Independent oscillatory patterns determine performance fluctuations in children with attention deficit/hyperactivity disorder

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The maintenance of stable goal-directed behaviour is a hallmark of conscious executive control in humans. Notably, both correct and error human actions may have a subconscious activation-based determination. One possible source of subconscious interference may be the default mode network that, in contrast to attentional network, manifests intrinsic oscillations at very low (<0.1 Hz) frequencies. In the present study, we analyse the time dynamics of performance accuracy to search for multisecond periodic fluctuations of error occurrence. Attentional lapses in attention deficit/hyperactivity disorder are proposed to originate from interferences from intrinsically oscillating networks. Identifying periodic error fluctuations with a frequency <0.1 Hz in patients with attention deficit/hyperactivity disorder would provide a behavioural evidence for such interferences. Performance was monitored during a visual flanker task in 92 children (7- to 16-year olds), 47 with attention deficit/hyperactivity disorder, combined type and 45 healthy controls. Using an original approach, the time distribution of error occurrence was analysed in the frequency and time–frequency domains in order to detect rhythmic periodicity. Major results demonstrate that in both patients and controls, error behaviour was characterized by multisecond rhythmic fluctuations with a period of ~12 s, appearing with a delay after transition to task. Only in attention deficit/hyperactivity disorder, was there an additional ‘pathological’ oscillation of error generation, which determined periodic drops of performance accuracy each 20–30 s. Thus, in patients, periodic error fluctuations were modulated by two independent oscillatory patterns. The findings demonstrate that: (i) attentive behaviour of children is determined by multisecond regularities; and (ii) a unique additional periodicity guides performance fluctuations in patients. These observations may re-conceptualize the understanding of attentive behaviour beyond the executive top-down control and may reveal new origins of psychopathological behaviours in attention deficit/hyperactivity disorder.

Keywords: action monitoring; ADHD; error processing; multisecond oscillations; time–frequency analysis
Abbreviations: ADHD = attention deficit/hyperactivity disorder; PACS = parental account of childhood symptoms
Introduction

The maintenance of goal-directed behaviour is a hallmark of conscious executive control in humans (Carter et al., 1998; Ullsperger et al., 2004). In the continuous stream of decision making, free decisions for actions are predicted by cortical activation patterns up to 10 s before these decisions enter awareness (Soon et al., 2008). This points to an activation-based determination of human actions emerging out of awareness. Performance errors are likewise foreshadowed by region-specific haemodynamic and neuroelectric patterns in the brain that precede errors by ~20–30 s (Weissman et al., 2006; Eichele et al., 2008; O’Connell et al., 2009). The explanation that performance failures are ‘programmed’ by the executive systems of the brain long before the action is made is problematic in view of basic adaptation principles. Instead, neural activations out of awareness may be responsible for interruptions of controlled task processing.

Indeed, temporally evolving activation patterns in a system-wide neural foundation have been found to predict errors (Weissman et al., 2006). One major neural system is associated with the maintenance of goal-directed attention. This system manifests an error-predictive decline of activation. The second system functions in parallel with the first one and comprises the default mode network of the resting brain (Gusnard and Raichle, 2001; Raichle et al., 2001). The default mode network is routinely attenuated during goal-directed tasks, but it is predictively less deactivated before errors (Fox et al., 2005, 2006; Padilla et al., 2006; Weissman et al., 2006; Li et al., 2007, 2008; Eichele et al., 2008). Thus, an insufficient default mode network deactivation in combination with a disproportionately low activation of the attention system may be a key source of error-prediction states (Fox et al., 2005). Since attentional systems sustain a stable level of activation to subserve goal-directed processing (Weissman et al., 2006), variability of performance in this perspective should be basically modulated by the temporal characteristics of the default mode network (Castellanos et al., 2005; Sonuga-Barke and Castellanos, 2007; Di Martino et al., 2008). Functional MRI, EEG, magnetoencephalographic and single-neuron recordings have repeatedly demonstrated that the intrinsic resting activity of the default mode network oscillates at very low (<0.1 Hz) frequencies (Gusnard and Raichle, 2001; Raichle et al., 2001; Broyd et al., 2009). Although the key role of the default mode network for modifying performance is increasingly being focused on (Broyd et al., 2009), no behavioural evidence has been provided so far for the presence of oscillatory patterns in the occurrence of errors.

In the present study, we analyse the time dynamics of errors to explore if task performance fluctuates with a specific periodicity. Given the presumed activation stability of the attentional system, identifying periodic fluctuations of errors with frequency <0.1 Hz would provide a behavioural evidence for interference from the default mode network. As a model promoting the expression of default mode network in active behaviour, we used the attention deficit/hyperactivity disorder (ADHD). Neuroimaging and neurophysiological studies support the hypothesis that resting state networks of the ‘default mode’ comprising the medial prefrontal, posterior cingulate and precuneus regions are deviant in ADHD (Zang et al., 2007; Castellanos et al., 2008; Tian et al., 2008; Broyd et al., 2009). On these grounds, behavioural deficits and periodic attentional lapses in ADHD have been proposed to originate from intrusions by insufficiently deactivated default mode network (Castellanos et al., 2005; Sonuga-Barke and Castellanos, 2007; Di Martino et al., 2008; Buzy et al., 2009; Fassbender et al., 2009). Details of the default mode interference hypothesis for ADHD (Sonuga-Barke and Castellanos, 2007) are presented in the online Supplementary material.

The aim of the present study was to provide direct behavioural evidence that performance accuracy in ADHD is determined by very slow (<0.1 Hz) periodic fluctuations. For this aim a continuous monitoring of correct and error responses was carried out in 92 children and adolescents (7- to 16-year olds), 47 with ADHD combined type and 45 healthy controls matched for age and IQ, while they performed a visual flanker task. To detect rhythmic periodicity in behaviour, an original approach was applied to enable the analysis of the time distribution of error occurrence in frequency and time–frequency domains. This approach revealed multisecond regularities in attentive behaviour of children and could also identify a unique periodicity of performance fluctuations leading to rhythmic episodes of attention lapses only in patients with ADHD.

Materials and methods

Subjects

Within the framework of a multi-centre study on central nervous regulatory mechanisms and child psychiatric disorders (for details, see Albrecht et al., 2008), a total of 92 subjects participated in the experiment. They belonged to two groups: healthy controls (n = 45) and patients with ADHD (n = 47), matched for age and IQ. Detailed group characteristics are presented in Table 1.

In the present study, European Caucasian subjects, all aged 7–16 years with an estimated full-scale IQ above 80 (Sattler, 1992; Twees et al., 1999) and no known child psychiatric disorder that may mimic ADHD were included. Recruitment of children suffering from ADHD combined type according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) was conducted as part of the International Multi-Centre ADHD Gene study (IMAGE; Asherson, 2004; Kuntsi et al., 2006). Children of the control group were recruited from regular schools around Göttingen, Germany and had no known family history of ADHD. For the selection of the groups used in the present study, a total of 398 children were screened, with 276 children of this sample having family history of ADHD. The selection of the groups was done according to the criteria described below. Ethical approval was obtained from the local ethical review board. Detailed information sheets were provided and informed consent from children above 9 years and parents of all children were obtained. Children being under stimulant treatment were off medication for at least 48 h before testing. All children earned small prizes. Parents did not receive any financial reward except travel expense reimbursements.

To assess cognitive ability, all children were screened for global learning difficulties with pro-rated full IQ scores derived from
Table 1 Sample description

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls n = 45 Mean (SD)</th>
<th>ADHD n = 47 Mean (SD)</th>
<th>ANOVA F(1,91) Partial $\eta^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>134.9 (27.0)</td>
<td>135.6 (20.4)</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Estimated total IQ</td>
<td>107.8 (12.6)</td>
<td>104.1 (10.5)</td>
<td>2.4</td>
</tr>
<tr>
<td>Strengths and Difficulties Questionnaire</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent rated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>2.2 (1.9)</td>
<td>8.2 (1.6)</td>
<td>268.9**</td>
</tr>
<tr>
<td>Prosocial behaviour</td>
<td>7.9 (1.8)</td>
<td>6.7 (2.1)</td>
<td>8.4**</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>1.6 (1.6)</td>
<td>4.7 (2.6)</td>
<td>46.7**</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>1.1 (1.2)</td>
<td>5.0 (2.0)</td>
<td>129.4**</td>
</tr>
<tr>
<td>Peer problems</td>
<td>0.8 (1.5)</td>
<td>4.3 (2.6)</td>
<td>60.3**</td>
</tr>
<tr>
<td>Teacher rated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperactivity$^a$</td>
<td>2.2 (2.7)</td>
<td>8.6 (1.5)</td>
<td>196.30**</td>
</tr>
<tr>
<td>Prosocial behaviour$^b$</td>
<td>7.4 (2.3)</td>
<td>5.6 (3.0)</td>
<td>9.40**</td>
</tr>
<tr>
<td>Emotional symptoms$^b$</td>
<td>1.2 (1.7)</td>
<td>3.3 (2.8)</td>
<td>17.30**</td>
</tr>
<tr>
<td>Conduct problems$^a$</td>
<td>0.7 (1.5)</td>
<td>3.2 (2.1)</td>
<td>41.70**</td>
</tr>
<tr>
<td>Peer problems$^a$</td>
<td>1.4 (2.0)</td>
<td>4.1 (2.7)</td>
<td>30.0**</td>
</tr>
</tbody>
</table>

Conners Parent rated

| Parameter                     | Controls Mean (SD) | ADHD Mean (SD) | F(1,91)     Partial $\eta^2$ |
|-------------------------------|--------------------|----------------|-------------|----------------------------|
| Oppositional score            | 51.7 (7.7)         | 72.0 (11.1)    | 101.5**     | 0.53                       |
| Cognitive/inattention score   | 49.9 (8.5)         | 66.8 (8.8)     | 87.9**      | 0.49                       |
| Hyperactivity score           | 50.2 (8.9)         | 76.9 (11.3)    | 158.5**     | 0.64                       |
| Anxious-shy score             | 51.9 (11.6)        | 60.0 (14.0)    | 9.1**       | 0.09                       |
| Perfectionism score           | 51.1 (8.5)         | 62.9 (11.1)    | 32.3**      | 0.26                       |
| Social problems score         | 50.6 (9.0)         | 66.0 (14.2)    | 38.3**      | 0.30                       |
| Psychosomatic score           | 48.8 (7.6)         | 60.6 (13.2)    | 27.5**      | 0.23                       |
| ADHD index                    | 48.9 (8.1)         | 68.7 (8.1)     | 138.5**     | 0.61                       |
| Global index: restless-impulsive | 49.8 (8.5)      | 74.8 (8.7)     | 195.6**     | 0.69                       |
| Global index: emotional liability | 48.2 (5.5)     | 69.4 (12.3)    | 111.7**     | 0.55                       |
| Global index: total           | 49.2 (7.0)         | 75.0 (9.1)     | 233.1**     | 0.72                       |
| DSM-IV inattentive score      | 49.8 (8.3)         | 66.6 (8.3)     | 93.7**      | 0.51                       |
| DSM-IV hyperactive impulsive score | 50.3 (9.5)    | 75.6 (11.2)    | 136.5**     | 0.60                       |
| DSM-IV total                  | 50.2 (8.9)         | 72.2 (9.6)     | 129.2**     | 0.59                       |

Conners Teacher rated

| Parameter                     | Controls Mean (SD) | ADHD Mean (SD) | F(1,90)     Partial $\eta^2$ |
|-------------------------------|--------------------|----------------|-------------|----------------------------|
| Oppositional score            | 50.6 (7.0)         | 62.0 (11.0)    | 35.3**      | 0.28                       |
| Cognitive/inattention score   | 48.6 (8.8)         | 63.1 (8.8)     | 62.2**      | 0.41                       |
| Hyperactivity score           | 50.4 (8.1)         | 68.0 (9.8)     | 87.9**      | 0.49                       |
| Anxious-shy score             | 53.7 (8.7)         | 64.9 (11.4)    | 28.0**      | 0.24                       |
| Perfectionism score           | 50.6 (7.8)         | 58.5 (10.6)    | 16.7**      | 0.16                       |
| Social problems score         | 48.6 (7.0)         | 61.5 (12.6)    | 36.3**      | 0.29                       |
| Psychosomatic score           | (missing)          |                |             |                            |
| ADHD index                    | 50.0 (9.2)         | 70.0 (7.8)     | 126.6**     | 0.59                       |
| Global index: restless-impulsive | 49.7 (10.0)   | 71.2 (8.0)     | 129.5**     | 0.59                       |
| Global index: emotional liability | 48.2 (5.9)     | 65.8 (12.0)    | 78.3**      | 0.47                       |
| Global index: total           | 49.2 (8.5)         | 72.3 (8.6)     | 169.6**     | 0.65                       |
| DSM-IV inattentive score      | 50.0 (10.8)        | 67.5 (8.1)     | 77.7**      | 0.46                       |
| DSM-IV hyperactive impulsive score | 49.0 (7.6)    | 67.1 (10.2)    | 92.7**      | 0.51                       |
| DSM-IV total                  | 49.8 (9.1)         | 69.1 (8.4)     | 112.7**     | 0.56                       |

a Missing for one control subject, thus df = 1,90.
b Missing for three controls, thus df = 1,88.
$^{*} P < 0.05$; $^{**} P < 0.001$.
$\eta^2$ = effect size; SD = standard deviation.

Four subtests of the Wechsler Intelligence Scale for children (Children WISC-III UK; Tewes et al., 1999): picture completion, block design, similarities and vocabulary. Individuals with pro-rated IQ < 80 were excluded from the study. The diagnostic assessment was performed with long versions of Conners’ rating scales (Conners et al., 1998a, b) and Strengths and Difficulties Questionnaires (Goodman, 1997; Rothenberger and Woerner, 2004) for parents and teachers. The hyperactivity scale of
the Strengths and Difficulties Questionnaire consists of five items. Also the n-score of the Conners’ 18 items, that are similar to the DSM-IV ADHD checklist, was used. In the Conners’ Scales, two subscales L (inattentive—nine items) and M (hyperactive-impulsive—nine items) combine to yield summary n-scores. For the Strengths and Difficulties Questionnaire hyperactivity scale, a comparable procedure obtaining an age- and gender-standardized profile was carried out. If T-scores on Conners ADHD scales (L, M, n) exceeded 62 and scores on Strengths and Difficulties Questionnaire hyperactivity scale exceeded the 90th percentile, a semi-structured clinical interview [Parental Account of Childhood Symptoms (PACS); Taylor et al., 1986a, b, 1987; Andreou et al., 2007; Uebel et al., 2010] was applied to verify ADHD diagnosis and control for symptoms from other child psychiatric disorders. To ensure that control subjects were free of susceptibility for ADHD, children with T-scores > 62 on both parent and teacher scales of the Conners’ total symptoms scale were excluded from that group.

The PACS is a semi-structured and standardized clinical interview administered with parents by trained investigators to obtain an objective measure of child behaviour in a range of specified situations (e.g. watching TV, playing alone or with friends) during the last week and year. A standardized algorithm based on PACS and Conners’ teacher ratings resemble the 18 DSM-IV criteria for ADHD, while situational pervasiveness was indicated if symptoms occurred in more than one situation within PACS. Since inter-rater reliability of PACS for ADHD scale is r > 0.9 with internal consistency of Cronbach’s α = 0.89, it is capable of providing accurate diagnosis of ADHD in a multi-centre study (Taylor et al., 1986a; Brookes et al., 2006). Diagnosis of frequent comorbidities also relied on scales with good inter-rater reliability, e.g. 0.89–0.95 for defiance and 0.79–0.90 for emotional disorders. Further, the parents were asked for other comorbidities, such as epilepsy, structural lesion of CNS or specific developmental disorders, and this information was scored as ‘not present’, ‘possible’, ‘sure’ or ‘not assessable’.

All subjects had normal or corrected to normal vision and understood task instructions as verified during a practice block. Groups were matched for age and did not differ for estimated total IQs (Table 1). In the ADHD group, PACS interview yielded susceptibility for mood disorder (n = 3), Tourette syndrome (n = 2), substance abuse (n = 1), obsessive compulsive disorder (n = 1), anxiety disorder (n = 23), oppositional defiant disorder (n = 33) and conduct disorder (n = 13). In order to exclude disorders of the autism spectrum that might confound the analysis of ADHD, participants were screened using the Social Communication Questionnaire (≥ 15; Chandler et al., 2007) in conjunction with the pro-social scale from the Strengths and Difficulties Questionnaire (≥ 4). Participants falling above these thresholds were excluded from analysis and were further evaluated using the autism spectrum disorder section of the PACS interview.

A standardized algorithm for PACS was applied to all raw PACS data to yield diagnoses based on operational DSM-IV criteria for ADHD (Table 1). Age adjustment for symptom threshold was built into the PACS algorithm. Situational pervasiveness was captured by the different situations investigated within the PACS interview as well as the presence of some symptoms reported by teachers using the Conners’ ADHD sub-scale.

**Procedure**

Assessments of children were carried out on 2 days. The neurophysiological session took place before the neuropsychological testing or vice versa, following a randomization scheme. The data analysed here were collected as part of the neurophysiological test-session that was carried out in a video-controlled, noise-shielded and slightly dimmed room at the Child and Adolescent Psychiatry Department of the University of Göttingen. Subjects sat on a comfortable seat during electrode attachment and task performance. The flanker task was administered after 5 min of resting EEG followed by a continuous performance test lasting 11 min and, if desired, a short break.

**Stimuli and task**

The flanker task consisted of 10 blocks of 40 trials each, modelled after Kopp et al. (1996). The blocks were separated by 20-s rest epochs. Columns of black arrowheads (equilateral triangles with 18 mm edge length at three positions with 23 mm distance centre to centre) were presented in the centre of a 17 in. monitor with 800 × 600 points resolution against a light grey background at 120 cm viewing distance. On every trial, a fixation mark in the centre of the screen was replaced by the stimuli. In the beginning of each trial, only flankers (two arrowheads pointing in the same direction and below the position of the fixation mark) were presented for 100 ms, before the target arrowhead appeared between the flankers. Target duration was 150 ms. Subjects had to press response buttons with the index finger of their hand corresponding to the direction indicated by the target. Accordingly, responses were produced with the right and the left hand. On congruent trials, flanker and target arrowheads pointed in the same and on incongruent trials—in opposite directions. A stimulus was presented every 1600 ms, and the task took ~ 13 min. On 50% of the trials (n = 200) the target and the flankers had the same direction (congruent stimuli). On the other 50% of the trials (n = 200) the target and the flankers had opposite directions (incongruent stimuli). Half of the trials indexed a right-hand response (n = 200), and the other half indexed a left-hand response (n = 200). In this way, four stimulus types with equal probability of 25% were formed: right congruent, right incongruent, left congruent and left incongruent (n = 100 for each stimulus type). For each subject, a random series of trials was generated online.

Feedback appeared on the screen at the end of each block. A child was instructed to be more accurate if > 10% errors on congruent or > 40% errors on incongruent trials were made. In case of < 10% errors on the congruent and < 40% errors on incongruent trials, it was stressed to respond faster; otherwise the child was told to go on the same way. This was done in order to control for accuracy, which might influence error processing (Gehring and Fencsik, 2001; Yordanova et al., 2004). Two practice blocks with 24 trials each were administered first.

In this experimental session, behavioural and EEG data were collected simultaneously. In the current report, only results from the behavioural parameters will be presented.

**Data analysis**

For each trial, individual performance was monitored by recording the reaction time and response accuracy (error number and error type). Trials with reaction time faster than 180 ms were identified as premature responses, and trials with reaction time longer than 1500 ms were identified as delayed responses. Premature and delayed responses were excluded from analyses of reaction time to prevent real response speed evaluation from being confounded by performance deficiencies such as disinhibition or attentional slips. In the present study, tools for data analysis were chosen to enable determination if changes in behaviour, as reflected by response accuracy, occur randomly or with a specific periodicity. Details on the standard analysis of performance accuracy are presented elsewhere (Yordanova et al., in press).
Detecting periodic oscillations in error occurrence

To reveal cyclic dynamic patterns of error fluctuations, the timing of errors was analysed. Other performance indices were not targeted because in this task, stimulus-specific processing (congruent versus incongruent) produces large variations in response speed and variance that may exceed and obscure variations due to periodic fluctuations.

Time series of error distribution

As a first step of error dynamics analysis, the time distribution of error occurrence was characterized by coding the positions of error and correct trials in each block for each subject (Fig. 1A). Then the coded trials (40 trials in each block) were averaged across the 10 experimental blocks (Fig. 1B). If incorrect responses occur in a fully random manner, no peaks are expected to emerge in the average obtained thus. In contrast, if errors occur with some consistent periodicity during a block, accumulation of incorrect responses at specific sequence positions would result in higher values in the average and accordingly, in the formation of peaks. The consecutive absolute values of individual averages were used as a time series signal (Fig. 1B).

Additionally, two artificial signals were generated to extend analyses, simulated and shuffled. The simulated signal was based on artificially generated time series of error distribution, in which the same error rate as in the original blocks was used. In these simulated time series, error positions of each subject’s errors in each block were defined in a statistically random manner. The shuffled signal was based on the original time distribution of errors in each block. However, this time series was obtained after random shuffling 200 times the positions of block onsets while preserving block structure of error distribution.

Analysis in the frequency domain

To assess if errors occur periodically and to determine the frequency of their appearance in the course of the experimental block, analysis in the frequency domain was made by means of fast Fourier transform (Fig. 1C). The analysed signal was the time series of error occurrence. In the currently employed experimental design, the sampling rate of the time series signal was 0.625 Hz (dwell time 1.6 s) corresponding to the rate of stimulation. The length of each experimental block of 66 s (40 stimuli per block) limited the slowest frequency to be analysed to 0.015 Hz. According to the Nyquist theorem, the highest cut-off frequency that could be reliably analysed was 0.31 Hz. To attenuate edge effects associated with the beginning and the end of each block, a Hanning window of 5% was applied before the fast Fourier transform. To reduce spurious peaks resulting from the averaging, the time series of error occurrence were smoothed by a three-point digital smoothing before fast Fourier transform calculation. The presence of peaks in the fast Fourier transform indicates that the time series of the analysed signal contains nearly rhythmic oscillations at specific frequencies. In Fig. 1C, fast Fourier transform of the time series of error distribution is illustrated for a representative subject. Two spectral peaks at 0.05 Hz and at 0.07–0.09 Hz are evident indicating oscillatory patterns of rhythmic error fluctuations.

Analysis in the time–frequency domain

Because analysis in the frequency domain can extract frequency-specific information about the signal, but cannot describe the temporal dynamics of frequency-specific oscillations, the temporal evolution of
oscillatory error behaviour was further evaluated by time–frequency decomposition. As a relevant approach, the continuous wavelet transform with Morlet basis function was used (Tallon-Baudry et al., 1997). Complex-valued Morlet wavelets are Gaussian in both the time and frequency domains. Complex Morlet wavelets \( w(t, f) \) can be generated in the time domain for different frequencies, \( f \), according to the equation:

\[
w(t, f) = A \exp(-t^2/2\sigma_t^2) \exp(2\pi i ft),
\]

where \( t \) is time, \( A = (\sigma_t \sqrt{2})^{-1/2} \), \( \sigma_t \) is the wavelet duration, and \( i = \sqrt{-1} \).

For analysis, a ratio of \( f_0/\sigma_t = 5 \) was chosen, where \( f_0 \) is the central frequency and \( \sigma_t \) is the width of the Gaussian shape in the frequency domain. The choice of the ratio \( f_0/\sigma_t \) was oriented to the expected slow-frequency components in the signal, which had an effect on the shape of the Morlet wavelet and decreased its decay (e.g. Yordanova et al., 2004). Continuous wavelet transform was performed for each individual average, with central frequencies varying from 0.02 to 0.2 Hz in steps of 0.003 Hz. For different \( f_0 \), time and frequency resolutions can be calculated as \( 2\sigma_t \) and \( 2\sigma_r \), respectively (Tallon-Baudry et al., 1997). \( \sigma_t \) and \( \sigma_r \) are related by the equation \( \sigma_t = 1/(2\pi \sigma_r) \). The signal for each individual average was convolved with the complex Morlet wavelet designated for \( f_0 \). The dimension of obtained results was in squared arbitrary units.

Figure 1C shows the time–frequency decomposition plot of a time series of error occurrence of the same representative subject. It indicates that the \( \sim 0.05 \) Hz oscillatory dynamic of error occurrence is not specific to an isolated time period of the experimental block. Rather, it characterized the whole analysis epoch of the block. The time–frequency decomposition also demonstrates that the faster \( \sim 0.07-0.09 \) Hz periodic pattern emerged in the second half of the experimental block, and existed there in parallel with the slower periodic pattern.

### Parameterization and statistical evaluation

After identification of frequency-specific components for the error data, a statistical comparison between the two groups (controls and ADHD) was performed for each frequency bin within the frequency range of the identified peak. The statistical evaluation was done by using the Student’s \( t \)-test. Before the test, spectral values were \( \log_{10} \) transformed to achieve a normal distribution of the data. The statistical outcome was corrected for multiple testing by means of the Bonferroni correction procedure. In the frequency domain, spectral peaks were detected up to 0.1 Hz. Accordingly, 10 analyses were conducted for the consecutive frequency bins from 0.01 to 0.1 Hz and a criterion of \( P < 0.005 \) would satisfy the correction for multiple tests.

To analyse temporal dynamics, after wavelet transform, relevant scales (frequency-specific components) were extracted. Mean values for the first and second halves of the analysed epoch (block duration) were measured. Before statistical evaluation, the power values of the wavelet scales were \( \log_{10} \) transformed to normalize data distribution. For each group, measures from first and second half of the block were compared by means of a paired-samples \( t \)-test.

In addition to original time series of error distributions, the same analyses were performed for the time series of simulated and shuffled data.

### Results

#### General performance

In the conflict-processing condition used here, the total error rate was significantly higher \( [F(1,91) = 13.4, P < 0.001] \) in children with ADHD [mean 19\%, standard error (SE) = 0.87] relative to healthy controls (mean 14\%, SE = 1.03). Yet, the effects of conflict processing were similar in the two groups as reflected by group-independent increase in error rate after incongruent trials compared to congruent trials \( [F(1,91) = 379.1, P < 0.0001] \). The overall response speed did not differ between the two groups of children \( [F(1,91) = 1.2, P > 0.3] \); mean for ADHD = 427 ms, SE = 11.8; mean for controls = 408 ms, SE = 12.4] whereas response speed variance was significantly larger in ADHD children \( [F(1,91) = 23.3, P < 0.001] \). More details are presented in the online Supplementary material 2.

#### Slow frequency-specific fluctuations of error occurrence in ADHD

Figure 2A shows that errors were not evenly distributed over time but their occurrence fluctuated (increased and decreased) in the course of the experimental block. These time variations were much more conspicuous for children with ADHD relative to controls.

Analysis of error distribution in the frequency domain revealed a prominent spectral peak within 0.035–0.06 Hz with a maximum at 0.05 Hz in the group of patients with ADHD (Fig. 2B). This corresponds to a time variation of error occurrence with a period of \( \sim 17–30 \) s, most stable at 20 s. Though smaller, an additional spectral peak <0.1 Hz was observed within 0.07–0.09 Hz (\( \sim 0.08 \) Hz) indicating faster error fluctuations with a period of \( \sim 12 \) s in the ADHD group. Group averaging in the frequency domain extracted the most stable across-subjects spectral components (Fig. 2B). Group averaging in the time domain followed by fast Fourier transform emphasized the between-subjects consistency in the time localizations of error oscillations and confirmed that the groups differed dramatically in error variations within the \( \sim 0.05 \) Hz frequency band (Fig. 2D).

In the control group, no spectral components at \( \sim 0.05 \) Hz were present at all (Fig. 2B, D). It is important to note that the \( \sim 0.08 \) Hz peak was observed in controls, although it was smaller than in patients with ADHD. The differences in spectral components between the two groups were statistically significant for the frequency bins of 0.04, 0.05 and 0.06 Hz (Student’s \( t \)-test, Bonferroni corrected to \( P = 0.005 \), \( P < 0.001 \) for each comparison, Cohen’s \( d \) ranging between 0.71 and 1.02, and effect size ranging between 0.33 and 0.45 for these comparisons; Fig. 2B and C). No such effects were observed for \( \sim 0.08 \) Hz bins (0.07, 0.08 and 0.09 Hz). Between-group differences for 0.04, 0.05 and 0.06 Hz frequencies were further confirmed by MANOVA where total error rate was included as a covariate, but the significance of the group factor was preserved [Bonferroni corrected to \( P = 0.015 \), \( F(1,91) = 7.3, 10.3, 9.4, P = 0.008, 0.002, 0.003 \) for the three variables].
Moreover, the ~0.05 Hz variation of error occurrence in ADHD persisted in the whole 66-s long analysis epoch (Fig. 2E). In contrast, the ~0.08 Hz error variations in the two groups occurred mainly in the second half of the experimental block. Paired \( t \)-tests of the time dynamics of extracted wavelet scales corresponding to relevant frequency bands indicated that the ~0.05 Hz fluctuations did not vary with time in ADHD (\( P > 0.5 \)), whereas the ~0.08 Hz component was significantly larger in the second than in the first half of the block in patients (\( P = 0.003 \), Supplementary material 4, Supplementary Fig. 3B). Though expressed, the detected time dynamics of the ~0.08 Hz oscillations did not reach significance in the control group (\( P = 0.16 \)). This effect was confirmed by a significant interaction group (controls versus ADHD) × dynamics (first versus second half) yielded by a repeated-measures ANOVA \( [F(1,91) = 5.6, P = 0.02] \). The observed oscillatory patterns were validated by comparisons with artificially generated (simulated) time series of error distribution. In the simulated data, no spectral peaks were detected in the fast Fourier transform of ADHD (Supplementary material 3, Supplementary Fig. 2), which verifies the presence of rhythmic oscillations in the original data set of patients. Paired \( t \)-tests comparing spectral activity between original and simulated data
revealed significant differences for 0.04, 0.05 and 0.06 Hz as well as 0.08 and 0.09 Hz bins only in the group of ADHD (P < 0.002 for each comparison, Bonferroni-corrected P < 0.005). No differences were found for the control group.

Effects of task initiation on error distribution

To determine if the oscillatory patterns in the original data depended on the initiation of the task, time series with error positions in each block were shuffled 200 times to randomize the positions of block onsets, and were subsequently subjected to the same analyses. If the oscillatory error dynamics was determined by task initiation, no oscillatory patterns would be present after shuffling. In ADHD, the slow ~0.05 Hz spectral component was fragmented after shuffling but no statistically significant differences were found between original and shuffled data (Supplementary material 4, Supplementary Fig. 3A). However, the ~0.08 Hz component emerging with a delay after task initiation in the original data, was no more evident with clear time localization in the time–frequency plots of shuffled data of both ADHD and control subjects (P = 0.7 and P = 0.5 for the comparisons of the first and second half of the block), indicating a clear resetting effect of task onset. Only in the ADHD group, however, was the difference between original and shuffled ~0.08 Hz oscillations significant for the second half of the block (P = 0.01).

Thus, the ~0.05 Hz component appeared to be a persistent feature of error distribution in ADHD, whereas the delayed appearance of the faster ~0.08 Hz fluctuations was triggered by task initiation in both groups, which could be validated for the patients. Figure 2F illustrates these effects by showing that the distinctiveness of the ~0.05 Hz and ~0.08 Hz oscillatory error patterns in ADHD increases when the contribution of random error distribution is eliminated.

Interindividual variability of error patterns in ADHD

Observation of individual time series of error occurrence revealed that subjects differed substantially with respect to the mode of error occurrence. In the group of control subjects, errors occurred typically as single errors preceded by sequences of correct responses (Fig. 3A). As a rule, sequences of three or more errors did not occur in healthy children.

In contrast, a specific pattern of error occurrence was detected in ADHD (Fig. 3C) characterized by the frequent emergence of groups of three and more errors (bouts). Notably, this pattern was found in 18 out of 47 patients (38%). The rest of the ADHD children, despite having high error rates, manifested either only single errors [n = 18 (38%), Fig. 3A], or single errors plus only episodic groupings of two consecutive errors [n = 11 (25%), Fig. 3B]. In the control group, only three subjects had brief episodes of two consecutive errors (7% in controls versus 63% in ADHD altogether).

This outcome raises the question of whether the ~0.05 Hz behavioural oscillation in ADHD is produced mainly by error bouts, or if it is inherent to ADHD psychopathology irrespective of the specific pattern of error grouping. Analyses were made separately for subjects with ADHD who did (n = 18) or did not manifest bouts of errors (n = 19). In both ADHD subgroups, a spectral peak was detected at 0.04–0.06 Hz indicating that the periodic cycling of error emergence with ~20-s period appears related to the ADHD psychopathology (Supplementary material 5, Supplementary Fig. 4). However, these fluctuations were significantly larger for the ADHD subgroup with error bouts (P < 0.005 for each comparison from 0.03 to 0.055 Hz). The differences between ADHD subgroups were not significant for the ~0.08 Hz spectral activity. Although the ~0.05 Hz peak was pronounced in the ADHD subgroup with single errors, its spectral power did not differ significantly from that of controls (P > 0.01) indicating that lapses in performance manifested by bouts of consecutive errors were accompanied by a significant increase in periodic cycling of error emergence (P < 0.001 for each comparison between the ADHD subgroup with bouts and controls).

The psychopathological scores and performance indices of the two ADHD subgroups were compared by means of MANOVA. None of the psychopathological scores differentiated the subgroups [F(1,35) < 0.9, P > 0.3], nor were there between-group differences in response speed [F(1,35) < 0.24, P > 0.6] and total error rate [F(1,35) = 3.2, P = 0.08]. However, the ADHD subgroup with error bouts had a significantly more variable performance [F(1,35) = 23.4, P < 0.0001 after correct and F(1,35) = 54.2, P < 0.0001 after error trials] and, as expected, a significantly higher error rate after errors [F(1,35) = 42.6, P < 0.0001; normalized to post-correct trials F(1,35) = 78.1, P < 0.0001]. Verbal IQ was lower in the subgroup with versus without bouts of errors [F(1,35) = 9.4, P = 0.004].

In addition to the selection of subjects with ADHD based on the presence or absence of error bouts, to further verify that oscillatory pattern of error dynamics was not due to bout-dependent accumulation of errors but emerges with specific periodicity independently of whether bouts will follow or not, the same analyses were repeated with bout positions being replaced by a single error. This approach was taken to preserve the event of error emergence in the respective time position, but to avoid a possible contribution of increased number of errors. The removal of bouts did not abolish the expression of the ~0.05 spectral peak in the ADHD group.
confirming that this pattern was not produced by bouts (Supplementary material 5, Supplementary Fig. 5). Rather it was produced by the specific cycling of incorrect behaviour irrespective of whether it was manifested as a single error or as a virtual lapse in performance reflected by consecutive errors.

Discussion

The present study demonstrates that specific patterns of cyclic fluctuations characterize the performance of children in a visuo-motor conflict task. One pattern revealed ~0.08 Hz behavioural oscillations producing regular increases and decreases of error responses with ~12-s periods. Consistent with the concept of the default mode system in the brain (Raichle et al., 2001; Fox et al., 2005), these ~0.08 Hz (~12 s) behavioural fluctuations emerged with a delay of ~30–40 s after task initiation, although they were triggered by the start of task-related processing. These observations exactly follow the predictions of default mode network models of Castellanos and Sonuga-Barke according to which default mode networks are deactivated by task-directed attention but, in specific conditions, activations from default mode networks may gradually re-emerge with time on task and may interfere with active task performance (Castellanos et al., 2005; Sonuga-Barke and Castellanos, 2007; see also Supplementary material 1, Supplementary Fig. 1). Notably, the ~0.08 Hz oscillatory pattern was detected in both healthy controls and subjects with ADHD although it significantly modulated performance accuracy in patients with ADHD.

In the context of default mode network models, this result provides original behavioural evidence for the dynamic effects of the default mode networks on performance quality. It demonstrates that in children and adolescents, cyclic oscillations of ~0.08 Hz progressively emerge with time-on-task and increasingly impose modulations of performance accuracy. This finding is suggested to reflect the capacity of default mode network to recover in the course of task processing mainly in psychopathological conditions such as ADHD (Sonuga-Barke and Castellanos, 2007). Although the neural system of goal-directed attention is suggested to support a stable level of activation, this finding also may reflect an oscillatory mode of functioning of the active processing system. This mode may be activated with a delay after task onset, alone or due to anti-correlational relations with the default mode network (Weissman et al., 2006; Castellanos et al., 2008; Fassbender et al., 2009).

A second major result was that a unique pattern of behavioural fluctuations existed in children with ADHD. First, in ADHD, periodic error fluctuations with a frequency of ~0.05 Hz were found to emerge in addition to the ~0.08 Hz error fluctuations, reflecting the independent occurrence of regular performance lapses in 20–30 s periods. Secondly, this slow oscillation pattern was not detected in healthy controls indicating specific associations with ADHD psychopathology. Thirdly, the pathological ~0.05 Hz performance fluctuations were not attenuated at transition to active task processing as detected for the periodic ~0.08 Hz performance fluctuations, nor did they vary substantially over time. Also, the ~0.05 Hz oscillatory behaviour correlated with performance deficits in patients by being significant only in those subjects with ADHD who manifested attention lapses reflected by error bouts. Therefore, the well-recognized deficits in post-error corrective adaptation in ADHD (van Meel et al., 2007) may represent the continuation of the same breakdown of processing that caused the error (Gehring and Fencsik, 2001).

Thus, we not only found that there was an enhancement of a delayed task-modulated ~0.08 Hz oscillation of errors in ADHD, but also an independent ADHD-specific oscillatory pattern of ~0.05 Hz that persisted in active task processing. This finding extends the original default mode interference model of ADHD (Sonuga-Barke and Castellanos, 2007) by demonstrating that performance accuracy in ADHD is determined by the co-existence of two independent sources of oscillatory fluctuations with different time dynamics in terms of both frequency of oscillations and effective temporal expression after task initiation. Identification of the neurofunctional level of the association between these behavioural fluctuations with default mode and pathologically pervasive oscillatory networks in ADHD (Castellanos et al., 2009), or with unique oscillating modes of active processing systems in psychopathological conditions (Rothenberger, 2009), appears to be of utmost importance to pursue the characterization of this disorder.

The presence of dynamic behavioural oscillations on the multi-second scale opens essentially new perspectives to investigate task-related brain processes. Similar to stimulus/event processing on the millisecond time scale (Demiralp et al., 1999), the switching of goal-directed attention may induce task-specific oscillatory brain dynamics in time periods of longer duration (e.g. on the multi-second time scale). These multisecond dynamics may reflect the reorganization, time-evolving dynamics and short-term restructuring of brain processes during a continuous task performance, as well as the specific interactions of these variables with default mode network oscillations or with oscillatory processes from shorter duration time scales within the second or millisecond range (Buzsaki and Draguhn, 2004). Thus, multisecond task-related oscillation patterns detected at the behavioural, neurophysiological or neuroimaging levels may provide new insights to state- and trait-dependent differences in the active maintenance of information processing.

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Supplementary material

Supplementary material is available at Brain online.

References


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