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Cognitive function predicts neural activity associated with pre-attentive temporal processing ☆

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ABSTRACT

Temporal processing, or processing time-related information, appears to play a significant role in a variety of vital psychological functions. One of the main confounds to assessing the neural underpinnings and cognitive correlates of temporal processing is that behavioral measures of timing are generally confounded by other supporting cognitive processes, such as attention. Further, much theorizing in this field has relied on findings from clinical populations (e.g., individuals with schizophrenia) known to have temporal processing deficits. In this study, we attempted to avoid these difficulties by comparing temporal processing assessed by a pre-attentive event-related brain potential (ERP) waveform, the mismatch negativity (MMN) elicited by time-based stimulus features, to a number of cognitive functions within a non-clinical sample. We studied healthy older adults (without dementia), as this population inherently ensures more prominent variability in cognitive function than a younger adult sample, allowing for the detection of significant relationships between variables. Using hierarchical regression analyses, we found that verbal memory and executive functions (i.e., planning and conditional inhibition, but not set-shifting) uniquely predicted variance in temporal processing beyond that predicted by the demographic variables of age, gender, and hearing loss. These findings are consistent with a frontotemporal model of MMN waveform generation in response to changes in the temporal features of auditory stimuli.

1. Introduction

Temporal processing refers to the act of processing time-related information and is thought to play a significant role in a variety of cognitive and psychological processes including speech, language, and even one's subjective well-being (Wittmann & Paulus, 2008). The construct of temporal processing is complex and associated with a variety of processes from simple sensory perceptions of time to more elaborate higher-level concepts of temporal reproduction, time estimation, and even processes needed to remember and engage in future activities (e.g., time-based prospective memory) (Barkley, Murphy, & Bush, 2001; Mäntylä, Carelli, & Forman, 2007). Given the plethora of tasks subsumed under the construct of temporal processing, it is not surprising that there have been conflicting findings regarding the neural substrates of this construct and the relationships between temporal processing and other cognitive processes (Coull, Vidal, Nazarian, & Macar, 2004; Harrington & Haaland, 1999).

One of the main confounds to assessing the basic neural underpinnings of temporal processing is that most measures of timing involve other supporting cognitive processes, such as decision making or working memory (Paul et al., 2011). The recruitment of these other cognitive processes has made identifying neural substrates associated with timing difficult. One method of assessing temporal processing that has emerged over the past decade is the use of pre-attentive electrophysiological methods. Specifically, a pre-attentive event-related brain potential (ERP) waveform, the mismatch negativity (MMN), has been utilized to measure neural activity elicited by a temporal "deviant" in order to assess timing abilities in the absence of attention demands (Davalos, Kisley, Ellis, & Freedman, 2003; Grimm, Widmann, & Schröeger, 2004; Kisley et al., 2004; Näätänen, Jiang, Lavikainen, Reinikainen, & Paavilainen, 1993; Näätänen, Syssoeva, & Takegata, 2004; Pakarinen, Takegata, Rinne, Huotilainen, & Näätänen, 2007; Tse & Penney, 2006). More specifically, neural responsivity to a deviation in either the duration of a stimulus or in the inter-stimulus interval (ISI) between stimuli is compared to neural activity associated with a standard duration stimulus or standard

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ISI, respectively, which is presented with much greater frequency. The difference between these measures of neural activity is calculated and known as the MMN waveform. It is measured passively by engaging the participant in a distraction task, such as watching a movie, while auditory stimuli are presented and brain responses are measured via scalp electrodes. While the MMN is not entirely insusceptible to certain types of attentional effects (Woldorff, Hackley, & Hillyard, 1991), it is an ERP that allows for the measurement of neural responses to timing stimuli in the absence of motor response, motivational demands, decision making and other potential cognitive demands that may affect temporal processing performance. Temporal deviation MMN paradigms have been used with a variety of clinical populations for whom traditional behavioral timing tasks may be difficult (e.g., schizophrenia) (Davalos, Kisley, Polk, & Ross, 2003; Michie, 2001; Todd, Michie, & Jablensky, 2003). In addition, these paradigms have been used to study development of temporal processing abilities from infancy to late adulthood (Brannon, Libertus, Meck, & Woldorff, 2008; Brannon, Roussel, Meck, & Woldorff, 2004; Cheour, Kushnerenko, Ceponiene, Fellman, & Näätänen, 2002; Gomes et al., 1999). Findings within these populations suggest, albeit indirectly, that pre-attentive temporal processing may be dependent on intact frontal lobe functioning.

While temporal deviance MMN studies have been quite useful for assessing perceptual timing abilities, there has been relatively little research directly addressing either the specific neural substrates associated with these event-related potentials or the relationship between the MMN and cognitive variables. It has been argued that the earliest neural process involved in the MMN relates to detection of the change in stimuli by the auditory cortices. This early perceptual or "pre-attentive" process is proposed to precede a frontal-cortex activation associated with directing conscious attention to the change in the stimuli (e.g., a tone duration or ISI which is different than the preceding tone duration or ISI) (Alho et al., 1998; Näätänen, Jacobsen, & Winkler, 2005; Rinne, Alho, Ilmoniemi, Virtanen, & Näätänen, 2000; reviewed by Deouell, 2007; Näätänen, Kujala, & Winkler, 2011; Winkler, 2007). Neuroimaging studies that have sought to identify the neural substrates of temporal processing utilizing stimuli presented in a manner similar to the temporal deviance MMN paradigms have generally found early processing in the superior temporal gyrus (STG) followed by frontal activation, specifically the inferior, medial, and superior frontal gyri in addition to the dorsolateral prefrontal cortex (DLPFC) (Molholm, Martinez, Ritter, Javitt, & Foxe, 2005; Rinne et al., 2000; Rinne, Degerman, & Alho, 2005; Tregellas, Davalos, & Rojas, 2006). Other studies using lesion methodology (Alain, Woods, & Knight, 1998), positron emission tomography (Müller, Jüptner, Jentzen, & Müller, 2002), and event-related optical imaging (Tse, Tien, & Penney, 2006; Tse & Penney, 2007) suggest involvement of a frontotemporal network in the generation of the MMN in response to temporal deviation.

The recruitment of the prefrontal cortex in the temporal deviation MMN suggests that "pre-attentive" or "perceptual" timing may share neural substrates with higher order cognitive processes that are also dependent on the frontal lobe (i.e., "executive functions"). Studies that have explored the potential relationship between perceptual timing and executive functioning have typically focused on the duration MMN within populations that exhibit executive dysfunction or have known frontal cortical dysfunction (e.g., schizophrenia) (Light & Braff, 2005; Toyomaki et al., 2008). The question remains, therefore, whether perceptual timing is associated with executive functioning and/or other cognitive functions in healthy individuals.

There appears to be a growing consensus that timing abilities, or at least temporal processing skills assessed behaviorally, are necessary for a number of tasks described as executive functioning. Mäntylä et al. (2007), among others, argue that most goal-directed activities require some form of temporal integration and monitoring of action (Fuster, 1993, 2002; Norman & Shallice, 1986). Research examining this question, however, has been limited to pediatric populations primarily, with only a few studies including young adults. The findings have been mixed, with only select executive tasks relating to time processing skills. Specifically, study findings have suggested that those types of executive tasks that depend primarily on the prefrontal cortex appear to be more closely related to time processing abilities. For example, tests of inhibition and updating show robust relationships to behavioral indices of timing (Barkley, 1997; Mäntylä et al., 2007). A number of investigators have noted a relationship between increased errors on response inhibition tasks and deficits in time reproduction (Gerbing, Ahadi, & Patton, 1987; Montare, 1977). Specifically, those with poor inhibition generally make more timing errors than those with good inhibition. However, it has been argued frequently that attentional abilities may be at the root of both inhibition and timing deficits (Barkley, Edwards, Laneri, Fletcher, & Metevia, 2001; Brown, 1985; Zakay, 1992). It is therefore questionable whether the relationship between timing and response inhibition would persist if the attentional demands were removed from the timing task (e.g., through the use of a pre-attentive measure, such as temporal deviance MMN). In contrast, executive tasks focusing on shifting within the task (e.g., from color to number) have not demonstrated the same relationship with timing abilities. Mäntylä et al. (2007) have argued that shifting is different from other executive functioning tasks as the parietal cortex plays a larger role in shifting than the prefrontal cortex. This argument has been supported both via neuropsychological studies and neuroimaging studies (Collette & Van der Linden, 2002; Gehring & Knight, 2002).

The question remains whether the relationship between executive functioning and temporal processing reflect shared neuroanatomical substrates *only* when timing is assessed behaviorally. Given that most behavioral timing tests engage working memory, decision making, and other cognitive processes, it is unclear whether it is those processes that drive the relationships between executive functioning and temporal processing or basic timing skills themselves. The current study seeks to examine whether temporal processing, measured in the absence of other cognitive demands (via ISI-based MMN), is also significantly related to cognitive tasks dependent on the prefrontal cortex in a healthy population.

To date, only one study has addressed the potential relationship between temporal processing, as measured by the MMN waveform, and cognitive abilities directly. This study (Kisley, Davalos, Engleman, Guinther, & Davis, 2005) found that in a sample of older adults auditory-verbal acquisition, planning time on a tower task, and accuracy of a conditional reaction time measure were related to MMN amplitude in response to temporal deviation (specifically ISI-deviance). The direction of these relationships was such that more intact cognition was related to greater neural activity associated with pre-attentive temporal processing. However, in addition to utilizing only a portion of the available older adult group for that analysis, the study did not control for demographic variables that may impact MMN amplitude and cognitive function, including gender and sensory loss (e.g., hearing threshold).

Given the paucity of research exploring the relationship between pre-attentive measures of temporal processing and cognitive variables in a healthy adult sample, this study sought to expand upon the findings of Kisley et al. (2005) by studying the relationship between pre-attentive temporal processing and cognitive functions associated with a frontotemporal neural network