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Sustained attention abnormalities in breast cancer survivors with cognitive deficits post chemotherapy: An electrophysiological study

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HIGHLIGHTS

- Our study examined if the ability to maintain sustained attention could be a feature of the cognitive difficulties reported by some breast cancer survivors (BCS).
- We found that BCS were less likely to maintain attention towards the task, and displayed reduced P3 amplitude to task relevant stimuli relative to healthy controls.
- This data underscores the utility of a new combination of laboratory-based measures for assessing self-reported attentional impairments in BCS.

ABSTRACT

Objective: Many breast cancer survivors (BCS) report cognitive problems following chemotherapy, yet controversy remains concerning which cognitive domains are affected. This study investigated a domain crucial to daily function: the ability to maintain attention over time.
Methods: We examined whether BCS who self-reported cognitive problems up to 3 years following cancer treatment ($n = 19$) performed differently from healthy controls (HC, $n = 12$) in a task that required sustained attention. Participants performed a target detection task while periodically being asked to report their attentional state. Electroencephalogram was recorded during this task and at rest.
Results: BCS were less likely to maintain sustained attention during the task compared to HC. Further, the P3 event-related potential component elicited by visual targets during the task was smaller in BCS relative to HC. BCS also displayed greater neural activity at rest.
Conclusions: BCS demonstrated an abnormal pattern of sustained attention and resource allocation compared to HC, suggesting that attentional deficits can be objectively observed in breast cancer survivors who self-report concentration problems.
Significance: These data underscore the value of EEG combined with a less traditional measure of sustained attention, or attentional states, as objective laboratory tools that are sensitive to subjective complaints of chemotherapy-related attentional impairments.

1. Introduction

Cognitive impairments are commonly reported by breast cancer survivors (BCS) who have undergone post-operative adjuvant chemotherapy, with a reported prevalence of 17–75% (Ahles et al., 2002; Brezden et al., 2000; Ganz et al., 2013; Kreukels

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et al., 2006; Schagen et al., 1999, 2001; van Dam et al., 1998). These cognitive complaints are associated with reduced quality of life and emotional well-being (van Dam et al., 1998; Schagen et al., 1999; Ahles et al., 2002), which highlights the importance of establishing objective measures of these deficits and their underlying neural mechanisms. While recent meta-analyses found a small to medium effect of chemotherapy in the post-treatment period on verbal and visuospatial abilities (Jim et al., 2012) as well as memory and attentional abilities (Lindner et al., 2014), research has yet to converge on a reliable profile of these cognitive impairments (e.g., Jansen et al., 2011; Kreukels et al., 2005, 2006, 2008a,b; Lepage et al., 2014; Quesnel et al., 2009; Tager et al., 2010; Wefel et al., 2015). Thus far, the focus has been on identifying a profile of deficits as indexed by a wide range of neuropsychological tests covering multiple sensory-motor and cognitive domains (Jansen et al., 2011; Quesnel et al., 2009; Tager et al., 2010; Wefel et al., 2011), yet to date this has lacked specificity in determining the effects of chemotherapy on a particular cognitive function. Despite concentration problems being one of the most common cognitive complaints by BCS (van Dam et al., 1998; Schagen et al., 1999), few studies have specifically addressed post-chemotherapy changes in the ability to maintain attention on the current task.

Sustained attention is an important cognitive domain that is crucial to our daily functioning, and can have a substantial impact on numerous other areas of cognitive function. It serves the purpose of focusing attention over time on a salient, task-relevant input to which neural resources are allocated, while simultaneously disregarding distractors not relevant to the task-at-hand. Recent research has revealed mixed findings regarding attentional abilities in BCS. For instance, Chen et al. (2014) reported that the alerting and executive control aspects of attentional networks were selectively impaired in BCS who have received adjuvant chemotherapy compared to BCS who did not. Likewise, BCS also performed poorly on tasks that require concentration, such as the Digit Span and Digit Symbol tests (Schagen et al., 1999). In contrast, other studies showed intact attentional abilities in BCS (Ahles et al., 2002; van Dam et al., 1998). The inconsistency of these findings may stem from the variety of tasks used to assess attention and the fact that performance on some attention tasks likely involves other cognitive processes that may also be impaired in BCS, including response inhibition and psycho-motor functioning.

In our daily life, successful performance on a task typically requires sustained attention for a time much longer than that used in experimental trials, which require focused attention for relatively short intervals of time and in which performance is evaluated on a trial-by-trial basis. Given a relatively inconsistent correspondence between subjective cognitive complaints and objective cognitive task performance assessed in the laboratory (Ahles et al., 2002; Pullens et al., 2010; Schagen et al., 1999; van Dam et al., 1998), one potential explanation is that BCS can perform competently when they focus their attention on a relatively short laboratory task. Unlike each experimental task within a neuropsychological test battery that typically lasts a few minutes, the completion of a house chore or work assignment generally takes much more time. In losing their concentration as commonly reported (van Dam et al., 1998; Schagen et al., 1999; Kreukels et al., 2006), BCS may also consequently lose their ability to perform their task-at-hand. Accordingly, we aimed to address the potential effects of chemotherapy on the ability to stay on-task for an extended period of time.

Our attention towards an ongoing task naturally waxes and wanes over time. On average, the general population report being off-task or mind wandering around 30–50% of the time, suggesting it is a regularly occurring experience that occupies a notable portion of our mental life (Killingsworth and Gilbert, 2010). In the context of an experiment, mind wandering is characterized as our attention drifting away from the demands of the external environment, or the processing required by the task-at-hand, towards the internal milieu. Converging lines of evidence suggest that mind wandering is associated with an attenuation of a broad array of neurocognitive processing (O'Connell et al., 2009; Barron et al., 2011; Kam and Handy, 2013; Kam et al., 2014). Moreover, there is a robust relationship between mind wandering episodes and performance failure, as observed in both experimental tasks conducted in the laboratory (Smallwood et al., 2003; Cheyne et al., 2009), and our chores and duties in everyday life (Carriere et al., 2008; McVay et al., 2009). The experience of mind wandering and its associated disruption in neurocognitive processing has not been assessed in BCS, and may provide valuable and novel insight into the cognitive complaints reported by BCS.

Given the prevalence and impact of mind wandering on our daily functioning, much research has been devoted to develop a measure that captures this ubiquitous experience and quantifies its frequency of occurrence. The most straightforward manner to investigate mind wandering is to directly ask participants to report their attentional state. This method of experience sampling has been used extensively in the literature in both experimental and observational studies (Smallwood et al., 2003; Christoff et al., 2009; Braboszcz and Delorme, 2011; Kam et al., 2011). Importantly, there is a high correspondence in the reported frequency of mind wandering between these two settings (McVay et al., 2009). In an experimental setting, participants are asked at unpredictable intervals to report their attentional state in the moment while they perform a task. This methodology has been used to demonstrate reliable and replicable differences in neurocognitive functioning between on-task and mind wandering states (Talairach and Tournoux, 1988; Smallwood et al., 2008; Kam et al., 2011, 2014; Kirschner et al., 2012). For instance, this self-report classification of attentional states has been associated with a systematic down-regulation of both sensory (Braboszcz and Delorme, 2011; Kam et al., 2011) and cognitive processing (Kam et al., 2014; Smallwood et al., 2008) during mind wandering states, as well as an up-regulation of activity in the brain's default mode network (Kirschner et al., 2012). Our current understanding of mind wandering and the neural correlates associated with this phenomenon allows us to consider ways in which this experience can be engaged in a non-normative manner in BCS.

The current study aimed to examine whether BCS who report persistent cognitive impairment following adjuvant chemotherapy for breast cancer show an abnormal pattern of sustained attention. To address this question, we measured both the frequency of mind wandering and the extent of cognitive processing of external stimulus as participants performed a sustained attention task. Throughout the task, we occasionally asked participants to report their attentional state as a way to quantify the frequency of mind wandering. We recorded their event-related potentials (ERP) during the task as an objective measure of the extent of cognitive processing of task-relevant stimulus engaged during periods of on-task and mind wandering. Specifically, the P300 ERP component reflects an attention-related cognitive process that involves stimulus evaluation and classification (Polich, 2009). Its amplitude indicates the intensity of neuronal activity reflecting the amount of attentional resources engaged, while its latency indicates the speed and duration of the neural process involved during task performance. Further, we also examined participants' electroencephalogram (EEG) at rest, as it has been linked to variations in cognitive task performance (Finnigan and Robertson, 2011; Stam et al., 2002) and has reliably differentiated healthy individuals from neurological and clinical populations, such as Alzheimer's disease and depression (Babiloni et al., 2013; Thibodeau et al., 2006). Resting EEG can be measured in terms of power within specific