Clinical Neurophysiology 125 (2014) 1576–1588

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Effects of stimulus-driven and goal-directed attention on prepulse inhibition of the cortical responses to an auditory pulse

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ARTICLE INFO

Article history:
Accepted 6 December 2013
Available online 17 December 2013

Keywords:
Prepulse inhibition
Auditory evoked potential
Continuous performance test
Attention
Source localization

HIGHLIGHTS

- We evaluated the effect of attention on sensory gating of cortical responses to a pulse.
- Stimulus-driven attention influenced prepulse inhibition of the N100 component and goal-directed attention influenced prepulse inhibition of the P200 component.
- Cortical sources of N100 and P200 were modulated by brain areas involved in attention.

ABSTRACT

Objective: Inhibition by a prepulse (prepulse inhibition, PPI) of the response to a startling acoustic pulse is modulated by attention. We sought to determine whether goal-directed and stimulus-driven attention differentially modulate (i) PPI of the N100 and P200 components of the auditory evoked potential (AEP) and (ii) the components' generators.
Methods: 128-channel electroencephalograms were recorded in 26 healthy controls performing an active acoustic PPI paradigm. Startling stimuli were presented alone or either 400 or 1000 ms after a visual prepulse. Three types of prepulse were used: to-be-attended (goal-directed attention), unexpected (stimulus-driven attention) or to-be ignored (non focused attention). We calculated the percentage PPI for the N100 and P200 components of the AEP and determined cortical generators by standardized weighted low resolution tomography.
Results: At 400 ms, the PPI of the N100 was greater after an unexpected prepulse than after a to-be-attended prepulse, the PPI of the P200 was greater after a to-be-attended prepulse than after a to-be ignored prepulse. At 1000 ms, to-be-attended and unexpected prepulses had similar effects. Cortical sources were modulated in areas involved in both types of attention.
Conclusions: Stimulus-driven attention and goal-directed attention each have specific effects on the attentional modulation of PPI.
Significance: By using a new PPI paradigm that specifically controls attention, we demonstrated that the early stages of the gating process (as evidenced by N100) are influenced by stimulus-driven attention and that the late stages (as evidenced by P200) are influenced by goal-directed attention.

1. Introduction

Filtering out irrelevant information is a crucial way of protecting the cognitive resources required for goal-directed activities. One of the physiological indices of these protective neural processes is referred to as prepulse inhibition (PPI), an index of sensorimotor gating. It corresponds to the attenuation of the startle reflex amplitude to an intense tactile, visual or acoustic stimulus (called the pulse) when a weaker, non-startling stimulus (the prepulse) precedes the pulse by approximately 30–500 ms. The prepulse attenuates not only motor responses (e.g., the eye-blink reflex) but also cortical responses to a sound pulse, such as the N100 and P200 components of the auditory evoked potential (AEP) (Perlstein et al., 1993, 2001) or the auditory evoked theta, alpha and gamma oscillations (Kedzior et al., 2006, 2007). The

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1388-2457/$36.00
http://dx.doi.org/10.1016/j.clinph.2013.12.002

N100 component of the AEP is thought to represent the processing of the auditory stimulus's physical attributes, e.g., its intensity (Davis and Zerlin, 1966), and is thus a measure of the initial registration, processing and attribute selection of an auditory stimulus (Hillyard and Picton, 1979). The P200 component of the AEP reflects a later stage of stimulus processing and is viewed as an index of some aspects of the stimulus classification process (Garcia-Larrea et al., 1992). Therefore, PPI of these AEP components could be a marker of sensory and cognitive gating. According to Inui et al. (2012), PPI of cortical responses could be a valuable tool for understanding the mechanisms of sensory gating and the impairments of these mechanisms in disease. Perriol et al. (2005) used PPI of cortical responses to a pulse to compare attention disorders in patients with Lewy body dementia, Parkinson's disease dementia and Alzheimer's disease. They observed disruption of PPI of the N100 and P200 components of the AEP in patients with Lewy body dementia and Parkinson's disease dementia but not in patients with Alzheimer's disease, this suggested the involvement of dopaminergic subcorticothalamocortical networks in PPI regulation.

Data from animal studies have suggested that sensorimotor gating is mediated by the corticostriatal and pallidothalamic circuitry, which includes the prefrontal cortex, thalamus, amygdala, hippocampus, nucleus accumbens, striatum, ventral pallidum, and globus pallidum (Swerdlow et al., 2001). In a functional magnetic resonance imaging (fMRI) study, Campbell et al. (2007) described a primary pontine circuitry for sensorimotor gating that interconnects with inferior parietal, superior temporal, frontal and prefrontal cortices via the thalamus and striatum. Hence, PPI is mediated by a broad network that includes cortical regions known to be involved in cognitive processes (namely attention). Moreover, although the magnitude of PPI is influenced by the prepulse-pulse lead interval (Filion et al., 1998), the PPI can also be modulated by attention processes. Several researchers have reported that in an active PPI paradigm (when participants are explicitly asked to attend to the prepulse), PPI is greater after a to-be-attended prepulse than after a to-be-ignored prepulse (Dawson et al., 1993; Filion et al., 1993). Rissling et al. (2007) combined an active PPI paradigm with a continuous performance test (CPT) involving rapid perceptual discrimination and working-memory processes. In Rissling et al.'s experiment, participants were presented a series of single digits (from 0 to 9) and were instructed to (i) press a response button after they saw a 0–0 sequence and (ii) refrain from pressing the button at any other time. The auditory pulses were presented just after the visual stimuli, which were used as a prepulse. Hence, the "0" was the to-be-attended visual prepulse and the other digits served as to-be-ignored visual prepulses. With a lead interval of 240 ms, startle eye-blink inhibition was greater after the to-be-attended prepulse than after the to-be-ignored prepulse. However, the attentional modulation of PPI has only been investigated for the eye-blink reflex. Furthermore, only passive PPI paradigms (i.e., with no tasks to be performed and no instructions concerning the prepulse) have been used to modulate the amplitude of the N100 and P200 components of the AEP (Abduljawad et al., 2001; Perriol et al., 2005; Inui et al., 2012; De Pascalis et al., 2013). The effect of attention on these markers of sensory and cognitive gating has not previously been investigated. Moreover, attention is a complex neurocognitive process. It can be either goal-directed (i.e., focused on relevant signals derived from task demands) or stimulus-driven (i.e., captured by salient properties of stimuli that are sometimes irrelevant for the task) (Desimone and Duncan, 1995; Kastner and Ungerleider, 2000). To the best of our knowledge, it has not been established whether goal-directed attention and stimulus-driven attention differ in their modulation of PPI.

Given that (i) PPI of the N100 and P200 components of the AEP is a marker of sensory and cognitive gating and (ii) the effect of attention on these cortical indexes had not previously been investigated (especially in terms of their differential modulation by stimulus-driven and goal directed attention), the main objective of the present study was to evaluate the effect of stimulus-driven and goal-directed attention on PPI of the AEP N100 and P200 components. Moreover, modulation of the anatomical sources of these AEP components by a prepulse had never previously been investigated. Anatomical sources of potentials recorded on the surface of the scalp can be studied with source reconstruction methods. Of the various methods, standardized low-resolution electromagnetic tomography (sLORETA), introduced by Pascual-Marqui (2002) is an interesting tool for modeling spatially distinct source activities in the absence of prior knowledge of the generators' anatomical location. Standardized weighted low-resolution electromagnetic tomography (swLORETA) is a recent modification of sLORETA, which compensates for variations in the sensors' sensitivity to current sources at different depths (Palmero-Soler et al., 2007). Hence, our secondary objective was to use swLORETA to determine how the cortical generators of N100 and P200 components of the AEP were modulated by the nature type of attention paid to the prepulse.

To this end, we combined an active acoustic PPI paradigm with a visual CPT as in Rissling et al. (2007) and studied inhibition of the cortical responses by recording the N100 and P200 components of the AEP. In contrast to previous studies using active PPI paradigms, we used three types of prepulse in the present work: one on which the subject's attention was voluntary focused (to-be-attended), one on which the subject's attention has not to be focused (to-be-ignored) and a third one that involuntarily captured the subject's attention (unexpected). To control for the attentional resources allocated to each type of prepulse, the event-related potential P300 component was recorded. It has been demonstrated that the amplitude of P300 varies according to the amount of attentional resources allocated to the task (Donchin et al., 1986). In the present study, we expected that the to-be-attended prepulse (involved in goal-directed attention) would be associated with the late, centroparietal P300 component which is observed when an infrequent, task-relevant stimulus is presented, whereas the unexpected prepulse (involved in stimulus-driven attention) would be associated with the early, frontocentral P300 which occurs when the subject is presented with an unexpected stimulus in the absence of any instructions (Squires et al., 1975). We hypothesized that the degree of inhibition of cortical responses to the pulse would depend on the prepulse type, with (i) greater inhibition after a to-be-attended prepulse or an unexpected prepulse than after a to-be-ignored prepulse and (ii) greater inhibition after a to-be-attended prepulse than after an unexpected prepulse. We also assumed that each type of prepulse would differentially modulate the N100 and P200 components and the latter's generators.

2. Methods

2.1. Participants

The study populations comprised 26 right-handed, healthy volunteers (10 female, 16 male; mean (*SD*) age: 22.4 (*2.7*) years). According to self-reports, none of the participants had a history of neurological or psychiatric disorders. None was taking psychoactive drugs, including tobacco or cannabis. Subjects with a history of visual or auditory impairments were excluded from the study. All participants gave their informed consent to participation in the study. The study protocol was approved by the local institutional review board ("Comité de Protection des Personnes Nord-Ouest IV", reference 2008-006842-25).