E., Stekelenburg, J. J., Roelofs, K., & De Gelder, B. (2013). Perception of face and body expressions using electromyography, pupillometry and gaze measures. *Frontiers in psychology, 4,* 28.

Kriegeskorte, N., Formisano, E., Sorger, B., & Goebel, R. (2007). Individual faces elicit distinct response patterns in human anterior temporal cortex. *Proceedings of the National Academy of Sciences, 104*(51), 20600-20605.

Kubzansky, L. D., Mendes, W. B., Appleton, A. A., Block, J., & Adler, G. K. (2012). A heartfelt response: oxytocin effects on response to social stress in men and women. *Biological psychology, 90*(1), 1-9.

Kuraoka, K., & Nakamura, K. (2007). Responses of single neurons in monkey amygdala to facial and vocal emotions. *Journal of Neurophysiology, 97*(2), 1379-1387.

LeDoux, J. E. (1996). *The Emotional Brain.* Simon and Schuster, New York.

Lee, H. J., Macbeth, A. H., Pagani, J. H., & Young, W. S. (2009). Oxytocin: the great facilitator of life. *Progress in neurobiology, 88*(2), 127-151.

Le Gros Clark, W. E. (1929). The thalamus of Tupaia minor. *Journal of anatomy, 63*(Pt 2), 177-206.5.

Leknes, S., Wessberg, J., Ellingsen, D. M., Chelnokova, O., Olausson, H., & Laeng, B. (2012). Oxytocin enhances pupil dilation and sensitivity to 'hidden'emotional expressions. *Social cognitive and affective neuroscience, 8*, 741-749.

Lieberman, M. D. (2007). Social cognitive neuroscience: a review of core processes. *Annu. Rev. Psychol., 58,* 259-289.

Lim, M. M., Bielsky, I. F., & Young, L. J. (2005). Neuropeptides and the social brain: potential rodent models of autism. *International Journal of Developmental Neuroscience, 23*(2), 235-243.

Lindhardt, K., Ólafsson, D. R., Gizurarson, S., & Bechgaard, E. (2002). Intranasal bioavailability of diazepam in sheep correlated to rabbit and man. *International journal of pharmaceutics, 231*(1), 67-72.

Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E., & Barrett, L. F. (2012). The brain basis of emotion: a meta-analytic review. *Behavioral and Brain Sciences, 35*(03), 121-143.

Lischke, A., Gamer, M., Berger, C., Grossmann, A., Hauenstein, K., Heinrichs, M., Herpertz, S. C., & Domes, G. (2012). Oxytocin increases amygdala reactivity to threatening scenes in females. *Psychoneuroendocrinology, 37*(9), 1431-1438.

Loewenfeld, I. E., & Lowenstein, O. (1993). *The pupil: Anatomy, physiology, and clinical applications (Vol. 2).* Wiley-Blackwell.

Lomber, S. G. (2002). Learning to see the trees before the forest: reversible deactivation of the superior colliculus during learning of local and global visual features. *Proceedings of the National Academy of Sciences, 99*(6), 4049-4054.

Loup, F., Tribollet, E., Dubois-Dauphin, M., Pizzolato, G., & Dreifuss, J. J. (1989). Localization of oxytocin binding sites in the human brainstem and upper spinal cord: an autoradiographic study. *Brain research, 500*(1), 223-230.

Luminet, O., Grynberg, D., Ruzette, N., & Mikolajczak, M. (2011). Personality-dependent effects of oxytocin: greater social benefits for high alexithymia scorers. *Biological psychology, 87*(3), 401-406.

Lundqvist, D., Flykt, A., & Öhman, A. (1998). *The Karolinska Directed Emotional Faces –KDEF [CD ROM]*. Stockholm, Sweden: Department of Clinical Neuroscience, Psychology section, Karolinska Institutet. ISBN 91-630-7164-9.

Lynn, S. K., Hoge, E. A., Fischer, L. E., Barrett, L. F., & Simon, N. M. (2014). Gender differences in oxytocin-associated disruption of decision bias during emotion perception. *Psychiatry research, 219*(1), 198-203.

Mandal, M. K., Pandey, R., & Prasad, A. B. (1998). Facial expressions of emotions and schizophrenia: A review. *Schizophrenia bulletin, 24*(3), 399.

Marsh, A. A., Henry, H. Y., Pine, D. S., & Blair, R. J. R. (2010). Oxytocin improves specific recognition of positive facial expressions. *Psychopharmacology, 209*(3), 225-232.

Mathison, S., Nagilla, R., & Kompella, U. B. (1998). Nasal route for direct delivery of solutes to the central nervous system: fact or fiction?. *Journal of drug targeting, 5*(6), 415-441.

Matsumoto, D., & Ekman, P. (1989). American-Japanese cultural differences in intensity ratings of facial expressions of emotion. *Motivation and Emotion, 13*(2), 143-157.

Merkus, P., Romeijn, S. G., Verhoef, J., Merkus, F. W., & Schouwenburg, P. F. (2001). Classification of Cilio-Inhibiting Effects of Nasal Drugs. *The laryngoscope, 111*(4), 595-602.

Mikolajczak, M., Gross, J. J., Lane, A., Corneille, O., de Timary, P., & Luminet, O. (2010). Oxytocin makes people trusting, not gullible. *Psychological Science, 21*(8), 1072-1074.

Moeller, S., Freiwald, W. A., & Tsao, D. Y. (2008). Patches with links: a unified system for processing faces in the macaque temporal lobe. *Science, 320*(5881), 1355-1359.

Monstein, H. J., Grahn, N., Truedsson, M., & Ohlsson, B. (2004). Oxytocin and oxytocin-receptor mRNA expression in the human gastrointestinal tract: a polymerase chain reaction study. *Regulatory peptides, 119*(1), 39-44.

Moos, F., & Richard, P. (1989). Paraventricular and supraoptic bursting oxytocin cells in rat are locally regulated by oxytocin and functionally related. *The Journal of physiology, 408*(1), 1-18.

Morris, J. S., Frith, C. D., Perrett, D. I., Rowland, D., Young, A. W., Calder, A. J., & Dolan, R. J. (1996). A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature, 383*(6603), 812-815.

Morris, J. S., Öhman, A., & Dolan, R. J. (1998). Conscious and unconscious emotional learning in the human amygdala. *Nature, 393*(6684), 467-470.

Neumann, I. D. (2008). Brain oxytocin: a key regulator of emotional and social behaviours in both females and males. *Journal of neuroendocrinology, 20*(6), 858-865.

Noesselt, T., Driver, J., Heinze, H. J., & Dolan, R. (2005). Asymmetrical activation in the human brain during processing of fearful faces. *Current Biology, 15*(5), 424-429.

O'Brien, B. J., Abel, P. L., & Olavarria, J. F. (2001). The retinal input to calbindin-D28k-defined subdivisions in macaque inferior pulvinar. *Neuroscience letters, 312*(3), 145-148.

Ochsner, K. N., & Lieberman, M. D. (2001). The emergence of social cognitive neuroscience. *American Psychologist, 56*(9), 717.

Oosterhof, N. N., & Todorov, A. (2009). Shared perceptual basis of emotional expressions and trustworthiness impressions from faces. *Emotion, 9*(1), 128.

Pantic, M., & Rothkrantz, L. J. (2004). Facial action recognition for facial expression analysis from static face images. *Systems, Man, and Cybernetics, Part B: Cybernetics, IEEE Transactions on, 34*(3), 1449-1461.

Pardridge, W. M. (2005). The blood-brain barrier: bottleneck in brain drug development. *NeuroRx, 2*(1), 3-14.

Parvizi, J., Jacques, C., Foster, B. L., Withoft, N., Rangarajan, V., Weiner, K. S., & Grill-Spector, K. (2012). Electrical stimulation of human fusiform face-selective regions distorts face perception. *The Journal of Neuroscience, 32*(43), 14915-14920.

Perry, A., Bentin, S., Shalev, I., Israel, S., Uzefovsky, F., Bar-On, D., & Ebstein, R. P. (2010). Intranasal oxytocin modulates EEG mu/alpha and beta rhythms during perception of biological motion. *Psychoneuroendocrinology, 35*(10), 1446-1453.

Phelps, E. A., Delgado, M. R., Nearing, K. I., & LeDoux, J. E. (2004). Extinction learning in humans: role of the amygdala and vmPFC. *Neuron, 43*(6), 897-905.

Phillips, M. L., Bullmore, E. T., Howard, R., Woodruff, P. W., Wright, I. C., Williams, S. C., Simmons, A., Andrew, C., Brammer, M., & David, A. S. (1998). Investigation of facial recognition memory and happy and sad facial expression perception: an fMRI study. *Psychiatry Research: Neuroimaging, 83*(3), 127-138.

Phillips, M. L., Young, A. W., Senior, C., Brammer, M., Andrew, C., Calder, A. J., Bullmore, E. T., Perrett, D. I., Rowland, D., Williams, S. C. R., & David, A. S. (1997). A specific neural substrate for perceiving facial expressions of disgust. *Nature, 389*(6650), 495-498.

Prehn, K., Kazzer, P., Lischke, A., Heinrichs, M., Herpertz, S. C., & Domes, G. (2013). Effects of intranasal oxytocin on pupil dilation indicate increased salience of socioaffective stimuli. *Psychophysiology, 50*(6), 528-537.

Purves, D., Augustine G. J., Fitzpatrick. D., Katz, L. C., LaMantia A.-S., McNamara, J. O., Williams, S. M. (Eds.). (2001). *Neuroscience (2nd ed.).* Sunderland, MA: Sinauer Associates.

Raine, A., Lencz, T., Bihrle, S., LaCasse, L., & Colletti, P. (2000). Reduced prefrontal gray matter volume and reduced autonomic activity in antisocial personality disorder. *Archives of general psychiatry, 57*(2), 119-127.

Rimmele, U., Hediger, K., Heinrichs, M., & Klaver, P. (2009). Oxytocin makes a face in memory familiar. *The Journal of Neuroscience, 29*(1), 38-42.

Robinson, D. L., & Petersen, S. E. (1992). The pulvinar and visual salience. *Trends in neurosciences, 15*(4), 127-132.

Rolls, E. T. (2000). The orbitofrontal cortex and reward. *Cerebral cortex, 10*(3), 284-294.

Rosenkranz, J. A., Moore, H., & Grace, A. A. (2003). The prefrontal cortex regulates lateral amygdala neuronal plasticity and responses to previously conditioned stimuli. *The Journal of Neuroscience, 23*(35), 11054-11064.

Rossion, B., Caldara, R., Seghier, M., Schuller, A. M., Lazeyras, F., & Mayer, E. (2003). A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. *Brain, 126*(11), 2381-2395.

Rossion, B., Gauthier, I., Tarr, M. J., Despland, P., Bruyer, R., Linotte, S., & Crommelinck, M. (2000). The N170 occipito-temporal component is delayed and enhanced to inverted faces but not to inverted objects: an electrophysiological account of face-specific processes in the human brain. *Neuroreport, 11*(1), 69-72.

Rotshtein, P., Henson, R. N., Treves, A., Driver, J., & Dolan, R. J. (2005). Morphing Marilyn into Maggie dissociates physical and identity face representations in the brain. *Nature neuroscience, 8*(1), 107-113.

Russell, J. A. (1980). A circumplex model of affect. *Journal of personality and social psychology, 39*(6), 1161.

Sahin, N. H., & Sahin, N. (1992). Reliability and validity of the Turkish version of the automatic thoughts questionnaire. *Journal of Clinical Psychology, 49*(6); 751-763.

Sakane, T., Akizuki, M., Taki, Y., Yamashita, S., Sezaki, H., & Nadai, T. (1994). Direct drug transport from the rat nasal cavity to the cerebrospinal fluid: the relation to the dissociation of the drug. *Journal of pharmacy and pharmacology, 46*(5), 378-379.

Sakane, T., Akizuki, M., Taki, Y., Yamashita, S., Sezaki, H., & Nadai, T. (1995). Direct drug transport from the rat nasal cavity to the cerebrospinal fluid: the relation to the molecular weight of drugs. *Journal of pharmacy and pharmacology, 47*(5), 379-381.

Sakane, T., Akizuki, M., Yamashita, S., Nadai, T., Hashida, M. & Sezaki, H. (1991). The transport of a drug to the cerebrospinal fluid directly from the nasal cavity: the relation to the lipophilicity of the drug. *Chemical and pharmaceutical bulletin, 39*(9), 2456-2458.

Savaskan, E., Ehrhardt, R., Schulz, A., Walter, M., & Schächinger, H. (2008). Post-learning intranasal oxytocin modulates human memory for facial identity. *Psychoneuroendocrinology, 33*(3), 368-374.

Schmidt, L. A., & Trainor, L. J. (2001). Frontal brain electrical activity (EEG) distinguishes valence and intensity of musical emotions. *Cognition & Emotion, 15*(4), 487-500.

Schmolck, H., & Squire, L. R. (2001). Impaired perception of facial emotions following bilateral damage to the anterior temporal lobe. *Neuropsychology, 15*(1), 30.

Schrammel, F., Pannasch, S., Graupner, S. T., Mojzisch, A., & Velichkovsky, B. M. (2009). Virtual friend or threat? The effects of facial expression and gaze interaction on psychophysiological responses and emotional experience. *Psychophysiology, 46*(5), 922-931.

Schulze, L., Lischke, A., Greif, J., Herpertz, S. C., Heinrichs, M., & Domes, G. (2011). Oxytocin increases recognition of masked emotional faces. *Psychoneuroendocrinology, 36*(9), 1378-1382.

Sergent, J., Ohta, S., & MacDonald, B. (1992). Functional neuroanatomy of face and object processing: a positron emission tomography study. *Brain, 1*(15), 15–36.

Shahrestani, S., Kemp, A. H., & Guastella, A. J. (2013). The impact of a single administration of intranasal oxytocin on the recognition of basic emotions in humans: a meta-analysis. *Neuropsychopharmacology, 38*(10), 1929-1936.

Shamay-Tsoory, S. G., Fischer, M., Dvash, J., Harari, H., Perach-Bloom, N., & Levkovitz, Y. (2009). Intranasal administration of oxytocin increases envy and schadenfreude (gloating). *Biological psychiatry, 66*(9), 864-870.

Smith, J. D., Masek, G. A., Ichinose, L. Y., Watanabe, T., & Stark, L. (1970). Single neuron activity in the pupillary system. *Brain research, 24*(2), 219-234.

Sprengelmeyer, R., Rausch, M., Eysel, U. T., & Przuntek, H. (1998). Neural structures associated with recognition of facial expressions of basic emotions. *Proceedings of the Royal Society of London B: Biological Sciences, 265*(1409), 1927-1931.

Sprengelmeyer, R., Young, A. W., Calder, A. J., Karnat, A., Lange, H., Homberg, V., Perrett, D., I., & Rowland, D. (1996). Loss of disgust: Perception of faces and emotions in Huntington's disease. *Brain, 119*(5), 1647-1665.

Sprengelmeyer, R., Young, A. W., Mahn, K., Schroeder, U., Woitalla, D., Büttner, T., Kuhn, W., & Przuntek, H. (2003). Facial expression recognition in people with medicated and unmedicated Parkinson's disease. *Neuropsychologia, 41*(8), 1047-1057.

Sprengelmeyer, R., Young, A. W., Pundt, I., Sprengelmeyer, A., Calder, A. J., Berrios, G., Winkel, R., Vollmöeller, W., Kuhn, W., Sartory, G., & Przuntek, H. (1997). Disgust implicated in obsessive–compulsive disorder. *Proceedings of the Royal Society of London B: Biological Sciences, 264*(1389), 1767-1773.

Stark, C. E., & Squire, L. R. (2000). Intact visual perceptual discrimination in humans in the absence of perirhinal cortex. *Learning & Memory, 7*(5), 273-278.

Stefanacci, L., & Amaral, D. G. (2002). Some observations on cortical inputs to the macaque monkey amygdala: an anterograde tracing study. *Journal of Comparative Neurology, 451*(4), 301-323.

Steinhauer, S. R. (2002). Pupillary responses, cognitive psychophysiology and psychopathology. Retrieved from http://www.wpic.pitt.edu/research/biometrics/Publications/PupilWeb.htm.

Steinhauer, S. R., Boller, F., Zubin, J., & Pearlman, S. (1983). Pupillary dilation to emotional visual stimuli revisited. *Psychophysiology, 20*, 472.

Takayanagi, Y., Yoshida, M., Bielsky, I. F., Ross, H. E., Kawamata, M., Onaka, T., Yanagisawa, T., Kimura, T., Matzuk, M. M., Young, L., J., & Nishimori, K. (2005). Pervasive social deficits, but normal parturition, in oxytocin receptor-deficient mice. *Proceedings of the National Academy of Sciences of the United States of America, 102*(44), 16096-16101.

Talegaonkar, S., & Mishra, P. R. (2004). Intranasal delivery: An approach to bypass the blood brain barrier. *Indian journal of pharmacology, 36*(3), 140.

Taylor, S. E., Gonzaga, G. C., Klein, L. C., Hu, P., Greendale, G. A., & Seeman, T. E. (2006). Relation of oxytocin to psychological stress responses and hypothalamic-pituitary-adrenocortical axis activity in older women. *Psychosomatic Medicine, 68*(2), 238-245.

Theodoridou, A., Rowe, A. C., Penton-Voak, I. S., & Rogers, P. J. (2009). Oxytocin and social perception: oxytocin increases perceived facial trustworthiness and attractiveness. *Hormones and behavior, 56*(1), 128-132.

Thorne, R. G., & Frey II, W. H. (2001). Delivery of neurotrophic factors to the central nervous system. *Clinical pharmacokinetics, 40*(12), 907-946.

Todorov, A., Harris, L. T., & Fiske, S. T. (2006). Toward behaviorally inspired social neuroscience. *Brain Research*, 1079, 76-85.

Tomita, H., Ohbayashi, M., Nakahara, K., Hasegawa, I., & Miyashita, Y. (1999). Top-down signal from prefrontal cortex in executive control of memory retrieval. *Nature, 401*(6754), 699-703.

Tsao, D. Y., Moeller, S., & Freiwald, W. A. (2008). Comparing face patch systems in macaques and humans. *Proceedings of the National Academy of Sciences, 105*(49), 19514-19519.

Ugwoke, M. I., Verbeke, N., & Kinget, R. (2001). The biopharmaceutical aspects of nasal mucoadhesive drug delivery. *Journal of pharmacy and pharmacology, 53*(1), 3-22.

Unkelbach, C., Guastella, A. J., & Forgas, J. P. (2008). Oxytocin selectively facilitates recognition of positive sex and relationship words. *Psychological Science, 19*(11), 1092-1094.

Van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2012). A sniff of trust: meta-analysis of the effects of intranasal oxytocin administration on face recognition, trust to in-group, and trust to out-group. *Psychoneuroendocrinology, 37*(3), 438-443.

Veening, J. G., de Jong, T., & Barendregt, H. P. (2010). Oxytocin-messages via the cerebrospinal fluid: behavioral effects; a review. *Physiology & Behavior, 101*(2), 193-210.

Vignozzi, L., Filippi, S., Luconi, M., Morelli, A., Mancina, R., Marini, M., Vannelli, G. B., Granchi, S., Orlando, C., Gelmini, S., Ledda, F., Forti, G., & Maggi, M. (2004). Oxytocin receptor is expressed in the penis and mediates an estrogen-dependent smooth muscle contractility. *Endocrinology, 145*(4), 1823-1834.

Vuilleumier, P., Armony, J. L., Driver, J., & Dolan, R. J. (2001). Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron, 30*(3), 829-841.

Vuilleumier, P., Richardson, M. P., Armony, J. L., Driver, J., & Dolan, R. J. (2004). Distant influences of amygdala lesion on visual cortical activation during emotional face processing. *Nature neuroscience, 7*(11), 1271-1278.

Vyas, T. K., Babbar, A. K., Sharma, R. K., Singh, S., & Misra, A. (2006). Intranasal mucoadhesive microemulsions of clonazepam: preliminary studies on brain targeting. *Journal of pharmaceutical sciences, 95*(3), 570-580.

Vyas, T. K., Shahiwala, A., Marathe, S., & Misra, A. (2005). Intranasal drug delivery for brain targeting. *Current drug delivery, 2*(2), 165-175.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063-1070.

Weiner, K. S., & Grill-Spector, K. (2010). Sparsely-distributed organization of face and limb activations in human ventral temporal cortex. *Neuroimage, 52*(4), 1559-1573.

Weiss, G. M. (1971). Cortisol and epinephrine relationships associated with stress adaptation in swine.

Wicker, B., Keysers, C., Plailly, J., Royet, J. P., Gallese, V., & Rizzolatti, G. (2003). Both of us disgusted in my insula: the common neural basis of seeing and feeling disgust. *Neuron, 40*(3), 655-664.

Willis, J., & Todorov, A. (2006). First impressions making up your mind after a 100-ms exposure to a face. *Psychological science, 17*(7), 592-598.

Winslow, J. T., & Insel, T. R. (2004). Neuroendocrine basis of social recognition. *Current opinion in neurobiology, 14*(2), 248-253.

Winston, J. S., Strange, B. A., O'Doherty, J., & Dolan, R. J. (2002). Automatic and intentional brain responses during evaluation of trustworthiness of faces. *Nature neuroscience, 5*(3), 277-283.

Wiseman, R., & Watt, C. (2010). Judging a book by its cover: the unconscious influence of pupil size on consumer choice. *Perception, 39*(10), 1417.

Zak, P. J., Kurzban, R., & Matzner, W. T. (2005). Oxytocin is associated with human trustworthiness. *Hormones and Behavior, 48*(5), 522-527.

Zak, P. J., Stanton, A. A., & Ahmadi, S. (2007). Oxytocin increases generosity in humans. *PLoS one, 2*(11), e1128.

Zbrożyna, A. W., & Westwood, D. M. (1991). Stimulation in prefrontal cortex inhibits conditioned increase in blood pressure and avoidance bar pressing in rats. *Physiology & Behavior, 49*(4), 705-708.

APPENDICES

APPENDIX A: BRAIN REGIONS INVOLVED IN FACE RECOGNITION

The visual system

To perceive a visual stimulus begins with the arrival of the photons reflected by the stimulus on the retina. These photons activate the photoreceptor cells of the retina ensuring transduction of light information into nerve messages. The retina is made up of different types of photoreceptor cells (i.e., bipolar, ganglion, amacrine cells) and photoreceptors called rods and cones.

Each photoreceptor has its own sensitivity to light. The rods (about 120 million cells) are very sensitive to light. Their activity is often saturated in normal illumination condition. Because of this high sensitivity, they rather participate in the night vision. On the other hand, the cones (about 5 million cells) have a lower sensitivity and therefore participate more in daytime vision, when the brightness is normal. The cones have a different spectral sensitivity than the rods, allowing them to participate in color vision while the rods are involved in only an achromatic (black and white) vision. The distribution of photoreceptors is not uniform. The concentration of the cones is maximum at the center of the retina, called the fovea, allowing a precise and significant vision in the center of the visual field. The further away from the fovea, the number of cones decreases, and consequently, the visual acuity gets low.

Each photoreceptor encodes a specific point of the visual field and the visual information is then transmitted to ganglion cells. The ganglion cells which receive inputs from several nerve cells, integrate the information from the photoreceptors. The photoreceptor has a smaller receptive field, while the ganglion cells that will be activated by many photoreceptors have a larger receptive field.

The ganglion cells, whose axons form the optic nerve, generate the action potentials propagating towards the lateral geniculate nucleus (LGN). In the LGN, two types of cell layers were identified: four parvocellular layers that receive inputs from the P-type ganglion cell and two magnocellular layers that receive the information transmitted by M-type cells. The parvocellular system is involved in the discrimination of form and color whereas the magnocellular system is involved in detection of motion. Then, the information processed at the LGN is transmitted to the primary visual cortex (V1). V1 (area 17 according to the architecture described by Brodmann) is located on the internal surface of the occipital lobe of each hemisphere, within the calcarine fissure. It is called striate cortex because of its particular cell architecture.

Furthermore, V1 is organized in a retinotopic fashion. In other words, there is a “topographic map” built point by point via using the visual field from information

received from the ganglion cells. A partial decussation of sensory fibers in the optic chiasm is found between the retina and the LGN. Therefore, the information from ganglion cells comes from one visual hemifield.

Brain areas involved in face recognition

The first hypotheses concerning the location of specific brain regions activated in the processing of faces emanate from case studies of brain-damaged patients.

For example, data from neuropsychology have shown that prosopagnosics patients which are unable to recognize faces at the individual level have lesions in the posterior regions (ventral occipito-temporal regions including in particular the lingual gyrus, the fusiform gyrus and parahippocampal cortex) (De Renzi, Perani, Carlesimo, Silveri, & Fazio, 1994). On the contrary, people with agnosia which is loss of the concept of the person, rather have more anterior lesions including temporal gyrus and medial temporal structures (Joubert et al., 2003, 2006; Gainotti, Barbier, & Marra, 2003).

Brain imaging techniques such as functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) have helped better define these different brain regions. A broad network of brain regions gets activated specifically in response to faces compared to other categories of objects (Sergent, Ohta, & MacDonald, 1992; Halgren et al., 1999; Haxby et al., 1999; Gauthier, Skudlarski, Gore, & Anderson, 2000; Rossion et al., 2000).

The hypothesis of the existence of a broad network of brain areas was confirmed by fMRI studies conducted in monkeys. Indeed, Tsao, Moeller, & Freiwald (2008) identified a wide network of specialized brain areas in face processing. It even seems that these regions are largely interconnected forming a hierarchically organized network (Moeller, Freiwald, & Tsao, 2008).

In humans, three main areas have been reported: (1) the fusiform face area (FFA) located at the junction of the occipital lobe and the inferior temporal lobe, at the fusiform gyrus, (2) the occipital face area (OFA) located at the inferior occipital gyrus (Kanwisher, McDermott, & Chun, 1997; Gauthier et al., 2000), and (3) the posterior superior temporal sulcus (STS) (Haxby et al., 1999; Weiner & Grill-Spector, 2010).

Some authors have questioned the organization of these three regions and whether the mechanisms involved in face processing was conducted in a purely feed-forward pattern as suggested by the hierarchical organization of the ventral visual pathway. To test this hypothesis, Rossion et al. (2003) report a case of a prosopagnosic patient which has a lesion in the OFA but has a preserved FFA. Conducting a study using fMRI, the authors show that the FFA of the patient is activated during the presentation of face stimuli and in the absence of any information from the OFA. This study suggests that the integrity of the OFA is necessary for normal face processing and the feedback connections from the FFA would properly handle faces.

In this sense, a meta-analysis by Bouvier & Engel (2006) reported 92 cases of patients with achromatopsia, which is loss of the color vision, have lesions in the ventral occipital cortex. The authors use patients with prosopagnosia reported in the literature as control lesions. Interestingly and completely independently of Rossion et al. (2003), the authors report that the regions affected in all prosopagnosics patients are located at the OFA and not in the FFA.

Apart from the comparison of the category of the faces with other categories of objects, several fMRI studies tried to evaluate the representation of different facial features and in particular the coding of identity. A study conducted by Rotshtein, Henson, Treves, Driver, & Dolan (2005), shows that certain brain regions are involved in the processing of the physical characteristics of the image while others seem to have a role in the processing of selective identity. The analysis of the blood oxygenation level dependent (BOLD) signal shows that the inferior occipital gyrus is selective to the physical characteristics of the image. On the contrary, the fusiform gyrus is selective to identity and its hemodynamic response is modulated only when the identity is different, independently of the physical characteristics of the image.

In addition, the subjects performed a familiarity judgment on the different personalities presented in order to investigate the possible correlation between the BOLD activity in the whole brain and the strength of familiarity. Thus, the researchers demonstrate a strong correlation between the level of familiarity and the activity in the anterior temporal regions (hippocampus and anterior temporal gyrus).

This study suggests in a hierarchical processing of faces where the inferior occipital gyrus is involved in the processing of the physical properties of the image, the FFA have a crucial role in the processing of identity. Also, the structures located in the more anterior regions of temporal lobe are involved in the processing of long-term familiarity.

However, this finding is controversial. For example, another study of fMRI conducted by Kriegeskorte, Formisano, Sorger, & Goebel (2007) suggests that the individualization of the face would be carried out both at the level of FFA and in the anterior part of inferior-temporal cortex. The latter region is thought to produce a different pattern depending on the identity.

Furthermore, another fMRI study conducted by Ishai, Haxby, & Ungerleider (2002) addresses the issue of mental imagery of faces. The authors show that a wide range of brain regions, including the FFA, the OFA, the STS and the amygdala, is activated when the famous faces are shown. Interestingly, when the participants were asked to imagine the famous faces, other regions in addition to the aforementioned regions are activated. Indeed, the authors report activation of the hippocampus, the precuneus, the intraparietal sulcus and the inferior frontal gyrus during this imaging task.

Finally, although the role of these regions is not yet clear, it appears that the processing of familiar faces is underpinned by a broad network of brain areas (Haxby, Hoffman, & Gobbini, 2000; Ishai, 2008) .

Moreover, studies using intracranial recordings have confirmed the distributed nature of brain regions involved in face processing. In a study conducted by Allison, Puce, Spencer, & McCarthy (1999), the recordings from grid electrodes implanted in the ventral occipital-temporal cortex of epileptic patients (in the diagnosis of their severe refractory epilepsy) confirmed the involvement of the occipital-temporal cortex in face processing.

Similarly, in a recent study conducted by Parvizi et al. (2012) addressed the question of the role of the fusiform gyrus in face perception in epileptic patients implanted with subdural electrodes in the temporal lobe. In this study, the researchers combine three neuroimaging techniques; electrocorticography, fMRI and brain electrical stimulation. Using fMRI, they identify two selective regions previously reported selective to faces that are the FFA and the OFA. The recording of the electrophysiological signal in the FFA, indeed shows a selective activity to faces. In addition, when the electrodes in these regions were stimulated, the patients reported that the faces of people in the room were "transformed". On the contrary, this stimulation did not disturb the perception of objects or the process of naming famous people. Therefore, this study using a multimodal approach provides converging data on the specificity of the fusiform gyrus in face perception.

APPENDIX B: STRUCTURES INVOLVED IN RECOGNITION OF FACIAL EXPRESSIONS

The amygdala

The role of amygdala in emotional processing is complex. This functional complexity of the amygdala is linked to its structure which is consisted of various groups of cores and multiple connections. The perceptual representation of stimuli from the visual cortex seems to penetrate through the lateral nuclei, while the central nuclei could send a signal back to the cortex, brain stem, hippocampus and basal ganglia in order to modulate cognition and emotional response (Amaral, 2003).

Lesion studies on the human amygdala

The bilateral amygdala lesions induce a deficit in the recognition of the most salient facial expressions especially fear (Adolphs, Tranel, Damasio, & Damasio, 1994). However, patients with bilateral amygdala lesions are able to discriminate subtle changes in the expression even if it is not recognized, indicating that the perceptual stage is completed (Adolphs et al., 1998). These patients even realize extremely difficult tasks of visuospatial discrimination (Stark & Squire, 2000). The gender and age of the faces are also well recognized (Anderson & Phelps, 2001).

The variability of emotions poorly recognized by patients with amygdalar lesions make any attempt to draw a simple conclusion difficult. While the recognition of fear is often impaired, some studies emphasize a deficit on the recognition of sadness and other negative emotions in general (Adolphs, Russell, & Tranel, 1999; Schmolck & Squire, 2001). The preponderant role of the amygdala in the perception of the most salient negative emotions gives it a function in the detection of danger and threat (Adolphs et al., 1999), and consequently in the avoidance behavior (Anderson & Phelps, 20001). Therefore, it is mainly hypothesized that it would be particularly useful in reading the social messages from the facial expressions depending on the expression of fear (Adolphs et al., 2005).

Functional imaging studies on the human amygdala

Both pioneer studies using PET (Morris et al., 1996) and fMRI (Breiter et al., 1996) showed activation of the amygdala by the presentation of faces expressing fear, without any special attention being laid on the expression. Regression analysis showed that the activation of the left amygdala modulates the activity of the occipito-temporal visual cortex in response to facial expressions (Morris et al., 1996). This specific modulation on the occipital-temporal cortex disappears when the amygdala is injured (Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004).

Some studies showed involvement of the amygdala in the recognition of other expressions. In addition to fearful faces, the recognition of facial expression of

happiness (Breiter et al., 1996) and sadness (Blair et al., 1999) also induces an increase in the amygdalar activity. These differences may be related to individual strategies required for each experiment (Adolphs et al., 2005).

The lateralization of the amygdalar functions is also investigated in various studies even the results are complicated to come up with a concise conclusion. Morris, Öhman, & Dolan (1998) suggest that the right amygdala is involved in the processing of subliminal messages whereas the left amygdala plays a role in the recognition of stimuli perceived consciously. Other studies suggest that the left amygdala is involved in processing negative emotions, while the right amygdala does not react differently depending on the expression (Iidaka et al., 2001). It cannot be concluded that a single amygdala is simply responsible of the recognition of facial expressions. Also, the actual strategies used by the subjects might not be controlled precisely. Furthermore, statistical analysis seems crucial to interpret these studies. Recently, a direct comparison of the two amygdala activities was carried out after presentation of facial expressions by visual hemifield (Noesselt, Driver, Heinze, & Dolan, 2005). This study showed a clear preference of the right amygdala to fearful stimuli if it is presented in the left visual field since its activity is correlated with better performance in detection of emotions in the same hemifield. Conversely, it seems that the left amygdala prefers a central presentation of emotional stimuli.

The amygdala should not be considered as the temple of knowledge of emotions but as a mediator between the perception of emotional stimuli and building knowledge of the emotional concept. After acquiring "bottom-up" perceptual information, the amygdala may participate in three ways to the recognition of facial expressions: 1) it can modulate perceptual representations via retrograde information; 2) it may participate in the activation of knowledge associated with emotion via its connections with other regions of the neocortex and hippocampus; 3) it can finally start the process resulting in an emotional reaction to finalize the conceptual knowledge of every emotion through simulation or execution of emotional process.

The orbitofrontal cortex

The orbitofrontal cortex, strongly interconnected with the amygdala (Stefanacci & Amaral, 2002), plays an important role in the analysis of facial expressions. The close connections between the prefrontal cortex and the temporal cortex are also necessary for further processing of visual stimuli (Tomita, Ohbayashi, Nakahara, Hasegawa, & Miyashita, 1999). Patients with orbitofrontal lesions show impaired recognition of facial expressions, especially fearful stimuli (Hornak et al., 1996). Thus, this region is involved in both the emotional experience and emotion recognition. Functional imaging studies have shown activation of left orbitofrontal region during a mental task of maintaining an expression of happiness (Dolan et al., 1996), and right orbitofrontal region after the presentation of expression of fear (Vuilleumier, Armony, Driver, & Dolan, 2001). Studies using transcranial magnetic stimulation (Harmer, Thilo, Rothwell, & Goodwin, 2001) or PET (Blair et al., 1999) have shown that the prefrontal areas, especially middle orbitofrontal and anterior cingulate gyrus, are also involved

in the recognition of anger. Anger and fear induce greater vegetative reactions that could be triggered by these prefrontal areas at late latency.

The orbitofrontal cortex plays a major social role, especially in the interpersonal relationship, social cooperation, moral behavior and reactions to social stress (Damasio, 1994). Developmental psychoses have also been associated with structural abnormalities of the prefrontal regions (Raine, Lencz, Bihrle, LaCasse, & Colletti, 2000). A deficit in the recognition of facial expressions was also highlighted in groups of schizophrenic patients (Mandal, Pandey, & Prasad, 1998). The orbitofrontal frontal structures could play a role in the inhibition of responses to emotional stimuli in a given social context (Blair, 1995; Phelps, Delgado, Nearing, & LeDoux, 2004). Abnormal aggressive behaviors could thus be related to a defective inhibition of subcortical structures such as the amygdala. The orbitofrontal cortex is also activated during the decision making, the selection response and reward and self-control (Rolls, 2000). Therefor, it seems to play a key role in integration of social messages from the surrounding world, motivations and their interactions.

The somatosensory and motor cortices

The somatosensory and motor cortices participate in the "construction of knowledge" by the genesis of the response activation. Patients with a lesion of primary and secondary somatosensory cortices, and right insula show a significant change in their capacity for empathy (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000). These areas have large capacity to integrate somatotopic body maps.

It is beneficial to recognize emotions in others in order to initiate a proper response. Recognition of facial expressions can be considered as the perception of an action in others (Gallese, Keysers, & Rizzolatti, 2004). The motor and somatosensory cortices are essential in imitation of expressions. But this role could be partly supported by the basal ganglia and the motor nuclei of brainstem.

The insula

The insular cortex participates in the modulation of the autonomic nervous system through the connections with the amygdala (Amaral, 2003). In humans, impairment in the recognition of the facial expression of disgust was demonstrated in patients with lesion in central insula or a disease involving a wider neural network. Researchers observed a selective deficiency in a patient with a lesion in the central insula and left putamen (Calder, Keane, Manes, Antoun, & Young, 2000). This patient had difficulty not only in recognizing facial expression of disgust, but also in experience of disgust.

The first functional imaging study performed to support the role of the insula in the recognition of disgust was conducted by Phillips and his team, using faces expressing fear and disgust in a gender discrimination task (Phillips et al., 1997). These results were confirmed by other researchers as well (Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998; Gorno-Tempini et al., 2001).

These results demonstrate that very central region of the insula is involved in the recognition of facial expressions in humans. This region of the insula is particularly interconnected with neural circuits associated with the systems of gustatory, olfactory and visceral motors. These different networks participate in certain aspects of disgust as an emotional concept. Another fMRI study by Wicker et al. (2003) confirmed involvement of the anterior region of the insula in the integration of several aspects of this emotion. The anterior ventral insula could be a decisive crossroads in the aggregation of these perceptive aspects, and perhaps has a cognitive function in the construction of conceptual knowledge of that emotion. This multimodal integration could help build a conceptual knowledge of disgust.

The basal ganglia

The lesions of the basal ganglia, especially on the right hemisphere, seem to imply a deficit in emotion recognition (Cancelliere & Kertesz, 1990). Functional imaging studies showed an activation in the right basal ganglia in response to the expressions of happiness, fear (Morris et al., 1996) and sadness (Phillips et al., 1998). The ventral striatum is particularly involved in the recognition of stimuli with aggressiveness, particularly the expression of anger (Calder, Keane, Lawrence, & Manes, 2004).

Three diseases involving the basal ganglia were explored: obsessive-compulsive disorder (OCD), Parkinson's disease and Huntington's disease. Patients with OCD have difficulty in recognition of the expression of disgust (Sprengelmeyer et al., 1997). There also seems to be a deficit in the recognition of certain facial expressions (e.g., disgust, fear) in Parkinson's disease (Sprengelmeyer et al., 2003). The impairments in the recognition of facial expressions with disgust have also been demonstrated in patients with Huntington's disease (Sprengelmeyer et al., 1996), but these results have not been confirmed. Recognition of anger and aggressive stimuli in general could be more deficient in this disease.

It is likely that the basal ganglia are a part of a network including the insula, and orbitofrontal cortex, involved in the processing of disgust and aggressive stimuli. These observations highlight the close relationship between emotional experience, production (motor) of facial expressions and recognition of these facial expressions.

The ventral (Everitt et al., 1999) and posterior (Han, McMahan, Holland, & Gallagher, 1997) basal ganglia are intimately connected with the amygdala. The connections with the prefrontal cortex, especially the orbitofrontal cortex, are also important (Eblen & Graybiel, 1995). The ventral regions appear involved in the motivational aspects related to the attractiveness of faces (Kampe, Frith, Dolan, & Frith, 2001). Relations between orbitofrontal cortex, ventral striatum and amygdala are highlighted in decision making, reward and phenomena of drug addiction (Everitt et al., 1999). This network of striatum and amygdala could introduce elementary notions of reward/punishment in these structures, primarily in the orbitofrontal cortex which has a primary role in the social context and motivations.

Aversive emotional stimuli are good candidates for early subcortical processing since they do not necessarily access the level of consciousness. They preferentially occur in the periphery of the visual field. A route through the superior colliculus, the pulvinar nuclei and amygdala might be particularly involved in the rapid processing of emotional visual stimuli requiring urgent behavioral response. This type of organization is known for the auditory system. Indeed, in rats, the thalamo-amygdala pathway seems sufficient to process the tonal stimuli in fear conditioning, while complex stimuli also conditions the fear must be processed by the auditory cortex (LeDoux, 1996). For visual stimuli, the thalamo-amygdala pathway has been described in monkeys. It receives information from the superior colliculus which projects on the lateral, anterior and inferior pulvinar nuclei (Robinson & Petersen, 1992). Pulvinar nuclei also receive direct retinal afferent information (O'Brien, Abel, & Olavarria, 2001). It projects on the amygdala by monosynaptic pathway (Robinson & Petersen, 1992) and this path deals with mainly magnocellular information (Lomber, 2002).

All these data suggest a relatively automatic processing of facial expressions in the amygdala, modulated by prefrontal structures depending on the context and motivations. Electrophysiological alterations located in the amygdala may be inhibited by the electrical stimulation of the medial prefrontal cortex (Zbrożyna, & Westwood, 1991). This can be attributed to the influence of modulating prefrontal projections and controlling sensory stimuli received from the basolateral amygdala region (Rosenkranz, Moore, & Grace, 2003; Phelps et al., 2004).

Thus, the amygdala can be engaged on two routes and therefore at least two different roles in the processing of emotional stimuli: 1) early and by an automatic thalamo-amygdala path, particularly involved in very specific conditions. Its main function would be warning and triggering a cascade of hormonal and neuro-cognitive body modification for the rapid response to danger; 2) later (after the first cortical responses to faces) and by a cortical pathway to a more complete judgment of the emotional stimuli. It would operate through a retrograde neuromodulation to extract the parameters needed to interpret the emotional expression of the face.

APPENDIX C: INTRANASAL ADMINISTRATION

In recent years, the interest in the intranasal drug delivery has increased. The nasal mucosa has many advantages as a route for administration of pharmaceuticals. It is easily accessible ensuring good drug availability and enables rapid onset of action. In addition, the intranasal administration prevents the degradation of the active ingredient in the gastrointestinal tract and in the liver. The intranasal route is suitable for the local and systemic therapy and for the treatment of diseases in the brain.

Overview and importance of the intranasal application

The blood-brain barrier is one of the most stringent barriers for drug delivery (Pardridge, 2005; Talegaonkar & Mishra, 2004). The intranasal application provides the ability to substances, bypassing through the blood brain barrier into the brain tissue (Talegaonkar & Mishra, 2004; Hanson & Frey II, 2008), and has been used as administration tool for various active ingredients in the animal models and in humans in recent years (Illum, 2004).

Also as a non-invasive application technique for rapid systemic substance uptake in the blood, the subsequent absorption of subtances from there to the brain is shown in several studies (Gizurarson, Gudbrandsson, Jónsson, & Bechgaard, 1999; Lindhardt, Ólafsson, Gizurarson, & Bechgaard, 2002). Nasal cavity and brain are connected to each other via the trigeminal nerve and olfactory nerve. This results in the ability of the substance transportation from the nasal cavity to the brain (Talegaonkar & Mishra, 2004; Hanson & Frey II, 2002). In anatomical studies of the nasal cavity in connection with the transfer of pathogens from the nose into the central nervous system (Le Gros Clark, 1929; Faber, 1937; Holl, 1980), it was shown that various dyes migrated from nasal epithelium in the brain.

Structure of the nasal epithelium

The nasal epithelium mainly consists of four cell types (Gizurarson, Bechgaard, & Hjortkjær, 2006): 1) Ciliary cells whose main function is to transport by wavelike motions of the cilia to the mucus toward the pharynx; 2) Goblet cells that secrete mucus which is renewed every 10 to 15 min (Vyas, Shahiwala, Marathe, & Misra, 2005); 2) Basal cells, so-called replacement cells, that mount the basement membrane and do not contact with the nasal lumina; 4) Columnar cells whose function is rapid fluid transport.

Occasionally, non-epithelial cells such as inflammatory cells are found in the nasal epithelium. The theoretical half-life of mucosal clearance in humans is 15 minutes (Vyas et al, 2005). In humans, the major part of the nasal cavity (approximately 92%) is responsible for respiratory functions and a small proportion (8%) is associated with olfactory system (Merkus, Romeijn, Verhoef, Merkus, & Schouwenburg, 2001; Vyas

et al., 2005). In the rat, the percentage of respiratory and olfactory epithelium is found at approximately 50% (Merkus et al., 2001).

The epithelial cells of the nasal mucosa are interconnected via tight junctions (Vyas et al., 2005). The mucosa is in spatial communication with the subarachnoid space (Thorne & Frey II, 2001). Since the cerebrospinal fluid (CSF) therein flows around the axon bundles of the olfactory nerve, the trigeminal nerve and the brain; the nose leads the CSF in the nasal lymphatics (Hanson & Frey II, 2002). Therefore, the olfactory epithelium is the portal of entry for substances from the nose into the brain or the CSF (Vyas et al., 2005).

Neural transportion routes

Basically, there are two pathways from nasal cavity to the brain: intraneuronal and extraneuronal pathways (Hanson & Frey II, 2002; Vyas et al., 2005). As a passive way of transportation, the intraneuronal transport which takes place in the axons of the olfactory nerve and the trigeminal nerve is slow. It may take up to hours and days for the substances to reach certain brain regions (Hanson & Frey II, 2002). The extraneuronal transport includes the substance passing through the mucosa and the underlying tissues into the CSF-stuffed subarachnoid space or directly into the brain parenchyma by the help of perineural channels (Hanson & Frey II, 2002; Mathison, Nagilla, & Kompella, 1998; Thorne and Frey II, 2001). Lipophilic substances can be taken extraneuronally by receptor-mediated endocytosis, diffusion or transcytosis via carrier vesicles in the subarachnoid space (Vyas et al., 2005). The extraneuronal transportation of hydrophilic substances from the mucosa into the CSF is slowly done by passive paracellular transportation via the tight junctions (Vyas et al., 2005). This form of extraneuronal transportation is positively correlated with the hydrophilic property and the molecular weight of substances (Vyas et al., 2005).

Factors influencing the effectiveness of intranasal administration

Chemical properties of a substance and the method of the application have a strong influence on whether how quickly and in what quantity substances enter from the nasal cavity into the central nervous system or the CSF by extraneuronal or intraneuronal pathways. Sakane et al. (1995) found that an increase in molecular weight is negatively correlated with the transport efficiency. The data shows that molecules up to a size of 2 kDa can be transported from the nasal cavity into the CSF (Sakane et al., 1995). Furthermore, the transportation efficiency of substances is positively correlated with the lipophilicity of the substances (Sakane et al., 1991). The transport is also affected by the degree of ionization (e.g., undissociated substances are better transported) (Sakane et al., 1994).

Other factors influencing the effectiveness of transportation are the physiological conditions of the nasal cavity. Thus, the ciliary cells of the respiratory epithelium are a limiting factor for the retention of the administered substance on the mucosa (Barakat, Omar, & Ahmed, 2006). The use of mucoadhesive carriers, such as cellulose,

dextran, chitosan or polymers, can prolong the retention time of the substances on the nasal mucosa and as a result increase the amount intake (Illum, Jørgensen, Bisgaard, Krogsgaard, & Rossing, 2002; Ugwoke, Verbeke, & Kinget, 2001; Vyas, Babbar, Sharma, Singh, & Misra, 2006).

Also, location of the substance delivery, administered volume and positioning of the animal during application influence the transportation (Gizurarson et al., 2006). Since the nasal feeding capacity is limited, the solubility of substances is a limiting factor for the intranasal application (Gizurarson et al., 2006).

APPENDIX D: BECK DEPRESSION INVENTORY

Aşağıda, kişilerin ruh durumlarını ifade ederken kullandıkları bazı cümleler verilmiştir. Her madde, bir çeşit ruh durumunu anlatmaktadır. Her maddede o ruh durumunun derecesini belirleyen 4 seçenek vardır. Lütfen bu seçenekleri dikkatle okuyunuz. Son bir hafta içindeki (şu an dahil) kendi durumunuzu göz önünde bulundurarak, size en uygun ifadeyi bulunuz. Daha sonra o maddenin yanındaki harfin üzerine (X) işareti koyunuz.

1. (a) Kendimi üzgün hissetmiyorum.
   (b) Kendimi üzgün hissediyorum.
   (c) Her zaman için üzgünüm ve kendimi bu duygudan kurtaramıyorum.
   (d) Öylesine üzgün ve mutsuzum ki dayanamıyorum.

2. (a) Gelecekten umutsuz değilim.
   (b) Geleceğe biraz umutsuz bakıyorum.
   (c) Gelecekten beklediğim hiçbir şey yok.
   (d) Benim için bir gelecek yok ve bu durum düzelmeyecek.

3. (a) Kendimi başarısız görmüyorum.
   (b) Çevremdeki birçok kişiden daha fazla başarısızlıklarım oldu sayılır.
   (c) Geriye dönüp baktığımda, çok fazla başarısızlığımın olduğunu görüyorum.
   (d) Kendimi tümüyle başarısız bir insan olarak görüyorum.

4. (a) Her şeyden eskisi kadar zevk alabiliyorum.
   (b) Her şeyden eskisi kadar zevk alamıyorum.
   (c) Artık hiçbir şeyden gerçek bir zevk alamıyorum.
   (d) Bana zevk veren hiçbir şey yok. Her şey çok sıkıcı.

5. (a) Kendimi suçlu hissetmiyorum.
   (b) Arada bir kendimi suçlu hissettiğim oluyor.
   (c) Kendimi çoğunlukla suçlu hissediyorum.
   (d) Kendimi her an için suçlu hissediyorum.

6. (a) Cezalandırıldığımı düşünmüyorum.
   (b) Bazı şeyler için cezalandırılabileceğimi hissediyorum.
   (c) Cezalandırılmayı bekliyorum.
   (d) Cezalandırıldığımı hissediyorum.
7. (a) Kendimden hoşnutum.
   (b) Kendimden pek hoşnut değilim.
   (c) Kendimden hiç hoşlanmıyorum.
   (d) Kendimden nefret ediyorum.

8. (a) Kendimi diğer insanlardan daha kötü görmüyorum.
(b) Kendimi zayıflıklarım ve hatalarım için eleştiriyorum.
(c) Kendimi hatalarım için çoğu zaman suçluyorum.
(d) Her kötü olayda kendimi suçluyorum.

9. (a) Kendimi öldürmek gibi düşüncelerim yok.
(b) Bazen kendimi öldürmeyi düşünüyorum, fakat bunu yapmam.
(c) Kendimi öldürebilmeyi isterdim.
(d) Bir fırsatını bulsam kendimi öldürürdüm.

10. (a) Her zamankinden daha fazla ağladığımı sanmıyorum.
(b) Eskisine göre şu sıralarda daha fazla ağlıyorum.
(c) Şu sıralarda her an ağlıyorum.
(d) Eskiden ağlayabilirdim, ama su sıralarda istesem de ağlayamıyorum.

11. (a) Her zamankinden daha sinirli değilim.
(b) Her zamankinden daha kolayca sinirleniyor ve kızıyorum.
(c) Çoğu zaman sinirliyim.
(d) Eskiden sinirlendiğim şeylere bile artık sinirlenemiyorum.

12. (a) Diğer insanlara karşı ilgimi kaybetmedim.
(b) Eskisine göre insanlarla daha az ilgiliyim.
(c) Diğer insanlara karşı ilgimin çoğunu kaybettim.
(d) Diğer insanlara karşı hiç ilgim kalmadı.

13. (a) Kararlarımı eskisi kadar kolay ve rahat verebiliyorum.
(b) Şu sıralarda kararlarımı vermeyi erteliyorum.
(c) Kararlarımı vermekte oldukça güçlük çekiyorum.
(d) Artık hiç karar veremiyorum.

14. (a) Dış görünüşümün eskisinden daha kötü olduğunu sanmıyorum.
(b) Yaslandığımı ve çekiciliğimi kaybettiğimi düşünüyor ve üzülüyorum.
(c) Dış görünüşümde artık değiştirilmesi mümkün olmayan olumsuz değişiklikler olduğunu hissediyorum.
(d) Çok çirkin olduğumu düşünüyorum.
15. (a) Eskisi kadar iyi çalışabiliyorum.
(b) Bir işe başlayabilmek için eskisine göre kendimi daha fazla zorlamam gerekiyor.
(c) Hangi iş olursa olsun, yapabilmek için kendimi çok zorluyorum.
(d) Hiçbir iş yapamıyorum.

16. (a) Eskisi kadar rahat uyuyabiliyorum.
(b) Şu sıralarda eskisi kadar rahat uyuyamıyorum.

(c) Eskisine göre 1 veya 2 saat erken uyanıyor ve tekrar uyumakta zorluk çekiyorum.

(d) Eskisine göre çok erken uyanıyor ve tekrar uyuyamıyorum.

17. (a) Eskisine kıyasla daha çabuk yorulduğumu sanmıyorum.
(b) Eskisinden daha çabuk yoruluyorum.
(c) Şu sıralarda neredeyse her şey beni yoruyor.
(d) Öyle yorgunum ki hiçbir şey yapamıyorum.

18. (a) İştahım eskisinden pek farklı değil.
(b) İştahım eskisi kadar iyi değil.
(c) Şu sıralarda iştahım epey kötü.
(d) Artık hiç iştahım yok.

19. (a) Son zamanlarda pek fazla kilo kaybettiğimi sanmıyorum.
(b) Son zamanlarda istemediğim halde üç kilodan fazla kaybettim.
(c) Son zamanlarda istemediğim halde beş kilodan fazla kaybettim.
(d) Son zamanlarda istemediğim halde yedi kilodan fazla kaybettim.
Daha az yemeye çalışarak kilo kaybetmeye çalışıyorum.
Evet ( ) Hayır( )

20. (a) Sağlığım beni pek endişelendirmiyor.
(b) Son zamanlarda ağrı, sızı, mide bozukluğu, kabızlık gibi sorunlarım var.
(c) Ağrı, sızı gibi bu sıkıntılarım beni epey endişelendirdiği için başka şeyleri düşünmek zor geliyor.
(d) Bu tür sıkıntılarım beni öylesine endişelendiriyor ki, artık başka hiçbir şey düşünemiyorum.

21. (a) Son zamanlarda cinsel yaşantımda dikkatimi çeken bir şey yok.
(b) Eskisine oranla cinsel konularla daha az ilgileniyorum.
(c) Şu sıralarda cinsellikle pek ilgili değilim.
(d) Artık cinsellikle hiçbir ilgim kalmadı.

APPENDIX E: POSITIVE AND NEGATIVE AFFECT SCALE (PANAS)

Bu ölçek farklı duyguları tanımlayan bir takım sözcükler içermektedir. Şu anda nasıl hissettiğinizi düşünüp her maddeyi okuyun. Uygun cevabı her maddenin yanında ayrılan yere (puanları daire içine alarak) işaretleyin. Cevaplarınızı verirken aşağıdaki puanları kullanın.

1. Çok az veya hiç
2. Biraz
3. Ortalama
4. Oldukça
5. Çok fazla

1. İlgili	1	2	3	4	5
2. Sıkıntılı	1	2	3	4	5
3. Heyecanlı	1	2	3	4	5
4. Mutsuz	1	2	3	4	5
5. Güçlü	1	2	3	4	5
6. Suçlu	1	2	3	4	5
7. Ürkmüş	1	2	3	4	5
8. Düşmanca	1	2	3	4	5
9. Hevesli	1	2	3	4	5
10. Gururlu	1	2	3	4	5
11. Asabi	1	2	3	4	5
12. Uyanık (dikkati açık)	1	2	3	4	5
13. Utanmış	1	2	3	4	5
14. İlhamlı (yaratıcı düşüncelerle dolu)	1	2	3	4	5
15. Sinirli	1	2	3	4	5
16. Kararlı	1	2	3	4	5
17. Dikkatli	1	2	3	4	5
18. Tedirgin	1	2	3	4	5
19. Aktif	1	2	3	4	5
20. Korkmuş	1	2	3	4	5

APPENDIX F: ETHICAL APPROVAL FORM

UYGULAMALI ETİK ARAŞTIRMA MERKEZİ
APPLIED ETHICS RESEARCH CENTER

ORTA DOĞU TEKNİK ÜNİVERSİTESİ
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26.11.2014

Gönderilen : Y. Doç. Dr. Didem Gökçay
Bilişsel Bilimler

Gönderen : Prof. Dr. Canan Sümer
IAK Başkanı Vekili

İlgi : Etik Onayı

Danışmanlığını yapmış olduğunuz Bilişsel Bilimler Bölümü öğrencisi Fatma Gülhan Saraçaydın ve Sağlık Bilişimi Bölümü öğrencisi Anıl Karabulut'un "Fizyolojik Tepkilerle Bilişsel Seçimlerin Doğal Endojen ve Eksojen Oksitosin Seviyelerine Göre Değişiminin İncelenmesi" isimli araştırması "İnsan Araştırmaları Komitesi" tarafından uygun görülerek gerekli onay verilmiştir.

Bilgilerinize saygılarımla sunarım.

Etik Komite Onayı

Uygundur

26/11/2014

Prof.Dr. Canan Sümer
Uygulamalı Etik Araştırma Merkezi
(UEAM) Başkanı Vekili
ODTÜ 06531 ANKARA

APPENDIX G: CONSENT FORM

Orta Doğu Teknik Üniversitesi Enformatik Enstitüsü Sağlık Bilişimi Bölümü öğretim üyelerinden Y. Doç. Dr. Didem Gökçay danışmanlığında yürütülen ve yüksek lisans öğrencilerinden Fatma Gülhan Saraçaydın ile Anıl Karabulut'un tez çalışmaları kapsamındaki "Fizyolojik tepkilerle bilişsel seçimlerin doğal endojen ve eksojen oksitosin seviyelerine göre değişiminin incelenmesi" adlı araştırmaya katılmak için seçildiniz. Çalışmaya katılım gönüllülük esasına dayalıdır. Kararınızdan önce araştırma hakkında sizi bilgilendirmek istiyoruz. Bilgileri okuyup anladıktan sonra araştırmaya katılmak isterseniz lütfen bu formu imzalayınız.

Günlük hayatımızda insanlarla ilişkilerimizin önemli bir kısmı karşımızdakinin duygu durumunu doğru tanıma üzerinedir. Örneğin, bir iletişim sırasında yüzünde kızgın bir ifade bulunan kişinin yüzündeki ifadeyi doğru tanımlamak iletişimin devamlılığını ve sizin davranışlarınızı etkilemektedir. Veya aynı kişiyi mutlu bir ifadeyle gördüğünüzde iletişiminizden memnun olduğu varsayımında bulunabilirsiniz. Bu ve buna benzer olaylarda vücudumuzda salgılanan ve bize avantaj sağlayarak yardımcı olan çeşitli moleküller bulunmaktadır. Bu moleküllerden biri de oksitosindir. Oksitosin, memelilerde esas olarak çiftler arası bağ kurma, çiftleşme ve de anne-çocuk arasındaki sevgi bağı kurulmasında rol oynamaktadır. Son yıllarda, oksitosinin bilişsel ve duygusal etkileri üzerine odaklanan bir dizi çalışma, eksojen (intranazal) oksitosinin duygusal durumların tanınmasını değiştirdiğini göstermiştir.

Bu çalışmada da farklı deney grupları arasında duygusal ifadelerin değerlendirilmesi ile oksitosin arasındaki ilişki araştırılacaktır.

Çalışma sırasında sizden yaklaşık 100 resmi değerlendirmeniz istenmektedir. Değerlendirmeyi iki farklı şekilde yapacaksınız.

1. Duygusal ifadelere göre (şaşkın, üzgün, bıkkın, korkmuş, kızgın, mutlu, nötr)
2. Güvenilirlik skalasında (1'den 9'a kadar değişen sayılarla)

Bu çalışmada gözbebeği büyümesini ve hareketlerini takip edip kayıt altına almak için bir göz izleme cihazı kullanılmaktadır. Bu cihazlar insan sağlığı ya da ruhsal durumu açısından en ufak bir risk teşkil etmemektedir. Öte yandan, çalışma öncesinde eksojen oksitosin ve endojen oksitosin koşullarına maruz kalmış katılımcı grupları oluşturulacaktır. Bu gruplama işlemi daha önce yapılan benzer çalışmalardaki uygulamalara göre belirlenmiştir. Katılımcılardan bir grup nazal yolla salin solüsyonu, diğer grup ise eksojen oksitosin alacaktır. Hangi gruba dahil olduğunuz size deney sonrasında açıklanacaktır. Bu şekilde tamamlanmış çalışmaları içeren makaleler size verilecektir. Salin solüsyonun ve eksojen oksitosinin vücuttaki etkisinin çok kısa sürede yok olduğu gözlenmiştir ve bilimsel olarak ispatlanmıştır (Striepens ve ark., 2013). Dolayısıyla çalışmamızın kısa süreli dahi invaziv bir etkisi bulunmamaktadır.

Bu formu imzalayarak araştırmaya katılım için onay vermiş olacaksınız. Çalışmayı tamamladığınız takdirde, kimlik bilgileriniz çalışmanın herhangi bir aşamasında açıkça kullanılmayacaktır. Doldurduğunuz anketlere verdiğiniz cevaplar ve araştırma süresince görsel cihaz kullanılarak edinilen her türlü bilgi yalnızca bilimsel amaçlar için kullanılacaktır. Bilgileriniz hiçbir kimse ile ya da ticari bir amaç için paylaşılmayacaktır.

Çalışmaya katılmayı kabul ettiğiniz takdirde, deneyin işleyişi hakkında bilgilendirileceksiniz. Çalışma süresi yaklaşık bir saat olarak planlanmıştır.

Çalışma hakkında daha fazla bilgi edinmek için aşağıda belirtilen araştırmacılarla iletişime geçebilirsiniz.

Y. Doç. Dr. Didem Gökçay, ODTÜ Enformatik Enstitüsü, A-216, xxx, xxx
Fatma Gülhan Saraçaydın, ODTÜ Enformatik Enstitüsü, xxx, xxx
Anıl Karabulut, ODTÜ Enformatik Enstitüsü, xxx, xxx

Referans:

Striepens, N., Kendrick, K. M., Hanking, V., Landgraf, R., Wüllner, U., Maier, W., & Hurlemann, R. (2013). Elevated cerebrospinal fluid and blood concentrations of oxytocin following its intranasal administration in humans. *Scientific reports, 3,* 3340.

"Fizyolojik tepkilerle bilişsel seçimlerin doğal endojen ve eksojen oksitosin seviyelerine göre değişiminin incelenmesi" çalışması hakkında bilgilendirildim. Çalışmayı istediğim zaman terk edebileceğimi ve bana ait kişisel bilgilerle beraber benden toplanan kişisel değerlendirmelerin hiçbir zaman açıkça kullanılmayacağını biliyorum. Bu çalışmaya gönüllü olarak katılıyorum.

Ad, Soyad:
Tarih:
İmza:

APPENDIX H: DEMOGRAPHIC INFORMATION FORM

Kişisel Bilgiler:

Adı Soyadı: Uygulama Tarihi: … / … / …
Cinsiyeti: Kadın ( ) Erkek ( )
Doğum Tarihi: … / … / …
Yaşı: …
Medeni Hali: Evli ( ) Bekar ( ) Dul ( ) Boşanmış ( )
Mesleği: ……
El Tercihi: Sağ ( ) Sol ( )
Eğitim Durumu: İlkokul (0-5 yıl) ( )
Ortaokul (6-8 yıl) ( )
Lise (9-12 yıl) ( )
Üniversite (12+) ( )

Sağlık Durumuna İlişkin Bilgiler:

İşitme Bozukluğu: Var ( ) Yok ( )
Varsa düzeltilmiş mi? ……
Görme Bozukluğu var mı? Var ( ) Yok ( )
Varsa hangisi? Miyop ( ) Astigmat ( ) Hipermetrop ( )
Varsa düzeltilmiş mi? ……
Renk Körlüğü: Var ( ) Yok ( )
Fiziksel Özür: Var ( ) Yok ( )
Varsa türü: ……

Geçirdiği Önemli Rahatsızlıklar (özellikle Psikiyatrik, Nörolojik veya Psikolojik):

Halen Kullanmakta Olduğu İlaç: Var ( ) Yok ( )
Varsa ilacın/ilaçların adı: ……
Uzun Süre Kullanıp Bıraktığı İlaç: Var ( ) Yok ( )
Varsa ilacın/ilaçların adı: ……
Varsa kullanım süresi: ……
Kadın ise, son menstrual kanama tarihi: ……

APPENDIX I: SELECTED STIMULI FROM KDEF

Stimuli used in the gender classification tasks

First gender classification task

Presentation order	Images
1	AM34NES
2	AF17NES
3	AF01NES
4	AM33NES
5	AF15NES
6	AM10NES
7	AF04NES
8	AF13NES
9	AM17NES
10	AM11NES
11	AF06NES
12	AM30NES
13	AF11NES
14	AM29NES
15	AF10NES
16	AM28NES
17	AM26NES
18	AF08NES
19	AF07NES
20	AM23NES

Second gender classification task

Presentation order	Images
1	AM31NES
2	AF18NES
3	AF34NES
4	AM27NES
5	AM01NES
6	AF32NES
7	AM02NES
8	AF29NES
9	AM04NES
10	AF20NES
11	AM21NES
12	AF22NES
13	AF27NES
14	AM13NES
15	AF26NES
16	AM07NES
17	AM08NES
18	AF28NES
19	AF24NES
20	AM06NES

Stimuli used in the trustworthiness evaluation task

Trustworthiness evaluation task

Presentation order	Images	Presentation order	Images
1	BM24NES	34	AM21NES
2	BM16NES	35	AF14NES
3	AF05NES	36	AM08NES
4	AM05NES	37	AF30NES
5	AF18NES	38	AF21NES
6	AM35NES	39	AM18NES
7	AF08NES	40	AM30NES
8	AM20NES	41	AF12NES
9	AM14NES	42	AF33NES
10	AF07NES	43	AM25NES
11	AM10NES	44	AM27NES
12	AF24NES	45	BM19NES
13	AM13NES	46	AF03NES
14	AF13NES	47	AF13NES
15	AF23NES	48	BM12NES
16	AF04NES	49	AF31NES
17	AM03NES	50	AF22NES
18	AF02NES	51	AF25NES
19	AM29NES	52	AM33NES
20	AM32NES	53	AM34NES
21	AF19NES	54	AF15NES
22	AF10NES	55	AF17NES
23	AM02NES	56	AF09NES
24	AF28NES	57	AM17NES
25	AM28NES	58	AF20NES
26	AM15NES	59	AM23NES
27	AM01NES	60	AF27NES
28	AF01NES	61	AF26NES
29	AF29NES	62	AM22NES
30	AM13NES	63	AM11NES
31	AF11NES	64	AM06NES
32	AM09NES	65	AM31NES
33	AF32NES	66	AF16NES

Stimuli used in the facial expression recognition task

Facial expression recognition task

Presentation order	Images	Presentation order	Images
1	AM31HAS	36	AF34SUS
2	AM22AFS	37	AM05NES
3	AM31DIS	38	AM31SAS
4	AM08NES	39	AM22DIS
5	AF22DIS	40	AF22NES
6	AF21SAS	41	AF21AFS
7	AF13SUS	42	AF13DIS
8	AF06NES	43	AF06SUS
9	AF21ANS	44	AF34NES
10	AM01DIS	45	AF21SUS
11	AM05SUS	46	AF06AFS
12	AM08DIS	47	AM01SAS
13	AM22SAS	48	AM05HAS
14	AM31AFS	49	AM22NES
15	AM05ANS	50	AM31ANS
16	AM34HAS	51	AM08SUS
17	AF13AFS	52	AM31NES
18	AF06ANS	53	AF34ANS
19	AF22SAS	54	AF21DIS
20	AM01NES	55	AF22AFS
21	AM08SAS	56	AF06HAS
22	AM31SUS	57	AF13ANS
23	AM22ANS	58	AM22HAS
24	AM08AFS	59	AF06SAS
25	AF34SAS	60	AM01AFS
26	AF22SUS	61	AF13HAS
27	AF21HAS	62	AM05DIS
28	AF13NES	63	AM08ANS
29	AF22ANS	64	AM01SUS
30	AF06DIS	65	AM05SAS
31	AM22SUS	66	AF21NES
32	AM08HAS	67	AM01HAS
33	AF34AFS	68	AF13SAS
34	AM01ANS	69	AM05AFS
35	AF22HAS	70	AF34DIS

APPENDIX J: DEBRIEFING FORM

Bu çalışma daha önce de belirtildiği gibi ODTÜ Enformatik Enstitüsü Sağlık Bilişimi Bölümü öğretim üyelerinden. Y. Doç. Dr. Didem Gökçay danışmanlığında yürütülen ve yüksek lisans öğrencilerinden Fatma Gülhan Saraçaydın ile Anıl Karabulut'un yüksek lisans tezi araştırmasıdır. Oksitosin hormonunun yüzlerdeki duygu durumu ve güven duygusu üzerindeki etkisini saptamayı amaçlayan bu çalışma aynı zamanda oksitosinin göz bebeği büyüklüğü üzerindeki etkisi ve ilişkisine de bakmaktadır.

Dünyada intranazal oksitosin kullanımını içeren çok sayıda çalışma bulunmaktadır. Bunun yanı sıra, duygusal ve duyusal olaylarla gözbebeği büyümesi arasındaki ilişki uzun yıllardır çalışılmaktadır. Görsel uyaranlardaki içeriğin insanlarda ölçülebilen bir gözbebeği reaksiyonu oluşturduğu açıkça bilinmektedir. Bu araştırmayı yapma nedenimiz, vücudumuzda sentezlenen veya dışarıdan alınan oksitosinin çeşitli duygu durumlarını içeren görsel uyaranların değerlendirilmesindeki rolü ve bunun gözbebeği büyümesi ile ilişkisini ortaya koymaktır. Ayrıca oksitosinin nötr ifade içeren uyaranların güvenilirlik açısından değerlendirilmesi üzerindeki etkisi de bir diğer inceleme konumuzdur.

Bilgimize göre Türkiye'de ilk kez böyle bir çalışma yapılmaktadır. Bu çalışmadan alınacak tüm verilerin Aralık 2015 sonunda elde edilmesi amaçlanmaktadır. Elde edilen bilgiler sadece bilimsel araştırma ve yazılarda kullanılacaktır. Çalışmanın sonuçlarını öğrenmek ya da bu araştırma hakkında daha fazla bilgi almak için aşağıdaki isimlere başvurabilirsiniz.

Bu araştırmaya katıldığınız için tekrar çok teşekkür ederiz.

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