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Neurophysiological markers of alert responding during goal-directed behavior: A high-density electrical mapping study

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The ability to dynamically modulate the intensity of sustained attention (i.e., alertness) is an essential component of the human executive control system, allowing us to function purposefully in accordance with our goals. In this study we examine high-density ERP markers of alert responding during the fixed sequence sustained attention to response task ($SART_{fixed}$). This paradigm has proven to be a sensitive clinical metric in patient populations with deficits in their ability to sustain attention (e.g., attention deficit hyperactivity disorder). In this task subjects withhold a button press to an infrequent no-go target ('3') embedded within a predictable sequence of numbers ('1' to '9'). Our data reveal a complex pattern of effects across the trial sequence of the SART, with clear contributions from frontal and parietal cortices to sustained attentional performance. Over occipito-parietal regions, early visual attention processes were increased during trial 2 (i.e., trial in which the digit '2' was presented) and trial 3, giving rise to the so-called selection negativity (SN). Two prominent late components were manifest during trial 2: LP1 (550–800 ms) and LP2 (850–1150 ms) over occipito-parietal and central sites. We interpret the LP1 component on trial 2 as reflecting retrieval of the task goal and the subsequent LP2 as reflecting competition between the currently relevant go response and the subsequent no-go response. On trial 3, an enhanced "no-go N2" (250–450 ms) was seen fronto-centrally in the absence of the "no-go P3" that typically follows. Fronto-polar activity was also seen across all trials and may be indicative of subgoal processes to integrate the association between stimulus and goal. Prior to a lapse of attention (i.e., failure to inhibit a response to "3") the LP1 was significantly attenuated on the preceding trial 2 indicating a failure of anticipatory goal-directed processing. The results are discussed in terms of models of sustained attention involving frontal and parietal cortices.

Keywords: Sustained attention; Go/no-go task; High-density ERPs; Lapses of attention; Early visual attention; Selection negativity; Goal-directed behavior; Delayed intentions

Introduction

A driver approaches a crossroads, notes the red light and pulls to a stop. Harried and worn out from a fairly dismal day at the office, his eyes are fixed on the lights; his only thoughts are for home, slippers, a Manhattan and an evening in front of the TV. The lights, after what feels like an age, change back to green and he hits his accelerator, relieved to be on his way again. Unfortunately, he has somehow neglected to notice that the car in front of him has yet to pull away. This, he ultimately understands, only as his car's forward progress is all too abruptly arrested by the rear fender of the car in front. Such momentary lapses in attentional re-allocation are unfortunately all too commonplace in life. Avoiding them relies particularly on our ability to sustain attention and to flexibly redeploy our attention to additional environmental factors that might be relevant. This latter function often requires reactivation of a subgoal, outside the immediate spotlight of attention. That is, the primary goal above is to go when the light is green, but an important subgoal is to ensure that there is nothing in the way. Although the example above is of a relatively benign circumstance where a lapse in attention results in an inappropriate response to current environmental circumstances, such lapses can also have catastrophic consequences. For example, a considerable proportion of major road traffic accidents can be attributed to momentary lapses in goal maintenance—that is, distraction or lapses in sustained attentional mechanisms (see, e.g., National survey of distracted and drowsy driving attitudes and behaviors: 2002[1]). As such, it is of great interest to understand the neural mechanisms that support sustained attention and subgoal activation.

Sustained attention requires an intrinsic maintenance of the alert state in the absence of exogenous inputs (Posner and DiGirolamo,

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[1] The Gallup organization (2002). National Survey of Distracted and Drowsy Driving Attitudes and Behaviors: 2002, http://www.nhtsa.dot.gov/people/injury/drowsy_driving1/survey-distractive03/index.htm.

2000; Posner and Peterson, 1990; Sturm et al., 1999). Lapses of sustained attention occur when there is a transient reduction in the alert state that can give rise to momentary loss of endogenous control over behavior. Recent positron emission tomography (PET) studies (Sturm et al., 1999, 2004) suggest that an extended right hemisphere network is involved in sustained attention including the right anterior cingulate, the right dorsolateral prefrontal cortex, the right inferior parietal lobule with projections to the thalamus and noradrenergic brainstem targets. Sturm and colleagues propose that right hemisphere brain structures exercise top-down control, via the thalamus, on noradrenergic structures in the brainstem.

A task that has proven very effective in assessing this type of attentive responding is the sustained attention to response task (SART) (Manly et al., 1999, 2002, 2003; Robertson et al., 1997). In one version of this task, a predictable series of single digits are presented (1–9) and subjects are required to make a response to each number (go trials) with the exception of the number 3 (no-go trial). A PET study showed that this task increased activation in both the right dorsolateral prefrontal cortex and the right superior/posterior parietal cortex compared to a more challenging version of the SART in which the numbers were presented randomly (Manly et al., 2003). These findings suggest that right fronto-parietal regions are responsible for maintaining a goal-directed focus in unarousing contexts where exogenous stimuli are not present to increase alertness through novelty, demand or perceived difficulty (Robertson and Garavan, 2004).

The SART has also proven to be a sensitive clinical measure, discriminating between traumatically brain injured (TBI) patients and healthy control subjects (Dockree et al., 2004; Manly et al., 2003; McAvinue et al., 2005; Robertson et al., 1997) and between ADHD children and controls (Shallice et al., 2002). Clinical groups exhibit increased errors of commission (false presses on the 3) during this task and fail to show anticipatory slowing on the trials before the upcoming no-go trial, a general finding in subjects who are successful at this task (Dockree et al., 2004), suggesting a loss of endogenous control at strategically important points during the task. Although, the functional anatomical correlates of the SART have been investigated (Fassbender et al., 2004; Manly et al., 2003; O'Connor et al., 2004), only one study (Dockree et al., 2004) has examined the electrophysiological dynamics during the task. In the latter study, alpha (~10 Hz) desynchronization was observed in healthy controls before the no-go trial. By contrast, TBI patients failed to show this modulation. This state of desynchronization has been associated with increased attentive processing (Klimesch et al., 1998; Mulholland, 1965; Pfurtscheller and Lopes da Silva, 1999) in the transition from a relaxed to an alert state, and with anticipatory preparation of visual cortices during selective attention tasks (Foxe et al., 1998; Fu et al., 2001; Worden et al., 2000). No studies to date have characterized the broad-band ERP componentry of the SART in neurologically normal adults.

In the present study, we utilize the excellent temporal resolution of high-density electrical mapping to examine the spatiotemporal dynamics of electro-cortical activity during the fixed sequence SART (hereafter referred to as the $SART_{fixed}$). Our first aim was to examine event-related potentials (ERPs) and their topographical distributions during periods of accurate sustained attention performance described as 'successful runs' of trials 1 through 9 (i.e., when subjects successfully withhold responses to trial 3). In previous investigations of the $SART_{fixed}$, adequate characterization of errors of commission has not been possible due to the rarity of their occurrence. In this study we addressed this limitation by testing subjects over the course of a full day (with regular breaks) so that adequate numbers of errors were committed. A criticism of this approach pertains to the ecological validity of the task. Can long-term engagement with a laboratory task over ~108 min relate to a more naturalistic situation? We argue that the task has features in common with everyday scenarios that require this kind of sustained attentional effort over long periods. For example, taking a long distance trip in the car interspersed with regular breaks may require similar periods of sustained attention to critical events during largely routine behavior. The SART also correlates with everyday reported cognitive failures in patients with traumatic brain injury (Robertson et al., 1997) suggesting that the propensity for attentional lapses on the task is related to greater everyday slips of attention.

Accordingly, as a second aim, we conducted an exploratory analysis of correct withholds and commission errors as well as the trials that preceded and followed these responses. The current study, in neurologically healthy subjects, will provide an important baseline for future understanding of clinical populations and their documented sustained attention deficits on this task. We acknowledge that we would not be able to test clinical groups for long periods of time due to excessive fatigue. However, in these groups the number of errors mounts up much more rapidly, circumventing the need to test for long periods.

We outline a number of predictions regarding the ERP componentry during the critical anticipatory period before the upcoming no-go target that will serve as important markers for alert responding during the task. On trial 2, we predict that early visual attentional processes will be mobilized because of the significance of this trial as an upcoming cue for the critical target trial. The most commonly reported attentional modulation is that of the P1 and N1 components that show increased amplitudes when spatial attention is directed to the stimulus location (i.e., stimuli are validly cued) compared to when it is directed elsewhere (Mangun and Hillyard, 1991; Mangun et al., 1987). In contrast, selectively attending to relevant visual features has been shown to elicit the so-called selection negativity (SN) (Anllo-Vento and Hillyard, 1996; Harter et al., 1984; Kenemans et al., 1993; Smid et al., 1999; Molholm et al., 2004). Although the $SART_{fixed}$ is not a selective visual feature attention paradigm per se, it is reasonable to propose that similar processes of visual selection might be engaged as the relevance of trials in the sequence increase before the critical target trial. Indeed, previous work has demonstrated that increased ventral-stream visual object-recognition processes underlying SN can be elicited by relevant visual stimuli when relevance is defined on the basis of a non-spatial feature(s) (Anllo-Vento and Hillyard, 1996; Harter et al., 1984; Kenemans et al., 1993; Smid et al., 1999).

We further predict that the recollection of the task goal ("withhold response to 3") will be critical on trial 2. Research investigating the dynamics of prospective remembering (West et al., 2001; West and Krompinger, 2005) has shown that the realization of a delayed intention is associated with two ERP modulations: an N300 and a "prospective positivity". They propose that the N300 is associated with detection of prospective memory cues and is seen as a phasic negativity over occipito-parietal scalp between 300 and 500 ms. Additionally, the later prospective positivity, seen as a broadly distributed positivity (500–1000 ms) over parietal areas, may reflect neural processes