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The effects of reward on width discrimination and tactile processing in humans

Os efeitos de recompensa na discriminação de distância ativa e processamento táctil em humanos

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palavras-chave EEG, processamento táctil, discriminação de distância, neuroquímica, neuropsicologia, toque activo

resumo

O processamento de informação tátil durante a discriminação de distância pelo toque envolve múltiplos processos cognitivos, entre eles a recompensa. Apesar de este processo ter sido extensivamente descrito em roedores, ainda há pouca informação relativamente à base neruobiológica deste tipo de processamento em humanos. Neste estudo analisou-se o efeito da atribuição de recompensas monetárias associadas ao desempenho numa tarefa de discriminação de distância pelo toque. Para tal utilizou-se o registo eletroencefalográfico e a análise neuroquímica. A análise dos resultados não demonstrou qualquer efeito da recompensa monetária no desempenho ou na latência de resposta dos sujeitos. Também não se verificou nenhuma alteração clara na quantidade de cortisol medido na saliva. A análise do sinal eletrofisiológico demonstrou que a introdução da recompensa monetária levou a alterações em todas as bandas de frequências, sendo que a maior expressão se verificou na banda gama baixa (30-45Hz). No seu conjunto, estes resultados sugerem que a recompensa monetária altera o processamento neuronal da distância através do toque, não se tendo, no entanto, verificado qualquer evidência no sentido de alterar o desempenho comportamental.

keywords EEG, tactile processing, width discrimination, neurochemistry, neuropsychology, active touch

abstract

Tactile information processing, during width discrimination, is associated with multiple cognitive processes such as reward. Even though this has been extensively studied in rodents, there is still very little information on the neurobiological basis of this process in humans. Here, the effects of monetary reward in active tactile width discrimination performance in humans were studied. For this, electrophysiological signals and neurochemical measurements were performed. Analysis of results did not demonstrate an effect of monetary reward in behavioural performance nor in response latency. Also, no changes were found in cortisol levels. Meanwhile, analysis of the electrophysiological signal revealed changes in the power of all frequency bands, with particularly large differences being present in the low gamma frequency band (35-40Hz). Altogether, these results suggest that monetary reward changes neurophysiological processing of active tactile width discrimination, but no evidence was found regarding changes in behavioural performance.

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Table of abbreviations

EEG	Electroencephalogram
EOG	Electrooculogram
ECG	Electrocardiogram
BSS	Blind source separation
ICA	Independent component analysis
CCA	Canonical correlation analysis
EMD-BSS	Empirical mode decomposition and blind source separation
SVM	Support vector machines
ERP	Event-related potential
LFP	Local field potential
MRI	Magnetic resonance imaging
R	Reward
NR	Non-Reward
CFP	Center-Finger Place
GUI	Graphical User Interface
R1	Ratio 1
R2	Ratio 2
NR run	Non rewarded run
R Run	Rewarded run
fNIRS	Functional near-infrared spectroscopy
n.s.	Non-significant
LFP	Local field potential

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Chapter I – Introduction & background information

EEG

Neurons are nerve cells responsible for the conduction of nervous impulses, they represent the fundamental unit of the brain.

Electroencephalography (EEG) is a non-invasive technique used to study neuronal activity that records electrical potential using electrodes placed on the scalp (Tudor 2005). EEG can be measured by means of electrodes placed on the scalp or directly on the cortex (Blinowska and Durka 2006).

EEG is typically is used to study the electrophysiology dynamics of the brain (Cohen 2017). EEG is particularly useful for evaluating patients with suspected seizures, epilepsy, and unusual brain activity (St. Louis et al. 2016). A typical EEG display graphs voltages on the vertical domain and time on the horizontal domain, providing a near real-time display of ongoing cerebral activity (figure 1).

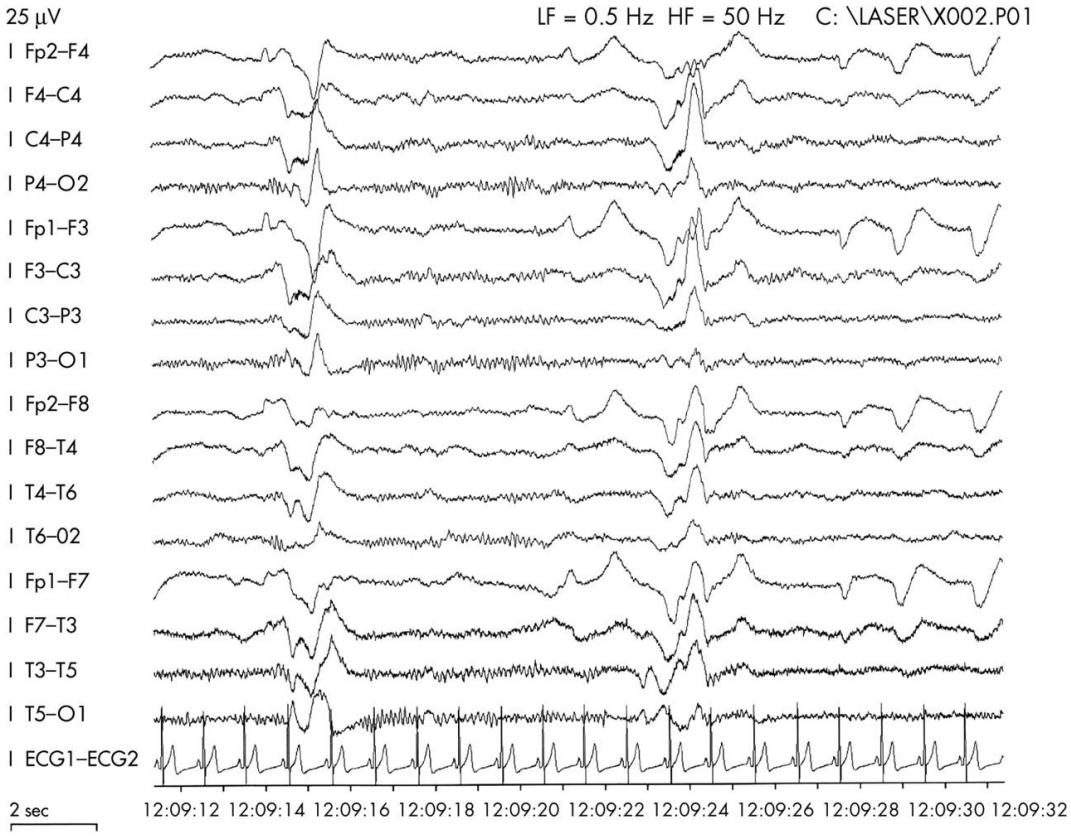

Figure 1. Typical EEG reading. Figure adapted from "EEG in neurological conditions other than epilepsy" (Smith 2005)

EEG enables analysis and interpretation of brain disorders; it is a tool with both clinical and research utility. (Chen et al. 1995) There are several types of EEG systems that range from 4 electrodes to 256 electrodes (Lau, Gwin, and Ferris 2012).

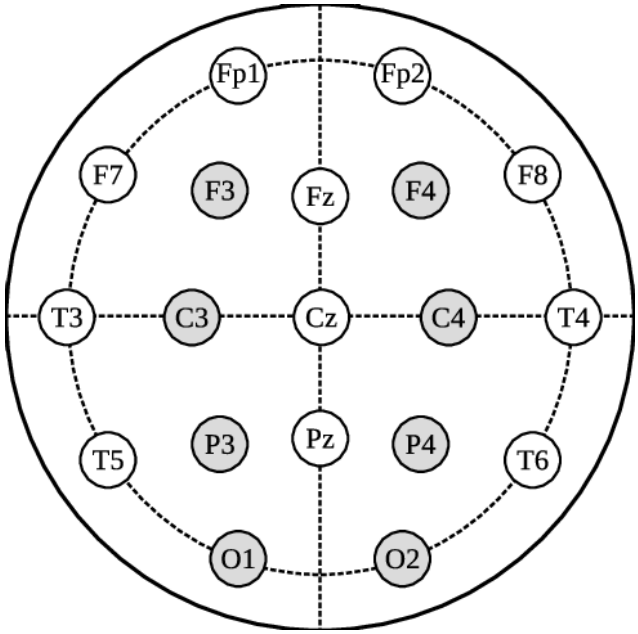

Figure 2. 16 electrode EEG system. Adapted from "Computer Science Technical Report Echo State Networks for Modeling and Classification of EEG Signals in Mental-Task Brain-Computer Interfaces"

There are several technics used to study brain activity, including EEG. Table 1 demonstrates a comparison between current used brain analysis tools.

Table 1. Comparison of different techniques used to study brain activity, adapted from "On-Chip Integrated Functional Near Infra-Red Spectroscopy (fNIRS) Photoreceiver for PorTable Brain Imaging" (Kamrani and Sawan Frédéric 2014)

	Image/Data Quality	Temporal Resolution	Spatial Resolution	Mobility Tolerance	Scale	Safety	Cost
MRI	High	Low (~30s)	Very-High (3-6 mm)	Medium	Bulky	High	High
fMRI	High	Low (~30s)	Very-High (3-6 mm)	Medium	Bulky	High	High
X-Ray	Low	Medium (1s-10s)	Very-High (1 mm)	Low	Bulky	Low*	Low
CT-Scan	Low	Medium (10s)	Very-High (1mm)	Low	Bulky	Low*	Low
Ultrasound	Low	Hi (~1ms)	Depends on the probe element width	Low	Medium	Very-High	Low
PET	High	Low (30s-40s)	High (5mm)	Very-high	Bulky	Low*	Very-high (1-2M$)
SPECT	Medium	Very-Low	Medium (1cm)	Medium	Bulky	Low	High (0.5-1M$)
MEG	Medium	Very-High (~1ms)	Low (1cm - 2cm)	Medium	Bulky	Low	High
EEG/ERP	Medium	Very-High (~1ms)	Medium (1cm)	Low	Small	High	Low
fNIRS	High	High (0.5s-1s)	Low-Medium (0.5cm-2cm)	Medium	Small	Very-High	Very-low

Observing the above Table, we can conclude that EEG provides a high safety with a very high temporal resolution in comparison to other methods.

EEG is analysed in frequencies that typically range from 0.01 Hz to 100 Hz but recent studies also show that spikes up to 500 Hz can be recorded and analysed (Urrestarazu et al. 2007). These frequency bands (figure 3), (Abo-Zahhad, Ahmed, and Abbas 2015) are divided in five different bands: delta(2–4 Hz), theta (4–7 or 8Hz) alpha (8–12Hz) beta (16–25Hz), Low gamma (30–50 Hz) and gamma (50-500Hz) (Klimesch 2018).

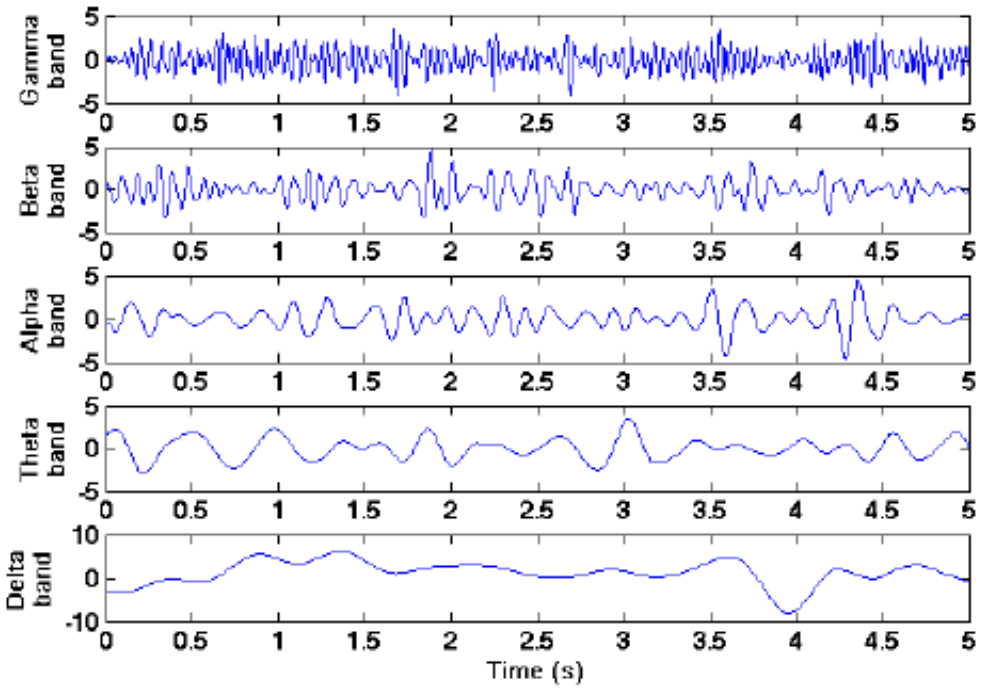

Figure 3. EEG frequency bands, adapted from "A New EEG Acquisition Protocol for Biometric Identification Using Eye Blinking Signals"(Abo-Zahhad et al. 2015)

EEG Signal processing and pre-processing

EEG signals are characterized by oscillatory behaviour, but they can also have patterns that are not necessarily rhythmic. Consequently we can observe two types of phenomena in EEG readings: oscillations and transients (Osorio et al. 2019), (figure 3).

EEG signals are easily contaminated by undesired noise, which will result in various artifacts (Jiang, Bian, and Tian 2019). Artifacts can arise due to the measurement instrument and human subjects (Ge et al. 2017). Artifacts related to measurement instrument like faulty electrodes, line noise and high electrode impedance can be prevented by more precise recording system and strict recording procedures. On the other hand, physiological artifacts - eyeblinks, eye movements, cardiac and muscle activity present a bigger challenge to remove (Fatourechi et al. 2007). Physiological artifacts may interfere with neural information and even be used as normal phenomena to misleadingly drive a practical application such as brain-computer interface (Mannan et al. 2018). Another issue

that could derive from artifacts is the imitation of cognitive or pathologic activity which could lead to wrongful interpretation of data and wrongly diagnostics in studies as a sleep disorders and Alzheimer's disease (Bassis, Esposito, and Morabito 2015; Tamburro et al. 2018). Therefore, artifacts identification and removal, either in clinical diagnosis or practical applications, is the most critical step prior to performing any type of data processing (Jiang et al. 2019).

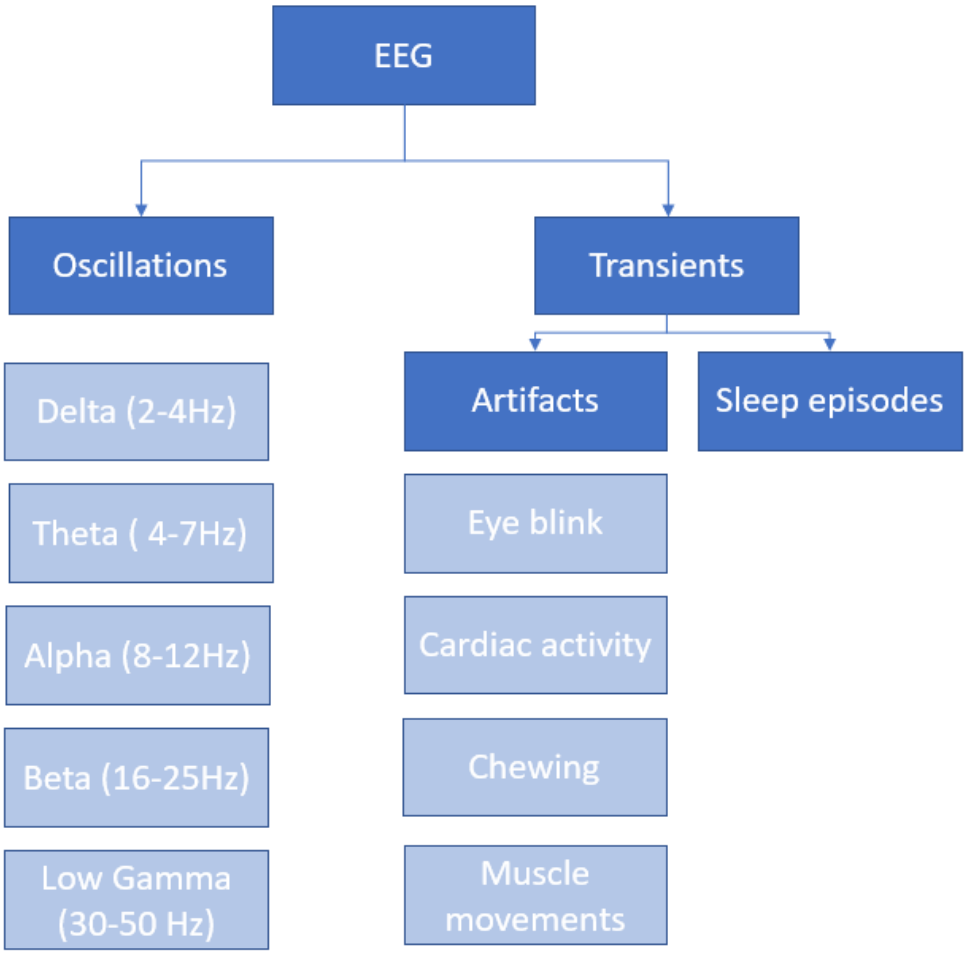

Figure 4. EEG Oscillations and transients, adapted from "A New EEG Acquisition Protocol for Biometric Identification Using Eye Blinking Signals" (Abo-Zahhad, Ahmed and Abbas, 2015)

Artifacts can be removed using algorithms or automatic removal via software. The artifact removal process can be separated into two categories: estimation of the artifactual signal using a reference channel, or by decomposing the EEG signal into other domains (Jiang et al. 2019). These techniques vary from regression (Al-Nuaimi et al. 2018), Blind Source

Separation (Sweeney, Ward, and McLoone 2012) and Wavelet Transform algorithm to their hybrid methods (Teixeira et al. 2006).

Physiological Artifacts

Physiological Artifacts originate from the subject's physiological activity like movement or blinking.

Ocular artifacts derive from eye movement and blinks which travel over the scalp and are recorded by EEG (Wallstrom et al. 2004). The amplitude of EOG is bigger than EEG and its frequency is similar with the frequency of EEG signals (Schlögl et al. 2007).

Muscular artifacts are originated by many different muscle groups close to the recording site and it's poses challenges when collecting EEG data (Goncharova et al. 2003). If the subject talks, sniffs, swallows it causes a muscular artifact (Urigüen and Garcia-Zapirain 2015).

Finally, cardiac artifacts can be introduced when placing an electrode close to a blood vessel. These artifacts are typical called pulse artifacts with a frequency of 1.2Hz, and due to their waveform being similar to EEG, makes them hard to remove. (Hamal and bin Abdul Rehman 2013). ECG is a known method to measure cardiac activity. The data collected from ECG can be acquired at the same as performing a EEG making artifact removal by a possible solution.(Lee, Park, and Lee 2015)

Artifact removal

Single Artifacts Removal Techniques

There are many methods used for artifact removal. The traditional method is the regression method (Woestenburg, Verbaten, and Slangen 1983). It works on the assumption that that each channel is the cumulative sum of the pure data and proportion of artifact.(Sweeney et al. 2012) This means that this method requires external reference data (EOG, ECG).

Wavelet transform is the act of transforming a time domain signal into time and frequency domain, that has good time-frequency features relative to Fourier transform due to the better tunable time-frequency tradeoff and superiority of non-stationary signal analysis.(Safieddine et al. 2012)

BSS (Blind source separation)

The other group of artifact removal methods are BSS (Blind source separation**)**. These methods involve using unsupervised learning algorithms without prior information and extra reference channels.

Canonical Correlation analysis – BSS assumes mutually uncorrelated sources which are maximally autocorrelated. It can be applied for the separation of muscle and brain activity sources because of the relative low autocorrelation of muscle artifacts in comparison with brain activity.(De Clercq et al. 2006)

Filtering methods are used in cancelation of the artifacts produced by EEG. These techniques are used to minimize the mean square error between the predicted EEG and primary EEG.(He et al. 2006) The two main filtering techniques are adaptive filtering (Marque et al. 2005) and Wiener filtering (Somers, Francart, and Bertrand 2018). All the techniques mentioned above can be used to together forming hybrid methods for artifact removal. Some of these methods include: EMD-BSS (Chen, Wang, and McKeown 2016), wavelet-BSS (Calcagno, La Foresta, and Versaci 2014) and BSS-SVM (Shoker, Sanei, and Chambers 2005).

Comparing the methods above:

The methods above represent the most common techniques used in EEG artifact removal. Comparing these methods showcases their differences demonstrates that their usage is dependent on application. The Table below presents a short comparison between artifact removal methods (Table 2)

Table 2. Comparison between Artifact removal methods

Method	***Additional Reference***	***Automatic***	***Online***	***Can Perform on Single Channel***
Regression	Y	Y	N	N
Wavelet	N	Y	N	Y
ICA	N	N	Y	N
CCA	N	N	Y	N
Adaptive filter	Y	Y	Y	Y
Wiener filter	N	Y	N	Y

Wavelet BSS	N	N	N	Y
EMD BSS	N	N	N	Y
BSS-SVM	N	Y	Y	N

When we consider EEG applications, often it is required to have real-time processing. This involves trying to manage methods with automatic processing that have low computational cost. Regression and filtering can process data automatically when they have a reference signal. In summary, artifact removal is a key part of analysing EEG data.

Neural Networks

In the past 20 years several research efforts concentrated in understanding how multiple brain regions interacted with each other in cognitive and sensory tasks (Rosazza and Minati 2011). Neural networks are patterns of heterogeneous structural connections that support a wide range of cognitive processes and behaviours, they represent the wiring of the brain (Lynn and Bassett 2019) .

EEG has been used to study responses to several forms of stimuli events where neural networks can be identified.

ERPs are rebounds in electrophysiological signals such as local field potentials (LFPs) that are triggered by external events or internal cognitive processes (Lopes-dos-Santos et al. 2018), (Freeman and Quiroga 2012) (figure 6). Local field potentials (LFPs) are a measurement of brain activity that facilitates the study of the flow information across a neural network. (Herreras 2016)

Studying LFPs showed that this signal scan be correlated with rat sleep cycles (Adler et al. 2014). During these studies it was also demonstrated that brain state transitions occur simultaneously across multiple forebrain areas as specific spectral trajectories with characteristic path, duration, and coherence bandwidth. During state transitions, striking changes in neural synchronization are affected by the prominent narrow-band LFP oscillations that mark state boundaries (Gervasoni, S. C. Lin, et al. 2004).

Somatosensory evoked potentials (SEP) are generated in response to a touch stimuli. SEPs consist of a series of positive and negative peaks that represent the sequential activation related to touch. Generally, SEP consists of an early cortical component provoked in the contralateral primary somatosensory cortex correlated with the physical characteristics of

the touched stimulus, such as N20, P27, and P50. Later components, such as N140 and P200, are typically larger in amplitude and more distributed over the scalp, mainly above the secondary somatosensory cortex and frontal cortex, indicating a higher cognitive processing (Hämäläinen et al. 1990).

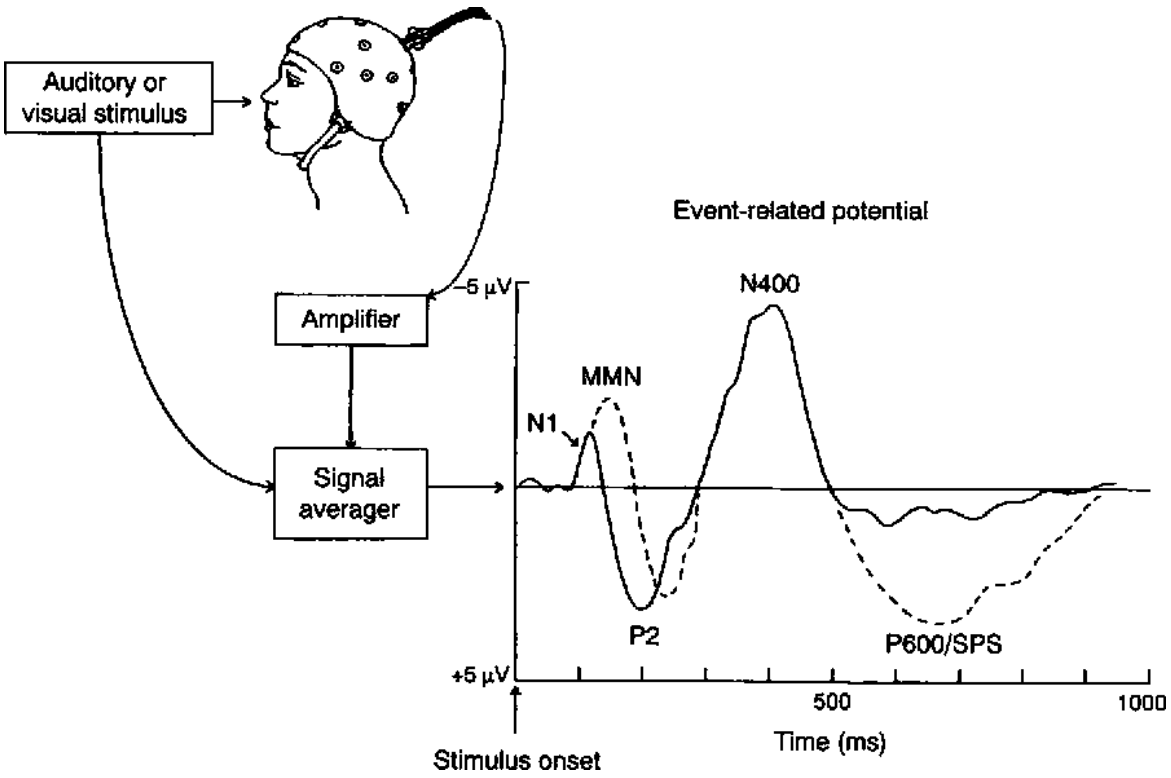

figure 5. Example of an ERP adapted from " Event-Related Potentials and Language Processing: A Brief Overview" (Kaan 2007)

Neurohaptics

Neurohaptics is the field of study that aims to understand the neural processes associated with touch and kinesthetic stimuli (Alsuradi, Park, and Eid 2020). Every moment our brains transform the perceived information into cognition creating knowledge and understanding of our surroundings (Alsuradi et al. 2020). We use touch in our daily lives to navigate our different tasks (interacting with objects, navigating the environment) and to establish emotional contact with other humans and objects (McGlone, Wessberg, and Olausson 2014b).

Despite advances in understanding the neural practices of tactile processing the mechanisms involved with processing tactile information are still unclear (Spitzer and Blankenburg 2011).

The somatosensory cortex is a one of the regions of the brain that receives and processes sensory information.

Measuring EEG shows that zones of the Cortex around C3, C4, and Cz locations deal with sensory and motor functions (De Clercq et al. 2006). Locations near P3, P4, and Pz contribute to activity of perception and differentiation (De Clercq et al. 2006). Recent studies of tactile width discrimination investigated changes in the power of Gamma waves in humans (Perrotta et al. 2020) and C3 and C4 electrodes. For example, changes in alpha and beta frequency bands were present in the C3 and C4 electrodes when subjects perform active and passive tactile discrimination tasks which are located above the primary somatosensory cortex (Eldeeb et al. 2020).

The neurophysiological basis of width discrimination has been studied in rodents and has shown that active and passive tactile discrimination trigger different neural networks (Krupa et al. 2001). In humans, a recent study show that EEG recordings showed that active and passive tactile discrimination versions of the same task are associated with neural signatures networks (Perrotta et al. 2020). Other EEG studies of active and passive tactile discrimination in humans have also shown activation of the parietal region contralateral to the stimulated finger (Moungou et al. 2016).

Studies of tactile discrimination in rats, have demonstrated synchronization of the fronto-parieto-occipital cortical areas, suggesting that active tactile discrimination maybe more widespread and dynamic that previously thought (Kunicki et al. 2019).

While animal models enable investigations of the genetic, molecular, cellular, circuit-level and neurophysiological mechanisms underlying these processes. Non-invasive technologies such as magnetic resonance imaging (MRI), magnetoencephalography (MEG) and electroencephalography help assessing the human brains structure and neural responses to complex behaviours (Anon 2017). Very few studies have used human models to understand width discrimination. Studies show that different regions of the brain have also been described as being involved in tactile discrimination (Zangaladze 2008) such as in the primary somatosensory cortex, intraparietal sulcus, occipito-temporal cortex, dorsal

and ventral premotor cortex, medial superior frontal cortex, lateral inferior frontal cortex, thalamus and cerebellar hemispheres (Stoesz et al. 2003), (Yeon et al. 2017).

The visual cortex is involved in nonvisual perception in blind humans (Zangaladze 2008), (Kujala et al. 1995), (Sadato et al. 1998). This has been associated with neural brain plasticity but visual processing can also influence some aspects of human tactile perception (Klatzky, Lederman, and Reed 1987).

Tactile processing and width discrimination

Touch is part of our lives allowing us to interact with our environment and play a key role in our survival (Hunt et al. 2017) but little is known about width discrimination in humans (Perrotta et al. 2020).

Using EEG we can visualize spontaneous activation of different areas of the brain (Custo et al. 2017). Signal analysis has engendered EEG with the temporal resolution but can lack spatial resolution for status of brain mapping (Michel and Murray 2012) and a brain imaging method capable of providing spatio-temporal information. EEG activity in the lower gamma frequency band (30–49 Hz) suggests that width discrimination is useful to study the neural dynamics underlying active and passive tactile processing (Perrotta et al. 2020). We can detect roughness and spatial position of an object using touch, this contact with the objects leads to skin vibration and the stimulation of the peripheral and then central neuros involved in tactile sensation (Baghdadi et al. 2021), (Lieber and Bensmaia 2019). Methods typically used to trigger mechanisms associated with tactile processing: passive, active and dynamical passive. Passive processing involves the subject being touched by the object (e.g., a pen that touches the subject's finger), active processing involves the subject touching the object (e.g., the subject moves the finger towards the pen until making contact and possibly exploring through movement), and in the dynamical passive the subject is touched by the object, but the object surface is moved such that there is continuous contact with multiple parts of the object and/or the subjects body (e.g., another person is touching with the different parts of the pen, the subjects' finger. (Baghdadi et al. 2021). The way we touch a surface can change the pattern of neural responses and how we perceive object we are interacting with (Callier, Suresh, and

Bensmaia 2019), (Muñoz et al. 2014), (Yoshioka et al. 2011), suggesting that several brain networks are involved in the way we process touch and tactile discrimination.

Somatosensory processing is associated with the ability to process tactile stimuli, namely touch, pressure, temperature, position, movement, and vibration (Pons et al. 1987). The neural basis of somatosensory processing is associated with a network of regions involving the primary and secondary somatosensory cortices, and the tactile thalamus but also as well other regions such as those associated with pre-frontal (Zhao et al. 2017), parietal (Kropf et al. 2019), and occipital cortices (Ortiz et al. 2011).

The involvement of such a large number of regions, namely some that have repeatedly been related to higher cognitive processing, support the notion that somatosensory processing can be modulated by multiple other ongoing processes.

Tactile width discrimination is a specific type of somatosensory processing characterized by the ability to detect different distances between two objects (e.g., to walls in a narrow corridor) which is known to be of critical relevance for rodents (Vincent 1912), (Knutsen, Pietr, and Ahissar 2006), (Carvell and Simons 1990). For example, a large number of studies in rats have described the neuronal correlates of tactile width discrimination in multiple paradigms demonstrating that learning (Wiest et al. 2010), motor, and reward contingencies can all influence tactile width discrimination. In other words, it is likely to be of increased relevance for species that significantly depend on small burrows to live in. Still, the existence of a large number of studies in this area constitutes a significant source of potential theories for somatosensory processing in humans. With the goal of exploring this vast potential, recent studies have developed and evaluated neural activity in a width discrimination task adapted for human subjects (Perrotta et al., 2020, Pais-Vieira et al., 2021 *submitted*). These studies have suggested that a network of regions involving the primary somatosensory cortex, but also frontal, parietal, and occipital regions through delta, alpha, and beta bands may be involved in tactile width discrimination.

The involvement of such a large network of regions is suggestive that functions such as attention (Whitmarsh et al. 2017), visual (Vermaercke et al. 2014), emotional (Kelley and Schmeichel 2014), may play a key role in this type of tactile discrimination. Also, processing of affective touch has been associated with the involvement of central-parietal regions and occipital regions, typically through the theta and beta frequency bands

(Grunwald et al. 2014), (von Mohr et al., 2017). Thus, functions that are related to attention, in tactile processing are expected to involve sensorimotor networks.

Neuropsychology and Neurochemistry

Neuropsychology is the field of study dedicated to comprehending the relationship between behaviour and the brain. Despite the relationship between behavioural performance and neurological basis, it remains difficult to classify the individual person in higher levels of brain function or brain damage (Wang 2018). Using reward conditions in neuropsychology can be a strong reinforcement to trigger, induce a behaviour or enhance learning (Berridge 2000). Studies shows that reward conditions improve performance in animal models (Blodgett 1929), (Klaus et al. 2009), (Everitt and Robbins 2005). In humans, performance has been associated with competition, reward, and even audience presence (Raja and Salah 2016). Monetary rewards play a high impact role on human performance, an example of this are payment models based on job performance. As a result, the approach to studying reward effects on performance today is to consider human beings as goal-directed and conscious information processors, who carefully weigh reward- and task-related information to optimize their performance (Zedelius et al. 2014). Another interesting influencer of performance is stress levels. Stress levels are measured using neurochemistry and is typically assessed using cortisol values in collected salivary samples. A study of 2009 showed that high cortisol levels in men caused a decrease in performance while the opposite was observed in woman performing the same task (van den Bos, Harteveld, and Stoop 2009). The role of stress and rewarded conditions in task performance can potentially unlock ways of optimizing human activity.

Reward processing is a function that is associated with emotional as well as attentional processing (Pleger, Blankenburg, Christian C. Ruff, et al. 2008), (Chikara et al. 2018), (Kim and Anderson 2021). The regions that are most often associated with reward processing are ventromedial and orbital prefrontal cortex and the dorsal anterior cingulate cortex (Lesage and Stein 2016). Tactile discrimination in the presence of monetary rewards with different magnitudes has been associated with a specific reactivation of the primary somatosensory cortex according to the amount of monetary reward (Pleger, Blankenburg, Christian C Ruff, et al. 2008) while studies associated with tactile attentional modulation have been characterized by a network of regions in somatosensory cortex and visual cortex (Bauer et al. 2006).

The reward system has influence in multiple other physiological systems, namely in stress. For example, cortisol is a glucocorticoid that has been associated with reward and tactile processing (Bray 2017), (Dinse et al. 2017) and therefore may play a significant role in reward during tactile width discrimination. A recent study showed that elevated cortisol levels block human tactile perceptual learning (Dinse et al. 2017).

Also, the neuropeptide substance P, which is known to be associated with the cuneate fasciculus (Suvas 2017) and has more often been associated with pain processing, has been previously proposed to play a relevant role in reinforcement (Huston and Oitzl 1989), (Borsook et al. 2016).

The presence of substance P in nervous structures suggests such as microglia, as well as immune cells (Mashaghi et al. 2016) suggest it plays a role in pain processing with its inhibition being studied for chronic pain management. Studies also showed that injecting substance P peripheral on the brain reinforced learning, suggesting that increased substance P can help during task performance (Huston and Oitzl 1989).

Here, we set to describe the effects of monetary reward in tactile width discrimination. The main objective was to test the hypotheses that:

- H1) Monetary rewards improve tactile width discrimination,
- H2) Neurophysiological correlates of tactile width discrimination are affected by monetary rewards.

To identify additional physiological correlates of the effects of reward in somatosensory processing we also tested the hypothesis that:

- H3) Cortisol levels correlate to tactile discrimination performance,

and that

- H4) Substance P levels correlate to tactile discrimination performance.

To test our hypotheses, EEG signals were recorded from human subjects performing the tactile width discrimination task (Perrotta et al., 2020) in the presence or absence of monetary rewards. To study the role of substance P and cortisol, saliva samples were collected before and after each run.

Chapter II – Materials & Methods

This experiment involved having a subject perform a width discrimination task twice. Once under a reward and other non-reward. Saliva samples were collected and EEG recording were performed during the task for posterior analysis.

Experimental protocol and data collection

The present study was approved by the ethics committee of the Escola de Medicina da Universidade do Minho (SECVS 148/2016). Male and female participants without history of severe neurological disease were studied. After an initial contact and brief explanation of the project, its potential outcomes, as well as the actions required during testing, participants signed an informed consent and performed the tactile width discrimination session.

Width discrimination task

The tactile width discrimination task is presented in figure 7 and has been previously described in detail (Perrotta et al., 2020). Briefly, this task is akin to a rodent width discrimination task (Krupa et al., 2001) and requires the subject to insert the index finger in an aperture width formed by two movable bars that can be set as a “Narrow” or a “Wide” stimulus. This action was indicated to the participant with a yellow light appearing on top of the aperture. After the software detected the subject’s finger, a green light turned on and the subject was allowed sampling the aperture width (1000ms). At this point the light turns red, and the subject is required to remove the finger and press one of two buttons (i.e., make a response). Choosing one button indicated that the participant evaluated the aperture as being “Narrow” while making a response in the other button indicated that participant evaluated the aperture as being “Wide”.

Sessions

Each session consisted of two runs, counterbalanced across subjects. One run – No Reward -consisted of performing the tactile discrimination task, and the other run – Rewarded Run -consisted in the same task, but higher performances were associated with higher monetary rewards. The monetary reward was a check (not actual money) that could be used to buy items in a local store.

After EEG placement and index finger measurement (using the box software), subjects were allowed to interact with the tactile discrimination box for 5-10 trials to ensure they were familiar with the sequence of lights (yellow, green, red) and the associated actions (insert finger, finger detected, remove finger and press response button).
Each session lasted approximately for 20 minutes and contained two runs, as indicated previously. Each run was composed by a total of 40 trials, 20 “Wide” (1.0 cm) and 20 “Narrow” (0.2 mm distance).
Saliva samples for evaluation of substance P and cortisol were collected in five different points, namely: baseline, before and after Run 1, and before and after Run 2. This allowed detection of changes occurring between the baseline and the session, as well as effects that were due to a particular run. Saliva samples were later processed and analyzed in in a different laboratory (Saliva Tech, Universidade Católica Portuguesa, Portugal).

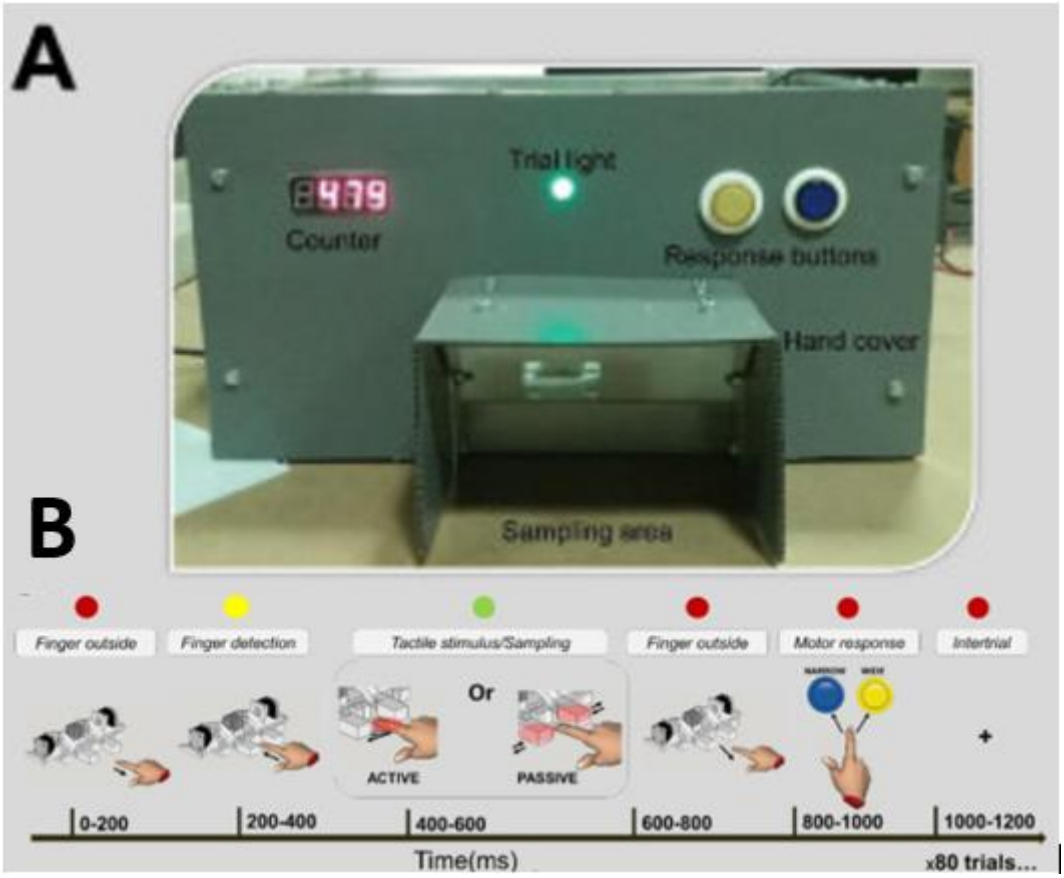

Figure 6. Device and experimental design of the active touch experiment. A) Device used during the trial B) Process followed by the subject during each trial adapted from "Differential width discrimination task for active and passive tactile discrimination in humans"

Data cleaning & processing

EEG recordings were acquired with a 16-channel amplifier using a 10-20 placement (V-Amp, actiCAP; Brain Products GmbH, Gilching, Germany). Signals were recorded using the Brain Vision Recorder (version 2.1.0, Brain Products, Gilching, Germany) and analyzed using Brain Vision Analyzer (version 2.2.1, Brain Products, Gilching, Germany) and Matlab (Mathworks, 2018b, Natick, USA), as well as Matlab (version R2020a Academic), Excel and GraphPad prism (version 9.0).

Pre-processing was performed using a common reference formed by the activity of all channels. Then a notch filter was applied (50Hz). Lastly, removal of EOG artifacts was performed using the Gratton and Coles algorithm (Di Flumeri et al. 2016) in Visual Analyzer.

Data was analyzed solely during the Discrimination period, which corresponded to a window of 1500ms (-500 up to 1000ms after each marker). This large window was used to

ensure that differences between participants, differences in the detection algorithm (i.e., initial detection of index finger), as well as movements occurring during the tactile sampling period were all included in the analysis. Due to the variability of how subjects deal with the task we preferred to look at the data as a whole, ensuring we didn't miss any relevant aspects.

Analysis of frequency bands was made using a Fast Fourier Transform with a resolution of 0.5 Hz. Frequency bands were defined as: delta (0.5-4.5Hz), theta (4.5- 8.5Hz), alpha (8.5-13.5Hz), beta (13.5-30.5Hz), and low gamma (30.5-45Hz). Data was only analysed up to 45Hz (described here as low gamma frequency band), to match the state map values used in a previous study (Pais-Vieira et al. 2019).

Two ratios were calculated as described in (Pais-Vieira et al. 2019) where state maps are defined using a modification of original method first presented by Nicolelis and colleagues (Gervasoni, S. C. Lin, et al. 2004). These ratios (Ratio 1 and Ratio 2) were calculated with the average power found in higher and lower frequencies, namely: Ratio1, R1:(0.5-20Hz)/(0.5-45Hz)] and Ratio 2, R2: (0.5-4.5Hz)/(0.5-9Hz). Each of these ratios was then be used as a coordinate (Ratio 1: abscissa, Ratio 2: ordinate) to form a state map.

Neurochemistry analysis

Saliva samples were collected during the experiment. After collection samples were stored in freezing conditions to preserve the sample. For analysis, samples were centrifuged at 10.000 xg for 10 minutes at 4ºC. The supernatant was then collected and stored. To calculate the concentration, volume and pH samples were re-suspended using a vortex. Samples were then stored for future analysis at -80ºC.

Statistical analysis

Statistical analysis was performed using Graph Pad Prism version 9 (GraphPad Software Inc in California), Matlab (version R2020 academic) and Excel (Professional, 2019). P values were considered significant for an alpha of 0.05, except when multiple comparisons were made, where Bonferroni corrections were used (Weisstein 2004). Comparison of average values between runs were made using paired samples T test or the non-parametric counterpart when necessary. Correlations between variables were studied using linear regression. Where indicated (see cortisol in saliva samples analysis) subjects with values

above three standard deviations of the remaining of the sample, were removed from the analysis (Sebert 1997).

Chapter III - Results

A total 19 subjects (36% male, 10% female and 54% undisclosed) with an average age of 32 ± 10 years (min=19, max=48) completed the behavioral protocol. Neural recordings from a total of 38 runs during both runs from the 19 subjects were analyzed here.

Behavioural results

As presented in figure 8, no significant differences were found between behavioral performances in Rewarded (80% ± 11%) and Non-rewarded runs (80% ± 12%) figure 8 n.s.; (paired samples T test, t=0.0.05870, df=18, P=0.9538). Also, comparison of response latencies did not reveal differences between rewarded and non-rewarded runs of the task (non-Rewarded: 1362 ± 325 ms; Rewarded: 1481.43 ± 464 ms; t=1.491, df=18, P=0.1532, n.s.), as shown:

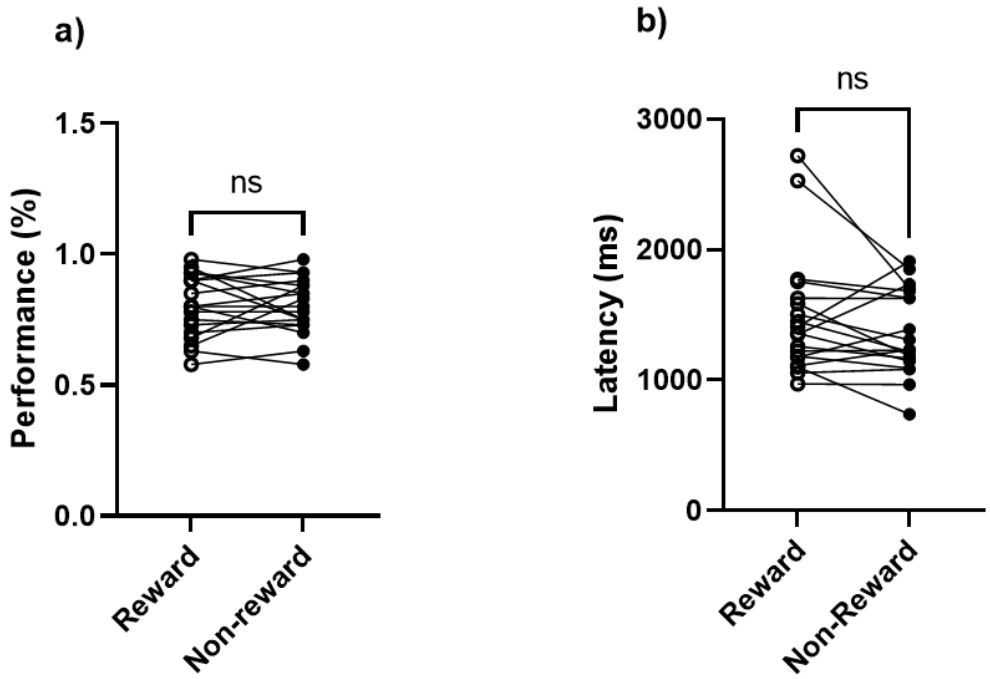

Figure 8. – Behavioural performances. a) No significant differences in performance were observed between rewarded and non-rewarded versions of the task. b) Response latencies were similar in both versions of the task.

Saliva samples results

Analysis of cortisol in saliva samples, revealed several relevant changes. Throughout the session a total of five different saliva samples were collected. An overall reduction was observed (Anova repeated measures , F (4, 85) = 1.024, P=0.3998). One subject was removed from all analysis since cortisol was higher than three standard deviations and therefore this subject was considered as an outlier (Population average: 1.988±1.528 pg/ml; Subject 13: average: 17.798± 4.423 pg/ml; 3 standard deviations=6.571 pg/ml).

Table 3. Cortisol measurements over the course of the trial (pg/mL)

	Reward		No reward	
Subject	before	after	before	after
1	0.609	0.822	1.042	0.537
2	0.516	0.659	0.841	0.697
3	17.500	11.790	19.800	22.100
4	4.408	2.831	1.955	2.454
5	4.507	4.591	4.832	3.425
6	0.707	1.025	0.939	0.948

7	0.688	0.396	0.716	0.820
8	6.610	5.509	5.058	4.798
9	2.345	2.062	3.381	2.313
10	2.982	2.867	2.663	2.440
11	1.995	2.518	6.712	4.643
12	1.389	1.142	1.214	1.281
13	0.279	0.199	0.439	0.292
14	1.949	1.677	2.883	2.235
15	1.255	1.028	1.718	1.328
16	0.692	0.838	0.864	0.782
17	1.272	1.239	1.160	1.134
18	1.743	1.816	1.866	2.030
19	1.846	2.475	1.992	2.323

Average cortisol levels tended to decrease over the trials and no correlation between cortisol levels and performance of the task was found person correlation (Non-reward: R=-0.03197, P= 0.8998, n.s; Reward: R=-0.1340, P= 0.5959).

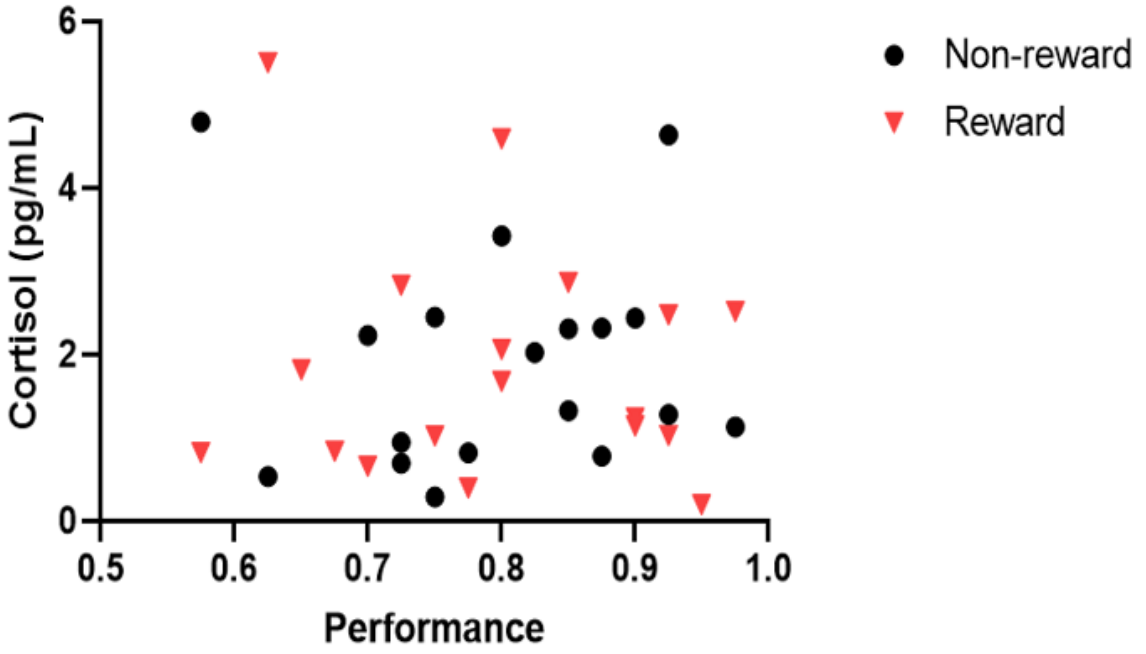

Figure 9. correlation between performance and cortisol levels after reward and non-reward runs

Substance P values were also collected with the same frequency of cortisol levels but due to technical issues, most concentration values were missing and due to that reason Substance P values were not included in any analysis.

Analysing the differences between cortisol levels (figure 10) before and after each trial run revealed no significant differences (paired samples T test t=0.224. df= 34, P=0.8328 (NR); t=0.6232, df= 34, P=0.5374 (R)).

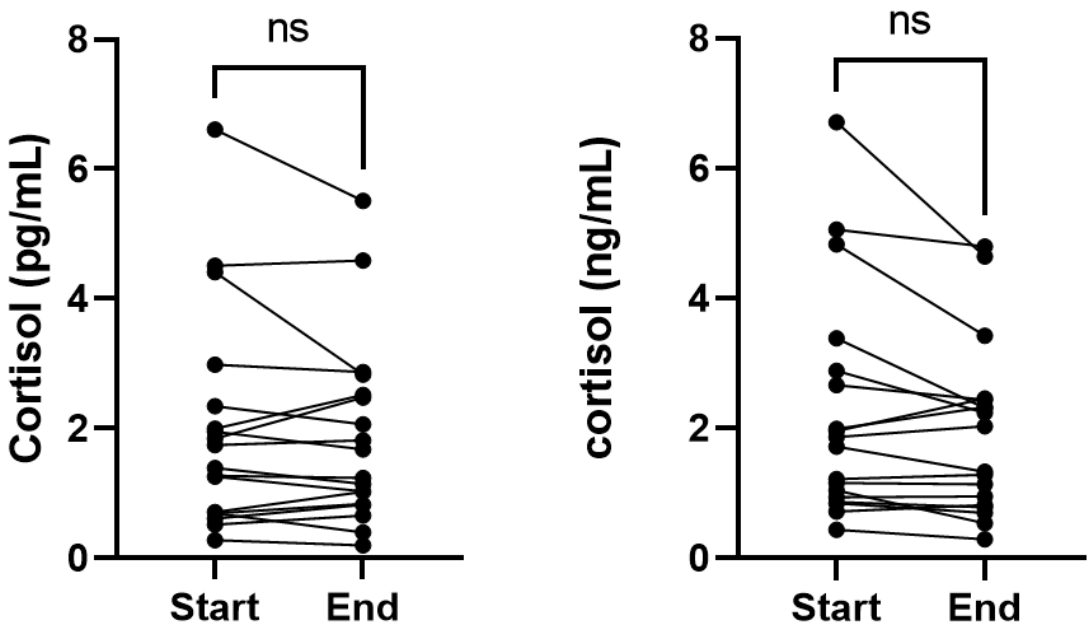

Figure 10. Changes in cortisol a) difference between cortisol at the start and end of the task for a) Non reward b) reward

To study if cortisol levels could influence performance levels during each version of the trial, we compared cortisol with the individual performances in the task using a linear regression (figure 11), no significant results were found. Reward: before r2 = 0.03971, P=0.4279; after r2 = 0.01797, P=0.5959; Non reward: before r^2 = 0.0001576, P=0.9606; after r^2 = 0.001022, P=0.8998). No significant correlations were found.

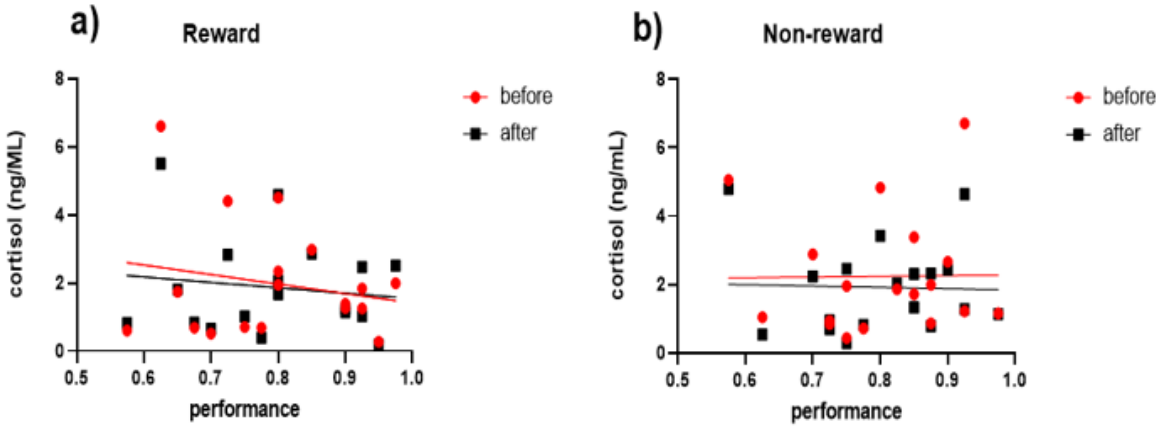

Figure 1. Relation between performance and cortisol before and after a) reward run b) non-reward run

Analysis of EEG recordings

In Table 2 significant differences in power for the different frequency bands are presented for Rewarded and Non-Rewarded runs. Differences in delta (1-3Hz), theta (3-7Hz), alpha (7 -12Hz), beta (12-30Hz), and low gamma (30-45Hz) frequencies were found during the tactile discrimination.

Table 4. Significant differences in power for the different frequency bands

Channel	Frequency band	No Reward (Mean±StDev)	Reward (Mean±StDev)	W	P	sig
Fp1	theta (3-7Hz)	0.358±0.575	0.468±0.646	49	0.0003	***
	beta (12-30Hz)	0.097±0.239	0.142±0.271	37	0.0199	*
	Low gamma (30-45Hz)	0.008±0.075	0.067±0.169	45	0.0155	*
Fp2	theta (3-7Hz)	0.552±0.664	0.323±0.407	-63	0.0209	*
	Low gamma (30-45Hz)	0.032±0.270	-0.031±0.038	-1	0.0073	**
F4	delta (1-3Hz)	4.571±2.065	3.899±1.745	-81	0.0040	**
	alpha (7-12 Hz)	0.177±0.308	0.070±0.131	-61	0.0258	*
	Low gamma (30-45Hz)	0.027±0.211	-0.022±0.064	-11	0.0116	*
T3	Low gamma (30-45Hz)	0.045±0.142	0.046±0.133	11	0.0123	*
C3	beta (12-30Hz)	0.124±0.235	0.089±0.166	-1	0.0302	*
C4	Low gamma (30-45Hz)	0.050±0.193	0.159±0.251	83	0.0144	*
T4	alpha (7-12 Hz)	0.125±0.261	0.077±0.211	-17	0.0308	*
P3	Low gamma (30-45Hz)	0.028±0.058	-0.016±0.052	18	0.0144	*
Pz	beta (12-30Hz)	0.092±0.168	0.143±0.251	43	0.0258	*
P4	Low gamma (30-45Hz)	0.008±0.069	0.071±0.195	79	0.0430	*
O1	delta (1-3Hz)	3.992±2.235	4.238±2.592	29	0.0015	**
	theta (3-7Hz)	0.889±0.768	1.014±0.944	25	0.0230	*
	alpha (7-12 Hz)	0.714±0.614	0.725±0.768	-11	0.0005	***
	beta (12-30Hz)	0.351±0.444	0.417±0.460	51	0.0001	***
	Low gamma (30-45Hz)	0.237±0.514	0.262±0.474	25	0.0030	**
O2	Low gamma (30-45Hz)	0.281±0.281	0.279±0.467	9	0.0050	**
A2	theta (3-7Hz)	0.358±0.575	0.468±0.646	49	0.0003	***
	beta (12-30Hz)	0.097±0.239	0.142±0.271	35	0.0241	*
	Low gamma (30-45Hz)	0.008±0.075	0.067±0.169	45	0.0155	*

Comparison of neurophysiological differences in power in rewarded and non-rewarded revealed fundamentally different networks of electrodes and frequency bands. As detailed in figure 12 and Table 4, low-gamma frequency band was associated with changes in a vast number of electrodes, while beta frequency band was only associated with changes in electrodes F4 and O1.

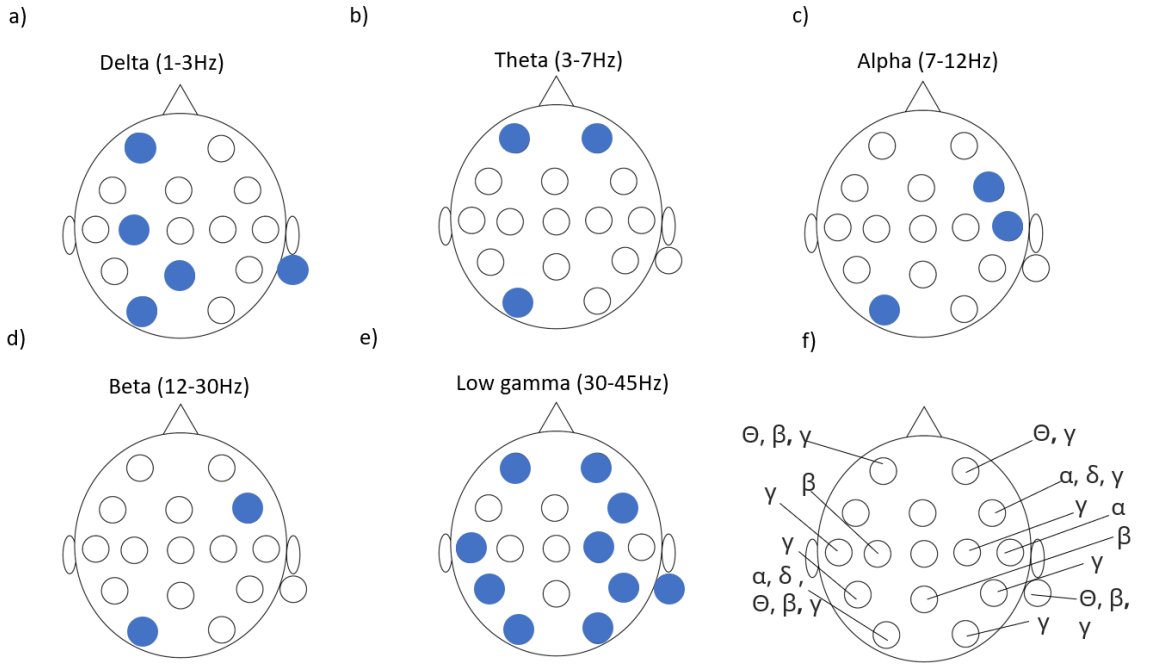

Figure 12. Representation of frequency specific networks. The blue spots indicate significant changes in specific frequencies depending on the nature of the trial (reward vs non reward). a) delta, b) theta, c) alpha, d) beta, e) low gamma f) All frequencies.

To determine if the neurophysiological changes observed in these networks of electrodes were associated with the participants' performances, we then investigated if changes in the power could predict performance in non-reward and reward runs of the trial.

To further understand changes in brain dynamics during tactile processing we asked if performance could be related to changes in broad states, as defined by ratios of LFP frequency bands first described by Gervasoni and colleagues (Gervasoni, S.-C. Lin, et al. 2004). The two ratios of frequencies were calculated (Ratio 1: 0.5–20 Hz/0.5–45 Hz; and Ratio 2 (0.5–4.5 Hz/0.5–9 Hz) and used to define broad state maps. The first ratio (Ratio 1) is the ratio of very low-middle frequencies (0.5–20 Hz) over very low-high frequencies (0.5–45.0 Hz). The second ratio (Ratio 2) is the ratio of very low frequencies (0.5–4.5 Hz) over low frequencies (0.5–9.0 Hz; Ratio2).

To identify if the presence of Reward significantly affected either Ratio, a comparison was made between for the rewarded and non-rewarded runs within each ratio (ratio 1 and 2). R1 and R2 between non-reward and reward runs (figure 13) held no significant difference (paired samples T test for a) ratio 1 (t=0.8694, df=30, P=0.3915) and b) ratio 2 (t=0.3581, df=30, P=0.3581).

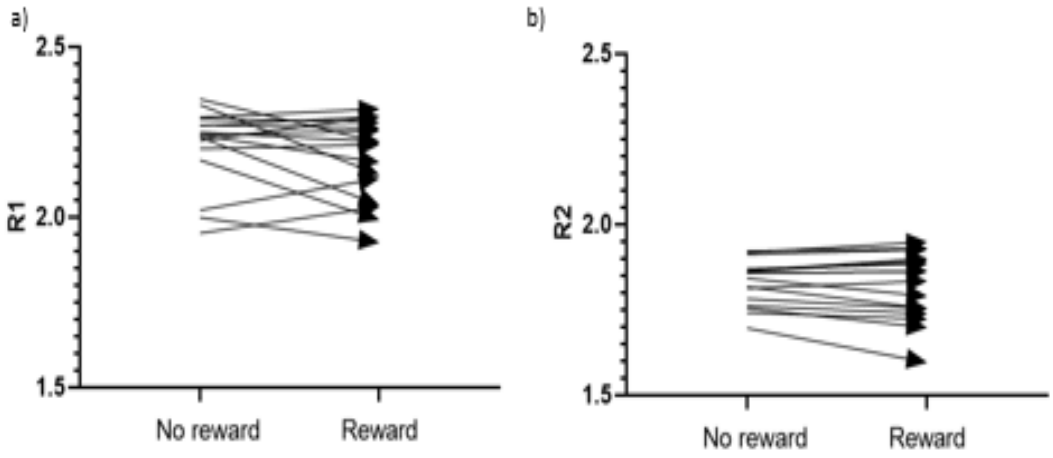

Figure 13. Changes from NR and R runs

We then asked if cortisol interacted with the above ratios used to describe state maps, no significant associations were discovered (Spearman correlation for FP1 r=0.1446, P=0.5789, n.s; F3 r=-02941, P=0.9134, n.s; C3 r=0.1495, P=0.5659, n.s ; A2 r=0.1446, P=0.5789, n.s).

Chapter IV – Discussion

In this dissertation electroencephalography signals, cortisol levels, and substance P levels were studied while human subjects performed a tactile discrimination task with or without monetary reward. No differences in behavioural performance or response latencies were found between runs with or without reward. Saliva analysis revealed that cortisol levels were not affected by reward, and no clear results could be obtained from substance P analysis. Comparison of power between rewarded and non-rewarded runs suggested the involvement of a large network of electrodes throughout the scalp and across several frequency bands. We have only recorded from 16 channels, source analysis could not be performed (Scherg, Vajsar, and Picton 1989) and therefore, it is not possible to determine from the present results if the changes observed in a particular electrode correspond to the underlying cortex where the electrode is placed. The remaining of this discussion will therefore refer to the electrode and not to the cortical region typically associated with it. during active tactile discrimination. Changes in the power of this network of electrodes, nor cortisol levels predicted the behavioural performance in the task. Lastly, analysis of ratios of frequencies indicated that higher frequencies were not predictive of behavioural performances during non-rewarded runs, supporting the notion that monetary reward has no effect in active tactile width discrimination, as no significance correlations between the studied variables was discovered.

We have not found an effect of monetary reward in the tactile discrimination, in contrast to a previous report (Pleger, Blankenburg, Christian C. Ruff, et al. 2008). Several factors can account for the lack of an effect of monetary reward in our task. First, we have used an active version of the task, while these previous authors have used a passive version. Second, in the previous study the tactile stimulus was delivered via a two-alternative forced-choice frequency discrimination task, while we have used width discrimination. Frequency stimulation is known to involve contralateral primary somatosensory cortex (Chung et al. 2013) and mechanoreceptor skin receptors (Tommerdahl et al. 2005) while tactile width discrimination is unlikely to involve the same receptors. Third, it is also possible that the amount of reward used was not enough to generate a significant difference between the two runs in the task (Capa and Bouquet 2018), or otherwise that task was not difficult enough. Fourth, it is possible that the psychological profile of subjects (Winegard, Winegard, and Boutwell 2017) or their previous experience with the use of the EEG or

tactile discrimination setup may have influenced the results (also see remaining of discussion). These findings do not allow rejecting the null hypothesis that reward has no influence on width discrimination processing.

P2 changes in power in C3/C4

Changes in the power of different frequency bands were found between rewarded and non-rewarded runs in a network of electrodes involving Fp1, Fp2, F4, T3, C3, C4, T4, P3, Pz, P4, O1, O2 and A2. This finding supports the hypothesis that monetary rewards affect neurophysiological correlates of somatosensory processing (H2). Previous studies of tactile width discrimination have found changes in the power of Gamma waves in humans (Perrotta et al. 2020) and C3 and C4 electrodes. For example, changes in alpha and beta frequency bands are often present in the C3 and C4 electrodes when subjects perform active and passive tactile discrimination tasks which are located above the primary somatosensory cortex (Eldeeb et al. 2020). However, previous studies, namely those involving monetary rewards, have not reported changes in Alpha and Beta frequencies (Mei et al. 2018) It is not clear from the present results if these differences could be due to an effect of the subject knowing in advance that one of the runs would be rewarded and the other not; due to the long time periods analysed (1500ms), or otherwise, if some other variable not addressed here may explain this.

Changes in the power of signals recorded from prefrontal and/or frontal electrodes were present in delta, theta, alpha, beta, and low gamma frequency bands. This region is typically associated with decision making in motor processing (Alegre et al. 2004), this suggests involvement of these regions on the decision process during the trial. Observing the parietal and occipital electrodes revelated wider change of frequency changes. This has been investigated before in rats suggesting that active tactile discrimination may be coordinated by widespread and dynamically complex bidirectional link between the primary somatosensory cortex and other cortical areas located in the frontal, parietal, and even the occipital cortex (Kunicki et al. 2019).

Ratios of higher (Ratio1) and lower (Ratio 2) frequency bands were not associated with performance in the rewarded as well as in the non-rewarded runs. In a recent study, using the passive version of this task (Pais-Vieira et al., 2021, *submitted*), electrodes in a network involving frontal, parietal, temporal, and occipital regions were predictors of width

discrimination performance. Here a different result was present, possibly due to the methodological differences (i.e., testing active or passive versions of the task). However, there were several changes in electrophysiological signals suggesting that a frequency specific network is activated during rewarded runs, even though a difference in means between rewarded and non-rewarded runs was found, no significant correlations were present.

No clear effect of reward was observed in cortisol levels in this study and therefore the null hypothesis that cortisol levels were associated with the introduction of monetary reward could not be rejected. According to previous studies, cortisol levels were expected to decrease with performance (Lautenbach et al. 2014). Namely, previous measurements of cortisol levels in the discrimination of other sensorial modalities have revealed that cortisol influences our capacity in discriminating sensorial stimuli (Tops et al. 2006), (Reynolds, Lane, and Thacker 2012) and the introduction of monetary rewards has been associated with increased performance (Zedelius et al. 2012), (Klaus et al. 2009). Several factors could account for the present findings. First, even though an overall decrease in cortisol levels was observed throughout the sessions, no significant differences were observed when other comparisons, that controlled for this effect, were made. For example, solely analysing the difference between the initial and final values in each run still did not indicate differences between rewarded and non-rewarded runs. Second, due to the difficulty to find subjects during the pandemic state, experiments were run in the morning and in the afternoon. Therefore, we cannot exclude that the absence of findings in cortisol levels could be due to a circadian effect (Hellhammer, Wüst, and Kudielka 2009)

It is possible, that cortisol levels could reflect, for example, an effect of “first contact” with EEG paraphernalia which could account for an additional level of stress in some of the subjects studies (Poppenk, Köhler, and Moscovitch 2010). Also, we have observed that the introduction of monetary rewards significantly changed the overall behaviour and attitudes of subjects in a period of seconds. For example, a small number of subjects became extremely nervous when making an incorrect discrimination after the introduction of the monetary reward, while others started laughing. Another group of subjects presented an overall competitive profile where they were highly concerned with achieving perfect performances independently of the monetary reward, while others reported only making an effort to perform accurately when monetary rewards were involved.

In future studies it will be important to start with the subjects' psychological profile (Van Zomeren and Brouwer 1994) and to increase the number of subjects studied accordingly, therefore allowing for analysis of subgroups with specific profiles. In addition, more controlled studies were different levels of monetary reward (Bonner and Sprinkle 2002), "live money", or active and passive versions of the task are compared (Perrotta et al., 2020) are performed, may allow identifying the role of cortisol and substance P in tactile width discrimination during monetary reward. Altogether, the analysis of neurochemistry results, when combined with the observation of the individual subjects' behaviour suggests that future studies of tactile width discrimination involving analysis of neurochemistry levels should include a baseline psychological evaluation.

The neurophysiological correlates of tactile width discrimination have been extensively described in rodents (Pais-Vieira et al. 2019), (Krupa et al. 2001), (Kunicki et al., 2019). In these previous studies learning (Wiest et al. 2010), motor activity and reward have been associated with changes in neural activity in cortical and subcortical regions such as postcentral gyrus, (Kim et al. 2017) and fronto-parietal (Pessoa and Engelmann 2010). While a direct comparison between rodent and human studies cannot be made, the findings from this and other recent studies (Perrotta et al., 2020; Pais-Vieira et al., 2021 *submitted*) suggest that a network of regions involving the frontal, temporal, parietal, and occipital regions. regions are involved in tactile width discrimination. More, the analysis of rodent studies has indicated that information transfer and coherence (Douglas et al. 2006) may also involve a network of regions close to the ones described here. It will be important for future studies to perform these additional analyses in the present data to accurately describe the dynamics present in the networks of electrodes identified here.

The present findings suggest that a network involving the Fp1, Fp2, F4, T3, C4, P3, P4, O1, O2 and A2, electrodes may be associated with reward processing during active width discrimination. These findings are in line with previous studies indicating that somatosensory processing in humans involves a network or regions such as somatosensory cortex, occipital regions and ventral striatum (Gervasoni, S. C. Lin, et al. 2004; Perrotta et al. 2020), (McGlone, Wessberg, and Olausson 2014a) and (Pleger, Blankenburg, Christian C. Ruff, et al. 2008) reflecting not only the somatosensory processing *per se*, but also higher cognitive functions often associated with it. For example, the effects of motor activity (Simões-Franklin, Whitaker, and Newell 2011) , reward (Pleger, Blankenburg,

Christian C. Ruff, et al. 2008), learning (Kao et al. 2020), attention (Genna et al. 2017), and multimodal stimulation (Kim et al. 2015), can all significantly modulate somatosensory processing. The findings of the present study are in line with these previous reports and suggest that a distributed network involving high and low frequencies may play a relevant role in reward processing during tactile width discrimination.

When observing the change in frequencies while performing the same task with different reward conditions we can observe a potential network related to rewarded conditions of the activity. Frequency specific networks have been described before as high-frequency cortical oscillations to be thought to coordinate neural activity locally, while low-frequency oscillations play a role in coordinating activity between more distant brain regions Networks related to spatial attention have also been described as synchronization of low band frequencies. (Daitch et al. 2013).

Low gamma frequencies are often associated with higher brain function such as cognition and emotion (Jia and Kohn 2011). Comparing specific frequency activity in reward versus non reward runs showed a significant difference between both trials with differences in the low gamma frequency band appearing in the majority of the electrodes recorded.

The occipital region also showed increases in power for all frequency bands analyzed here. These findings are, to some extent, in line with a previous study in rats where a significant role for the occipital cortex was found while rats performed a width discrimination task in the dark (Kunicki et al. 2019).

In regard to the neurochemistry results, there was an average decline of cortisol levels throughout the two runs, with no correlation being observed with performance and speed of which the subject performed the task. This is an unclear result, as current literature describes a relationship between cortisol and performance as well as reward processing (Kinner, Wolf, and Merz 2016), (Lautenbach et al. 2014). The same non-significant relationship is represented with the analysis of the ratios.

Active tactile width discrimination was not affected by the introduction of monetary rewards. Also, no differences between cortisol were present in rewarded and non-rewarded versions of the task. Neurophysiological correlates of tactile width discrimination support the notion that a prefrontal-parietal-occipital network involving low-gamma frequencies is associated with monetary reward influences, suggesting a frequency specific

synchronization. This suggests a relevant role for low-gamma bands during reward processing, with low-gamma in the occipital region being related to attention (Marshall et al. 2018).

Caveats of the study and future work

The main caveat of the present study is the small number of viable Substance P samples, which prevented a proper analysis and comparison with other variables. Other points that can be raised, or improved, relate to source analysis which could not be performed due to the reduced number of channels recorded here (16 channels) (preventing a proper comparison between the findings from the electrodes and the origin of the changes recorded.

We have not analyzed ERP, information transfer, coherence, nor have we described in detail the response period. While this additional analysis would not the change the fact that monetary rewards did not clearly change the behaviour of the subjects, it is possible that these variables could help explain some of the verbal responses (not described here in detail) obtained after subjects performed the task. In addition, it is not known if motor activity could contribute to the present findings (Simões-Franklin et al. 2011), or if using a passive version of the task could potentially lead to different results (Pleger et al., 2008).

For future work we plan to increase the number of subjects performing the task, perform a pre-testing psychological evaluation to better group different psychological profiles (Van Zomeren and Brouwer 1994).

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