THE EFFECTS OF INTRANASAL OXYTOCIN DURING TRUSTWORTHINESS EVALUATION: CONTEXT MATTERS

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ABSTRACT

THE EFFECTS OF INTRANASAL OXYTOCIN DURING TRUSTWORTHINESS EVALUATION: CONTEXT MATTERS

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Social domain of human life is thought to be regulated majorly by the factors present in the immediate surroundings. Aside from environmental factors, as one of the agents connecting neurochemical mechanisms and social processes, the neuropeptide oxytocin is also suggested to be involved in social cognition and prosocial behavior including approach and trust. Thus, the current study is conducted towards understanding the effects of intranasally administered oxytocin on pupil dilation and on trustworthiness evaluation during two different social cognitive tasks that differ only with respect to situational context. We used computer generated faces as stimuli from the Trustworthiness Data Set 2 which contains faces manipulated on the axis of facial trustworthiness in three levels (trustworthy, neutral, and untrustworthy). Additionally, we managed to collect task evoked pupil diameter changes during subjective evaluation of trustworthiness tasks. In order to prevent any sex-dependent effects of oxytocin, only heterosexual male participants were invited to participate in the study. The findings revealed that intranasal oxytocin indeed exerts its effects in a task-dependent manner. While the same faces were rated as being more trustworthy in approach task, they were rated as being less trustworthy in trust task under the influence of oxytocin. Aside from that, participants in the oxytocin group were faster at judging the trustworthiness levels of the faces in both approach and trust task. In terms of pupil dilation, there was a significant but subtle difference between the placebo and oxytocin groups. The current study is a facilitator towards understanding the situation variant nature of oxytocin and it enables us to conduct more refined theories about the social effects of oxytocin in humans.

Keywords: trustworthiness, approach, trust, oxytocin, pupillary response

ÖZ

İNTRANAZAL OKSİTOSİNİN GÜVENİLİRLİK DEĞERLENDİRMESİ SIRASINDAKİ ETKİLERİ: BAĞLAM ÖNEMLİDİR

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İnsanların sosyal ilişkilerinin, büyük çoğunlukla yakın çevrelerinde yer alan etkenler tarafından kontrol edildiği düşünülmektedir. Çevresel faktörlerin yanı sıra, sosyal işlemleri düzenleyen nörokimyasal elementlerden biri olan oksitosinin de yaklaşma ve güven davranışlarını içeren sosyal biliş ve toplum yanlısı davranış ile ilişkili olduğu önerilmiştir. Bu nedenle, bu çalışma, sadece durumsal bağlam açısından değişen iki farklı sosyal bilişsel görev sırasında, intranazal yolla uygulanan oksitosinin göz bebeği açılımı ve güvenilirlik üzerindeki etkisini anlamak için yürütülmüştür. Çalışmada, güvenirlilik ekseni etrafında geliştirilmiş (güvenilir, yüksüz (nötr), güvenilmez) bilgisayar ürünü yüzler içeren Trustworthiness Data Set 2 veritabanından seçilen görsel uyaranlar kullanılmıştır. Ek olarak, öznel güvenirlik değerlendirmesi sırasında göz bebeği açılım verileri toplandı. Oksitosinin cinsiyete bağlı etkisini engellemek için, çalışmaya sadece heteroseksüel erkek katılımcılar davet edildi. Sonuçlar, intranazal alınan oksitosinin etkisinin göreve bağlı olarak değiştiğini ortaya çıkarmıştır. Oksitosinin etkisi altında, aynı yüzler, yaklaşma görevinde daha çok güvenilir bulunurken güven görevinde daha az güvenilir olarak değerlendirilmiştir. Bunun yanında, oksitosin grubundaki katılımcılar hem güven hem yaklaşım görevlerinde yüzlerin güvenilirlik seviyesine daha hızlı karar vermişlerdir. Göz bebeği açılımı açısından, oksitosin ve placebo grupları arasında anlamlı fakat çok az bir fark gözlemlenmiştir. Bu çalışma oksitosinin duruma bağlı değişken doğasını anlamak için bir aracı olmuş ve oksitosinin insanlar üzerindeki sosyal etkilerini tanımlayacak yeni teoriler üretmemize olanak sağlamıştır.

Anahtar kelimeler: güvenilirlik, yaklaşma, güven, oksitosin, göz bebeği tepkisi

To Cupid and Salem,

who are bundles of cashmere fur, unconditional love, element of tranquility and a little bit of insanity,

……gırrrr……

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CHAPTER 1

INTRODUCTION

Social engagement with people for whom we have zero acquaintance frequently requires making social judgments such as deciding on whether to trust them in different contexts (M. L. Willis, Dodd, Palermo, Richards, & Mathews, 2013). However, rather than feeling unconditional trust, the ability to make a proper social judgment requires careful assessment of the conditions of the current situation as well as caution regarding the outcome of the situation that potentially bears high risk (Greenspan, Loughlin, & Black, 2001). If these individuals were close partners, friends or someone in our family, making a social judgement against them would be relatively easier considering the large amount of information you might use to infer about their reliability. Quite the contrary, there is little information for us to be able to evaluate trustworthiness of the unfamiliar people. For this kind of interactions, facial appearances are the most pivotal and informative as an external sources (Adolph et al., 1998; Willis and Todorov, 2006, Willis et al., 2011a, b). Reliability of these non-verbal hints which shape our evaluative process is another issue. Nonetheless, facial characteristics inform us about the intentions of the other individual and our ability to make proper social judgements are based on intuition which is based on the gut-feeling in these circumstances (Fetchenhauer, Groothuis, & Pradel, 2010; Stewart et al., 2012; Stirrat & Perrett, 2010; Todorov & Uleman, 2002; Toscano & Schubert, 2015). Besides the facial cues acquired from the target people, there are internal mechanisms playing also an essential role in subjective social perceptions. Based on the recent literature, the neuropeptide oxytocin is a strong candidate to be regarded as one of the modulatory element of our social judgements.

Neuropeptide oxytocin[1] is studied extensively for its role during parturition and nursing where it acts to stimulate muscle contraction during parturition and milk ejection, respectively (Anne Campbell, 2008). Aside from that, oxytocin can directly

[1] Oxytocin is a nonapeptide belonging to the family of neuropeptides (Thomas R. Insel, 2010). Oxytocin coupled to its carrier molecule is synthesized in the cells of paraventricular nucleus (PVN) and supraoptic nucleus (SON) of the hypothalamus. As being a neuropeptide, oxytocin serves as a neurohormone in the peripheral system, whereas it can act as a neuromodulator in the central system (Gimpl, Fahrenholz, & Gene, 2001; Moos & Richard, 1989). In order to act as a neurohormone, in times of need, oxytocin pass to the bloodstream via the connections of blood capillaries and magnocellular neuronal circuitry (Bealer, Armstrong, & Crowley, 2010; Gainer, 2012).

access to the wide variety of brain structures to induce modulatory effects in the neural populations within these destinations (Veening, de Jong, & Barendregt, 2010). Accordingly, oxytocin has been discovered to have fundamental roles to regulate both social and reproductive behavior, including maternal care, parental behavior, attachment and bonding in a species specific manner (Donaldson & Young, 2008; Goodson, 2005). A growing list of studies have further investigated whether the findings of animal research on social behavior and affiliation can be extended to humans as well (A. Bartz & Hollander, 2006; Heinrichs, von Dawans, & Domes, 2009). For this purpose, intranasal administration appealed most researchers since this method provides an indirect but non-invasive way to study effects of neuropeptides on social effects in humans in experimental contexts (Born et al., 2002).

Over the past years, substantial progress has been achieved towards understanding the effects of exogenous oxytocin administration on social cognition and prosocial behavior in humans. Building on this research, oxytocin is demonstrated to have modulatory role in interpersonal trust behavior and cooperation (J. Bartz et al., 2011; Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008; Declerck, Boone, & Kiyonari, 2010, 2013; Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005; Moïra Mikolajczak, Pinon, Lane, de Timary, & Luminet, 2010), generosity (Zak et al., 2007), attachment (J. A. Bartz, Zaki, Ochsner, et al., 2010; Buchheim et al., 2009), subjective perception of trustworthiness (Andari et al., 2010; Theodoridou, Rowe, Penton-Voak, & Rogers, 2009), approachability (Rimmele, Hediger, Heinrichs, & Klaver, 2009), social memory (Guastella, Mitchell, & Mathews, 2008; Heinrichs, Meinlschmidt, Wippich, Ehlert, & Hellhammer, 2004; Savaskan, Ehrhardt, Schulz, Walter, & Schächinger, 2008), inferring internal state of others (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007), and recognition of facial expression (Bakermans-Kranenburg & van IJzendoorn, 2013; J. A. Bartz, Zaki, Bolger, et al., 2010; Guastella et al., 2010). Involvement of oxytocin on positive prosocial behavior and social cognition clearly has ground for excitement which justifies oxytocin to be referred as "liquid trust", "love hormone" (Domes et al., 2007; Ferguson, Young, & Insel, 2002; Guastella, Mitchell, & Mathews, 2008; Morhenn, Park, Piper, & Zak, 2008; Taylor, 2006).

However, a closer look at the effects of oxytocin in social domain challenges its perspective due to increasing number of studies revealing inconsistent results or weak effect sizes. Moreover, it turns out that regulated behaviors via the neuropeptide oxytocin are not limited with only beneficial positive prosocial behaviors. In fact, it has been shown to produce antisocial effects such as envy and gloating (Shamay-Tsoory et al., 2009), diminished trust when others are portrayed untrustworthy or anonymous (Declerck et al., 2010; M Mikolajczak et al., 2010), ethnocentrism and out-group derogation (C. K. W. De Dreu, Greer, Van Kleef, Shalvi, & Handgraaf, 2011; Carsten K W De Dreu et al., 2010), negative recollections of maternal care in individuals with high attachment insecurity (J. Bartz et al., 2011; J. A. Bartz, Zaki, Ochsner, et al., 2010). Therefore, it should be taken into consideration that treating oxytocin as a powerful elixir which leads to increased trust behavior in anybody might

be misleading, because situational factors or personality differences could override the effects of oxytocin in social domain of humans.

The current study is conducted with curiosity about the sources of variations in the relatively inconsistent literature of oxytocin with respect to social cognition and prosocial behavior. Therefore, the possible context-dependent nature of oxytocin is examined within the current study to see how intranasal administration oxytocin would manipulate the trustworthiness judgments of participants in two different social cognition tasks with different scenarios in a placebo controlled study. In order to see whether exogenous oxytocin influences the trustworthiness evaluation of participants towards faces with different level of trustworthiness, a stimulus set consisting of computer-adjustments – with faces are used. The faces are manipulated on the axis of trustworthiness in three levels (untrustworthy, neutral, trustworthy) – is used. Building on the context-dependent nature of social effects of exogenous oxytocin, it is hypothesized to find an interaction between the variables of the current study. Possible sexual dimorphic effects of oxytocin in humans are controlled by only recruiting heterosexual male participants.

Remainder of the current thesis consists of five chapters. In chapter 2, literature review covers current knowledge about the studies of pupil psychophysiology and the neuropeptide oxytocin alongside with the motivation for the conducted study and hypotheses related with it. Chapter 3 consists of the materials used in the study, recruited participants, stimulus selection and subject preparation processes, methodology and procedure describing how the study conducted. Results of the conducted experiments are presented in chapter 4. In the chapter 5, results are interpreted and discussed in a comprehensive manner. Lastly, chapter 6 presents a concise conclusion.

CHAPTER 2

LITERATURE REVIEW

In this chapter, building on previous studies, pupillary dynamics and oxytocin is reviewed. In the first section of this chapter, pupillary anatomy and its physiology is outlined as well as, psychophysiological responses given during different cognitive and affective tasks. In the second section, literature on the neuropeptide oxytocin is reviewed with respect to its psychophysiological effects. Effect of oxytocin on trust behavior, social cognition and facial expression, its gender-related effects and context and subject-dependent nature is reviewed. Lastly, the chapter is completed with the section presenting the motivation for the initiation of this thesis, research questions and hypothesis.

2.1 Pupillary anatomy and physiology

Through visual perception, light coming from the environment has to pass through the eye to reach the posterior part of it. In this process, light enters the eye through pupil – an opening found in the center of the iris, a pigmented area located in front of the eye. Hence, pupil is not a structure rather it is a hole, the size of which is regulated through iris in order to adjust the amount of light allowed to enter the eye (Stanfield, 2012, ch. 10). In that sense, the functioning of iris and pupil resembles how cameras work; where incoming light enters through the aperture instead of pupil, the diameter of which is adjusted by the diaphragm instead of iris (Beatty & Lucero-Wagoner, 2000).

The regulation of the size of the pupil is adjusted by two antagonistically working smooth muscles found in the iris. These two smooth muscles are found as layers wrapped around each other, thereby surrounding the pupil (Figure 2.1). Of these two, the innermost layer of smooth muscle is called constrictor muscle, whereas outermost layer is called dilator muscle. The shape of the constrictor muscles is circular and resembles rings such that each layer of ring is embedded each other. On the other hand, the outer dilator muscles fibers are in the form of straight lines radiating from the center of the iris such that the alignment resembles spokes of bicycle tires.

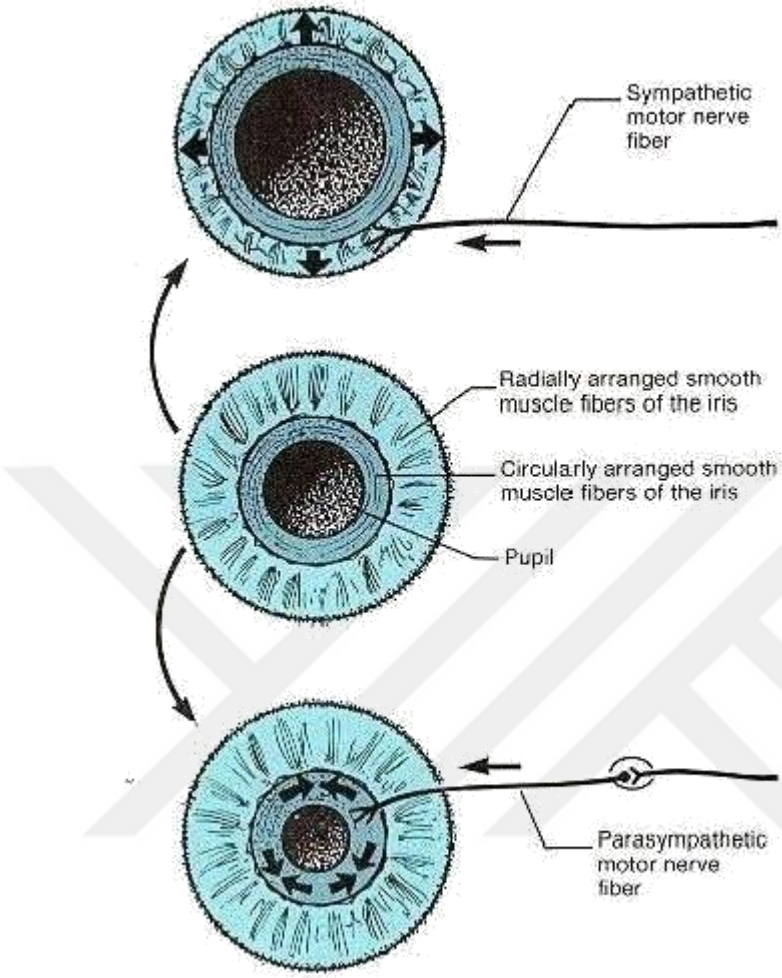

Figure 2.1 The anatomy and mechanics of pupil and iris (Hole, JW Jr., 1990)

The constriction and dilation of pupillary diameter are primarily governed by the autonomous nervous system (ANS) which innervates the aforementioned smooth muscles (Figure 2.1). In detail, the pupillary constriction is mediated by parasympathetic nervous system (PNS) such that initiation of PNS pathway is originated in the Edinger-Westphal nucleus located in the midbrain. From the nucleus, the efferent fibers of PNS pathway are tracking along the 3rd cranial nerve (oculomotor nerve) in order to make synapse at the ciliary ganglion, to reach the constrictor muscle at the iris. The parasympathetic stimulation of the circular muscles of pupil results in the concentric contraction, thereby pupillary constriction. On the other hand, pupillary dilation is mediated by sympathetic nervous system (SNS) such that initiation of SNS pathway is mediated through hypothalamus. From the hypothalamus, the efferent nerves of SNS pathway distribute along the spinal cord down to the lower cervical and upper thoracic segment of the spinal cord. Then, the

course of the fibers leaves the cord to make synapse at the superior cervical ganglion to finally, run to the radial muscles at the iris. The sympathetic stimulation of the radial muscles results in the concentric contraction, thereby pupillary dilation (Loewenfeld & Lowenstein, 1999). The innervation of pupillary constriction and dilation through autonomous nervous system is outlined in detail in Figure 2.2 (Albert, D. M., Miller, J. W., & Azar, D. T, 2008).

Therefore, instantaneous diameter of pupil is a reflection of the combined triggered activity in the SNS and PNS pathways, innervating dilator muscles and constrictor muscles of the iris, respectively.

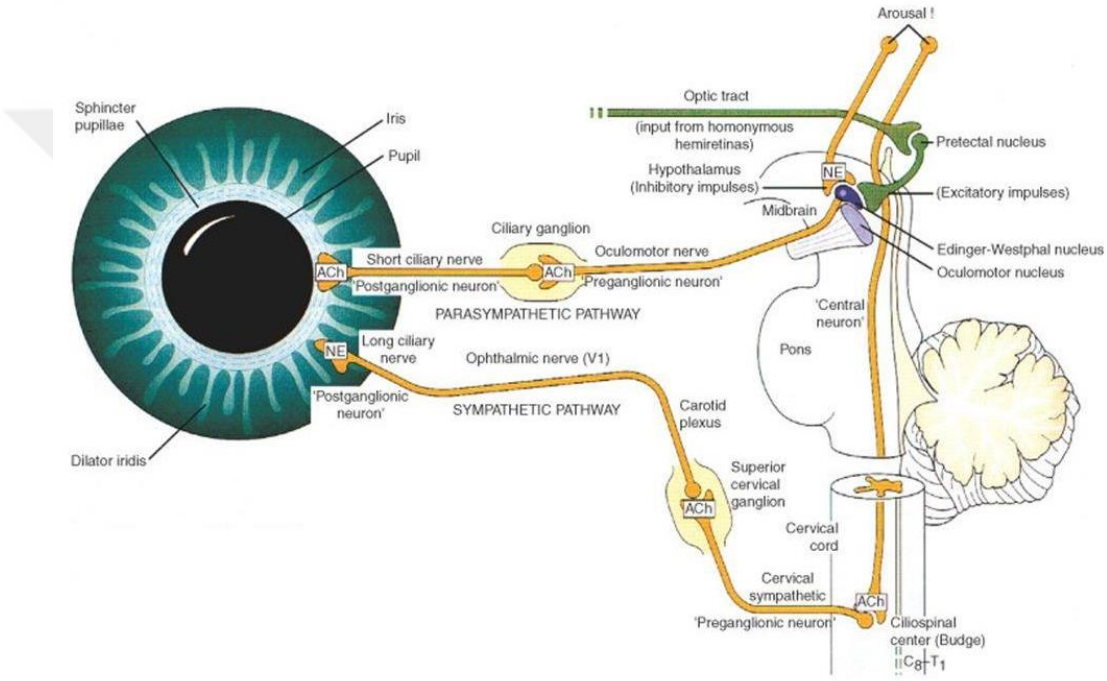

Figure 2.2 SNS and PNS pathways controlling the dilation and constriction of pupil, respectively (Albert, D. M., Miller, J. W., & Azar, D. T, 2008).

2.1.1 Non-psychophysiological pupil movements

Pupillary aperture is a dynamic structure, the size of which is under control by reciprocal activities of the iridic musculature innervated by different branches of ANS. Primarily, the adjustment on the size of the pupillary diameter serves for better visual processing with respect the luminance level of the environment. This reflexive behavior of the eye is called pupillary light reflex (Andreassi, 2000, ch. 10). Permitting certain amount of light before it falls on the retina is required for better optical acuity. Basically, under bright light constriction of circular sphincter muscle layer can decrease the size of the diameter up to 2 mm for allowing less light to come in. On the other hand, under dim light pupil is dilated by the contraction of pupillary

radial muscles thus its diameter can be increased up to 8 mm for allowing more light to enter the posterior of the eye. The changes of the size of the pupillary can be responsive as fast as .2 seconds to an existing stimulus with maximum response occurring approximately .5 to 1.0 sec later (Guyton, 1977; Loewenfeld & Lowenstein, 1999). The enlargement of pupils under dim light enhances visual performance by allowing more light to fall on the retina. The light reflex is an autonomic cranial reflex and exerts its effects on both eyes even if the light is projected only the one eye. Besides that, photoreceptors present in the retina are light sensitive such that excessive lightning of the surrounding environment damages them to bleach out. Thus, pupillary light reflex also provides protective features by modifying the size of the pupillary aperture such that photoreceptors of the retina gather only the required amount of light.

In addition to pupillary light reflex, accommodation reflex is also an important factor which determines the diameter of the pupils for optical functioning. The accommodation reflex, also called the near reflex aims adjusting the focus for visual acuity (Silverthorn, Johnson, Ober, Ober, & Silverthorn, 2016). In response to focusing on an object located nearby, reduction in the diameter of the pupils is observed due to this reflex, which in turn enables visual system to focus properly. Otherwise, pupils which are unable to accommodate leads to improper focusing which in turn results in blurry image of that object. Therefore, the main purpose for this reflex is trying to maximize the depth of field by constricting pupils.

Careful examination of pupillary diameter would result in rhythmic but irregular series of decrease and increase in pupil size which happened quite irrelevantly from the illumination of the surrounding (McLaren, Erie, & Brubaker, 1992). Rather than being neurologically significant symptom, those movements – which are called hippus (from the Greek *hippos* meaning horse) were observed in healthy population and were considered as the reflection of activity in pupillary musculature governed by central processes underlying human cognition. Since the movements were in synchronization within the two eyes they were admitted as being central process rather than peripheral process.

2.1.2 Psychophysiological pupil movements

The diameter of pupillary aperture is largely determined by light reflex and accommodation reflex. Alongside with these large scale pupillary movements which are heavily based on optical purposes, it is observed that there are tiny fluctuations within the diameter of pupils which are too small to be perceived with unaided observation. Cognitive psychophysiologists are interested in those tiny fluctuations in consideration of the words admitted by Oswald Bunke in 1911 that “every active intellectual process, every psychological effort, every exertion of attention, every active mental image, regardless of content, particularly ever affect just as truly

produces pupil enlargement as does every sensory stimulus." (Eckhard H. Hess, 1975). Charles Darwin (1872) was among the first people to recognize the bridge between the pupillary movements and central processes in his book "*The Expression of the Emotions in Man and Animals*", though he was researching on emotion and fear in animals. He claimed that an affectively intense stimulus is capable of inducing pupillary dilation, in as quick as .2 milliseconds and reaching to maximum in .5 to 1 seconds (Darwin, 1998).

Neural underpinnings of psychophysiological pupil movements are relatively difficult to address since pupil dilation is under the influence of external sensory input in different modalities (tactile, olfactory, auditory, gustatory and noxious) as well as internal processes including the affective system and mental activities (Beatty & Lucero-Wagoner, 2000). Therefore, there are substantial amounts of afferent paths to reach pupillary musculature through ANS. So far varying sources which have influence on pupillary diameter have been published including fatigue (Lowenstein & Loewenfeld, 1951, 1964), alertness-relaxation (Bartlett, Faw, & Liebert, 1967), alcohol usage (Skoglund, 1943), psychiatric diagnosis (Duke-elder, 1971; Rubin, 1964; Steinhauer & Hakerem, 1992), information processing load (Beatty & Kahneman, 1966; Simpson & Hale, 1969), incentive (Daniel Kahneman & Peavler, 1969; D Kahneman, Peavler, & Onuska, 1968), political attitude (Eckhard H. Hess & H., 1965), semantic stimuli (Hutt & Anderson, 1967).

Rather than being a direct consequence, task-evoked pupillary responses (TEPR) are correlational reporter markers of the central mechanisms behind the human cognition. Although correlation does not imply causation, application of reporter markers is commonly utilized in scientific literature. In molecular biology, expression profile of a gene of interest can be studied via utilization of reporter genes. Protein of the reporter genes are easily detected or measurable such as GFP – a bioluminescent protein called as green fluorescence protein. In this approach a reporter gene segment is inserted within the regulatory region of a gene of interest and thereby, whenever or wherever the gene of interest is expressed the GFP is expressed. In consequence, the cell would be identified via illumination in bright green under specific wavelength of light (Lodish, 2008). The application of reporter gene facilitates the research towards understanding regulatory processes of human genome. Similarly, the application of pupillometry makes it possible to infer about the psychophysiology of the human mental processes since it offers reliable and consistent index of human cognition with respect to central nervous system (Beatty & Lucero-Wagoner, 2000).

The psychophysiological pupil movements which range from .1 to .5 millimeters are comparatively small in contrast to large scale pupillary movements which range from 1 to 9 millimeters. Thus relatively sophisticated machinery is used for observing any pupillary change given in response to human mental processes (Beatty, 1982a, 1982b; Goldwater, 1972). With the development of practical machinery measuring pupil size changes with high precision, task-evoked pupillary responses (TEPR) are measured and calculated by averaging specific points in an experimental task with respect to significant events (Beatty, 1986). Thus, pupillometry becomes precise, stable and

accurate measure of human cognitive processes which are tested in an experimental paradigm (Beatty, 1986). The approach requires using a reliable baseline pupil diameter with respect to the task being tested and this methodology enables TEPR to be enhanced to stand out by diminishing any noise in the pupillary signal.

TEPR is a useful tool to study human cognition for cognitive psychophysiologist since it is a powerful correlational index of underlying brain processes. Yet, taking sensible precautions is necessary when studying with phasic pupillary responses which are not reflexive since it is possible that pupillary light reflex and accommodation reflex may interfere with the TEPR considering the scale of change in pupils by the aforementioned reflexes (Beatty & Lucero-Wagoner, 2000; Tryon, 1975). In order to prevent large scale pupillary movement to effect the TEPR, luminance level of the surrounding and brightness level of the experimental stimuli should be kept constant. Besides, experimental stimuli should be fixed in an optimum distance that the presented stimuli during experimental tasks should not be induced pupillary constriction via accommodation reflex.

2.1.3 Effect of Cognition & Behavior on Pupillometry

The idea of using TEPR towards understanding biological basis of several human cognitive, emotional and behavioral processes induced great interest among cognitive psychophysiologists starting with early 60s. Hess was one of the great facilitators of this movement due to his extensive research on this topic which gathered attention of contemporary researchers to build the bridge between pupillary movements and human cognition alongside with affective loading.

Novelty Effect

Earlier studies investigating the pupillary responses and affective loading of experimental stimuli linked pupillary dilations to sexual arousal and sexual orientation (Hess & Polt, 1960; Hess, Sheltzner, and Shlien, 1963). In the study conducted by Hess, greater pupillary diameter is obtained when female participants when presented with pictures of male nude and baby, and when male participants were presented with pictures of female nude. It was postulated that the reason why greater pupillary responses are gathered is the result of interest in the nudes of opposite sex. However, a subsequent study claimed that rather than viewing the nudes of opposite sex, it was the orientation of sexual interest of the participant was the determinant factor in the obtained pupillary response that homosexual males reacted with higher pupillary diameter towards to male nudes as compared to heterosexual males which reacted with higher pupillary diameter towards to female nudes. Although these early studies were too quick in concluding that the obtained TEPR during sexual stimulus was the result of sexual arousal of the participants, the studies were criticized by the bias towards explanation of the nature of the relationship between the pupillary response and the experimental stimuli (Andreassi, 2000, ch. 10). Another explanation for the connection was the novelty of the stimulus that the

explanation can be further extended to capture the sexual context of it since after all a stimulus with sexual context is novel in nature. The study conducted by Hamel (1974) suggested that the novelty rather than the sexual arousal may be the key indicator in interpreting the obtained pupillary diameter when participants viewed the stimuli with sexual content.

Affective Value

Another controversial issue on connecting the pupillary response to the affective valence of the experimental stimuli is the directionality of the pupillary movement. Perceptual aversion hypothesis claimed by Hess (1972) suggested that a negative stimulus which is unpleasant induces pupillary constriction as opposed to pupillary dilation. On the other hand, a positive stimulus which is pleasant induces a pupillary dilation. However, despite the presence of the arousing context of the negative stimulus is present, pupillary response would be in favor of pupillary dilation at first which is followed by lasting pupillary constriction. The 'dual' nature of pupillary response took attention of the contemporary psychophysiologists and there was extensive research on the topic in order to investigate the possible constriction effect due to negative affect of the experimental stimulus (Lowenfield, 1966; Woodmanse, 1967; Libby, Lacey, and Lacey, 1973; Janisse, 1974). Lowenfield (1966) conducted a study and revealed that the only factor capable of inducing pupillary constriction was light reflex and no other stimuli would induce it. On the contrary, all the collected psychosensory stimuli in the study was able to produce pupillary response in favor of pupil dilation. On the other hand, studies conducted by Woodmansee (1967) and Libby, Lacey, and Lacey (1973) partially supported the aversion-constriction hypothesis of Hess such that small sample of their participants were observed to have pupillary constriction in reaction to unpleasant stimuli. Moreover, Hess' studies were reviewed and criticized for having methodological flaws so that the notion that stimuli with negative affect induced pupillary constriction remained controversial (Janisse, 1977). Janisse also did a follow-up study to investigate the relationship between affective value of the stimulus and psychophysiological pupillary response; the study concluded that both negative and positive affective stimulus were capable of inducing pupillary dilations as opposed to what had been hypothesized by Hess with regard to aversion-constriction notion (1974). Bradley, Miccoli, Escrig, & Lang, 2008). Thus, the Hess hypothesis was perceived as controversial based on the findings of majority of follow up studies.

In more recent studies extreme points of the affective dimension in terms of high pleasant and aversive stimulus were shown to be inducing greater pupillary dilations (Steinhauer, Boller, Zubin, & Pearlman, 1983; Bradley, Miccoli, Escrig, & Lang, 2008). A relatively recent study conducted by Bradley et al. (2008) re-touched the aforementioned controversial topic on the relationship between psychophysiological pupillary response and affective content of the stimulus. In comparison to previous ones, the study was methodologically well controlled, and employed modern technology for monitoring pupillary responses. The experimental material employed in the study was rich and reliable since it was adopted from well controlled database

of International Affective Pictures System (IAPS: Lang et al. 2005). Hereby, affective domain was studied with regard to two axes; hedonic valence and emotional arousal. The study revealed that as the emotional content of the visual stimulus increases, the observed pupillary diameter would be larger. Thus neutral pictures induced smaller pupillary dilation as compared to emotionally arousing pleasant and unpleasant pictures. This study holds a strong position on the relationship between emotional loading and pupil response. The study is also valuable for characterizing the link between obtained psychophysiological pupillary response and the two branches autonomous nervous system. Building on their study, the pupillary dilation observed during passive viewing of the visual stimulus was found to be elicited by the activity of sympathetic pathway rather than parasympathetic pathway. Mechanism of action is further proposed as starting from the basolateral nucleus of amygdala followed by central nucleus in response to an affective stimulus. The activity in amygdala further reflects on the lateral hypothalamus, hereby projecting on sympathetic pathway which eventually innervates iridic dilator muscles to increase pupillary diameter. Although the functionality of this connection between emotionally arousing stimulus and pupillary response is rather ambiguous, the connection is possibly a vestigial heritage from our evolutionary history (Lang & Bradley, 2010).

Moreover, Bradley et al. (2008) conducted studies in which the experimental setting was controlled for level of luminance of the visual stimuli that the pictures used in the study was manipulated for low, moderate and high luminance. Based on that, initial light reflex of the pupil was found to be correlated with the luminance level of the visual stimulus which is confirming the previous studies in a well-controlled manner. Thus, it is crucial to control for the brightness of the visual stimuli when collecting psychophysiological pupillary responses.

Cognitive Load

The psychophysiological pupillary response was also assessed during several cognitive tasks including short term memory (D Kahneman & Beatty, 1966), and mental mathematical calculation (E. H. Hess & Polt, 1964). In the study conducted by Hess and Polt (1964), subjects were asked to perform a multiplication problem mentally, during which their pupillary response was collected. The study revealed important findings with respect to the relationship between pupillary dynamics and cognitive tasks such that initially a pupillary dilation was observed in response to the multiplication problem. The initial dilation remained and enlarged until the solution was found. Then, a sudden decrease in pupillary response was observed following the deposition of the answer. Moreover, the task difficulty was modified in the study and task evoked pupillary process was found to be correlated with the increasing task difficulty. The findings revealed the relationship between cognitive load during a mental multiplication task and TEPR.

On top of that, Kahneman and Beatty (1966) investigated the possible link between psychophysiological pupillary response and memory in a short term memory task. The task requirement was based on memorizing three to seven digit numbers. First,

each number was listened, then memorized and verbally repeated in corrected order. During the whole process, pupillary response was collected from participants and initial pupillary dilation was observed with the start of listening the first digit. The pupillary dilation remained and enlarged through the listening and reaching its maximum at the last digit. Following that, pupillary constriction was observed along with verbal repeatition of the first digit. The constriction remained until the last digit was repeated. The findings of two study was similar with respect to the observed pupillary response pattern. The task difficulty was also changed during the experiment such that memorizing a three-digit series was easier than memorizing a seven-digit series. Correspondingly, observed pupillary response was larger in memory tasks with seven-digit series than three-digit series. The findings reveal the relationship between cognitive load during a short term memory task and TEPR.

Moreover, language processing and its relationship with task-evoked pupillary response was also investigated. Likewise, the task difficulty was manipulated through the complexity of the sentences which participants had to process. The effect of task difficulty on pupillary response was preserved in the language processing task: greater pupillary dilation was observed for processing more complex sentences (Ahern, 1978; Ahern & Beatty, 1979).

Finally, the link between psychophysiological pupil response and cognitive tasks was established. Each cognitive task including mental calculation, short term memory, perception and reasoning requires an evaluative process which have a cognitive loading. That processing period requires effortful attention of the perceiver and such cognitive processing and relative attention reflects itself in the corresponding TEPR (Beatty, 1982b).

2.2 Neuropeptide oxytocin

Oxytocin is a nonapeptide belonging to the family of neuropeptides. Up to now, there are approximately one hundred neuropeptides discovered to be functioning in the mammalian brain (Thomas R. Insel, 2010). Among the neuropeptides, the family of nonapeptides to which oxytocin and its close relative vasopressin belong is conserved through mammalian evolution for their fundamental roles to regulate both social and reproductive behavior in a species specific manner (Donaldson & Young, 2008; Goodson, 2005). The evolutionary roots of the genes responsible for the aforementioned nonapeptides are considered to be dating back to 700 million years ago and their primary role was regulating homeostasis through water cycle between environment and within the cell. However, the evolutionary path to modern era added additional properties to their functioning with respect to social domain. Among the conserved commonalties which are shared by variety of species including vertebrates and invertebrates, all nonapeptides have facilitator roles in social behavior, gender and sex-steroids which affect them as well as their receptors, and sites of action including brain and gonads. Hence, Sir Henry Dale after discovering this small

neuropeptide gave the name of oxytocin which is combination of two Greek words of 'ωκυξ' = *fast, quick* and 'τοκοξ' = *birth,* pointing its facilitator role at parturition during which its primary role is contracting the muscles of uterus (Dale, 1906). Discovery of structure of oxytocin was a remarkable study with respect to the facts that it became the first polypeptide for which structure is identified. This study brought Nobel to Du Vigneaud in Chemistry in the year of 1955 (Du Vigneaud, Ressler, & Trippett, 1953).

Being a neuropeptide, oxytocin is not a mere neurotransmitter. While it serves as a neurohormone in the peripheral system, it can act as a neuromodulator in the central system (Gimpl et al., 2001; Moos & Richard, 1989). Oxytocin coupled to its carrier molecule - neurophysin is synthesized in the cells of paraventricular nucleus (PVN) and supraoptic nucleus (SON) of hypothalamus. The neurons within which oxytocin is produced are called magnocellular neurons named in referencing to its size being large. The magnocellular neurons in the PVN and supraoptic nuclei have projections to the neurohypophysis (posterior pituitary gland) through which oxytocin travelled. During this route, oxytocin is accompanied with its carrier counterpart neurophysin that it helps targeting, packaging and storing of oxytocin. In order to act as a neurohormone, in times of need, oxytocin pass to the bloodstream via the connections of blood capillaries and magnocellular neuronal circuitry (Bealer et al., 2010; Gainer, 2012).

Moreover, aside from acting as a neurohormone in the periphery, it is observed that oxytocin has neuromodulator properties in the central nervous system. Commonly, a neurotransmitter is released to synaptic cleft from the axonal terminal of a presynaptic neuron to convey the neurotransmission. However, routes of central oxytocin are relatively more complicated than that, hence it is regarded as a neuromodulator in addition to its neurotransmitter role in conveying neurotransmission (Carter, 2014; Churchland & Winkielman, 2012). On central level, as shown in Figure 2.3 by the dotted lines, neuropeptide oxytocin can diffuse from dendrites as well (Ludwig & Leng, 2006). This diffusion results in oxytocin to travel in broader sense and diffuse to extra hypothalamic regions. In addition to that, synthesis of oxytocin is not limited to magnocellular neurons of PVN and SON in the central level such that it can be also produced at the parvocellular cells of PVN. With the help of neuronal projections of parvocellular neurons diffusing through ECS (extracellular space) and subsequently CSF (cerebrospinal fluid), oxytocin can directly reach the wide variety of brain structures to induce modulatory effects in the neural populations within these destinations (Veening et al., 2010). The areas where oxytocin can reach and influence are amygdala, hippocampus, striatum, nucleus accumbens (NAc), superchiasmatic nucleus (SCN), bed nucleus of stria terminalis (BNST), ventral tegmental area, frontal cortex and spinal cord and brain stem (Argiolas & Gessa, 1991; Huber, Veinante, & Stoop, 2005; Purves et al., 2004; Veening et al., 2010). Central release of oxytocin is considered to be unrelated to the peripheral release of oxytocin due to the fact that in response to several stimuli plasma oxytocin levels are not parallel with oxytocin levels in CSF (T R Insel, Young, & Wang, 1997).

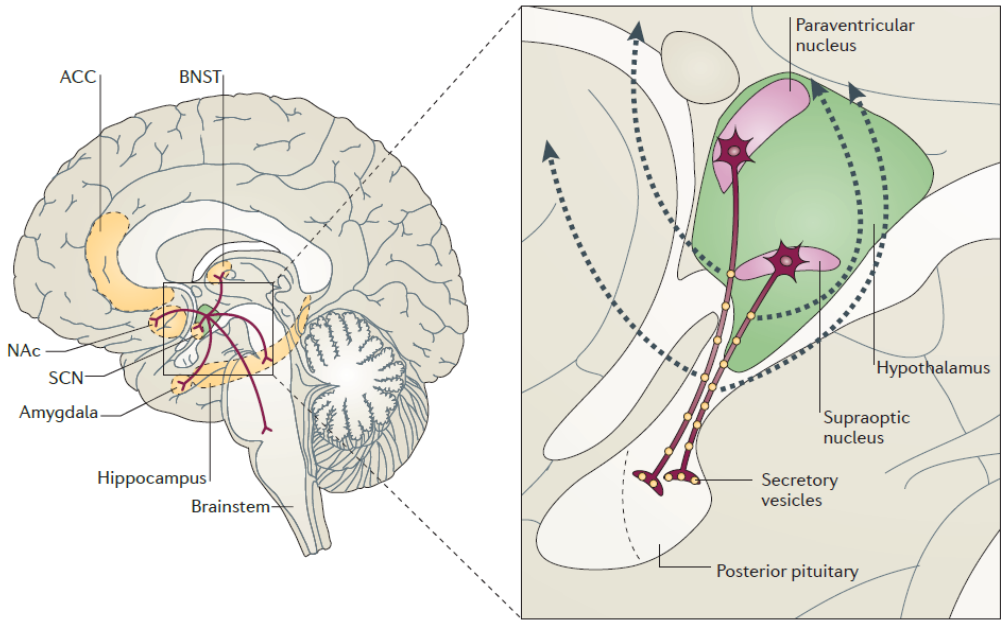

Figure 2.3 Central and peripheral routes for neuropeptide OXT (Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011). ACC = anterior cingulate cortex; BNST = bed nucleus of the stria terminalis; NAc = nucleus accumbens; SCN = suprachiasmatic nucleus.

Coinciding with its etymologic roots, neuropeptide oxytocin is studied extensively for its role during parturition and nursing where it acts to stimulate muscle contraction during parturition and milk ejection, respectively (Anne Campbell, 2008). Aside from that, extensive research on the neurohypophyseal neuropeptides revealed the discovery of additional regulatory roles of oxytocin in mammalian physiology with a broader spectrum with respect to reproduction and sexual behaviors. It has been shown that central release of oxytocin alongside with neuronal activity can be triggered in response to both sexual and non-sexual stimuli. Copulation, stimulation of genitals or breast stimulation, giving birth, olfactory stimuli and suckling are categorized as sexual stimuli whereas grooming, massage and engaging with the offspring are categorized as non-sexual stimuli.

In humans as well as other mammals, there are four receptors for nonapeptides. While three of them were for vasopressin, one of them serves as an oxytocin receptor (OXTR). However, cross-binding activity among them is observed such that vasopressin can bind to all four receptors (Thomas R. Insel, 2010). Receptors of the nonapeptides are commonly GPCRs (G protein-coupled receptors). The receptor for oxytocin molecule (OXTR) has been discovered in 1992 and it is a polypeptide

composed of 389 amino acids with 7 transmembrane domains (Kimura, Tanizawa, Mori, Brownstein, & Okayama, 1992).

The idea that involvement of the nonapeptides in species-specific reproductive and social behavior comes from the animal research. Based on the literature both the structure of peptide and the receptor and their expression are evolutionarily conserved (T R Insel et al., 1997). Despite this fact, the regulated behaviors via these nonapeptides are not limited. Although mostly being related to social and reproductive behavior, the repertoire of the regulated behaviors are quite distant across species, because every behavior regulated by them is dependent on the species itself (Donaldson & Young, 2008). This variability in the species-specific behaviors certainly cannot be easily explained by highly conserved peptide structure of these nonapeptides. Rather, this variation is thought to be mediated by the diversity in the expression patterns of receptors for these nonapeptides in central system. The animal research conducted in rats revealed that there are oxytocin receptors can be found in variety of brain regions including olfactory system, basal ganglia, limbic system, thalamus, hypothalamus, brain stem and spinal cord (Gimpl et al., 2001). Moreover, research conducted on primates revealed the presence of oxytocin receptors also in orbitofrontal cortex in addition to hypothalamus, amygdala and hippocampus (M. L. Boccia, Goursaud, Bachevalier, Anderson, & Pedersen, 2007). Alongside with variance in expression patterns among species, the nonapeptides are also observed to have sexually dimorphic characteristics in their expression pattern in vertebrates. Thus, the behavioral outcomes may differ between the two sex as a consequence (De Vries & Panzica, 2006).

In humans, studies investigating the presence of oxytocin receptors in peripheral level discovered that there are oxytocin receptors in kidney, digestive tract, heart, pancreas, thymus and adypocytes (Kiss & Mikkelsen, 2005). On the other hand, methodological difficulties prevented researchers to study the areas in human central nervous system where oxytocin receptor is present. In spite of difficulties, there was an autopsy study conducted by Loup et al. (1991) to investigate the locations of oxytocin binding sites in brains of 12 deceased individuals. Although, the study supports the animal research by showing localization of oxytocin binding sites in human brains, the distribution of oxytocin binding sites is not overlapping with the animal research in some areas. The study detected that there are sites which oxytocin can bind in substantia nigra and nucleus basalis of Meynert in human brain, whereas it was unable to locate any oxytocin binding sites on olfactory bulb, entorhinal cortex, hippocampus and amygdala (Loup et al., 1991). Another autopsy study was conducted in human brains was managed to reveal presence of oxytocin binding sites in hypothalamus, anterior cingulate cortex, olfactory nucleus and amygdala (M. L. L. Boccia, Petrusz, Suzuki, Marson, & Pedersen, 2013). The authors of second study claim that controversial findings of the outcomes of these two studies may be resulted due to the methodological differences to some extent. The results of research on finding possible oxytocin binding sites in human central system indicate that there are differences in distribution of oxytocin receptors in human brains as compared to animal research, although there are similarities between them.

2.2.1 Intranasal administration of oxytocin

Animal research conducted towards understanding central effects of oxytocin utilizes some invasive methodologies which help researchers to increase the availability of the oxytocin in central nervous system of the animal being studied (Gimpl et al., 2001). However, the same invasive techniques of genetic manipulations or central administration of the substance are not applicable for human subjects. Early studies investigating in the behavioral outcomes of oxytocin in humans used peripheral administration via intravenous infusion. Elevated plasma levels of oxytocin via systemic administration put a question mark on whether systemically administered oxytocin can cross blood-brain barrier (BBB). Unfortunately, systemic administration of oxytocin is not capable of passing the blood-brain barrier (BBB); only very small amount of oxytocin can pass through it (Kang & Park, 2000). BBB is an important protective barrier which prevents molecules circulating in bloodstream to freely pass to the central system in an uncontrolled manner. Thus, it has to be taken into consideration for drug delivery either for therapeutic or experimental purposes (Illum, 2000; Pardridge, 1999). While molecules which are lipophilic with smaller molecular weights can cross BBB, a hydrophilic molecule has smaller chance to cross it. Considering that the nonapeptides are hydrophilic large molecules, their chance of crossing BBB is low (McEwen, 2004). Moreover, systemic administration of oxytocin is short-lived in blood – approximately 3-9 minutes (Churchland & Winkielman, 2012). Thus, short life span, poor blood-brain barrier penetration capability and metabolic instability hindered the early studies utilizing intravenous administration of oxytocin to study its central effects. Alongside with that, peripheral infusion of oxytocin can trigger endocrinologic response through circulating bloodstream such as uterine contraction in females, which in turn having side effects through influencing other hormonal systems (Meyer-Lindenberg et al., 2011).

In order to accomplish drug delivery to the central system, researchers developed several approaches to circumvent BBB. Intranasal administration appealed most researchers since this method provides an indirect but non-invasive way to study effects of neuropeptides on social effects in humans in experimental contexts as well as in animal models (Dal Monte, Noble, Turchi, Cummins, & Averbeck, 2014; Illum, 2000). This method of administration gathered great interest to study social effects of oxytocin since the experimental researches on the area was successful to produce replicable results in behavior, perception and functioning of brain (Bakermans-Kranenburg & van IJzendoorn, 2013). Intranasal administration provides a great tool since it offers a rapid way for the administered substance to reach to central system, at the same time it is protected from being degraded through absorption through gastrointestinal tract. Although intranasal administration offers a convenient way to study neuropeptides on human social behavior, the literature on whether it reaches the brain and if so, how it reaches the brain after being administered via this method is limited. The precious work of Born et al., (2002) disambiguate the uncertainties surrounding intranasal administration of neuropeptides to some extent by measuring the levels of neuropeptides in CSF after intranasal administration. In their study, it was observed that after 30 minutes of substance administration, levels of these

compounds in CSF were elevated. The outcomes of the study confirm the hypothesis that intranasal administration is efficient for delivering a drug to reach brain by circumventing BBB (Born et al., 2002).

2.2.2 Effect of oxytocin on trust behavior

Trust is a central concept for human life because we have to judge others and show trust/distrust to maintain social domain of our life. Because of having such a central role, inevitably trust has been interest to many disciplines such as psychology and economy. Especially consideration of the modified trust by oxytocin towards strangers, towards family and towards romantic partners have been interesting avenues that were explored. Each study contributed to this rich environment of trust in terms of their definition such that sometimes trust is conceptualized as behavioral intention based on assessment of potential risks and deciding on whether the benefits outweigh the loses. On the other hand, trust can be more affect-based that it can be based on 'gut feeling' which is derived from intuition. Multidisciplinary perspective cherished the definition of trust and as a consequence cherished the research studying relationship between oxytocin and trust. Since oxytocin is viewed as the physiological facilitator of the social domain of human life, the possible link between trust and oxytocin has gathered great interest since under intranasal oxytocin administration people engage in behaviors perceived as more trusting, generous and altruistic (Barraza & Zak, 2009; Baumgartner et al., 2008; Kosfeld et al., 2005; Moïra Mikolajczak et al., 2010; Zak et al., 2007).

Theodoridou et al. (2009) studied trust-oxytocin relationship in terms of facial recognition which is an inevitable component of social cognition. They utilize the fact that on daily basis, our willingness to approach and socially engage with others is primarily based on our social judgments of trust. One possible source of the information which is relied on while evaluating others in terms of trustworthiness and approachability is facial cues. In their study, the only reliable source of information was facial characteristics of the presented pictures and it is revealed that trustworthiness judgments of participants are influenced by intranasal oxytocin. Facial appearance of an individual certainly helps us through social interaction to feel trust or not and oxytocin has been shown to have facilitator properties in this process.

In addition to the effects of oxytocin on social perception, it has been shown that oxytocin promotes social behavior by manifesting its effects in the decisions of individuals during a trust game which involves monetary share (Kosfeld et al., 2005). Effect on exogenous oxytocin is observed when participants were engaging with another person but not when engaging with the computer itself, suggesting that oxytocin promotes prosocial behavior in the presence of a social agent. Presence of social agent is important for controlling the possibility that oxytocin might lead to increased risk taking behavior in general or decrease the perception of risk in a scenario which involves monetary share. Since the improvements of trusting behavior

were only observed in participants who were playing against another human being but not in players who were playing against computers, it was suggested by the authors that effects of oxytocin are limited to situations where the situation bears a "social risk", possibly referring to the effects of oxytocin on social behavior. However, the same study is also important for characterizing the underpinning mechanisms of oxytocin with regard to social behavior. The increased prosocial behavior is only observed in the participants who are investors not the trustee. Hence we can infer that oxytocin is involved in prosocial behavior but it is not effective in reciprocity.

Oxytocin and its possible effects on trusting behavior is studied well in the context of scenarios which involve monetary share. However, it is a fact that trusting others comes with a risk; the risk of betrayal. Whether someone who is faced with betrayal of trust would still be able to trust again is a subject of interest of the study conducted by Baumgartner et al. (2005). The literature of oxytocin implies that oxytocin increase willingness of participants to trust the others with their money however it was not shown that whether this increased ability to trust by oxytocin is resilient to resist betrayals. In the study of Baumgartner et al. (2005), participants were recruited to play a trust game similar to the study of Kosfeld et al. (2005). However, in the former study, participants were provided with feedback on whether they are betrayed by their counterparts in half of the experiment. It was observed that ability to trust others is decreased in participants receiving placebo after they learnt they they had been betrayed. On the contrary, trusting behavior was not diminished in oxytocin group. Hence oxytocin was shown to be decreasing betrayal aversion and replenish the ability of trusting others, even when the participants faced exploitation of their trust by someelse. In order to understand the outcomes of this study, it should be noted that after the betrayal of trust, participants played against a different counterpart to be able to investigate the ability to trust others after being betrayed by someone else (Baumgartner et al., 2008).

Additionaly, Zak et al. (2007), conducted a study to explain the positive effects of oxytocin on social effects by investigatin wether oxytocin increased generousity in humans by way of engaging in more trusting behaviors under the effect intranasal oxytocin. In their study, participants were engaged in a decision making game which involves monetary sharing. In brief, the participants were provided with money and asked to give some of it to share the money with their counterparts in the experiment. The other partner has the right to refuse to given amount and if that happens both parties gain nothing. Upon intranasal administration of oxytocin, participants engange in more generous decisions as compared to participants who were administered placebo. Since it was also shown that exogenous oxytocin did not increase altruistic decision making process where the other partner has no right to reject the amount of money given, it is suggested that increased altruism is not the potential source for the observed effect of intranasal oxytocin in their study (Zak et al., 2007).

The studies mentioned above investigate the possible relationship of oxytocin and and trust in scenarios which involves monetary share. Whether this beneficial effects of

oxytocin on social domain of life with respect to trust behavior is extendable to non-monetary context was studied by Mikolajczak et al. (2010). The study investigates the effects of oxytocin in an interesting yet distinctive scenario as compared to trust game. In their study the sign of trust is not the amount of money sent to the partner, rather it is sharing highly personal information about themselves and trusting that their privacy will not be violated. As compared to placebo, oxytocin influenced willingness of participants to loosen protective behavior about their privacy, thereby promoting trust in a totally different scenario. Alongside with monetary share, the link between trust and oxytocin persisted with respect to sharing personal and confidential information. So it can be concluded that oxytocin influences social behavior in humans in a broader sense (Moïra Mikolajczak et al., 2010).

2.2.3 Context and situation dependent effects of oxytocin

Building on the literature, it is thought that exogenous oxytocin indiscriminately produces positive social behavior and improves social cognition (J. A. Bartz, Zaki, Bolger, & Ochsner, 2011; M Mikolajczak et al., 2010). However, this view is doubted by the increasing number of studies revealing inconsistent results upon investigating social effects of oxytocin in humans. Empirical support in animals revealed that effect of increased availability of oxytocin predicted social behaviors in animals in situation dependent fashion (Anne Campbell, 2008). Studies in animal research report that upon giving birth, levels of oxytocin in the female rodents in boosted. This increment on the level of oxytocin in the body of female rodent leads to decreased aggressive behavior against her pups while at the same the mother engange in more defensive behavior in order to protect her offspring against potentially harmful other females (Debiec, 2005; Pedersen, 2004). Therefore, it should be taken into consideration that treating oxytocin as powerful elixir which leads to increased trust beheavior in anybody might be misleading. Situational factors or personality differences could override the effects of oxytocin in social domain of humans.

Mikolajczak et al. (2010), investigated wether effect of intranasal administration of oxytocin on trusting behavior is always unidirectional. In order to discover the moderating role of contextual influences in the relationship between exogenous oxytocin and prosocial behavior, their study involved a contextual manipulation. Their experimental design was similar to the Kosfeld et al., (2005) such that participants were engaging in a trust game which involves monetary share. However, in that study, they were able to manipulate the trustworthiness of the partners which the participants had played with by portrayal. If a participants choose to trust an untrustworthy partner, the unfair partner would not respond the trusting behavior of the participants in reciprocity, thereby the participant could lose everything (M Mikolajczak et al., 2010). The participants in that study could play against three different partners; fair partner, unfair partner and computer. Therefore, the study was precious in order to understand wether exogenous oxytocin has situation-invariant or context-dependent effect on the trusting behavior. Their results revelaed that under

the intransal administration of oxytocin, participants trusted more to the reliable partners as compared to placebo and showed mistrust against unreliable partners. By contextually manipulating the trustworthiness level of the partners, Mikolajczak et al. (2010) was able to show that the effects of oxytocin is moderated by the features of the condition where oxytocin is administered. The study suggested that although intranasal oxytocin does make people more trusting, more altruistic and more generous, it does not make people more gullible. Moreover, their study also reported an interesting result such that the boosting effect of intranasal oxytocin on trust behavior was observed to be higher in the computer agent condition. This finding is contradictory to what Kosfeld et al. (2005) suggested where exogenous oxytocin was shown to be uneffective while playing the trust game with a computer agent. Therefore, future studies could try to find explanation to whether effects of oxytocin in trust behavior are extendable to non-social environment.

Declerk et al. (2010), conducted a study where upon intranasal administration of oxytocin participants were required to engage in a coordination game. In that study, effect of intranasal administration on the performance in cooperation game was also investigated in a context-dependent manner. Upon arrival before playing the coordination game, one group of participants were not allowed to socially engage with anybody other than the experimenter such that participants in that group did not meet with the person whom they would play against. There was another group of participants who were allowed to briefly communicate and socially engage with other participants prior to starting to play the game. The contextual manipulation was the presence/absence of social contact in advance of playing the coordination game. Their results support the context-dependent nature of oxytocin such that intranasal administration exerts differential effects in terms of coordination across the prior contact with participants. Oxytocin increased cooperation rate of participants in the socially engaged group, but diminished trust and lead participants to behave protectively in the anonymous group (Declerck et al., 2010).

In another study, it is shown that intranasally administered oxytocin enhances the ability of participants to read emotions in the eyes in a mind reading task (Domes et al., 2007). RMET (Reading the Mind in the Eyes Test) is commonly used to asses the capacity of individuals to interpret the social cues in order to determine the mental state of others. Results of that study confirmed the view that oxytocin has a crucial role in social cognition. However, the study also revealed that enhancing effects of oxytocin in ability of mind reading is more pronounced in the difficult items. In fact, the effect of intranasally administered oxytocin on easy items resulted in the same RMET scores from both participants receiving placebo and oxytocin. Moreover, in another study conducted with patients with ASD (Autism Spectrum Disorder), opposite effects of exogenous oxytocin are detected (Guastella et al., 2010). Intranasally administered oxytocin specifically improved the performance of patients with ASD to infer affective mental state of others only in easy items but it did not effect the performance in difficult items. As it is mentioned earlier, effect of intranasally administered oxytocin seemed to produce inconsistent results with respect to mind reading ability, a very crucial process of human social life. However,

it should be noted that in the second study, the easy items are already difficult for patients with ASD since they have difficulties in emotion recognition (Guastella et al., 2010). Furthermore, the performance on easy items was not effected by exogenous oxytocin in healthy population since easy items were to also easy for the participants who received placebo and equally did well on those as compared to participants who received oxytocin ('ceiling' effect). Thus, it can be postulated that effect of increased aviliability of oxytocin in performance on the mind reading through emotion recognition might be moderated by task difficulty. Additionaly, it seems that there is a limit for intranasally administered oxytocin to improve performance in such tasks.

2.2.4 The effect of intranasal oxytocin on pupillary responses

Literature on the physiological effects neuropeptide oxytocin with respect to pupillary response is relatively limited because studies conducted in this area are rare. To the best of our knowledge, pupillary responses have been the subject of interest of two studies which investigate the connection between exogenous oxytocin and facial expression recognition (Leknes et al., 2013; Prehn et al., 2013). The dosages of the administered substance in two studies were different: in Prehn's (2013) study participants received 24 IU of oxytocin, whereas in Leknes' (2013) study participants received higher (40 IU) amount of oxytocin. However, both studies involve facial expression recognition with respect to different emotions. The findings of the conducted studies reveal that administration of oxytocin triggered a pupillary dilation in response to emotional facial expression recognition. These findings are commentary to the previous literature such that empirical data supports oxytocin to improve prosocial behavior and facilitate social cognition. With respect to perceptual selectivity model proposed to explain social effects of oxytocin (J. A. Bartz et al., 2011), it gathers attention of the participants to socially relevant cues specific for the features of the situation in which oxytocin has been administered (Leknes et al, 2013).

2.2.5 Gender related effects of oxytocin

Oxytocin has been studied in variety of topics related to social cognition and emotion recognition. However, the observed effects of intranasal oxytocin are limited to the findings obtained from the male participants so far. In addition to that, even though some studies do include female participants, it remains unanswered whether there is an actual link between the intranasal administration and the gender of the participants on the observed effects due to inadequate research in the field. 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; Guastella, Howard, Dadds, Mitchell, & Carson, 2009; Savaskan et al., 2008; Shamay-Tsoory et al., 2009; Theodoridou et al., 2009). However, significant gender differences have been reported in more recent studies (Anna Campbell, Ruffman, Murray, & Glue, 2014; Fischer-Shofty, Levkovitz, & Shamay-Tsoory, 2013; Gordon, Zagoory-Sharon,

Leckman, & Feldman, 2010; Hoge et al., 2014; Kubzansky, Mendes, Appleton, Block, & Adler, 2012; Lynn, Hoge, Fischer, Barrett, & Simon, 2014).

Therefore, in order to eliminate possible gender related effects of oxytocin on social behavior, current study is accomplished by recruiting only heterosexual male participants.

2.3 Motivation, Research Questions and Hypotheses

Experimental studies reveal that intranasal administration of oxytocin promotes social interaction and related behavior including trust and approach in different scenarios. In addition, recent studies report that intranasal administration of oxytocin results in pupil diameter changes in response to trust-related behavior which requires people to make social judgments. In the current study, it is aimed to examine whether the simple appearance and evaluation of a visual stimuli with specific trustworthiness content trigger pupil dilation in a social judgment task. Possible effects of oxytocin are evaluated specially for two aspects of the trust behavior: 1. Trustworthiness of the faces when the task requires participants to hypothetically approach and ask information 2. Trustworthiness of the faces when the task requires participants to hypothetically trust and share something. Due to possible sexual dimorphism of oxytocin intake in humans, only heterosexual male participants are recruited in the study. Dependent variables that are investigated are subjective trustworthiness ratings, reaction times and pupil diameter.

The research questions and hypotheses are as follows:

Approach task related research questions and hypotheses

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

Hypothesis 1: Since oxytocin is found to be related with approach related social cognition and prosocial behavior such as trust inspired by others, participants receiving oxytocin will rate the faces as more trustworthy than participants receiving placebo in approach context.

Hypothesis 2: Since oxytocin facilitates the social interaction with others, participants receiving oxytocin will rate the faces faster than participants receiving placebo in approach context.

Research Question 2: Will the general effect of oxytocin on pupils, which is increased pupil diameter, hold during trustworthiness judgments?

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

Trust task related research questions and hypotheses

Research Question 3: Is there a relationship between intranasal oxytocin intake and trustworthiness judgments in trust task?

Hypothesis 4: Since social effects of oxytocin are not always beneficial and are shown to be influenced by contextual features of the situation, participants receiving oxytocin and placebo will differ in their trustworthiness judgments in trust task.

Hypothesis 5: Despite the task requiring trust and sharing something, since oxytocin facilitates social interaction, participants receiving oxytocin will rate the faces as faster than participants receiving placebo in trust context.

Research Question 4: Will the general effect of oxytocin on pupils, which is increased pupil diameter, hold during trustworthiness judgments?

Hypothesis 6: Participants receiving oxytocin will show larger pupil diameters compared to participants receiving placebo while judging trustworthiness in trust context.

Task comparison related research questions and hypotheses

Research Question 5: Do the requirements of the task affect trustworthiness judgments?

Hypothesis 7: Since trusting someone to share something is more demanding than trusting someone to ask something, participants will rate the faces as less trustworthy during trust task than approach task.

Hypothesis 8: Since it is a crucial decision to share something rather than ask something, trustworthiness judgments of the faces in trust task will take longer time than the ones in approach task.

Hypothesis 9: Since trust is more demanding than approach task and the pupil dilation is affected from cognitive load, trustworthiness

judgments of the faces in trust task will elicit larger pupil dilation than the ones in approach task.

Face manipulation related research questions and hypotheses

Research Question 6: Does the trustworthiness level of the faces affect trustworthiness judgments?

Hypothesis 10: Since the faces have already been evaluated by people in terms of trustworthiness, trustworthy face will have higher ratings compared to neutral faces while untrustworthy faces will have lower ratings compared to neutral faces.

Research Question 7: Is there a relationship between trustworthiness level of the faces and pupil size?

Hypothesis 11: Since pupillary changes reflect the arousing state and attention of the individual, trustworthy faces will differ in terms of initiation of pupillary responses. Thus, trustworthy and untrustworthy faces will elicit larger pupil diameters compared to neutral faces.

Table 2.1 Summary table for hypotheses.

	Approach	Trust	Task Comparison	Face Manipulation
Behavioral Rating	**H1** OXT > PLC	**H4** OXT ≠ PLC	**H7** Approach < Trust	**H10** T> N > U
Reaction Time	**H2** OXT < PLC	**H5** OXT < PLC	**H8** Approach < Trust	
Pupil Response	**H3** OXT > PLC	**H6** OXT > PLC	**H9** Approach < Trust	**H11** U ≠ N ≠ T

CHAPTER 3

METHOD

3.1 Overview

The method chapter is composed of scale-based materials, experimental materials, stimulus creation and preprocessing steps, participants and experimental design of pre study and main study. In the main study, participants were instructed to rate the trustworthiness and approachability of the presented stimuli. One aim of the study was to find how individuals react differently to trustworthy, neutral and untrustworthy faces. Therefore, firstly a pre study was conducted to reveal which of the faces are perceived as trustworthy, neutral or untrustworthy. Thereafter, main study was conducted based on the stimuli from the pre study. Detailed information about both main study and pre study can be found below.

3.2 Materials

3.2.1 Scale-Based Materials

In the current study, Beck Depression Inventory (BDI), Positive and Negative Affect Scale (PANAS) were used as scale-based materials.

Beck Depression Inventory (BDI)

Beck Depression Inventory (BDI), invented by Dr. Aaron T. Beck, is a standardized test which is widely used to measure the level of the depression in humans (Beck, 1961). The inventory is based on self-report and contains 21 questions with four possible answers (see Appendix B). Each question in the inventory reflects several aspects of the depression; hopelessness, irritability, physical symptoms and cognitions. The answers to each question differ in intensity starting from non-severe (score 0) to severe (scored 3). According to that, the scores range from 0 (lowest score) to 63 (highest score). Having a score of 1-10 is evaluated as normal, 11-16 as mild mood, 17-20 as borderline clinic depression, 21-30 as moderate depression, 31-40 as major and over 40 as extreme depressions.

Adaptation of BDI into Turkish population was done by Hisli (1988) and Sahin and Sahin (1992). Reliability coefficient of the adapted inventory is .74 (Cronbach's alpha). With regard to results of Turkish society, having a score lower than 17 is

evaluated as non-depressed. In order to control that the participants are not depressed, any participants having a larger score is excluded from the current study. The inventory used in the current study is provided in Appendix B.

Positive and Negative Affect Schedule (PANAS)

Positive and Negative Affect Scale is a psychometric test which is used to quantify affect or mood quantitatively (Watson et al, 1988). The scale is based on self-report and contains 20 items in 5-point Likert type scale, ranging from 1= very slightly to 5= very much. The items in the scale are divided in two sets, one of which is covering positive affect and the other negative affect (See Appendix C). Positive affect (PA) concerns the alertness and activeness of a participant whereas negative affect (NA) concerns how much anger and fear that participant experience. In order to complete PANAS, participants were asked to evaluate each 20 emotions based on how much they experience that particular emotion currently. The scale is frequently used and has a high reliability with internal consistency (Cronbach's alpha) of .88 and .87 for positive and negative affect, respectively. Adaptation of PANAS into Turkish was carried out by Gençöz (2000) and reliability of the scale was found .86 and .83 for positive affect set and negative affect set, respectively.

Calculations were done separately to get a positive and negative affect score. While calculation of positive affect score was done by summing the responses taken from the items 1, 3, 5, 9, 10, 12, 14, 16, 17 and 19, whereas calculation of negative score was done by summing the responses taken from the items 2, 4, 6, 7, 8, 11, 13, 15, 18 and 20. Thus, scores are ranged from 10 (lowest score) to 50 (highest score) for both positive and negative affect set. Accordingly, having a higher score from a set reflects increased degree of that affect type. In order to be considered in positive mood, a participant's positive affect score has to be greater than her/his negative affect score. Likewise, in order to be considered in negative mood, a participant's negative affect score has to be greater than her/his positive affect score. In order to control that the participants are not in negative mood, any participants having a greater score of negative affect than positive affect is excluded from the current study. The inventory used in the current study may be seen in Appendix C.

3.2.2 Experimental Materials

Trustworthiness Face Data Set 2

Experimental material consists of computer-generated face stimuli chosen from the freely available database of Trustworthiness Face Data Set 2, created by Oosterhof and Todorov (2008). The data set is composed of 300 pictures based on 100 facial identities manipulated on the axis of trustworthiness in 3 different levels, untrustworthy, neutral and trustworthy. The facial identities in the dataset are all

Caucasian bald males, depicted from frontal view with eyes open and having neutral facial expression. The faces were created by using a software called FaceGen Modeller Program Version 3.1 (Singular Inversions, 2006) and manipulated according to the trustworthiness face model explained in Oosterhof and Todorov (2008). With the help of that model, the group was able to change facial features important in terms of trustworthiness of each face, thus, to turn them into less or more trustworthy. In order to define which facial features are important with regard to trustworthiness of the face, at first the group randomly created 300 computer-generated emotionally neutral faces via the modeling program. Then, trustworthiness ratings of each face were scored by 29 raters on a 9 point Likert scale. The facial features which are at great importance for facial trustworthiness were identified mathematically. It was found that orientation of the mouth and the eyebrows are important with respect to perceived trustoworthiness. Thus, the group was able to create a new data set composed of faces which varied, along the axis of trustworthiness systematically, by manipulating the orientation of the mouth region (changing the distance between the nose and the mouth) and eyebrows (changing the inner ridge by increasing or decreasing). Any distance between subsequent levels along the axis represented by standard deviation units (SD). Simply, trustworthiness face model created two different versions of each facial identity: trustworthy version (3 SD away from the original face) and untrustworthy version (-3 SD away from the original face). Examplars of the face stimuli are displayed in Figure 3.1.

The data set provides good control on eliminating effect of any facial features (e.g. skin, texture, hair, freckles, etc). Being able to use the untrustworthy and trustworthy versions of the same facial identity makes it possible to observe any effect of stable facial features specific to trustworthy appearance. The distance between different versions of the same face along the trustworthiness axis is set carefully in order to preserve the emotionally neutral expression of the faces and to prevent participants from differentiating which two versions are generated from the same face and also not to cause faces to look too unrealistic (Todorov et al 2008).

3.3 Stimuli Creation

For studying trustworthiness, The Trustworthiness Face Data Set 2 was chosen since it is designed with great elaboration to eliminate any confounding facial features such as skin, texture, and hair. On the other hand, in order to study pupil dynamics, brightness, color and illumination of the visual stimuli should be controlled to avoid their influence on pupils' reaction. Hence, pre-processing was applied on each face. The steps of pre-processing were done according to the methods described in Hepsomalı (2013) and Saracaydin (2015). A flowchart further explaining the steps of stimuli creation is provided in Figure 3.2.

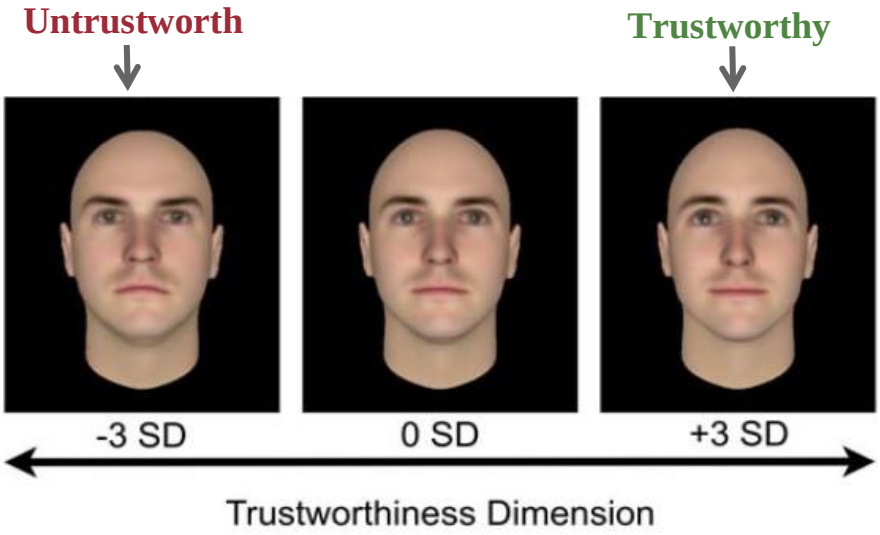

Figure 3.1 Sample stimuli from Trustworthiness Face Data Set 2

3.3.1 Image Pre-Processing

Image pre-processing was accomplished in 4 steps including screening and selection of the faces based on face size, cropping the face area, creating gray versions of the RGB images and brightness adjustment. All these steps were performed by using Adobe Photoshop CS6.

3.3.1.1 Face Size Screening and Selection

In order to control the perception of visual stimuli, a selection process was implemented based on the head size differences. Average width and length of all the 100 facial identities in the data set were 235.07 pixels *(SD = 9.19)* and 389.2 pixels *(SD =1.92)*, respectively (only the neutral faces were used in this step). Since the variances in length are negligible, a selection criterion is applied only depending on the width of the faces. Only faces of which width value lies within 1 SD of the mean were selected for further processing. This resulted in 72 facial identities (72 faces x 3 versions = 216 faces).

3.3.1.2 Converting from RGB to Gray Scale

The colored (RGB) images were converted into gray scale. Conversion is done by choosing Image>Mode>Grayscale in Photoshop CS6. The conversion to the grayscale was done in order to reduce the effect of illumination which is critical on pupillary responses.

3.3.1.3 Cropping Face Area

The present study was interested in only the facial area, hence any remaining parts of the faces were removed. First, the background is removed by using Magic Eraser Tool. Then, in order to keep only the facial area, neck region of the face images was cropped by using Quick Selection Tool. The edges of selection are softened via Refine Edge Option (Smooth: 20, Feather: 3.8, Contrast: 72). A gray background layer (R: 128 G: 128 B: 128) is created with 400 x 477 pixels.

3.3.1.4 Brightness Adjustment

In order to control brightness, mean intensity values of all images were obtained by using the histogram panel of Photoshop CS6. The average mean intensity values of all images were calculated as 131.18. Then, mean intensity values of all the images in the data set were set to the values that are similar to the averaged value by moving the slider in the Image>Brightness adjustment.

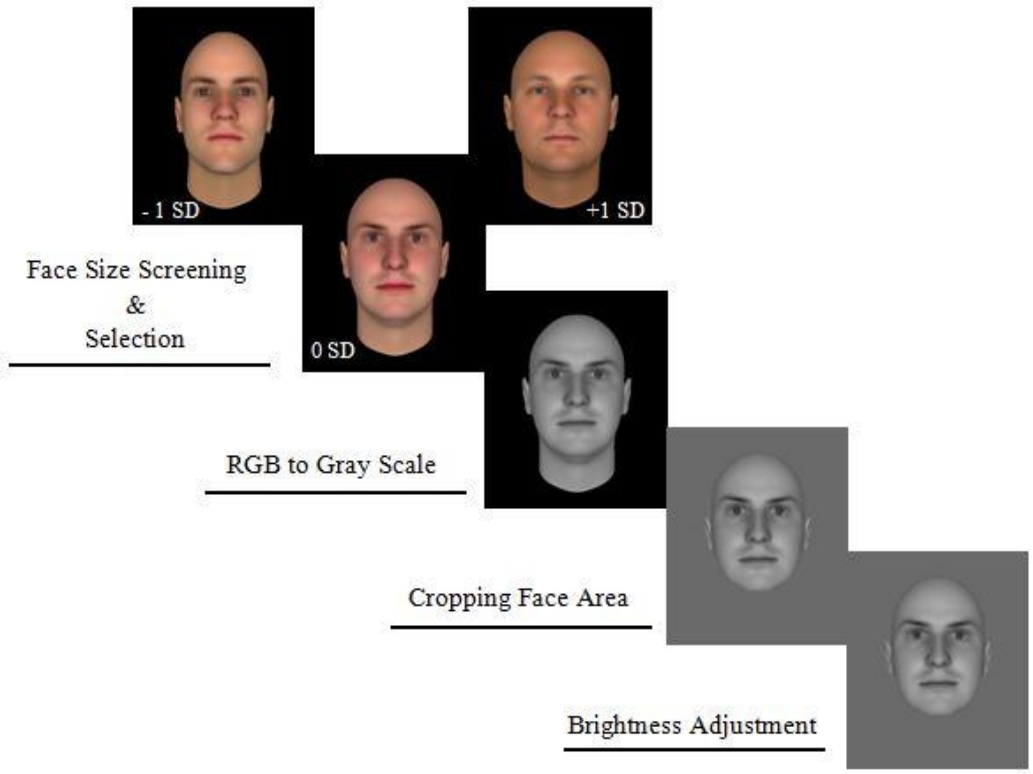

Figure 3.2 Flowchart of image pre-processing

3.4 Preliminary Study: Manipulation Check

Trustworthiness Face Data Set 2 is created by using a well validated method described in Oosterhof and Todorov (2008). Although the data set is composed of Caucasian facial identities manipulated along the trustworthiness dimension, some of the faces are found to be culturally distant and the manipulation on trustworthiness was found to be weak, subjectively. Thus, we conducted a preliminary study to serve as a manipulation check, to guarantee that faces in the data set are perceived in accordance with the trustworthiness manipulation by Turkish male participants. By this means, the main study would contain only a subset of the faces from the database, those that were the strongly recognizable to be trustworthy, neutral and untrustworthy.

3.4.1 Participants

The preliminary study participants were 14 heterosexual male the age of whom ranged from 22 to 34 *(M = 27.93, SD = 3.45)* with normal or corrected to normal visual ability. All the participants were healthy, did not have any neurological or psychiatric disorders and were not under any psychoactive, neurological medication. In terms of depression, only one participant, the BDI score of whom was higher than 20 was excluded from the pre study. In terms of mood, none of the participants were excluded because all participants were in positive mood with higher positive PANAS scores than negative PANAS scores. One participant did not complete the experiment by his own will such that his data were not used in subsequent analysis. Due to technical problems, the first half of one participant's data could not be used.

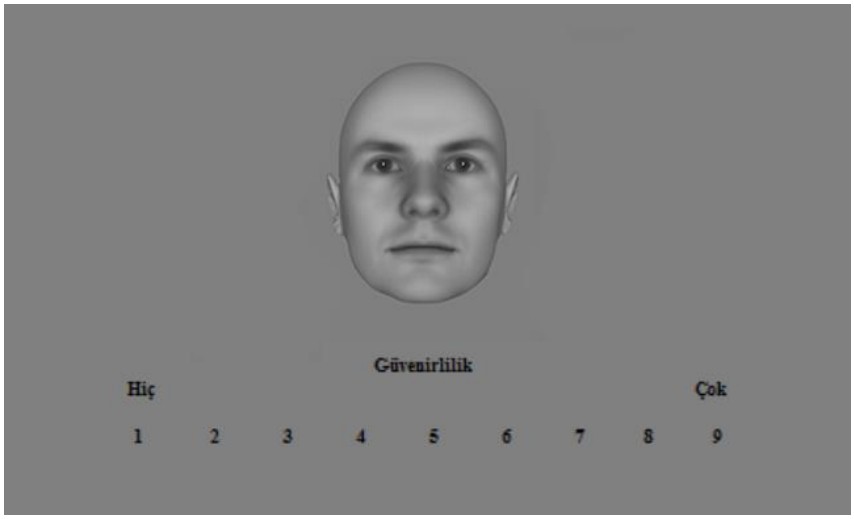

Figure 3.3 The stimulus display screen from pre study

3.4.2 Apparatus

The pre study was designed in E-Prime 2.0 software that the software was used for presentation of the stimuli and data recording purposes. All stimuli were presented on a 60 Hz 17" TFT monitor with 1280 x 768 pixels resolution screen based on Windows 10 desktop system. The data collection process was held in METUNeuro Lab in Middle East Technical University Informatics Institute.

3.4.3 Procedure

The preliminary study was conducted in a well-lit quiet room. Before the experiment, participants were asked to fill in demographic information form, BDI and PANAS. All the questionnaires were generated by using the online survey platform Qualtrics (www.qualtrics.com). The whole experiment took approximately 20 minutes.

In the preliminary study, participants were randomly presented 216 faces (72 facial identities in 3 different versions, trustworthy, neutral and untrustworthy) as experimental stimuli. In order to overcome boredom effect, the experiment was conducted in two sessions and in each session participants were presented with 108 faces. The visual stimuli were presented on the center of a gray background (R: 128 G: 128 B: 128). The order of the presentation of faces in each session was pseudo-randomized and order of the sessions was counterbalanced.

Before the initiation of the experiment, a brief verbal explanation about the experiment is delivered alongside with written instructions presented on the monitor screen. In the experiment each trial begun with a black fixation cross on the gray background (R: 128 G: 128 B: 128) which remained on the screen for 1 second. Following the fixation cross, the experimental stimulus was presented on the screen. Participants were asked to rate how trustworthy is the presented face on a 9 point Likert scale, ranging from 1= not at all to 9= very much. Each stimulus is shown to the participants until a response is given. The scale was always displayed below the experimental stimuli in each trial. Responses were given by pressing the numeric keys on the keyboard representing the trustworthiness scale. Although, there was no time constraint, participants were asked to respond as quickly as possible and rely on their gut feelings and not think about the pictures too much.

3.4.4 Results

Data was analyzed by using SPSS 21 (Statistical Package for the Social Sciences). Descriptive analysis was applied on the ratings of trustworthiness. The mean trustworthiness values of faces generated by trustworthiness model was calculated for each versions of trustworthiness (trustworthiness, neutral, untrustworthy). Untrustworthy faces were rated in the trustworthiness scale with a mean of 3.92 (*SD = 0.86*). Neutral faces were rated in the trustworthiness scale with a mean of 5.28 (*SD*

= *0.52*). Trustworthy faces were rated in the trustworthiness scale with a mean of 6.06 (*SD = 0.55*). Perceived trustworthiness ratings followed the trend proposed by the model, *F (1, 12) = 45.31, p < .001* (see Figure 3.4). In addition to that, item-wise analysis was applied on the data in order to reveal how trustworthiness ratings varied for each face. Although, each groups' ratings differed from each other significantly, item-wise analysis revealed trustworthiness ratings of groups have boundaries overlapping each other (see Figure 3.5 and Figure 3.6). In order to successfully determine which faces in the data set are perceived accordingly with trustworthiness manipulation, a selection process is applied based on the trustworthiness ratings. Only the faces, each version of which were clearly distinct from each other, were selected in terms of trustworthiness ratings. By that means, it would be possible to select only the faces, each version of which is strongly recognizable as according to the trustworthiness model. After the selection process, a subset of 40 faces was extracted (see Figure 3.4, 3.5, 3.6)

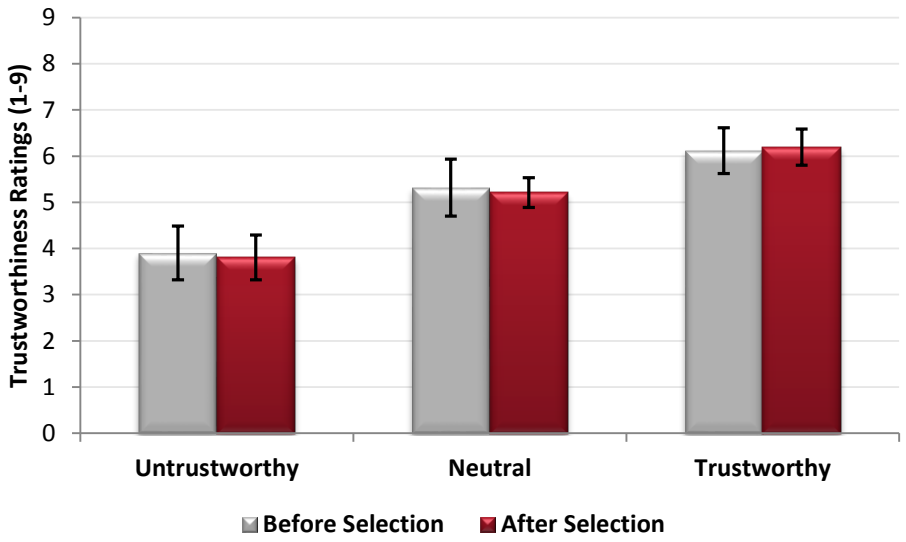

Figure 3.4 Mean trustworthiness ratings of faces - before and after the selection process (error bars represent standard deviation)

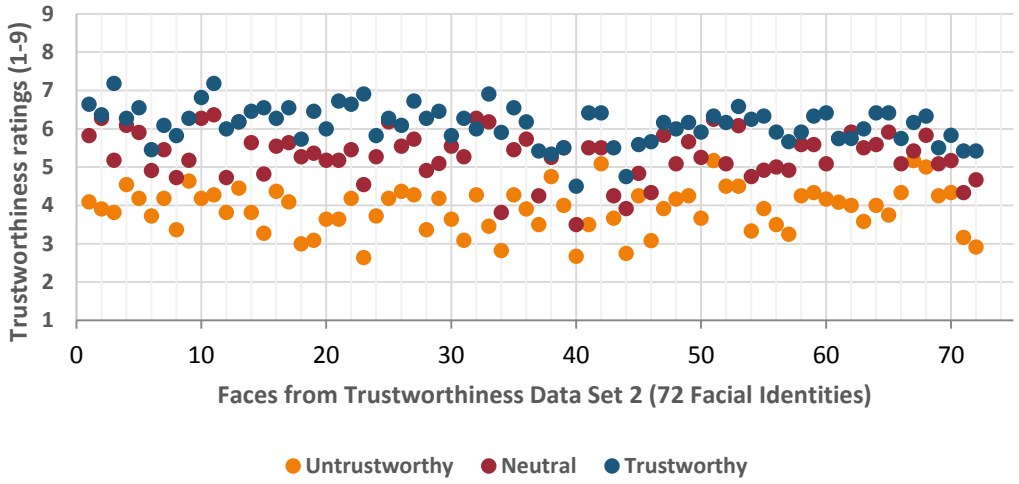

Figure 3.5 Trustworthiness ratings of the faces from Trustworthiness Face Data Set 2 acquired from the preliminary study. x-axis represents the faces from the data set. Colors are representing the versions of each face on different trustworthiness level.

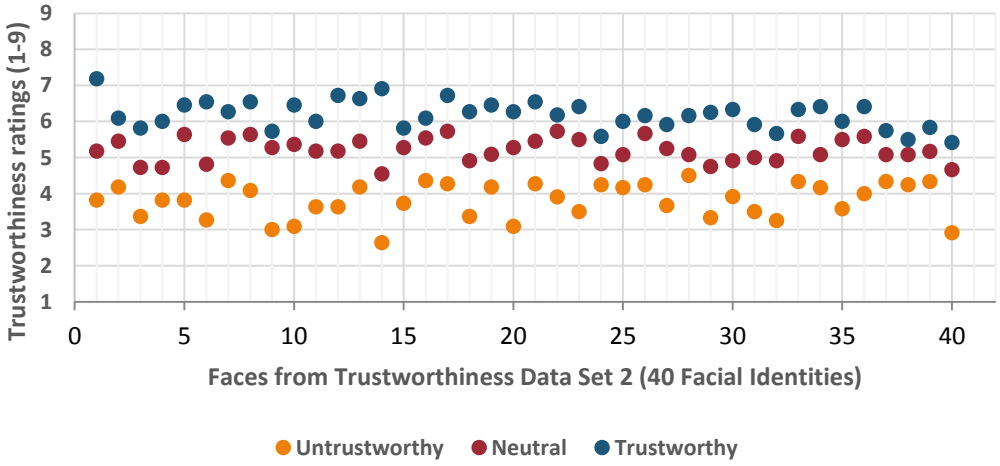

Figure 3.6 Trustworthiness ratings of the faces selected for main study. x-axis represents the faces from the data set. Colors are representing the versions of each face on different trustworthiness level.

Table 3.1 The mean values and standard deviations of the faces before and after selection process

FACES	Trustworthiness Ratings			
	Before Selection Process		After Selection Process	
	Mean	*SD*	*Mean*	*SD*
Untrustworthy	3,91	0,58	3,81	0,48
Neutral	5,32	0,61	5,21	0,32
Trustworthy	6,12	0,50	6,20	0,39

3.5 Main Study

The main study aims to find possible effects of intranasally administered oxytocin on pupil dilation and perceived trustworthiness rating during contextually different social cognition tasks in a subset of Trustworthiness Face Data Set 2.

3.5.1 Participants

The main study participants were 25 male subjects mainly from student population of METU and other neighboring universities (mean age = 22.88 ± 2.94, age range = 18-28). The participants were randomly assigned to oxytocin and placebo groups. Participant recruitment was achieved via advertising posters and handouts being distributed throughout the university and social media. The study was approved by METU Ethics Committee (see Appendix D) and all the subjects participated in the study provided written informed consent and were given an incentive of 20 TRY plus 8 GB flash disk for their contribution.

Inclusion Criteria:

Age 18-28, heterosexual male, non-smoker, normal visual ability (not corrected by glasses or contact lenses), not being on any prescribed psychoactive or neurological medication, not having a history of any neurological, psychiatric or relevant endocrinologic disorder, and not having nasal draining or lachrymation.

Exclusion Criteria:

In terms of depression, none of the participants were excluded (BDI scores of all the participants were 17 or lower). In terms of mood, only one participant, the negative PANAS score of whom was higher than positive PANAS score, was excluded from the study.

3.5.2 Apparatus

Stimulus presentation was handled via Experiment Builder (ver. 2.1.1), the display software for EyeLink System. Pupillometric data were recorded monocularly with EyeLink 1000 Plus eye tracker located at the Eye Tracking Lab at METU Informatics Institute (AZ-18)[2]. A desktop mount was used with forehead and chin rest enabling the participant to hold their head still by tactile support. Using chin rest is recommended while using desktop mount since it reduces head movements substantially. All stimuli were presented via Experiment Builder with 1024x768 pixel resolution and pupillary responses were collected via EyeLink 1000 Plus eye tracker monocularly from the right eye of the participants with data rate of 1000 Hz, on a 17" VGA monitor under the control of desktop computer with Windows 7 environment. The Eyelink 1000 Plus provides high precision measurement for estimating pupil diameter. Its resolution in detecting change in diameter of the pupil is .01% (Eyelink 1000 Plus User Manual, ver 1.09). The lightning of the room was set to dim light with 32.0 lux. Participants were positioned so that eyes align with the top quarter of the monitor and the distance from eyes to monitor was 75 cm (Distance A in Figure 3.7).

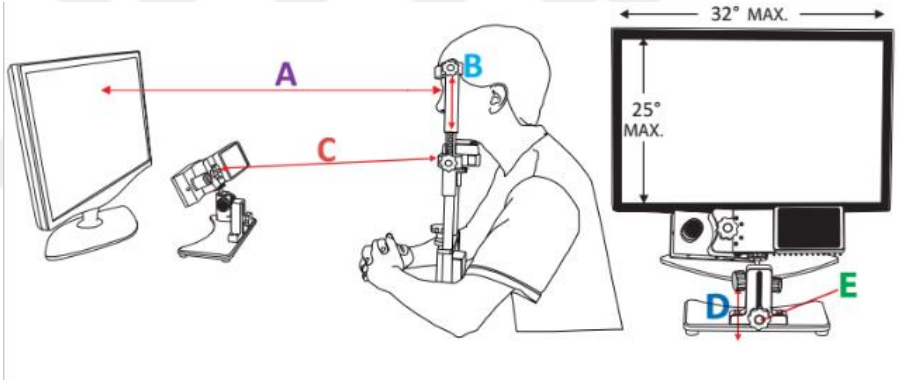

Figure 3.7 The apparatus and the position of the participant (Eyelink 1000 Plus Quick Start Guide, ver 1.00w)

3.5.3 Procedure

One day before the experimental days, participants were instructed to abstain from beverages with caffeine, nicotine, alcohol and any prescribed medication especially

[2] We are grateful to the cognitive science department and Assist. Prof. Cengiz Acarturk for letting us use the equipment for this thesis.

analgesics for 24 hours before experiment and abstain from any food and drink, except water, for 2 hours prior experiment. On arrival, participants were informed about the experimental procedure, intranasal administration of neuropeptide or saline solution and experimental stimuli. Subsequently, each volunteer filled demographic information (Appendix F), the BDI (Appendix B) for measuring level of depression, PANAS (Appendix C) for mood assessment, after they provided written consent (Appendix D). All questionnaires were generated by using the online survey platform Qualtrics (www.qualtrics.com). Completion of admission procedure generally took 10 minutes.

The overview of the experimental procedure for main study is presented in Figure 3.9. Accordingly, the main study is composed of two succeeding sessions, treatment session followed by experimental session. Treatment session involves intranasal administration of neuropeptide oxytocin or saline solution (0.9% saline). Based on recent research on neuropeptide oxytocin and its effects on CNS, administration of such neuropeptides (e.g. vasopressin and oxytocin) via nasal route enables them to directly pass to central nervous system (Born et al., 2002) which makes the intranasal administration a great tool to study oxytocin in humans without observing any harmful side effects (Heinrichs et al., 2003, 2004).

Applying the standardized protocol of administration of intranasal oxytocin, each volunteer received either a single dose of 24 IU of oxytocin (Syntocinon Spray; Novartis; three puffs per nostril = 6 puffs) or saline solution. Participants were randomly assigned to either oxytocin or placebo groups that it was a single-blind experiment design. Thus, the experimenter (A.K.) was aware of the content of the bottle the participant received, while the participant was unaware of it. This was verified by the end of the experiment. Participants self-administered neuropeptide or saline solution according to their assigned group under supervision of the experimenter (A.K.) and waited 40 minutes before the experimental session commenced. During this waiting period, each participant was seated alone and was asked to remove their mobile phones outside the lab and refrain from any type of social interaction. Duration of waiting period is consistent with time when the neuropeptide oxytocin to reach a plateau level in central nervous system (Born et al., 2002).

Experimental session was composed of two blocks conducted subsequently with a 5 minutes break between them (Task 1 and Task 2). In each block, participants performed a trustworthiness rating task in which a subset of Trustworthiness Face Data Set 2 was used as experimental stimuli. The subset was composed of 40 facial identities (40 x 3 levels = 120 faces) chosen as a result of the aforementioned preliminary study. Three different levels of trustworthiness of each facial identity were present in the dataset. The constructed subset is equally distributed to two runs and in order to make sure that there is no difference between the faces allocated to two runs, trustworthiness ratings of each face were analyzed by t-test and found to be non-significant for each trustworthiness level ($p = 0.31$ for trustworthy, $p = 0.27$ for neutral, $p = 0.81$ for untrustworthy). Therefore, each run contained 20 trustworthy

faces, 20 neutral faces and 20 untrustworthy faces with non-overlapping boundaries between the levels and the experimental stimuli used in experiments were identical with regard to trustworthiness level. The complete list of experimental stimuli used in experiments is listed in Appendix H.

The waiting period ended forty minutes after substance administration. Following that, participants were asked to perform a perceived trustworthiness rating task in two runs where 60 faces were presented in each block at the center of a monitor screen where gray background (R:128 G:128 B:128) is used while face images were precisely arranged to fall in the 15^{o} visual angle of the participant. Before initiation of the experiment, the instructions on how the tasks should be performed were read aloud and explained; written instructions were also provided on the monitor screen. At the beginning of each block, the participant was provided with a scenario to base their judgement on as they rate the trustworthiness level of the presented faces. The scenarios were containing contextual informations for being in a specific situation while making the trustworthiness judgements. While scenario of task 1 contained an approach related context, the scenario of task 2 involved a trust related context.

Task 1 – Approach Context

"You are in a foreign city and need to find an address. You have decided to ask for directions. Will you approach and ask directions to the person whose face appears on the screen?"

Task 2 – Trust Context

"You are at the subway station abroad. Somebody comes up and asks your mobile phone for an urgent call. Will you trust him and give your phone to the person whose face appears on the screen?"

In each block, every trial started with a black fixation cross presented on the gray background (R: 128 G: 128 B: 128) for 2 seconds. Following the fixation cross, each face was shown one at a time and remained on the screen for four seconds for participants' evaluation. After four seconds, facial image is replaced with a response screen and remained until a response was given (see Figure 3.8). Participants made their judgments by a wireless mouse click, on a 9-point Likert scale, ranging from 1= not trustworthy at all to 9= very trustworthy. Although, there was no time constraint, participants were asked to respond as quickly as possible and rely on their gut feelings since there is no right or wrong answer. The order of the tasks was counterbalanced among the participants. The order of the experimental stimuli was randomized in a way that no more than two faces of the same trustworthiness level occur consecutively. Participants were tested individually in an empty lab with a dim light (32.0 lux) where a curtain was present in the room to separate the experimenter and the participant during each run. At the beginning of each run, 9-point calibration of EyeLink 1000 Plus System was applied.

3.5.4 Analysis

Item-based analysis was conducted by separate 2x2x3 mixed design analysis of variances (mixed ANOVA) for trustworthiness ratings, reaction times and pupillary responses separately. Since the item size (N=120) was five times greater than the participant size (N=24), this analysis was mandatory to increase statistical power. Drug administration (2: oxytocin, placebo) was taken as within-subjects factor while task (2: approach, trust) and trustworthiness level of face images (3: untrustworthy, neutral, trustworthy) were taken as between-subjects factors. Bonferroni correction was applied for pairwise comparisons after significant main effects. The results are reported in the following section.

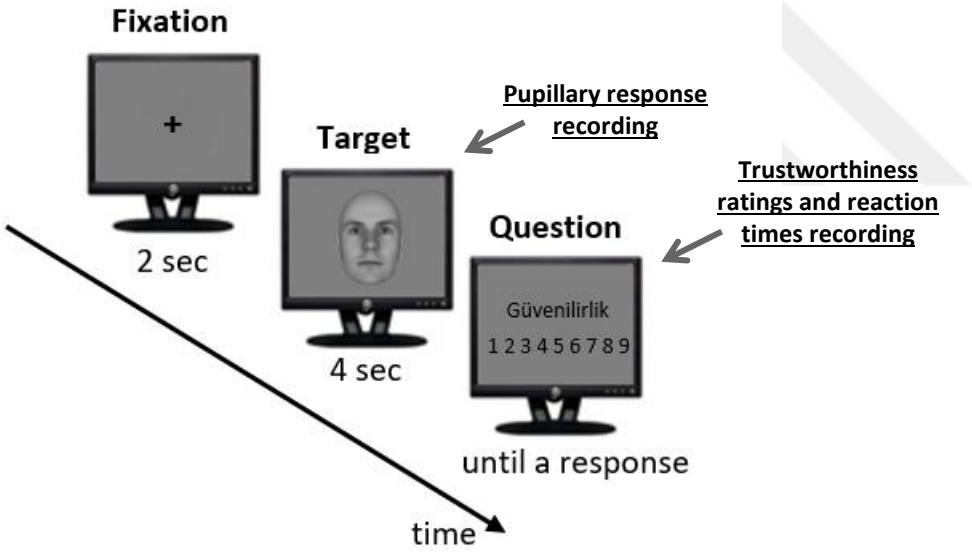

Figure 3.8 Overview of experimental flow for trustworthiness judgment task.

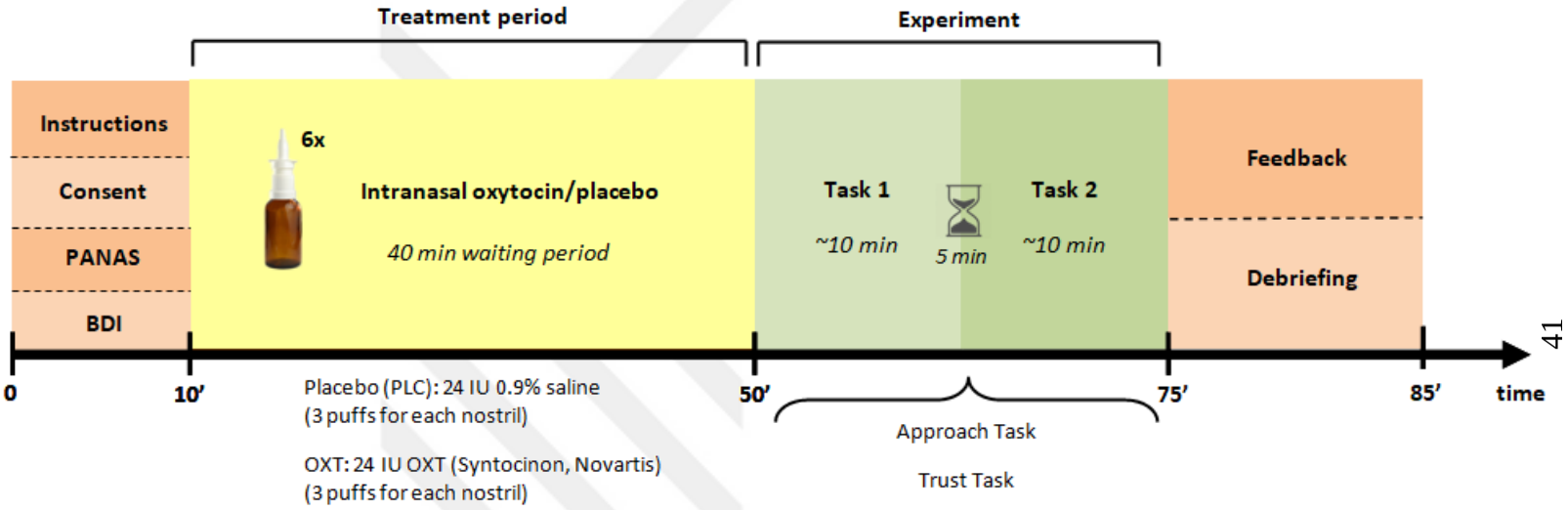

Figure 3.9 Overview of the study design (Adapted from Leknes et al., 2013)

CHAPTER 4

RESULTS

4.1 Behavioral Data

4.1.1 Item-wise Analysis on Trustworthiness Ratings

Taking into consideration that the number of items (i.e. the face images N = 120) in the conducted study is much larger than the number of subjects (N = 24) participated in the study, an item-wise approach is favored to analyze the outcome of the study. In contrast to conventional participant-wise analysis, applying an item-wise analysis is expected to enhance statistical significance of the current study. For the results of conventional participant-wise analysis on behavioral data, please see Appendix A.

In the item-wise analysis, the experimental stimuli are regarded as participants such that drug condition (oxytocin and placebo) becomes a within-subjects factor whereas trustworthiness level of the face images (untrustworthy, neutral and trustworthy) and task type (approach task and trust task) were studied as between-subjects factors. Therefore, a 2 (task: approach, trust) x 3 (face: untrustworthy, neutral, trustworthy) x 2 (drug: oxytocin, placebo) mixed ANOVA was applied on the trustworthiness ratings given to each face image by participants who received oxytocin and placebo in approach and trust tasks. There was a significant main effect of drug condition that ratings from participants who received oxytocin differed significantly from participants who received placebo, $F\ (1, 114) = 8.754,\ p = .004,\ \eta = .07$ (See Figure 4.1 for overall distrubition of scores in both oxytocin and placebo groups).

4.1.1.1 Manipulation Check

There was also a significant main effect of the task where participants evaluated faces in different scenarios, on the ratings of trustworthiness, $F\ (1, 114) = 94.53,\ p < .001,\ \eta = .99$. According to that, trustworthiness ratings of faces were higher in the approach task $(M = 4.71,\ SD = 1.01)$ as compared to trust task $(M = 4.01,\ SD = .97)$. Thus, the different scenarios given in approach and trust task were effective in prompting different trustworthiness ratings.

There was also a significant main effect of the level of trustworthiness of the faces on the ratings of trustworthiness, *F (1, 114) = 290.08, p < .001, η = .84*. Following contrasts revealed that, while untrustworthy faces *(M = 3.21, SD = .61)* were rated significantly lower than neutral faces *(M = 4.54, SD = .5, p < .001)*, trustworthy *(M = 5.32, SD = .59)* faces were rated significantly higher than neutral faces *(p < .001)*. In addition to that, there was no significant face type x task interaction on the trustworthiness ratings of the faces, *F (2, 114) = .114, p = .892, η = .002*. Hence, all these findings revealed that the manipulation on the trustworthiness levels of the faces, and manipulation on task difference were verified (see Figure 4.2 and 4.3).

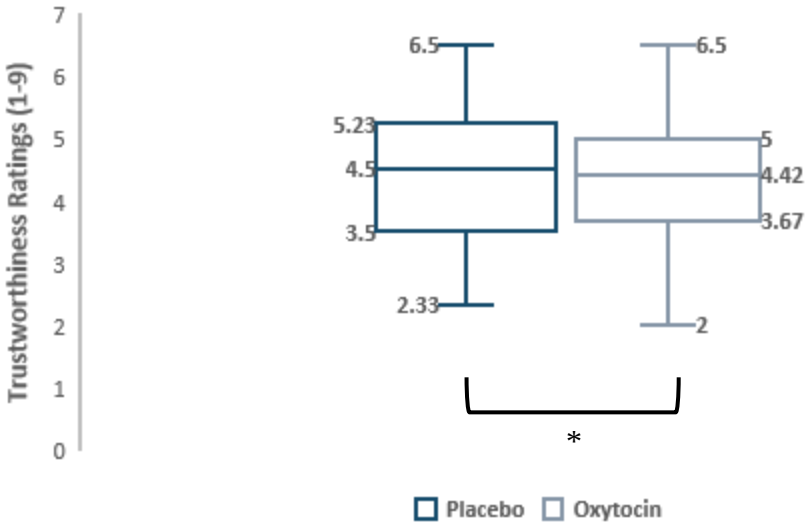

Figure 4.1 Trustworthiness ratings of faces in oxytocin and placebo groups:
* p = .004

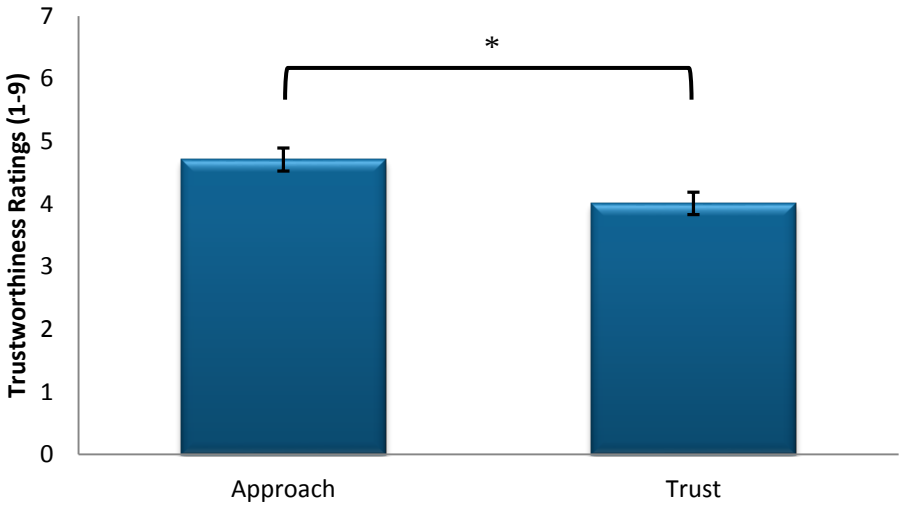

Figure 4.2 Trustworthiness ratings of faces in both approach and trust tasks (error bars represent standard error): *p < .001.

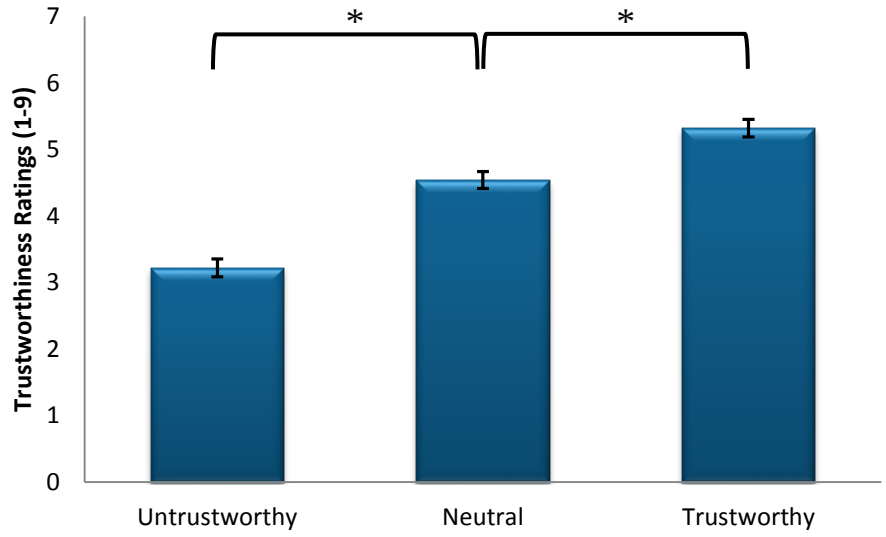

Figure 4.3 Trustworthiness ratings of trustworthy, neutral and untrustworthy faces (error bars represent standard error): *p < .001.

4.1.1.2 The interaction between drug and task

There was also a significant interaction effect such that the drug the participant received interacted with the task in which the faces were evaluated according to different scenarios (approach vs. trust), $F\ (1,\ 114) = 45.81,\ p < .001,\ \eta = .29$. This

effect indicates that the trustworthiness ratings given to faces in two different tasks were affected differently by the placebo and oxytocin conditions. The same faces in the approach task were rated more trustworthy by the participants who received oxytocin *(M = 4.78, SD = .87*) as compared to participants who received placebo *(M = 4.64, SD = 1.14)*. On the other hand, the same faces in the trust task were rated more untrustworthy by the participants who received oxytocin *(M = 3.83, SD = .98)* as compared to participants who received placebo *(M = 4.19, SD = .93)*. According to that, while oxytocin increased the trustworthiness ratings of the faces in the approach task, it lowered them in the trust task (see Figure 4.4).

4.1.1.3 The interaction between drug and trustworthiness level of the faces

There was also a significant interaction effect such that the drug the participants received interacted with the trustworthiness level of the faces being evaluated (untrustworthy, neutral, trustworthy) in approach and trust tasks combined, $F\ (2, 114) = 8.43$, $p < .001$, $\eta = .13$. This effect indicates that the trustworthiness ratings given to faces of different trustworthiness level were affected differently by the placebo and oxytocin conditions. The graph in Figure 4.5 presents the nature of this interaction. According to that, untrustworthy faces *($M_{OXT} = 3.21$, $SD_{OXT} = .71$; $M_{PLC} = 3.23$, $SD_{PLC} = .51$)* and neutral faces *($M_{OXT} = 4.55$, $SD_{OXT} = .62$; $M_{PLC} = 4.53$, $SD_{PLC} = .52$)* were rated similarly across the oxytocin and placebo groups. However, participants in oxytocin group rated trustworthy faces *($M_{OXT} = 5.16$, $SD_{OXT} = .61$; $M_{PLC} = 5.48$, $SD_{PLC} = .52$)* as less trustworthy when compared to participants in placebo group (See Figure 4.5). This interaction is further broken down below where the interaction between drug, task and trustworthiness level of the faces were reported.

4.1.1.4 The interaction between drug, task and trustworthiness level of the faces

The three-way interaction analyzes whether the drug x task interaction described above is same for each trustworthiness level of the faces. Finally, there was a significant drug (placebo, oxytocin) x task (approach, trust) x trustworthiness level of faces (untrustworthy, neutral and trustworthy) interaction effect, $F\ (2, 114) = 8.81$, $p < .001$, $\eta = .13$. The interaction points out that, the combined effect of the drug the participants received and the task according to which the faces were evaluated significantly differ in different levels of trustworthiness of faces. The overall nature of the interaction is presented in Figure 4.6. This interaction is further broken down for each trustworthiness level of the faces below (see Figure 4.7, 4.8 and 4.9.).

Untrustworthy faces were rated lower in trust task as compared to approach task by the participants who received placebo. However, this difference in the trustworthiness ratings of untrustworthy faces was increased in the oxytocin condition. Untrustworthy faces were rated as more trustworthy in approach task and less trustworthy in trust task by the participants who received oxytocin as compared to ratings of participants

who received placebo. Thus, while oxytocin decreases the trustworthiness ratings of untrustworthy faces in trust task (oxytocin, M = 2.61, SD = .36; placebo, M = 3.11, SD = .41, $p < .001$), it increased the trustworthiness ratings in approach task (oxytocin, M = 3.80, SD = .38; placebo, M = 3.36, SD = .55, $p < .001$; see Figure 4.7).

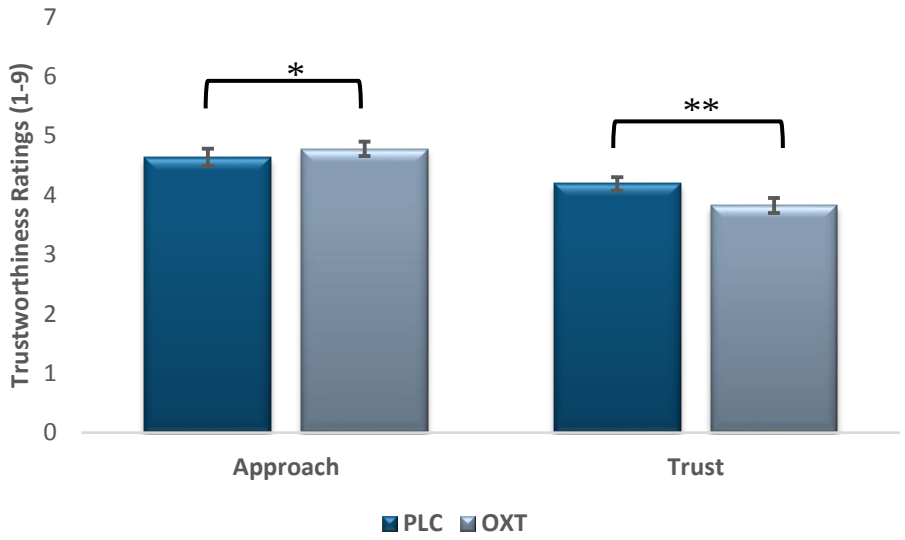

Figure 4.4 Trustworthiness ratings of approach and trust tasks in both oxytocin and placebo groups (error bars represent standard error): *p = .008, **p < .001.

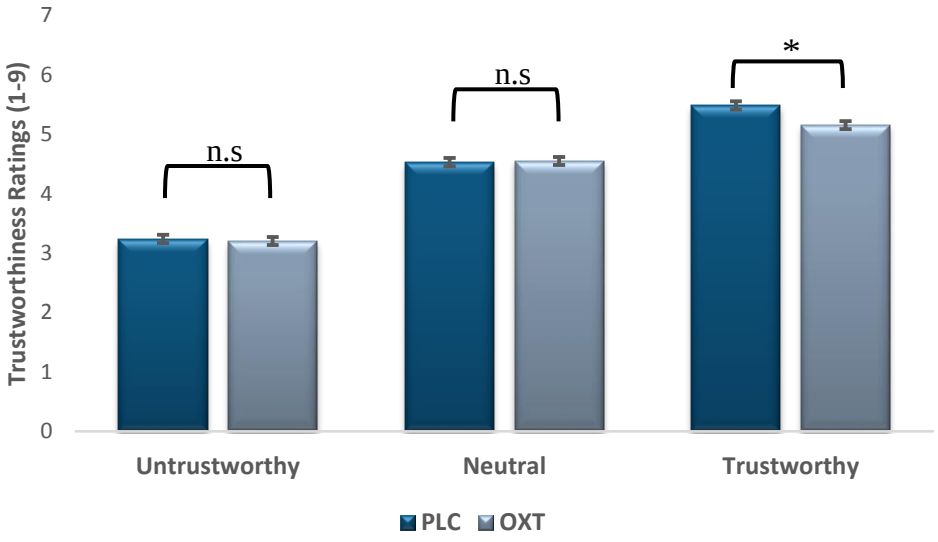

Figure 4.5 Trustworthiness ratings of trustworthy, neutral and untrustworthy faces in both oxytocin and placebo groups (error bars represent standard error): *p < .001.

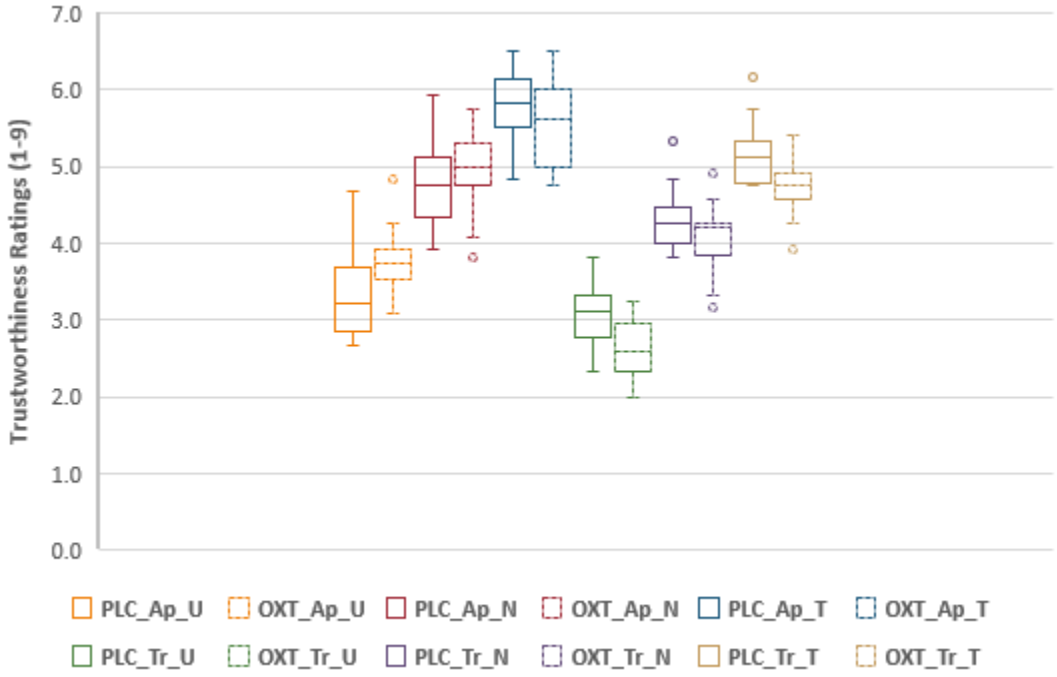

Figure 4.6 Trustworthiness ratings of trustworthy, neutral and untrustworthy faces in both oxytocin and placebo groups during approach and trust tasks.

(PLC=Placebo, OXT=Oxytocin, Ap=Approach, TR=Trust, U=Untrustworhty, N=Neutral, T=Trustworthy)

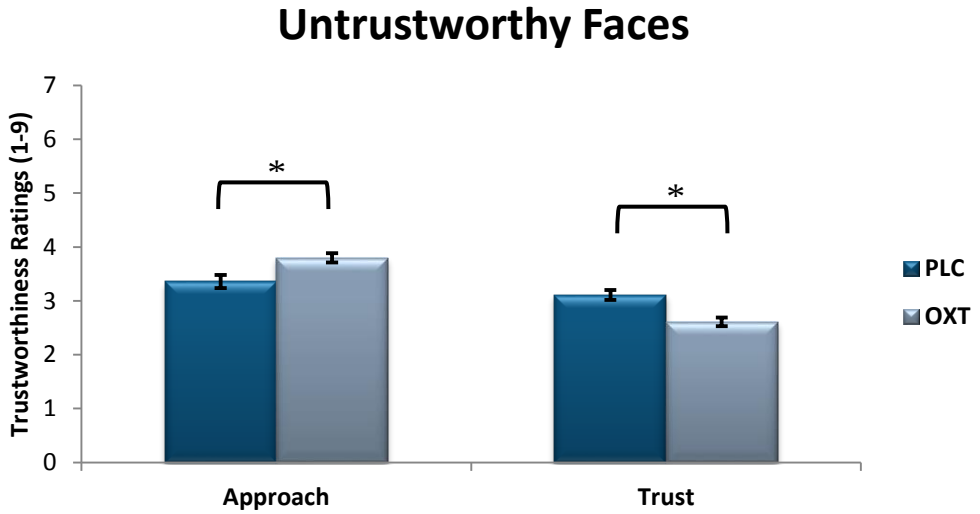

Figure 4.7 Trustworthiness ratings of untrustworthy faces evaluated in approach and trust tasks in both oxytocin and placebo groups (error bars represent standard error): *p < .001.

Likewise, neutral faces were rated lower in trust task as compared to approach task by the participants who received placebo. However, this difference in the trustworthiness ratings of neutral faces was increased in the oxytocin condition that neutral faces were rated as more trustworthy in approach task and less trustworthy in trust task by the participants who received oxytocin as compared to ratings of participants who received placebo. Thus, while oxytocin decreased the trustworthiness ratings of neutral faces in trust task (oxytocin, M = 4.12, SD = .42; placebo, M = 4.30, SD = .36, p = .049), it increased the trustworthiness ratings in approach task (oxytocin, M = 4.98, SD = .45; placebo, M = 4.75, SD = .54, p = .014; see Figure 4.8).

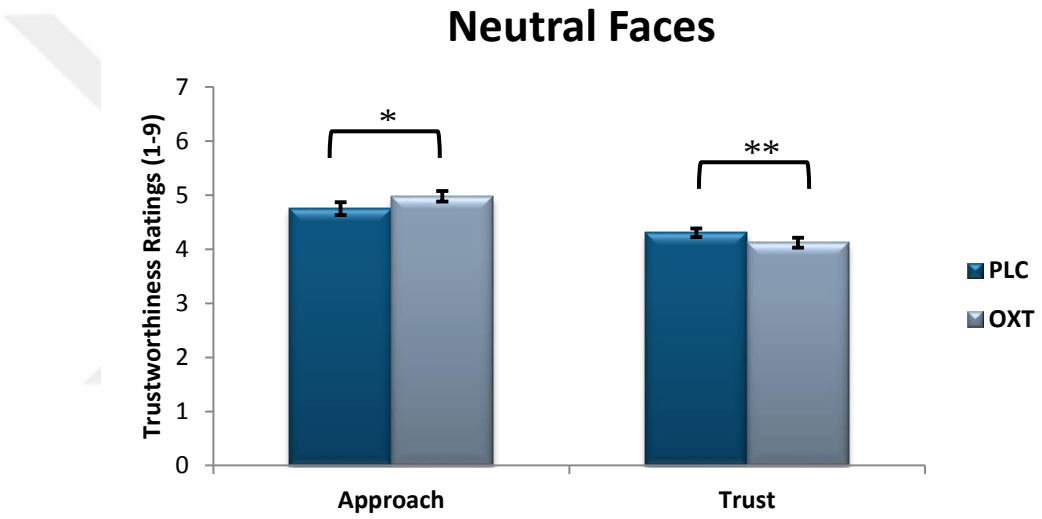

Figure 4.8 Trustworthiness ratings of neutral faces evaluated in approach and trust tasks in both oxytocin and placebo groups (error bars represent standard error): *p = .014, **p = .049.

Trustworthy faces were rated lower in trust task as compared to approach task by the participants who received placebo. Contrasting to other face groups, this difference in trustworthiness ratings of trustworthy faces between approach and trust tasks remained in oxytocin condition as well. Thus, the interaction between the task and the drug is diminished in the trustworthiness ratings of trustworthy faces. Therefore, oxytocin decreases the trustworthiness ratings of trustworthy faces in both approach task (oxytocin, M = 5.57, SD = .52; placebo, M = 5.80, SD = .44, p = .011) and trust task (oxytocin, M = 4.75, SD = .34; placebo, M = 5.16, SD = .36, p < .001) where participants rated faces according to different scenarios (see Figure 4.9).

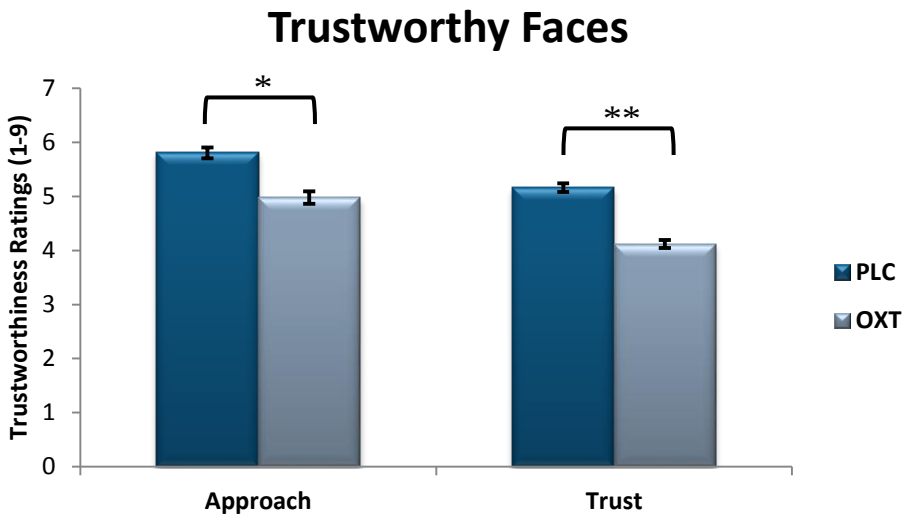

Figure 4.9 Trustworthiness ratings of trustworthy faces evaluated in approach and trust tasks in both oxytocin and placebo groups (error bars represent standard error): *p = .011, **p < .001.

4.1.2 Item-wise Analysis on Reaction Times

Analyzing reaction time requires removal of excessive durations and spotting any outliers found in the data. In order to set thresholds for reaction time duration, descriptive statistics of the data were analyzed, *M = 1491.3, SD = 963.19*. Any reaction time above or below 2.5 SD of the mean is set to be as an excessive duration and removed. In addition to that, any reaction time shorter than 300 ms is also set to be an excessive duration and removed, since a response given in such short time interval thought to be an artifact. Based on excessive duration criteria, 3.54% of the data (102/2880 trials) were excluded from the further analysis. Any participants of whom 30% of trials were excluded as outliers would also be excluded from the study, but none of the subjects participated in the study were met this condition. To search for any outliers within the groups, reaction times for placebo and oxytocin groups were transformed into z-scores, then any score falling within the interval of, higher than 2 and lower than -2 were spotted and removed as outliers, .24% of the data (7/2880 trials). For item-wise analysis on reaction time, similar statistical designs described for trustworthiness ratings were applied.

A 2 (task: approach, trust) x 3 (face: untrustworthy, neutral, trustworthy) x 2 (drug: oxytocin, placebo) mixed ANOVA was applied on the reaction time during trustworthiness evaluation for each face image by participants who received oxytocin and placebo in approach and trust tasks. There was a significant main effect of drug condition that reaction time from participants who received oxytocin differed

significantly from participants who received placebo, *F (1, 107) = 112.81, p < .001, η = .51*. On average, participants who received oxytocin *(M = 1245.34, SD = 159.67)*, significantly were faster while evaluating trustworthiness of the faces than participants who received placebo *(M= 1485.03, SD = 184.45;* see Figure 4.10*)*.

There was a significant main effect of the trustworthiness level of the faces on the reaction time during trustworthiness evaluation of faces, *F (1, 107) = 7.74, p = .001, η = .13* (see Figure 4.11). Bonferonni post-hoc tests revealed that, corrected pairwise comparisons revealed that untrustworthy faces *(M = 1423.23, SD = 202.80)* were evaluated longer than both neutral faces *(M = 1322.12, SD = 212.56, p = 001)* and trustworthy faces *(M = 1363.10, SD = 203.17, p = .044)*, difference in evaluation time of neutral faces and trustworthy faces were found not to be significant *(p=.473)*.

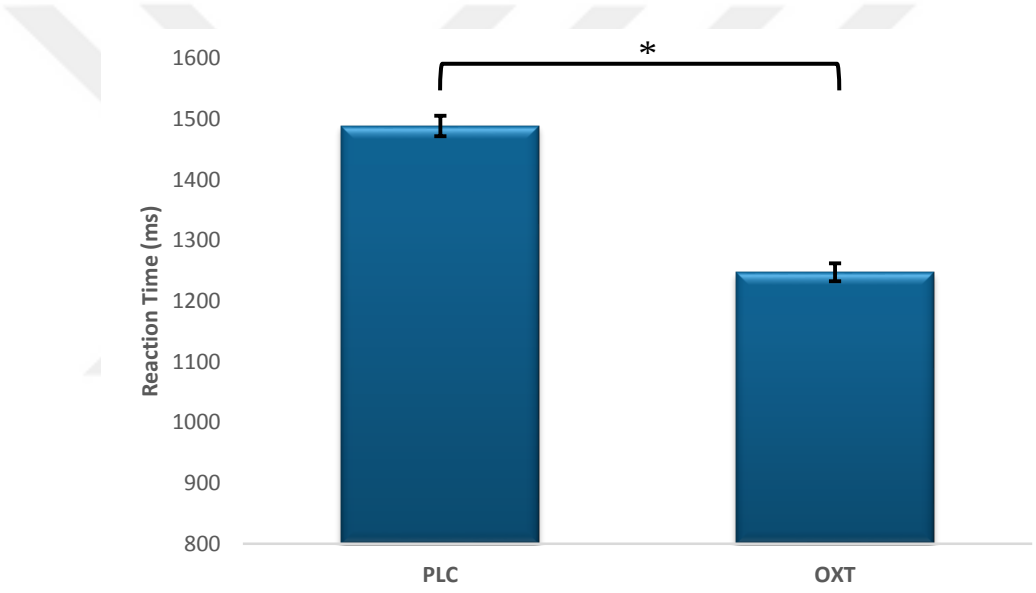

Figure 4.10 Reaction times of faces in both oxytocin and placebo groups (error bars represent standard error): *p < .001.

However, there was not a significant main effect of the task on reaction time during trustworthiness evaluation where faces were rated according to different scenarios, *F (1, 107) = .031, p = .86, η = .00* (see Figure 4.12). According to that, participants did not differ in their reaction time while evaluating faces in approach task *(M = 1367.01, SD = 213.09)* and trust task *(M = 1370.58, SD = 206.93)*.

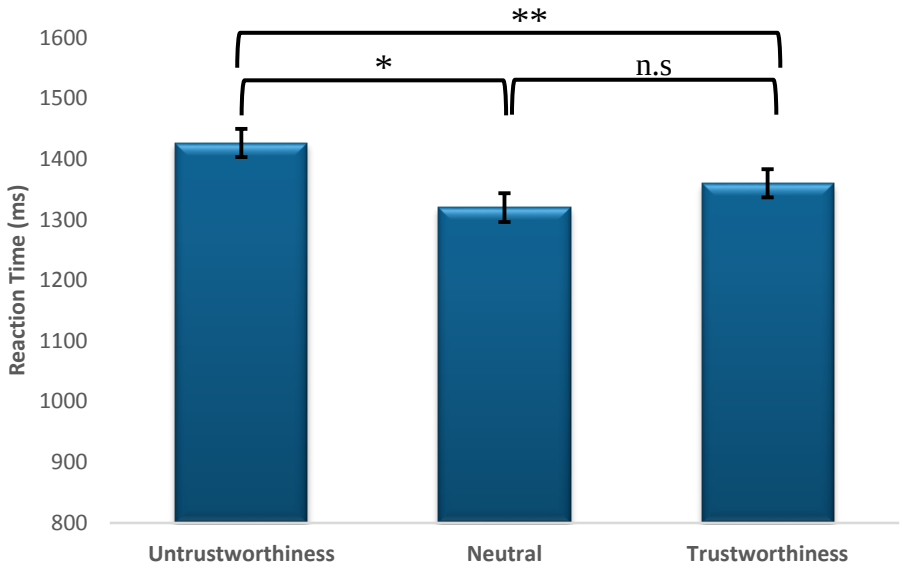

Figure 4.11 Reaction times of trustworthy, neutral and untrustworthy faces (error bars represent standard error): *p < .001, **p = .044.

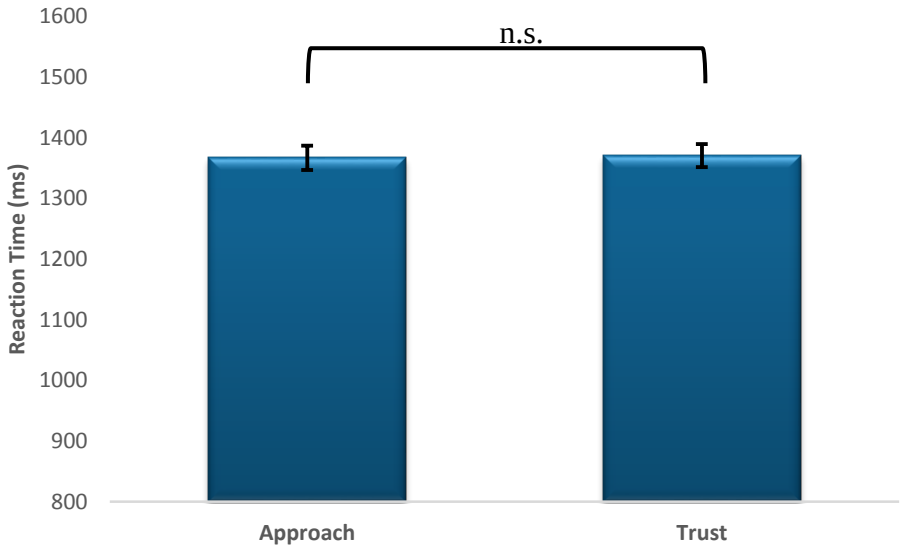

Figure 4.12 Reaction times of faces in both approach and trust task (error bars represent standard error)

4.1.2.1 The interaction between drug and task

There was no 2-way significant interaction such that the drug the participants received did not interact with the task in which the faces were evaluated according to different

scenarios (approach vs. trust), $F\ (1,\ 107) = .58,\ p < .45,\ \eta = .01$ (see Figure 4.13). The absence of the interaction effect indicates that the reaction times during trustworthiness evaluation of the faces on two different tasks were affected similarly by the placebo and oxytocin conditions. In other words, oxytocin did not affect the reaction times of trustworthiness evaluation in a task dependent manner (approach: M_{PLC} = 1495.63 SD_{PLC} = 169.69, M_{OXT} = 1236.13 SD_{OXT} = 168.98; trust: M_{PLC} = 1482.10 SD_{PLC} = 196.29, M_{OXT} = 1259.07 SD_{OXT} = 150.18; see Figure 4.4).

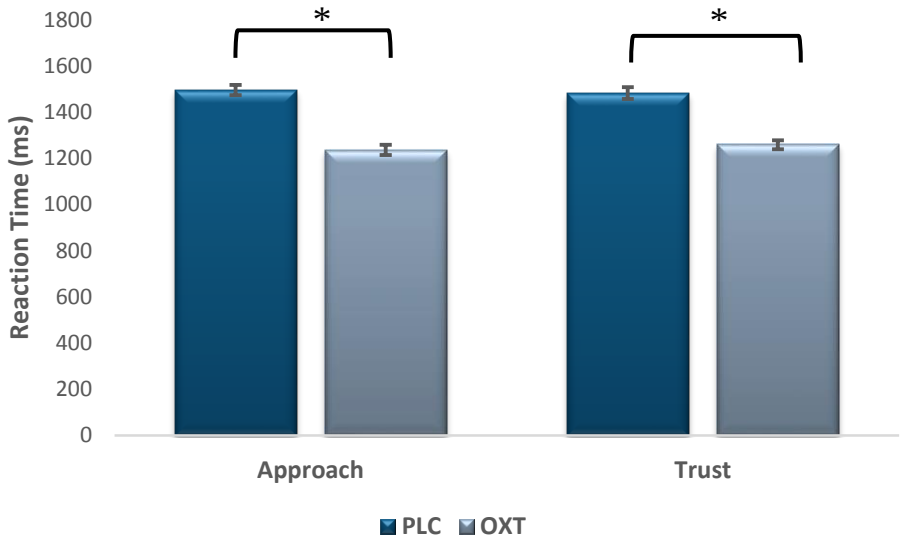

Figure 4.13 Reaction times of approach and trust tasks in both oxytocin and placebo groups (error bars represent standard error): *p < .001.

4.1.2.2 The interaction between drug and trustworthiness level of the faces

There was no 2-way significant interaction such that the drug the participants received did not interact with the trustworthiness level of the faces being evaluated (untrustworthy, neutral, trustworthy), $F\ (2,\ 107) = .07,\ p < .94,\ \eta = .00$. The absence of the interaction effect indicates that the reaction times during trustworthiness evaluation of the faces on different trustworthiness level of the faces were not affected differently by the placebo and oxytocin conditions. According to that, oxytocin did not affect the reaction times of trustworthiness evaluation according to the trustworthiness level of the face.

4.1.2.3 The interaction between drug, task and trustworthiness level of the faces

The three-way interaction analyzes whether the drug x task interaction described above is same for each trustworthiness level of the faces. However, unlike two-way interactions, there was a significant drug (placebo, oxytocin) x task (approach, trust)

x trustworthiness level of faces (untrustworthy, neutral and trustworthy) interaction effect, $F\ (2, 107) = 3.20$, $p = .045$, $\eta = .06$. The interaction points out that, the combined effect of the task according to which the faces were evaluated and the different levels of trustworthiness of faces interacted significantly differs across the participants who received placebo and oxytocin.

The nature of the interaction is presented in Figure 4.14. According to that, neutral faces were evaluated faster in approach task as compared to trust task by both participants who received oxytocin and placebo. On the other hand, while trustworthy faces were evaluated slower in approach task compared to trust task by the participants who received placebo, they were evaluated in opposite fashion by the participants who received oxytocin that participants in oxytocin group evaluated trustworthy faces faster in approach task compared to trust task. Alongside with that, while untrustworthy faces were evaluated faster in approach task compared to trust task by the participants who received placebo, they were evaluated in opposite fashion by the participants who received oxytocin that participants in oxytocin group evaluated untrustworthy faces slower in approach task compared to trust task. Therefore, oxytocin converges reaction times towards different trustworthiness level of faces in the trust task, whereas it diverges reaction times towards different trustworthiness level of faces in the approach task.

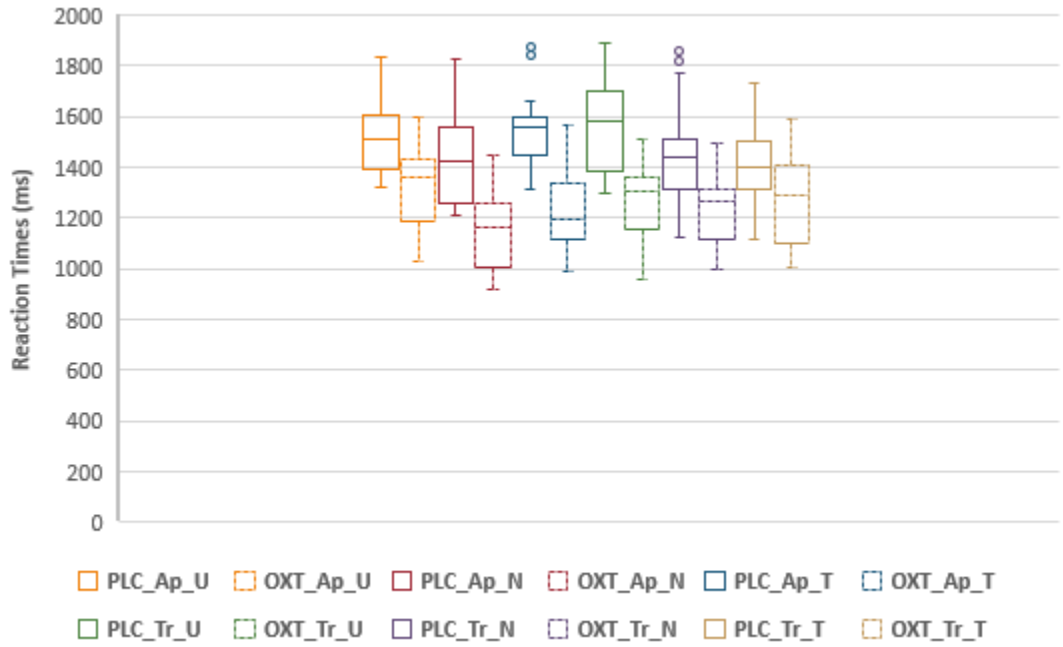

Figure 4.14 Reaction times of trustworthy, neutral and untrustworthy faces evaluated in approach and trust tasks in both oxytocin and placebo groups

(PLC=Placebo, OXT=Oxytocin, Ap=Approach, TR=Trust, U=Untrustworhty, N=Neutral, T=Trustworthy)

4.2 Physiological Data

4.2.1 Item-wise Analysis on Pupillary Responses

For the current study, only pupillary responses collected as pupil diameter were used for analysis. The collected data is extracted by selecting the 4-second display time of the face images plus 200 ms before this display time (last 200 ms of fixation cross screen). Since the data collection rate was 1000 Hz, there were 4200 data points which were gathered for each trial (see Figure 4.15). Therefore, data during the response screen were discarded from analysis. Preprocessing steps of pupillary response include the reconstruction of the region in the signal with eyeblinks using interpolation, median filtering and smoothing of the signal, as well as baseline correction. Any pupillary signal which lacks light-reflex or lacks a dilation peak is discarded. All the pre-processing steps were applied using MATLAB (R2014b) and Python (version 3.6.1).

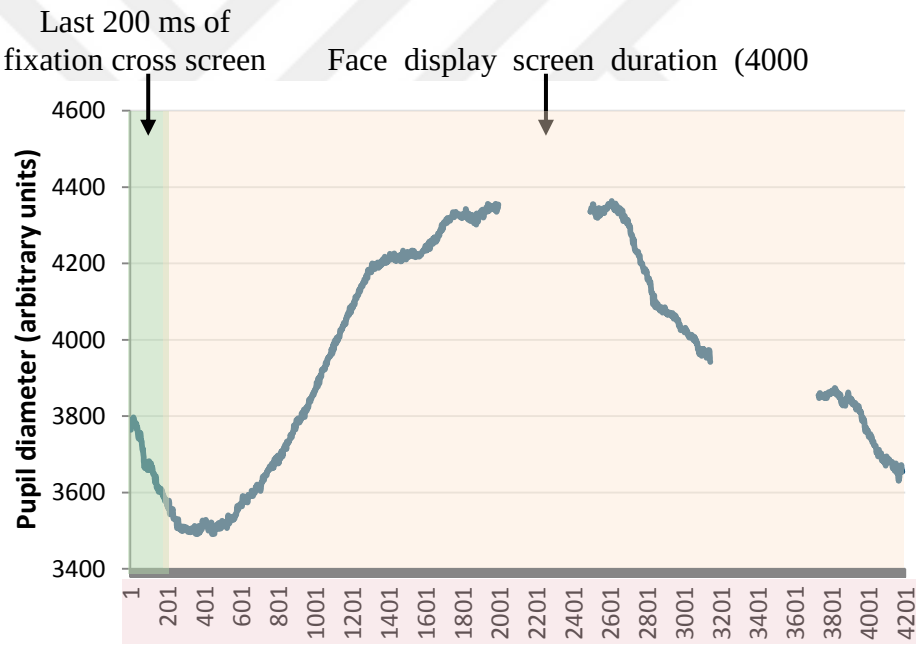

Figure 4.15 Sample trial with 4200 pupil diameter data points

First of all, any blinks found in the pupillary data were spotted and if it met any exclusion condition, the trial for which pupillary data belongs was removed from the analysis (Figure 4.16 and 4.17). Blink exclusion criteria includes having a total blink duration more than 1500 milliseconds in a trial (more than 1/3 of the duration of the trial), having a blink more than 150 milliseconds found within the 200 milliseconds of the beginning of the trial where the baseline correction applied and having a blink more than ¾ of a second (750 milliseconds). Based on blink exclusion criteria, 1.18 % (34/2880 trials) of the data were removed.

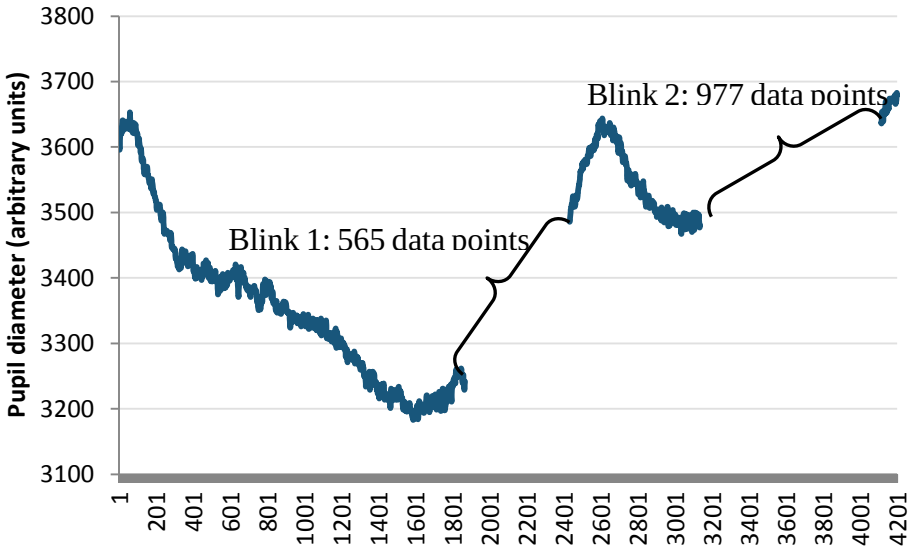

Figure 4.16 Excessive blink removal: single blinks longer than 750 data points (Blink 2) and total blink duration longer than 1500 data points (Blink 1 + Blink 2= 1542)

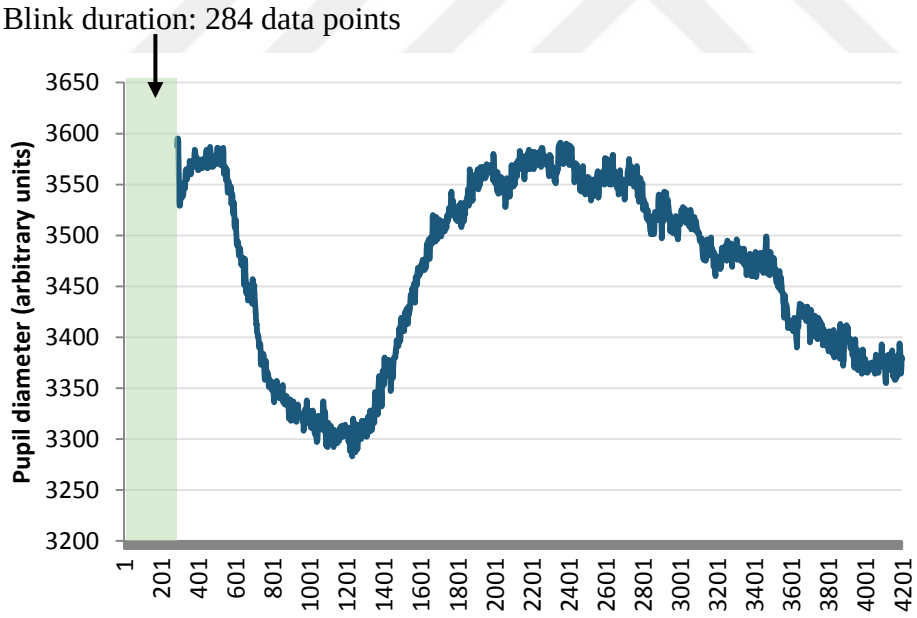

Figure 4.17 Excessive blink removal: blinks longer than 150 data points in first 200 ms

After the exclusion of any trials which contain excessive blinks, among the remaining trials, any trial with shorter blinks were interpolated by using the algorithm developed by Mathôt (2013). Briefly, what the algorithm does is spotting the regions where there is an excessive decrease (or an increase) in pupillary data and marking them as blinks,

then, any blink found is reconstructed via cubic-spline interpolation. Amount of decrease in pupillary data to be counted as a blink can be given as a parameter to the algorithm that in the current study, any decrease or increase greater than 4 artificial-units was regarded as blink onset (see Figure 4.18).

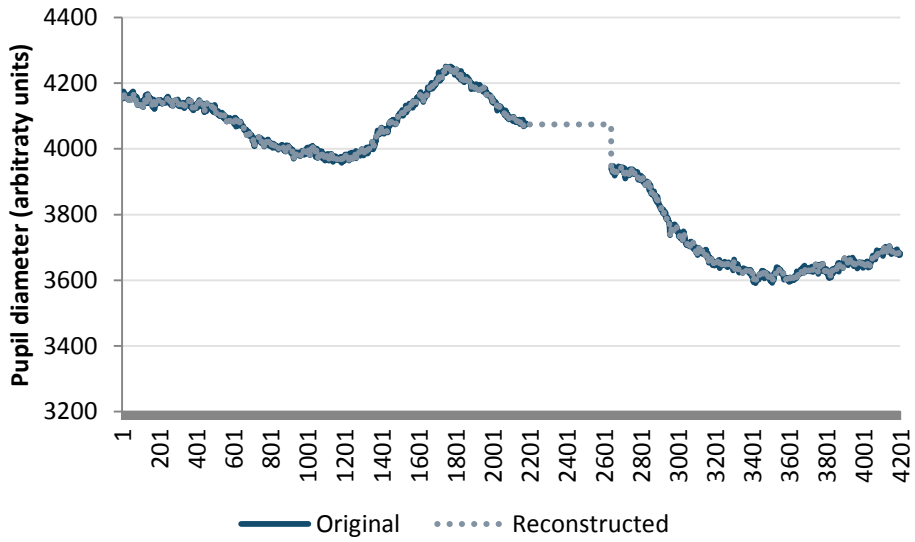

Figure 4.18 Blink reconstruction by cubic-spline interpolation (Mathôt 2013)

Preprocessing of the pupillary data continued with applying a median filter in order to remove any artifacts present in the signal and smoothing of the signal via moving-average filter (see Figure 4.19 and 4.20). Windowing size for both applications were set to 251 data point that the windowing size is determined accounting the data collection rate, 1000 Hz.

Following that, in order to obtain comparable pupillary responses across trials and across participants, a baseline correction was applied on the pupillary data (see Figure 4.21). Baseline for each trial was set as the median of the last 200 milliseconds of the fixation screen which was immediately before the stimulus display. Baseline correction was applied individually for each trial that the baseline value was subtracted from all the following data points within that trial.

Since the blink reconstruction algorithm is unable to interpolate blinks occurring towards the very end of the trials as good as others, the pupillary data for each trial was truncated to 3750 data points which were last 250 milliseconds of each trial was removed.

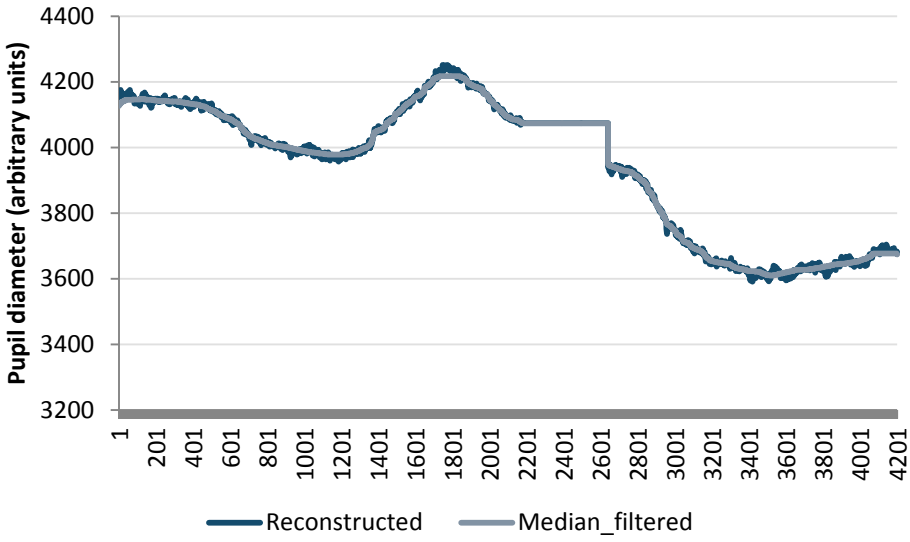

Figure 4.19 Artifact removal with median filter (window size: 251 data point)

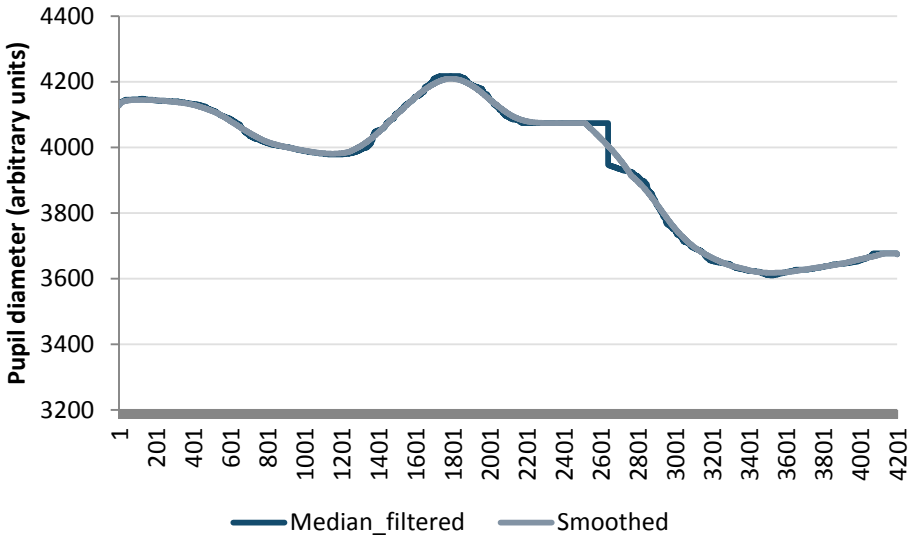

Figure 4.20 Smoothing of the signal via moving average filter (window size: 251 data point)

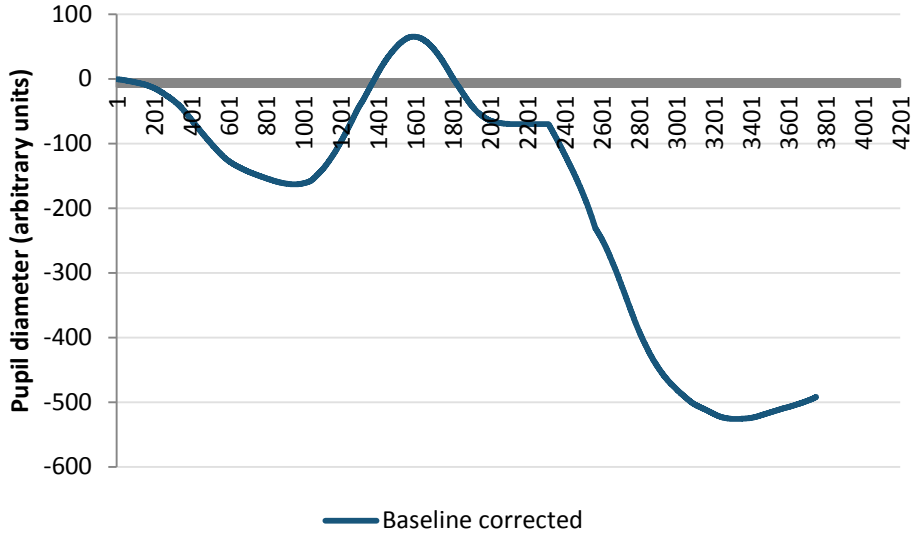

Figure 4.21 Baseline correction with the median of the last 200 ms of fixation cross screen

Finally, any trials lacking a light-reflex within the first 1600 milliseconds were removed (Figure 4.22). In order to detect the presence of light-reflex which indicates a constriction, two curves with 3rd order and 6th order polynomials were fitted to the first 1600 milliseconds of the pupillary data and any trial lacking local minima where the pupil signal followed a concave up trend in constriction regions were removed. Alongside with light-reflex criterion, trials which did not manage to dilate after the constriction were removed (see Figure 4.23 for monotonically decreasing trials).

Based on light-reflex criterion, 3.26 % of the data were removed (94/2880 trials), whereas based on negative-peak criterion, 1.98 % of the data were removed (57/2880 trials).

Rather than using absolute peak values for the pupillary analysis, the constriction values for each trial were subtracted from the peak values such that pupillary data for each trial reflects how much the eyes dilated after the constriction (Figure 4.24). In order to spot any outliers among the relative peaks, the data was transformed into z-scores and any value higher than 2 and lower than -2 were considered an outlier and removed from the further analysis 4.44% of the data (128/2880 trials). Thus, in total % 10.87 of the collected data were removed (313 / 2880 trials). The exclusion criterion for the participants was that any participants with 30% of trials which were removed would be excluded from the trial. Only 1 of the participants met this criterion that this participant was removed from the further analysis for pupillary response analysis.

No local minima where the pupil signal follows a concave up

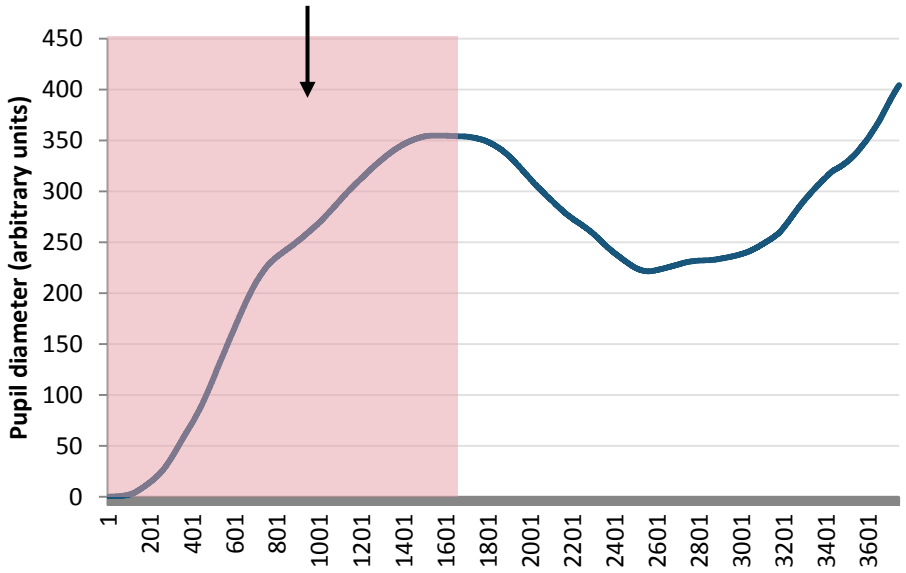

Figure 4.22 Exclusion criteria: lacking light reflex within first 1600 ms

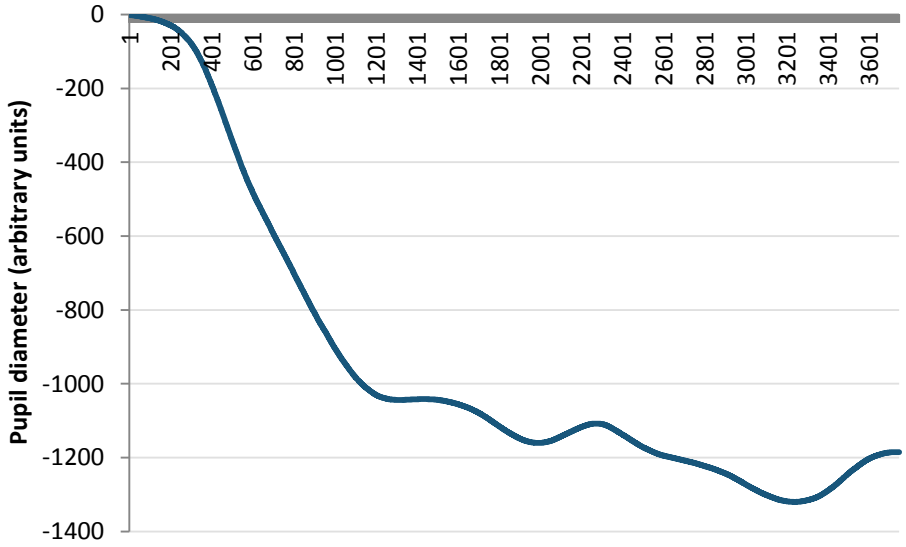

Figure 4.23 Exclusion criteria: monotonic decreasing

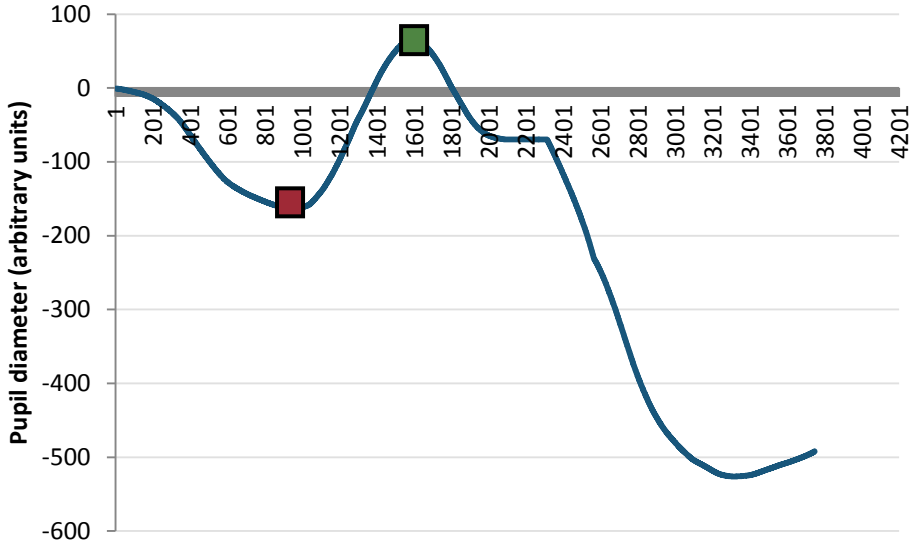

Figure 4.24 Relative peak calculated by subtracting the constriction value (red square) from the peak value (green square)

Since all pupil diameter values were collected in arbitrary units, a conversion was applied in order to obtain pupil data in milimetric scale. This would allow comparison of the findings of the current study with the literature on pupil psychophysiology. In order to do that, an 8-mm black dot was printed on a white A4 paper and its diameter was measured by the EyeLink 1000 eye-tracker. The mean pupil dimeter of the artificial pupil was measured as ~7600 arbitrary units (a.u.) across 10 trials. Hence, any pupil diameter values reported in this section was converted to millimeter by the following formula:

$$Pupil\ diameter\ (mm) = \frac{Pupil\ diameter\ (a.u.) \times 8\ (mm)}{7600\ (a.u.)}$$

For item-wise analysis on pupil diameter difference, similar statistical designs described for trustworthiness ratings and reaction time above were applied. A 2 (task: approach, trust) x 3 (face: untrustworthy, neutral, trustworthy) x 2 (drug: oxytocin, placebo) mixed ANOVA was applied on the mean relative peaks collected during trustworthiness evaluation of the faces with varying trustworthiness levels by participants who received oxytocin and placebo across approach and trust tasks. There was a significant main effect of drug condition such that pupil diameter difference collected from participants who received oxytocin differs significantly from participants who received placebo, $F\ (1, 114) = 15.93, p < .001, \eta = .12$. On average,

eyes of the participants who received placebo *(M=.32, SD = .06)* dilated significantly larger than the eyes of the participants who received oxytocin *(M = .30, SD = .05)*. According to that, administration of oxytocin induced pupils to dilate less during trustworthiness evaluation compared to administration of placebo (see Figure 4.25 and 4.26).

There was also a significant main effect of the task difference on the pupil diameter difference where participants evaluated the presented faces according to different scenarios, $F\ (1, 114) = 4.91,\ p = .03,\ \eta = .04$ (see Figure 4.27 and 4.28). On average, eyes of the participants who were evaluating the trustworthiness of the faces according to the scenarios given in the approach task *(M = .32, SD = .06)* were dilated significantly larger as compared to trust task *(M = .30, SD = .06)*.

However, there was not a significant main effect of the trustworthiness level of the face being evaluated on pupil diameter difference during trustworthiness evaluation, $F\ (2, 114) = .52,\ p = .60,\ \eta = .01$ (see Figure 4.29 and 4.30). According to that, during trustworthiness evaluation eyes of the participants were dilated similarly while evaluating faces of untrustworthy *(M =.63, SD =.08)*, neutral *(M =.62, SD =.08)* and trustworthy *(M =.61, SD =.08)*.

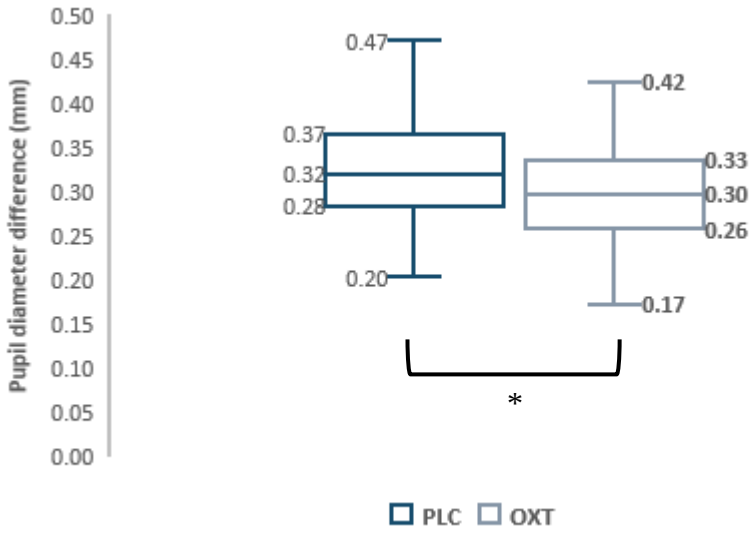

Figure 4.25 Pupil diameter changes of the participants for faces in both oxytocin and placebo groups (error bars represent standard error): *p < .001.

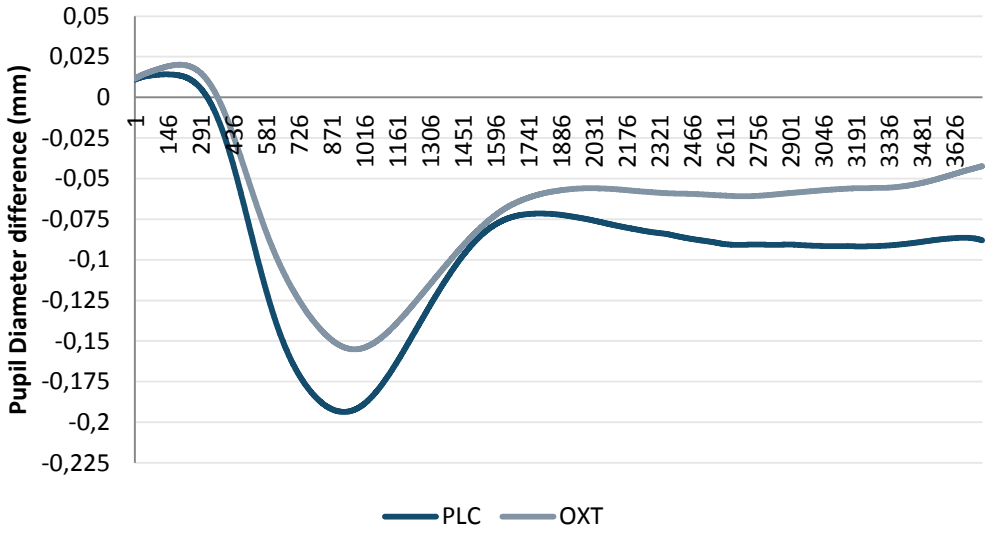

Figure 4.26 Pupil diameter changes for faces in both oxytocin and placebo groups (x axis: each data point corresponds to 1/1000 seconds). It is obtained by averaging pupillary responses of all trials across oxytocin and placebo groups.

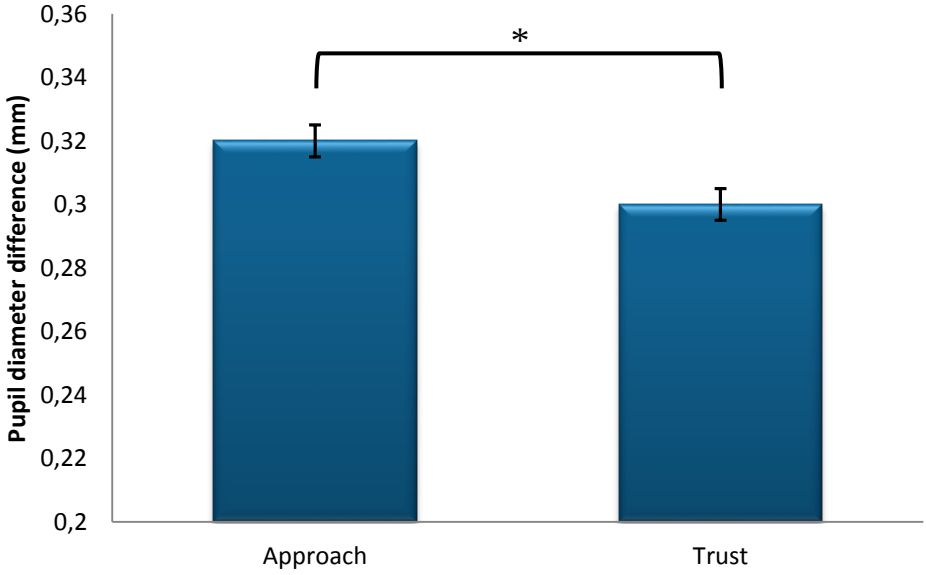

Figure 4.27 Pupil diameter changes of participants for faces evaluated in both approach and trust tasks (error bars represent standard error), *p = .03.

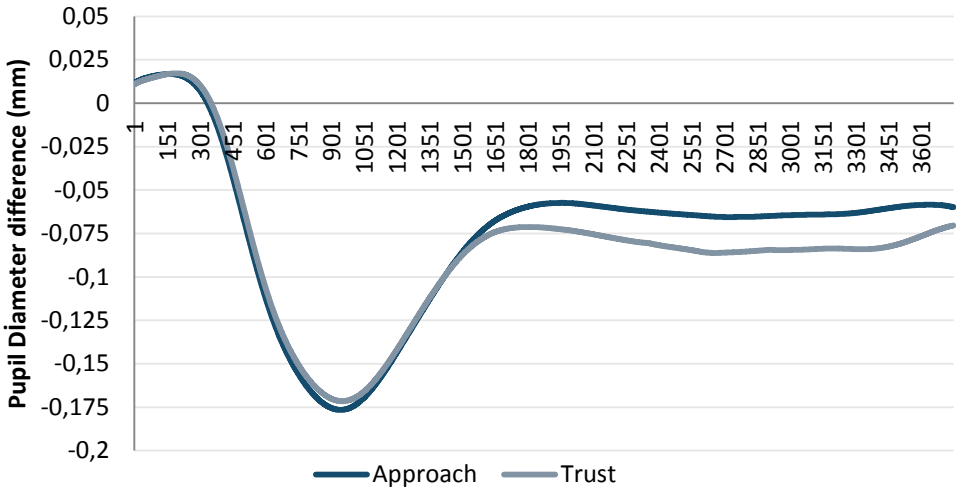

Figure 4.28 Pupil diameter changes for faces evaluated in both approach and trust tasks (x axis: each data point corresponds to 1/1000 seconds). It is obtained by averaging pupillary responses of all trials across approach and trust tasks.

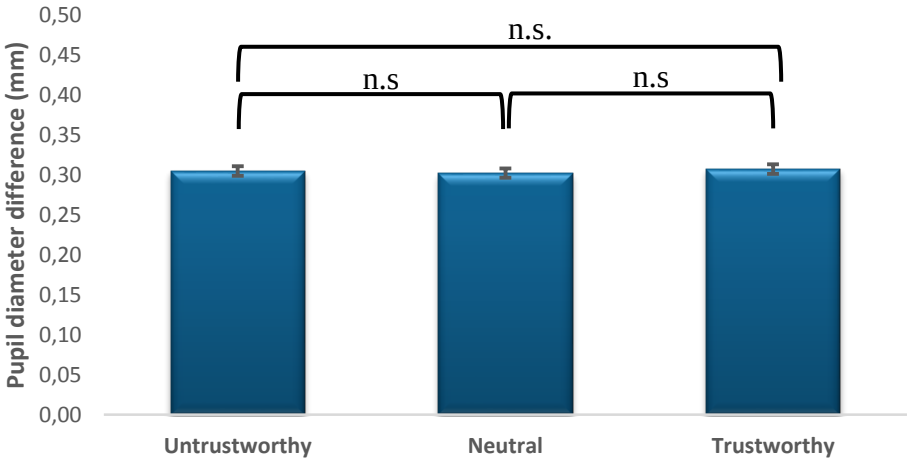

Figure 4.29 Average pupil diameter changes for untrustworthy, neutral and trustworthy faces (error bars represent standard error).

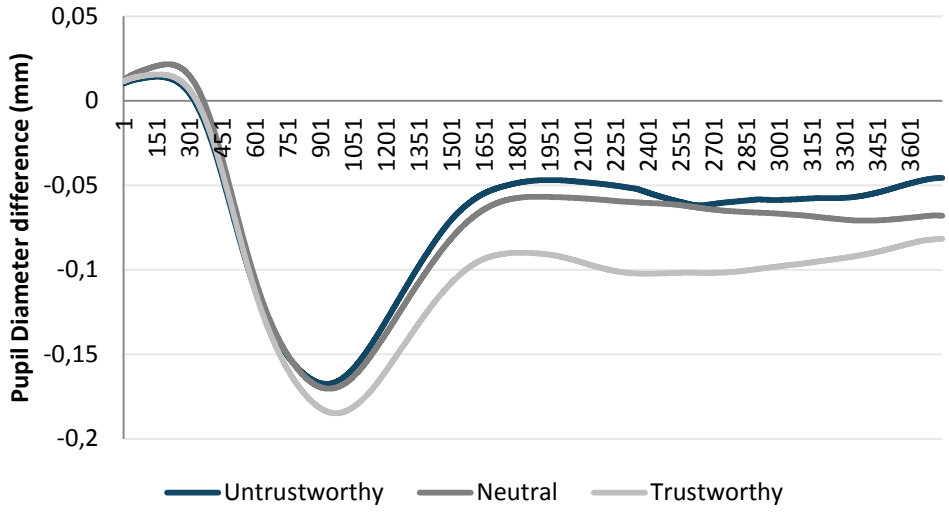

Figure 4.30 Pupil diameter changes for untrustworthy, neutral and trustworthy faces (x axis: each data point corresponds to 1/1000 seconds). It is obtained by averaging pupillary responses of all trials across trustworthy, neutral and untrustworthy faces.

4.2.1.1 The interaction between drug and task

There was also a significant interaction effect such that the drug the participants received interacted with the task in which the faces were evaluated according to different scenarios (approach vs. trust), $F\ (1, 114) = 4.72, p = .03, \eta = .04$. This effect indicates that the mean pupil diameter changes during trustworthiness evaluation in two different tasks were differently modified by the placebo and oxytocin conditions (see Figure 4.31 and 4.32). While evaluating trustworthiness of the faces according to the scenario given in the approach task participants who received oxytocin exhibits less pupil diameter change as compared to participants who received placebo (oxytocin, $M = .30$, $SD = .05$; placebo, $M = .34$, $SD = .05$, $p < .001$, see Figure 4.34 and 4.36). On the other hand, the difference between the pupil diameter change is diminished in the trust task where both groups of participants of whom eyes were dilated in similarly ($M_{PLC} = .31$, $SD_{PLC} = .06$, $M_{OXT} = .30$, $SD_{OXT} = .06$, $p = .201$, see Figure 4.35 and 4.37).

4.2.1.2 The interaction between drug and trustworthiness level of the faces

There was no 2-way significant interaction such that the drug the participants received did not interact with the trustworthiness level of the faces being evaluated (untrustworthy, neutral, trustworthy), $F\ (2, 107) = .38, p < .68, \eta = .01$. The absence of the interaction effect indicates that the pupil diameter changes during trustworthiness evaluation of the faces with different trustworthiness level were not affected differently by the placebo and oxytocin conditions. According to that,

oxytocin did not affect the pupil diameter difference during the trustworthiness evaluation of faces with different level of trustworthiness (Figure 4.33).

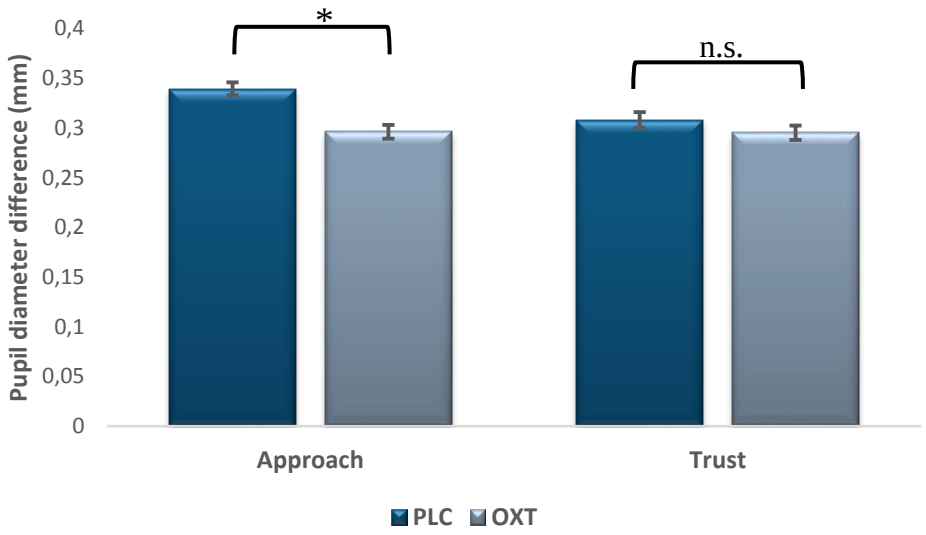

Figure 4.31 Pupil diameter changes of participants for faces evaluated in approach and trust tasks in both oxytocin and placebo groups (error bars represent standard error), *p < .001.

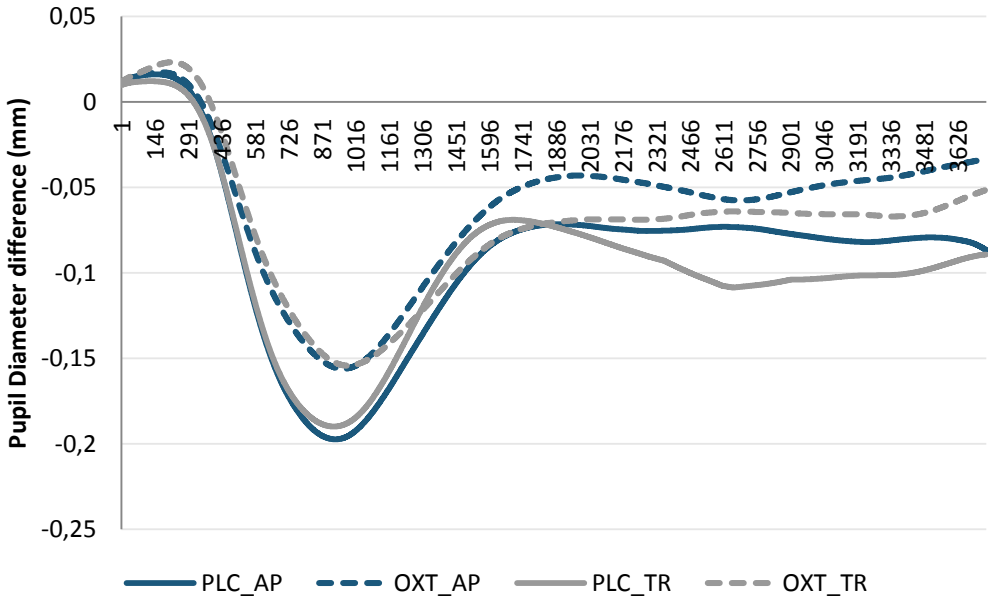

Figure 4.32 Pupil diameter changes for faces evaluated in approach and trust tasks in both oxytocin and placebo groups (x axis: each data point corresponds to 1/1000 seconds). It is obtained by averaging pupillary responses of all trials across placebo and oxytocin groups for both approach and trust tasks.

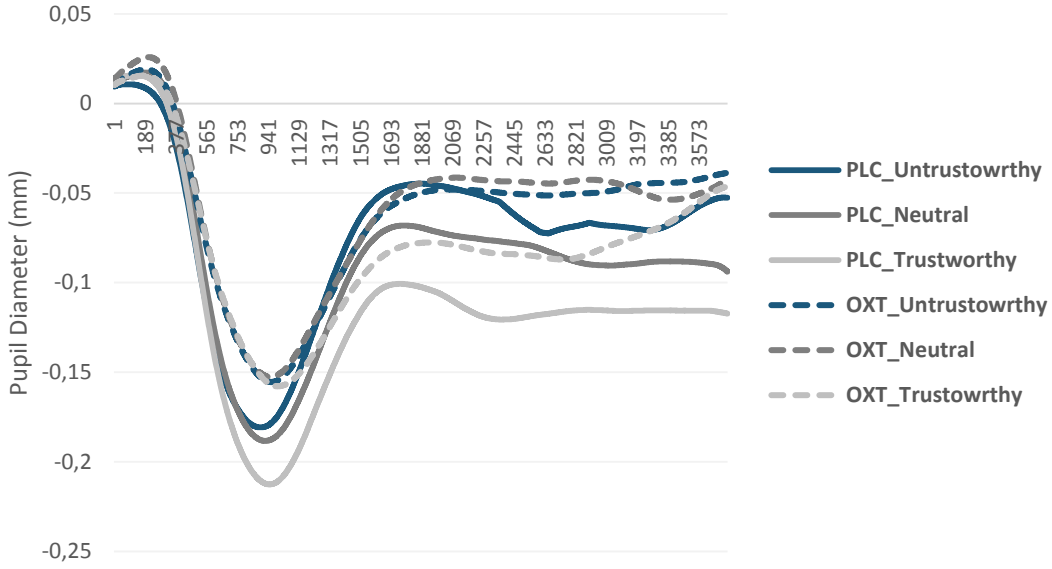

Figure 4.33 Pupil diameter changes for trustworthy, neutral and untrustworthy faces in both oxytocin and placebo groups (x axis: each data point corresponds to 1/1000 seconds). It is obtained by averaging pupillary responses of all trials across placebo and oxytocin groups for trustworthy, neutral and untrustworthy faces.

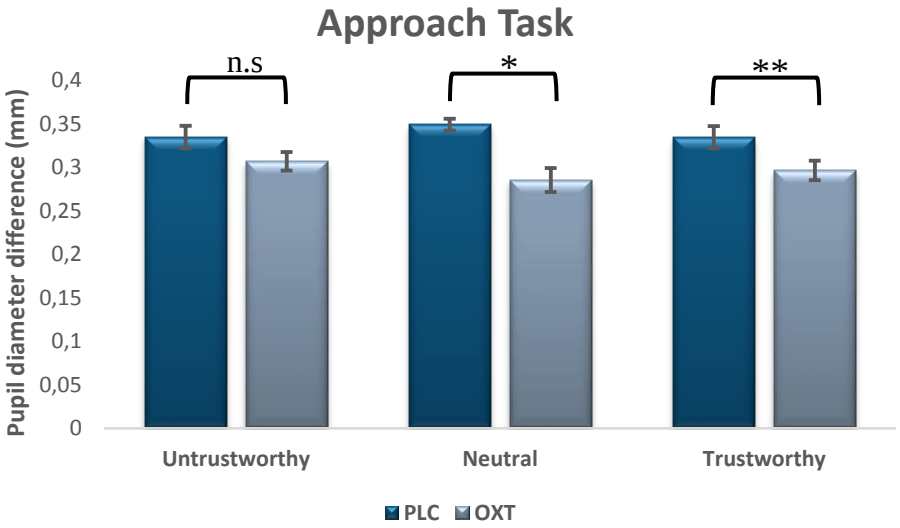

Figure 4.34 Pupil diameter changes for untrustworthy, neutral and trustworthy faces in approach task (error bars represent standard error), *p < .001, **p = .028.

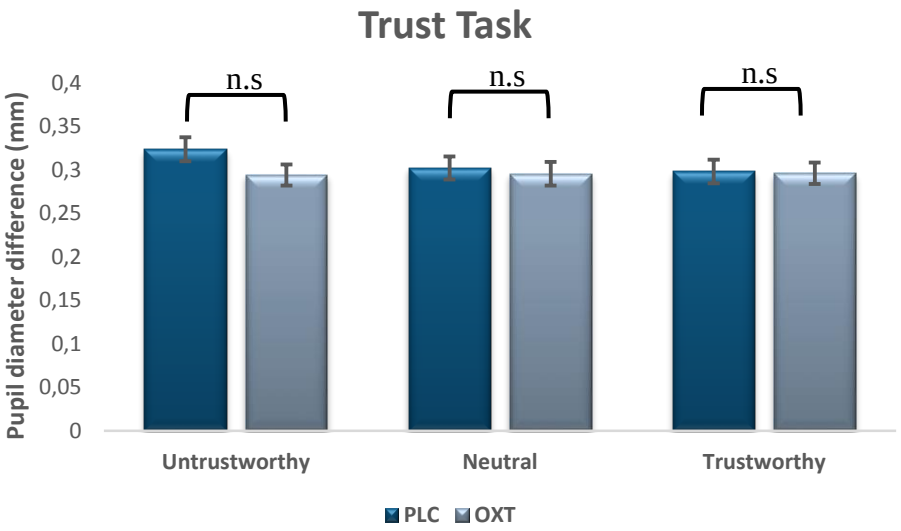

Figure 4.35 Pupil diameter changes for untrustworthy, neutral and trustworthy faces in trust task (error bars represent standard error)

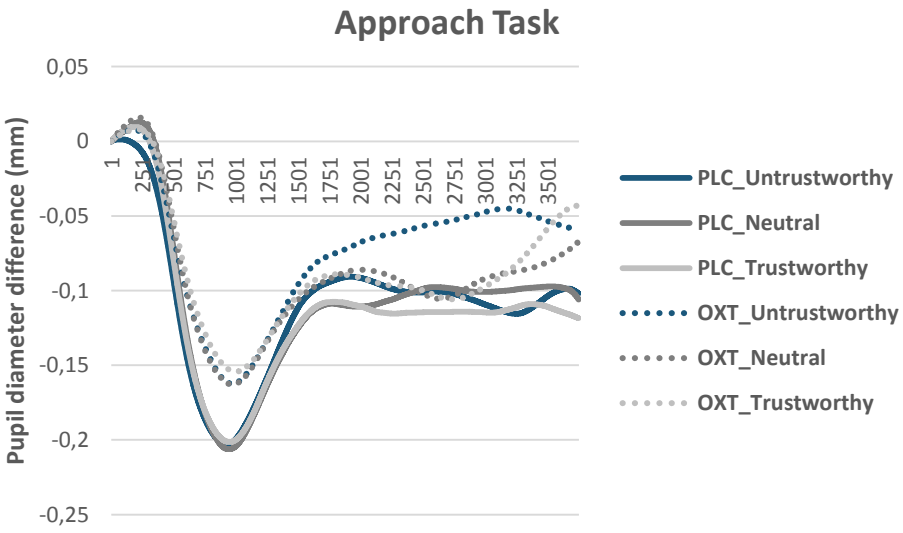

Figure 4.36 Pupil diameter changes for untrustworthy, neutral and trustworthy faces in approach task (x axis: each data point corresponds to 1/1000 seconds). It is obtained by averaging pupillary responses of all trials across placebo and oxytocin groups for trustworthy, neutral and untrustworthy faces in approach task.

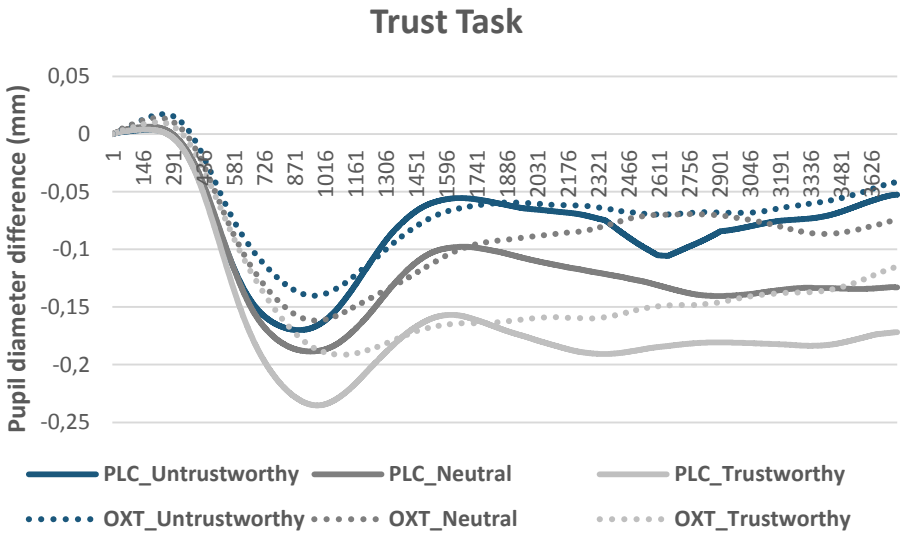

Figure 4.37 Pupil diameter changes for untrustworthy, neutral and trustworthy faces in trust task (x axis: each data point corresponds to 1/1000 seconds). It is obtained by averaging pupillary responses of all trials across placebo and oxytocin groups for trustworthy, neutral and untrustworthy faces in trust task.

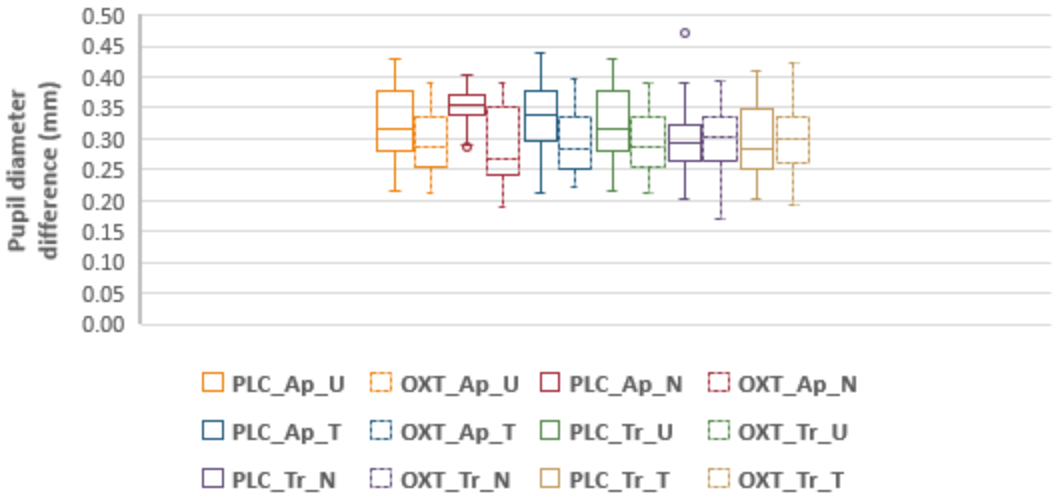

Figure 4.38 Pupil diameter changes for untrustworthy, neutral and trustworthy faces in both oxytocin and placebo groups during approach and trust task

(PLC=Placebo, OXT=Oxytocin, Ap=Approach, TR=Trust, U=Untrustworhty, N=Neutral, T=Trustworthy)

CHAPTER 5

DISCUSSION

The current study aims to investigate how trustworthiness evaluation of participants would differ under the effect of neuropeptide oxytocin in response to untrustworthy, neutral, and trustworthy faces. Behavioral findings of the study involve trustworthiness ratings given to each face and reaction time. Based on recent research, oxytocin has been shown to exert physiological effects alongside with behavioral outcomes with respect to pupillary physiology (Leknes et al., 2013; Prehn et al., 2013). Thus, aside from behavioral effects of oxytocin, the current study also aims to investigate pupillary responses obtained during trustworthiness evaluation of faces. On top of that, the main motivation behind the current study is characterizing the context dependent nature of oxytocin in order to enable more refined theorizing on the social effects of oxytocin in humans. Building evidence on oxytocin literature revealed the "dual nature" of oxytocin that it does not always promote approach or trust in a situation-independent manner (C. K. W. De Dreu et al., 2011; Declerck et al., 2010; Carsten K W De Dreu et al., 2010; Shamay-Tsoory et al., 2009). In order to disambiguate the relationship between oxytocin and social domain of human life, the focus of the current study is towards investigating contextual cues during two different social cognition tasks differing only with respect to situational settings. While one task involves a scenario where the participants had to trust and approach the trustee in order to seek help, the other task involves a scenario where the participants had to trust the trustee to give help through letting him to use the mobile phone that participants carried with him.

In order to prevent any influence of sex-dependent effect of oxytocin, only heterosexual male participants were invited to participate in the study. Behavioral data of the current study includes the trustworthiness ratings given to each face and the reaction times of the response. Physiological data includes pupillary responses obtained during evaluation of facial trustworthiness. While physiological data were recorded in the duration of visual stimuli presentation, the behavioral data were recorded after the passive gazing of the visual stimuli ended.

Building on the literature presented in Chapter 2, there were 3 hypotheses in relation to approach behavior, 3 hypotheses in relation to trust behavior, 3 hypotheses for comparisons of the task and 2 hypotheses with face manipulation that there were 11 hypotheses in total, as listed in tables 5.1, 5.2, 5.3 and 5.4, respectively. The results with respect to these hypotheses are presented in the tables side by side with the hypotheses.

Table 5.1 Results of hypotheses for approach task

Hypotheses	Significance	Finding
H1, Trustworthiness Ratings: OXT > PLC	p < .008	**Confirmed**
H2, Reaction Times: OXT < PLC	p < .001	**Confirmed**
H3, Pupillary Response: OXT > PLC	p < .001	**Not confirmed (Reverse effect)**

Table 5.2 Results of hypotheses for trust task

Hypotheses	Significance	Finding
H4, Trustworthiness ratings: OXT ≠ PLC	p < .001	**Confirmed**
H5, Reaction times: OXT < PLC	p < .001	**Confirmed**
H6, Pupillary responses: OXT > PLC	p = .20	**Not confirmed**

Table 5.3 Results of hypotheses for comparison of the tasks

Hypotheses	Significance	Finding
H7, Trustworthiness ratings: Approach < Trust	p < .001	**Confirmed**
H8, Reaction times: Approach < Trust	p = .86	**Not confirmed**
H9, Pupillary responses: Approach < Trust	p = .03	**Not confirmed (Reverse effect)**

Table 5.4 Results of hypotheses for face manipulation

Hypotheses	Significance	Finding
H10, Trustworthiness ratings: T > N > U	p < .001	**Confirmed**
H11, Pupillary responses: T ≠ N ≠ U	p = .60	**Not confirmed**

Analyses revealed that there is a main effect of drug on trustworthiness ratings such that participants who received oxytocin rated the faces as less trustworthy as compared to participants who received placebo. At first sight, this finding looks contradictory to the majority of studies in the literature which shows beneficial positive effects of oxytocin in trust behavior. However, this main effect only tells us how intranasal administration of oxytocin influence judgements of participants in task independent manner. On account of increasing number of studies, effect of exogenous oxytocin in social cognition and prosocial behavior is reported to be interacting with either situational features of task or variables of stimuli (J. A. Bartz, Zaki, Bolger, et al., 2010; Di Simplicio, Massey-Chase, Cowen, & Harmer, 2009; Domes et al., 2007; Guastella et al., 2010; Guastella, Mitchell, & Mathews, 2008; Heinrichs et al., 2004; Marsh, Yu, Pine, & Blair, 2010; Rimmele et al., 2009; Savaskan et al., 2008; Schulze et al., 2011). Therefore, instead of main effect of oxytocin condition, interactions of oxytocin with task variable (approach and trust) and stimuli variable (trustworthy, neutral, untrustworthy) are more informative for better understanding the mechanism of oxytocin with respect to social behavior in humans. In the current study, results revealed both significant interaction effect between drug condition and task variable and between drug condition and face manipulation such that intranasal oxytocin administration is shown to have differential effects with respect to contextual differences in tasks and stimuli. Presence of significant interactions in trustworthiness judgments are supporting the aforementioned and growing literature of context dependent nature of oxytocin in social behavior.

In order to broken down the interaction effect and analyze how intranasal administration of oxytocin modulates trustworthiness judgement of participants, pairwise comparisons in task level should be taken into consideration. First, in approach task, effect of exogenous oxytocin on trustworthiness judgements confirmed our **hypothesis 1** such that oxytocin increased trustworthiness ratings of participants in approach related context. Besides that, intranasal administration of oxytocin facilitates this process of trustworthiness evaluation such that participants receiving oxytocin were faster in responding as compared to participants receiving placebo which confirms our **hypothesis 2**. This finding of the study is in line with the studies investigating the effects of oxytocin on prosocial behavior and revealed the fact that oxytocin fosters trust (Baumgartner et al., 2008; Kosfeld et al., 2005; Moïra Mikolajczak et al., 2010; Theodoridou et al., 2009). The study of Theodoridou et al (2009), investigated the relationship between exogenous oxytocin and trustworthiness perception in a placebo controlled experimental paradigm. Their study revealed that participants who received intranasal oxytocin rated neutral faces as more trustworthy as compared to participants who received placebo. However, the study did not define any contextual constraint on the context of trust that participants rated the faces based on the question “How trustworthy is the face?”.

In addition to that, Saracaydin (2015) conducted a study where she investigated the possible link between intranasally administered oxytocin and trustworthiness judgments on the same approach-related context. In that study, the experimental stimuli were a subset of Karolinska Directed Emotional Faces (KDEF) - KDEF is

composed of human faces photographed while expressing variety of emotions such as happy, sad, fearful and neutral (Lundqvist, D., Flykt, A., & Öhman, A., 1998). Only neutral faces were used for the trustworthiness judgments. The results of the study are in line with our results such that participants under influence of intranasally administered oxytocin rated neutral faces as more trustworthy in an approach related context (Saraçaydin, 2015). It should be noted that in that study, the experimental stimuli are neutral real human faces whereas in our study it was computer generated human faces which are emotionally neutral. In comparison, our approach has advantages and disadvantages. On the one hand, computer generated faces allow controlling possible effects of any non-facial features (e.g. skin, texture, hair, freckles etc.) in trustworthiness judgements while at the same time preserving the emotionally neutral content of the face. Moreover, being able to manipulate the trustworthiness level of the face allows us to further explore effect of intranasal oxytocin in response to faces of different trustworthiness levels. On the other hand, there are obvious downsides of not using real faces such that computer generated faces are not perceived as realistic as a real face (Todorov, Dotsch, Porter, Oosterhof, & Falvello, 2013). More on the disadvantages of using artificial faces is further explained at the limitations and future studies section at the end of this chapter. However, results of both studies (i.e. Saracaydin, 2015 and ours) which explored real and computer generated faces are in parallel with respect to the effects of exogenous oxytocin in approach related trustworthiness judgments.

On the other hand, results of the current study revealed significant yet opposing effects of exogenous oxytocin on trustworthiness judgements in trust-related context. In other words, participants receiving oxytocin administration rated faces significantly less trustworthy as compared to participants receiving placebo which confirms **hypotheses 4**. Thus, it turned out that boosting effect of intranasal administration of oxytocin on trustworthiness evaluation is diminished in trust-related context. Nevertheless, facilitatory effect of intranasal administration of oxytocin remains in the trust task as well. In other words, participants receiving oxytocin were faster in responding as compared to participants receiving placebo in trust-related context which confirms our **hypothesis 5**. This finding is contradictory to the studies which reports positive effects of oxytocin, instead it is in line with the studies reporting undesired effects of oxytocin in prosocial and social cognition such as envy (Shamay-Tsoory et al., 2009), mistrust (J. Bartz et al., 2011; Declerck et al., 2010; M Mikolajczak et al., 2010), insecurity in attachment (J. A. Bartz, Zaki, Ochsner, et al., 2010), outgroup derogation (C. K. W. De Dreu et al., 2011).

Additionally, results showed that in contrast to approach-related context, in the trust-related context, participants receiving oxytocin rated faces as less trustworthy as compared to participants receiving placebo. It should be noted that in both of the tasks, participants had to make the same social judgment – trustworthiness evaluation. However, only difference between the two tasks was the scenarios which were given in the beginning of each task such that participants were asked to make judgments by considering the contextual information in the provided scenario. This experimental design allowed us to observe whether effect of intranasal administration on social

judgment of trustworthiness interacted with the contextual cues. Empirical data support this view such that exogenous oxytocin enhance the tendency to evaluate the faces as more trustworthy in approach-related context. In contrast, intranasal administration of oxytocin did not increase trustworthiness ratings in trust related context, instead the participants rated the faces as less trustworthy as compared to placebo. Thus, the present study demonstrated the context-dependent nature of oxytocin with respect to social effects of oxytocin in humans. Therefore, it could be postulated that contextual features could be key to understand the mechanism of exogenous oxytocin in humans while interpreting the inconsistent findings of the oxytocin in the literature.

There are other studies in which intranasal administration also interacted with either stimulus or task variables. In the study conducted by Declerk et al. (2010), the relationship between rate of cooperation and intranasal administration of oxytocin was found to be moderated by the presence of social cues such that increased availability of oxytocin only promoted increased trust when participants were allowed to briefly socially engage with each other. However, when the participants were anonymous to each other, due to the lack of social contact direct the relationship between the oxytocin and cooperation to other direction that participants engage in protective behavior under the effect of intranasal oxytocin as compared to placebo. Moreover, Mikolajczak et al. (2010) also reported dual nature of oxytocin that in their study participants played a well-known trust game with a computer agent, reliable person and unreliable person. Results revealed that upon intranasal administration, participants were found to be trusting the people who are portrayed as reliable more. In contrast, when participants were playing against someone who is portrayed as untrustworthy the trust inducing effect of oxytocin was diminished. Thus, it was shown that the effect of oxytocin was moderated with the trustworthiness level of the partner. Accordingly, it was suggested that although oxytocin has ability to make people more trusting, it seems that it does not make people trust in a situation-invariant manner.

Social engagement with people we have zero acquaintance frequently requires making social judgments about them such as deciding on whether to trust them in different contexts (M. L. Willis et al., 2013). However, rather than feeling unconditional trust, the ability to make a proper social judgment is in line with careful assessment of the conditions of the current situation and be cautious when the outcome of the situation bears potential high risk (Greenspan et al., 2001). In the current study, as compared to approaching behavior which involves asking a question, trust condition can be perceived as riskier and indeed our results yielded that this is the case since participants perceived the faces as more untrustworthy in the trust scenario as compared to approach scenario which confirms our **hypothesis 7.** In spite of that, this difference is not observed in reaction times of the two tasks such that participants evaluated the trustworthiness of the faces in the trust task and approach task at the same rate. This finding is not confirming our **hypothesis 8**. In fact, asking for address is not harmful for the individual that you can always ask to another person and verify the answer you got earlier. However, giving your cell phone bears risk of

theft. In addition to that, since cell phones contains personal and confidential information, the risk is not limited to monetary loss.

Moreover, the dual nature of oxytocin may also present in the in-group and out-group bias such that it in another study, oxytocin influenced participants to favor in-group members and promoted distrust to out-group members (Carsten K W De Dreu et al., 2010). This distinction may extend to the current study as well. In the trust condition participants are being approached by a stranger who might be perceived as an out-group member. In contrast, in approach task, participant himself had to overcome this barrier and approach that person which does not make him an out-group member anymore. In accordance with that, under the effect of intransal administration of oxytocin, perceived trustworthiness of the faces increased in approach condition wheras it decreased in the trust condition.

In the light of our behavioral results on trustworthiness perception, there is evidence that oxytocin, as an ancient neuropeptide also has modulatory role in a crucial survival skill: preventing exploitation financially and socially. In other words, behavioral results of the conducted study revealed that intranasal oxytocin treatment is successful in promoting trust in relatively safer situations and dealing with in-group members but it does not make people more 'gullible' that it may increase tendency to people to evaluate others as less trustworthy or induce defensive agression when the present situation involves risky outcomes or social engagement with out-group member which is consistent with the literature as well (Declerck et al., 2010; Carsten K W De Dreu et al., 2010; M Mikolajczak et al., 2010).

Additionally, De Dreu et al. (2012) studied how exogenous oxytocin could influence decision making process of participants in selection of allies for their group in an intergroup competition. Similar to the current study, De Dreu et al. (2012) also used computer generated faces which are manipulated to look either trustworthy or untrustworthy. By creating in-group out-group boundary, they managed to manipulate context to determine whether intranasal administration of oxytocin has an effect with respect to that aspect. It is observable that humans alongside with some of the other mammals, form coalitions which serve to increase in-group benefits while protecting the group from outside threats. Darwin who also studied the human survival and commented as follows: "Groups with a greater number of courageous, sympathetic and faithful members, who were always ready to warn each other of danger, to aid and defend each other … would spread and be victorious over other tribes" (Darwin, 1873, p. 156). Hence, one of the strategies to choose allies for the group is to engage with allies which are strong enough to benefit the group by defending the group from threat of rival out-group members. The results of the study revealed that intranasal oxytocin administration has influence on the process of alliance selection such that exogenous oxytocin administration let participants to choose allies which had greater threat potential. In addition to that, oxytocin did not induce affiliative behavior towards untrustworthy faces such that under the intranasal administration of oxytocin participants rated untrustworthy faces as being more useful in a possible inter-group conflict. Although their study did not investigate whether

trustworthiness judgements were due to exogenous oxytocin, the fact that participants rated untrustworthy faces as being more useful suggests that perceived trustworthiness of the faces remained unaffected in that context (Carsten K. W. De Dreu, Greer, Handgraaf, Shalvi, & Van Kleef, 2012).

Analysis on the trustworthiness ratings in response to faces with different trustworthiness levels indicated that our face manipulation is validated in both tasks, confirming our **hypothesis 10**. On average, while untrustworthy faces were rated lower than neutral faces, trustworthy faces were rated significantly higher than neutral faces. The trustworthiness ratings of the faces follows the same trend as proposed by the model (Todorov, Baron, & Oosterhof, 2008).

The current study also revealed that context-dependent nature of intranasal oxytocin on trustworthiness judgements are not limited with task variable (approach vs trust). Results showed that social effects of exogenous oxytocin were found to be interacting with stimuli variable alongside with the our task variable – which provided another contextual cue in quantifying the level of trustworthiness of the presented face (Todorov & Duchaine, 2008; J. Willis & Todorov, 2006; M. L. Willis et al., 2013). This interaction tells us that increased availability of oxytocin induced differential outcomes in response to different levels of trustworthiness of the faces.

Without considering the task difference, the results revealed that on average the trustworthiness ratings were significantly altered when participants evaluated only the trustworthy faces. The differences in neutral and untrustworthy faces found to be non-significant. By virtue of the existence of significant 2-way interaction of task x drug condition and significant 3-way interaction of drug, task and trustworthiness level of the face, the effects of intranasal oxytocin in response to different levels of trustworthiness should be investigated in task level in order to better understanding of the outcomes of the current study.

In approach task, while intranasal administration of oxytocin decreased trustworthiness ratings of trustworthy faces, it increased them in response to neutral and untrustworthy faces. On the other hand, in trust task, trust inducing effect of increased availability of oxytocin is diminished such that it decreased trustworthiness ratings of the faces irrespective of the trustworthiness level of the faces. Trust-related context can be thought as being relatively riskier as compared to approach-related context, but the difference between the two tasks was not limited with that. While approach task requires participants to imagine themselves approaching someone to seek for help, trust task requires participants to image being approached by a stranger and giving help to that stranger. Based on that, as compared to approach-related context, trust-related context is better categorized as involving more prosocial behavior which is defined as engaging in behaviors which would benefit others by your own will (Eisenberg & Miller, 1987). Previous research showed that people are inclined to make emphatic responses and help others when they feel that their help is required (Penner., Dovidio., Piliavin., & Schroeder., 2005). Moreover, it was also reported that willingness of prosocial behavior could be altered by the facial cues of

the other party who seeks for help. While fearful faces can be perceived as giving clues about a potential danger which is in the close proximity and convey information that the individual is in a stressful mood, sad faces can trigger emphatic response and increase our desire to help (Hasson, 1997) In fact, it was previously reported that, people tend to make more donations to charity events in response to sad faces as compared to happy or neutral faces (Small & Verrochi, 2009). Although significant 3-way interaction (drug x task x face) suggested that social effects of exogenous oxytocin is moderated by the trustworthiness level of the face, the variance in the trustworthiness evaluation of trustworthy faces can be partially explained with emotions. When the participants did not receive sign of help from trustworthy faces, they rated them as less trustworthy to give help. This view is also supported by the feedbacks deposited from the participants upon completion of the experiment.

On the other hand, approach task requires participants to imagine themselves as approaching the presented face, but this does not involve a prosocial behavior in comparison to trust task. Results of the current study is consistent with the studies investigating the link between facial cues and approachability: faces having negative expressions are rated as less approachable as compared to faces bearing positive expressions (M. L. Willis, Palermo, & Burke, 2011a, 2011b). Furthermore, it seems that intranasally administered oxytocin modulates this relationship between facial cues and trustworthiness judgements with respect to approach behavior. Increased availability of oxytocin makes participants to decrease their trustworthiness ratings in response to trustworthy faces wheras increase their trustworthiness ratings in response to neutral and untrustworthy faces. This interaction of drug x face could be counted towards an empirical support for the context-dependent nature of oxytocin as well.

To the best of our knowledge, literature on psychophysiological responses acquired upon receiving exogenous oxytocin via intranasal administration is limited. There are only a few studies investigating the link between exogenous oxytocin and pupillometry (Leknes et al., 2013; Prehn et al., 2013; Saracaydin, 2015). Both studies of Leknes et al. (2003), and Prehn et al., (2013) reported that under the intranasal administration of oxytocin, pupil of the participants increased in diameter in response to recognition of facial expressions with varying emotions. In addition to that, in the study conducted by Saracaydin (2015), it is reported that pupil dilatory effect of intranasal administration of oxytocin is held during trustworthiness evaluation as well. Based on these studies measuring psychophysiological pupillary response under the effect of exogenous oxytocin, it was hypothesized that intranasal administration of oxytocin would induce additional pupil dilation during trustworthiness evaluation. In contrast, present study revealed conflicting results with the current literature of psychophysiological effects of exogenous oxytocin which rejected our hypotheses regarding the pupillary responses. In accordance with the significant 2-way (task and drug) interaction, the pupil data of the current study will be discussed in task dependent manner. The interaction suggests that psychophysiological effects of the intranasal administration of oxytocin differed across the two tasks. In approach task, pupils of the participants receiving oxytocin dilated significantly less than the pupil of the participants receiving placebo while evaluating the trustworthiness of the faces

in approach-related context. This finding caused rejection of our **hypothesis 3**. On the other hand, in trust task, results revealed that dilatory effect of intranasal administration of oxytocin on pupils found to be diminished when participants were evaluating the trustworthiness level of the faces which caused rejection of our **hypothesis 6**. Psychophysiological results of the current study are surprising considering that it was hypothesized that general effect of oxytocin which is increased pupillary dilation would hold during the trustworthiness evaluation of the faces both in approach and trust related contexts. Literature on the pupil physiology claims that phasic rather than tonic changes in pupil diameter correlates with the processing demands of the task which makes task-evoked pupillary responses a great correlational index to study underlying brain processes (Beatty & Lucero-Wagoner, 2000; Steinhauer & Hakerem, 1992). On the other hand, exogenous administration of oxytocin is thought to have facilitatory effects in social cognition and prosocial behavior in humans (J. A. Bartz et al., 2011; Churchland & Winkielman, 2012). This view is also supported with the reaction time data of the present study which revealed that under the intranasal administration of oxytocin participants were faster at evaluating trustworthiness level of the faces in both approach- and trust-related contexts. In the same manner, increased competence in social cognition and prosocial behavior under the effect of intranasal administration of oxytocin could have manifested itself in the pupillary responses.

Moreover, Gamer and Bücher (2010) conducted a study in order to determine under which branch of autonomous nervous system, oxytocin exerts its effects. Measuring skin conductance and heart rate at the same time while participants were engaged in an emotion classification task under the intranasal administration of oxytocin helped them to characterize the effects of oxytocin. Results of the study revealed that intranasal administration of oxytocin did not have any effect on skin conductance which is mediated by sympathetic activity. However, it was also revealed that it did have an effect on the phasic responses of heart rate which is mediated by parasympathetic activity. The results of the study constructed an empirical support for the view that it was the parasympathetic activity which oxytocin influences (Gamer, Zurowski, & Buchel, 2010). Hence, the decrease in the pupillary responses that we observed can be the consequences of the change in the parasympathetic activity which is modulated by the intranasal administration of oxytocin (Steinhauer & Hakerem, 1992). However, it should also be noticed that intranasal administration of oxytocin did not have any impact on the trust-related context. Thus, new research is needed to characterize whether context-dependent effects of intranasal administration of oxytocin could be extended to pupillary response as well.

Literature on task-evoked pupillary response revealed that psychophysiological pupil movements are reliable indices of human cognitive processes: dilation of the pupil is in correlation with the cognitive load of the task (Beatty & Kahneman, 1966; D Kahneman et al., 1968). In line with cognitive load view, we expected that in trust-related context there will be large pupillary dilations as compared to approach-related context. The results of the current study revealed that while participants evaluated the trustworthiness of the faces in an approach related-context, their eyes dilated

significantly more as comparing to evaluating trustworthiness level of the faces in the trust-related context which cause rejection of **hypotheses 9**. Moreover, it is also well studied that emotional content of the stimulus is capable of inducing pupillary response such that greater pupil dilations were obtained in response to emotional stimulus as compared to neutral ones (Bradley et al., 2008). Furthermore, in the study conducted by Saracaydin (2015), largest pupillary dilations were observed during trustworthiness evaluation of the untrustworthy faces in approach-related context, whereas smallest pupillary dilations were observed during trustworthiness evaluation of the neutral faces. Thus, it was hypothesized that obtained pupillary responses would differ among the faces of different trustworthiness levels. The findings of the current study revealed conflicting results such that there is no difference in pupillary dilations in response to evaluation of trustworthiness of the faces which caused rejection of **hypotheses 11**.

On top of that, it should be taken into consideration that the obtained pupillary responses of the current study are in the range of .1 to .5 which is in line with the literature of pupillometry (Beatty & Lucero-Wagoner, 2000). Therefore, it could be postulated that our experimental stimulus of the current study is capable of inducing task-evoked pupillary responses. On the other hand, the observed differences in pupil responses between the placebo and exogenous oxytocin group are too small to compound on interpretations between conditions. For example, although participants receiving intranasal administration of oxytocin showed significantly larger diameters than participants receiving placebo in approach task, this difference is only .04 mm. Therefore, pupillometry results of the current study should be interpreted with caution.

For the analysis of the psychophysiological data of the present study, pupillary responses which were collected during the 4-sec duration of the trustworthiness evaluation were used. Instead of using the peak value of pupillary dilations within this period, relative pupillary dilations were calculated and used for further steps of the analysis. Calculation of the relative peaks was as follows; for each trial the peak values were subtracted from the pupillary diameter recorded at the initial constriction of the pupil upon the presentation of the stimulus. Thus, relative peaks are representing how much the eyes of the participants were dilated after the initial constriction. On the other hand, other studies investigating pupillary responses under the intranasal administration of oxytocin used absolute peaks for their analysis (Leknes et al., 2013; Prehn et al., 2013; Saracaydin, 2015). Accordingly, their peaks represented how much the eyes of the participants were dilated with respect to the presentation of the stimulus – by taking the start of the stimulus as baseline. This difference in the methods of analyzing the pupillary responses could be accounted for the conflicting findings of the current study. Besides that, it is not known whether exogenous oxytocin administration has any influence on the amplitude of the initial constriction of the pupils. If that is so, direct comparison of the relative peaks of the current study with the studies which uses absolute peaks might be misleading. Future studies would shed light on this issue by investigating possible link between the

amplitude of the initial constriction of the eyes and the administration of exogenous oxytocin.

Furthermore, it was hypothesized that effects of oxytocin in prosocial behavior and social cognition can be better conceptualized by an interactionist approach where situational features under which oxytocin is administered and stable characteristics of the participants of whom administering the oxytocin plays a role in modulating the social effects of oxytocin (J. A. Bartz et al., 2011). Task difficulty, valence of the stimuli, reliability, familiarity of the opponent and conflict between in-out group can be categorized as contextual cues which can moderate the effects of intranasally administered oxytocin. On the other hand, competency in social cognition, personality trait differences, can be counted towards person-dependent moderators of oxytocin. Confirmation of hypotheses 1 and hypotheses 4 and reported significant 3-way interaction (drug x task x face) empirically supporting the interactionist model for social effects of oxytocin in humans. In accordance with the model, intranasally administered oxytocin in trustworthiness judgment is moderated by the contextual features of the situation where oxytocin is administered and trustworthiness level of the face to whom administered person socially engage with.

In addition to the context-dependent and person-dependent moderators, according to the interactionist model there are possible mechanisms through which increased availability of oxytocin induce social effects in humans; increasing affiliative motivation in humans, reducing anxiety and increasing saliency of the socially relevant information. Affiliative motivation hypothesis suggests that intranasal administration of oxytocin replenish the diminished the interest to the stimulus within the environment, thereby increased the motivation of the individual with respect to motivation. Although this hypothesis could be accounted for explaining positive effects of oxytocin in the literature, its explanatory role in explaining undesired effects of oxytocin is somewhat limited. Increased trustworthiness ratings in response to neutral and untrustworthy faces upon receiving intranasal administration of oxytocin in approach-related context supports this view. On the other hand, the diminished trust-inducing effect of exogenous oxytocin in trust-related context is not easy to interpret with affiliative motivation mechanism.

In addition to that, it is suggested that increased availability of exogenous oxytocin induce anxiolytic effects in humans which in turn facilitates people to engage in more prosocial behavior. Reduced anxiety hypothesis stems from the animal research where exogenous oxytocin has been shown to modulate fear and anxiety in animals(McCarthy, McDonald, Brooks, & Goldman, 1996). Moreover, decreased amygdala activity is observed in response to fearful and several social stimuli in humans as well (Kirsch, 2005). This mechanism is also promising in explaining the enhancement in emotion recognition performance of patients who suffer from social anxiety, and increased approach related and prosocial behavior. However, likewise affiliative motivation hypothesis, it lacks power to underpin the induced negative social emotions of exogenous oxytocin. Our reaction time data supports this mechanism: upon intranasal administration participants were able to respond faster

while evaluating trustworthiness level of the faces. However, it is still not explanatory to the context-dependent effects of exogenous oxytocin administration.

Last but not least, increased perceptual saliency mechanism may explain the effect of exogenous oxytocin on social cognition and prosocial behavior with respect to both beneficial and undesired effects of oxytocin. This mechanism suggests that intranasal administration of oxytocin increases the attention of people towards socially relevant cues. According to the saliency hypothesis, oxytocin acts as a social magnifier to better perceive the circumstances of the current situation by paying attention to contextual information. This is also empirically supported with the studies revealing that intranasal administration of oxytocin shifted eye gaze of the participants to the eye region in face processing (Andari et al., 2010; Guastella, Mitchell, & Dadds, 2008). Hence, this mechanism can account for the context-dependent effects of exogenous oxytocin administration such that both beneficial and undesirable effects of intranasal administration of oxytocin can be explained. While exogenous oxytocin facilitates prosocial behavior when socially engaging with reliable people or the situation involves cooperative interactions, it induces protective withdrawal behavior in response to competitive, uncertain situations and socially engaging with an unreliable person. Likewise, perceptual saliency hypothesis can account for better understanding of both trustworthiness ratings and reaction time results obtained in the current study in which oxytocin acted as a social magnifier to better perceive the current situation by considering both facial features related to perception of trustworthiness and contextual cues and utilize them for making a social judgement. It turned out that, upon oxytocin administration while contextual conditions of approach task guided people to trust more, conditions of the trust task directed participants to be more cautious.

Limitations and future work

Experimental material consists of computer-generated face stimuli chosen from the freely available database of Trustworthiness Face Data Set 2, created by Oosterhof and Todorov (2008). While the use of computer generated faces allows exploration of the effects of facial features related to the trustworthiness level of the faces in a well-controlled manner, there are immediate undesired secondary effects. Using computer-generated faces obviously decreases mundane realism, thereafter it is possible that some of the faces might fall to the category of 'uncanny valley'. 'Uncanny valley' is the hypothesis as suggested by Mashiro Mori in 1970 that as a replica of human being approaches to being closer to real human, it triggers greater emphatic response in humans. However, there is a certain level where the real-like human replica begins to trigger aversive feelings and induce repulsion against it (MacDorman & Ishiguro, 2006). Accordingly, it cannot be excluded that 'uncanny valley' might explain some of the variance in trustworthiness judgements.

Moreover, another limitation of using Trustworthiness Data Set 2 is that, the database consists of only bald males. While it allows you to test your hypotheses in a well-controlled manner by excluding non-facial characteristics (e.g. hair), it lowers the external validity of the study. On other hand, this choice was mandatory to some extent since it has been shown that there is a tendency to classify faces with no hair as male even if the faces has female characteristics (Dotsch & Todorov, 2012). Therefore, future studies could contribute with an improvement to the current models of computer-generated faces by making them realistic (near-photographic) and developing newer models to include female faces. Apart from that, cropping the facial area to exclude any non-facial parts could be an alternative approach for studying with these faces for now. It is possible that the baldness of the faces would not be too noticeable then.

Furthermore, the faces in Trustworthiness Face Data Set 2 are manipulated to look more trustworthy or untrustworthy, while preserving the emotionally neutral content of the face (Oosterhof & Todorov, 2008). The model used by Todorov and Oosterhof (2008), is based on changing facial features which are important with respect to the trustworthiness of the face. With the help of that model, the group was able to change facial features (orientation of the mouth region, distance between the nose and the mouth, increasing/decreasing inner ridge of the eyebrows) which are important in terms of trustworthiness of each face, thus, to turn them into less or more trustworthy. A shortcoming of this approach is that manipulated facial features cause participants to identify emotions from the faces to a certain level although they are manipulated to have a neutral facial expression (Oosterhof & Todorov, 2009). It has been suggested that dimensions of valence of trustworthiness share a common perceptual basis such that trustworthiness level of a face refers to the overall valence of the face. Empirical data support this view such that, these two dimensions are found to be correlated (Montepare & Dobish, 2003; Todorov & Duchaine, 2008).

In addition to that, the faces in the dataset are not controlled for eye-gaze direction. Based on subjective evaluation, some faces are found to look straight forward whereas some of them have diverted eye-gaze. However, this feature of the faces has a significant importance with respect to the social effects of exogenous oxytocin such that it has been shown that eye-gaze direction is moderating the effects of oxytocin in humans (Petrovic, Kalisch, Singer, & Dolan, 2008). In a fMRI study where effect of intranasal administration of oxytocin is investigated, participants were presented with faces having direct or diverted eye-gaze conditioned with either an electric shock (conditioned faces) or nothing (control). The participants were required to make judgments on how sympathetic the faces looked. It has been demonstrated that negative ratings towards conditioned faces diminished upon intranasal administration of oxytocin. Moreover, the effect of oxytocin was stronger for the faces with direct gaze which is more socially relevant. Thus, it has been suggested that effects of exogenous oxytocin in social judgements are moderated by the eye-gaze of the target stimuli.

Last but not least, the current study is conducted towards identifying context-dependent nature of oxytocin. It has been suggested the social effects of oxytocin are also moderated by the stable individual differences of the person to whom oxytocin is administered (Bartz, Zaki, Bolger, & Ochsner, 2011). Future research assessing whether intranasal administration of oxytocin has differential effects with respect to certain personality differences (e.g. attachment avoidance/insecurity, social anxiety, state/trait anxiety) and if so, characterizing the circumstances under which effects of oxytocin is moderated by these person-dependent features would be fruitful.

CHAPTER 6

CONCLUSION

The current study is conducted to understand how trustworthiness judgements of participants would differ under the effect of exogenous oxytocin as compared to placebo in response to untrustworthy, neutral, trustworthy faces and in response to different contextual information (approach-related vs trust-related context). While one task involved a scenario where the participants had to trust and approach the trustee in order to seek help by asking an address (approach-related context), the other task involved a scenario where the participants had to trust the trustee to give help through letting the other person to use the mobile phone that participants owned (trust-related context). For this purpose, we used computer generated faces which are manipulated on the axis of trustworthiness in three levels (trustworthy, neutral, and untrustworthy). To characterize psychophysiological effects of oxytocin, we managed to collect task evoked pupil diameter changes during subjective evaluations with EyeLink 1000 Plus, provided to us as a courtesy of the EyeTR eyetrack lab at METU Informatics Institute. In order to prevent any sex-dependent effects of oxytocin, only heterosexual male participants were invited to participate in the study.

In approach task, participants who received oxytocin intranasally rated the faces as more trustworthy such that oxytocin increased trustworthiness ratings of participants in approach related context as compared to placebo. Besides that, intranasal administration of oxytocin facilitated the process of trustworthiness evaluation such that participants receiving oxytocin were faster in responding as compared to participants receiving placebo. This finding of the current thesis is consistent with the literature research demonstrating beneficial effects of oxytocin in social domain of life and revealing trust-enhancing effects of oxytocin (Baumgartner et al., 2008; Kosfeld et al., 2005; Moïra Mikolajczak et al., 2010; Theodoridou et al., 2009).

On the other hand, in trust task, participants under intranasal oxytocin administration rated faces significantly less trustworthy as compared to participants receiving placebo. Thus, it turned out that trust-inducing effect of intranasal administration of oxytocin on trustworthiness evaluation is diminished in trust-related context. In spite of that, facilitatory effect of intranasal administration of oxytocin is prevailed for the trustworthiness evaluation in the trust-related context. In other words, participants receiving exogenous oxytocin judged the trustworthiness of the presented face quicker as compared to participants receiving placebo in trust-related context. This finding is contradictory to the studies which reports positive effects of oxytocin, instead it is confirmatory to the studies reporting undesired, anti-social effects of oxytocin such as envy and gloating (Shamay-Tsoory et al., 2009), mistrust (J. Bartz

et al., 2011; Declerck et al., 2010; M Mikolajczak et al., 2010), insecurity in attachment (J. A. Bartz, Zaki, Ochsner, et al., 2010), outgroup derogation (C. K. W. De Dreu et al., 2011).

Moreover, the current study also revealed that context-dependent nature of intranasal administration on trustworthiness judgements are not limited with our task variable (approach vs trust). It was demonstrated that social effects of exogenous oxytocin interacted with trustworthiness level of the face of whom participants make social judgements about. To put otherwise, increased availability of oxytocin induced differential outcomes in response to different levels of trustworthiness of the faces.

In terms of psychophysiological findings of the current thesis, in approach task, pupils of the participants receiving oxytocin dilated significantly less than the pupil of the participants receiving placebo while evaluating the trustworthiness of the faces in approach-related context. On the other hand, in trust task, results revealed that dilatory effect of intranasal administration of oxytocin on pupils found to be diminished when participants were evaluating the trustworthiness level of the faces. The present study revealed conflicting results with the current literature of psychophysiological effects of exogenous oxytocin which rejected our hypotheses regarding the pupillary responses. On the other hand, observed differences (i.e. effect sizes) in pupil responses between the placebo and exogenous oxytocin group were too small to derive any solid interpretation. Therefore, psychophysiological results of the current study should be taken into consideration with caution.

This experimental design allowed us to observe whether effect of intranasal administration on social judgment of trustworthiness interacted with the contextual cues. The present study empirically demonstrated that intranasally administered oxytocin in trustworthiness judgment is moderated by the contextual features of the situation where oxytocin was administered and trustworthiness level of the face with whom the participant socially engaged with. Therefore, it could be postulated that contextual features could be key to understand the mechanism of exogenous oxytocin in humans while interpreting the inconsistent findings about oxytocin in the literature.

The current study is a facilitator towards understanding the situation-variant nature of oxytocin. Our findings will lead us to conduct more refined theories on social effects of oxytocin in humans. Rather than having situation-invariant effects, increased availability of oxytocin could alter the saliency of interpersonal cues; resulting in both affiliative and protective social perceptions of trustworthiness and approachability.

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APPENDICES

APPENDIX A: PARTICIPANT-WISE ANALYSIS ON BEHAVIORAL DATA

Trustworthiness ratings

Approach Task

A 2 (drug: oxytocin, placebo) x 3(face: trustworthy, neutral, untrustworthy) repeated-measures ANOVA was applied to compare the trustworthiness ratings of participants who received oxytocin and placebo in the approach task. There was a significant main effect of the type of faces on ratings of trustworthiness, $F\ (1.26, 27.76) = 48.48$, $p<.001$, $\eta = .69$. Following contrasts revealed that ratings of untrustworthy faces *(M = 3.58, SD = .97)* were significantly lower than neutral faces *(M = 4.86, SD = .80)* in approach task, $F\ (1, 22) = 81.75$, $p<.001$, $\eta = .79$, and ratings of trustworthy faces *(M= 5.69, SD = 1.02)* were significantly higher than neutral faces *(M = 4.86, SD = .80)* in approach task, $F\ (1, 22) = 17.30$, $p<.001$, $\eta = .44$.

However, there was a non-significant main effect of drug condition on the ratings of trustworthiness, $F\ (1, 22) = .237$, $p=.631$, $\eta = .01$, indicating that ratings of trustworthiness of participants in oxytocin *(M = 4.78, SD = .21)* and placebo *(M = 4.64, SD = .21)* groups were similar. In addition, there was no significant interaction effect between drug condition and face type on trustworthiness ratings during approach task, $F\ (1.26, 27.76) = 1.28$, $p= .278$, $\eta = .06$.

Trust task

A 2 (drug: oxytocin, placebo) x 3(face: trustworthy, neutral, untrustworthy) repeated-measures ANOVA was applied to compare the trustworthiness ratings of participants who received oxytocin and placebo in the trust task. There was a significant main effect of the type of faces on ratings of trustworthiness, $F\ (1.49\ 32.69) = 41.01$, $p<.001$, $\eta = .65$. Following contrasts revealed that ratings of untrustworthy faces *(M = 2.86, SD = 1.39)* were significantly lower than neutral faces *(M = 4.21, SD = 1.60)* during the trust task, $F\ (1, 22) = 50.18$, $p<.001$, $\eta = .70$, and ratings of trustworthy faces *(M= 4.95, SD = 1.54)* were significantly higher than neutral faces *(M = 4.21, SD = 1.60)* in trust task, $F\ (1, 22) = 13.20$, $p = .001$, $\eta = .38$.

However, there was a non-significant main effect of drug condition on the ratings of trustworthiness during the trust task, $F\ (1, 22) = .419$, $p=.524$, $\eta = .02$, indicating that ratings of trustworthiness of participants in oxytocin *(M = 3.87, SD = .40)* and

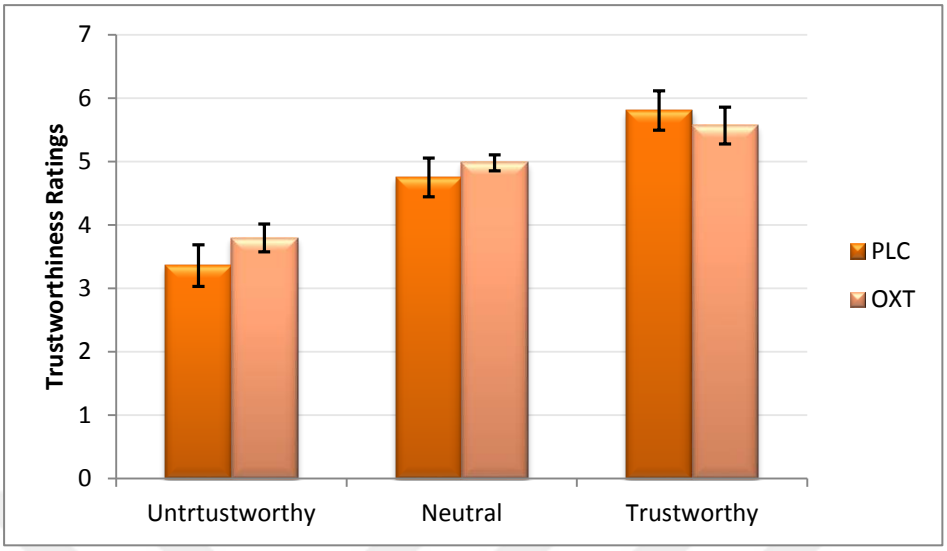

Figure A.1 Trustworthiness ratings of untrustworthy, neutral and trustworthy faces evaluated in approach task in both oxytocin and placebo groups (error bars represent standard error)

placebo *(M = 4.19, SD = .40)* groups were similar. In addition, there was no significant interaction effect between drug condition and face type on trustworthiness ratings during the trust task, $F(1.49, 32.69) = .24$, $p = .72$, $\eta = .01$.

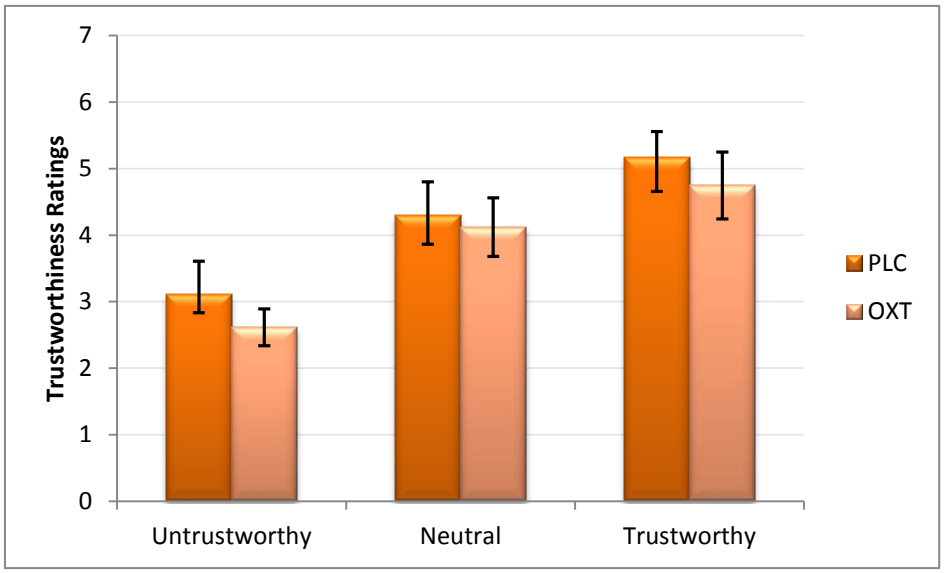

Figure A.2 Trustworthiness ratings of untrustworthy, neutral and trustworthy faces evaluated in trust task in both oxytocin and placebo group (error bars represent standard error)

Reaction Times

Approach Task

A 2 (drug: oxytocin, placebo) x 3(face: trustworthy, neutral, untrustworthy) repeated-measures ANOVA was applied to compare the reaction times of participants in oxytocin and placebo groups while performing trustworthiness evaluation in the approach task. There was a significant main effect of the type of faces on reaction times of participants, $F (2, 44) = 6.34, p<.004, \eta = .22$. Following contrasts revealed that participants evaluated neutral faces $(M = 1255.55, SD = 71.52)$ significantly faster than untrustworthy faces $(M = 1404.27, SD = 68.52)$ and trustworthy faces $(M= 1378.47, SD = 73.02)$ in approach task, $F (1, 22) = 10.50, p<.004, \eta =.32$. However, there was not any significant difference between trustworthy and untrustworthy faces in terms of reaction times that participants were evaluated those face rather in similar fashion in approach task in approach task, $F (1, 22) = 7.36, p<.013, \eta = .25$.

Moreover, there was a marginally significant main effect of drug condition on the reaction time of participants during the approach task, $F (1, 22) = 3.74, p=.066, \eta = .15$, that participants received oxytocin $(M= 1218.09, SD = 238.18)$ were faster than participants received placebo $(M = 1474.11, SD = 425.08)$ in terms of reaction times. In addition, there was no significant interaction effect between drug condition and face type on reaction times during the approach task, $F (2, 44) = .254, p= .777, \eta = .01$.

Trust Task

A 2 (drug: oxytocin, placebo) x 3(face: trustworthy, neutral, untrustworthy) repeated-measures ANOVA was applied to compare the reaction times of participants in oxytocin and placebo groups while performing trustworthiness evaluation in the trust task. Unlike approach task, there was a non-significant main effect of the type of faces on reaction times of participants, $F (2, 44) = 1.684, p<.197, \eta = .07$, indicating that reaction times of participants when evaluating untrustworthy faces $(M = 1407.36, SD = 342.46)$, neutral faces $(M = 1329, SD = 323.27)$ and trustworthy faces $(M = 1327.78, SD = 344.93)$ were similar.

Similar to approach task, there was a marginally significant main effect of drug condition on the reaction times of participants during the trust task, $F (1, 22) = 3.882, p=.062, \eta = .15$, that participants received oxytocin $(M= 1238.70, SD = 202.69)$ were faster than participants received placebo $(M = 1471.26, SD = 397.30)$ in terms of reaction times. In addition, there was no significant interaction effect between drug condition and face type on reaction times during the trust task, $F (2, 44) = .946, p= .396, \eta = .04$.

APPENDIX B: 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 dâhil) 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 C: POSITIVE AND NEGATIVE AFFECT SCALE

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 D: ETHICAL APPROVAL FORM

UYGULAMALI ETİK ARAŞTIRMA MERKEZİ
APPLIED ETHICS RESEARCH CENTER

ORTA DOĞU TEKNİK ÜNİVERSİTESİ
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08 MART 2017

Konu: Değerlendirme Sonucu

Gönderen: ODTÜ İnsan Araştırmaları Etik Kurulu (İAEK)

İlgi: İnsan Araştırmaları Etik Kurulu Başvurusu

Sayın Yrd. Doç. Dr. Didem GÖKÇAY;

Danışmanlığını yaptığınız doktora öğrencisi Anıl KARABULUT ve Fatma Gülhan SARAÇAYDIN'ın ***"Fizyolojik Tepkilerle Bilişsel Seçimlerin Doğal Endojen ve Eksojen Oksitosin Seviyelerine Göre Değişiminin İncelenmesi"*** başlıklı araştırması İnsan Araştırmaları Etik Kurulu tarafından uygun görülerek gerekli onay **2017-FEN-009** protokol numarası ile **26.03.2017 – 01.09.2018** tarihleri arasında geçerli olmak üzere verilmiştir.

Bilgilerinize saygılarımla sunarım.

APPENDIX E: 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.

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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 F: 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 G: 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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Anıl Karabulut, ODTÜ Enformatik Enstitüsü, xxx, xxx

APPENDIX H: SELECTED STIMULI FROM THE TRUSWORTHINESS FACE DATASET 2

Untrustworthy	Neutral	Trustworthy
fs100_002_0.bmp	fs100_002_1.bmp	fs100_002_2.bmp
fs100_008_0.bmp	fs100_008_1.bmp	fs100_008_2.bmp
fs100_009_0.bmp	fs100_009_1.bmp	fs100_009_2.bmp
fs100_015_0.bmp	fs100_015_1.bmp	fs100_015_2.bmp
fs100_018_0.bmp	fs100_018_1.bmp	fs100_018_2.bmp
fs100_019_0.bmp	fs100_019_1.bmp	fs100_019_2.bmp
fs100_020_0.bmp	fs100_020_1.bmp	fs100_020_2.bmp
fs100_022_0.bmp	fs100_022_1.bmp	fs100_022_2.bmp
fs100_023_0.bmp	fs100_023_1.bmp	fs100_023_2.bmp
fs100_024_0.bmp	fs100_024_1.bmp	fs100_024_2.bmp
fs100_026_0.bmp	fs100_026_1.bmp	fs100_026_2.bmp
fs100_029_0.bmp	fs100_029_1.bmp	fs100_029_2.bmp
fs100_030_0.bmp	fs100_030_1.bmp	fs100_030_2.bmp
fs100_032_0.bmp	fs100_032_1.bmp	fs100_032_2.bmp
fs100_033_0.bmp	fs100_033_1.bmp	fs100_033_2.bmp
fs100_036_0.bmp	fs100_036_1.bmp	fs100_036_2.bmp
fs100_038_0.bmp	fs100_038_1.bmp	fs100_038_2.bmp
fs100_039_0.bmp	fs100_039_1.bmp	fs100_039_2.bmp
fs100_040_0.bmp	fs100_040_1.bmp	fs100_040_2.bmp
fs100_042_0.bmp	fs100_042_1.bmp	fs100_042_2.bmp
fs100_047_0.bmp	fs100_047_1.bmp	fs100_047_2.bmp
fs100_048_0.bmp	fs100_048_1.bmp	fs100_048_2.bmp
fs100_054_0.bmp	fs100_054_1.bmp	fs100_054_2.bmp
fs100_058_0.bmp	fs100_058_1.bmp	fs100_058_2.bmp
fs100_062_0.bmp	fs100_062_1.bmp	fs100_062_2.bmp
fs100_064_0.bmp	fs100_064_1.bmp	fs100_064_2.bmp
fs100_068_0.bmp	fs100_068_1.bmp	fs100_068_2.bmp
fs100_071_0.bmp	fs100_071_1.bmp	fs100_071_2.bmp
fs100_074_0.bmp	fs100_074_1.bmp	fs100_074_2.bmp
fs100_075_0.bmp	fs100_075_1.bmp	fs100_075_2.bmp
fs100_077_0.bmp	fs100_077_1.bmp	fs100_077_2.bmp
fs100_078_0.bmp	fs100_078_1.bmp	fs100_078_2.bmp
fs100_080_0.bmp	fs100_080_1.bmp	fs100_080_2.bmp
fs100_081_0.bmp	fs100_081_1.bmp	fs100_081_2.bmp
fs100_087_0.bmp	fs100_087_1.bmp	fs100_087_2.bmp
fs100_089_0.bmp	fs100_089_1.bmp	fs100_089_2.bmp
fs100_091_0.bmp	fs100_091_1.bmp	fs100_091_2.bmp
fs100_095_0.bmp	fs100_095_1.bmp	fs100_095_2.bmp
fs100_096_0.bmp	fs100_096_1.bmp	fs100_096_2.bmp
fs100_099_0.bmp	fs100_099_1.bmp	fs100_099_2.bmp