Behavioral Consequences of Aberrant Alpha Lateralization in Attention-Deficit/ Hyperactivity Disorder

Niels ter Huurne, Marten Onnink, Cornelis Kan, Barbara Franke, Jan Buitelaar, and Ole Jensen

Background: Attention-deficit/hyperactivity disorder (ADHD) is characterized by problems in directing and sustaining attention. Recent findings suggest that alpha oscillations (8–12 Hz) are crucially involved in gating information between brain regions when allocating attention. The current study investigates whether aberrant modulation of alpha oscillations contributes to attention problems in ADHD patients.

Methods: Magnetoencephalographic signals were recorded in adults with ADHD ($n = 17$) and healthy control subjects ($n = 18$) while they performed a visuospatial attention task. Cues directed attention to the left or right visual hemifield with an 80% validity with respect to the upcoming target.

Results: Unlike the control group, subjects with ADHD showed a higher accuracy for invalidly cued right targets compared with invalidly cued left targets ($p = .04$). This coincided with an inability of the ADHD subjects to sustain the posterior hemispheric alpha lateralization in the period before the target for the left cue condition ($p = .011$). Furthermore, the control group showed a strong correlation between the degree of alpha lateralization and the magnitude of the cueing effect assessed in terms of accuracy ($r_s = .71$, $p = .001$) and reaction times ($r_s = -.81$, $p < .001$). These correlations were absent in the ADHD group.

Conclusions: Our results demonstrate that subjects with ADHD have a failure in sustaining hemispheric alpha lateralization when cued to the left, resulting in an attentional bias to the right visual hemifield. These findings suggest that aberrant modulations of alpha oscillations reflect attention problems in ADHD and might be related to the neurophysiological substrate of the disorder.

Key Words: ADHD, attention, bias, electroencephalography, magnetoencephalography (MEG), oscillations

Attention-deficit/hyperactivity disorder (ADHD) is a neuropsychiatric disorder characterized by a developmentally inappropriate pattern of inattentiveness, impulsivity, and restlessness that leads to impairment in multiple areas of life (1). Once thought to be solely a childhood disorder, ADHD has now been recognized as an important clinical condition in adults as well. The estimated prevalence of ADHD is approximately 5% in children and adolescents and 3%–4% in adults (2,3). One of the clinically most marked features of ADHD includes problems in directing and sustaining attention. The neuronal substrate of these problems is still relatively unknown.

The allocation of attention involves both focusing on the relevant information and at the same time suppressing competing and possibly distracting information (4). An increasing number of studies indicate that the allocation of attention and processing resources in the brain is linked to oscillatory activity (brain rhythms) in the alpha band (8–12 Hz) (5–17). For instance, a decrease in alpha activity typically reflects the engagement of a given area. This might result in a gain increase associated with increased attention. Also, increases in alpha activity have been shown to actively inhibit neuronal activity and processing (18,19), which would serve to suppress incoming distracting information. The alpha modulation is likely, on the basis of these findings, to play an important role in attentional processes by gating streams of information through the brain [for reviews see (20–25)].

Hypothetically, abnormal modulation of alpha band activity could explain symptoms of inattentiveness and distractibility in ADHD. If the modulation of alpha activity should fail, control over which stimuli to process and which to ignore would be lost, which in turn would cause attention problems. Attention-deficit/hyperactivity disorder has been associated with alterations in alpha, theta, and beta band oscillatory activity in resting state electroencephalography [for a review see (26)]. Also, a study using a cross-model (visual and auditory) cueing paradigm showed an absence of a decrease of alpha in response to a cue in children with ADHD (27). These results could indicate that ADHD is associated with problems in modulating the alpha activity. Further research is needed to corroborate this hypothesis.

A larger part of the research on the functional role of the alpha activity has focused on allocation of visuospatial covert attention with spatial cues to direct attention to either visual hemifield. It is now well-established that alpha power decreases in occipital regions contralateral to the attended visual field, whereas there is relative increase in alpha power in the ipsilateral occipital regions (6,9–11,13,15–17). This hemispheric alpha lateralization has often been shown to correlate with spatial detection (11,13,15,16) and also with response-inhibition abilities (17). This marks the importance of alpha modulation in effectively directing and sustaining attention to a visual stimulus and shaping behavior.

Although the hemispheric lateralization of the alpha activity by spatial cueing has proven a highly robust phenomenon, its consequence for behavior has as not yet been studied in an

From the Centre for Cognitive Neuroimaging (NtH, JB, OJ), Department of Psychiatry (NtH, MO, CK, BF), Department of Cognitive Neuroscience, (JB), Centre for Neuroscience, Donders Institute for Brain, Cognition and Behavior; and the Department of Human Genetics (BF), Radboud University Medical Centre, Nijmegen, The Netherlands.

Address correspondence to Niels ter Huurne, M.D., Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behavior, PO Box 9101, Nijmegen, NL-6500 HB, The Netherlands; E-mail: n.terhuurne@psy.umcn.nl.

Received Sep 11, 2012; revised Jan 11, 2013; accepted Feb 1, 2013.

0006-3223/$36.00
http://dx.doi.org/10.1016/j.biopsych.2013.02.001

ADHD population. In the present study we set out to investigate: 1) whether attention problems in ADHD could be partly explained by a reduced ability to modulate and sustain oscillatory activity in the alpha band; and 2) whether abnormal alpha oscillations were related to behavioral performance. To that end we used magnetoencephalography (MEG) to record the hemispheric lateralization in the alpha band in typically developed adults and adults diagnosed with ADHD.

Methods and Materials

Subjects

A total of 41 adults (ages 21–40 years) were recruited for this study from an existing database of adult ADHD patients and healthy control subjects (Dutch cohort of the IMpACT [International Multicenter Persistent ADHD Collaboration] study) (28). Participants included adult ADHD patients ($n = 17$) and IQ-, age-, and gender-matched healthy control subjects ($n = 18$). Six subjects (two ADHD patients, four control subjects) were not included in the final data analysis for reasons described in the following text. Patients were included if they met DSM-IV-TR criteria for ADHD in childhood as well as adulthood (1). All participants were assessed with the Diagnostic Interview for Adult ADHD (29). The Structured Clinical Interview for DSM-IV was used for comorbidity assessment. Assessments were carried out by trained professionals (psychiatrists or psychologists). In addition, a quantitative measure of clinical symptoms was obtained with the ADHD DSM-IV Rating Scale (30). Subjects with comorbid psychiatric or neurological disorders were excluded. Subjects using ADHD-medication other than psychostimulant drugs were also excluded. Seven subjects were using methylphenidate regularly. All of them temporally discontinued their medication for a 20-hour period before participation, securing wash-out. For all subjects IQ was estimated with a subset (block design and vocabulary assessments) of the Wechsler Adult Intelligence Scale. Handedness was determined with the Edinburgh Handedness Inventory (31). For demographic information, see Table 1. The study was approved by the local medical-ethical committee (committee for protection of human subjects of the Arnhem/Nijmegen region; CMO protocol number 2009/260) and was performed according to the Declaration of Helsinki. Written informed consent was obtained from all participants before study entry.

Task

Each trial was composed of a .6-sec baseline period with a fixation cross presented at the center of the screen (Figure 1). Two random dot kinematograms were then displayed in the right and the left visual hemifield. In 5 of 6 of the trials, a left or a right arrow was shown simultaneously in the center for .2 sec. In 1 of 6 of the trials a question mark (neutral cue condition) was shown instead of the cue. The random dot kinematograms were each composed of 350 dots moving in random directions, each covering $11^\circ \times 11^\circ$, centered 10° right and left of the fixation cross. After a .6- to 1.1-sec preparation interval, 50% of the dots would coherently move horizontally (leftward or rightward), whereas in the other hemifield dots would move vertically (upwards or downwards) for the duration of .3 sec. Subjects were instructed to detect the horizontal coherent movements but not the vertical movements. The movement direction (left or right) was reported by pressing one of two buttons with the dominant hand. In 80% of the trials the horizontal coherent movement change would occur in the cued hemifield (valid cue trials). In 20% of the trials horizontal movement would occur in the uncued hemifield (invalid cue trials). After each trial, feedback was given on accuracy. The response period depended on the button press. All conditions were presented randomly and interleaved. A total of 864 trials were presented lasting 2–2.5 sec. A session lasted approximately 45 min/subject. Before the recordings, subjects participated in a practice session with 120 trials lasting 5 min. During the experiment subjects were seated in front of a projector screen, with a distance of 72 cm between eyes and screen. Subjects were instructed to move their heads as little as possible during the experiment. The visual stimuli were presented with an EIKI-XL-100 projector (Eiki International, Rancho Santa Margarita, California) with 60-Hz refresh rate. Behavioral responses were collected with a Current Designs HH-1x4-C fiber optic response device. We used the software MATLAB 7.5.0 Psychtoolbox (MathWorks, Natick, Massachusetts) for presenting the stimuli.

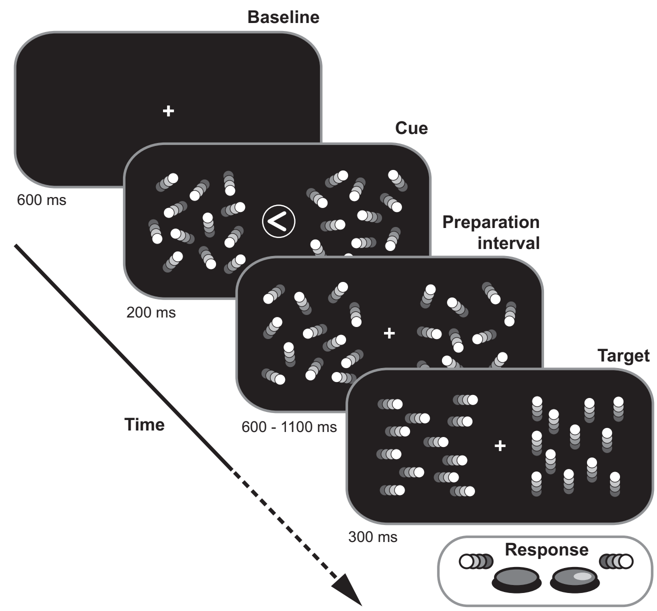

Figure 1. Schematic overview of the experimental paradigm. After a baseline period subjects were attentionally cued to the left or the right visual hemifield, and random dot kinematograms (RDKs) were shown in each visual hemifield. After a 600- to 1100-msec preparation interval, in one of the RDKs 50% of the dots started moving coherently in the left or right direction—in the other RDK, up or down. Subject had to report the direction of the horizontal movement by pressing a button. In 80% of the trials the horizontal movement occurred in the cued hemifield (valid cue trial), as shown here, whereas in 20% surprise trials it occurred in the other hemifield (invalid cue trial).

Table 1. Demographic Information

	Control	ADHD	Statistics	
Age, yrs	30.9 ± 5.05	31.8 ± 6.22	−.46	ns[a]
IQ Estimation[b]	11.7 ± 2.39	12.2 ± 2.32	−.62	ns[a]
ADHD Self-Report	2.28 ± 2.76	11.1 ± 3.09	−8.9	$p < .001$[a]
Sex (Men, Women)	10, 8	7, 10	.72	ns[c]
Handedness (Right, Left)	16, 2	15, 2	.004	ns[c]

Values are mean and SD, unless otherwise indicated.
ADHD, attention-deficit/hyperactivity disorder; ns, not significant.
[a] t test, accepted level of significance $p < .05$.
[b] IQ estimations of four control subjects were missing.
[c] χ^2 test, accepted level of significance $p < .05$.