



# Association of Preterm Birth With Attention-Deficit/Hyperactivity Disorder–Like and Wider-Ranging Neurophysiological Impairments of Attention and Inhibition

Anna-Sophie Rommel, PhD, Sarah-Naomi James, MSc, Gráinne McLoughlin, PhD, Daniel Brandeis, MD, PhD, Tobias Banaschewski, MD, PhD, Philip Asherson, MD, PhD, Jonna Kuntsi, PhD

**Objective:** Preterm birth has been associated with an increased risk of attention-deficit/hyperactivity disorder (ADHD)–like symptoms and cognitive impairments similar to those seen in ADHD, including attention and inhibitory control difficulties. Yet data on direct comparisons across ADHD and preterm birth on cognitive-neurophysiological measures are limited.

**Method:** We directly compared 186 preterm-born adolescents to 69 term-born adolescents with ADHD and 135 term-born controls on cognitive-performance and event-related potential measures associated with attentional and inhibitory processing from a cued continuous performance test (CPT-OX), which we have previously shown to discriminate between the adolescents with ADHD and controls. We aimed to elucidate whether the ADHD-like symptoms and cognitive impairments in preterm-born individuals reflect identical cognitive-neurophysiological impairments in term-born individuals with ADHD.

**Results:** Go-P3 amplitude was reduced, reflecting impaired executive response control, in preterm-born adolescents compared to both controls and adolescents with ADHD. Moreover, in preterm-born adolescents, as in

term-born adolescents with ADHD, contingent negative variation amplitude was attenuated, reflecting impairments in response preparation compared to controls. Although the ADHD group showed significantly increased NoGo-P3 amplitude at FCz compared to preterm group, at Cz preterm-born adolescents demonstrated significantly decreased NoGo-P3 amplitude compared to the control group, similar to term-born adolescents with ADHD.

**Conclusion:** These findings indicate impairments in response preparation, executive response control, and response inhibition in preterm-born adolescents. Although the response preparation and response inhibition impairments found in preterm-born adolescents overlap with those found in term-born adolescents with ADHD, the preterm group also shows unique impairments, suggesting more wide-ranging impairments in the preterm group compared to the ADHD group.

**Key words:** ADHD, preterm birth, EEG, event-related potential, neurocognitive impairment

*J Am Acad Child Adolesc Psychiatry* 2017;56(1):40–50.

In the developed world, 8.6% of individuals are born preterm (i.e., before 37 completed weeks of gestation).<sup>1</sup> Although survival rates of preterm-born individuals have increased greatly,<sup>2,3</sup> preterm birth is associated with the risk of adverse long-term outcomes.<sup>4,5</sup> A meta-analysis demonstrated that preterm-born children ( $n = 1,556$ ) were at heightened risk (relative risk [RR] = 2.64) for developing attention-deficit/hyperactivity disorder (ADHD) relative to controls ( $n = 1,720$ ).<sup>4</sup> A population-based study of Norwegian adults further reported a 1.3- and 5-fold increased risk for ADHD in adults born preterm (<37 weeks) and extremely preterm (<28 weeks), respectively.<sup>6</sup>

ADHD is characterized by developmentally inappropriate and impairing levels of hyperactivity, impulsivity,

and/or inattention.<sup>7</sup> A meta-analysis in children with ADHD showed impairments in sustained attention (indexed by increased numbers of omitted responses or omission errors), impairments in response inhibition (indexed by increased numbers of error responses or commission errors), and intraindividual fluctuations in reaction times (reaction time variability [RTV]) compared to controls.<sup>8</sup> In adults with ADHD, similar impairments have been reported.<sup>9–12</sup> A cognitive profile that resembles that of individuals with ADHD, including impairments in attention and inhibitory control, is also frequently associated with preterm birth.<sup>13</sup> A meta-analysis of nine studies found that teacher- and parent-rated attention problems in very preterm children (<33 weeks' gestation) were 0.43 to 0.59 standard deviations higher than for controls, respectively.<sup>13</sup> Furthermore, impairments in response inhibition have been found in children<sup>14</sup> and young adults<sup>15</sup> born preterm.

Although research has provided strong support for the link between preterm birth and ADHD, little is known



Supplemental material cited in this article is available online.

about the underlying risk pathways. Cognitive performance data alone provide only indirect insight into covert processing as various covert mechanisms may result in indistinguishable overt performance on cognitive tasks. The study of event-related potentials (ERPs), which are electrical potentials generated by the brain in response to internal or external events such as stimuli and responses,<sup>16</sup> allows direct investigation of covert brain processes with millisecond temporal resolution.<sup>17,18</sup> ERP measures permit a sensitive comparison of the cognitive-neurophysiological profiles associated with preterm birth and ADHD, enabling us to investigate whether the symptoms and impairments seen in individuals born preterm are identical to those associated with ADHD or whether they are part of more wide-ranging impairments. Consequently, neurophysiological assessments have the potential to further elucidate the risk pathways underlying preterm birth and ADHD.

Although countless ERP studies have been conducted in preterm-born infants in neonatal intensive care units<sup>19,20</sup> and in the postnatal period,<sup>21-23</sup> less ERP research has been carried out in children, adolescents, or adults born preterm. The ERP studies that have been conducted in preterm-born children have focused mainly on auditory ERP components.<sup>24-26</sup> Auditory ERP components are neurophysiological correlates of cortical sound processing and sound discrimination: they are generated involuntarily by the brain during basic auditory encoding (indexed by the ERP component P1) or as a response to a perceived change in continuously repeated sounds (indexed by the ERP components N2, mismatch negativity [MMN] and P3a).<sup>16</sup> Responses to novel sounds (as indexed by N2, MMN, and P3a amplitudes) are hypothesized to reflect an individual's capacity to allocate attention.<sup>16,25</sup> Auditory ERPs are therefore useful to study attention in participants who cannot easily respond behaviorally, such as young infants and children. In auditory ERP studies, increased N2 amplitudes, interpreted as reflecting impaired attention orienting, have been found in children born very preterm (<32 weeks).<sup>24,26</sup> Preterm-born children have also demonstrated abnormalities in other early sensory and attentional ERP components (MMN, P1 and P3a).<sup>24-26</sup> Despite this initial evidence for impairments in ERP measures of attentional processing in preterm-born individuals, the research overall is limited, and no studies of preterm birth to date have investigated ERP components that sensitively capture the attentional and inhibitory impairments seen in individuals with ADHD.

One of the most common cognitive tasks used to study attentional processing and response inhibition in individuals with ADHD is the cued continuous performance test (CPT-OX). The CPT-OX requires participants to detect target stimuli among a sequence of distractor stimuli. Omission errors (OE; the lack of a response to a target) are assumed to represent impairments in sustained attention, whereas commission errors (CE; responses to distractor stimuli) are an index of response inhibition. ERPs associated with the CPT are the Go-P3, which is an electrical potential generated by the brain in response to the target stimulus, the NoGo-P3, which is an electrical potential generated by the brain in response to the distractor stimulus and reflects response

inhibition, as well as the Cue-P3 and contingent negative variation (CNV), which occur in response to the cue stimulus and are thought to reflect attentional orienting to a cue and motor response preparation respectively. CPT performance is typically impaired in individuals with ADHD, who usually demonstrate increased reaction time variability, a greater number of OEs, and a greater number of CEs.<sup>8</sup> In addition, ERP studies using the CPT-OX have found that individuals with ADHD also show impaired response inhibition, response preparation, and attentional orienting as indexed by reduced NoGo-P3, contingent negative variation (CNV), and Cue-P3 amplitudes.<sup>27-29</sup> Yet, not all studies have reported case-control differences in Cue-P3 amplitude.<sup>30,31</sup> Although some studies report attenuated Go-P3 amplitude in individuals with ADHD,<sup>32-34</sup> indexing impaired executive response control, others show no case-control differences.<sup>27,28,35</sup> Finally, case-control differences in N2 amplitude in response to distractor stimuli (NoGo-N2) are typically not found in the CPT-OX.<sup>28,31,36</sup>

Direct comparisons on ERP measures between preterm-born individuals and term-born individuals with ADHD are scarce. One ERP study investigated attentional processing in very-low-birthweight children born preterm (<1,501 g and <34 weeks) with and without ADHD, as well as in term-born controls and term-born individuals with ADHD.<sup>37</sup> Term- and preterm-born children with ADHD, who showed increased mean reaction time (MRT), RTV, and a greater number of commission and omission errors on a visual oddball paradigm, also demonstrated an increased NoGo-N2 amplitude compared to term-born controls and preterm-born participants without ADHD. However, the sample size was small (n = 41 across four groups). No study to date has compared ERP components associated with attentional and inhibitory processing in both ADHD and preterm birth using a detailed measure of attention and inhibitory control such as the CPT-OX.

We previously reported findings on ADHD case-control differences on cognitive and neurophysiological markers of ADHD. With the use of the CPT-OX, we demonstrated that sustained attention (indexed by omission errors), response inhibition (indexed by commission errors and NoGo-P3 amplitude), intraindividual fluctuations in reaction times (RTV), response preparation (indexed by CNV amplitude), and attentional orienting (indexed by Cue-P3 amplitude) successfully discriminated between adolescents with ADHD and controls.<sup>38</sup> Conflict monitoring as indexed by NoGo-N2 amplitude was not previously investigated in this sample of ADHD and control adolescents.<sup>38</sup> Having established the cognitive-performance and ERP measures that sensitively capture the attentional and inhibitory impairments in adolescents with ADHD, we now compare new data obtained from adolescents born preterm on identical measures to the data previously obtained from the ADHD and control participants.

In the current study, we therefore aim to establish whether the cognitive impairments associated with preterm birth, including attention and inhibitory control difficulties, reflect neurophysiological impairments identical to those observed in term-born individuals with ADHD.

Download English Version:

<https://daneshyari.com/en/article/4931593>

Download Persian Version:

<https://daneshyari.com/article/4931593>

[Daneshyari.com](https://daneshyari.com)