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Effects of inter-stimulus interval (ISI) duration on the N1 and P2 components of the auditory event-related potential

Diana R. Pereira [a,*], Susana Cardoso [a,b], Fernando Ferreira-Santos [a], Carina Fernandes [a,c], Cassilda Cunha-Reis [a], Tiago O. Paiva [a,c], Pedro R. Almeida [a,d], Celeste Silveira [c,e], Fernando Barbosa [a], João Marques-Teixeira [a]

[a] *Laboratory of Neuropsychophysiology, Faculty of Psychology and Educational Sciences, University of Porto, Rua Alfredo Allen, 4200-135 Porto, Portugal*
[b] *Center of Psychology, Faculty of Psychology and Educational Sciences, University of Porto, Rua Alfredo Allen, 4200-135 Porto, Portugal*
[c] *Faculty of Medicine, University of Porto, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal*
[d] *School of Criminology, Faculty of Law, Rua dos Bragas, 223, 4050-123 Porto, Portugal*
[e] *Department of Psychiatry, Hospital de São João, Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal*

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ABSTRACT

The N1 and P2 components of the event-related potential are relevant markers in the processing of auditory information, indicating the presence of several acoustic phenomena, such as pure tones or speech sounds. In addition, the expression of these components seems to be sensitive to diverse experimental variations. The main purpose of the present investigation was to explore the role of inter-stimulus interval (ISI) on the N1 and P2 responses, considering two widely used experimental paradigms: a single tone task (1000 Hz sound repeated in a fixed rhythm) and an auditory oddball (80% of the stimuli were equal to the sound used in the single tone and the remaining were a 1500 Hz tone). Both tasks had four different conditions, and each one tested a fixed value of ISI (600, 1000, 3000, or 6000 ms). A sample of 22 participants performed these tasks, while an EEG was recorded, in order to examine the maximum amplitude of the N1 and P2 components. Analysis of the stimuli in the single tone task and the frequent tones in the oddball task revealed a similar outcome for both tasks and for both components: N1 and P2 amplitudes were enhanced in conditions with longer ISIs regardless of task. This response pattern emphasizes the dependence of both the N1 and P2 components on the ISI, especially in a scenario of repetitive and regular stimulation. The absence of task effects suggests that the ISI effect reported may depend on refractory mechanisms rather than being due to habituation effects.

1. Introduction

In the context of the event-related potentials (ERPs), the occurrence of one auditory stimulus, such as a pure tone, a click, or a speech sound, can lead to the manifestation of several deflections, including the negative N1 component which appears approximately 75 to 150 ms after the stimulus onset, and the positive P2 component that emerges in the interval of 150 to 250 ms. The P2 tends to present maximum amplitude in the vertex (Cz) (Crowley and Colrain, 2004), and the N1 has a fronto-central topographic distribution (Rosburg et al., 2008). This central topographic convergence instigated a theoretical integration of these components in the so-called vertex complex (Davis et al., 1966; Fitzgerald and Picton, 1981; Nelson and Lassman, 1973). Nevertheless, it has been suggested that the N1 and P2 exhibit distinct sensitivities to stimulus characteristics (Näätänen and Picton, 1987; Roth et al., 1976) and divergent neuronal generators (Crowley and Colrain, 2004), thus showing independent properties.

The inter-stimulus interval (ISI) consists of the period of time that separates two consecutive stimuli, starting from the offset of the first stimulus until the onset of the second. The ISI plus the stimulus duration defines the Stimulus Onset Asynchrony (SOA), but when all stimuli have the same duration, the ISI and SOA can be considered equivalent measures (Colman, 2014). This experimental variable has been scarcely investigated in recent years, although it is considered relevant in the study of auditory sensory memory (Čeponiené et al, 1998; Grossheinrich et al., 2010), since it allows the exploration of maintenance properties for auditory stimulation (Cowan, 1984). Previous studies comparing experimental conditions with long and short ISIs showed that the amplitude of the auditory evoked potential components tends to increase with larger ISIs (Muller-Gass et al., 2008; Roth et al., 1976; Schucard and Callaway, 1974). It has been suggested that ISIs of at least 6 to 10 s are required to elicit maximal N1 and P2 amplitudes (Davis et al., 1966; Nelson and Lassman, 1968). In the case of N1,

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* Corresponding author. Tel.: +351 226 079 700; fax: +351 226 079 725.
E-mail addresses: diana.r.pereira@gmail.com (D.R. Pereira), susanacardoso2004@yahoo.es (S. Cardoso), frsantos@fpce.up.pt (F. Ferreira-Santos), carinastfernandes@gmail.com (C. Fernandes), cassilda_reis@hotmail.com (C. Cunha-Reis), tiago.paiva1989@gmail.com (T.O. Paiva), palmeida@fpce.up.pt (P.R. Almeida), celestesilveira@gmail.com (C. Silveira), fbarbosa@fpce.up.pt (F. Barbosa), teixeira@fpce.up.pt (J. Marques-Teixeira).

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its amplitude tends to decrease with the ISI reduction (Alcaini et al. 1994; Fitzgerald and Picton, 1981; Javitt et al., 2000; Nelson and Lassman, 1968; Steiner et al., 2014; Teder et al., 1993). Considering the peak latency of N1, there are studies that point to a latency increment with an augmented ISI (e.g., Alcaini et al., 1994), while other studies show peak latency stability regardless of the ISI manipulation (e.g., Nelson and Lassman, 1968; Teder et al., 1993).

The findings reviewed above reveal that the N1 and P2 properties seem to be influenced by variations in the ISI, and two possible frameworks have been discussed in this regard: the habituation and the refraction proposals. According to the habituation approach, the living organism tends to adapt its response repertoire according to the novelty present in the surrounding environment. Hence, when confronted with the repetition of (innocuous) stimuli in stable environment conditions, responses tend to fade with repetition, revealing a process of habituation oriented to a particular stimulus (Özemi et al., 2000). The concept of habituation in the context of ERP findings has been demonstrated for the N1 and P2 components in an early study by Rust (1977): both N1 and P2 showed an amplitude decrease from the first to the second stimulus in a context of 31 stimuli separated by a long ISI of 33 s. More specifically, the auditory N1 component has been described as a clear exemplar of the habituation process, since it diminishes in amplitude across stimuli repetitions, while its latency remains stable (Bruin et al., 2000; Jiang et al., 2013; Polich, 1986) or decreases in the case of short ISIs (Rosburg et al., 2010). N1 habituation can be viewed as process of novelty oriented loss, in which there is an establishment of a neuronal representation for the repeated stimuli (Budd et al., 1998).

Research on habituation seems to be intricately associated with ISI manipulations, since distinct intervals, short or long, can lead to different response patterns. Furthermore, the study of habituation can be accomplished comparing the response between stimuli of the same group or between different blocks of stimuli (Özemi et al., 2000). In theory, when short ISIs are used, it is possible to obtain a transitory habituation which is quickly reached, and thus called short-time habituation. Another habituation process evolves progressively with time through the application of long ISIs, so it is considered a long-time habituation process. Näätänen and Picton (1987) mention that the decreased response reached after extended periods of time and various blocks is close to the authentic habituation mechanism, and this perspective is supported by different studies (e.g., Rosburg et al., 2002; Roth and Kopell, 1969; Sambeth et al. 2004; Schucard and Callaway, 1974). Even so, the diminished amplitude of N1 and P2 can also be identified when the analysis is centered on contrasting stimuli of the same block/group, i.e., by comparing the response between the first and the second stimulus, and so on (Lange, 2010; Özemi et al., 2000; Roth and Kopell, 1969; Sambeth et al., 2004).

The process of refraction is an alternative, non-exclusive explanation, and can be defined as the time needed for the potential response recovery of the neuronal sources to reach a level identical to the one found in the pre-stimulation context. The refraction cycle has been primarily observed in isolated neurons, which need a temporal window to reestablish their ability to emit action potentials, and it has been argued that this concept can be applied to neuronal network functions and potentially detected via ERPs (Budd et al., 1998; Näätänen and Winkler, 1999). In this sense, after the activation evoked by an initial stimulus, the neural sources need time to return to baseline levels. This recovery process can be disrupted by iterated stimulus presentations characterized by rapid cadences (Ross and Tremblay, 2009; Tremblay et al., 2004) that prevent the neural generators from fully recovering and result in diminished scalp ERP amplitudes (Gonsalvez and Polich, 2002). According to Nelson and Lassman (1973), at a given stimulus intensity, the amplitude of auditory evoked vertex responses increases as a logarithmic function of the recovery period, that is, every constant ratio increase in recovery period results in a constant microVolt growth in the evoked response. Thus, a facilitated recuperation of the neuronal sources and larger component amplitudes are expected when long ISIs are used. Overall, refraction appears to be sensitive to variations operated in ISI parameters (Näätänen and Picton, 1987), and it is also likely that different neuronal populations demonstrate distinct refraction periods (Coch et al., 2005). Even so, the precise neuronal mechanisms possibly responsible for these refraction effects remain unclear (Budd et al, 1998). One possible way to address which mechanism, habituation or refraction, best accounts for the effects previously reported is to examine how different ISIs affect the N1 and P2 ERP components under conditions that lead to different levels of habituation. Accordingly, the present study seeks to address this issue by systematically examining the effect of different ISIs on the N1 and P2 responses in two distinct and typical ERP tasks, namely a single tone repeated stimulation task and an auditory oddball task. The presentation of a single tone at a regular ISI leads to strong habituation effects, which are mitigated in tasks where stimulus delivery is less predictable, such as the oddball task. The habituation approach described above would then predict that N1 and P2 amplitudes would be smaller in the single tone task than for frequent stimuli in the oddball task. On the other hand, the refraction approach would predict that N1 and P2 amplitudes depend solely on the duration of the ISI regardless of task. In line with these hypotheses, the present investigation aimed to explore the specific impact of ISI manipulations in the N1 and P2 response in two tasks that are expected to induce different levels of habituation, namely a single tone task (where higher levels of habituation are expected) and an oddball task (where lower levels of habituation should be observed). Based on previous findings and considering a context of repetitive stimulation, the N1 and P2 amplitudes are expected to be increased in conditions with long ISIs when compared to short ISIs. The novelty of the present study is to test whether these effects depend on the level of habituation induced by the task, which we expect will provide evidence regarding which mechanism, habituation or refraction, may be responsible for this effect.

We were also interested in testing whether the N1 and P2 exhibited independent response functions to different ISI variations. This goal may be emphasized by considering that the properties of the auditory P2 component are still not well understood even after decades of ERP research, as noted in several studies (e.g., Bell et al., 2010; Ferreira-Santos et al., 2012; Giaquinto et al., 2007; Hämäläinen et al., 2007; Näätänen and Picton, 1987; Salisbury et al., 2010; Sussman et al., 2008). In the review by Crowley and Colrain (2004), the authors describe that the majority of studies focused on the experimental manipulation of stimulus parameters date back to the 1960s and 70s, with only a modest amount of work conducted in the following years. These authors further note that the ISI parameter has been scarcely studied in the case of P2. A better understanding of the different experimental factors which have an impact on the ERP characteristics is an essential step to explore their functional significance.

2. Method

2.1. Participants

Twenty-two healthy adult participants with normal hearing (12 females, all right-handed) were recruited from the academic community of the University of Porto. Mean age was 23.14 years ($SD = 3.82$; range: 19–33). Inclusion criteria were delineated in order to guarantee the homogeneity of relevant characteristics with known impact in the EEG recordings, including sex, age, years of formal education, and laterality (see Picton et al., 2000): (a) ages between 18 and 35 years old; (b) approximately equal numbers of female and male participants in the experimental group; and (c) minimum of 12 years of formal education. Additional inclusion criteria were the absence of sensory–motor impairments that could influence the participant's performance in the experimental tasks, neurologic and/or psychiatric conditions, substance abuse, and intake of psychoactive medication.