



MATILDE ANTUNES FAIAL

Bachelor of Science in Biomedical Engineering

**EFFECTS OF OXYTOCIN AND TESTOSTERONE
ADMINISTRATION ON EMPATHIC REACTIONS
ELICITED IN INTERPERSONAL AGGRESSION
CONTEXTS**

AN ELECTROENCEPHALOGRAPHY INVESTIGATION

MASTER IN BIOMEDICAL ENGINEERING

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**Effects of oxytocin and testosterone administration on empathic reactions elicited in interpersonal aggression contexts
an electroencephalography investigation**

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ABSTRACT

Violence perpetrated by men against women continues to persist in contemporary society, manifesting in various forms and social contexts. In an attempt to understand the cognitive processes linked to men's responses to aggressive contexts, the current study aimed to investigate the effect of Oxytocin (OT) and Testosterone (T) on men's empathic reactions to female victims and male aggressors.

In order to reach the proposed research goal, it was employed a double-blind placebo-controlled experimental design with a randomized cross-administration of OT and T. Electroencephalography data was recorded from 60 participants while they engaged in a psychological task, the Interpersonal Aggression Paradigm. Different analyses were conducted for the 2 types of blocks in the task: Passive Viewing Block and Empathy Blocks. The Event-related Potentials (ERPs) elicited during the stimuli presentation were analysed along with behavioural self-report measures of empathy.

The behavioural results revealed that the OT and T administrations did not modulate the participants' empathic response. However, participants were able to empathize with the victim by experiencing increased feelings of fear and with the aggressor by experiencing higher levels of anger. ERP analysis findings also showed that the hormones had no significant effect on the P300 and LPP ERP components. Regarding the P300, it was found that the neutral stimuli elicited enhanced P300 amplitudes. During the empathy blocks, LPP amplitudes were increased when focusing on emotionally charged pictures. These results suggest that the neutral stimuli elicited stronger responses in the early stage of the empathic process, while the emotional stimuli led to a more intense response in the latter phase.

The current findings serve as preliminary groundwork for understanding the complex relationship between exogenous OT and T and the neural dynamics of empathy, particularly towards interpersonal aggression.

Keywords: Empathy, Interpersonal Aggression, Oxytocin, Testosterone, Event-related Potentials

RESUMO

A violência contra mulheres perpetrada por homens continua a persistir na sociedade atual, manifestando-se sob diversas formas. Numa tentativa de compreender os processos cognitivos subjacentes à reação a contextos de agressão, o presente estudo teve como objetivo estudar o efeito da Oxitocina (OT) e da Testosterona (T) em reações empáticas masculinas perante vítimas do sexo feminino e agressores do sexo masculino.

Para atingir o objetivo proposto, foi implementada uma experiência com um *design* duplamente cego, controlado por placebo, randomizado, com uma administração cruzada de OT e T. Foram adquiridos dados electroencefalográficos de 60 participantes enquanto realizavam uma tarefa psicológica, o *Interpersonal Aggression Paradigm*. Foram efetuadas análises diferentes para os 2 tipos de blocos do paradigma: Bloco de Observação Passiva e Blocos de Empatia. Os potenciais evocados durante a apresentação dos estímulos foram analisados, juntamente com as medidas comportamentais de empatia relatadas pelos participantes.

Os resultados comportamentais revelaram que as administrações de OT e T não modularam a resposta empática dos participantes. No entanto, estes foram capazes de empatizar com a vítima, ao sentirem mais medo, e com o agressor, ao sentirem maiores níveis de raiva. O resultado da análise dos potenciais evocados mostrou também que a administração das hormonas não teve um efeito significativo nos potenciais P300 e LPP. Relativamente ao P300, verificou-se que os estímulos neutros aumentaram a sua amplitude. Durante os blocos de empatia, as amplitudes do LPP aumentaram quando os participantes se focavam nas imagens com maior carga emocional. Estes resultados sugerem que os estímulos neutros provocaram respostas mais fortes na fase inicial do processo empático, enquanto os estímulos emocionais conduziram a uma resposta mais intensa na fase final.

Estes resultados servem de base para a compreensão da relação complexa entre a OT e a T exógenas e os mecanismos neuronais da empatia, particularmente perante agressão interpessoal.

Palavras-chave: Empatia, Agressão Interpessoal, Oxitocina, Testosterona, Potenciais Evocados

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ABBREVIATIONS

- ANOVA** Analysis of Variance (*pp. x–xii, 24, 25, 27, 29, 31, 55, 57, 60, 61, 64, 67, 70, 72, 75, 77–79, 81, 83*)
- EEG** Electroencephalography (*pp. 2, 3, 5, 6, 10–14, 18–20, 23, 25*)
- EQ** Empathy Quotient (*p. 40*)
- ERP** Event-Related Potential (*pp. viii, 3, 5, 6, 10–12, 14–17, 23–25, 28–32, 35–40, 75–84*)
- FCUL** Faculdade de Ciências da Universidade de Lisboa (*p. 19*)
- fMRI** Functional Magnetic Resonance Imaging (*pp. 4, 10, 12, 14*)
- IAP** Interpersonal Aggression Paradigm (*pp. viii, 2–5, 14, 18–22, 24, 25, 28, 33–37, 39, 40*)
- IBEB** Instituto de Biofísica e Engenharia Biomédica (*p. 19*)
- ICA** Independent Component Analysis (*p. 23*)
- IRI** Interpersonal Reactivity Index (*p. 40*)
- LH** Luteinizing Hormone (*p. 7*)
- LPP** Late Positive Potential (*pp. viii, ix, xi, xii, 6, 7, 11–13, 15–17, 23, 24, 28, 30–32, 36–40, 76–78, 81–84*)
- MET** Multifaceted Empathy Test (*p. 13*)
- OT** Oxytocin (*pp. 2, 3, 8–10, 13–17, 19, 20, 23, 33, 35, 38–40*)
- PL** Placebo (*pp. 12–17, 19, 20, 38, 40*)
- PVN** Paraventricular Nucleus (*pp. 8, 9*)
- RMET** Reading the Mind in the Eyes Test (*pp. 12, 13*)

SON Supraoptic Nucleus (*p. 8*)

T Testosterone (*pp. 2, 3, 7–10, 12, 14–17, 19, 20, 23, 33, 35, 38–40*)

INTRODUCTION

The research work described in this dissertation was carried out in accordance with the norms established in the ethics code of Universidade Nova de Lisboa. The work described and the material presented in this dissertation, with the exceptions clearly indicated, constitute original work carried out by the author.

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1.1 Context and Motivation

Social connections play a crucial role in maintaining the overall health of human beings. In order to build meaningful relationships, one must be able to identify and understand the emotional states and perspectives of other individuals [2], an essential skill referred to as empathy.

Empathy can be described as the ability to experience and understand other people's feelings or mental states [3]. Several variables can influence empathic reactions towards others, namely the ethnicity [4] or gender [5] of the target of empathy. Other factors can also modulate the observer's empathic responses, such as their cultural beliefs and subjective experiences [2].

It has been empirically proven that empathy can drive pro-social behaviours and inhibit aggressive tendencies, as some studies state that those who naturally feel for others are less likely to cause them harm [6]. On this basis, empathy can be investigated as a means to understand specific dimensions of aggressive behaviours, including the persistence of physical and psychological violence inflicted on women, particularly by men.

According to the World Health Organization, aggression towards women is considered a "global health problem of epidemic proportions", resulting in physical complications, impaired social functioning or mental health problems in the victims [7]. Investigating the cognitive processes behind men's aggressive behaviours is essential to identify the sources and possible motives for their emergence. Moreover, it is important to identify possible

inhibitors or triggers for that kind of behaviour towards women. One way to achieve this goal is through the investigation of empathic responses towards female targets.

This dissertation focuses specifically on studying men's empathic reactions towards female victims and male aggressors in interpersonal aggression contexts. Furthermore, two hormones that can be implicated in empathic and aggressive processes, and modulate neural responses towards different targets, were selected for this study: **Oxytocin (OT)**, which is associated with social bonding and empathy [8] and **Testosterone (T)**, commonly linked to anti-social behaviours and aggressive tendencies [9].

This investigation was carried out using **Electroencephalography (EEG)**. The EEG methodology has been employed in the study of intricate psychological mechanisms such as selective attention or memory and it can be a powerful vehicle for the investigation of social cognition processes [10]. Only relatively recently, the topic of empathy has been more prevalent in EEG investigations, as it enables researchers to better understand subjects' responses to specific stimuli and possibly predict future behaviours when confronted with similar conditions. The present study employed the **Interpersonal Aggression Paradigm (IAP)** [11], a psychological task where participants watched emotional (interpersonal aggression contexts) and neutral interactions between 2 individuals. In this experimental task, they were instructed to watch the pictures without focusing on any specific target as well as attempting to empathize with the different targets.

1.2 Objectives

The present research aims to provide new insights into the cognitive processes associated with men's perception of female victims as well as male aggressors and how exogenous **OT** and **T** can influence those neural reactions when compared to placebo conditions.

Therefore, the research question that this dissertation aims to answer is: **Does OT and T influence male empathic reactions to interpersonal aggression situations?**

In order to accurately answer the proposed question, EEG data collected during the IAP was analysed, as well as behavioural measures.

1.3 Document Structure

This document is divided into eight chapters. The first and current chapter introduced this dissertation and its motivation as well as the main research goals. The second chapter provides the theoretical concepts required for the development of this dissertation. The third chapter encompasses a literature review on the main topics addressed in this study. In chapter four, the proposed hypotheses are presented. The fifth chapter provides a comprehensive description of the methodology adopted to fulfil the objectives of this study. Chapter six presents the results obtained within this investigation and in chapter seven these results are critically analysed and discussed. Lastly, the eighth chapter concludes this document by presenting the main findings and future research suggestions.

THEORETICAL CONCEPTS

In this chapter, the theoretical concepts required to address the main topics of this dissertation are presented. The first section of this chapter explains the concept of empathy and its neural basis. In the second section, a thorough description of the IAP is presented. In the third section, EEG is introduced as well as Event-Related Potentials (ERPs), including the components of interest for this research. The fourth and fifth sections are about the hormones examined in this study: OT and T.

2.1 Empathy

Numerous definitions have been created for the term empathy, most of them connected by the general idea of blurring the boundaries between other people's experiences and self-experience [12]. Empathy can be generally described as a complex physiological phenomenon where processes such as observation, reasoning, and memory are employed to infer and understand the thoughts and feelings expressed by others [13]. Based on this, one can understand that empathizing with someone encompasses a broad spectrum of human experiences, including the motivation to help and care for them or the automatic mirroring of that individual's emotional states, a common process known as emotional contagion [14].

Currently, most scholars and researchers agree that the empathic process can be divided into two different neurocognitive components: an automatic **emotional** bottom-up process, in which one's perception is shaped solely by the other person's expression of emotion, stimulating a mirroring response in the observer; and a latter **cognitive** top-down component where the perceiver is able to understand the cognitive aspects and perspectives of others without necessarily sharing their emotional state [11], [12], [14]. It is the combination of the emotional and cognitive components that leads to a complete empathic experience since it combines an understanding of the other person's perspective as well as the emotional significance of the particular situation [15].

2.1.1 Empathy and the Brain

A crucial milestone in the psychology and empathy research was the discovery of mirror neurons in monkeys. It was found that these neurons in the ventral premotor and parietal cortices were activated when the monkeys observed or performed actions, therefore suggesting that the understanding of others' behaviours is based on the simulation of those observed states [16], [17].

Studies performed in humans, mostly with [Functional Magnetic Resonance Imaging \(fMRI\)](#), have also confirmed this mirroring effect. Researchers have found that both executing and perceiving a physical action will recruit the premotor cortex [18]. Other brain networks such as temporo-parietal junction [19] and inferior frontal cortex [20] have also been linked to behaviour mirroring. In terms of emotional perception, a similar discovery was found as studies show that the observation and imitation of human facial expressions or body postures will activate the same premotor regions [21].

As for the division of the empathic experience into emotional empathy and cognitive empathy, different brain structures have been allocated to these two complementary processes. A great amount of research has focused on emotional empathy, particularly studying the early response to different facial expressions. The emotional connotation in the face of the target of empathy is processed via temporal cortex from the visual cortex to the limbic areas [22]. However, subcortical structures such as the amygdala can also respond to facial stimuli, particularly to bolder expressions as opposed to more subtle emotional states [22]. Additionally, it has been shown that different facial emotions will activate different brain structures [23]. For instance, observing disgusted expressions will engage the insula, which is expected given its known role in the process of learning aversions, particularly related to taste [23]. It is important to emphasize that the early emotional response will also be affected by different variables such as attentional modulation [24]. As for cognitive empathy, research has shown that the structures implicated in the ability to understand other people's mental states are the temporal poles, the medial prefrontal cortex and the temporoparietal junction [25].

2.2 Interpersonal Aggression Paradigm

The [IAP](#) is a psychological task that was originally used by Nummenmaa et al. [11] in an [fMRI](#) investigation on the neural systems involved in cognitive and emotional empathy. In this paradigm, participants are instructed to watch pictures of emotional and neutral scenarios between two individuals. The emotional pictures depict interpersonal aggression scenarios like strangulation or threats with weapons, while the neutral pictures show routine, non-emotional interactions like conversing or looking through magazines.

The participants are given 2 types of instructions, either to empathize with one of the protagonists in the pictures or to watch the pictures in a passive way, without focusing on a specific target. In both neutral and emotional scenes, the participants are instructed

to empathize either with the person on the right or with the person on the left, that is, to try to mentally mimic what they would be feeling and thinking in the particular situation depicted in the image. The task is divided into blocks where each picture is shown one at a time. In total, the participants are presented with five types of blocks: passive-watching emotional scenes; passive-watching neutral scenes; empathizing with one of the individuals in a neutral scene; empathizing with the aggressor; and empathizing with the victim in the emotional pictures. The block in which the participants are requested to empathize with one of the targets in the neutral scene is meant to trigger cognitive empathy, while the blocks where they have to empathize with the victim or the aggressor should elicit emotional empathy.

In this dissertation, the IAP was also implemented for the assessment of empathic responses towards aggressors and victims in interpersonal aggression interactions. However, the experimental task underwent certain adaptations regarding the instructions, block organization and stimuli selection.

Additionally, in our investigation participants were instructed to complete a questionnaire regarding their empathic response to the stimuli presented in the IAP task. Specifically, participants rated 4 different emotions, i.e., Fear, Anger, Neutral and Pleasure, on a scale from 1 to 5, according to the intensity of their emotions when focusing on the different targets as well as their perception of the emotion intensity felt by the targets.

2.3 Electroencephalography

The EEG technique is used to measure electrical activity produced by the cooperative action of the brain cells. The most common way to collect the electrical activity of the brain is through the placement of electrodes on the scalp, as it is a practical and non-invasive method [26]. An EEG signal is composed of negative and positive fluctuations that can be studied in terms of amplitude, latency and frequency, all of which can be associated with specific cognitive processes [27].

The EEG recordings are captured from a specific type of neurons, the pyramidal neurons, because their structure allows them to be powerful dipoles. When the dipoles have opposite orientations, the charges will neutralize each other and the signal will not reach the scalp. Since the cortical pyramidal neurons are positioned perpendicularly to the scalp and parallel to each other, the summation of their dipoles will generate a significant signal. Thus, the EEG signal results from the sum of the postsynaptic potentials, which are the graded potentials created by the change of permeability of the postsynaptic membrane, from cortical pyramidal neurons [28].

The recording of the EEG signal can be time-locked to actions or external stimuli in order to study specific cognitive activity. The distinct waveforms found in those portions of the signal can be referred to as ERPs [26].

2.3.1 Event-Related Potentials

Research on cognition and perception, including emotion, and sensory processing, is frequently conducted using ERPs since they provide millisecond-level resolution of the brain activity underlying these processes. For that reason, investigating ERPs is especially beneficial for examining cognitive processes that happen rapidly or automatically, as well as assessing the temporal dynamics of these mechanisms [10], [29].

ERPs are direct measures of neural activity consisting of voltage deflections in the EEG signal that are temporally tied to a particular occurrence, like a reaction to a stimulus. The negative and positive fluctuations in the ERP waveform are referred to as ERP components and they translate specific neural processes [30].

2.3.1.1 Event-Related Potential Technique

In order to identify the ERP components in the EEG data, the temporal sections recorded during the event of interest have to be averaged across a large number of trials [30]. Once the ERPs are extracted, different types of information can be obtained from the underlying components for further analysis. The most common ways to analyse the ERP components are through the comparisons of their amplitude and latency [31].

There are two main approaches when extracting amplitude values from an ERP component. The first is the identification of the maximum voltage, positive or negative, in the time window of that particular component, i.e., peak amplitude. The second entails the assessment of the waveform mean amplitude across the selected time window, known as the mean amplitude [31]. As for latency, in the ERP context, it refers to the time delay between the onset of the stimulus and the occurrence of the ERP component.

In this dissertation, the mean amplitudes of the P300 and the Late Positive Potential (LPP) ERP components will be used to examine the impact of the hormones on the empathy levels for the different targets. The mean amplitude was chosen to quantify these ERP components because it remains unbiased in the presence of high-frequency noise within the signal, as opposed to the peak amplitude [31].

2.3.1.2 P300 ERP Component

The P300 is a positive ERP component that peaks at around 300 to 600 ms after stimulus presentation. Its amplitude reaches a maximum in the midline scalp sites of the centro-parietal region [32]. Research findings suggest that the P300 recorded on the scalp is produced through the activity of neural networks involving areas in the temporal-parietal neocortex, as well as limbic structures such as the anterior cingulate [33].

In 1965, Sutton et al. [34] labeled the P300 after observing a significant positive component that peaked around 300 ms after stimulus onset. This response was observed when the participants were unable to anticipate whether the upcoming stimulus would be auditory or visual. Once the experience was designed in a way that enabled the prediction

of the stimulus type, the component appeared much smaller. Since then, the P300 has been extensively studied across various contexts, and linked to a wide range of cognitive processes.

2.3.1.3 LPP ERP Component

The **LPP** component is a sustained positive deflection that typically begins at around 400 ms after stimulus onset and can last several hundreds of milliseconds depending on the type of stimulus and nature of the task. Its maximal amplitude is registered in the centroparietal electrodes [35]. Studies suggest that **LPP** is produced and modulated by cortical and subcortical structures linked to visual and emotional processing. These different brain systems may have a greater impact on regulating this component depending on the emotional content of the stimuli (positive, negative, or neutral) [36].

A significant body of research indicates that the **LPP** component is consistently modulated by emotion, as it is generally larger for emotionally significant stimuli, such as exciting or threatening information, compared to neutral information. However, depending on individual differences and self-relevance, specific types of stimuli can evoke larger amplitudes in the **LPP** component. For instance, if an individual is particularly sensitive to a specific type of emotional content, such as fear-inducing images, they might exhibit a greater **LPP** response when presented with those stimuli when compared to someone less sensitive to such content. Other factors that might influence **LPP** amplitudes are task demands as well as the overall context of the study [37].

2.4 Testosterone

T is a steroid sex hormone that plays numerous roles in women's and men's bodies [38]. In males, it is produced in the testicular interstitium by the Leydig cells [39]. Every 60 to 90 minutes, the gonadotropin-releasing hormone is released from the hypothalamus to signal the pituitary gland to produce the **Luteinizing Hormone (LH)** and release it into the bloodstream [40]. The **LH** will then bind to specific receptors in the plasma membrane of the Leydig cells and initiate a series of reactions that leads to the production of **T** [41]. The steroid hormone is then released in the peripheral circulation and transported to target tissues such as muscle, adipose tissue, prostate gland and gonadal tissue.

In order to carry out its androgenic functions, including the stimulation of the development of male sex characteristics, **T** has to bind to androgen receptors in the target cells that will allow the expression of the specified responsive genes. **T** is also responsible for modulating anabolic effects such as supporting muscle growth and bone density, therefore being referred to as an anabolic-androgenic steroid. Lastly, since some of its receptors are also expressed in the brain, **T** has a significant effect on cognition and behaviour [42].

2.4.1 Influence of Testosterone on Social Dynamics

Investigations on the social effects of **T** have been conducted by animal researchers in the last decades, leading to the confirmation of **T**'s role as a "social hormone" [9]. More recently, studies performed on humans have shown the causal effects of **T** in relation to different social dynamics including aggression and social status [9].

Several studies corroborate the hypothesis that men with higher levels of baseline **T** concentrations tend to have more aggressive tendencies in comparison to men with lower levels of this hormone [43], [44]. However, recent studies employing single dose administrations of **T** show that the link between **T** and human aggression is relatively weak, as the subjects' actions are modulated mainly by social context, provocation or personality traits [45], [46]. Nevertheless, single dose **T** administrations have been shown to decrease generosity in participants in a neuroeconomics paradigm [47], as well as increase propensity to punish opponents in behavioural experimental tasks [48].

On the other hand, exogenous **T** can also lead to pro-social behaviours performed with the intention to achieve and maintain social status or gain influence in group settings [49].

2.4.2 Exogenous Testosterone in Research Contexts

Studies investigating the effects of exogenous **T** have been more prevalent because they allow a deeper comprehension of the causality of this hormone in response to complex psychological paradigms created in laboratory environments [50].

There are 3 main routes for **T** administration in endocrinological studies: oral, intramuscular and transdermal [50]. The most commonly used methods of administration are oral and transdermal, since they are non-invasive. However, the oral administration results in a deficient absorption of **T** since it causes it to be metabolized and inactivated rapidly by the liver, leading to the requirement of larger dosages for the hormone to reach the desired level in the body [51]. The transdermal route offers distinct advantages over the aforementioned techniques since it allows an easy inspection of the **T** levels in the body through saliva collections [52]. Moreover, it allows **T** to be released into the systemic circulation at a consistent rate. **T**'s concentration reaches its maximum approximately 2 hours post-administration, and returns to its basal level after 12 hours, similarly to the natural fluctuation of **T** levels in men [53].

2.5 Oxytocin

OT is a neuropeptide that acts as a central neuromodulator and a peripheral hormone in both males and females. It is mainly produced in magnocellular neurons in the **Paraventricular Nucleus (PVN)** and the **Supraoptic Nucleus (SON)** of the hypothalamus [54].

A portion of the **OT** produced in the **PVN** and **SON** is carried through the neuron's axons to the pituitary gland, where it is stored in the secretory vesicles. The **OT** is

then secreted into the peripheral bloodstream for its hormonal effects, including uterine contractions and milk ejection during lactation [55].

As for its central effects, OT produced in the magnocellular neurons and in the parvocellular neurons (smaller cells located in the PVN) is transported along the axons and released as a neurotransmitter in specific brain regions in the brainstem and forebrain, as well as in structures within the limbic system [55]. In these regions, OT has a modulatory role on social behaviours and emotion expression [54].

2.5.1 Influence of Oxytocin on Social Dynamics

Research into OT's impact on human social dynamics earned prominence in the early 2000s, establishing it as a behaviour modulator [56]. Its administration in experimental settings is linked to various social effects such as trust [57] and cooperative behaviour [58], leading to OT being commonly referred to as the "love hormone" or "moral molecule" [59].

As opposed to T, OT is often associated with pro-social behaviours and social cognition [8]. It was discovered that OT delivered intranasally resulted in a decrease in fear and anxiety in humans when confronted with fearful or threatening contexts in experimental tasks [60], [61]. Moreover, the administration of OT has been shown to improve emotional empathy, i.e., the ability to understand and share the emotions felt by others, therefore contributing to more positive social interactions [62].

In addition to promoting pro-social behaviours, research has also shown the role of exogenous OT on participants' in-group bias and discriminating behaviour towards others they categorize as out-group, such as individuals of a different ethnicity [63]. Moreover, according to the Social Salience Hypothesis [64], OT can also heighten aggressive behaviours in provocative or competitive contexts.

2.5.2 Exogenous Oxytocin in Research Contexts

Most investigations examining OT's role in social cognition use intranasal spray administrations due to its simplicity and non-invasiveness [57].

The nasal delivery is preferred since it allows the OT to bypass the blood brain barrier and reach the central nervous system [65]. OT that is orally administered will not influence social cognitive processes since it will be metabolized by the intestinal fluid in the gastrointestinal tract [66]. OT also fails to be diffused through the respiratory system since the molecules are too large to be absorbed by the alveolar epithelium in the lungs [67].

Currently, there are 3 possible pathways that describe the transport of OT from the nasal cavity to the brain [65]. The olfactory pathway, where the OT reaches the brain and peripheral circulation through the olfactory sensory neurons located in the olfactory epithelium in the nasal cavity. Similarly, in the trigeminal pathway, the OT molecules travel from the epithelium to the trigeminal ganglion, which then extends to the brainstem. Lastly, in the peripheral pathway the OT is absorbed in the carotid arteries located in both olfactory and respiratory epithelia [65].

LITERATURE REVIEW

This chapter presents a comprehensive literature review on empathy, divided into 3 sections. The first section discusses empathy in EEG investigations, including the relationship between empathy and the ERPs of interest, as well as the concept of empathy in interpersonal aggression contexts. The second and third sections examine the correlation between empathy and T and OT, respectively.

3.1 Empathy and Electroencephalography Investigations

To gain a deeper understanding into the way people perceive and react to the emotional and mental state of others, researchers relied mostly on subjective ratings of empathy obtained through interviews or self-report questionnaires [68]–[70]. Electrophysiological measures, including electrodermal activity and electromyography, came in as an attempt to establish quantitative measures of empathy [71]–[73]. However, such measures could not provide information regarding the cognitive mechanisms underlying the empathic process. To shine a light on these neural dynamics, researchers resorted to brain imaging techniques (e.g., fMRI) and other measures of brain activity, such as EEG.

Empathy-related EEG investigations often revolve around the concept of empathy for pain. In 2008, Yan Fan et al. [74] assessed the temporal dynamics of the neural empathic process in an EEG study where subjects were presented with pictures and cartoons of hands in neutral and painful situations. It was confirmed that the empathic process involved two distinct phases that unfolded at different points in time: an affective sharing response that involved early ERP components, and a following cognitive evaluation that involved late ERP components. Additionally, during the presentation of painful stimuli, there was an increase in P300 amplitudes in comparison to the non-painful pictures. Moreover, when comparing the ERP modulations for painful depictions of human hands versus cartoons, it was found that the latter stimuli reflected a decrease in the modulation of the early components.

A great amount of literature corroborates these results, as an increase in amplitude in the early ERP components, such as the N100, N200 and P200 components, is linked

with the perception of pain [75], [76]. The N100 and N200 components are two negative fronto-central ERP components. While the N100 peaks at around 50 to 150 ms after stimulus onset [77], the N200 reaches its peak at around 250 to 350 ms post-stimulus [78]. As for the P200, it is described as a fronto-central positive ERP component that emerges approximately 200 ms after the stimulus onset [31].

Similarly to the approach followed by Yan Fan et al. [74], other studies investigated the effect of the target of the harmful behaviours in the modulation of the empathy-related ERP components and yielded similar results. For non-human targets, e.g., robots [79], or individuals of a different ethnicity or social group from the observer, which can be categorized as out-group, it was found a decrease in early ERP activity [80]–[82]. This disparity in early empathic responses observed between two distinct groups, such as individuals from different racial backgrounds, may indicate that the emotional component of empathy plays a significant role in the manifestation of prejudice [83]. In the research surrounding empathy for others' pain, a vast amount of contexts has been studied including the morality of the target of empathy [84], cooperation and competition [85], age of the observer [86] and life experience [87].

In addition to empathy for pain, the recognition and understanding of emotional facial expressions, which can reflect the level of empathic ability, have been studied in EEG investigations. A study showed that individuals with higher empathy scores obtained through self-report questionnaires exhibited enhanced amplitudes in the N170 and in the LPP ERP components when observing faces showing distinct emotions such as anger or surprise [88]. Groen et al. [89] corroborated this result by showing that participants with a tendency to experience distress when perceiving other people's distress displayed larger LPP responses to human interactions as opposed to other types of stimuli.

3.1.1 Empathy in Interpersonal Aggression Contexts

Similarly to the early stages of empathy research, there are analytical investigations based on self-report measures of empathy that study individuals' empathic levels towards interpersonal aggression situations, namely how the genders of the victim and perpetrator modulate empathic reactions in scenarios of sexual harassment [90]–[92].

Few EEG research follows a similar procedure to the one used in the current study, where participants are instructed to empathize with different targets in neutral and interpersonal aggression contexts. A study conducted by Dongen et al. [93] employed a similar method, where EEG signal was collected while participants viewed pictures of neutral and aggressive scenes between two individuals. The study analysed how psychopathic meanness modulated empathy towards the violent scenes. However, contrarily to the present study, participants only passively viewed the images, meaning that the study did not explore empathy levels toward specific targets but rather responses to the entire scenes. As a result, larger P300 and LPP amplitudes were found during the aggressive stimuli presentation as well as a decrease in LPP amplitudes for higher psychopathic

meanness scores. Furthermore, in a study that investigated individuals with an empathy dysfunction, researchers found that participants showed diminished LPP amplitudes when exposed to stimuli depicting someone being harmed by another person [94].

Aside from studying the ERP components associated with empathy and vicarious emotion processing, some EEG research focuses on frequency bands. Balconi et al. [95] analysed how different frequency bands were implicated with the early emotional empathic response towards different social interactions and how that neural response interplayed with the participants' autonomic reaction. The stimuli consisted of pictures of two individuals in positive, negative, or neutral situations and participants were instructed to try to experience the emotions that the targets were portraying. It was found that the type of emotion influenced the distribution of the brain's activity and that the low frequency theta and delta bands were closely linked with blood flow changes in the brain's cortex (empathic central measures).

3.2 Empathy and Testosterone

Early exposure of T has been shown to influence empathic responses. Chapman et al. [96] discovered that higher fetal T exposure correlated with a lower performance on the Reading the Mind in the Eyes Test (RMET) [97], where a low score typically indicates a weakened ability to understand another person's mental state. On the same note, a recent fMRI study found that prenatal T exposure was associated with a decrease in resting-state connectivity in brain regions involved in cognitive empathy [98].

As for T administration, Hermans et al. [99] investigated its effect on affective emotional sharing and facial mimicry with electromyography. It was found that the administration of T contributed to the attenuation of the mirroring effect. However, it did not modulate the self-report measures, suggesting that the effects of exogenous T may not reach the conscious brain and only modulate the early physiological responses.

Regarding EEG investigations, Zhuo et al. [100] studied the influence of exogenous T on empathy for pain. The investigation included two different experiments: the first consisted of a pain-judgement task, where participants rated pictures of hands in painful or non-painful situations as painful or non-painful, and a counting task where participants were instructed to count the number of hands in the pictures. From this experiment, it was found that while there were no significant differences in neural responses during the pain-judgment task between T and Placebo (PL), there were differences in the hands-counting task, as the participants showed lower accuracy in this task after T administration as well as larger LPP amplitudes. These results suggested that a late empathic response was evoked even when the focus was shifted away from pain cues. The second experiment consisted of rating the intensity of the pain portrayed in the stimuli. The self-report ratings were not significantly influenced by T, but it was found that it increased N100 and N200 amplitudes, meaning that it facilitated the automatic emotional empathic response to

others' pain when participants were actively empathizing with the stimuli (pain-rating task).

3.3 Empathy and Oxytocin

The impact of OT on various pro-social behaviors, including empathy, has been extensively studied [54]. Various studies found that the administration of OT led to heightened emotional empathic responses [62]. Moreover, an eye-tracker investigation conducted by Le et al. [101] showed that attention toward human faces, as opposed to body parts or their surroundings, increased with exogenous OT, suggesting an enhanced empathic response since attention to others' emotions can be indicative of a strong empathic ability.

In studies employing the **Multifaceted Empathy Test (MET)** [102], OT has also been proven to enhance emotional empathy [62], [103]. The MET is a test that evaluates both cognitive and emotional empathy. For the cognitive empathy measure, participants are asked to deduce the mental states of individuals shown in different pictures and afterward are informed of the accuracy of their answers. To evaluate emotional empathy, subjects are asked to assess their emotional reactions to the stimuli.

In addition to enhancing emotional empathy, OT can also improve mentalizing, which is the ability to infer others' mental states. Domes et al. [104] reached this conclusion in an investigation where participants were instructed to complete the **RMET**. It was revealed that the participants who were administered with intranasal OT performed better than the ones in the PL condition.

In 2013, Sheng et al. [105] investigated the effects of intranasal OT on empathic responses towards out-group individuals. In this study, participants were presented with pictures of neutral and pain-charged faces of individuals of the same and different racial identities. Results showed that the OT administration led to stronger empathic responses, as evidenced by increased P200 amplitudes, towards painful facial expressions in comparison to neutral expressions in the individuals from the same racial group. This effect was not observed in the individuals categorized as out-group, therefore emphasizing OT's role in promoting an in-group bias in the context of empathy.

Furthermore, a recent EEG investigation focused on the self-other distinction during the empathic response and how OT could interact with this process [106]. Participants were instructed to either assess the emotional state depicted in facial stimuli or evaluate their own emotional responses (sad versus neutral). It was found that OT attenuated the differences in P200 and LPP amplitudes between sad and neutral facial expressions in the self-evaluation task, meaning that it minimized the differences in neural empathic reactions towards expressions of sadness versus neutrality. Additionally, in the emotion assessment task, OT was found to enhance P200 amplitudes when participants perceived sad expressions. These results could validate OT's role in integrating rather than segregating self and others, a phenomenon that suggests a strong empathic response.

HYPOTHESES

The paradigm used in this study, the IAP, has only been employed in an fMRI investigation [11] and it has never been studied in combination with T and OT administration as well as in a ERP analysis. Moreover, the specific context of empathy towards individuals in interpersonal aggression contexts, particularly female victims and male perpetrators, has also not been taken into consideration under these circumstances.

On that account, EEG investigations surrounding similar topics allowed for hypotheses regarding the effect of OT and T on the ERP components of interest for this study. Moreover, the behavioural hypotheses were developed based on the literature review of the social effects of the two hormones.

The current hypotheses explore the 4 different administration groups that result from the cross-administration of the two hormones: active OT and active T; active OT and PL T; active T and PL OT; PL OT and T (control group).

4.1 Behavioural Hypotheses

The participants' self-reported empathic experiences, assessed with the IAP questionnaire, towards the different types of targets in the stimuli, i.e, victim and aggressor (male and female actors in the emotional pictures) and neutral male and neutral female (male and female actors in the neutral pictures), will be used to quantify their empathic responses. Participants with a greater understanding of the emotions expressed by the actors, and who also experience emotional resonance themselves, will be considered more empathic. For instance, when focusing on the victim of a violent action, assigning higher ratings for the emotion Fear when assessing the target's emotional experience will be deemed a more empathic response, as it signifies the recognition and acknowledgment of the feelings expressed by that target. When it comes to describing their personal experiences, participants who will give higher scores to emotions like Anger or Fear will also be considered to have a strong empathic reaction. On the other hand, if the Neutral or Pleasure emotions are rated higher, it could indicate that the emotions expressed by the victim did not elicit a contagious response, signaling a low empathic experience.

Taking into account the pro-social effects of OT explored in section 2.5.1 and its implication in the empathic ability, as mentioned in section 3.3, one can anticipate that the active OT and PL T administration group will lead to stronger empathic responses in the participants in comparison to the control group, meaning that they will have emotionally compatible experiences with the actors' and accurately recognize their feelings. It is also possible to predict that the OT administration will lead to stronger empathic responses towards the female in the emotional pictures, as opposed to the male, since this hormone can evoke pro-social behaviours and elicit compassionate feelings towards the target that is being harmed.

On the other hand, T has been found to reduce the mentalizing ability and enhance non-prosocial behaviours. This thus suggests that the administration group with the active T compound and PL OT could exhibit impaired empathic responses when compared to the PL OT and PL T group. This impairment will be evidenced by a lack of emotional sharing, reflected in higher ratings of the neutral emotion when focusing on both victim and aggressor targets, as well as pleasurable feelings from the observation of the victim's painful expressions or the aggressor's violent actions. Research has also shown that T administration could enhance emotional reactivity, which could lead to stronger feelings of anger and fear in response to aggressive stimuli. Considering this, one could also expect a more pronounced empathic reaction towards the perpetrator of the violent behaviours. Given the intricate nature of the relationship between T and social stimuli, which can be influenced by various factors, it is challenging to accurately predict a straightforward effect from its administration, particularly considering the complexity of the empathic experience.

As for the administration of both OT and T active compounds, the interplay of the two hormones will possibly lead to a complex reaction in the participants. However, it is expected that the OT will counteract the effect of the T and that the participants under this condition will show enhanced empathic reactions towards the actors, especially the female protagonist in the emotional pictures, similarly to the anticipated effect of the active OT and PL T administration group.

4.2 Neural Hypotheses

To shine a light on the cognitive mechanisms underlying the empathic process, the analysis of the neural data will be focused on the P300 and LPP ERP components.

4.2.1 P300 ERP Component

The P300 component is implicated with a significant amount of cognitive processes and it is highly dependent on task requirements [107]. Studies show that this component is modulated by emotionally salient stimuli, meaning that stimuli with emotional significance, either positive or negative, will elicit larger P300 amplitudes compared to neutral stimuli.

Additionally, information that will capture the participant's attention or require increased cognitive processing will also lead to greater P300 amplitudes [108]. These results are noteworthy since increased attention to others' emotions can be considered an indicator of a stronger empathic ability as well as heightened cognitive activity.

As mentioned in section 3.1, stimuli depicting painful situations generated larger P300 amplitudes in comparison to non-painful stimuli in empathy for pain investigations [74]. Few studies explore the effect of empathic responses towards emotional and neutral interpersonal scenarios on P300 activity. However, it has been shown that larger P300 amplitudes were found during the presentation of aggressive stimuli in comparison to neutral ones in a passive viewing empathy task [93].

Considering the active OT and PL T administration group, it is expected that the participants show greater empathic abilities, which will result in larger P300 amplitudes, in comparison to the control condition. It is worth mentioning that OT can also heighten aggressive behaviours. However, since the employed experimental task has a passive nature, it should not trigger aggressive reactions in the subjects [64]. Furthermore, within this administration group, it is expected that when passively viewing the images, greater P300 amplitudes will be found during the presentation of the emotional scenes. In the empathy blocks, which are meant to trigger empathy towards the actors in the pictures, the P300 should appear larger when participants empathize with the individuals in the emotional pictures, with a particularly pronounced effect for the victims since that type of target may elicit compassionate feelings, which could be enhanced by the OT administration.

As for the active T and PL OT administration group, considering the hypothesis that T could lead to weaker empathic responses, one can predict that lower P300 amplitudes will be found in the participants within this group when compared to the control group. However, in line with the hypothesis for the behavioural data, it is also plausible to expect that during the empathy blocks of the experimental task, the P300 could be increased for the aggressor role in comparison to the other targets, reflecting a higher empathy level and possible identification with that character.

Bearing in mind the hypothesis that OT counteracts the effect of T, for the active OT and T administration group, it is expected that the participants under this condition will demonstrate higher empathy levels compared to the control group and therefore enhanced P300 amplitudes. We hypothesize that the amplitudes should be notably larger for the female protagonist in the emotional stimuli, similarly to the anticipated effect of the active OT and PL T administration group.

4.2.2 LPP ERP Component

The LPP ERP component is closely associated with emotional processing. Stimuli that generate a strong affective response or are personally relevant or meaningful to the individual will evoke larger LPP amplitudes as opposed to more neutral and impersonal

information [109], [110]. Moreover, socially charged stimuli depicting facial expressions or human interactions will also result in greater LPP amplitudes [89].

Since higher empathy levels tend to be associated with increased sensitivity to emotionally or socially charged stimuli, these modulations of the LPP component could suggest that stronger empathic abilities are positively related to LPP amplitudes.

As for empathy investigations, as mentioned in section 3.1, a study found that individuals with higher self-report empathy levels showed enhanced amplitudes of the LPP ERP component when observing faces showing strong emotions, such as anger [88]. Additionally, research has shown that heightened empathic abilities lead to larger LPP amplitudes when perceiving people in distress [89], while subjects with empathy dysfunctions show decreased LPP amplitudes in response to that type of stimuli [94]. Enhanced LPP amplitudes were also found during the presentation of aggressive pictures in comparison to neutral ones in a passive viewing empathy task [93].

With these results in mind and considering the empathic effect of the OT, the hypothesis regarding the administration group containing the active OT and PL T is that the participants will have increased LPP amplitudes in comparison to the control condition, particularly in the empathy blocks of the task, since the LPP reflects the cognitive empathy process as opposed to earlier emotional responses (this heightened activity in the empathy blocks will be seen across all 4 groups). Similarly to the hypothesis for the P300 component, one can expect stronger empathic reactions towards the emotional stimuli, particularly when empathizing with the victim of aggression (female target), which will be evidenced by enhanced LPP activity.

For the active T and PL OT administration group, in line with the hypothesis that T impairs empathic ability, we predict a decrease in LPP amplitudes in comparison to the other administration groups. It is expected that the modulation of the LPP is more prominent in the emotional stimuli compared to the neutral. Moreover, similarly to the P300 hypothesis, an increase in LPP activity when empathizing with the aggressor compared to the other targets can also be expected.

Lastly, for the group with the active T and OT compounds, the hypothesis is similar to the one for the active OT and PL T group, as the effects of the T will be canceled out by the OT, leading to increased amplitudes of the LPP component compared to the control group. As previously mentioned, this effect might be amplified in the empathy blocks, particularly when participants empathize with the female target in the emotional pictures.

METHODOLOGY

This chapter describes the adopted methods to achieve the proposed objectives for this thesis, including the overview of the experimental protocol, the design of the IAP task, and a comprehensive description of the data acquisition and statistical analysis.

5.1 Participants

63 healthy men aged between 18 and 29 years old ($M = 21.44$, $SD = 2.36$) participated in an EEG experiment in exchange for a monetary compensation in the form of a 25€ FNAC e-voucher. All the participants were recruited from the community sample through advertisement on various online platforms as well as in person flyer distribution.

3 participants had incomplete EEG recordings, hence the neural analysis being carried out on a total of 60 participants, while the behavioural on the 63 participants.

5.1.1 Recruitment

The inclusion criteria for this study included being male, healthy, heterosexual, aged between 18 and 40 years old (inclusive), right-handed, and a native portuguese speaker. The heterosexuality condition was crucial to prevent that sexual attraction to different gender targets would differentially influence the empathy towards them.

Participants with any psychiatric or physical illnesses such as cardiovascular, hepatic, renal, pulmonary, endocrine, or skin diseases were excluded from the study, as well as anyone using hormonal or corticosteroid medication regularly. Participants with conditions resulting in chronic nasal obstruction were excluded since it could affect drug absorption via nasal roots. Furthermore, cigarette or alcohol consumption was also considered among the exclusion criteria (more than 5 cigarettes a day and 28 units of alcohol per week, 1 unit being 10 mL of pure alcohol).

After the recruitment process, all the participants were instructed to avoid consuming cannabis or other substances a week prior to the experiment. Additionally, they were requested to refrain from consuming caffeine, alcohol, tobacco or spicy foods and skip any intense physical activity, such as sports or sexual activity, in the 48 hours leading to

the session. 24 hours before the study they were also instructed to not use deodorant and to avoid washing their hair in order to improve the quality of the EEG signal.

5.2 Study Design

This study was approved by the [Faculdade de Ciências da Universidade de Lisboa \(FCUL\)](#) ethical committee and all the participants gave their written consent before participating in the experiment (REF: CEC/2/2022).

The experiment followed a double-blind, placebo-controlled design, with a randomized cross-administration of OT and T. It was also assured that all participants were unaware of the ultimate goals of the study.

5.3 Experimental Protocol Overview

The experiment was conducted at [Instituto de Biofísica e Engenharia Biomédica \(IBEB\)](#) in [FCUL](#). In the beginning of each session, the participant answered the pre-experiment questions in order to confirm whether he met the necessary requirements and to evaluate his mental state before the experiment. He was provided with an informative document outlining all the steps of the experiment and was asked to sign the informed consent form. Afterwards, the first saliva sample was collected and the participant was then instructed to wash his armpits with a neutral soap and wear a t-shirt with cotton pads for the sweat collection. This process was followed by the gel application (T or PL T). After this, the participant proceeded with the training for 2 experimental tasks, which were not considered in this dissertation. Once the training was finished, the EEG equipment was set-up. The OT or the corresponding PL was then self-administrated via nasal-spray approximately 25 minutes before the beginning of the EEG recording. Next, the second saliva sample was collected (3 minutes) and the experimental tasks started shortly after with the following order: Resting-state task, Taylor Aggression Paradigm, IAP, Rape Behaviour Aggression task and the Authenticity task. Once the experiment was finished, the third and last saliva sample and the sweat samples were collected, and the EEG cap was removed from the participant. Lastly, the participant was requested to fill several psychological questionnaires, including the IAP behavioural questionnaire. Once the procedure was concluded, the experimenter assessed if the participant was feeling any side effects, both physical and psychological, and the e-voucher was sent to the participant via e-mail. The full session lasted between 4 and half and 5 hours.

Some of the steps mentioned in the experimental protocol will not be addressed in this thesis nor be included in the analysis, namely the collection of the saliva and the sweat samples. Furthermore, electrodermal activity data was collected during the EEG recording but will not be analysed in this dissertation. EEG recordings during the IAP experimental task and the behavioural output from the IAP questionnaire comprise the data that will be analysed in order to answer the proposed research question.

5.4 Drug Administration

Before the experimental tasks, the **OT**, the **T** or the **PL** were administered to every participant in a double-blind placebo-controlled design, meaning that both the participant and the experimenters were unaware if the participant was receiving the **PL** or the active substance. The **T** or its **PL** were administered by applying a gel directly on the participant's skin on the upper arm. For the **T**, the gel used was the Testavan 20 mg/g transdermal gel and for the **PL** it was used a neutral gel in an identical bottle. A total of 69 mg of gel was applied approximately 2 hours before the **EEG** collection. For the **OT**, 24 Intranasal Units (IU) of the Syntocinon-Spray 40 IU/mL or the corresponding **PL** were self-administered after the experimenter instructed the participant on how to use the nasal spray correctly and after assessing the congestion of the nostrils (on a scale from 1 - completely blocked, to 10 - completely unblocked, if the participant rated one of his nostrils below 7, the spray would be administered only to the other nostril). This administration process took place 25 minutes before the first experimental task. On average, the **IAP** started 1 hour and 12 minutes after the **OT** administration and 2 hours and 48 minutes after the **T** administration. The distribution of the substances led to the formation of 4 distinct administration groups among the participants: **OT** and **T**; **OT** and **PL T**; **T** and **PL OT**, and **PL OT** and **PL T**. In the present thesis, the neural analysis included a total of 60 participants, which were distributed in the different drug groups as follows: Drug Group 1 (n = 14), Drug Group 2 (n = 16), Drug Group 3 (n = 17) and Drug Group 4 (n = 13).

5.5 Design of the Task: Interpersonal Aggression Paradigm

5.5.1 Stimuli

The set of pictures that constitutes the stimuli for this study was originally used by Nummenmaa et al. [11]. In this investigation, each participant watched a total of 56 images showing a man and a woman in two different situations: 28 images portraying neutral/non-emotional situations and 28 images showing interpersonal aggression scenes (emotional pictures), where the man appears as the perpetrator and the women the victim of the verbal or physical aggression, as seen in Figure 5.1. The neutral images are matched to the images portraying the aggressive scenes, i.e., the neutral scenes have a corresponding emotional scene, where the actors and their surroundings, including the location, clothes and lighting, remain the same. Images displaying two women were excluded from the original set since it was essential that the interactions were between a man and a woman for the context of this dissertation. From the total data set of 60 images (30 emotional and 30 neutral), 56 were kept (28 emotional and 28 neutral) for the purpose of this study. Also, some pictures were mirrored in order to standardize the positions of the actors, that is, the woman on the right and the man on the left. The images depict people from head to hip in the majority of the set and all pictures have similar luminance

levels and average contrast density [11] and a dimension of 2048 x 1536 Pixels.



(a) Male and Female Targets in neutral picture (b) Male and Female Targets in emotional picture

Figure 5.1: Stimuli used in the IAP experimental task.

5.5.2 Experimental Task

The task is divided in 3 blocks and for each block the participants watched the total set of 56 images, one by one, in a randomized order, creating a surprise factor as well as a stronger reaction associated with the emotional pictures.

In the first block, the participants were instructed to watch the images in a passive way, similarly to watching television or looking through a magazine. To reinforce this instruction, surrounding the images appeared 2 arrows pointing to the left of the picture, where the male protagonist is, and 2 arrows to the right, pointing to the location of the female target, to further emphasize that the participant should not focus on a specific target and simply watch the picture as a whole, as shown in Figure 5.2. The images stayed on the centre of the screen for 1500 ms and then a jittered fixation cross between 2000 to 3000 ms appeared.

The second and third blocks of the task are the empathy blocks. In the second block, the participants watched the 56 images in a random order and were instructed to focus on the person on the right, which is the woman in both neutral and aggressive scenarios. In addition to paying particular attention to the female target, the subjects were instructed to empathize with her, i.e., to mentally simulate what she is thinking and feeling in the specific situation portrayed in the image. Analogously to the first block, the pictures were surrounded by arrows, but this time the 4 arrows were pointing to the right, to the visual field of the target of the empathy in the scene, therefore emphasizing the previous instructions. Since this block is meant to trigger emotional and cognitive empathic responses in the participants, the images stayed on the screen for a longer amount of time (4000 ms) followed by a jittered fixation cross, identically to the first block.

The third and final block was similar to the second. The participants watched the full set of 56 images in a random order but contrarily to the previous block, they were

requested to empathize with the person on the left, which is the male target in both neutral and emotional scenes, where he is portrayed as the aggressor. The arrows surrounding the pictures were pointing to the left and the images stayed on the screen for the same amount of time as the previous block, followed by a jittered fixation cross.

Each block was preceded by the instruction screens and the participants stated when they were ready to start by pressing the "Enter" key on the keyboard. The order of appearance of the second and third block was randomised across participants. The images were presented on a screen with 1920 x 1080 resolution. The task was coded in MatLab 2023a [111], using the Psychophysics Toolbox [112].

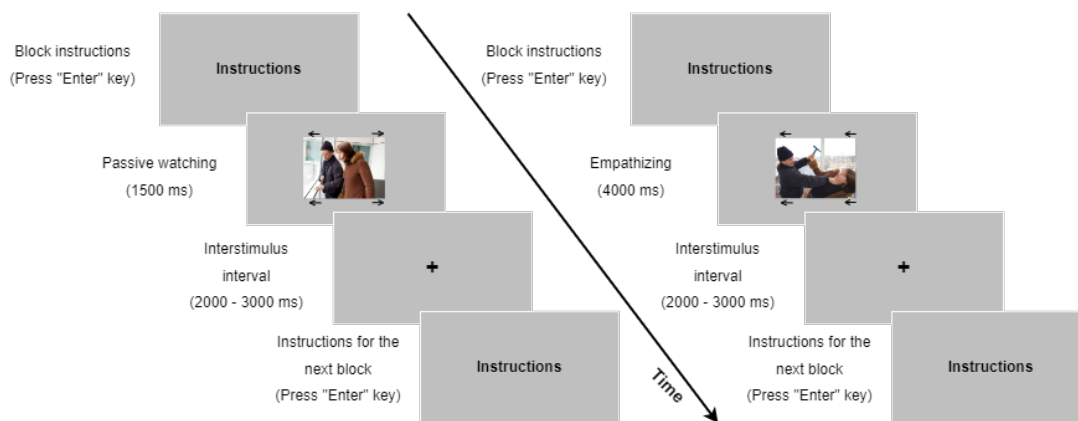


Figure 5.2: Illustration of the IAP task. Passive Block (left) and Empathy Block (right).

5.6 Interpersonal Aggression Paradigm Questionnaire

As explained in section 5.3, once the experiment was finished, participants filled the behavioural questionnaire for the IAP experimental task. This questionnaire was used to assess, at an explicit level, the empathy towards the different targets (female and male) in the two types of pictures (emotional and neutral).

The questionnaire consisted of 224 questions. For each of the 56 images, participants were asked to rate their own emotions when observing the person on the right, i.e., the female target, on a scale from 1 to 5, 1 being “do not feel at all” and 5 being “feel very much”. Participants rated 4 different emotions: Fear, Anger, Pleasure and Neutral. The second question was similar to the first but now focusing on the target on the left. In the third and fourth questions participants were requested to rate their perception of the emotions felt by the male and the female protagonists, i.e., what they thought they were feeling in the specific situations portrayed in the pictures, using the same four emotions and rating system as the previous questions. The questionnaire was created using Google Forms and the images were added in a random order. Annex III includes the 4 questions that were asked for each of the pictures.

5.7 Data Acquisition and Analysis

In order to study the effect of OT and T on empathic responses elicited in interpersonal aggression contexts, neural and behavioural data were collected and analysed.

5.7.1 Neural Data

Continuous electrophysiological data was recorded with the BrainVision system (ActiCap64 system, BrainProducts GmbH, Gilching, Germany) including a 64 electrode ActiCap and BrainChamp amplifier. The FCz electrode served as the reference and the Fp as the ground. During the acquisition, the impedance was kept at 10 k Ω or below for all the electrodes.

The preprocessing of the EEG signal was performed using the EEGLAB toolbox 2021.0 [113] on Matlab 2023a [111]. Raw data was down sampled to 250 Hz and filtered with a 0.1 - 40 Hz band-pass filter. Bad channels and artifacts found when visually inspecting the signal were eliminated and the data was then re-referenced to the average. In order to remove eye movement, muscle or heart artifacts embedded in the EEG signal, an Independent Component Analysis (ICA) was performed. Lastly, the eliminated channels were interpolated.

The EEG data was divided into epochs separately for the passive viewing block and empathy blocks using the ERPLAB toolbox [114]. The total length of the epochs consisted of the full stimuli presentation duration, meaning that, for the passive block, the epochs had a total length of 1700 ms: 200 ms before the picture display onset and 1500 ms after; and for the empathy blocks, a total of 4200 ms: 200 ms before the picture display onset and 4000 ms after. Furthermore, to guarantee that the epochs were not contaminated with possible artifactual voltages, epochs containing channels exceeding the ± 100 μ V voltage limits were removed. The ERP waveforms were then averaged and the mean amplitudes were extracted. The time windows selected for each component were chosen based on previous literature and further visual inspection of the grand-averaged ERP waveforms. The analysis of the P300 ERP component was conducted within the 210-310 ms interval. The analysis of the LPP ERP component was fragmented into early LPP and late LPP because it allowed a more nuanced understanding of the temporal dynamics of the empathic process. For the early LPP, its amplitude values were inspected in the 300-600 ms time window. The late LPP amplitude was studied in the 600-4000 ms time window for the empathy blocks and in the 600-1500 ms time window for the passive block. The electrodes selected to analyse these components were chosen based on the topographical scalp maps in the time windows of each component. On that regard, data from the PO3, PO4, PO8, O2, and O1 electrodes was analysed for the P300 for both the passive viewing and empathy conditions, data from the PO4, PO8 and P6 electrodes for the early LPP for the passive viewing and empathy conditions, data from the P3, P1, Pz, P2, P4, P6 and PO3 electrodes was investigated for the late LPP within the empathy condition,

and from the P4 and P6 electrodes for the passive viewing condition.

5.7.2 Behavioural Data

The behavioural data consisted of the ratings of the IAP questionnaire from 63 participants. One subject had to be excluded for giving the same rating for all of the questions, hinting to an attention lack during the questionnaire answering. For each emotion (Fear, Anger, Neutral and Pleasure), all answers were averaged across Targets (Female or Male) and Picture Types (Emotional or Neutral).

5.7.3 Statistical Analysis

The statistical analysis was performed on RStudio (version 2023.03.1) [115]. For the neural data, separate analyses were conducted for the empathy blocks and the passive block. In the first case, in order to study the effect of the hormones on the empathic response to the different targets, it was conducted a mixed repeated-measures Analysis of Variance (ANOVA) for the each of the components. The mean amplitude values of the ERP component (P300, early LPP or late LPP) served as the dependent variable, while the Target of Empathy (i.e., Female and Male), and the Picture Type (i.e., Emotional and Neutral), the within-subject factors and the Drug Group (i.e., 1, 2, 3 and 4) as the between-subject factor. For the passive block analysis, the participant's reaction to the picture as a whole was analysed. One two-way mixed ANOVA was conducted with the mean amplitude values of the P300 ERP component, one with the early LPP mean amplitude, and a third with the late LPP mean amplitude as the dependent variable, all having the Picture Type as the within-subject factor and the Drug Group the between-subject. At the behavioural level, a mixed repeated-measures ANOVA was conducted for each of the emotions that were rated in the IAP questionnaire (i.e., Fear, Anger, Neutral and Pleasure). The average ratings of each emotion for each Target of Empathy across the different Picture Types served as the dependent variable. The Target of the empathy (i.e., Female or Male) and the Picture Type (i.e., Emotional or Neutral) were the within-subject factors, and the Drug Group (1, 2, 3 and 4) the between-subject factor. Two distinct analyses were performed with this approach. The first considering the subjective emotional experience of the participant when looking at the specific targets, and the other considering the participant's perception of the actor's emotions.

For both neural and behavioural data, the results were considered statistically significant if $p < .05$ and tendencies were set if $p < .07$. All preparation for the statistical analysis was conducted in Matlab 2023a [111], including the averaging and organization of the data.

RESULTS

This chapter presents the statistical analysis results from the participants' self-report data, the behavioural results, and from the ERP measurements extracted from the EEG data collected during the IAP task, i.e., neural results.

6.1 Behavioural Results

Two different analysis were performed for each type of self-report data obtained from the IAP questionnaire: the Personal emotional experience and the Perceived emotions.

6.1.1 Personal Experience

The results from a mixed repeated-measures ANOVA on the emotion Fear showed a statistically significant main effect of the Picture Type ($F(1,59) = 73.253, p < .001, \eta_p^2 = 0.289$). Pairwise comparisons showed that participants felt more Fear when watching the Emotional pictures ($M = 2.07, SE = 0.13$) in comparison to the Neutral pictures ($M = 1.07, SE = 0.02$) ($p < .001$). Furthermore, the main effect of the Target of Empathy was found to be statistically significant ($F(1,59) = 36.722, p < .001, \eta_p^2 = 0.068$). The *post-hoc* analysis revealed that participants were more fearful when focusing on the Female ($M = 1.78, SE = 0.09$) as opposed to the Male target in the pictures ($M = 1.35, SE = 0.07$) ($p < .001$). Lastly, the Picture Type \times Target of Empathy interaction also reached statistical significance ($F(1,59) = 39.943, p < .001, \eta_p^2 = 0.065$). Pairwise comparisons showed that, for the Emotional pictures, focusing on the Female target caused more fearful reactions among the participants ($M = 2.49, SE = 0.16$), compared to the Male target ($M = 1.65, SE = 0.12$) ($p < .001$). As for the Neutral pictures, there were no significant differences between the Male and Female targets ($p = 0.502$). No other main effects or interactions were found to be statistically significant ($p \geq 0.291$).

For the emotion Anger, the ANOVA results showed a statistically significant main effect of the Picture Type ($F(1,59) = 102.631, p < .001, \eta_p^2 = 0.362$). Pairwise comparisons between Picture Types revealed that participants felt angrier towards the Emotional pictures ($M = 2.13, SE = 0.11$) in comparison to the Neutral ones ($M = 1.04, SE = 0.01$)

($p < .001$). The main effect of the Target of Empathy also reached statistical significance ($F(1,59) = 86.77, p < .001, \eta_p^2 = 0.168$). Results from the *post-hoc* analysis showed that the Male characters elicited higher Anger levels ($M = 1.91, SE = 0.08$) than the Female ($M = 1.26, SE = 0.05$) ($p < .001$). Moreover, results showed that the Picture Type x Target of Empathy interaction was found to be statistically significant ($F(1,59) = 85.30, p < .001, \eta_p^2 = 0.156$). *Post-hoc* pairwise comparisons revealed that, for the Emotional pictures, participants felt more Anger when focusing on the Male ($M = 2.77, SE = 0.16$) in comparison to the Female target ($M = 1.50, SE = 0.10$) ($p < .001$). There were no significant differences between the Male and Female targets for the Neutral pictures ($p = 0.041$). No other main effects or interactions reached statistical significance ($p \geq 0.734$).

As for the Neutral emotion, results revealed a significant main effect of the Picture Type ($F(1,59) = 162.433, p < .01, \eta_p^2 = 0.457$). Pairwise comparisons between Picture Types showed that the emotion Neutral was rated higher for the Neutral pictures ($M = 4.29, SE = 0.10$) in comparison to the Emotional pictures ($M = 2.29, SE = 0.18$) ($p < .001$). No other main effects or interactions reached statistical significance ($p \geq .280$).

Lastly, for the emotion Pleasure, the analysis showed a significant main effect of the Picture Type ($F(1,59) = 37.694, p < .001, \eta_p^2 = 0.146$). The *post-hoc* analysis showed that the participants felt more Pleasure when focusing on the individuals in the Neutral pictures ($M = 1.31, SE = 0.05$) as opposed to the Emotional pictures ($M = 1.05, SE = 0.02$) ($p < .001$). Moreover, The Picture Type x Target of Empathy interaction was found to be statistically significant as well ($F(1,59) = 9.066, p = .004, \eta_p^2 = 0.008$). The *post-hoc* analysis showed that the participants felt more Pleasure towards the Female targets in the Neutral pictures ($M = 1.33, SE = 0.06$) in comparison to the same targets in the Emotional pictures ($M = 1.02, SE = 0.01$) ($p < .001$). The same effect was verified for the Male targets (Neutral pictures: $M = 1.28, SE = 0.05$; Emotional pictures: $M = 1.08, SE = 0.04$) ($p < .001$). No other main effects or interactions were found to be statistically significant ($p \geq 0.176$). Appendix A contains a full report of the aforementioned results.

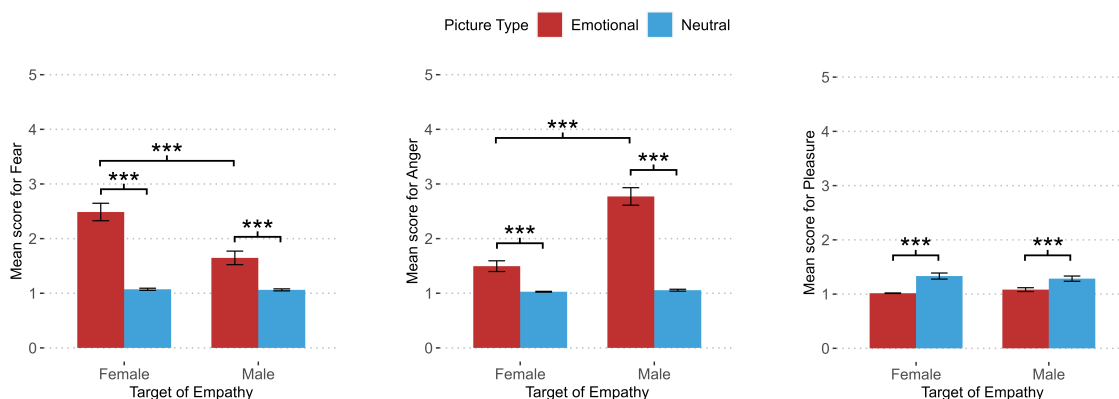


Figure 6.1: Ratings of the participants' emotional experience (Fear, Anger, and Pleasure) by Target of Empathy and Picture Type. Abbreviations: *** $p \leq .001$

6.1.2 Perceived Experience

As described in chapter 5, the self-report data of the participants' perceptions of the emotions felt by the individuals in the pictures was analysed using the same method as their subjective emotional experience.

Regarding the emotion Fear, the results from a mixed repeated-measures ANOVA revealed a statistically significant main effect of the Picture Type ($F(1,59) = 1618.974, p < .001, \eta_p^2 = 0.840$). Pairwise comparisons between Picture Types showed that the participants perceived the individuals in the Emotional pictures as more fearful ($M = 3.07, SE = 0.05$) in comparison to the actors in the Neutral ones ($M = 1.13, SE = 0.02$) ($p < .001$). The ANOVA results also showed a statistically significant main effect of the Target of Empathy ($F(1,59) = 915.13, p < .001, \eta_p^2 = 0.768$). The *post-hoc* analysis showed that participants perceived that the Female target was feeling more fear ($M = 2.87, SE = 0.04$), as opposed to the Male target ($M = 1.33, SE = 0.05$) ($p < .001$). Additionally, the two-way interaction between Picture Type and Target of Empathy also reached statistical significance ($F(1,59) = 677.22, p < .001, \eta_p^2 = 0.731$). It was found that for the Emotional pictures, the Female target ($M = 4.54, SE = 0.06$) was perceived as more fearful than the Male ($M = 1.60, SE = 0.09$) ($p < .001$). The same effect was verified for the Neutral pictures but with lower ratings for both individuals (Female: $M = 1.20, SE = 0.03$; Male: $M = 1.06, SE = 0.01$; $p < .001$). Other main effects or interactions were not found to be statistically significant ($p \geq 0.426$).

For the Anger emotion, the simple main effect of the Picture Type was found to be statistically significant ($F(1,59) = 911.91, p < .001, \eta_p^2 = 0.795$). When looking into the differences between the Picture Types, results showed that participants considered that the emotion Anger was more represented in the Emotional pictures ($M = 2.85, SE = 0.06$) than in the Neutral pictures ($M = 1.07, SE = 0.01$) ($p < .001$). The ANOVA results also revealed a statistically significant main effect of the Target of Empathy ($F(1,59) = 539.19, p < .001, \eta_p^2 = 0.665$). Pairwise comparisons showed that the Male target ($M = 2.60, SE = 0.04$) was perceived as more angry than the Female ($M = 1.32, SE = 0.04$) ($p < .001$). The Picture Type x Target of Empathy two-way interaction reached statistical significance as well ($F(1,59) = 469.19, p < .001, \eta_p^2 = 0.657$). The *post-hoc* analysis revealed that for the Emotional pictures, participants attributed higher ratings of Anger to the Male ($M = 4.12, SE = 0.08$) when compared to the Female protagonist in the pictures ($M = 1.59, SE = 0.08$) ($p < .001$). As for the Neutral pictures, no significant differences were found between the Male and Female targets ($p = 0.141$). No other main effects or interactions reached statistical significance ($p \geq 0.184$).

Concerning the emotion Neutral, the analysis showed that the simple main effect of the Picture Type was found to be statistically significant ($F(1,59) = 617.72, p < .001, \eta_p^2 = 0.844$). The *post-hoc* analysis revealed that higher ratings of this emotion were attributed to the Neutral pictures ($M = 3.85, SE = 0.10$) when compared to the Emotional ones ($M = 1.15, SE = 0.04$) ($p < .001$). Moreover, results also showed a statistically significant main effect of the Target of Empathy ($F(1,59) = 6.744, p = .012, \eta_p^2 = 0.001$). Pairwise comparisons

revealed that participants perceived the Male target as more Neutral ($M = 2.52$, $SE = 0.06$) in comparison to the Female target ($M = 2.48$, $SE = 0.05$) ($p = .0119$). No other main effects or interactions were found to be statistically significant ($p \geq 0.108$).

Lastly, for the Pleasure emotion, results showed a statistically significant main effect of the Picture Type ($F(1,59) = 32.396$, $p < .001$, $\eta_p^2 = 0.137$). Pairwise comparisons revealed that the participants perceived the Neutral interactions as more pleasurable for the targets ($M = 1.75$, $SE = 0.06$) as opposed to the Emotional ones ($M = 1.40$, $SE = 0.04$) ($p < .001$). The main effect of the Target of Empathy reached statistical significance as well ($F(1,59) = 93.104$, $p < .001$, $\eta_p^2 = 0.177$). Pairwise comparisons between Targets of Empathy revealed that the Male targets ($M = 1.78$, $SE = 0.06$) were always considered to be experiencing more Pleasure than the Female targets ($M = 1.37$, $SE = 0.03$) ($p < .001$). Lastly, the interaction between Picture Type and Target of Empathy was found to be statistically significant ($F(1,59) = 45.14$, $p < .001$, $\eta_p^2 = 0.079$). It was discovered that, for the Emotional pictures, higher ratings of Pleasure were attributed to the Male protagonist ($M = 1.74$, $SE = 0.08$) in comparison to the Female target ($M = 1.06$, $SE = 0.02$) ($p < .001$). That same effect was verified for the Neutral pictures (Male: $M = 1.83$, $SE = 0.07$; Female: $M = 1.68$, $SE = 0.06$; $p < .001$). Other main effects or interactions did not reach statistical significance ($p \geq 0.231$).

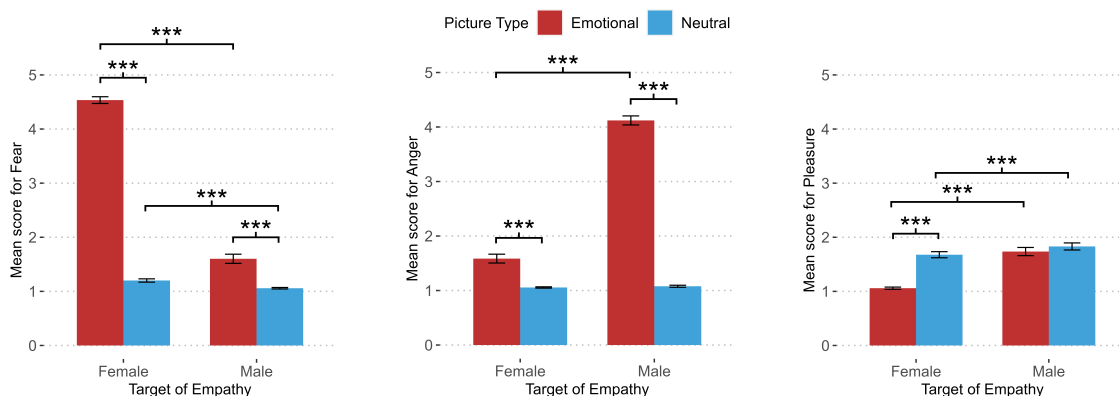


Figure 6.2: Ratings of the participants' perceived emotions (Fear, Anger, and Pleasure) by Target of Empathy and Picture Type. Abbreviations: *** $p \leq .001$

6.2 Neural Results

Two different analyses were performed for the 2 block types of the IAP: the passive viewing block and the empathy blocks. For each type of block, different analyses were run for the P300, early LPP and late LPP ERP components. For the passive block, only 59 participants were analysed, out of the 60, due to a pre-processing error on one of the signals. A full report of the neural results can be found in Appendix A.

6.2.1 Passive Block: P300 ERP Component

For the passive viewing block, the grand-averaged ERP waveforms are represented in Figure 6.3, where a P300 component is evident as well as the difference in amplitude between the 2 conditions, i.e., passive viewing Emotional pictures and passive viewing Neutral pictures. The topographical scalp map shows an increased activity in the parietal and occipital regions.

When running a two-way mixed ANOVA on the P300 mean amplitudes, the main effect of the Picture Type was the only to reach statistical significance ($F(1,55) = 13.30$, $p < .001$, $\eta_p^2 = .004$). *Post-hoc* pairwise comparisons between Picture Types revealed that P300 amplitudes were increased when viewing Neutral pictures ($M = 13.7$, $SE = 0.87$) when compared to the Emotional ones ($M = 12.9$, $SE = 0.87$) ($p < .001$). No other main effects or interactions were found to be statistically significant ($p \geq .150$).

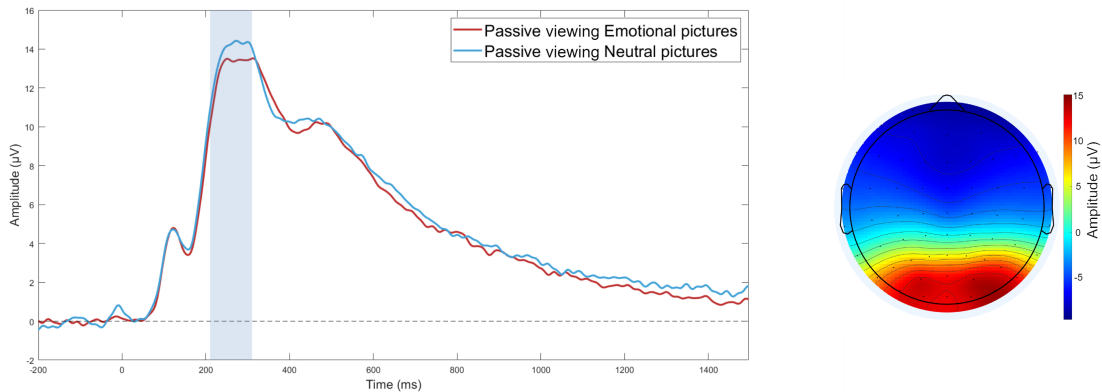


Figure 6.3: Grand-averaged ERP waveforms during the stimuli presentation in the passive viewing block collapsed across electrodes PO3, PO4, PO8, O2, and O1. The highlighted time window was used for the analysis of the P300 ERP component (210-310 ms). On the right is the topographical distribution of the 210-310 ms time window.

6.2.2 Passive Block: LPP ERP Component

Concerning the early LPP component, Figure 6.4 illustrates the grand-averaged ERPs and the scalp topography in the 300-600 ms time frame.

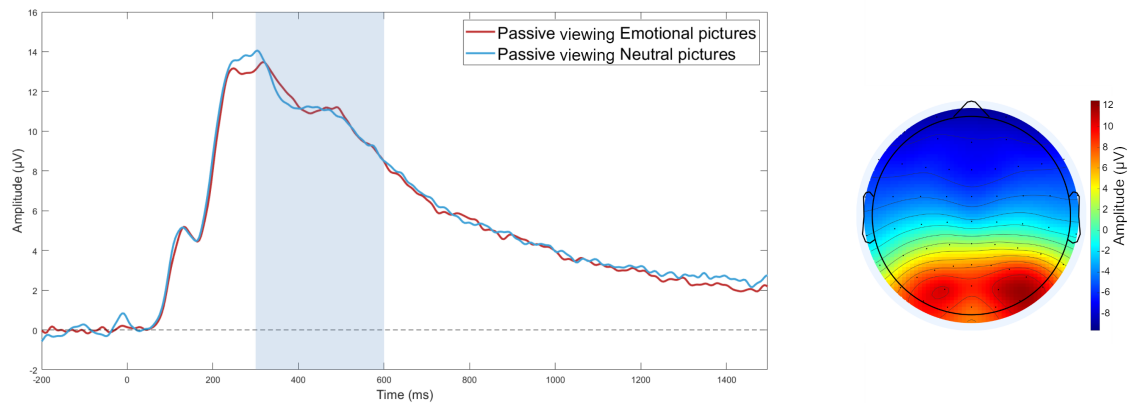


Figure 6.4: Grand-average ERP waveforms during the stimuli presentation in the passive viewing block collapsed across electrodes PO4, PO8, and P6. The highlighted time window was used for the analysis of the early LPP ERP component (300-600 ms). On the right is the topographical distribution of the 300-600 ms time window.

As for the late LPP component, the grand-averaged ERPs and the topographical distribution for the 600-1500 time window can be seen in Figure 6.5.

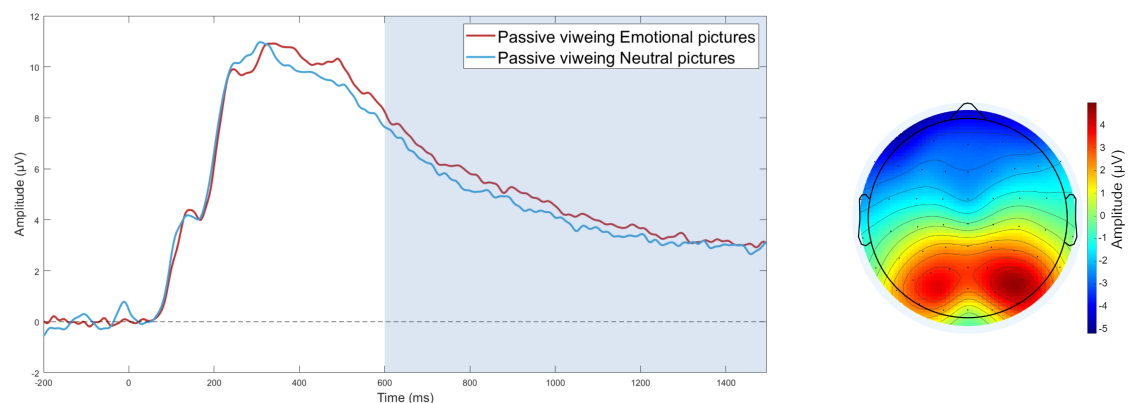


Figure 6.5: Grand-average ERP waveforms during the stimuli presentation in the passive viewing block collapsed across electrodes P4 and P6. The highlighted time window was used for the analysis of the late LPP ERP component (600-1500 ms). On the right is the topographical distribution of the 600-1500 ms time window.

The analysis of both early and late components of the LPP did not yield statistically significant main effects or interactions: $p \geq .531$ for the early LPP component, and $p \geq .117$ for the late LPP component.

6.2.3 Empathy Blocks: P300 ERP Component

The computed grand-averaged ERP waveforms show that the P300 is evident in the 4 conditions, i.e., empathizing with the Female in the Emotional pictures (victim); empathizing with the Male in the Emotional pictures (aggressor); empathizing with the Female in the Neutral pictures, and empathizing with the Male in the Neutral pictures. The topographical distribution in Figure 6.6 shows that, in the 210-310 ms time window, higher activity was found in the occipital and parietal regions.

Results from a mixed repeated-measures ANOVA showed that the main effect of the Picture Type was the only statistically significant effect ($F(1,56) = 7.601, p = .008, \eta_p^2 = 0.002$). Pairwise comparisons between Picture Types revealed that the P300 amplitudes were increased for the Neutral pictures ($M = 12.3, SE = 0.75$) compared to the Emotional pictures ($M = 11.7, SE = 0.82$) ($p = .008$). Furthermore, no other main effects or interactions reached statistical significance ($p \geq .392$).

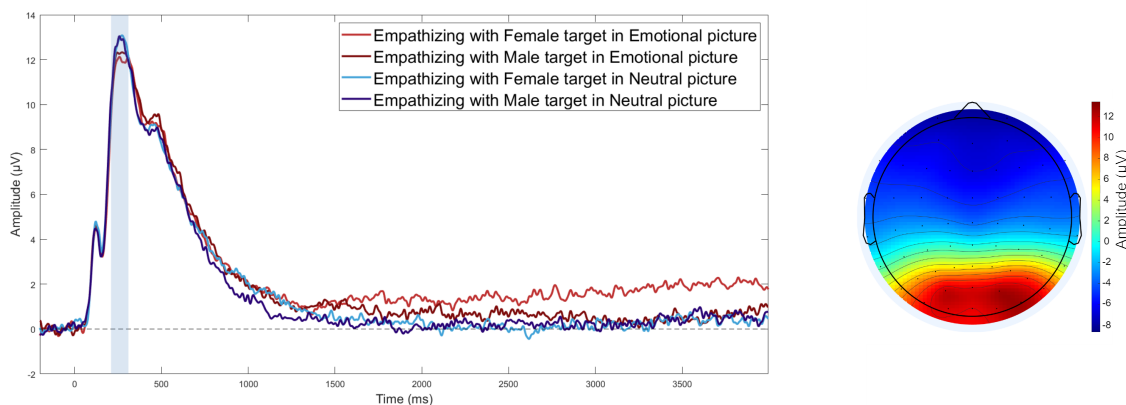


Figure 6.6: Grand-average ERP waveforms during the stimuli presentation in the empathy blocks collapsed across electrodes PO3, PO4, PO8, O2, and O1. The highlighted time window was used for the analysis of the P300 ERP component (210-310 ms). On the right is the topographical distribution of the 210-310 ms time window.

6.2.4 Empathy Blocks: Early LPP ERP Component

Figure 6.7 illustrates the grand-averaged ERPs and the topographical distribution in the 300-600 ms time window.

For the early LPP component, the main effect of Picture Type was found to be statistically significant ($F(1,56) = 5.07, p = .028, \eta_p^2 = .002$). Pairwise comparisons between Picture Types showed that the early LPP mean amplitude was higher for the Emotional pictures ($M = 10.04, SE = 0.66$) in comparison to the Neutral pictures ($M = 9.59, SE = 0.62$) ($p = 0.028$). No other main effects or interactions reached statistical significance ($p \geq .107$).

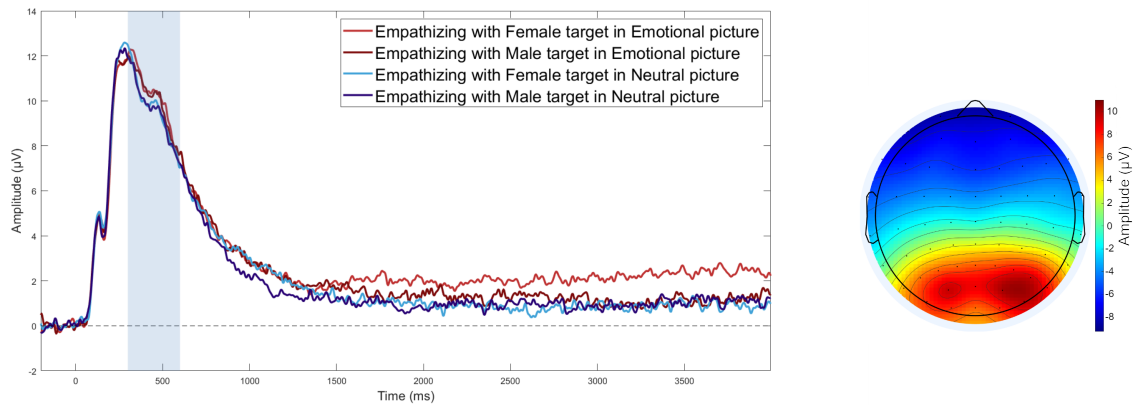


Figure 6.7: Grand-average ERP waveforms during the stimuli presentation in the empathy blocks collapsed across electrodes PO4, PO8 and P6. The highlighted time window was used for the analysis of the early LPP ERP component (300-600 ms). On the right is the topographical distribution of the 300-600 ms time window.

6.2.5 Empathy Blocks: Late LPP ERP Component

The grand-averaged ERP waveforms are represented in Figure 6.8 as well as the topographical distribution of the 600-4000 ms time window during stimuli presentation.

The analysis of the late LPP component, revealed that the only statistically significant effect was the main effect of the Picture Type ($F(1,56) = 9.69, p = .003, \eta_p^2 = .026$). The *post-hoc* analysis revealed that late LPP amplitudes were larger for the Emotional pictures ($M = 2.61, SE = 0.34$) in comparison to the Neutral ones ($M = 1.71, SE = 0.32$) ($p = .0029$). The remaining main effects and interactions were not statistically significant ($p \geq .215$).

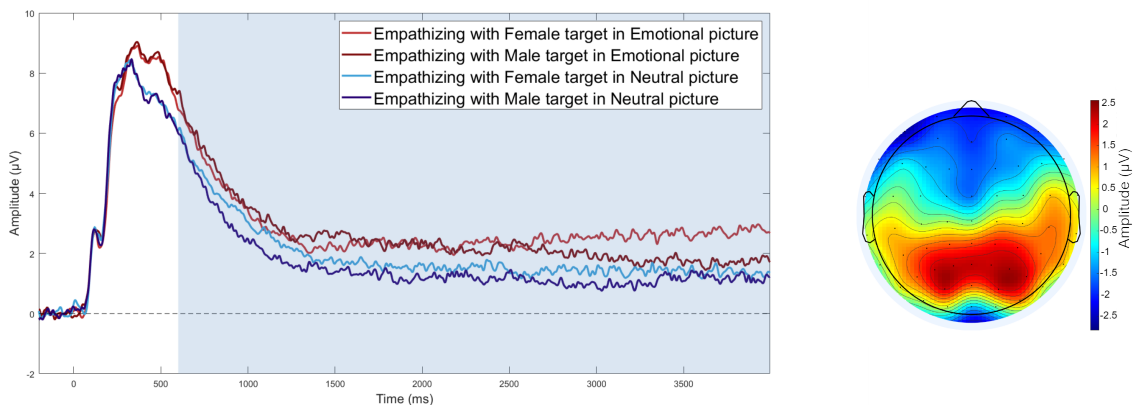


Figure 6.8: Grand-average ERP waveforms during the stimuli presentation in the empathy blocks collapsed across electrodes P3, P1, Pz, P2, P4, P6, and PO3. The highlighted time window was used for the analysis of the late LPP ERP component (600-4000 ms). On the right is the topographical distribution of the 600-4000 ms time window.

DISCUSSION

The present study aimed to provide new insights into the empathic neural response and how exogenous OT and T could modulate the response to different targets in interpersonal aggression contexts. During the IAP task, participants watched pictures of Female and Male characters in Neutral and Emotional interactions. In the first block of the experimental task, participants were instructed to watch the pictures without focusing on any specific target. In the second and third blocks, participants had to focus their attention either on the Female or the Male target and attempt to feel what they were feeling in the presented scenario. This task organization allowed for a deeper understanding of the emotional and cognitive components that constitute the empathic experience. The behavioural aspect of the data consisted of the participants' answers to the IAP questionnaire, which was filled after the experimental task.

In this chapter, the main results from the behavioural and neural analysis are discussed. However, it is important to mention that the Drug Groups were kept blinded since the investigation was only recently concluded and this dissertation does not include the full set of participants.

7.1 Behavioural Data

7.1.1 Personal Emotional Experience towards the Stimuli

When asked to rate their feelings towards the different targets, participants gave higher ratings of the emotion Fear when focusing on the Female target compared to the Male target ($p < .001$). Moreover, the difference in ratings between the Male and Female targets was significant for the Emotional pictures ($p < .001$), where the Female character appears as the victim of violent behaviours. Since Fear is the primary emotion that the Female targets portray in the pictures, this could mean that, to some degree, the participants were able to recognize and slightly mimic their emotions. Considering that the process of emotion contagion is a part of emotional empathy, it is possible to infer that the stimuli had the desired effect on the participants, that is, to trigger emotional empathy responses towards the targets. For the Anger emotion, the same contagion effect was verified. For

the Emotional stimuli, participants reported feeling higher levels of Anger towards the Male target compared to the Female ($p < .001$), which is in line with the expression of the Male actors, who appear as the perpetrators of the aggressive behaviours. Regarding the ratings of the Neutral emotion, the statistical analysis revealed that higher ratings of this emotion were attributed to the Neutral pictures ($p < .001$), which suggests that the lack of emotional content in the interactions in the Neutral picture type also translated to a neutral emotional experience for the participants.

As for the Pleasure emotion, results showed that the participants felt more Pleasure towards the individuals in Neutral pictures in comparison to the Emotional ones ($p < .001$), with no significant differences in ratings for Male and Female targets. This outcome could be expected considering the natural human aversion to violence and the context-sensitive nature of aggressive behaviours [116].

7.1.2 Perceived Emotional Experience of the Targets of Empathy

In the IAP questionnaire, participants were also asked to rate the emotions felt by the individuals in the pictures as a way to assess the cognitive aspect of the empathic response since these ratings involve an understanding of the target's feelings and mental state.

For the Fear emotion, the Female character was perceived as more fearful than the Male in the Emotional and in the Neutral pictures ($p < .001$), where none of the targets portray emotionally charged expressions. A possible explanation for this result could be the societal bias in perceptions of dominance, as some studies suggest that men tend to perceive women as less dominant and more submissive, which are states that could be associated with fearful expressions [117].

Regarding the ratings of Anger, the analysis revealed that the Male targets in the Emotional pictures were perceived as angrier than their Female counterparts ($p < .001$). This result suggests that the participants were able to accurately identify the emotional state of the Male target of empathy. Furthermore, given that emotion recognition is a primary component of the empathic response, this finding serves as an additional indicator that the stimuli had the intended effect on the participants.

For the Neutral emotion, higher ratings were attributed to the Neutral pictures, as expected, and for the Emotional pictures, participants perceived the Male target as more neutral than the female ($p = .0119$). The same trend was found for the Pleasure ratings, since the participants reported that the Male targets were experiencing more Pleasure than the Female in both neutral and aggressive interactions ($p < .001$). This result is expected considering that the female character appears as the victim of the aggressive behaviours and it is in line with literature findings that suggest that men may derive pleasure or satisfaction from engaging in violent actions [118], [119], which could have led the participants to assume that the aggressor took pleasure in harming someone.

7.1.3 Influence of Oxytocin and Testosterone on Personal and Perceived Emotions

The data from both personal and perceived emotional experiences revealed that the **OT** and **T** administrations did not influence the participants' ratings on the **IAP** questionnaire. This result is corroborated by studies that also found that the effect of **OT** and **T** may modulate physiological responses but not reach the conscious brain, therefore not being translated to this kind of self-report data [99], [120]. Moreover, the fact that the participants only filled out the questionnaire after completing the 5 experimental tasks could also justify this result. The first task started when both hormones reached their highest concentration, that is around 25 minutes after administration for the **OT** and approximately 2 hours for the **T**. The exact start time of filling out the questionnaire varied for each participant due to the various factors involved in a laboratory experiment. However, considering that the baseline levels of **OT** are re-established 90 minute post-administration for most individuals [121], it is possible to infer that the impact of this hormone may not have been as pronounced as intended. Additionally, it is worth noting that the fatigue that participants might have felt while answering the questionnaire could also have affected their answers.

7.2 P300 ERP Component

Previous literature findings report that early **ERP** components, such as the **N100** and **P200 ERP** components, are influenced by **OT** and **T** administrations in empathy-related investigations [100], [105]. It has also been proven that empathy can modulate the **P300** component [74] and given the social effects of the **OT** and **T** [8], [9], one could expect that the combination of the empathy-inducing stimuli and the hormones' effects on cognition and social behaviour would result in the modulation of the **P300** waveform for the different administration groups. However, unexpectedly, for the passive viewing block and the empathy blocks, the Drug Group did not modulate **P300** amplitudes.

It is possible to attribute this result to a wide range of explanations, namely the fact the **IAP** task started, on average, 1 hour and 12 minutes after the **OT** administration and 2 hours and 48 minutes after the **T** administration, which is long after the hormones had reached their maximum concentration. Additionally, one could argue that the relationship between the hormones and empathic responses towards emotionally charged stimuli, particularly in interpersonal aggression contexts, is complex and that the participants' neural responses can be modulated by a large number of variables that are impossible to control in an experimental setting. Moreover, due to the complexity of the empathic process, it is also plausible that the **P300** component alone could not translate the neural dynamics resulting from the **OT** and **T** administrations. Other factors such as the inherent empathic abilities of the participants and other personality traits could also have influenced the **P300** activity.

Nevertheless, in the computed waveforms for the passive viewing and the empathy

blocks, the P300 component is very evident, which generally indicates that the stimuli had a strong effect on the participants and that they were actively engaging with the task [122]. This enhanced P300 activity could also imply that the empathy reaction was so strong that a plateau was reached, meaning that no drugs could increase any further the response. Furthermore, the absence of significant differences in the P300 for the different targets, i.e., Female and Male, in the empathy blocks, could signify that perhaps in this specific task, the P300 ERP component is not modulated by the gender of the target, which participants could perceive as out or in-group, or the aggression role variable.

Moreover, results showed that the Picture Type, was the only modulator of the P300 component for the passive viewing and the empathy blocks, meaning that the emotional content of the stimuli (aggressive or neutral) influenced the amplitude of the P300 component. It was found that the neutral pictures led to enhanced P300 activity in both types of blocks. This result goes against the initial hypothesis that stated that the emotional pictures would elicit larger P300 amplitudes. However, the IAP questionnaire results showed that the participants felt more pleasure when focusing on the individuals in the Neutral pictures versus the Emotional ones. With that result in mind, the positive valence attributed to the neutral stimuli may be the reason for the larger P300 amplitudes, as positive valence has also been associated with increased P300 activity [123]. Lastly, studies employing an Oddball Paradigm, a common type of task that is frequently used in ERP investigations, have shown that the P300 is enhanced when the stimuli are unexpected [124]. Therefore, it is possible that the salience of the emotional pictures is so high that the neutral stimuli are perceived as different and unexpected when presented among the emotional ones, thus resulting in larger amplitudes of the P300 component.

7.3 LPP ERP Component

The LPP ERP component is modulated by emotionally charged stimuli as well as stimuli containing social content. Studies suggest that strong empathic abilities have also been linked to enhanced LPP activity [37]. Therefore, similarly to the P300 component, it was expected that the interplay between the two hormones and the emotions elicited by the IAP task would lead to modulations of the LPP component across the 4 administration groups.

Nevertheless, it was found that for both early and late components of the LPP during the passive viewing and the empathy blocks, the Drug Group did not produce significant changes in the LPP mean amplitudes. The previous section discusses potential explanations for this outcome, such as the drug administration timing and the fact that the relationship between the hormones and empathic reactions toward interpersonal aggression stimuli might not be straightforward and that the interplay between the two can be influenced by a large number of factors.

Considering the empathy blocks, results showed that for both early and late LPP components, the Picture Type was the only variable that modulated the LPP amplitudes.

It was found that amplitudes were larger when participants tried to empathize with the targets in the Emotional pictures. This result manifested in both early and late LPP components and is in line with the expected hypothesis that empathizing with the Emotional pictures should increase the LPP activity. However, the Target of Empathy did not influence LPP amplitudes, meaning that the gender and aggression role variables did not affect this component in a significant manner.

For the passive block, the analysis of the early and late LPP components did not lead to statistically significant results. It is possible that this result was due to the fact that the stimulus presentation in this particular block was shorter, i.e., 1500 ms, in comparison to the empathy blocks, i.e., 4000 ms. The LPP is a late component so, in the context of the IAP task, the duration of the stimuli presentation might not have been long enough to have a significant impact on the late LPP amplitudes. Furthermore, since the participants are only passively watching the pictures and not actively trying to empathize with one of the targets, this block of the task requires a decreased cognitive load. Since the engagement of cognitive resources has been associated with changes in LPP amplitudes [37], it is possible that it could have influenced the results.

7.4 Drug Group Hypotheses

Results showed an absence of a statistically significant Drug Group effect at a neural and behavioural level. Despite this lack of statistical significant results, the influence of the Drug Group was deeper investigated to understand if some distinct patterns could be observed and possibly lead to speculations regarding the correspondence of each group to their drug combinations.

On a behavioural level, the hypotheses regarding the Drug Groups' content were developed considering the personal emotional experiences reported by the participants in the IAP questionnaire, as these measurements are meant to reflect the emotional aspect of the empathic process. For the neural results, since participants are actively empathizing with the different targets in the empathy blocks, the mean ERP amplitudes from those blocks were considered.

At a neural level, the Drug Group 3 showed enhanced P300 and LPP amplitudes in comparison to other administration groups for each of the conditions: empathizing with the Female target in Emotional pictures; empathizing with the Male target in Emotional pictures; empathizing with the Female target in Neutral pictures; and empathizing with the Male target in Neutral pictures (P300: $M_{\text{Group1}} = 10.7$, $SE = 0.67$; $M_{\text{Group2}} = 11.7$, $SE = 0.76$; $M_{\text{Group3}} = 13.2$, $SE = 0.82$; $M_{\text{Group4}} = 12.3$, $SE = 0.83$; early LPP: $M_{\text{Group1}} = 7.96$, $SE = 0.46$; $M_{\text{Group2}} = 8.61$, $SE = 0.55$; $M_{\text{Group3}} = 11.6$, $SE = 0.74$; $M_{\text{Group4}} = 11.1$, $SE = 0.71$; late LPP: $M_{\text{Group1}} = 1.36$, $SE = 0.43$; $M_{\text{Group2}} = 2.02$, $SE = 0.40$; $M_{\text{Group3}} = 2.92$, $SE = 0.31$; $M_{\text{Group4}} = 2.33$, $SE = 0.32$), which suggests a heightened empathic response. The illustrations of the mean P300 and LPP amplitudes by Target of Empathy, Picture Type, and Drug Group can be seen in Appendix A. Furthermore, the mean amplitudes of the

early and late LPP components were larger for the Female target in the Emotional pictures (early LPP: $M_{\text{Female, Emotional}} = 12.3$, $SE = 1.41$; late LPP: $M_{\text{Female, Emotional}} = 3.41$, $SE = 0.57$) which appears as the victim of the aggressions, in comparison to the Male (early LPP: $M_{\text{Male, Emotional}} = 11.7$, $SE = 1.71$; late LPP: $M_{\text{Male, Emotional}} = 2.57$, $SE = 0.78$). These results were complemented by the emotional experience ratings. Specifically, participants in Drug Group 3 felt higher levels of Fear and Anger for both Male ($M_{\text{Fear, Male}} = 1.93$, $SE = 0.30$; $M_{\text{Anger, Male}} = 2.97$, $SE = 0.28$) and Female targets ($M_{\text{Fear, Female}} = 2.97$, $SE = 0.31$; $M_{\text{Anger, Female}} = 1.67$, $SE = 0.20$) in the Emotional pictures when compared to the other Drug Groups. Additionally, within the Drug Group 3, participants felt less Neutral towards all the different conditions. According to the proposed hypothesis which states that OT administration could lead to enhanced empathic responses, with higher empathy levels towards the Female target, these neural and behavioural results suggest that Drug Group 3 could be composed of the active OT and PL T.

In contrast, Drug Group 1 appeared to have a decrease in P300 and LPP amplitudes across all the conditions in comparison to the other Drug Groups, hinting a weakened empathic ability. Additionally, it was noticeable that the P300 and LPP activity was enhanced for the Male target in both Neutral and Emotional Picture Types (P300: $M_{\text{Male}} = 10.9$, $SE = 0.98$; early LPP: $M_{\text{Male}} = 8.06$, $SE = 0.65$; late LPP: $M_{\text{Male}} = 1.55$, $SE = 0.67$), in comparison to the Female target (P300: $M_{\text{Female}} = 10.4$, $SE = 0.94$; early LPP: $M_{\text{Female}} = 7.86$, $SE = 0.66$; late LPP: $M_{\text{Female}} = 1.22$, $SE = 0.55$). On the behavioural level, participants in Drug Group 1 felt more Neutral towards both Picture Types when compared to the other Drug Groups ($M_{\text{Neutral, Group1}} = 3.53$, $SE = 0.19$; $M_{\text{Neutral, Group2}} = 3.19$, $SE = 0.20$; $M_{\text{Neutral, Group3}} = 2.97$, $SE = 0.18$; $M_{\text{Neutral, Group4}} = 3.48$, $SE = 0.18$). No other distinct significant behavioural pattern was found in the self-report data. Nevertheless, the results appear to be in line with the active T and PL OT hypothesis which suggest that T can weaken the empathic ability but also enhance the reaction towards Male targets, leading to the belief that that is the content of the Drug Group 1.

Results showed that the ERP amplitudes in Drug Group 4 were larger in comparison to Drug Groups 1 and 2. As for the behavioural measures, a distinct pattern was not observable. However, given that both the P300 and LPP ERP amplitudes in Drug Group 4 were the most similar to those observed in the Drug Group 3, it is plausible to infer that this may be attributed to the combined effect of the active OT and T compounds, as it was hypothesized that the OT would counteract the effect of the T, suggesting a similar result to the active OT and PL T condition.

Lastly, given the aforementioned results, it can be speculated by a deduction logic that the Drug Group 2 is composed of the PL OT and PL T.

CONCLUSION

The present study aimed to investigate, for the first time, the effects of **OT** and **T** on men's empathic responses to interpersonal aggression contexts. It represents an attempt to provide new insights into the modulatory role of each of these hormones, and their combination, on the neural dynamics of the complex human phenomenon that is empathy.

The analysis of the behavioural results revealed that the participants were able to feel the emotions that the targets were portraying, as evidenced by a heightened experience of fear when empathizing with the victim and increased feelings of anger when empathizing with the aggressor. Participants also accurately recognized the emotions expressed by the targets. Interestingly for both Picture Types, the male target was perceived as experiencing more pleasure, while the female target was associated with greater feelings of fear.

The **ERP** analysis revealed that the P300 component was sensitive to the Picture Type for both passive viewing and empathizing conditions, with the neutral stimuli enhancing P300 activity. Contrary to the P300, increased **LPP** amplitudes were found when focusing on the emotional pictures during the empathy blocks. For the passive viewing blocks, none of the factors that were considered for the analysis, i.e., Picture Type and Drug Group, had an effect on **LPP** activity. These findings suggest that the neutral stimuli elicited stronger responses during the early stages of the empathic process, whereas the emotional stimuli led to a more pronounced response in the latter phase.

It is worth mentioning that the present dissertation does not include the full sample of 88 participants required to complete this study. Once the full data sample is obtained, the drug groups will be unblinded, allowing for a thorough analysis of the effects of **OT** and **T**. At the current stage, due to the incomplete dataset, the statistical power of the analysis is compromised and the effects of the hormones on men's empathic responses in interpersonal aggression contexts remain ambiguous.

With the current data sample, the Drug Group was not found to modulate the behavioural nor the neural responses associated with the **IAP** task. This lack of statistically significant Drug Group results did not facilitate the formulation of an hypothesis regarding the content of the Drug Groups, and for this reason, a deeper inspection was carried out on the neural and behavioral data given our a priori hypotheses. Drug Group 3 showed

increased P300 and LPP mean amplitudes in comparison to the other groups, as well as stronger emotional reactions to the stimuli, assessed with the IAP questionnaire's mean scores, which indicated a potential effect of the active OT and PL T. Furthermore, it was found that the P300 and LPP mean amplitudes in Drug Group 4 were the closest to the amplitudes in Drug Group 3, which suggested that the Drug Group 4 could be composed of the active OT and T compounds. Decreased ERP amplitudes in Drug Group 1, as well as a more neutral emotional response to the stimuli, led to the belief that Drug Group 1 contained the active T and PL OT. Lastly, it was hypothesized that the Drug Group 2 was composed of the PL OT and PL T.

In conclusion, the current findings serve as preliminary groundwork for understanding the complex relationship between exogenous OT and T and the neural dynamics of empathy, particularly towards interpersonal aggression. Additional investigation is necessary to further explore these findings and the possible modulatory role of the two hormones.

8.1 Future Research

In the current study, participants filled various psychological questionnaires, including the Interpersonal Reactivity Index (IRI) [125] and the Empathy Quotient (EQ) [126], which allow for an assessment of the participants inherent empathic abilities. The scores from these questionnaires were not studied in the context of this dissertation but will be further analysed for a scientific paper, as it has been demonstrated that empathy levels and other personality traits can modulate the effects of OT and T [45], [64].

Furthermore, different adaptations could be made in the current investigation in order to further understand the implications of the hormones in the empathic process. For instance, to facilitate a comparative study between the two types of blocks in the IAP task, one could modify the task to ensure that stimuli presentation durations were standardized across blocks. Therefore, in addition to comparing the ERPs across different stimuli, this adaptation would facilitate comparisons between the two task requirements: passive viewing and empathizing. Also, it could be interesting to explore how different concentrations of OT and T could affect empathy in the interpersonal aggression context.

Moreover, future research should aim to include a more diverse sample of participants, encompassing individuals of varying demographics. Additionally, since gender differences have already been explored in the context of empathy [127], conducting a comparative study between men and women in the context of empathy towards male aggressors and female victims could provide valuable insights into potential gender differences in the empathic cognitive process.

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SUPPLEMENTARY MATERIAL

A.1 Behavioural Data

A.1.1 Personal Experience

Table A.1: Descriptive statistics of the Personal ratings of the emotion Fear.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	2.21	1.28
		Male	15	1.67	0.913
	Neutral	Female	15	1.07	0.148
		Male	15	1.10	0.248
2	Emotional	Female	15	2.53	1.36
		Male	15	1.54	0.851
	Neutral	Female	15	1.03	0.059
		Male	15	1.03	0.056
3	Emotional	Female	18	2.97	1.30
		Male	18	1.93	1.28
	Neutral	Female	18	1.12	0.228
		Male	18	1.08	0.122
4	Emotional	Female	15	2.24	1.09
		Male	15	1.44	0.717
	Neutral	Female	15	1.08	0.107
		Male	15	1.04	0.091

Table A.2: Results from a mixed repeated-measures ANOVA on the personal ratings of the emotion Fear.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	1.18	1.18	.026	.33
Picture Type	1,59	0.85	73.25	.29	<.001***
Target of Empathy	1,59	0.31	36.72	.068	<.001***
Drug Group x Picture Type	3,59	0.85	1.28	.021	.29
Drug Group x Target of Empathy	3,59	0.31	0.79	.0050	.50
Picture Type x Target of Empathy	1,59	0.27	39.94	.065	<.001***
Drug Group x Picture Type x Target of Empathy	3,59	0.27	0.62	.0030	.60

Table A.3: *Post-hoc* analysis on the effect of Picture Type on the personal ratings of the emotion Fear.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	2.07	0.13	59	1.81	2.32
Neutral	1.07	0.017	59	1.03	1.10
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	1	0.12	59	8.559	<.001***

Table A.4: *Post-hoc* analysis on the effect of Target of Empathy on the personal ratings of the emotion Fear.

Estimated Marginal Means					
Target of Empathy	emmean	SE	df	UCL	UCL
Female	1.78	0.085	59	1.61	1.95
Male	1.35	0.068	59	1.22	1.49
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Female - Male	0.43	0.070	59	6.06	<.001***

Table A.5: *Post-hoc* analysis on the effect of Target of Empathy on the personal ratings of the emotion Fear per Picture Type, and the effect of Picture Type per Target of Empathy.

Estimated Marginal Means						
Picture Type	Type	emmean	SE	df	UCL	UCL
Emotional	Female	2.49	0.16	59	2.17	2.81
	Male	1.65	0.12	59	1.40	1.90
Neutral	Female	1.07	0.019	59	1.03	1.11
	Male	1.06	0.019	59	1.02	1.10

Pairwise Comparisons - Target of Empathy per Picture Type						
Picture Type	Contrast	estimate	SE	df	t.ratio	p.value
Emotional	Female - Male	0.84	0.14	59	6.23	<.001***
Neutral	Female - Male	0.011	0.016	59	0.68	.502

Pairwise Comparisons - Picture Type per Target of Empathy						
Target of Empathy	Contrast	estimate	SE	df	t.ratio	p.value
Female	Emotional - Neutral	1.41	0.15	59	9.35	<.001***
Male	Emotional - Neutral	0.59	0.11	59	5.13	<.001***

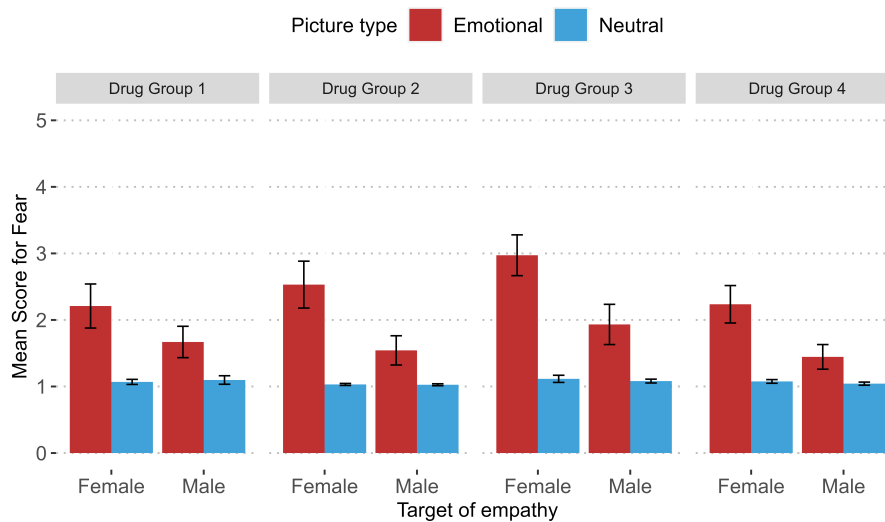


Figure A.1: Ratings of the participants' personal experience of Fear by Target of Empathy, Picture Type, and Drug Group.

Table A.6: Descriptive statistics of the Personal ratings of the emotion Anger.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	1.34	0.81
		Male	15	2.79	1.32
	Neutral	Female	15	1.03	0.071
		Male	15	1.07	0.15
2	Emotional	Female	15	1.53	0.88
		Male	15	2.80	1.47
	Neutral	Female	15	1.02	0.068
		Male	15	1.05	0.13
3	Emotional	Female	18	1.67	0.84
		Male	18	2.97	1.20
	Neutral	Female	18	1.04	0.059
		Male	18	1.07	0.17
4	Emotional	Female	15	1.45	0.51
		Male	15	2.53	1.06
	Neutral	Female	15	1.02	0.030
		Male	15	1.03	0.058

Table A.7: Results from a mixed repeated-measures ANOVA on the personal ratings of the emotion Anger.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	0.91	0.43	.0090	.73
Picture Type	1,59	0.73	102.63	.36	<.001***
Target of Empathy	1,59	0.31	86.77	.17	<.001***
Drug Group x Picture Type	3,59	0.73	0.41	.0070	.75
Drug Group x Target of Empathy	3,59	0.31	0.32	.0020	.81
Picture Type x Target of Empathy	1,59	0.29	85.30	.16	<.001***
Drug Group x Picture Type x Target of Empathy	3,59	0.29	0.25	.0020	.86

Table A.8: *Post-hoc* analysis on the effect of Picture Type on the personal ratings of the emotion Anger.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	2.13	0.11	59	1.91	2.36
Neutral	1.04	0.011	59	1.02	1.06
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	1.09	0.11	59	10.13	<.001***

Table A.9: *Post-hoc* analysis on the effect of Target of Empathy on the personal ratings of the emotion Anger.

Estimated Marginal Means					
Target of Empathy	emmean	SE	df	UCL	UCL
Female	1.26	0.051	59	1.16	1.36
Male	1.91	0.084	59	1.75	2.08
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Female - Male	-0.65	0.07	59	-9.32	<.001***

Table A.10: *Post-hoc* analysis on the effect of Target of Empathy on the personal ratings of the emotion Anger per Picture Type, and the effect of Picture Type per Target of Empathy.

Estimated Marginal Means						
Picture Type	Type	emmean	SE	df	UCL	UCL
Emotional	Female	1.50	0.098	59	1.30	1.69
	Male	2.77	0.16	59	2.45	3.09
Neutral	Female	1.03	0.0075	59	1.01	1.04
	Male	1.06	0.017	59	1.02	1.09
Pairwise Comparisons - Target of Empathy per Picture Type						
Picture Type	Contrast	estimate	SE	df	t.ratio	p.value
Emotional	Female - Male	-1.28	0.14	59	-9.32	<.001***
Neutral	Female - Male	-0.028	0.014	59	-2.085	.041
Pairwise Comparisons - Picture Type per Target of Empathy						
Target of Empathy	Contrast	estimate	SE	df	t.ratio	p.value
Female	Emotional - Neutral	0.47	0.094	59	4.98	<.001***
Male	Emotional - Neutral	1.72	0.153	59	11.19	<.001***

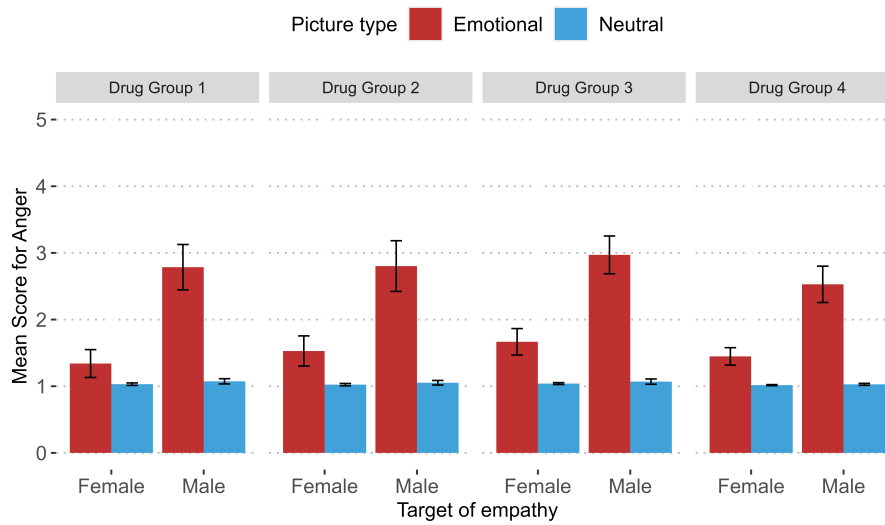


Figure A.2: Ratings of the participants’ personal experience of Anger by Target of Empathy, Picture Type, and Drug Group.

Table A.11: Descriptive statistics of the Personal ratings of the emotion Neutral.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	2.63	1.50
		Male	15	2.58	1.52
	Neutral	Female	15	4.48	0.624
		Male	15	4.44	0.754
2	Emotional	Female	15	2.18	1.45
		Male	15	2.16	1.47
	Neutral	Female	15	4.20	0.817
		Male	15	4.22	0.782
3	Emotional	Female	18	1.85	1.18
		Male	18	1.83	1.14
	Neutral	Female	18	4.11	0.912
		Male	18	4.08	0.928
4	Emotional	Female	15	2.61	1.49
		Male	15	2.49	1.45
	Neutral	Female	15	4.41	0.574
		Male	15	4.41	0.562

Table A.12: Results from a mixed repeated-measures ANOVA on the personal ratings of the emotion Neutral.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	3.48	1.31	.044	.280
Picture Type	1,59	1.55	162.43	.457	<.001***
Target of Empathy	1,59	0.02	2.36	<.001	.130
Drug Group x Picture Type	3,59	1.55	0.38	.006	.766
Drug Group x Target of Empathy	3,59	0.02	0.37	<.001	.774
Picture Type x Target of Empathy	1,59	0.02	1.86	<.001	.178
Drug Group x Picture Type x Target of Empathy	3,59	0.02	.76	<.001	.523

Table A.13: *Post-hoc* analysis on the effect of Picture Type on the personal ratings of the emotion Neutral.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	LCL
Emotional	2.29	0.1756	59	1.94	2.64
Neutral	4.29	0.0962	59	4.10	4.49
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	-2	0.157	59	-12.745	<.001***

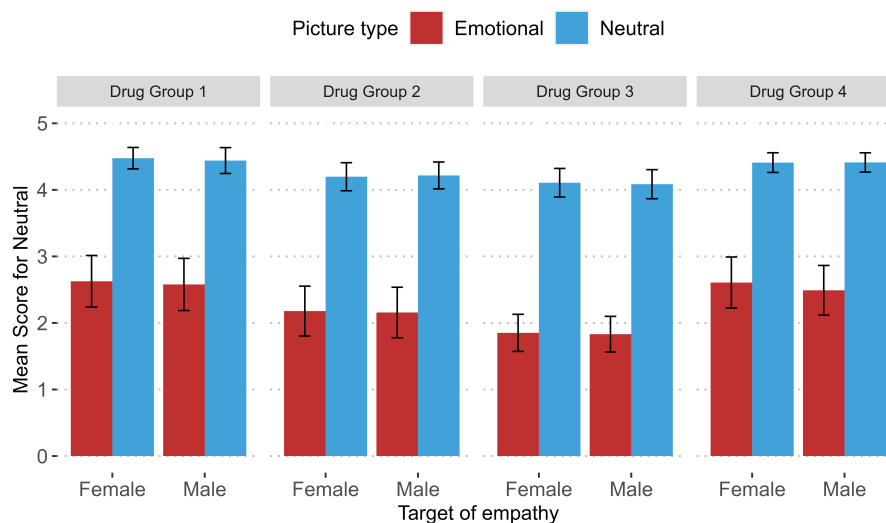


Figure A.3: Ratings of the participants' personal experience of the Neutral emotion by Target of Empathy, Picture Type, and Drug Group.

Table A.14: Descriptive statistics of the Personal ratings of the emotion Pleasure.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	1.01	0.021
		Male	15	1.04	0.138
	Neutral	Female	15	1.28	0.589
		Male	15	1.18	0.338
2	Emotional	Female	15	1.02	0.065
		Male	15	1.01	0.021
	Neutral	Female	15	1.41	0.523
		Male	15	1.26	0.306
3	Emotional	Female	18	1.01	0.035
		Male	18	1.18	0.451
	Neutral	Female	18	1.30	0.341
		Male	18	1.33	0.44
4	Emotional	Female	15	1.02	0.04
		Male	15	1.10	0.24
	Neutral	Female	15	1.34	0.254
		Male	15	1.37	0.406

Table A.15: Results from a mixed repeated-measures ANOVA on the personal ratings of the emotion Pleasure.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	0.22	0.41	.011	.745
Picture Type	1,59	0.11	37.69	.146	<.001***
Target of Empathy	1,59	0.06	0.09	<.001	.766
Drug Group x Picture Type	3,59	0.11	0.49	.007	.687
Drug Group x Target of Empathy	3,59	0.06	1.71	.012	.176
Picture Type x Target of Empathy	1,59	0.02	9.06	.008	.004**
Drug Group x Picture Type x Target of Empathy	3,59	0.02	0.39	.001	.757

Table A.16: *Post-hoc* analysis on the effect of Picture Type on the personal ratings of the emotion Pleasure.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	1.05	0.0181	59	1.01	1.09
Neutral	1.31	0.0485	59	1.21	1.41
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	-0.259	0.0423	59	-6.140	<.001***

Table A.17: *Post-hoc* analysis on the effect of Picture Type on the personal ratings of the emotion Pleasure per Target of Empathy, and the effect of Target of Empathy per Picture Type.

Estimated Marginal Means						
Target of Empathy	Type	emmean	SE	df	UCL	UCL
Female	Emotional	1.02	0.00539	59	1.01	1.03
	Neutral	1.33	0.05599	59	1.22	1.44
Male	Emotional	1.08	0.03506	59	1.01	1.15
	Neutral	1.28	0.04799	59	1.19	1.38
Pairwise Comparisons - Picture Type per Target of Empathy						
Target of Empathy	Contrast	estimate	SE	df	t.ratio	p.value
Female	Emotional - Neutral	-0.316	0.0549	59	-5.768	<.001***
Male	Emotional - Neutral	-0.202	0.0358	59	-5.658	<.001***
Pairwise Comparisons - Target of Empathy per Picture Type						
Picture Type	Contrast	estimate	SE	df	t.ratio	p.value
Emotional	Female - Male	-0.0664	0.0347	59	-1.915	.0603
Neutral	Female - Male	0.0477	0.0382	59	1.250	.2162

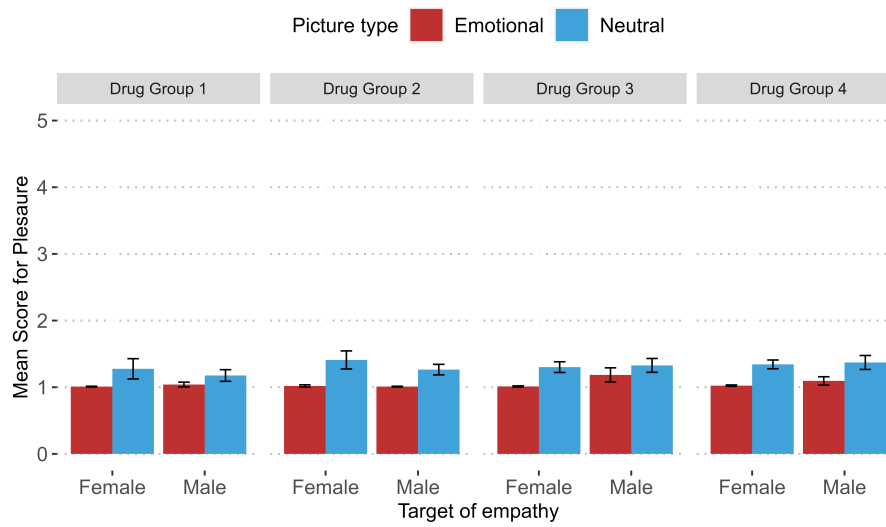


Figure A.4: Ratings of the participants' personal experience of Pleasure by Target of Empathy, Picture Type, and Drug Group.

A.1.2 Perceived Experience

Table A.18: Descriptive statistics of the Perceived ratings of the emotion Fear.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	4.43	0.497
		Male	15	1.58	0.443
	Neutral	Female	15	1.20	0.248
		Male	15	1.02	0.046
2	Emotional	Female	15	4.57	0.605
		Male	15	1.47	0.422
	Neutral	Female	15	1.14	0.213
		Male	15	1.06	0.097
3	Emotional	Female	18	4.60	0.381
		Male	18	1.56	0.896
	Neutral	Female	18	1.18	0.266
		Male	18	1.05	0.086
4	Emotional	Female	15	4.54	0.482
		Male	15	1.80	0.73
	Neutral	Female	15	1.29	0.221
		Male	15	1.1	0.168

Table A.19: Results from a mixed repeated-measures ANOVA on the perceived ratings of the emotion Fear.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	0.27	0.79	.014	.504
Picture Type	1,59	0.15	1618.97	.840	<.001***
Target of Empathy	1,59	0.16	915.13	.768	<.001***
Drug Group x Picture Type	3,59	0.15	0.15	.001	.930
Drug Group x Target of Empathy	3,59	0.16	0.33	.004	.801
Picture Type x Target of Empathy	1,59	0.18	677.22	.731	<.001***
Drug Group x Picture Type x Target of Empathy	3,59	0.18	0.94	.011	.426

Table A.20: *Post-hoc* analysis on the effect of Picture Type on the perceived ratings of the emotion Fear.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	3.07	0.0541	59	2.96	3.18
Neutral	1.13	0.0201	59	1.09	1.17
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	1.94	0.0482	59	40.236	<.001***

Table A.21: *Post-hoc* analysis on the effect of Target of Empathy on the perceived ratings of the emotion Fear.

Estimated Marginal Means					
Target of Empathy	emmean	SE	df	UCL	UCL
Female	2.87	0.0355	59	2.80	2.94
Male	1.33	0.0469	59	1.24	1.42
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Female - Male	1.54	0.0508	59	30.251	<.001***

Table A.22: *Post-hoc* analysis on the effect of Target of Empathy on the perceived ratings of the emotion Fear per Picture Type, and the effect of Picture Type per Target of Empathy.

Estimated Marginal Means						
Picture Type	Type	emmean	SE	df	UCL	UCL
Emotional	Female	4.54	0.0622	59	4.41	4.66
	Male	1.60	0.0845	59	1.43	1.77
Neutral	Female	1.20	0.0303	59	1.14	1.26
	Male	1.06	0.0136	59	1.03	1.09
Pairwise Comparisons - Target of Empathy per Picture Type						
Picture Type	Contrast	estimate	SE	df	t.ratio	p.value
Emotional	Female - Male	2.933	0.1017	59	28.850	<.001***
Neutral	Female - Male	0.143	0.0241	59	5.933	<.001***
Pairwise Comparisons - Picture Type per Target of Empathy						
Target of Empathy	Contrast	estimate	SE	df	t.ratio	p.value
Female	Emotional - Neutral	3.334	0.0673	59	49.574	<.001***
Male	Emotional - Neutral	0.544	0.0766	59	7.105	<.001***

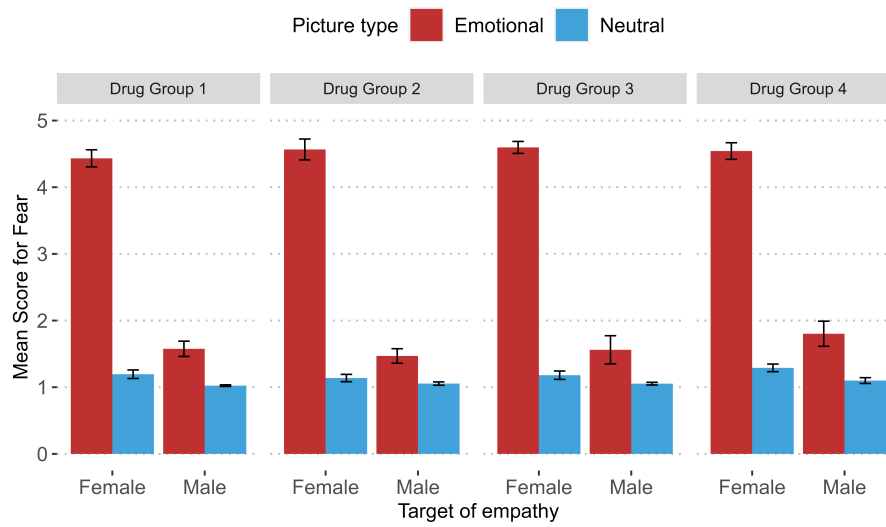


Figure A.5: Ratings of the participants' perception of Fear by Target of Empathy, Picture Type, and Drug Group.

Table A.23: Descriptive statistics of the Perceived ratings of the emotion Anger.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	1.54	0.493
		Male	15	3.85	0.754
	Neutral	Female	15	1.05	0.075
		Male	15	1.06	0.103
2	Emotional	Female	15	1.47	0.558
		Male	15	4.30	0.64
	Neutral	Female	15	1.02	0.052
		Male	15	1.06	0.128
3	Emotional	Female	18	1.56	0.623
		Male	18	4.25	0.606
	Neutral	Female	18	1.08	0.114
		Male	18	1.12	0.205
4	Emotional	Female	15	1.77	0.844
		Male	15	4.09	0.623
	Neutral	Female	15	1.07	0.118
		Male	15	1.07	0.12

Table A.24: Results from a mixed repeated-measures ANOVA on the perceived ratings of the emotion Anger.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	0.25	0.87	.013	.463
Picture Type	1,59	0.22	911.91	.795	<.001***
Target of Empathy	1,59	0.19	539.19	.665	<.001***
Drug Group x Picture Type	3,59	0.22	0.70	.009	.555
Drug Group x Target of Empathy	3,59	0.19	1.67	.018	.184
Picture Type x Target of Empathy	1,59	0.21	469.19	.657	<.001***
Drug Group x Type x Target of Empathy	3,59	0.21	1.09	.013	.360

Table A.25: *Post-hoc* analysis on the effect of Picture Type on the perceived ratings of the emotion Anger.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	2.85	0.0598	59	2.73	2.97
Neutral	1.07	0.0138	59	1.04	1.09
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	1.79	0.0591	59	30.198	<.001***

Table A.26: *Post-hoc* analysis on the effect of Target of Empathy on the perceived ratings of the emotion Anger.

Estimated Marginal Means					
Target of Empathy	emmean	SE	df	UCL	UCL
Female	1.32	0.0417	59	1.24	1.40
Male	2.60	0.0425	59	2.51	2.68
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Female - Male	-1.28	0.0551	59	-23.221	<.001***

Table A.27: *Post-hoc* analysis on the effect of Target of Empathy on the perceived ratings of the emotion Anger per Picture Type, and the effect of Picture Type per Target of Empathy.

Estimated Marginal Means						
Picture Type	Target of Empathy	emmean	SE	df	UCL	UCL
Emotional	Female	1.59	0.0811	59	1.42	1.75
	Male	4.12	0.0828	59	3.96	4.29
Neutral	Female	1.06	0.0120	59	1.03	1.08
	Male	1.08	0.0187	59	1.04	1.12
Pairwise Comparisons - Target of Empathy per Picture Type						
Picture Type	Contrast	estimate	SE	df	t.ratio	p.value
Emotional	Female - Male	-2.5353	0.1121	59	-22.611	<.001***
Neutral	Female - Male	-0.0223	0.0149	59	-1.494	.1406
Pairwise Comparisons - Picture Type per Target of Empathy						
Target of Empathy	Contrast	estimate	SE	df	t.ratio	p.value
Female	Emotional - Neutral	0.529	0.0807	59	6.563	<.001***
Male	Emotional - Neutral	3.042	0.0850	59	35.812	<.001***

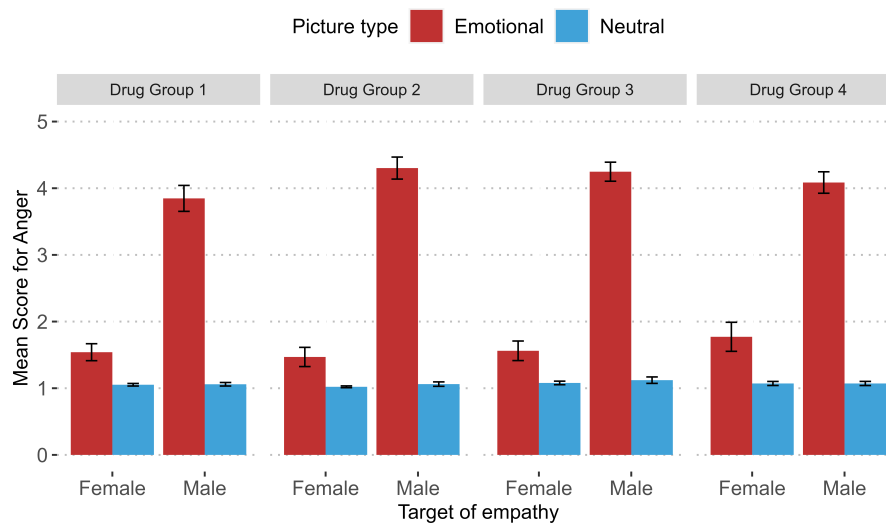


Figure A.6: Ratings of the participants' perception of Anger by Target of Empathy, Picture Type, and Drug Group.

Table A.28: Descriptive statistics of the Perceived ratings of the emotion Neutral.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	1.16	0.337
		Male	15	1.22	0.394
	Neutral	Female	15	4.00	0.691
		Male	15	4.11	0.772
2	Emotional	Female	15	1.08	0.157
		Male	15	1.09	0.114
	Neutral	Female	15	3.79	0.712
		Male	15	3.78	0.818
3	Emotional	Female	18	1.17	0.336
		Male	18	1.26	0.456
	Neutral	Female	18	3.80	0.818
		Male	18	3.79	0.806
4	Emotional	Female	15	1.04	0.057
		Male	15	1.15	0.124
	Neutral	Female	15	3.78	0.836
		Male	15	3.76	0.899

Table A.29: Results from a mixed repeated-measures ANOVA on the perceived ratings of the emotion Neutral.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	0.67	0.71	.017	.548
Picture Type	1,59	0.74	617.72	.844	<.001***
Target of Empathy	1,59	0.02	6.74	.001	.012*
Drug Group x Picture Type	3,59	0.74	0.31	.008	.821
Drug Group x Target of Empathy	3,59	0.02	0.87	<.001	.462
Picture Type x Target of Empathy	1,59	0.01	2.66	<.001	.108
Drug Group x Picture Type x Target of Empathy	3,59	0.01	1.80	<.001	.157

Table A.30: *Post-hoc* analysis on the effect of Picture Type on the perceived ratings of the emotion Neutral.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	1.15	0.0357	59	1.08	1.22
Neutral	3.85	0.0999	59	3.65	4.05
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	-2.71	0.109	59	-24.854	<.001***

Table A.31: *Post-hoc* analysis on the effect of Target of Empathy on the perceived ratings of the emotion Neutral.

Estimated Marginal Means					
Target of Empathy	emmean	SE	df	UCL	UCL
Female	2.48	0.0495	59	2.38	2.58
Male	2.52	0.0549	59	2.41	2.63
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Female - Male	-0.0431	0.0166	59	-2.597	.0119*

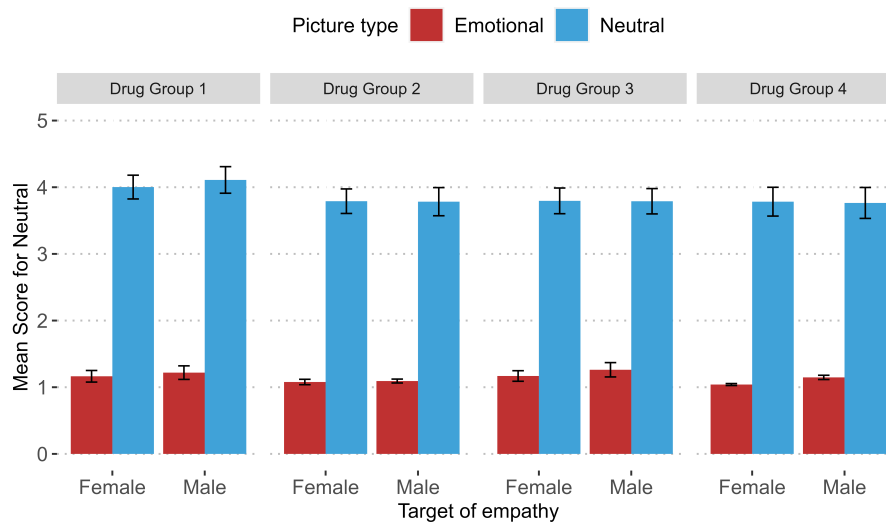


Figure A.7: Ratings of the participants' perception of the Neutral emotion by Target of Empathy, Picture Type, and Drug Group.

Table A.32: Descriptive statistics of the Perceived ratings of the emotion Pleasure.

Drug Group	Picture Type	Target of Empathy	n	M	SD
1	Emotional	Female	15	1.01	0.022
		Male	15	1.75	0.591
	Neutral	Female	15	1.56	0.451
		Male	15	1.67	0.461
2	Emotional	Female	15	1.09	0.234
		Male	15	1.56	0.562
	Neutral	Female	15	1.82	0.515
		Male	15	1.94	0.574
3	Emotional	Female	18	1.04	0.074
		Male	18	1.92	0.627
	Neutral	Female	18	1.64	0.397
		Male	18	1.80	0.494
4	Emotional	Female	15	1.09	0.218
		Male	15	1.71	0.604
	Neutral	Female	15	1.69	0.421
		Male	15	1.91	0.535

Table A.33: Results from a mixed repeated-measures ANOVA on the perceived ratings of the emotion Pleasure.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,59	0.39	0.44	.010	.726
Picture Type	1,59	0.25	32.40	.137	<.001***
Target of Empathy	1,59	0.12	93.10	.177	<.001***
Drug Group x Picture Type	3,59	0.25	1.47	.021	.231
Drug Group x Target of Empathy	3,59	0.12	1.25	.009	.300
Picture Type x Target of Empathy	1,59	0.10	45.14	.079	<.001***
Drug Group x Picture Type x Target of Empathy	3,59	0.10	1.35	.008	.265

Table A.34: *Post-hoc* analysis on the effect of Picture Type on the perceived ratings of the emotion Pleasure.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	1.40	0.0403	59	1.32	1.48
Neutral	1.75	0.0589	59	1.64	1.87
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	-0.356	0.0626	59	-5.692	<.001***

Table A.35: *Post-hoc* analysis on the effect of Target of Empathy on the perceived ratings of the emotion Pleasure.

Estimated Marginal Means					
Target of Empathy	emmean	SE	df	UCL	UCL
Female	1.37	0.0300	59	1.31	1.43
Male	1.78	0.0562	59	1.67	1.90
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Female - Male	-0.415	0.043	59	-9.649	<.001***

Table A.36: *Post-hoc* analysis on the effect of Target of Empathy on the perceived ratings of the emotion Pleasure per Picture Type, and the effect of Picture Type per Target of Empathy.

Estimated Marginal Means						
Picture Type	Target of Empathy	emmean	SE	df	UCL	UCL
Emotional	Female	1.06	0.0204	59	1.02	1.10
	Male	1.74	0.0756	59	1.58	1.89
Neutral	Female	1.68	0.0563	59	1.56	1.79
	Male	1.83	0.0653	59	1.70	1.96
Pairwise Comparisons - Target of Empathy per Picture Type						
Picture Type	Contrast	estimate	SE	df	t.ratio	p.value
Emotional	Female - Male	-0.677	0.0759	59	-8.925	<.001***
Neutral	Female - Male	-0.153	0.0314	59	-4.861	<.001***
Pairwise Comparisons - Picture Type per Target of Empathy						
Target of Empathy	Contrast	estimate	SE	df	t.ratio	p.value
Female	Emotional - Neutral	-0.6187	0.0599	59	-10.336	<.001***
Male	Emotional - Neutral	-0.0942	0.0855	59	-1.103	0.2747

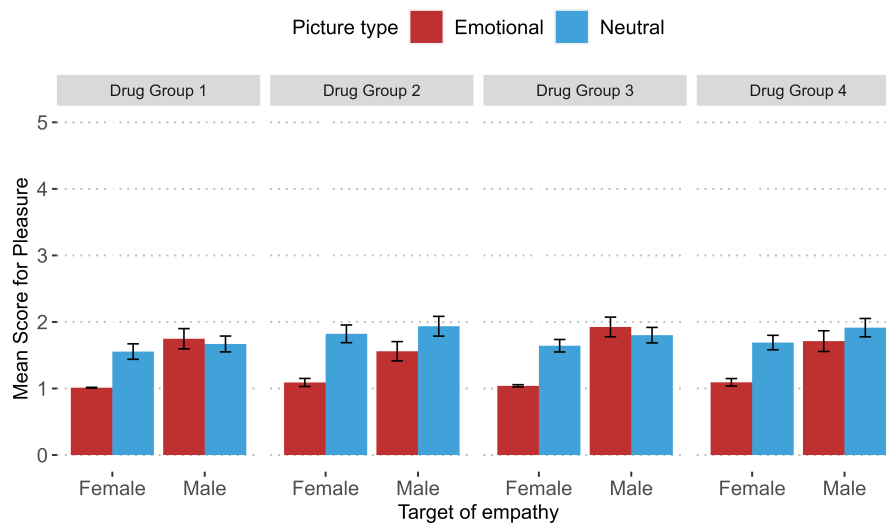


Figure A.8: Ratings of the participants' perception of Pleasure by Target of Empathy, Picture Type, and Drug Group.

A.2 Neural Data

A.2.1 Passive Block

A.2.1.1 P300 ERP Component

Table A.37: Descriptive statistics of the Amplitude of the P300 ERP Component during the passive block.

Drug Group	Picture Type	n	M (μ V)	SD (μ V)
1	Emotional	14	14.2	8.80
	Neutral	14	15.7	8.18
2	Emotional	15	12.0	5.50
	Neutral	15	13.1	6.05
3	Emotional	17	12.2	6.20
	Neutral	17	12.7	6.22
4	Emotional	13	13.3	5.82
	Neutral	13	13.4	5.85

Table A.38: Results from a two-way ANOVA on the Amplitude of the P300 ERP Component during the passive block.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,55	87.06	0.47	.025	.706
Picture Type	1,55	1.37	13.30	.004	<.001***
Drug Group \times Picture Type	3,55	1.37	1.85	.002	.150

Table A.39: *Post-hoc* analysis on the effect of Picture Type on the Amplitude of the P300 ERP Component during the passive block.

Estimated Marginal Means					
Type	emmean	SE	df	UCL	UCL
Emotional	12.9	0.873	55	11.2	14.7
Neutral	13.7	0.866	55	12.0	15.5
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	-0.79	0.217	55	-3.646	>.001***

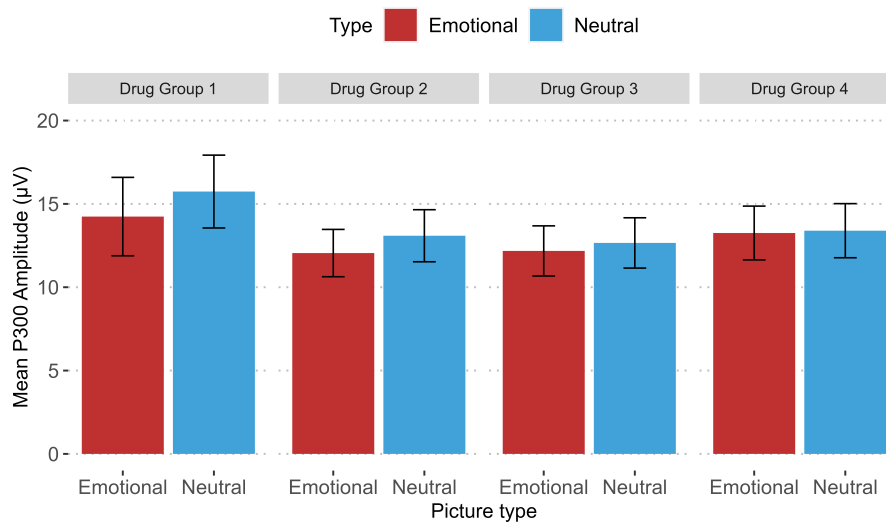


Figure A.9: Amplitude of the P300 ERP Component during the passive block by Picture Type and Drug Group.

A.2.1.2 LPP ERP Component

Table A.40: Descriptive statistics of the Amplitude of the early LPP ERP Component during the passive block.

Drug Group	Picture Type	n	M (µV)	SD (µV)
1	Emotional	14	11.6	6.86
	Neutral	14	11.9	7.06
2	Emotional	15	9.99	5.18
	Neutral	15	9.90	5.82
3	Emotional	17	10.6	5.49
	Neutral	17	10.6	5.34
4	Emotional	13	12.4	4.64
	Neutral	13	11.8	4.38

Table A.41: Results from a two-way mixed ANOVA on the Amplitude of the early LPP ERP Component during the passive block.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,55	62.70	0.45	.024	.716
Picture Type	1,55	1.63	0.14	<.001	.707
Drug Group x Picture Type	3,55	1.63	0.74	.001	.531

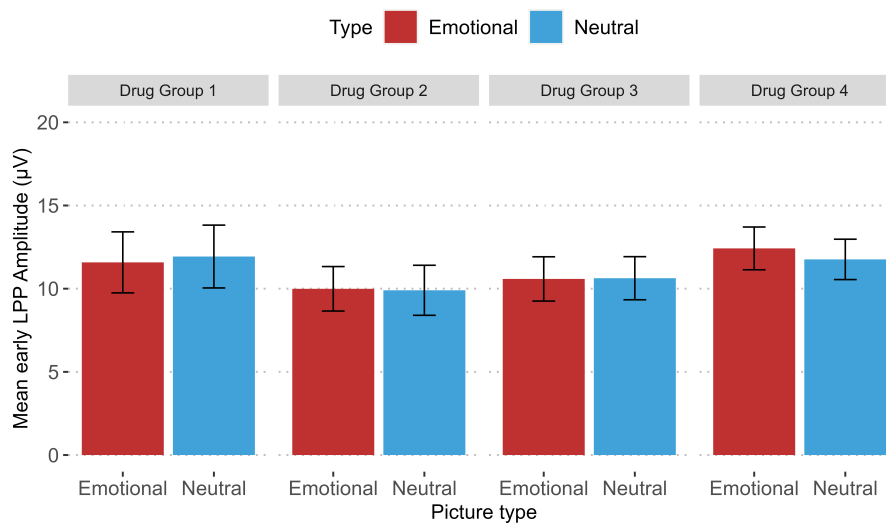


Figure A.10: Amplitude of the early LPP ERP Component during the passive block by Picture Type and Drug Group

Table A.42: Descriptive statistics of the Amplitude of the late LPP ERP Component during the passive block.

Drug Group	Picture Type	n	M (µV)	SD (µV)
1	Emotional	14	5.16	4.26
	Neutral	14	4.66	4.36
2	Emotional	15	3.80	2.94
	Neutral	15	3.14	2.93
3	Emotional	17	4.76	3.60
	Neutral	17	5.05	3.58
4	Emotional	13	4.80	3.03
	Neutral	13	4.10	2.79

Table A.43: Results from a two-way ANOVA on the Amplitude of the late LPP ERP Component during the passive block.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,55	22.57	0.62	.030	.606
Picture Type	1,55	1.81	2.53	.003	.117
Drug Group x Picture Type	3,55	1.81	0.97	.004	.414

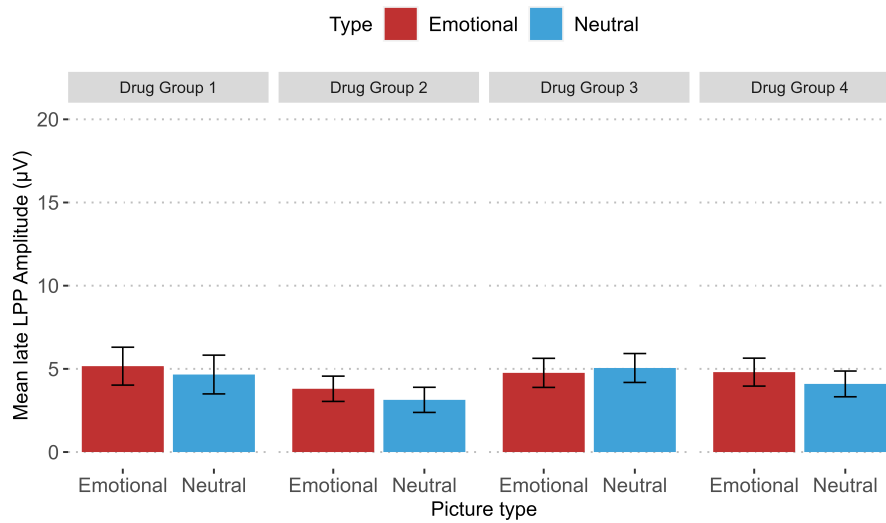


Figure A.11: Amplitude of the late LPP ERP Component during the passive block by Picture Type and Drug Group.

A.2.2 Empathy Blocks

A.2.2.1 P300 ERP Component

Table A.44: Descriptive statistics of the Amplitude of the P300 ERP Component during the empathy blocks.

Drug Group	Picture Type	Target of Empathy	n	M (μ V)	SD (μ V)
1	Emotional	Female	14	10.1	5.08
		Male	14	10.6	5.56
	Neutral	Female	14	10.8	5.00
		Male	14	11.3	4.95
2	Emotional	Female	16	11.3	6.64
		Male	16	11.5	6.64
	Neutral	Female	16	12.1	6.24
		Male	16	11.8	5.14
3	Emotional	Female	17	13.3	7.49
		Male	17	13.0	6.86
	Neutral	Female	17	13.4	6.31
		Male	17	13.1	6.89
4	Emotional	Female	13	11.4	5.5
		Male	13	12.3	6.95
	Neutral	Female	13	12.8	5.68
		Male	13	12.9	6.40

Table A.45: Results from a mixed repeated-measures ANOVA on the Amplitude of the P300 ERP Component during the empathy blocks.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,56	143.37	0.47	.023	.701
Picture Type	1,56	2.71	7.60	.002	.008**
Target of Empathy	1,56	4.45	0.37	<.001	.544
Drug Group x Picture Type	3,56	2.71	0.76	<.001	.524
Drug Group x Target of Empathy	3,56	4.45	0.55	<.001	.647
Picture Type x Target of Empathy	1,56	2.16	0.74	<.001	.392
Drug Group x Picture Type x Target of Empathy	3,56	2.16	0.23	<.001	.877

Table A.46: *Post-hoc* analysis on the effect of Picture Type on the Amplitude of the P300 ERP Component during the empathy blocks.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	11.7	0.820	56	10.0	13.3
Neutral	12.3	0.747	56	10.8	13.8
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	-0.589	0.214	56	-2.757	0.0079**

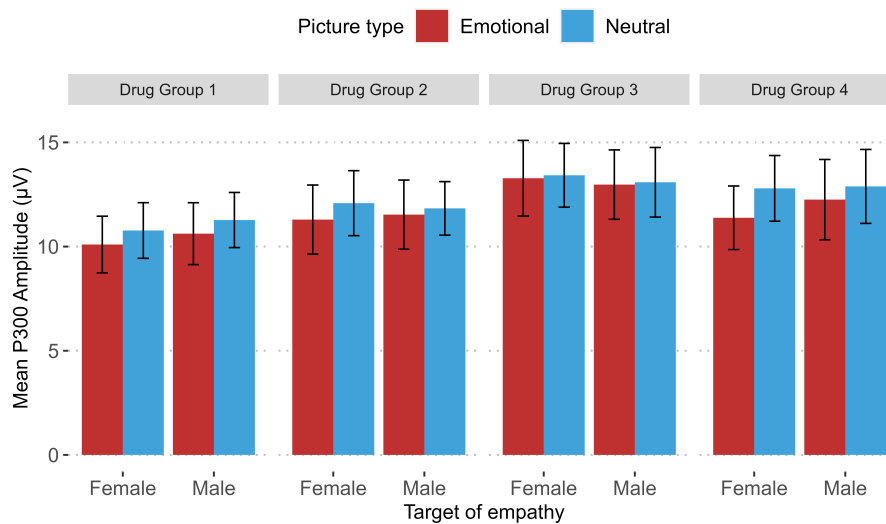


Figure A.12: Amplitude of the P300 ERP Component during the empathy blocks by Target of Empathy, Picture Type, and Drug Group.

A.2.2.2 LPP ERP Component

Table A.47: Descriptive statistics of the Amplitude of the early LPP ERP Component during the empathy blocks.

Drug Group	Picture Type	Target of Empathy	n	M (μ V)	SD (μ V)
1	Emotional	Female	14	7.81	3.91
		Male	14	7.82	3.38
	Neutral	Female	14	7.92	3.17
		Male	14	8.30	3.59
2	Emotional	Female	16	9.13	5.13
		Male	16	9.08	4.42
	Neutral	Female	16	8.53	4.45
		Male	16	7.70	3.88
3	Emotional	Female	17	12.3	5.81
		Male	17	11.7	7.04
	Neutral	Female	17	11.4	5.58
		Male	17	11.0	6.45
4	Emotional	Female	13	11.2	4.61
		Male	13	11.2	6.17
	Neutral	Female	13	10.6	4.87
		Male	13	11.3	6.04

Table A.48: Results from a mixed repeated-measures ANOVA on the Amplitude of the early LPP ERP Component during the empathy blocks.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,56	95.59	2.05	.092	.118
Picture Type	1,56	2.39	5.07	.002	.028*
Target of Empathy	1,56	4.03	0.08	<.001	.783
Drug Group x Picture Type	3,56	2.39	2.13	.003	.107
Drug Group x Target of Empathy	3,56	4.03	0.70	.001	.554
Picture Type x Target of Empathy	1,56	1.25	0.17	<.001	.678
Drug Group x Picture Type x Target of Empathy	3,56	1.25	1.22	<.001	.311

Table A.49: *Post-hoc* analysis on the effect of Picture Type on the Amplitude of the early LPP ERP Component during the empathy blocks.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	10.04	0.661	56	8.72	11.4
Neutral	9.59	0.623	56	8.34	10.8
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	0.453	0.201	56	2.253	0.0282*

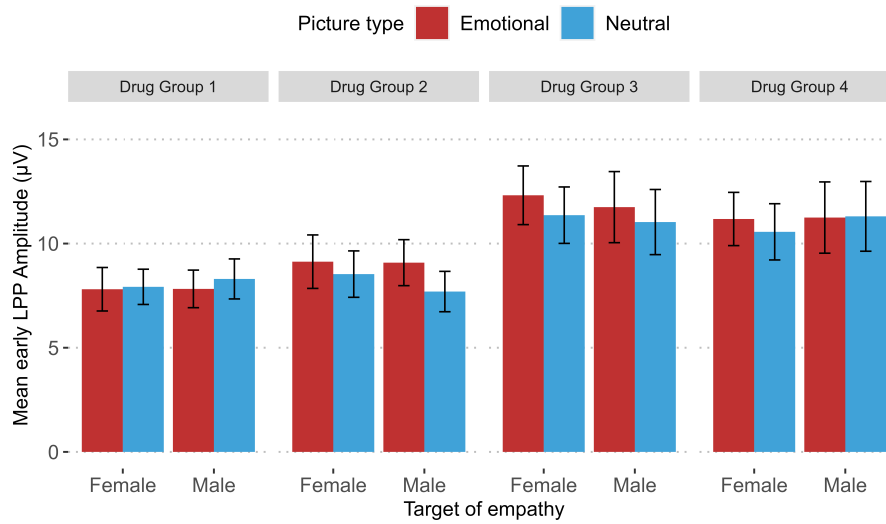


Figure A.13: Amplitude of the early LPP ERP Component during the empathy blocks by Target of Empathy, Picture Type, and Drug Group.

Table A.50: Descriptive statistics of the Amplitude of the late **LPP ERP** Component during the empathy blocks.

Drug Group	Picture Type	Target of Empathy	n	M (μ V)	SD (μ V)
1	Emotional	Female	14	1.60	3.10
		Male	14	2.03	2.67
	Neutral	Female	14	0.842	2.82
		Male	14	0.975	4.28
2	Emotional	Female	16	3.45	4.55
		Male	16	2.39	2.40
	Neutral	Female	16	1.37	2.98
		Male	16	0.871	1.61
3	Emotional	Female	17	3.41	2.34
		Male	17	2.57	3.23
	Neutral	Female	17	3.16	2.22
		Male	17	2.55	2.52
4	Emotional	Female	13	2.34	2.90
		Male	13	3.10	1.47
	Neutral	Female	13	2.13	2.22
		Male	13	1.76	2.38

Table A.51: Results from a mixed repeated-measures **ANOVA** on the Amplitude of the late **LPP ERP** Component during the empathy blocks.

Effect	df	MSE	F	η_p^2	p-value
Drug Group	3,56	21.09	1.22	.041	.310
Picture Type	1,56	5.00	9.69	.026	.003**
Target of Empathy	1,56	3.96	0.99	.002	.324
Drug Group x Picture Type	3,56	5.00	1.54	.013	.215
Drug Group x Target of Empathy	3,56	3.96	1.24	.008	.305
Picture Type x Target of Empathy	1,56	2.37	0.16	<.001	.690
Drug Group x Picture Type x Target of Empathy	3,56	2.37	0.82	.003	.489

Table A.52: *Post-hoc* analysis on the effect of Picture Type on the Amplitude of the late LPP ERP Component during the empathy blocks.

Estimated Marginal Means					
Picture Type	emmean	SE	df	UCL	UCL
Emotional	2.61	0.344	56	1.92	3.30
Neutral	1.71	0.319	56	1.07	2.35
Pairwise Comparisons					
Contrast	estimate	SE	df	t.ratio	p.value
Emotional - Neutral	0.904	0.29	56	3.113	0.0029**

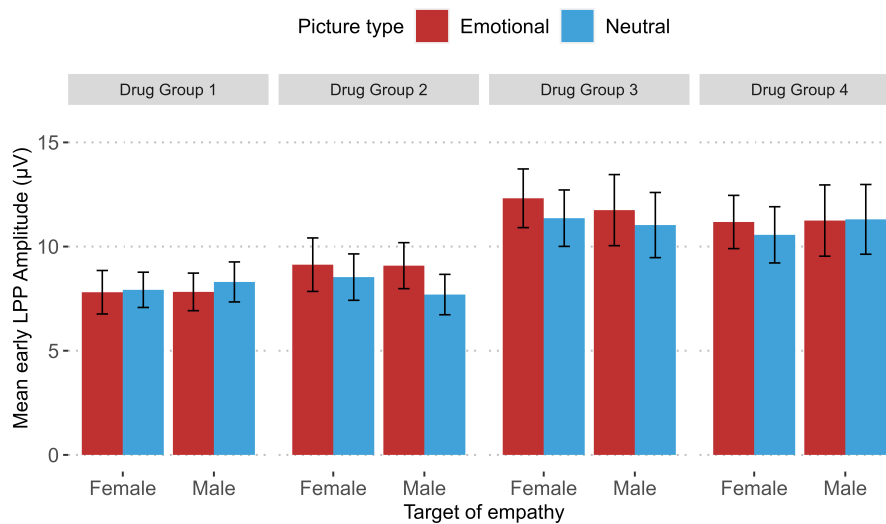


Figure A.14: Amplitude of the late LPP ERP Component during the empathy blocks by Target of Empathy, Picture Type, and Drug Group.

I

INFORMED CONSENT

This annex contains the Informed Consent that was signed by all the participants before the experiment.



Ciências
ULisboa

Comissão de Ética de Ciências

Formulário de Consentimento Informado

PROJECTO: [SOTO EXPL/PSI-GER/1148/2021]

INVESTIGADOR RESPONSÁVEL: Carlotta Cogoni

**Agradecemos o seu interesse e colaboração neste estudo.
Por favor, preencha o formulário que se segue. Receberá uma cópia quando sair.**

1. Confirmo que li e compreendi o folheto informativo associado ao projecto.
2. Foi-me dada a oportunidade de ler e considerar a informação apresentada, e fazer perguntas, as quais foram respondidas de forma satisfatória.
3. Compreendo que a minha participação é voluntária e que sou livre de desistir do estudo em qualquer altura, sem ter que dar quaisquer explicações e sem quaisquer consequências.
4. Compreendo que os dados recolhidos durante o estudo possam ser do conhecimento dos membros da equipa de investigação, sempre que necessário para o estudo. Autorizo que os membros da equipa tenham acesso a esses dados.
5. Compreendo que, caso esta investigação venha a ser publicada, todos os dados serão mantidos anónimos e nenhuma informação será identificável como sendo minha.
6. Gostaria que me fosse enviado o relatório final do estudo.
O meu endereço de e-mail é: _____
7. Gostaria de ser contactado para o endereço acima acerca de sessões ou estudos adicionais relacionados com este estudo.
8. Declaro que não comuniquei nenhuma razão potencial de qualquer natureza que constitua um eventual factor de risco para a minha saúde ou integridade física.
9. Declaro que participo neste estudo sem qualquer remuneração ou contrapartida, para além do ressarcimento das despesas em que tiver incorrido ou compensação simbólica pelo meu tempo.
10. Declaro que aceito que as minhas entrevistas sejam gravadas em áudio e vídeo.
11. Declaro que aceito que a saliva, o suor, e dados descritos no ponto 10 serão usados de forma anonimizada (i.e., sem o meu nome) em estudos de investigação follow-up.
12. Declaro que tomo a minha decisão de forma inteiramente livre.
13. Concordo em participar neste estudo.



Ciências
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Comissão de Ética de Ciências

Formulário de Consentimento Informado

_____/_____/_____
Nome do Participante Assinatura Data

Sou da opinião que o participante compreendeu os aspectos relevantes da informação fornecida e está apto a tomar uma decisão informada.

_____/_____/_____
Assinatura do Investigador Responsável Data

PARTICIPANTS' INFORMATION BROCHURE

This annex contains the Brochure with the information about the experimental protocol that participants were instructed to read before the experiment.



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Comissão de Ética de Ciências

Folheto Informativo

PROJECTO: [SOTO EXPL/PSI-GER/1148/2021]

INVESTIGADOR RESPONSÁVEL: [Carlotta Cogoni]

Vimos desta forma convidá-la/o a participar no nosso estudo de investigação focado em interações sociais.

Antes de decidir, gostaríamos de lhe apresentar os detalhes desta investigação, a sua razão de ser, a sua utilidade potencial e as implicações da sua participação. Um membro da equipa da investigação irá acompanhá-lo na leitura deste folheto e responderá a quaisquer perguntas que queira fazer.

1 - Em que consiste o estudo "DESIGNAÇÃO DO ESTUDO"?

Este estudo incide sobre a interação social entre pessoas através de um jogo de computador e pretende avaliar o efeito de 2 compostos nessa mesma interação social.

A sua participação, que será muito valorizada, consiste em jogar o jogo de computador que lhe será apresentado e preencher um questionário, e poderá durar cerca de 4 horas. Não existem riscos significativos expectáveis associados à participação no estudo. Ainda que possa não beneficiar diretamente com a participação no estudo, as suas respostas vão contribuir para melhor compreender as bases biológicas da interação social.

Em primeiro lugar, será realizada uma breve entrevista referente aos seus dados demográficos, personalidade, assim como hábitos e experiências sociais anteriores.

De seguida, pediremos que se deite numa cama e será colocado na sua cabeça um aparelho de electroencefalografia para que registemos a sua atividade cerebral, enquanto executa duas tarefas cognitivas (jogos) num computador. Também serão recolhidas medições não-invasivas sobre a movimento ocular e pupilar (eye-tracking), registando concomitantemente, as respostas de Condutância da pele (SRC), eletrocardiograma e eletromiografia (ECG e EMG).

Durante a experiência também irá fornecer 3 amostras de saliva, e duas amostras de suor para análise hormonal e genética.

Receberá depois um gel e um spray nasal que poderá ou não conter um ingrediente ativo (oxitocina e testosterona). Esse gel e spray (ingrediente ativo ou o seu placebo) serão administrados somente uma vez, são seguros e não estão associados a efeitos adversos ou efeitos colaterais na dose utilizada neste estudo – sendo o seu uso e comercialização aprovados pelo INFARMED em Portugal.

2 - Tenho de participar neste estudo?

A participação no estudo é totalmente voluntária. Vamos descrever o estudo e apresentar o conteúdo deste folheto informativo, incluindo os detalhes da sua participação. Se concordar em participar, irá assinar um Formulário de Consentimento. Serão-lhe fornecidas cópias deste documento e do Formulário de Consentimento informado.

3 - E se eu desejar desistir do estudo?

É livre de desistir, em qualquer altura, sem ter que fornecer quaisquer razões ou explicações.

4 - O que terei de fazer no âmbito do estudo?

No âmbito do estudo, irá participar em uma sessões de electroencefalografia.



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Cada sessão demorará um tempo máximo de 4 horas mas não tem um tempo mínimo obrigatório.

No âmbito do estudo, irá participar nalguns jogos de computador para verificar o efeito da formação de impressões na interação interpessoal. O primeiro jogo é composto por dois jogadores, que irão competir, dois de cada vez numa tarefa competitiva de tempo de reação. Durante o estudo, jogará um total de duas sessões, sendo que em cada sessão jogará com um jogador diferente. Num outro momento do jogo, estará envolvido em outras tarefas, que irá realizar sozinho. No final, ser-lhe-á pedido o preenchimento de uns questionários psicológicos e demográficos.

O objetivo da investigação é identificar e compreender de que forma as pessoas interagem. Não tem como objetivo avaliá-la/o a si. Todas as recomendações e melhorias sugeridas permitirão fazer evoluir a investigação e são bem-vindas.

5 - Quais as desvantagens e riscos de participar?

Não estão previstos quaisquer riscos associados e a expectativa da equipa de investigação é de que as sessões em que participar sejam uma experiência agradável para os participantes.

O horário das sessões será 9-19.

6 - Quais os possíveis benefícios de participar?

De acordo com a nossa experiência, as pessoas gostam de participar em estudos que promovem a comunicação com cientistas. O seu envolvimento irá ajudar a identificar e compreender de que forma as pessoas interagem umas com as outras. Independentemente da sua prestação, receberá uma compensação mínima de 25€ pelo seu tempo, deslocação e inconveniência.

7 - O que acontece quando o estudo terminar?

A análise dos dados terminará aproximadamente em dezembro de 2023. Os resultados do estudo serão publicados em conferências e revistas académicas. Se desejar saber detalhes sobre os resultados e implicações do estudo, fazer-lhe-emos chegar uma cópia do relatório do estudo, mas não antes de Julho 2024.

8 - E se ocorrer algum problema?

Se tiver alguma preocupação sobre qualquer aspecto deste estudo, deve falar com o investigador responsável, Dr. Carlotta Cogoni, que fará o seu melhor para o elucidar e responder às suas dúvidas, por telefone, 962055802 ou e-mail ccogoni@fc.ul.pt. Caso esteja descontente ou queira apresentar uma queixa formal, pode fazê-lo contactando o Diretor da Faculdade de Ciências da Universidade de Lisboa [e-mail: direccao@fc.ul.pt].

9 - A minha informação será mantida confidencial?

Sim. Seguiremos todas as práticas éticas e legais e toda a informação sobre si (incluído as amostras de saliva, e de suor) será tratada de forma absolutamente confidencial. Para garantir a anonimidade, os registos pessoais estarão apenas disponíveis na sua integralidade, para o investigador responsável, e os membros da equipa de investigação apenas terão acesso aos dados que necessitarem de conhecer. Se os seus dados forem usados para publicações ou apresentações, serão totalmente anonimizados, sem qualquer referência, directa ou indirecta, à sua identidade. Se forem tiradas fotografias, e for nossa intenção usá-las em alguma apresentação, será-lhe pedida autorização prévia. Se estiver disponível para que usemos fotografias ou vídeos para esse propósito, pedir-lhe-emos primeiro que assine autorizações específicas com esse objectivo.



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10 - O estudo passou por um processo de revisão?

[Sim]. Com efeito, este estudo foi revisto pela Comissão de Ética de Ciências (<https://ciencias.ulisboa.pt/pt/comissao-etica-ciencias>). Esta comissão analisou a proposta de estudo, bem como todos os seus materiais e não levantou objeções do ponto de vista ético.

11 - Quem posso contactar relacionado com este estudo?

<p>Dr. Carlotta Cogoni Instituto de Biofísica e Engenharia Biomédica – Fciências.ID ccogoni@fc.ul.pt Telefone 962055802</p>	<p>Dr. Nicoletta Cera Faculdade de Psicologia e de Ciências da Educação da Universidade do Porto (FPCE/UP) cera.nicoletta@fpce.up.pt Telefone 968059426</p>	<p>Dr. Diana Prata Instituto de Biofísica e Engenharia Biomédica – Fciências.ID diana.prata@kcl.ac.uk Telefone 966595936</p>
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Sinta-se à vontade para os contactar em qualquer matéria relacionada com este estudo.

Muito Obrigado.

Obrigado por nos ter dedicado este seu tempo e por considerar participar neste estudo.

O Investigador Responsável

INTERPERSONAL AGGRESSION PARADIGM QUESTIONNAIRE

This annex includes the 4 questions from the Interpersonal Aggression Paradigm questionnaire that were asked for each of the pictures presented in the experimental task.

1. De acordo com o que você sentiu ao observar a pessoa da direita , indique a [*] intensidade das suas emoções numa escala de 1 a 5. (1 = "eu não senti esta emoção"; 5 = "eu senti muito esta emoção")					
	1	2	3	4	5
Medo	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Raiva	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Neutro	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Prazer	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

1. De acordo com o que você sentiu ao observar a pessoa da esquerda , indique a [*] intensidade das suas emoções numa escala de 1 a 5. (1 = "eu não senti esta emoção"; 5 = "eu senti muito esta emoção")					
	1	2	3	4	5
Medo	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Raiva	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Neutro	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Prazer	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

1. De acordo com o que você achou que a **pessoa da direita** estava a sentir na situação da imagem, indique a intensidade dessas emoções numa escala de 1 a 5. *

(1 = "a pessoa não sentiu esta emoção"; 5 = "a pessoa sentiu muito esta emoção")

	1	2	3	4	5
Medo	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Raiva	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Neutro	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Prazer	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

1. De acordo com o que você achou que a **pessoa da esquerda** estava a sentir na situação da imagem, indique a intensidade dessas emoções numa escala de 1 a 5. *

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	1	2	3	4	5
Medo	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Raiva	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Neutro	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Prazer	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>



2024

Effects of oxytocin and testosterone administration on empathic reactions elicited in interpersonal aggression contexts:
an electroencephalography investigation

Matilde Faial

