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PSYCHIATRY AND PRECLINICAL PSYCHIATRIC STUDIES - SHORT COMMUNICATION

Stimulus-preceding negativity in ADHD

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Abstract Children with ADHD often show disrupted response preparation as indicated by attenuated stimulus-preceding negativity (SPN). This study examined response preparation in a relatively short cue–stimulus interval. No differences in SPN occurred between children with ADHD and their normal peers. A strong positive relationship was found between SPN and mean reaction time in both groups. Children with ADHD are able to mentally prepare themselves for upcoming events in short cue–stimulus intervals.

Keywords ADHD · Event-related potentials · Stimulus-preceding negativity · Contingent negative variation · Neurophysiology · Reaction time

Introduction

Cues that provide information about the timing of upcoming events can speed up response times because cues allow preparation for action. In many cognitive paradigms, cues are provided before the actual stimulus. Children with attention-deficit/hyperactivity disorder (ADHD) benefit from cues, but their reactions to stimuli remain characterized by slower responses compared to their healthy peers despite cues (Johnson et al. 2008). At the neurophysiological level, preparation is reflected by a slow negative component, often called contingent negative variation (CNV; Walter et al. 1964). In longer intervals, the CNV can be subdivided into an early and late phase, reflecting orienting, and expectancy/motor preparation, respectively (Boxtel and Böcker 2004). The late phase of the CNV is a combination of movement-preceding negativity and stimulus-preceding negativity (SPN; Brunia 1988). Attenuation of the CNV in ADHD has been found in both the early part (van Leeuwen et al. 1998), the late part (Johnstone and Clarke 2009), and the entire CNV (Banaschewski et al. 2008), and is regarded as a robust neurophysiological marker of ADHD. In a developmental study, the CNV remained attenuated in adults previously diagnosed with ADHD, while other ERP components showed normalization with development from childhood to young adulthood (Doehnert et al. 2013). In most CNV paradigms, the interval between cue and stimulus is typically around 1.5 s. It is known that children with ADHD perform poorer when the event rate is slow and the failure to allocate more effort during a slow event rate is also visible in the parietal P3 component (Wiersema et al. 2006). Perhaps, the interval of 1.5 s is too long for them to keep a prepared state of mind. Therefore, the question remains whether abnormalities in CNV and task performance could be explained by the relatively long cue–stimulus interval typically employed in CNV paradigms. According to the cognitive energetic model of Sergeant (2005), children with ADHD may have an energetic dysfunction resulting in difficulties with adjusting their energetic state to meet task demands. A longer cue–stimulus interval implies higher task demands, as an optimal energetic state has to be maintained for a longer period. This study aims to explore the relationship between the CNV and task performance in a paradigm that has a relatively short cue–stimulus interval and a normal event rate. To avoid confusion in terminology, we will use the term SPN instead of CNV, as the paradigm differs from classic CNV paradigms with a relatively long cue–stimulus interval.

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Methods

Twenty-four children with a DSM-IV diagnosis of ADHD (20 boys) and 23 normal controls (21 boys), all aged between 8 and 12 years (mean age 10.3 and 10.5 years, respectively), participated. ADHD diagnosis was verified using standardized assessment instruments (DBD, Pelham et al. 1992; DISC-IV, Shaffer et al. 2000). Both parent and teacher ratings for the ADHD group fell within the clinical range on the DBD. Twenty children met the criteria for ADHD combined subtype, three for ADHD inattentive subtype and one for hyperactive subtype. Fifteen children were also diagnosed with ODD. IQ was estimated with two performance and two verbal subtests of the Wechsler Intelligence Scale for Children, third edition (Wechsler 1991). The children's parents gave their written informed consent. The local Ethical Committee of the VU Medical Center approved the study. The task was to judge the pitch of 360 words that were preceded by a visual cue. Mean reaction time (MRT) was the dependent variable. The electroencephalogram (EEG; 0.05–200 Hz, sampling rate 1,000 Hz) was recorded with Scan 4.3 software (Compumedics) with a cap of 60 tin electrodes. EEG signals were off-line re-referenced to the average of both earlobes. Blinks and horizontal eye movements were monitored with electrodes placed at the outer canthi of each eye and below and above the left eye. The ground electrode was placed on the cheek. Impedances were kept below 10 kΩ. After additional filtering (0.05–30 Hz), blinks were corrected using a subtraction algorithm (Semlitsch et al. 1986). The interval between the cue (picture of an ear that blinked in blue for 300 ms) and the auditory stimulus (spoken words) was analyzed. The duration of the interval between the cue onset and the auditory stimulus onset varied between 750 and 850 ms. ISI varied between 3.8 and 4.2 s. Epochs were baseline corrected to a pre-cue interval of −100 and trials containing artifacts exceeding ±100 µV were excluded. The SPN was defined as the mean area in the window −170 ms to 0 ms relative to the auditory stimulus onset, corresponding to a mean interval of 630–800 ms after cue onset and was analyzed at Fz, Cz and Pz. The start of the SPN was defined by the most positive peak at Cz in the window 200 ms to 0 in the grand average of both groups (latency differed by 11 ms between the groups; the mean latency was chosen). For a more detailed description of participants, task design and electrophysiological recordings, the reader is referred to an earlier study (van Mourik et al. 2011). MRT and IQ were analyzed with univariate ANOVAs. SPN was analyzed with repeated measures ANOVA with one between factor, *Group* (ADHD group, control group), and one within factor, *Electrode* (Fz, Cz, Pz). If sphericity occurred, the Greenhouse Geisser correction was applied. Pearson's correlation coefficients were computed between mean reaction time (MRT) and SPN.

Results

Children with ADHD responded slower than normal controls [F (1, 46) $= 5.36$, $p < 0.05$] and had lower IQs [F (1, 46) $= 19.27$, $p < 0.000$]. No correlation between IQ and MRT or SPN was found; thus IQ was not entered as a covariate. For the SPN, no main effect of *Group* was found, nor did *Group* interact with *Electrode*. A main effect for electrode was found [F (2, 44) $= 33.95$, $p < 0.000$]: the SPN was larger (more negative) at Fz and Cz (Fig. 1) compared to Pz [F (1, 46) $= 46.12$, $p < 0.000$; F (1, 46) $= 40.09$, $p < 0.000$ respectively]. The SPN correlated significantly with MRT at Fz [$r = 0.451$, $p = 0.001$], Cz [$r = 0.549$, $p = 0.000$], and Pz [$r = 0.500$, $p = 0.000$] in a positive direction: a more negative SPN was related to faster reaction times. These correlations were also significant in the groups separately except the correlation between Fz and SPN in the control group, which just escaped conventional levels of significance [$r = 0.412$, $p = 0.051$]. Controlling the correlations between the SPN and MRT for age did not affect the main results. The correlation between MRT and SPN at Cz is illustrated in Fig. 2.

Conclusion and discussion

This study shows that SPN can be elicited in tasks with a relatively short interval between cue and stimulus. The strong correlation between SPN and reaction times in both groups lends further support that the observed negativity may be comparable to the late part of the CNV as measured in tasks with a long interval between cue and stimulus. The late part of the CNV has also been found to correlate with MRT (Dhar et al. 2010). A limitation of this study is that we did not

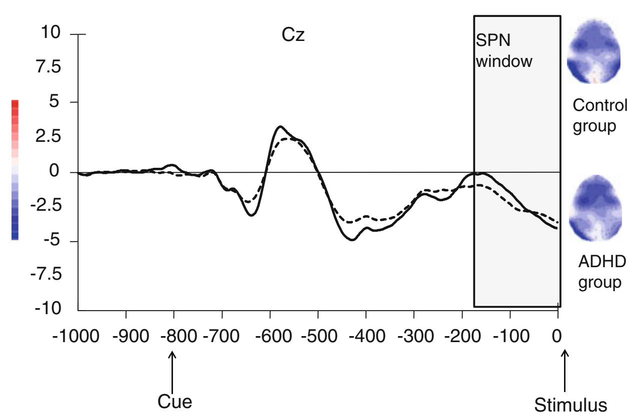

Fig. 1 SPN at Cz in the ADHD and control group. The *solid line* represents the control group, the *dashed line* the ADHD group. Topographic maps show the scalp distribution of the SPN in both groups in the selected window (scale ranges from −5 to 5 µV)

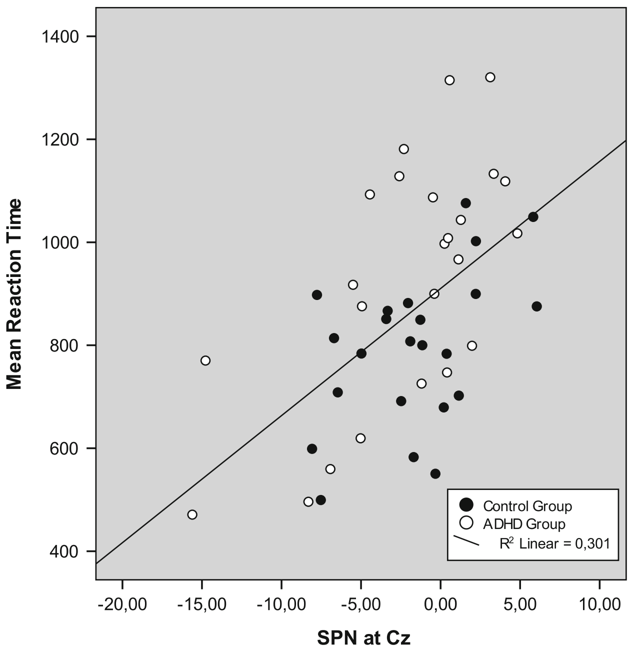

Fig. 2 Correlation between mean reaction time (ms) and the SPN (μV) at Cz

directly manipulate the cue–stimulus interval, which precludes conclusions about the comparability of this component in different cue–stimulus intervals. A second limitation is that ADHD is a heterogeneous disorder and our small subgroup ($n = 24$) may not be representative of the ADHD population, as a large part of the participants had comorbid ODD. It has been shown that the global field power of the cue–CNV microstate was reduced in children with ADHD, but not in children with ADHD + ODD/CD (Banaschewski et al. 2003). Thus, our results should be interpreted with caution. The most important result of this study is the finding that children with ADHD show similar neurophysiological preparation compared with normally developing children and that there is a strong relationship between neurophysiological preparation and reaction times in both groups. In both groups, children benefit from neurophysiological preparation, as expressed by shorter reaction times in children with a larger (more negative) SPN. If the interval between the cue and stimulus is short, children with ADHD seem to be able to prepare themselves equally to children without ADHD probably resulting in better overall task performance compared to studies that use long intervals between cue and stimulus. It should be noted that reaction times were slower in the ADHD group. This slowness could not be attributed to a lack of neurophysiological preparation, but may be due to lapses of attention in the ADHD group resulting in more extreme slow responses.

Conflict of interest The authors declare that they have no conflict of interest.

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