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Research Report

P300 amplitude alterations during inhibitory control in persons with Mild Cognitive Impairment

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ABSTRACT

Deficits in executive function are highly noticeable in Alzheimer's disease, and recent behavioral studies have shown that such deficits – particularly during inhibitory control – can also be found in persons with Mild Cognitive Impairment (MCI). Thus, the objective of this study was to investigate behavioral and electrophysiological correlates of inhibitory control in persons with MCI. A group of persons with MCI and a group healthy older adults performed a Go/NoGo task while electroencephalogram was recorded. Our results revealed that persons with MCI performed less accurately than healthy controls during the Go and NoGo conditions. In addition, we found reduced P300 amplitudes during Go and NoGo conditions relative to healthy older adults. Our results suggest that neurocognitive mechanisms associated with target detection and evaluation (Go P300) and response inhibition (NoGo P300) are compromised in persons with MCI.

1. Introduction

Mild Cognitive Impairment (MCI) is defined as a state of subjective and objective impairment in memory or some other aspect of cognition that is not severe enough to constitute dementia (Petersen, 2004). MCI may often be a prodromal stage of Alzheimer's disease: approximately 10–15% of persons with MCI transition to Alzheimer's disease, in contrast to a 1–2% conversion rate in the healthy older adult population (Petersen et al., 2001, Petersen et al., 2009). Thus, MCI research allows for the study of cognitive decline prior to the onset of dementia.

Executive function is a broad term that refers to several cognitive abilities thought to control and guide goal-oriented behavior. These cognitive abilities can include planning, behavior initiation, self-monitoring, decision-making, inhibitory control, abstract thinking, cognitive flexibility, divided attention, and multitasking (Alvarez and Emory, 2006, Chan et al., 2008). Inhibitory control may be defined as the process that suppresses access to irrelevant information and inappropriate responses that would disrupt the completion of the task at hand (Dempster, 1992, Bjorklund and Hasnishfeger, 1995). Inhibitory control is a crucial component of the executive function system because it allows for the completion of more complex tasks (Okonkwo et al., 2006), and is important for attention, working memory, social competence and emotion regulation (Kochanska et al., 1996). A deficit in inhibitory control is one of the most noticeable impairments in early Alzheimer's disease (Amieva et al., 1998, Amieva et al., 2004, Belleville et al., 2006). Some studies of MCI have not found differences in inhibitory control in persons with MCI relative to healthy older adults (Belleville et al., 2007, Zhang et al., 2007) while others have shown that MCI participants exhibit deficits in inhibitory control (Wylie et al., 2007, Bélanger and Belleville, 2009, Bélanger et al., 2010). In a comprehensive study that investigated multiple subdomains of executive function, severe impairments in inhibitory control were observed in persons with MCI, while mild impairments were observed in other domains, including divided attention, verbal fluency, and planning (Johns et al., 2012).

The conflicting results observed in inhibitory control studies may be due task complexity. For example, Duong et al. (2006) found that deficits during inhibitory control were salient during a modified version of the Stroop test but not during the classic version. In the classic version of the Stroop test, participants are presented with a congruent and an incongruent condition. In the

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congruent condition, they are asked to name a colour (e.g., a red circle) whereas in the incongruent condition, they are asked to read a colour that is printed in a different colour (e.g., the word "red" in blue ink). An interference effect is observed when comparing congruent and incongruent trials; that is, slower reaction times and lower accuracy are observed for incongruent than congruent trials. Duong et al.'s findings revealed no interference score differences between persons with MCI and healthy older adults during this test. However, in a modified version that required semantic processing, inhibition differences between persons with MCI and healthy older adults were salient. In their modified version of the Stroop, participants were presented with line drawings of animals along with letter strings below the figure. In the congruent condition, the word named the animal, while in the incongruent condition the word was not the name of the animal. When presented with the stimuli, participants were asked to name the drawing as fast as possible. Their results revealed that persons with MCI made more errors than healthy older adults during the incongruent condition. Thus, their results suggest that inhibitory control is more difficult for persons with MCI when other cognitive operations (in this case, semantic search) are required.

In another study that used a modified version of the Stroop test (Bélanger et al., 2010), inhibitory control deficits were also apparent in persons with MCI. Unlike in the classic version of the Stroop test, which presents the congruent and incongruent conditions in separate blocks, Bélanger et al. used a more complex measure of inhibitory control, which presented congruent and incongruent trials randomly intermixed. Presenting the trials in this manner allows for a more sensitive measure of interference. Their results revealed that the reaction time difference between congruent and incongruent trials was larger in the MCI group than in the healthy older adult group. Finally, in another modified version of the Stroop test that required participants to perform arithmetic in the incongruent condition (e.g., perform addition when seeing "$6 \times 2 = \_\_$"), persons with MCI exhibited greater interference effects than healthy older adults (Zamarian et al., 2007).

Semantic inhibition also seems to be unimpaired in persons with MCI, as measured by the Hayling test (Belleville et al., 2007). However, when the test is modified, differences between persons with MCI and healthy older adults are apparent (Bélanger and Belleville, 2009). In the Hayling test, participants are asked to complete sentences with a single word; the test has two different conditions: an automatic condition, where they are asked to provide the appropriate word that completes the sentence (e.g., "I eat soup with a *spoon*"), or an inhibition condition, where they are asked to complete the sentence with an unrelated word (e.g., "I eat soup with a *sock*"). Similar to the classic Stroop test, the classic version of the Hayling test presents the condition types in separate blocks. In order to avoid the use of strategies in the inhibition condition, Bélanger and Belleville modified the test by presenting the automatic and inhibition conditions randomly intermixed. Their findings revealed that persons with MCI responded less accurately than healthy older adults in the inhibition condition.

Another test of inhibitory control is the Flanker task. In this task, participants are asked to indicate the direction of an arrow situated in the center of a screen while ignoring flanking distractors positioned of the sides of the central stimulus. The task has a neutral condition (e.g., ♦ ♦ → ♦ ♦), a congruent condition (e.g., → → → → →), and an incongruent condition (e.g., ← ← → ← ←). Similar to the modified versions of the Stroop and Hayling tests (Bélanger and Belleville, 2009, Bélanger et al., 2010), the conditions in the Flanker task are presented randomly intermixed. Consistent with other studies, the magnitude of reaction time difference between congruent and incongruent trials was larger in the MCI group than in the healthy older adult group (Wylie et al., 2007).

Inhibitory control deficits in persons with MCI have also been found during the Go/NoGo task (Dwolatzky et al., 2003, Cid-Fernández et al., 2014), which is also considered to be a complex executive function task (Rubia et al., 2001). In a Go/NoGo task, participants are presented with two types of stimulus: Go trials, which require a motor response, and NoGo trials, which require the withholding of a motor response. According to Rubia et al. (2001), tasks that require motor inhibition are a more direct measure of inhibitory control because they involve "all-or-none decisions about action or non-action" (page 251) while other tasks require the control of interfering information that is irrelevant to the task at hand (e.g., Stroop test, Flanker task). Given that inhibitory control is the executive function sub-domain that is most affected in persons with MCI (Johns et al., 2012), the Go/NoGo task constitutes an ideal task for investigating mechanisms of inhibitory control in this population.

The electrophysiological correlates of inhibitory control can be studied with Event-Related Potentials (ERPs), which are derived from electroencephalographic recordings and thus provide very high temporal resolution. The major ERP components elicited during the Go/NoGo task are the N200 and P300. The N200 –a negative going wave peaking between 200 and 350 ms post-stimulus onset– is generated during the NoGo condition. Although its role is not yet clear, this component is thought to be associated with decision processes related to response inhibition (Bokura et al., 2001, Dong et al., 2009) or with conflict detection and response preparation (Donkers and van Boxtel, 2004, Randall and Smith, 2011). The P300 –a positive wave peaking between 300 and 600 ms post-stimulus onset– is larger in amplitude during the NoGo than the Go condition (Bokura et al., 2001). This effect is associated with motor response inhibition efficiency (Pfefferbaum et al., 1985, Roberts et al., 1994, Falkenstein et al., 1995).

To our knowledge, only one ERP study has investigated inhibitory control mechanisms in persons with MCI using the Go/NoGo task. In that study, the Go/NoGo task was mixed with a passive auditory oddball task (Cid-Fernández et al., 2014). Participants were presented with auditory-visual stimuli pairs and were asked to ignore the auditory oddball (which consisted of a series of repetitive auditory stimuli, intermixed with infrequent stimuli), only attending to the visual Go/NoGo stimuli. For the visual stimuli, they were asked to respond to numbers and letters (Go condition) and to inhibit their response to triangles (NoGo condition). Their results revealed reduced NoGo N200 amplitudes in persons with MCI relative to healthy older adults. However, no P300 differences during Go/NoGo were observed between persons with MCI and healthy older adults.

Other ERP studies have investigated inhibitory control during tasks that require the control of interference of irrelevant information. For example, Wang et al. (2013) found reduced N200 and P300 amplitudes in persons with MCI when compared to healthy older adults while performing a Flanker task, suggesting impairment in mechanisms associated with conflict detection and motor response inhibition. In addition, another research group investigated cognitive control during a Simon task (Cespón et al., 2013, 2015), which is a stimulus-response compatibility paradigm (i.e., in the incongruent condition the stimulus and response are incompatible; for example, a red dot appears on the left hand side of the screen but participants are asked to press a key with their right hand when they see a red dot). This task elicits ERP components that are different to those elicited during the Go/NoGo. The components associated with the Simon task are the N200 central contralateral (N2cc), which is associated with cognitive control exerted during withholding a response based on stimulus position (Praamstra and Oostenveld 2003, Praamstra, 2006, 2007), the N200 posterior-contralateral (N2pc), associated with attentional shifts towards relevant stimuli (Luck and Hillyard, 1994, Woodman and