



Research Paper

Pupil response and attention skills in Down syndrome

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ABSTRACT

Down syndrome (DS) is characterized by attentional problems. Little is known about the neural correlates of attention problems in DS due to difficulties in evaluation. Pupil dilation, associated with an increase in cognitive load and locus coeruleus-noradrenaline system activity in humans, is a neurophysiological measurement that may help to characterize such problems. The aim of this research was to investigate the link between a phasic pupil dilation response and target detection in people with DS, as compared with a control group with typical development (TD) matched by mental age. Participants performed an “oddball” task by means of an eye-tracker and a series of neuropsychological tests. Although the DS and control group demonstrated similar attentional skills and behavioral performance, the participants with DS showed greater pupil dilation. This result suggests that people with DS expend extra cognitive effort to achieve performance similar to those with TD. This finding is discussed in light of the attentional process in DS and the reliability of pupil dilation measurement in the study of attention and other cognitive processes in DS.

1. Introduction

1.1. Attention in Down syndrome

Down syndrome (DS), a genetic disorder caused by the presence of all or part of an extra copy of chromosome 21, is the most common cause of genetic intellectual disability (Lubec & Engidawork, 2002). Studies have reported attention deficits beginning in early childhood for people with DS (Clark & Wilson, 2003; Wilding, Cornish, & Munir, 2002). These include problems with the system of vigilance, causing difficulties in producing or maintaining optimal vigilance and performance during an activity (Breckenridge, Braddick, Anker, Woodhouse, & Atkinson, 2013; Cornish, Munir, & Cross, 2001; Lanfranchi, Jerman, Dal Pont, Alberti, & Vianello, 2010; Munir, Cornish, & Wilding, 2000); problems with the system of attentional orientation, causing difficulties in prioritizing sensory input by the selection of specific modalities or locations in the environment (Cornish et al., 2001; Cornish, Scerif, & Karmiloff-Smith, 2007; Munir et al., 2000); and problems of executive attention, causing difficulties in focalizing attention and monitoring target stimuli (Atkinson & Braddick, 2011, 2012; Cornish et al., 2001; Flanagan et al., 2007; Porter & Coltheart, 2006; Wilding et al., 2002). Although these difficulties are found in people with DS, there is also evidence of similar or better performance in certain areas, for example in vigilance, than in people with other intellectual disabilities but comparable mental age (Faught, Connors, & Himmelberger, 2016; Trezise, Gray, & Sheppard, 2008).

Several studies have examined the neurophysiological correlates of attention. A frequently used method for measuring attentional

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responses is the presentation of an “oddball” task while capturing event-related potentials. In this type of task, subjects are exposed to sequences of frequent and infrequent audiovisual stimuli. In active oddball tasks, participants are asked to press buttons in reaction to infrequent target stimuli; in passive tasks, they are only exposed to the stimuli. In passive oddball tasks, people with DS show longer latencies and higher amplitudes than typical development (TD) controls in the P300 component.¹ These results have been associated with slower detection of infrequent stimuli and the need to trigger more neural activation than TD controls (Diaz & Zurrón, 1995; Kakigi, Neshige, Matsuda, & Kuroda, 1994; Kaneko, Ehlers, Philips, & Riley, 1996; Seidl, Hauser, Marx, Freilinger, & Lubec, 1997). Although this electrophysiological research was a pioneering approach in the study of the neural correlates of attention in DS, the use of chronological age controls and passive oddball tasks limited its reach. Comparisons by chronological age could be disadvantageous for participants with DS because of their intellectual disability; they may require greater cognitive effort than those of the same chronological age without intellectual disabilities. A neurophysiological response is difficult to interpret when the experimental task is passive, as it is not correlated with a specific behavioral response. Electroencephalographic signals are also very sensitive to physiological factors such as blinking or muscular movement. It is thus necessary to consider alternative neurophysiological measures.

1.2. Attention and pupil dilation

According to Petersen and Posner (2012), attentional systems are dependent on multiple neural networks and neurotransmission systems. Although they involve the joint activation of multiple neural areas and neurotransmitters, the locus coeruleus and norepinephrine (LC-NA) system contributes actively in all attentional schemes: vigilance (Sturm & Willmes, 2001), orienting (Gabay, Pertzov, & Henik, 2011), and executive attention (Bunsey & Strupp, 1995; Nieuwenhuis, Aston-Jones, & Cohen, 2005). This contribution is related to the widely distributed projections from the LC-NA system throughout the forebrain and the neocortex (Costa & Rudebeck, 2016). Aston-Jones and Cohen (2005) suggested two different modes of LC activity: tonic, where LC activity is elevated but phasic activity is absent, which causes distractibility in the subject; and phasic, where the LC is characterized by bursts of activity and is associated with the presentation of target stimuli and the subject's response to a task.

The interaction of tonic and phasic activity is related to the functioning of each attentional system (Aston-Jones & Cohen, 2005). Phasic activity has been directly correlated to pupil diameter (Aston-Jones & Cohen, 2005). Pupil dilation and the LC-NA system have been linked to task performance, stimulus processing efficiency, and cognitive effort (Aston-Jones & Cohen, 2005; Beatty, 1958; Kahneman, 1973) in typical and atypical populations and different age ranges (for a review, see Karatekin, 2007). Pupil response usually includes two phases: the first is associated with pupillary sphincter relaxation by parasympathetic inhibition (in the interval 600–900 ms), and the second with pupillary contraction by sympathetic activation (after 900 ms) (Steinhauer & Hakerem, 1992). Pupil size has also been correlated with event-related potentials associated with attentional and high-level processing, like that in the P300 and N400² components (Thierry, 2011, 2013; Thierry, 2011, 2013; Seidl et al., 1997). It is thus clear that pupil dilation is a signature of brain and cognitive functioning, perhaps because the LC-NA system causes an increase in arousal levels, and therefore cortical and peripheral activation, that prepares the organism for a reorientation of cortical networks and an adaptive behavioral response (Sara & Bouret, 2012).

1.3. Pupillary Down response in down syndrome

The considerations presented above suggest that the measure of pupillary response could be useful in evaluating attention processes in people with DS. However, visual problems common in the DS population might affect the reliability of pupil measurements. Among people with DS, 20% have strabismus, 40% hyperopia, 14% myopia, 30% astigmatism, 10% nystagmus, and 1% cataracts (Down Syndrome Association, 2006). People with DS who develop Alzheimer's disease also tend to have a smaller number of LC cells (Manaye, McIntire, Mann, & German, 1995; Prasher et al., 1998). Pupil dilation can thus serve as a measure of cognitive processing only for participants without visual problems that affect pupillary response, and for those younger than 40, the approximate age at which people with DS develop Alzheimer's disease (Lott & Head, 2001).

1.4. Aims of the study

This study investigated the link between a phasic pupil dilation response and target detection in DS, compared with a healthy control group matched by mental age, to explore differences in the cognitive effort used to detect target stimuli. We tested participants in a simple active visual oddball task to evaluate the difference in pupil dilation between groups when participants correctly executed the task. Participants were asked to press a button when they saw an infrequent target stimulus. We hypothesized that participants with DS would show behavioral performance similar to that of the control group, but that those with DS would have greater pupil dilation. This result would suggest that participants with DS require greater cognitive effort to achieve similar performance than those with TD with comparable cognitive abilities. Furthermore, if the pupil dynamic is different for target and non-target stimuli, and if it is related to behavioral performance, pupil dilation could be a viable measure for the study of attention in DS. To our knowledge, this is the first study to examine pupil dilation as a measure of attention in DS; it proposes this new approach for

¹ P300 is a positive deflection in voltage with a post-stimulus latency of 250–500 ms (Ruhnau, Schröger, & Sussman, 2016).

² N400 is a negative deflection in voltage with a post-stimulus latency of 400 ms. This component is related to semantic incongruity (Kutas & Hillyard, 1980).

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