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Neurophysiological study of width discrimination in humans

Estudo neurofisiológico da discriminação de distância em humanos

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Dissertação apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Biomedicina Molecular, realizada sob a orientação científica do Doutor Miguel Santos Pais Vieira, Professor Auxiliar em Regime Laboral do Departamento de Ciências Médicas da Universidade de Aveiro

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palavras-chave EEG , discriminação de distância, tátil, sensoriomotor

resumo

O estudo do processamento tátil de distâncias encontra-se bastante desenvolvido em roedores, tendo sido útil para a demonstração de múltiplos mecanismos básicos relevantes. Apesar desta relevância, o estudo da discriminação de distâncias em humanos é ainda bastante reduzido. Durante a presente dissertação foram analisados os correlatos neurofisiológicos, através do registo de eletroencefalografia, em participantes que realizavam uma tarefa de discriminação de distância em modo ativo ou passivo. A análise da potência das bandas de frequências delta, teta, alfa, beta e gama revelou diferenças na potência do sinal para diferentes bandas de frequências e elétrodos. O processamento ativo era caracterizado por um aumento da potência nas bandas de frequências delta, teta e gama nos elétrodos F3, F4; e um aumento da atividade na banda de frequência gama no elétrodo T4. O processamento passivo era caracterizado por um aumento da potência de delta nos elétrodos Fp1 e T4 e um aumento da potência de gama em Tp10. No seu conjunto, estes resultados sugerem que o processamento ativo e passivo da distância são caraterizados por uma rede assimétrica envolvendo elétrodos pré-frontais, frontais e temporais nas bandas de frequência delta, teta e gama.

keywords EEG , width discrimination, tactile, sensorimotor

abstract

Tactile width discrimination processing has been extensively studied in rodents and has demonstrated multiple relevant basic mechanisms. Despite this relevance, the number of studies of width discrimination in humans has been scarce. During the present dissertation, neurophysiological correlates of width discrimination were analyzed through electroencephalography recordings in participants performing a width discrimination task in active or passive modes. Analysis of power in the delta, theta, alpha, beta, and gamma frequency bands revealed differences in the power for different frequency bands and electrodes recorded. Active width discrimination processing was characterized by an increase in the power of delta, theta and gamma frequency bands in electrodes F3 and F4, and an increase in power in the gamma frequency band in T4. Passive tactile width processing was characterized by an increase in the power of delta in electrodes Fp1 and T4, and an increase in gamma frequency band in Tp10. Altogether these results suggest that active and passive tactile width discrimination processing are characterized by an asymmetrical network involving prefrontal, frontal and temporal electrodes, in delta, theta, and gamma frequency bands.

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1. Introduction

The present dissertation is a neurophysiological and behavioural study of active and passive tactile discrimination in humans. This dissertation is organized as follows: i) the state-of-the-art for tactile processing and width discrimination will be presented, as well as the need to perform the present study; ii) a brief description of the somatosensory system; iii) a brief discussion of current findings on Discriminative touch, as well as studies of active and passive tactile discrimination.; iv) description of electroencephalogram (EEG) technique; v) Hypothesis and Objectives; vi) methods; vii) results; viii) discussion and conclusions.

1.1. State-of-the art

Tactile discrimination processing requires the integration of sensory, motor, and cognitive information in humans and animals [1]–[8]. Width discrimination is a specific type of tactile information processing that has been extensively studied in rodents [2]–[4], [9]–[12], but remains largely undescribed in humans [13]. Width discrimination in the sub-centimeter scale is not likely to constitute a critical survival skill for humans, contrary to rodents [14]–[16]. The formation of an exact and precise body schema, which is required for formulating novel movements, is facilitated by tactile discrimination. Nonetheless, the large body of knowledge gathered in the latter species, can significantly inform us about the neural basis of somatosensory processing and lead to new lines of inquiry regarding this function in humans. For example, studies in rodents have revealed that width discrimination performance is associated with widespread and dynamic interactions involving information transfer in theta, beta, and gamma frequency bands in a fronto-parieto-occipital network [17]. These regions and frequency bands are known to play a relevant role in tactile processing of shape, texture, and electrical stimuli detection in humans [18], [19], but their role in width discrimination remains unknown.

A recent study has developed a width discrimination task for humans [13] that mimics the original rodent task [9] (Figure 1).

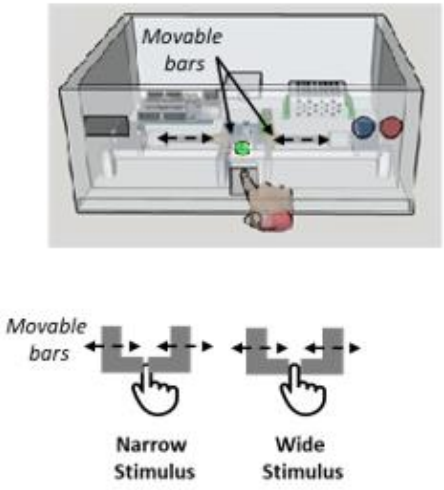

Figure 1 – Behavioral apparatus.

In the passive version, subjects were required to insert the index finger in a small chamber and wait for the tactile stimulus to be delivered by two movable and non-visible bars that moved towards the finger forming one of two widths: “Wide” or “Narrow”. In the active version subjects were required to insert the index finger in in the aperture and sample the tactile discriminanda. In both versions, the subject was then required to make a motor response in one of two pushbuttons, to indicate a narrow or wide aperture. Lastly, after the motor response, an auditory stimulus signalled a correct or incorrect choice. This behavioural task largely parallels the rodent task previously described [9] and is suited for electrophysiological studies, namely with electroencephalogram (EEG).

Although the original study has briefly described the neurophysiological correlates of tactile width discrimination in a small sample of participants performing active and passive versions of the task, this analysis did not allow making inferences about the underlying neurophysiological mechanisms. This study suggested that changes in the low gamma band across a network of

electrodes recording from multiple regions may be relevant for tactile width discrimination [13], however these preliminary findings need to be confirmed in a larger sample. In addition, as there is still very little research on this topic, it is not known if the same extensive network of regions and frequency bands involved in width discrimination in rodents [14]–[16] is also present in humans.

Active and passive tactile width discrimination require subjects identifying/sampling the discriminanda (i.e., the bars touch the index finger) and then compare the relative width of the current stimulus with a previously experienced width (e.g., a previous experience of the Narrow stimulus). These actions are expected to engage neural circuits involving somatosensory processing as well as higher cognition processes such as working memory [20] and attention [21]. Previous studies of tactile discrimination have explored EEG correlates of tactile processing using stimulation current, grating orientation, textures, or vibratory stimuli; due to their ability to generate EEG evoked responses. These studies have reported the engagement of a complex network of regions involving the somatosensory cortex, prefrontal cortex, occipital cortex, and the parietal cortex, typically in alpha, mu, and beta frequency bands ([8], [19], [29], [30], [20], [22]–[28]). Namely, changes in the alpha frequency band in the C3 electrode have been used as a predictor of tactile performance [30], and overall tactile discrimination seems to be associated with a recurrent network involving the somatosensory, parietal and pre-frontal regions through beta (feedforward) and gamma (recurrent) frequency bands [8].

Evidence from rodents indicates that active and passive tactile processing engage fundamentally different neural network dynamics in multiple systems [2]–[4], [10], [11], [31]–[35]. While passive tactile stimulation of the whiskers results in phasic increases (i.e., lasting tens of milliseconds) in single unit recordings from the ventral posterior medial (VPM) thalamus and somatosensory cortex (S1), fundamentally different neural modulations are found when awake behaving rats actively sample a tactile stimulus [2], [11]. Specifically, active tactile discrimination is characterized by longer neuronal responses (i.e., lasting hundreds of milliseconds) that can include both increased as well as decreased firing rates in populations of neurons that differ across the depth of an S1 cortical

column. This difference between active and passive tactile processing is also the result of multiple concurrent neural networks interacting and facilitating or inhibiting tactile related information depending on the specific action required at each moment in time [3], [4], [12]. Also, when rodents actively sample a tactile stimulus in the dark, the primary visual cortex, prefrontal cortex, and hippocampus all seem to play a fundamental role in task performance [33], [36].

Comparison of ratios of frequency bands has been previously used to describe neurophysiological correlates and state dynamics when relatively large time intervals are involved, namely for cortical function in rodents [5], [36], [37]. This analysis compares two ratios, one with higher frequencies and another with lower frequencies, generating two different coordinates that can be used to identify states and transitions. Such analysis has previously allowed making inferences about the neurophysiological bases of ongoing natural behaviours [37] or broad neurophysiological states induced by pharmacological manipulation [5]. These studies support the use of ratios of power in frequency bands in the identification of differences in the neurophysiological substrate of active and passive tactile width discrimination.

Having introduced the need to perform the present study, the key concepts, structures, techniques will now be described in more detail.

1.2. The somatosensory system and the somatic senses

The somatosensory system allows us to identify, grasp, evaluate, and manipulate objects. Sensory information is retrieved through a complex network of nerve endings, sensory neurons and touch receptors in the skin [38].

The somatic senses can be categorized into three physiological types: the mechanoreceptive somatic, the thermo-receptive, and pain senses [38]. The mechanoreceptive somatic senses, which include tactile and position sensations that are stimulated by mechanical displacement of some tissue of the body, the thermo-receptive senses, which detect heat and cold, and the pain sense, which is activated by factors that damage the tissues [39]. Touch, pressure, and vibration are different sensations, but they are all detected by the same types of receptors. Touch sensation generally results from stimulation of tactile receptors in the skin or in tissues beneath the skin [39]. Mechanoreceptors are specialized neural structures that provide information to the central nervous system (CNS), their physiological function is to convert physical forces into neuronal signals [39]. The main tactile receptors relevant for width discrimination are the free nerve endings, Meissner's corpuscles, Merkel cell-neurite complex, and Paccinian corpuscles. Free nerve endings are found in the skin and can detect touch and pressure. The Meissner's corpuscle is a touch receptor with great sensitivity, that is characterized by an elongated encapsulated nerve ending of a large (type Aβ) myelinated sensory nerve fiber. The Meissner's corpuscles are present in the non-hairy parts of the skin, in the fingertips, lips, and other areas of the skin where a person's capability to discriminate a spatial locations of touch sensations is highly developed. They are also important for giving out steady-state signals that allow one to determine continuous touch of objects against the skin [39]. The Merkel cell-neurite complex is formed by ending of myelinated, low-threshold nerve fibers (Aβ type) and specialized epidermal cells, these kind of mechanoreceptors are enriched in touch-sensitive regions of the skin [40]. The Merkell cells generate a slowly adapting response characterized by high-frequency firing at the onset of the mechanical stimulation and a sustained low-frequency firing during the static phase, these cells activate the sensory fibers to drive the sustained firing [40], [41].

Lastly, the Pacinian corpuscles are mechanical filters and chemicals modulators, that are categorized as type II RA mechanoreceptors, the firing activity of these corpuscles is observed during the dynamic phase of the mechanical stimulus but not the static one [40], [42]. A summary of the main characteristics of the receptors thought to be involved in tactile width discrimination is presented in Table 1.

Table 1- Main receptors thought to be relevant for tactile width discrimination.

Receptor	Characteristics	Main Function	Main location
Free nerve endings	Nerve ending	Touch, pressure	Skin
Meissner corpuscle	Encapsulated nerve ending of a large (type Aβ) myelinated sensory nerve fiber	Touch	Fingertips
Merkel neurite complex (Merkel disks)	Groups of disks from the same Aβ fiber	Light touch	Fingertips
Paccinian corpuscles	Encapsulated nerve ending	Vibration	Subcutaneous tissue and other locations

1.3. Central components of somatosensory processing

Besides this peripheral component, there is a central component that is associated with the specific spinal cord tracts (such as the medial lemniscus and spinothalamic pathways), thalamic nuclei [43], [44], as well as the primary and somatosensory cortices [45], [46]. More recently, it has been demonstrated that at the central nervous system level, somatosensory processing involves not only the traditional primary and secondary somatosensory cortices, but also multiple concurrent networks [3], [4], [17], [47–49], with some of the more recent studies suggesting that full understanding of somatosensory sensation requires the study of cross modal integration [50].

1.4. Discriminative touch and EEG

Discriminative touch has been associated with changes in frequency bands in Frontal (theta, alpha, beta, gamma), parietal (alpha, gamma), occipital (gamma and primary somatosensory cortices (beta and gamma) [8], [29], [51–54]. Part of the complexity of somatosensory processing is related to the fact that somatosensory processing often involves motor as well as cognitive components. For example, touching an object (active tactile processing) or being touched by the same object (passive tactile processing) are associated with fundamentally different neural networks [2], [55–57].

1.5. Active and passive tactile discrimination

Gibson was the first that proposed the notion that active and passive tactile exploration could involve distinct processes[58]. According to this author, active touch is when people perform voluntary finger movements, different neural mechanisms are recruited as compared to when same movement is produced externally, passive touch [59]. An early study of active and passive tactile discrimination, Huttunen and Homberg, (1991), found Frontal, Parietal, and Central components in EEG evoked potentials, which generally agrees with other studies of tactile processing previously mentioned [55].

Meanwhile, using a more refined technical approach, Ackerley et al., 2012 found differences in the BOLD (Blood oxygen level dependent) response in the primary somatosensory cortex (BA3) when active or passive touch was applied by the subject of by another person. Active self-touch was characterized by a positive response in the somatosensory cortex, while passive self-touch resulted in a negative response. Meanwhile, being touched by an experimenter was also associated with a positive response in the somatosensory cortex, but this response was smaller when passive stimulation was used. Even though the study of Ackerley and colleagues was solely focused in the somatosensory cortex, it demonstrated not only that active and passive tactile processing are associated with different neurophysiological correlates, but also that self-touch adds one more layer of complexity to this analysis [57]. Therefore, this study supports the

notion that primary sensory regions' processing involves multiple complex concurrent networks. This is also of relevance for the present study because the difference in neural responses described by these authors for the active and passive stimulation, also resembles previous findings obtained in width discrimination studies in rats [2], [3]. In Table 2 a summary of the main regions/electrodes associated with tactile discrimination is presented.

Table 2- Main regions/electrodes and EEG frequency bands associated with tactile processing.

Function	Region/Electrode	Frequency band
Tactile discrimination	Frontal	Alpha, Beta, Gamma
	Somatosensory/Parietal	Beta, Gamma
	Parietal	Gamma
	Occipital	Gamma

1.6. EEG

Electroencephalography (EEG) is a technique that records electrical potentials in the scalp allowing the study of neurophysiological correlates of brain activity. EEG was developed in 1929 by the German psychiatrist Hans Berger [60], providing a new neurological and psychiatric tool. The discovery of EEG was a breakthrough for the advancement of neuroscience and of neurologic and neurosurgical everyday practice, especially for patients with seizures [60]. EEG is an effective method that uses the surface area of the scalp to collect brain waves that correlate to different states [61].

During the procedure, electrodes consisting of small metal discs with thin wires are pasted onto the user scalp. The electrodes detect tiny electrical charges that result from the activity of the user's brain cells. The charges are amplified and appear as a graph on a computer screen, or as a recording that may be printed out on paper [62], [63].

The EEG is an electrophysiological technique that records changes in voltage potential and therefore allows analysis of electrical activity arising from the human brain [63]. EEG measures brain electrical fields via electrodes (which act as small antennas) sited on the head. The electrical fields are the result of electrochemical signals passing from one neuron to the next [64]. The electrical activity recorded on the scalp corresponds to the result of the inhibitory or excitatory postsynaptic potentials from thousands of pyramidal cells near each recording electrode. This activity can be represented as a field with positive and negative poles, that have an equal electrical charge or magnetic force, with a space between them, a dipole [65].

When billions of these microscopic signals are passed simultaneously in spatially extended and geometrically aligned neural populations, the electrical fields become powerful enough to be measured from outside the head [64]. EEG signals are typically analysed in frequency bands ranging from 0.01 Hz to around 100 Hz. However, higher frequencies have been described, such as 150-500Hz [66]. More often, these frequency bands are divided in five different bands, namely: delta(2–4 Hz), theta (4–7 or 8Hz) alpha (8–12Hz) beta (16–25Hz) and, gamma (30–50 Hz) [67]. These values, however, may change slightly according to the author [66].

While EEG is an extremely useful technique, it is prone to record artifacts not related to cerebral activity. This means that the presence of magnetic and/or electrical fields in the surrounding environment (e.g., electrical utility currents), can affect EEG recordings. Furthermore, biologically generated electrical activity (by scalp muscles, the eyes, the tongue, and even the distant heart) creates massive voltage potentials that frequently overwhelm the signal recorded from the scalp [63]. In short, biological and environmental electrical artifacts can interfere with the ability to accurately identify both normal rhythms and pathological patterns [68].

Artifacts possess many distinguishing characteristics that are identifiable by trained observers [63], as well as algorithms [68] .Artifacts are one of the problems that must be dealt when recording data with EEG. In particularly, when real-time analysis is performed, special care is needed with pre-processing data [68]. Pre-processing ensures that noise and artifacts (e.g., eye movements or

others), are not introduced into the decoding algorithm, as if they were neuronal signals.

The identification and removal of artifacts, either in clinical diagnosis or practical applications, is a key pre-processing step prior to the analysis of neural signals. One way to prevent this is to apply precautions to avoid unnecessary motion incurring artifacts, but if the subjects have inability to follow these instructions, this method is unmanageable either for clinical or household applications. There are a variety of efficient techniques for artifact removal, that have been previously published [68].

In the present study, EEG recordings were made from 16 channels 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 analysed using Brain Vision Analyzer (version 2.2.1, Brain Products, Gilching, Germany) and Matlab (Mathworks, 2018b, Natick, USA). Pre-processing included re-referencing using all channels as reference [69]. Then a notch filter was applied (50Hz). Ocular correction was performed using the Gratton and Coles algorithm (already implemented in Visual Analyzer). The data was then segmented according to the discrimination and response marker, with a window of 1500ms (-500 up to 1000ms after each marker), ensuring no overlap between the two actions. Fast Fourier Transform with a resolution of 0.5 Hz was then applied. Frequency bands were analysed 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 [5]. Power was then normalized across the different subjects and compared for the different periods (discrimination and response). Comparison of power was made between the two periods, instead of using a baseline, because we have observed in a previous study that large intertrial intervals quickly led to mental exhaustion of participants. Also, as the moving bars require a relatively long period of time to stimulate the subject, we have opted to analyse relatively long periods of time [5].

1.7. Hypothesis and Objectives

Based on the findings from the previous studies from humans and rodents presented, the following hypothesis were tested:

H1: Different neural networks communicate through different frequency bands in active and passive tactile width discrimination with changes in power of delta, theta and gamma in prefrontal, frontal and temporal regions.
H2: Ratios of frequencies that differ between active and passive versions of the task are correlated to the task performance.

To test these hypothesis electrophysiological correlates of tactile with discrimination were recorded and compared between participants (n=18) performing the active and passive versions of the task while EEG recording where performed. The power for the different frequency bands (delta: [0.5-4.5 Hz], theta. [4.5-8.5Hz], alpha [8.5-13.5 Hz], beta [13.5-30.5 Hz], and low gamma [30.5-45 Hz]) and electrodes was compared within subjects during the discrimination period (H1).
Also, the difference between ratios of higher [Ratio 1:(0.5-20 Hz)/(0.5-45 Hz)] and lower frequencies [Ratio 2: (0.5-4.5 Hz)/(0.5-9 Hz)] between the two versions was compared (H1).
Lastly, for the electrodes were differences between the two versions of the task were found, a Spearmen correlation was performed between the two ratios and the overall task performance (H2).

2. Methods

Literature review for similar study designs in the field, demonstrates a growing body of evidence for the reliable use of EEG to ascertain results, validating the hypothesis. The EEG signal has a millisecond-scale temporal resolution. Because postsynaptic changes are thus promptly reflected in the EEG, this approach is an ideal manner for monitoring abrupt changes in brain function. The robust electrical signals recorded at the scalp and the relatively easy and non-invasive methods by which they are obtained are useful for studies [70]. Nevertheless, obtaining high-quality signals frequently necessitates a sizable amount of training [70].

2.1. Tactile discrimination task

The tactile discrimination experimental apparatus consists of an electromechanical device that was specially constructed and is controlled by computer software that was specially created to provide tactile discrimination control in a reliable and consistent manner. The aperture is adjusted by moving two 40 mm x 20 mm stimulation bars (height, wide). There was a total of four runs of width discrimination in the experimental session. Twenty trials made up each run block and runs alternated between passive and active tactile versions of the same activity. To avoid many consecutive trials with the same stimulus, each run had an equal number of "wide" or "narrow" aperture trials (10 wide and 10 narrow), which were pseudorandomized. Wide and narrow were adjusted in the active version to +0.5 cm and +0.0 cm above finger size, respectively. Wide and narrow were set in the passive version of the task at, respectively, +0.2 cm above finger size and 0.2 cm below finger size. The subject will leave the finger in the CFP, and the experimenter will move the bars gradually until they touch the subject's index finger on each side to determine the finger size. Each trial with a "wide" or "narrow" aperture began when the center light became yellow, signaling that the subject had to insert their finger into the CFP (i.e., stimulus onset). The trial light then went green if the algorithm determined that the finger was in the

proper place. At this point, the participant was given some time to sample the aperture width (e.g., 500 ms). The aperture width may be sampled actively or passively. The patient might move the finger to investigate the aperture width if the block was activated. In contrast, if the block was active, the subject had to keep their finger in the CFP while the bars moved in the direction of their finger. Following the discrimination, the individual had to take their finger out of the frontal panel opening and touch one of the two push buttons to indicate the aperture width for that trial. The center light had gone red by this point.

After pressing a button, the four LED digital display would show whether the answer was accurate or incorrect and would update the overall number of correct answers. This coincided with the trial's conclusion. The center light would then flash red once more to signal an intertrial interval of 500–50 ms (Mean–SEM). The person should not stick their finger inside the front panel opening, according to this.

The participant was given a brief practice session (15 trials of each condition) before the EEG cap was applied so that the subject could get comfortable with the detailed instructions for each tactile discrimination condition [13].

2.2. Ratios of frequencies analysis

Analysis of state maps was based on an adaptation [5] of the original method described by Gervasoni and colleagues [37]. This method calculates two different ratios (ratio 1 and ratio 2) based on the average power found in higher and lower frequencies, namely: ratio1, R1:(0.5-20 Hz)/(0.5-45 Hz) and ratio 2, R2: (0.5-4.5 Hz)/(0.5-9 Hz).

2.3. Statistical analysis

Results are presented as mean and standard deviation (Mean±SD). Paired samples t tests or Wilcoxon signed ranks tests were used to compare power in each frequency band between the two different versions of the task. Spearman correlations were calculated to compare Ratios of frequencies with the performance in the behavioural task. An alpha value of 5% was considered except when specifically indicated. When multiple comparisons were performed the alpha value was divided by the number of comparisons made.

3. Results

The present study was approved by the Ethics Committee of the University of Minho (SECVS 148/2016; and the Comité para as Ciências da Saúde of the Catholic University of Portugal (39/2017), according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. All experiments were performed in accordance with relevant named guidelines and regulations. All participating subjects voluntarily filled an informed consent. Subjects were tested at the Catholic University of Portugal and at the University of Minho (see Appendix, section 2-4).

3.1. Behavioural results

A total of 18 subjects were tested. Four subjects performed only one block in the active and one block in the passive versions of the task. A total of 32 blocks were analysed here. Comparison of the behavioural performance in the active and passive versions of the task revealed an overall improved performance in the active version (paired samples t-test: $t=5.492$, $df=31$, $P<0.0001$). To further determine if this difference was due to some learning effect, we compared solely the performances of the second active and passive blocks (for the 14 subjects that performed them) and a significant difference was also found (paired samples t-test: $t=3.873$, $df=13$, $P=0.0019$).

3.2. Electrophysiology recordings

3.2.1. Power of frequency bands

EEG analysis revealed several differences between the power of specific frequency bands in the active and passive versions of the task. Comparison of the discrimination period (0-500) ms interval for delta, theta, alpha, beta, low gamma delta in each of the sixteen electrodes revealed that an increase in activity associated with left frontal and temporal electrodes during active processing and showed an increase activity in electrodes located in the left frontal and temporal regions during passive processing. These differences are presented in Table 3.

Comparison of power for the delta, theta, alpha, beta, and low gamma frequency bands in each channel during the discrimination period, revealed differences between active and passive runs. These differences are presented in Table 3 (Appendix supplementary Table 1 presents full details for other channels and non-significant frequencies) and summarized in Figure 2, to facilitate comprehension. Overall, only a small number of electrodes presented differences between the active and passive versions of the task, and these occurred mostly in the pre-frontal and frontal electrodes, namely: Fp1, F3, F4, T4, and Tp10; and included increases as well as decreases in power during the active version of the task.

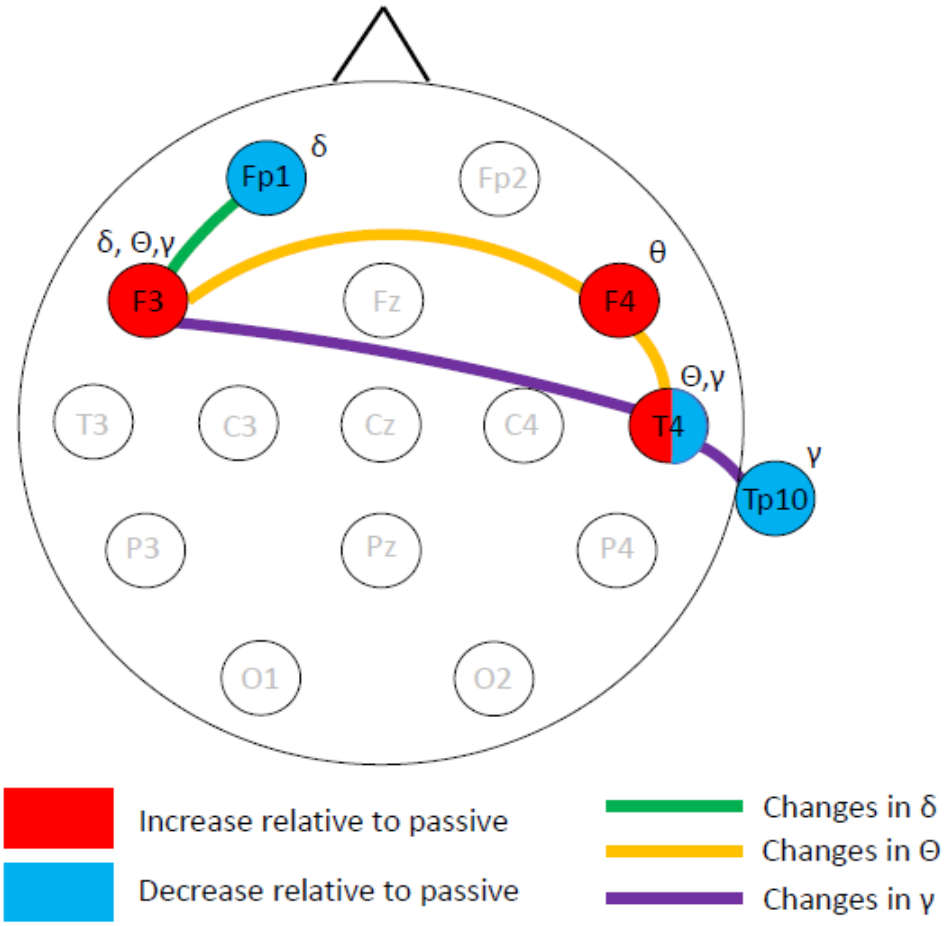

Figure 2 – Differences in power for most common frequency bands.

Table 3 – Significant differences in power for frequency bands in each channel during discrimination period. Channels Fp1, F3, F4, T4 and Tp10, presented significant differences between active and passive versions of the task. For p-value <0.05 (*); p < 0.005 (**).

		Active		Passive				
Channel	Band	Mean (a.u.)	Stdev	Mean (a.u.)	Stdev	W	p	Sig
Fp1	Delta	1.133	0.4656	1.302	0.4932	202.0	0.0479	*
F3	Delta	1.654	0.4899	1.435	0.4669	-212	0.0374	*
	Theta	0.082	0.2813	-0.033	0.06739	-234	0.0209	*
	Low Gamma	0.2165	0.09468	-0.1559	0.05806	288.0	0.0039	**
F4	Theta	0.07942	0.2264	0.01907	0.1747	-202.0	0.0479	*
T4	Theta	0.1252	0.4000	-0.01522	0.1977	-210.0	0.0394	*
	Low Gamma	-0.1908	0.1063	-0.1512	0.08380	226.0	0.0260	*
Tp10	Low Gamma	-0.2062	0.1103	-0.1571	0.06769	212.0	0.0374	*

In the electrode Fp1, a decrease in the power of the Delta frequency band was found during active tactile discrimination (Active: 1.133±0.4656; Mean±Stdev; Passive:1.302±0.4932; W=202.0; P=0.0479; Wilcoxon signed-rank test). In channel F3, power in Delta band was higher during active tactile discrimination (Active: 1.654±0.4899; Mean±Stdev; Passive:1.435±0.4669; W=-212; P=0.0209; Wilcoxon signed-rank test). In channel F3, power in Theta band was higher during active tactile discrimination (Active: 0.082±0.2813; Mean±Stdev; Passive: -0.033±0.06739; W=-234; P=0.0209; Wilcoxon signed-rank test). In channel F3, power in Low Gamma band was higher during active tactile discrimination (Active: 0.2165±0.09468; Mean±Stdev; Passive: -0.1559±0.05806; W= -288.0; P= 0.0039; Wilcoxon signed-rank test). In channel F4, power in Theta band was higher during active tactile discrimination (Active: 0.07942±0.2264; Mean±Stdev; Passive:0.01907±0.1747; W=-202; P=0.0479; Wilcoxon signed-rank test). In channel T4, power in Theta band was higher during active tactile discrimination (Active: 0.1252±0.4000; Mean±Stdev; Passive: -0.01522±0.1977; W=-210; P=0.0394; Wilcoxon signed-rank test). In channel T4, power in Low gamma band lower during active tactile discrimination (Active: -0.1908±0.1063; Mean±Stdev; Passive: -0.1512±0.08380; W=226.0; P=0.0260; Wilcoxon signed-rank test). In channel Tp10, power in Low Gamma band was lower during active tactile discrimination (Active: -0.2062±0.1103; Mean±Stdev; Passive -0.1571±0.06769; W=212; P=0.0374; Wilcoxon signed-rank test).

3.2.2. Analysis of Ratios

Analysis of ratios of higher and lower frequency bands, for the group of electrodes that presented statistically significant differences in power, demonstrated that Fp1 and F3 were associated with differences in ratio 1, while F3 and T4 presented significant differences in ratio 2. These differences are presented in more detail in Table 4 and in Figure 3.

Table 4 - Comparison of ratios of higher and lower frequencies in active and passive versions of the task. For p-value <0.05 (*); p < 0.005 (**).

Electrode	Ratio	W	p	Sig
Fp1	1	-206	0.0446	*
	2	-110	0.2855	No
F3	1	-222	0.0304	*
	2	-300	0.0034	**
F4	1	-132	0.1993	No
	2	-110	0.2855	No
T4	1	-72	0.4866	No
	2	-246	0.0164	*
TP10	1	-172	0.0938	No
	2	-190	0.0640	No

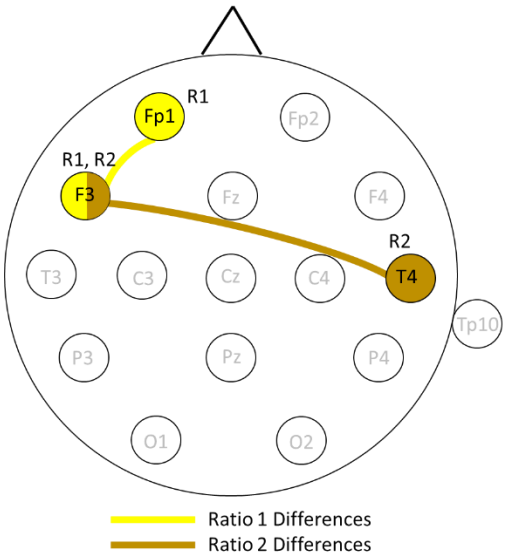

Figure 3 – Networks of electrodes associated with differences in ratios of higher (yellow) and lower (brown) frequencies during the active and passive versions of the task

To gain further understanding on the potential relation between the differences found between ratios in the active and passive versions of the tasks, the ratios of frequency bands were compared to the task performance. As presented in Table 5, no significant differences for the electrodes studied here were found. For electrodes Fp1 (Ratio 1 and Ratio 2 in the active version) and T4 (Ratio 1 in the passive version) near significant values were found (also see discussion).

Table 5 – Comparison of performance and ratios of frequencies. No significant correlation between the performance in the active or passive versions of the task and the ratios of higher (Ratio 1) or lower (Ratio 2) frequencies was found.

Electrode	Active		Passive	
Fp1	**R value**	**p value**	**R value**	**p value**
R1	-0.27786	**0.0156**	-0.02562	0.9551
R2	-0.17066	**0.0366**	0.162381	0.7239
F3	**R value**	**p value**	**R value**	**p value**
R1	-0.0209	0.2752	0.125959	0.4437
R2	-0.20131	0.1628	0.148754	0.4023
F4	**R value**	**p value**	**R value**	**p value**
R1	0.106637	0.6764	0.276986	0.0993
R2	-0.14371	0.6338	0.139542	0.686
T4	**R value**	**p value**	**R value**	**p value**
R1	-0.12874	0.5199	0.216047	**0.0285**
R2	-0.18699	0.3145	0.295694	0.1223
Tp10	**R value**	**p value**	**R value**	**p value**
R1	-0.1168	0.3486	-0.02672	0.9044
R2	0.029519	0.9376	-0.03916	0.9586

Note: Corrected alpha=0.05/10=0.005

4. Discussion

In the present study we have compared active and passive tactile width discrimination while EEG recordings were performed. Analysis of frequency bands revealed increases for the active version of the task in delta frequency band in electrode F3; an increase in theta frequency band in F3, F4, and a reduction in T4; and an increase in gamma in F3 and T4, and a reduction in Tp10. Meanwhile, comparison of ratios of higher and lower frequencies revealed that for the group of electrodes that presented statistically significant differences in power, demonstrated that Fp1 and F3 were associated with differences in ratio 1, while F3 and T4 presented significant differences in ratio 2. These results suggest that an asymmetrical network involving prefrontal, frontal and temporal electrodes, in delta, theta, and gamma frequency bands is associated with active and passive tactile width discrimination.

Before we begin the proper discussion of the results it is important to highlight that this study was performed using a 16-electrode setup. This means that source localization, which cannot be reliable with less than 64 electrodes [72–74] was not performed here. Therefore, all results presented here will be mainly considered in terms of their relation to the recording electrode and not necessarily the underlying cortical region, since it cannot be ascertained that the signal recorded corresponds to that region.

A difference in the power and ratios of frequencies was found for the passive and active version of the tactile width discrimination task. This finding supports our first hypothesis, regarding different neural substrates for active and passive tactile width discrimination. In addition, the differences in the power of frequency bands were found in a network of electrodes that roughly matches previous reports of EEG changes occurring in tactile processing [54]. These electrodes are placed in frontal (contralateral Fp1, contralateral F3, and ipsilateral F4) and temporal regions (ipsilateral T4) regions, with an additional difference found in electrode Tp10 (see detailed discussion of this electrode below).

The passive version of the task was characterized by an increase in the power of delta frequency in the electrode Fp1 and a decrease in delta frequency band in

F3. A previous study has reported changes in tactile processing when real or virtual stimuli were delivered to subjects these changes were, in addition, accompanied by changes in event related potential latencies, suggesting that frontal lobe electrodes are associated with real tactile stimulation while limbic electrodes are associated with virtual stimulation [74]. In addition, processing of a smooth surface has been associated with changes in the delta frequency band of signals recorded from electrodes Fp1 and F3 [75]. Even though the relation between processing of a smooth surface and width discrimination is not straightforward, these studies support a role for this frequency band and these electrodes in tactile processing. Future studies may help elucidate this potential relation. In a different, but relevant approach, a previous study evaluating stress, reported changes in delta frequency bands for the pair Fp1-F3 [76]. This is a potentially relevant finding that is, in part, supported by the behavioral reports of the subjects that indicated preferring the active version rather than the passive version of the task. Although the task was not considered to be stressful by most of the participants, the overall evaluation was that it was more difficult.

Another neurophysiological difference between the active and passive versions of the task was an overall decrease in theta frequency band for the subnetwork of electrodes in F3, F4 and T4. Frontal theta frequency power has been reported to increase during recall of haptic information [77]. These authors have shown that theta power was correlated to the mean exploration time spent by subjects and has therefore been associated with the hypothesis that fronto-central theta power is associated with the load of working memory [78]. The passive version of the task was considered to be more difficult that the active version and therefore it could be, at first expected, that the power of the theta band to be higher in the passive version of the task. However, during the passive version of the task subjects are not allowed to sample the discriminanda (i.e., they need to keep the finger in place and the bars will move towards the finger). This supports the notion that theta band is increased in the active version of the task, because subjects are allowed to sample the aperture width. It would be relevant in future studies to determine if the amount of time exploring the width aperture is also correlated to theta band power in the relevant electrodes. As the present task had a pre-determined time for the sampling interval, this could not be tested here.

One other subnetwork of electrodes presented differences between the active and passive versions of that in the low-gamma frequency band and involved F3, T4 and Tp10. The gamma frequency band plays a relevant role in tactile discrimination, namely in frontal, parietal, and occipital regions [54]. In the specific case of F3 electrode, an increase in gamma power has been associated with mental training [79], while increases in power in this frequency band have been reported for F3-T4 electrodes in cognitive impairment/Alzheimer Disease [80], depression [81]. In our study, we have found an increase in the gamma frequency band power for the Fp3 electrode during the active version of the task, but a decrease in the passive version of the task, and therefore the relation between these previous studies and the results obtained here is not clear. An increase in gamma in the F3 electrode could be interpreted as some form of increased mental effort [79], but subjects reported that the active version of the task was easier and therefore one would expect the opposite result (i.e., that the active version of would be associated with reduced gamma power).

We have not found a relevant role for electrodes in occipital, parietal regions, nor for C3 electrode (see discussion below). At this point it is important to note that: i) we have solely explored the discrimination period and therefore there may not be large differences between the two versions of the task for this particular interval for electrodes in these regions, ii) we have not explored phase synchronization, information transfer, nor event related potentials; which may reveal relevant differences between the two versions of the task not found with the present analysis.

The results from the TP10 electrode are difficult to interpret due to its location. This is an electrode that is above right mastoid process and therefore the underlying neural signal is largely attenuated. In fact, this electrode is used as reference in many studies, but it also has been implicated in relevant neural networks [82]. Meanwhile, a difference between the two versions of the task was found, and therefore this result should be acknowledged and discussed. In the present study this electrode presented a decrease in the gamma frequency band during the active version of the task. One potential explanation for this difference

could be related to the proximity of this electrode to the auditory cortex and the increased noise of the motors during passive stimulation. However, the possibility of increased auditory activity relating to the passive version of the task should be further investigated, for example, with an increased number of electrodes in the relevant regions [83], [84].

An unexpected outcome of the present study was the absence of differences for the electrode C3 (located above the somatosensory cortex) which has been associated with differences in active and passive stimulation in humans using other tasks [7], [24], [29], [55], [57] and in rodents [2], [3]. We speculate that this lack of differences may be related to a decreased sensitivity of the analysis performed here. We propose that future studies use classifiers to further determine if EEG signals recorded from the electrode C3 differ between active and passive versions of the task [29].

4.1. Ratios of frequencies

The differences found in the ratios of higher and lower frequency bands generally support the findings of the individual frequency bands. These results demonstrated a subnetwork where ratio 1 changed in Fp1 and F3 electrodes. Ratio 1 is sensitive to changes occurring in higher frequencies [37] and therefore this analysis allowed detection of a change occurring in gamma or beta band frequency in the electrode Fp1, that was not detected when the different frequency bands were compared. In the future it will be important to perform additional analysis to identify if this difference is due to an effect of beta, gamma or both frequency bands. Meanwhile the comparison of Ratio 2, which is sensitive to changes occurring in lower frequencies, revealed changes in lower frequencies occurring in electrodes F3 and T4, has identified in the comparison of the subnetwork of changes in the delta frequency band (discussed above).

4.2. Parallels between human and rodent studies

One of the goals of the present study was to identify potential parallels between the neurophysiological substrates of width discrimination in humans [13] and animals [2], [3], [17]. We have observed that active and passive tactile discrimination was significantly different for an asymmetrical network of electrodes placed in frontal and temporal regions for delta, theta and gamma frequency bands. Although tese findings are in line with the previous results from rodents, they suggest that the inclusion of additional periods of the task (before and after the tactile discrimination) and the use of more refined analysis (information transfer, phase synchronization, etc.) can significantly improve our current knowledge on the human and rodent parallels in width discrimination.

4.3. Caveats, potential bias, and technical discussion

A small number of caveats and potential bias should be considered. The number of electrodes used to record in this study does not allow for source analysis and therefore, the present findings are discussed regarding the position of each electrode rather than the cortical region beneath it. We have only included low (30.5-45.0Hz) but not the high gamma band frequencies which are relevant for tactile spatial attention [21] . We have opted for this because: i) visual inspection of the data showed little activity in the higher gamma band, and ii) we have previously seen that low gamma frequency band seems to capture several of the relevant characteristics for this task [85]. Even though, the present results and conclusions can be, to some extent, biased by this approach.

Another potential caveat of the present study is that active and passive versions of the task may correspond to different processing time intervals in the brain. Namely, it is possible that passive tactile discrimination, may require a longer period than the active discrimination. This is due to the fact that the subject need to introduce the finger, and wait for the bars to move, which ends up taking longer than just sampling the aperture width in the active version.

Lastly, for one of our subjects, performing the task proved to be a stressful event. Such an effect of the task was not predictable from our previous [13] or current experience (now including more than 30 subjects tested in different versions of the task), since subjects are always allowed to interact with the task before the session (i.e., they perform a small number of trials before the actual session begins until they indicate being comfortable with the procedure). Even though, in future studies, we propose implementing a short psychological evaluation of subjects before testing them in this apparatus.

5. Conclusion

The neurophysiological substrate of width discrimination suggests that a network involving electrodes recording from frontal and temporal regions in delta, theta and gamma frequency bands is responsible for active and passive tactile information processing.

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Appendix

1. Supplementary Table 1 – Power of all frequency bands in each channel during discrimination period

2. Informed consent

Modelo_de_Consentimento.pdf

3. Ethics approval Universidade Católica Portuguesa

Parecer Catolica Bial.pdf

4. Ethics approval Universidade do Minho

Parecer SECVS.pdf

Supplementary Table 1- Power of all frequency bands in each channel during discrimination period

		Active		Passive				
Channel	**Band**	**Mean**	**Stdev**	**Mean**	**Stdev**	**W**	**p**	**SIG**
FP1	Delta	1.133	0.466	1.302	0.493	202.000	0.048	*
	Theta	1.133	0.466	1.302	0.493	74.000	0.480	No
	Alpha	-0.069	0.057	-0.074	0.063	68.000	0.517	No
	Beta	-0.104	0.049	-0.117	0.050	-146.000	0.157	No
	Gamma	-0.119	0.072	-0.144	0.081	148.000	0.152	No
FP2	Delta	1.261	0.480	1.314	0.420	92.000	0.378	No
	Theta	-0.054	0.086	-0.010	0.223	46.000	0.664	No
	Alpha	-0.073	0.092	-0.073	0.095	-78.000	0.456	No
	Beta	-0.098	0.073	-0.122	0.053	-160.000	0.120	No
	Gamma	-0.145	0.091	-0.144	0.073	-38.000	0.721	No
F3	Delta	1.654	0.490	1.435	0.467	-212.000	0.037	*
	Theta	0.082	0.281	-0.033	0.067	-234.000	0.021	*
	Alpha	-0.049	0.129	-0.081	0.054	-78.000	0.456	No
	Beta	-0.148	0.058	-0.129	0.048	164.000	0.111	No
	Gamma	-0.217	0.095	-0.156	0.058	288.000	0.004	**
FZ	Delta	1.791	0.558	1.816	0.559	42.000	0.692	No
	Theta	0.263	0.422	0.199	0.311	-68.000	0.517	No
	Alpha	-0.072	0.078	-0.090	0.076	-138.000	0.182	No
	Beta	-0.188	0.067	-0.191	0.069	-24.000	0.824	No
	Gamma	-0.241	0.109	-0.226	0.091	28.000	0.794	No
F4	Delta	1.580	0.516	1.391	0.448	-150.000	0.146	No
	Theta	0.079	0.226	0.019	0.175	-202.000	0.048	Yes
	Alpha	-0.071	0.074	-0.082	0.026	-30.000	0.779	No
	Beta	-0.156	0.064	-0.132	0.053	174.000	0.090	No
	Gamma	-0.186	0.089	-0.153	0.073	172.000	0.094	No
T3	Delta	1.415	0.424	1.393	0.388	-34.000	0.750	No
	Theta	0.091	0.291	0.034	0.184	-8.000	0.946	No
	Alpha	-0.054	0.104	-0.057	0.080	8.000	0.946	No
	Beta	-0.120	0.086	-0.124	0.064	-18.000	0.870	No
	Gamma	-0.179	0.079	-0.163	0.063	84.000	0.421	No

		Active		Passive				
Channel	**Band**	**Mean**	**Stdev**	**Mean**	**Stdev**	**W**	**p**	**SIG**
C3	Delta	1.539	0.498	1.436	0.414	-82.000	0.433	No
	Theta	0.176	0.333	0.111	0.372	-164.000	0.111	No
	Alpha	-0.024	0.154	-0.052	0.142	-98.000	0.347	No
	Beta	-0.150	0.071	-0.141	0.055	90.000	0.388	No
	Gamma	-0.209	0.097	-0.178	0.079	124.000	0.232	No
CZ	Delta	1.539	0.517	1.588	0.487	14.000	0.900	No
	Theta	0.129	0.256	0.132	0.332	-4.000	0.977	No
	Alpha	-0.081	0.052	-0.072	0.120	-120.000	0.247	No
	Beta	-0.158	0.059	-0.167	0.066	-22.000	0.839	No
	Gamma	-0.184	0.087	-0.189	0.084	-16.000	0.885	No
C4	Delta	1.571	0.506	1.442	0.523	-52.000	0.622	No
	Theta	0.162	0.352	0.096	0.194	6.000	0.962	No
	Alpha	-0.005	0.169	-0.027	0.138	-32.000	0.765	No
	Beta	-0.162	0.073	-0.132	0.077	102.000	0.327	No
	Gamma	-0.211	0.113	-0.189	0.092	56.000	0.595	No
T4	Delta	1.361	0.519	1.268	0.498	-86.000	0.410	No
	Theta	0.125	0.400	-0.015	0.198	-210.000	0.039	*
	Alpha	-0.045	0.149	-0.050	0.220	-98.000	0.347	No
	Beta	-0.109	0.124	-0.093	0.091	122.000	0.240	No
	Gamma	-0.191	0.106	-0.151	0.084	226.000	0.026	*
P3	Delta	1.619	0.445	1.585	0.462	-42.000	0.692	No
	Theta	0.284	0.436	0.306	0.372	18.000	0.870	No
	Alpha	-0.033	0.115	-0.016	0.125	66.000	0.529	No
	Beta	-0.176	0.062	-0.177	0.073	14.000	0.900	No
	Gamma	-0.226	0.084	-0.227	0.101	-4.000	0.977	No
PZ	Delta	1.548	0.496	1.387	0.426	-146.000	0.157	No
	Theta	0.261	0.451	0.166	0.366	-108.000	0.299	No
	Alpha	-0.036	0.152	-0.068	0.086	-56.000	0.595	No
	Beta	-0.178	0.056	-0.151	0.062	186.000	0.070	No
	Gamma	-0.207	0.080	-0.170	0.078	174.000	0.090	No

		Active		Passive				
Channel	**Band**	**Mean**	**Stdev**	**Mean**	**Stdev**	**W**	**p**	**SIG**
P4	Delta	1.520	0.415	1.646	0.515	94.000	0.367	No
	Theta	0.254	0.441	0.352	0.480	106.000	0.308	No
	Alpha	-0.033	0.166	-0.010	0.114	140.000	0.176	No
	Beta	-0.177	0.074	-0.190	0.080	-44.000	0.678	No
	Gamma	-0.200	0.088	-0.239	0.114	-128.000	0.217	No
O1	Delta	1.595	0.462	1.549	0.475	-40.000	0.706	No
	Theta	0.313	0.433	0.318	0.410	-14.000	0.900	No
	Alpha	-0.023	0.087	0.018	0.160	64.000	0.542	No
	Beta	-0.145	0.106	-0.146	0.084	2.000	0.992	No
	Gamma	-0.251	0.107	-0.247	0.110	10.000	0.931	No
O2	Delta	1.609	0.494	1.637	0.459	14.000	0.900	No
	Theta	0.237	0.346	0.164	0.160	-78.000	0.456	No
	Alpha	0.015	0.214	-0.043	0.118	-176.000	0.087	No
	Beta	-0.160	0.061	-0.134	0.072	140.000	0.176	No
	Gamma	-0.235	0.105	-0.231	0.085	12.000	0.915	No
Tp10	Delta	1.523	0.551	1.396	0.407	-94.000	0.367	No
	Theta	0.170	0.434	-0.003	0.113	-150.000	0.146	No
	Alpha	-0.010	0.158	-0.058	0.132	-178.000	0.083	No
	Beta	-0.155	0.066	-0.129	0.050	174.000	0.090	No
	Gamma	-0.206	0.110	-0.157	0.068	212.000	0.037	*