

The Speed of Visual Attention and Motor-Response Decisions in Adult Attention-Deficit/Hyperactivity Disorder

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ABSTRACT

BACKGROUND: Adults with attention-deficit/hyperactivity disorder (ADHD) exhibit slowed reaction times (RTs) in various attention tasks. The exact origins of this slowing, however, have not been established. Potential candidates are early sensory processes mediating the deployment of focal attention, stimulus response translation processes deciding upon the appropriate motor response, and motor processes generating the response.

METHODS: We combined mental chronometry (RT) measures of adult ADHD ($n = 15$) and healthy control ($n = 15$) participants with their lateralized event-related potentials during the performance of a visual search task to differentiate potential sources of slowing at separable levels of processing: the posterior contralateral negativity (PCN) was used to index focal-attentional selection times, while the lateralized readiness potentials synchronized to stimulus and response events were used to index the times taken for response selection and production, respectively. To assess the clinical relevance of event-related potentials, a correlation analysis between neural measures and subjective current and retrospective ADHD symptom ratings was performed.

RESULTS: ADHD patients exhibited slower RTs than control participants, which were accompanied by prolonged PCN and lateralized readiness potentials synchronized to stimulus, but not lateralized readiness potentials synchronized to response events, latencies. Moreover, the PCN timing was positively correlated with ADHD symptom ratings.

CONCLUSIONS: The behavioral RT slowing of adult ADHD patients was based on a summation of internal processing delays arising at perceptual and response selection stages; motor response production, by contrast, was not impaired. The correlation between PCN times and ADHD symptom ratings suggests that this brain signal may serve as a potential candidate for a neurocognitive endophenotype of ADHD.

Keywords: ADHD, Decision-making, Electroencephalography, Neuro-cognitive endophenotypes, Psychophysics, Stimulus-response translation

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Attention-deficit/hyperactivity disorder (ADHD) frequently persists into adulthood (1–3). Due to developmental changes in symptom expression, however, the diagnosis of adult ADHD remains challenging (1–10). Latent neurocognitive traits might, thus, constitute endophenotypes of ADHD that 1) differentiate between affected and unaffected individuals, 2) are more closely related to the neurobiological changes associated with adult ADHD than the overt symptoms, and 3) might provide specific information about target functions for interventions (11). In this regard, various attention tasks have been used to study ADHD, with the general finding being that children and adults with ADHD exhibit slowed response times (RTs)¹ (except for the most basic

response tasks) (5,13–20). However, the exact contributions of the respectively engaged internal processes—which might be the source(s) of the overt RT slowing—are not specified unequivocally (4,5,7,10,13–16). Candidate processing levels are early sensory processes that guide the deployment of focal attention (4,10,21), stimulus-response translation processes that decide upon the correct motor response, and motor-response production processes (5,22–24).

Event-related potential (ERP) waves of the electroencephalogram (EEG) allow the assessment of the timing and magnitude of neural activity underlying several distinct processes during task performance (25–27). Thus, a systematic decomposition of potential perceptual and response-related sources underlying overt behavioral slowing is possible when combining ERPs with behavioral measures. This opens the potential for identifying latent internal traits of ADHD-related slowing that bear candidacy for neurocognitive endophenotypes (26–29). Of note, the few previous ERP studies of ADHD patients that investigated early sensory components provide some evidence

¹These findings indicate that behavioral slowing is a reliable finding across the life span. In the clinical symptomatology, this is reflected by inattention symptoms (i.e., sluggish orienting and responding to social and cognitive stimuli and difficulties to direct and maintain selective attention to motivationally relevant tasks) being more enduring than hyperactivity symptoms (6,12).

for alterations of sensory processes that mediate attentional (21) as well as subsequent response selection (22–24). However, none of these studies or those in children with ADHD (26) used a design capable of disentangling the respective potential contributions of the three distinct, consecutive substages of information processing to overt task performance.

Here, we assessed lateralized brain electrical activity in combination with RTs during a compound search task (30) in which the pop-out target to be detected (31,32) contained an additional feature that had first to be identified (e.g., vertical versus horizontal orientation) before a decision about the appropriate motor response could be reached (e.g., left versus right index finger) (32,33). This way, the feature that defined the target from its surroundings (e.g., color) was dissociated from the feature that determined the response (e.g., orientation), permitting target selection, response selection, and response production processes to be examined independently in terms of their respective ERP signatures both within the same participant and in the same task (Figure 1).

In particular, our analyses focused on the posterior contralateral negativity (PCN, also called N2pc) (34,35)—a negativity elicited over parieto-occipital areas contralateral to the location of an attended stimulus—as a marker of focal-attentional selection (36). Second, the lateralized readiness potential (LRP)—a negative-going deflection over the motor areas contralateral to the side of a unimanual response—was examined to index the activation and execution of effector-specific motor responses (37,38). When synchronized relative to stimulus onset (stimulus-locked LRP [sLRP]), its onset latency marks the speed of motor-response decisions, that is, the time it takes to select one out of several possible response alternatives (39). When synchronized relative to response onset (response-locked LRP [rLRP]), its onset reflects the time between response selection and response execution [e.g., (40,41)].

All behavioral and neural measures were compared between adult patients with ADHD, diagnosed in a comprehensive

procedure, and matched healthy control participants. We expected to replicate behavioral slowing of RTs in adults with ADHD (10,13–20). Since both perceptual (4,10,21) and response-related (5,22–24) processes have been suggested as candidate sources of overt RT slowing, we further expected to observe delays in at least one of the analyzed ERPs. Moreover, to assess the clinical relevance of affected ERPs, we further correlated ERP measures with symptom ratings of disease severity. First, we used the Conners Adult ADHD Rating Scales (CAARS) (42) as an index of the severity of subjective current ADHD symptoms. Second, we used the Wender Utah Rating Scale (WURS) (43) sum score as an index of the subjective retrospective severity of childhood symptoms.

METHODS AND MATERIALS

Participants

Fifteen adult ADHD patients (6 male patients; mean age 32.93 ± 10.36 years)² diagnosed at the Department of Psychiatry (Ludwig-Maximilians-University Munich) participated in the study. In the diagnostic procedure, two psychiatric interviews (according to DSM-IV) were conducted either by psychiatrists of the ADHD outpatient clinic or by psychiatrists in clinical practice and by experienced neuropsychologists. Patients were only included in the study when both psychiatrists and neuropsychologists rated them as ADHD patients. A psychologist trained in ADHD assessment collected collateral information from different sources. Elementary school reports or prior diagnoses during childhood and adolescence had to confirm childhood onset according to the obligatory DSM-IV symptoms for childhood ADHD. Patients were only included if descriptions of the respective symptoms were reported at an age <7 years and persisted for a long-term period in the subsequent developmental reports. In Germany, elementary school reports contain comprehensive descriptions of learning performance, social behavior, and daily structure, differentiated according to cognition, emotion, and motor behavior. Furthermore, prior psychiatric diagnoses or third-party informants (siblings, parents, and/or spouses) had to confirm that these symptoms were also displayed at home and that there had been no alternative suspected diagnosis.

Neuropsychological Testing

Current ADHD symptoms were assessed using the long version of the CAARS and retrospective childhood symptoms were assessed using the WURS. Average current ADHD symptom ratings in patients (Table 1) indicated significant subjective impairment in all subscales (mean *t* scores > 60), except for hyperactivity/restlessness (mean *t* score = 57),

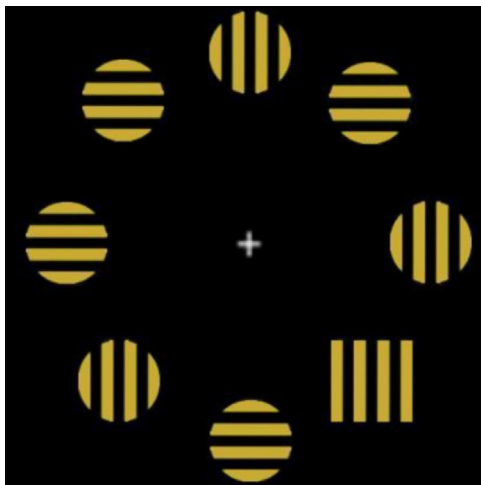


Figure 1. Example of stimulus displays used in the present study. Each display contained a pop-out target, defined in the feature dimension shape (square) or color (red circle), among distracters (yellow circles). The task was to indicate the target's (grating) orientation (horizontal vs. vertical) via pressing the respectively assigned mouse button (left vs. right).

²The relatively high rate of female participants in our study is consistent with a generally more balanced gender distribution of prevalence rates in adulthood compared with childhood ADHD studies (44). It has been argued that while in childhood, referrals from teachers and parents are biased toward male subjects; self-referrals in adulthood are more common and lead to diminishing differences in prevalence rates between male and female subjects (45).

Table 1. Group Demographics

| | ADHD (<i>n</i> = 15) | Control Subjects (<i>n</i> = 15) | <i>t</i> |
|---------------------|-----------------------|--------------------------------------|---------------------|
| Sex (F/M) | 9/6 | 10/5 | |
| Age | 32.93 (10.36) 17–48 | 30.13 (10.16) 19–48 | -.747 |
| School Years | 11.86 (1.64) 9–14 | 12.6 (.98) 10–14 | 1.48 |
| Occupational Status | 2.26 (.88) 2–3 | 2.73 (.45) 1–3 | 1.82 |
| IQ (MWT-B) | 99.00 (7.61) 85–110 | 94.64 (12.16) 80–125 | 1.17 |
| CAARS Subscales | | | |
| A | 72.33 (6.68) 59–80 | 47.87 (4.12) 41–56 | -12.07 ^a |
| B | 57 (8.28) 40–72 | 43.93 (5.06) 33–53 | -5.22 ^a |
| C | 64.73 (11.35) 44–86 | 46.40 (7.27) 31–61 | -5.27 ^a |
| D | 56.87 (11.87) 38–79 | 42.60 (5.77) 34–52 | -4.19 ^a |
| E | 76.53 (10.34) 58–90 | 47.93 (5.42) 38–56 | -9.49 ^a |
| F | 63.53 (10.82) 44–84 | 41.47 (7.47) 32–54 | -6.5 ^a |
| G | 73.87 (10.2) 59–90 | 44.2 (6.61) 33–54 | -9.5 ^a |
| H | 71.73 (7.5) 55–81 | 46.87 (6.1) 36–58 | -9.89 ^a |
| WURS | 46.53 (12.54) 25–71 | 11.2 (6.33) 2–20 | -9.74 ^a |
| BDI-II | 9.53 (6.52) 1–22 | 2.13 (2.53) 0–7 | -4.1 ^a |

Note. Group demographics: Sex distribution and mean, SD, and range of age, attended school years, occupational status (where 1 = labor employment, 2 = technical employment or training, 3 = professional work or university studies), IQ, ADHD rating scales, and depression for ADHD and control groups. *t* values are presented to indicate significant differences between the groups. Tests used: German Multiple-Choice Vocabulary Test (41), corrected according to Satzger *et al.* (46). Conners Adult ADHD Rating Scales (38) with *t* scores of subscales: A: inattention/memory problems; B: hyperactivity/restlessness; C: impulsivity/emotional instability; D: problems with self-concept; E: inattentive symptoms according to DSM-IV; F: hyperactive-impulsive symptoms according to DSM-IV; G: total ADHD symptoms according to DSM-IV; H: ADHD Index. Wender Utah Rating Scale (39). Revised Beck Depression Inventory (42).

ADHD, attention-deficit/hyperactivity disorder; BDI-II, Beck Depression Inventory-II; CAARS, Conners Adult ADHD Rating Scales; F, female; M, male; MWT-B, German version of the Multiple Choice Vocabulary Test; WURS, Wender Utah Rating Scale.

^a*p* < .01.

while retrospective symptoms were above cutoff for all patients except for two who were already medicated with methylphenidate during childhood. In accordance with previous reports on symptoms in adulthood (6), inattentiveness ratings were especially pronounced (mean *t* scores > 72).

IQ was screened using the German version of the Multiple Choice Vocabulary Test (47), ensuring that participants' IQ was above 85. The German version of the Beck Depression Inventory-II (BDI-II) (48) was administered to rule out significant depressive symptoms in control subjects. Depression is highly correlated with ADHD (49,50). Accordingly, ADHD patients with mild (*n* = 4), borderline (*n* = 2), and moderate (*n* = 1) depression levels (but not with severe levels) were included. Two patients were being treated with selective serotonin reuptake inhibitors and were not required to interrupt medication. Six patients were taking methylphenidate but were off medication for at least 24 hours before the experiment. The control group consisted of 15 healthy, demographically matched participants (5 male participants; mean age 30.13 ± 10.16 years) without psychiatric or neurological history. The groups showed no significant differences in IQ, age, gender, years of education, or occupational status (Table 1). A significantly higher level of depression

symptoms was found for the patient group ($t_{30} = 4.16$, $p > .001$); for this reason, separate statistical analyses with depression as covariate were conducted. As expected, ADHD-related symptom ratings (CAARS *t* scores and WURS scores) were significantly higher for the ADHD group and all control participants were below cutoff values. All participants gave informed consent according to the Declaration of Helsinki II and received payment for participating. The study was approved by the ethics committee of the medical faculty of Ludwig-Maximilians-University Munich.

Stimuli, Task, and Study Design

We used a compound search paradigm similar to that introduced by Töllner *et al.* (30). The search displays consisted of sets of eight items presented in a circular array against a black background, each with a distance of 3.0° of visual angle from a white fixation cross (Figure 1). Every trial contained a target randomly defined by a unique color (red circle, 1.2° radius) or a unique shape (square, 2.4° × 2.4°) among seven distractors (yellow circles, each with 1.2° radius). Both targets and distractors contained a grating randomly oriented either horizontally or vertically that determined the response. The gratings consisted of four bars (.4° × 2.4°) separated by three gaps (.3° × 2.4°). The singleton's position on each trial was assigned randomly to one of the six lateral locations. Participants were instructed to maintain central eye fixation and to respond as fast and accurately as possible to the target's orientation (vertical vs. horizontal) with their left/right thumb (pressing a left/right mouse button), respectively. Stimuli were presented on a 17-inch (43.18 cm) screen at a viewing distance of about 65 cm. The experiment consisted of 12 blocks of 72 trials, yielding a total of 864 trials. After the first 6 blocks, response button assignments were reversed. The initial response button assignments were counterbalanced across participants. Each trial started with a fixation cross for 500 milliseconds, followed by the search array for 200 milliseconds. The trial was terminated by the participant's response or timed out after 2 seconds. During the intertrial interval, a white fixation cross was shown variably for either 950, 1000, or 1050 milliseconds. Error responses or time-outs triggered the message Error (German: Fehler). The experiment was conducted in an electrically shielded, sound-attenuated experimental booth. Participants were seated comfortably on a padded chair, while holding the mouse on their lap with both hands, with thumbs placed directly over the response buttons. All participants performed a practice session 5 to 10 days before the actual EEG session to equally familiarize them with the task. During practice, participants performed two to four blocks until they achieved a mean performance of above 90% accuracy and RTs below 1 second. All participants achieved these criteria.

EEG Recording and Data Analysis

EEG was recorded using 63 silver/silver chloride active electrodes (actiCAP, BrainProducts, Gilching, Germany), with electrodes mounted on an elastic cap (Easy Cap, FMS, Herrsching, Germany) according to the international 10-10 system (51). Vertical and horizontal electrooculogram was registered from an electrode beneath the left eye and Fp1 and electrodes F9/10,

respectively. Data were recorded with a DC BrainAmp amplifier (BrainProducts) using a .1 Hz to 250 Hz band-pass filter and a digitization rate of 1 kHz. All data were referenced to FCz and re-referenced offline to averaged mastoids. Electrode impedances were kept below 5 k Ω . Before the EEG analysis, all recordings were visually inspected to eliminate nonstereotypical noise and then high-pass filtered using a .1 Hz (24 dB/Octave; half-power cutoff) infinite impulse response filter. Next, an infomax independent component analysis was run to identify and back-transform blinks and/or horizontal eye movements. Before EEG segmentation, a 40-Hz (24 dB/Octave) low-pass infinite impulse response filter was applied to all data. EEG recordings were segmented separately for each individual. Artifact rejection was performed based on multiple parameters, with a maximum allowed amplitude of $\pm 60 \mu\text{V}$, maximum allowed voltage steps of $50 \mu\text{V}$ between two sample points, and minimum required signal change of $.5 \mu\text{V}$ within 500 milliseconds, on an individual channel basis. To further control for horizontal eye movements, we rejected all segments with signals exceeding $\pm 25 \mu\text{V}$ at electrodes F9/10 before ERP averaging. (See Supplement 1 material for evidence that, following this procedure, the present ERL waves were not contaminated by residual eye-related activity).

For the PCN analysis, the EEG data were epoched into 400-millisecond periods following stimulus onset relative to a 200-millisecond prestimulus period used for baseline correction. The PCNs were computed by subtracting ipsilateral from contralateral activity at electrodes PO7/8 relative to the target side. PCN peak latencies were determined as the maximum negative deflection in the time window 130 to 350 milliseconds post-stimulus. PCN amplitudes were obtained by averaging ± 5 data points around this maximum deflection. PCN onset latencies were determined using the Ulrich and Miller (52) jackknife-based scoring method, defining the onset at 50% of the maximum amplitude. For the LRP analysis, the EEG data were first epoched into 1200-millisecond periods following stimulus onset relative to an 800-millisecond prestimulus period, so that baseline correction could be performed (based on the 200-millisecond prestimulus period). The LRP was computed by subtracting ipsilateral from contralateral ERPs at electrodes C3/4 relative to the response side. Stimulus-locked LRPs were then re-epoched into 800-millisecond periods following stimulus onset relative to a 200-millisecond baseline. Response-locked LRPs were re-epoched into periods of 800 milliseconds before to 200 milliseconds after response onset. Onset latencies of LRPs were computed—as recommended by Ulrich and Miller (52)—using 50% and 90% of the maximum amplitude as optimal criteria to determine the stimulus- and response-locked LRP onsets, respectively. Response-locked LRP amplitudes were calculated by averaging ± 5 data points around the maximum LRP deflection. The interval between PCN and sLRP was calculated by subtracting the PCN onset latency from the sLRP onset latency.

Separate analyses of variance were carried out on all behavioral (error rates, RTs) and neural measures (PCN amplitude, PCN peak latency, PCN onset latency, PCN to sLRP interval, LRP onset latency, rLRP amplitude, rLRP onset latency) for the between-subject factor group (ADHD, control). Trials with incorrect responses or RTs longer than 1 second were not entered into the analyses. In addition, due to significant between-group differences in BDI-II scores, we

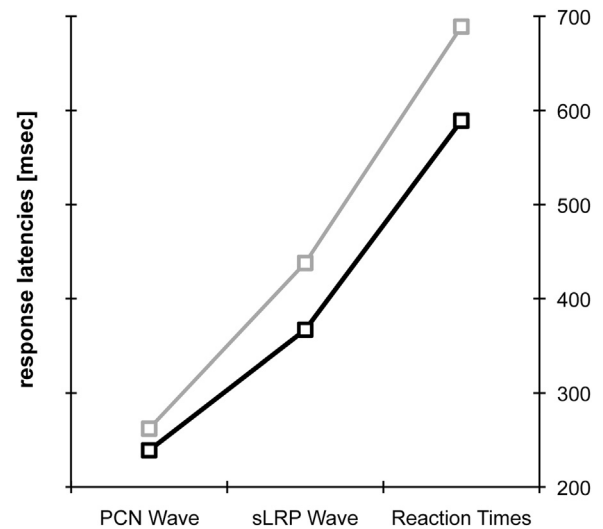


Figure 2. Mean posterior contralateral negativity (PCN), stimulus-locked lateralized readiness potential (sLRP), and response (response time) latencies separately for control subjects (black line) and attention-deficit/hyperactivity disorder patients (gray line).

submitted the variables that were not derived through the jackknife procedure (RT and PCN peak latency) to separate analyses of covariance with the BDI-II scores as covariates, as suggested by Thomas *et al.* (53). To provide information about the clinical relevance of the EEG timing in the adult ADHD patient group, we examined the relationship between ERP peak/onset latencies (54) and subjective symptom ratings of both current (CAARS ADHD index) and retrospective (WURS sum score) impairments.

RESULTS

Behavioral Data

The analysis of variance for error rates revealed no significant differences between patients (8.27%) and control subjects (6.52%) ($F_{1,28} = 1.15$; $p > .293$, $d = .39$). By contrast, RTs were significantly ($F_{1,28} = 15.36$; $p < .001$, $d = 1.43$) slower in ADHD patients (689 msec; SD = 71) than in control participants (590 msec; SD = 67) (Figure 2). This result also remained significant after including depression (BDI-II score) as a covariate ($F_{1,27} = 8.64$; $p < .007$).

PCN Data

The rise (217 vs. 195 msec) and the maximum (262 vs. 240 msec) of the PCN waves were markedly delayed for ADHD patients as compared with control participants (Figure 3). These observations were substantiated by significant group effects for PCN onset ($F_{c1,28} = 10.38$; $p < .003$, $d = 1.18$) and peak latencies ($F_{1,28} = 15.63$; $p < .001$, $d = 1.44$). As with the RT data, the difference in peak latencies remained significant after controlling for BDI-II scores ($F_{1,27} = 4.93$; $p = .035$). In addition, PCN peak latencies correlated significantly (Figure 4) with ADHD symptom scores of current and retrospective impairments (CAARS ADHD index: $r = .49$, $p = .032$; WURS

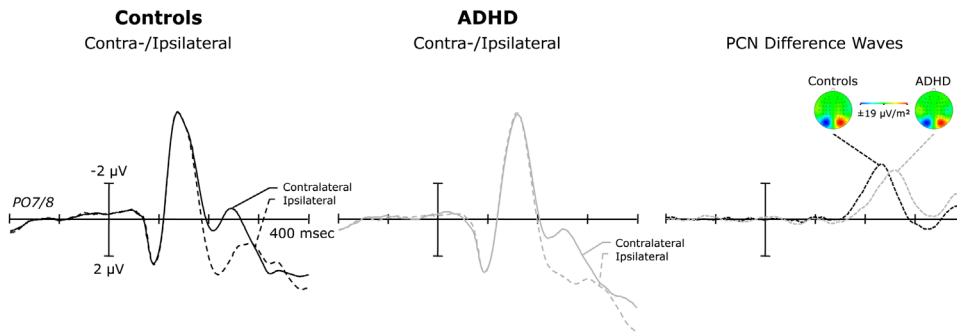


Figure 3. Target-synchronized grand average event-related potential (ERP) waves elicited at electrode sites PO7/8 for the control group (black lines) and the attention-deficit/hyperactivity disorder (ADHD) group (gray lines). Left: ERP waves contralateral (contra-) and ipsilateral to the target position for the control group. Center: ERP waves contra- and ipsilateral to the target position for the ADHD group. Right: posterior contralateral negativity (PCN) difference waves, obtained by subtracting ipsilateral from contralateral activity, for the control and ADHD groups. The topographic scalp distribution map shows the point in time

at which the difference between grand average contralateral and ipsilateral waves was maximal.

sum score: $r = .46$; $p = .041$; both one-sided).³ No significant difference was obtained for PCN onset amplitudes ($F_{1,28} = .27$; $p > .61$, $d = .19$).

LRP Data

The groups further differed in the sLRP onset latencies ($F_{c1,28} = 18.34$; $p_c < .002$, $d = 1.56$), with the latencies being prolonged in ADHD patients (438 msec, $SD = 3.43$) as compared with control participants (367 msec, $SD = 3.02$). However, there was no correlation with ADHD symptom scores of current and retrospective impairments (CAARS ADHD index: $r = .15$, $p = .301$; WURS sum score: $r = .16$; $p = .266$). Importantly, the PCN to sLRP interval of ADHD patients (221 msec, $SD = 3.22$) significantly exceeded that observed for control participants (172 msec, $SD = 2.30$) ($F_{c1,28} = 11.72$; $p_c < .002$, $d = 1.25$), showing that the delay in the sLRP latency exceeds, and is thus not completely attributable to, the delay in the preceding PCN. No significant differences were observed for the rLRP onset latencies ($F_{c1,28} = .80$; $p_c = .38$, $d = -.32$) and amplitude ($F_{1,28} = .02$; $p > .878$, $d = .06$), indicative of motor-related processing being comparable between the two groups (Figure 5).

DISCUSSION

The primary aim of the present study was to disentangle potential contributions of focal-attentional selection, stimulus-response translation, and motor-response production processes to RT slowing in adult ADHD. For this purpose, performances of an adult ADHD group and a healthy control group were compared in a compound search task, with simultaneous recording of lateralized ERPs. Behaviorally, our analyses replicate previous reports of prolonged RTs in adults, as well as children, with ADHD (55,56), further underlining the reliability of ADHD-dependent RT slowing in visual attention tasks. Mirroring this RT pattern, we found delayed PCN waves

for ADHD patients, indicating slowed attentional selection. The individual PCN delay correlated with impairment severity as revealed by subjective current and retrospective symptom ratings. In addition, the sLRP timing was prolonged overall and the interval between the PCN and the sLRP was considerably increased for ADHD patients. The latter finding provides evidence of an additional slowing at intermediate, stimulus-response translation processes. Groups did not differ in rLRP timing, which demonstrates that motor processing remains similar for both groups. Together, our results reveal a summation of deficits at two consecutive processing levels, focal-attentional selection and motor-response selection, which conjointly contribute to RT slowing in adult ADHD.

Because our study included only adults, we cannot tell whether this ERP pattern developed over the course of the disease or whether it would likewise be observable in children. To answer this question unequivocally, it would be necessary to assess children with ADHD. The RT cost might reflect either genuine (age-independent) slowing in ADHD or a compensatory strategy of adults who have learned to deal with their tendency to perform inaccurately by slowing—that is, it may reflect a speed-accuracy trade-off. At variance with the latter assumption, however, is that RT slowing in ADHD is found reliably in children as well as in adults (6,12), favoring the possibility that the current pattern might be equally present in children. Moreover, correlations of PCN timing with current ADHD symptomatology indicate that those participants who were less efficiently compensating for the difficulties brought about by the disease showed more delayed PCNs. Thus, we tentatively suggest that the PCN timing may reflect a neural correlate of genuine slowing in ADHD.

ADHD and the Speed of Visual Attention

The delayed PCN timing indicates that, already early, sensory attention-guiding processes are impaired in adult ADHD patients—even in a pop-out search task in which visual selection is largely bottom-up driven (57–59). Such a fundamental slowing of basic processes of attentional selection (required in most tasks using visual material) would be a major contributing factor to the deficits exhibited by ADHD patients in more complex visual tasks (60). While the PCN has not yet been used to assess visual attentional deficits in ADHD, previous ERP studies already pointed to an impairment of early and

³We further calculated correlations between onset latencies and symptom measures, as suggested by Stahl and Gibbons (54). These analyses revealed that PCN onsets were correlated significantly with ADHD symptom scores of current impairments (CAARS ADHD index: $r = .55$, $p = .017$); the correlation with retrospective impairments failed to reach statistical significance (WURS sum score: $r = .38$; $p = .082$). No significant correlations were found for LRP onsets (all p values $> .22$).

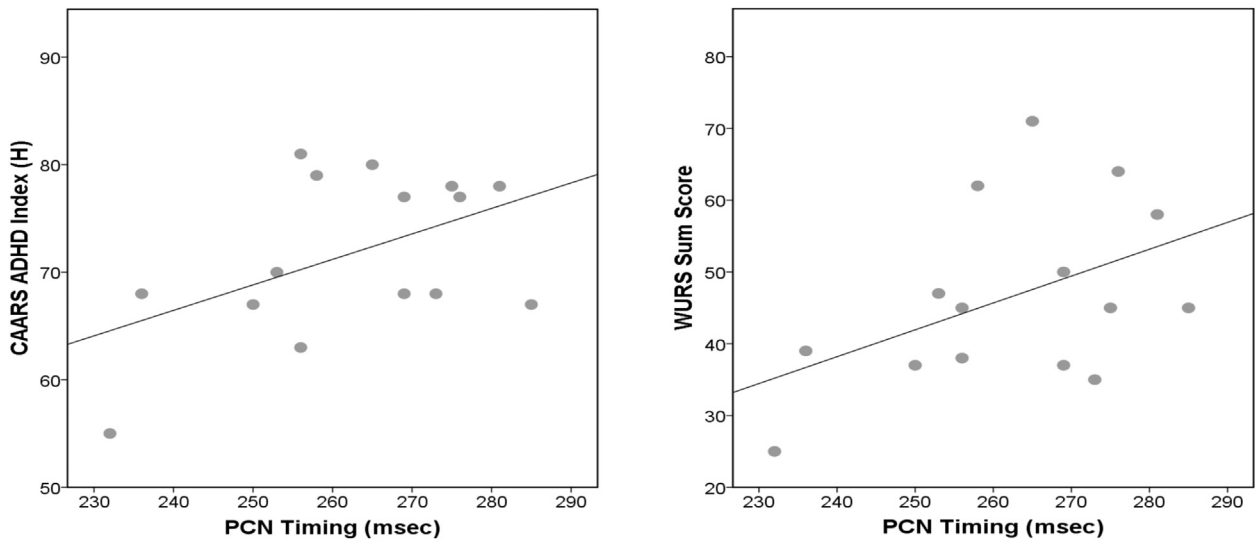


Figure 4. Correlations between the posterior contralateral negativity (PCN) timing and the scores in psychometric testing (for the attention-deficit/hyperactivity disorder [ADHD] group). Left: correlation with the ADHD Index (H) *t* score of the Conners Adult ADHD Rating Scales (CAARS). Right: correlation with the Wender Utah Rating Scale (WURS) Sum Score.

intermediate visual attentional processes in ADHD children, evidenced by N1 and N2 delays in a two-alternative forced-choice RT task (61). On the other hand, Prox *et al.* (21), using a go/no-go paradigm, reported enhanced activations but no changes in the timing of the N1 and N2 components in adult ADHD, without significant delays in RT performance. Based on their results, Prox *et al.* (21) surmised that adult ADHD patients have learned to gather greater neural resources for the perceptual analysis and identification of a single stimulus to achieve normal performance. In light of the current findings, we argue that such an adaptation is not feasible when, contrary to typical go/no-go tasks that use one stimulus only, a target has to be selected among multiple distractors.

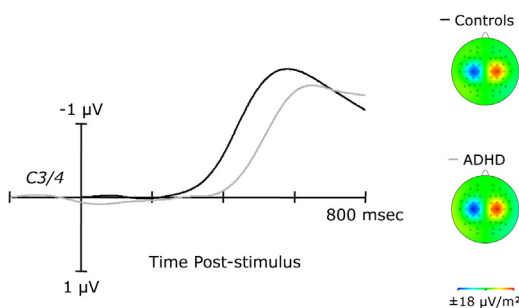
Several findings suggest that PCN delay may have candidacy for a neurocognitive endophenotype of adult ADHD (10,21,28). The first is its relationship to clinical indicators of the disease: the PCN timing was correlated to subjective symptom severity. Second, and in particular, the relationship of PCN timing with retrospective as well as current childhood symptoms was reliable and comparable in strength. Accordingly, despite the well-known overt symptom expression changes across the life span, the

timing of the PCN would appear to reflect disease severity in quite a stable manner. Third, the PCN delay seems to be related to ADHD in a relatively specific manner. In schizophrenia patients, for instance, Luck *et al.* (62) reported the PCN timing to be unaffected. Verleger *et al.* (63) showed that under challenging conditions with rapid visual information requirements, PCN amplitudes were reduced in schizophrenia and bipolar patients but they did not report latency differences for either of these patient groups. Note that the adult ADHD patients in the current study exhibited PCN amplitudes similar to the control group. Furthermore, PCN latency differences remained significant even after controlling for the influence of depression symptoms. Although further studies on other psychiatric and neurological disorders are clearly needed, it can be tentatively inferred that a delayed PCN not only indicates a rather unspecific liability for the development of any psychiatric symptoms but also bears a certain degree of disease specificity.

ADHD and the Speed of Motor-Response Decisions

In addition to delayed attentional selection, the interval between the PCN and the sLRP was increased in adults with

Stimulus-locked LRP



Response-locked LRP

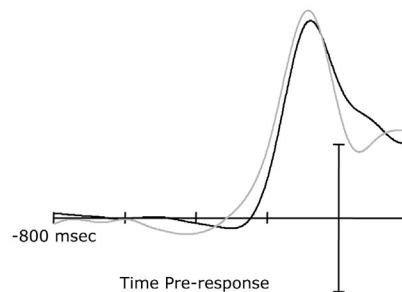


Figure 5. Grand-averaged lateralized readiness potential (LRP) (contralateral – ipsilateral difference) waves elicited at electrode sites C3/4 for the control group (black lines) and the attention-deficit/hyperactivity disorder (ADHD) group (gray lines). Left: for the stimulus-locked LRP elicited in the 800-millisecond interval after stimulus onset. Right: for the response-locked LRP elicited in the 800 milliseconds before response onset. Middle: scalp topographic map depicting the contralateral – ipsilateral difference waves of the LRP.

ADHD compared with control participants. Thus, the delay observed for the sLRP does not simply reflect a carryover of delays in attentional selection; rather, response selection appears to be additionally affected in patients, indicating slowed visuomotor integration processes. In particular, adult ADHD patients required significantly more time to decide upon the correct motor response based on the target's featural identity. By contrast, following response selection, the actual realization of the motor response was not affected, as evidenced by the rLRP. Of note, the current study is, to our knowledge, the first to assess motor processes in ADHD adults directly through the LRP and furthermore to dissociate response selection from response production components. In a study of ADHD children, Perchet *et al.* (25) took the absence of timing differences between the N2 and P3 (which have been associated with stimulus evaluation) in the presence of RT and accuracy changes as indirect evidence of alterations in response selection processes. However, these authors neither measured response-related ERPs nor differentiated between processes of preparation and execution. The present results, by contrast, clearly demonstrate that in adult ADHD, a slowing of response selection, rather than of the subsequent motor production, contributes to the overt RT slowing. Note, however, that owing to life span changes in symptomatology and in motor-related hyperactivity in particular, results relating the motor production stages derived by our methodology might conceivably differ in children [e.g., (6,24)]. The revealed impairment in response selection is in line with previous studies that reported an especially marked RT slowing in adult ADHD patients with increasingly difficult stimulus-response mappings (5,13–15).

Implications of Impaired Perceptual and Response Selection Decisions in ADHD

The observed impairments at the stages of focal attentional and response selection in adult ADHD are likely to summate in tasks that place demands on both processing stages. As suggested in a meta-analysis by Schoechlin and Engel (13), this is the case in complex attention tasks that include distractor elements, conditional responses, or both, in which adult ADHD patients exhibit a greater impairment compared with basic psychomotor tasks. Given that daily life tasks involve both processes, delays in attentional and response selection would jointly contribute to overt adult ADHD symptomatology. This conclusion is, at least in part, supported by the correlation obtained between PCN timing and subjective impairment severity.

Conclusion

The present findings disclose that adult ADHD patients have processing delays in at least two distinct substages of information processing, namely, attentional selection (indexed by the PCN) and response selection (indexed by the sLRP), which summate to produce an overall RT slowing. By contrast, they display no slowing in motor-response production (as indexed by the rLRP). Our direct demonstration of these delays adds to the mounting evidence that adult ADHD patients are more impaired in tasks placing greater demands on attentional and/or response selection, as compared with

simple RT tasks. The correlation of the PCN with ADHD symptom ratings further indicates that the PCN delay may bear candidacy as a neurocognitive endophenotype of adult ADHD. Arguably, the use of a compound search task along with neurochronometric measurements represents a methodological advantage that is sensitive to the interaction of these two distinct processes in task performance, providing further support for an understanding of ADHD as a multifactorial disorder (8).

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REFERENCES

- Davidson MA (2008): ADHD in adults: A review of the literature. *J Atten Disord* 11:628–641.
- Barkley RA, Fischer M, Smallish L, Fletcher K (2002): The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. *J Abnorm Psychol* 111:279–289.
- Biederman J, Faraone SV, Monuteaux MC, Bober M, Cadogan E (2004): Gender effects on attention-deficit/hyperactivity disorder in adults, revisited. *Biol Psychiatry* 55:625–700.
- Woods SP, Lovejoy DW, Ball JD (2002): Neuropsychological characteristics of adults with ADHD: A comprehensive review of initial studies. *Clin Neuropsychol* 16:12–34.
- Gallagher R, Blader J (2001): The diagnosis and neuropsychological assessment of adult attention deficit/hyperactivity disorder. *Ann N Y Acad Sci* 931:148–171.
- Biederman J (2005): Attention-deficit/hyperactivity disorder: A selective overview. *Biol Psychiatry* 57:1215–1220.
- Kaplan RF, Stevens M (2002): A review of adult ADHD: A neuropsychological and neuroimaging perspective. *CNS Spectr* 7:355–362.
- Castellanos FX, Sonuga-Barke EJ, Milham MP, Tannock R (2006): Characterizing cognition in ADHD: Beyond executive dysfunction. *Trends Cogn Sci* 10:117–123.

9. Nigg JT (2005): Neuropsychologic theory and findings in attention-deficit/hyperactivity disorder: The state of the field and salient challenges for the coming decade. *Biol Psychiatry* 57:1424–1435.
10. Armstrong CL, Hayes KM, Martin R (2001): Neurocognitive problems in attention deficit disorder. Alternative concepts and evidence for impairment in inhibition of selective attention. *Ann N Y Acad Sci* 931: 196–215.
11. Finke K, Schwarzkopf W, Müller U, Frodl T, Müller HJ, Schneider WX, *et al.* (2011): Disentangling the adult attention-deficit hyperactivity disorder endophenotype: Parametric measurement of attention. *J Abnorm Psychol* 120:890–901.
12. Solanto MV, Gilbert SN, Raj A, Zhu J, Pope-Boyd S, Stepak B, *et al.* (2007): Neurocognitive functioning in AD/HD, predominantly inattentive and combined subtypes. *J Abnorm Child Psychol* 35:729–744.
13. Schoechlin C, Engel RR (2005): Neuropsychological performance in adult attention-deficit hyperactivity disorder: Meta-analysis of empirical data. *Arch Clin Neuropsychol* 20:727–744.
14. Johnson DE, Epstein JN, Waid RL, Latham PK, Voronin KE, Anton RF (2001): Neuropsychological performance deficits in adults with attention deficit/hyperactivity disorder. *Arch Clin Neuropsychol* 16:587–604.
15. Faraone SV, Biederman J, Spencer T, Wilens T, Seidman LJ, Mick E, Doyle AE (2000): Attention-deficit/hyperactivity disorder in adults: An overview. *Biol Psychiatry* 48:9–20.
16. Hervey AS, Epstein JN, Curry JF (2004): Neuropsychology of adults with attention-deficit/hyperactivity disorder: A meta-analytic review. *Neuropsychology* 18:485–503.
17. Kovner R, Budman C, Frank Y, Sison C, Lesser M, Halperin J (1998): Neuropsychological testing in adult attention deficit hyperactivity disorder: A pilot study. *Int J Neurosci* 96:225–235.
18. Karalunas SL, Huang-Pollock CL, Nigg JT (2012): Decomposing attention-deficit/hyperactivity disorder (ADHD)-related effects in response speed and variability. *Neuropsychology* 26:684–694.
19. Sergeant JA (2005): Modeling attention-deficit/hyperactivity disorder: A critical appraisal of the cognitive-energetic model. *Biol Psychiatry* 57:1248–1255.
20. Soutschek A, Schwarzkopf W, Finke K, Hennig-Fast K, Müller HJ, Reidel M, *et al.* (2013): Interference control in adult ADHD: No evidence for interference control deficits if response speed is controlled by delta plot. *Acta Psychol (Amst)* 143:71–78.
21. Prox V, Dietrich DE, Zhang Y, Emrich HM, Ohlmeier MD (2007): Attentional processing in adults with ADHD as reflected by event-related potentials. *Neurosci Lett* 419:236–241.
22. Fisher T, Aharon-Peretz J, Pratt H (2011): Dis-regulation of response inhibition in adult attention deficit hyperactivity disorder (ADHD): An ERP study. *Clin Neurophysiol* 122:2390–2399.
23. Karch S, Thälmeier T, Lutz J, Ceroveckí A, Opgen-Rhein M, Hock B, *et al.* (2010): Neural correlates (ERP/fMRI) of voluntary selection in adult ADHD patients. *Eur Arch Psychiatry Clin Neurosci* 5:427–440.
24. Valko L, Doehner M, Müller UC, Schneider G, Albrecht B, Drechsler R, *et al.* (2009): Differences in neurophysiological markers of inhibitory and temporal processing deficits in children and adults with ADHD. *J Psychophysiol* 23:235–246.
25. Perchet C, Revol O, Fourmeret P, Mauguière F, Garcia-Larrea L (2001): Attention shifts and anticipatory mechanisms in hyperactive children: An ERP study using the Posner paradigm. *Biol Psychiatry* 50:44–57.
26. Barry RJ, Johnstone SJ, Clarke AR (2003): A review of electrophysiology in attention-deficit/hyperactivity disorder: II. Event-related potentials. *Clin Neurophysiol* 114:184–198.
27. Johnstone SJ, Barry RJ, Clarke AR (2013): Ten years on: A follow-up review of ERP research in attention-deficit/hyperactivity disorder. *Clin Neurophysiol*, 114, 184–198.
28. Mueller A, Candrian G, Kropotov JD, Ponomarev VA, Baschera GM (2010): Classification of ADHD patients on the basis of independent ERP components using a machine learning system. *Nonlinear Biomed Phys* 4(suppl 1):S1.
29. Mueller A, Candrian G, Grane VA, Kropotov JD, Ponomarev VA, Bacher GM (2011): Discriminating between ADHD adults and controls using independent ERP components and a support vector machine: A validation study. *Nonlinear Biomed Phys* 5:5.
30. Töllner T, Gramann K, Müller HJ, Kiss M, Eimer M (2008): Electrophysiological markers of visual dimension changes and response changes. *J Exp Psychol Hum Percept Perform* 34:531–542.
31. Treisman A, Gormican S (1988): Feature analysis in early vision: Evidence from search asymmetries. *Psychol Rev* 95:15–48.
32. Treisman AM, Gelade G (1980): A feature-integration theory of attention. *Cogn Psychol* 12:97–136.
33. Wiegand I, Finke K, Müller HJ, Töllner T (2013): Event-related potentials dissociate perceptual from response-related age effects in visual search. *Neurobiol Aging* 34:973–985.
34. Töllner T, Müller HJ, Zehetleitner M (2012): Top-down dimensional weight set determines the capture of visual attention: Evidence from the PCN component. *Cereb Cortex* 22:1554–1563.
35. Woodman GF, Luck SJ (1999): Electrophysiological measurement of rapid shifts of attention during visual search. *Nature* 400:867–869.
36. Eimer M (1996): The N2pc component as an indicator of attentional selectivity. *Electroencephalogr Clin Neurophysiol* 99:225–234.
37. Coles MG (1989): Modern mind-brain reading: Psychophysiology, physiology, and cognition. *Psychophysiology* 26:251–269.
38. Kutas M, Donchin E (1980): Preparation to respond as manifested by movement-related brain potentials. *Brain Res* 202:95–115.
39. Töllner T, Rangelov D, Müller HJ (2012): How the speed of motor-response decisions, but no focal-attentional selection, differs as a function of task set and target prevalence. *Proc Natl Acad Sci U S A* 109:1990–1999.
40. Miller J, Patterson T, Ulrich R (1998): Jackknife-based method for measuring LRP onset latency differences. *Psychophysiology* 35:99–115.
41. Hackley SA, Valle-Inclán F (2003): Which stages of processing are speeded by a warning signal? *Biol Psychol* 64:27–45.
42. Conners CK, Erhards D, Sparrow E (2002): *Conner's Adult ADHD Rating Scales (CAARS)*. North Tonawanda, NY: Multi Health Systems.
43. Ward MF, Wender PH, Reimherr FW (1993): The Wender Utah Rating-Scale: An aid in the retrospective diagnosis of childhood attention-deficit hyperactivity disorder. *Am J Psychiatry* 150:885–890.
44. Simon V, Czobor P, Bálint S, Mészáros Á, Bitter I (2009): Prevalence and correlates of adult attention-deficit hyperactivity disorder: Meta-analysis. *Br J Psychiatry* 194:204–211.
45. Gershon J (2002): A meta-analytic review of gender differences in ADHD. *J Atten Disord* 5:143–154.
46. Satzger W, Fressmann H, Engerl RR (2002): Liefern HAWIE-R, WST und MWT-B vergleichbare IQ-Werte? *J Indiv Differ* 23:159–170.
47. Lehl S (1999): *Mehrfachwahl-Wortschatz-Intelligenztest (MWT-B)*. Göttingen. Germany: Hogrefe.
48. Kühner C, Bürger C, Keller F, Hautzinger M (2007): [Reliability and validity of the Revised Beck Depression Inventory (BDI-II). Results from German samples]. [Article in German]. *Nervenarzt* 78:651–656.
49. Kessler RC, Adler L, Barkley R, Biederman J, Conners CK, Demler O, *et al.* (2006): The prevalence and correlates of adult ADHD in the United States: Results from the national comorbidity survey replication. *Am J Psychiatry* 163:716–723.
50. Sobanski E, Brüggemann D, Alm B, Kern S, Deschner M, Schubert T, *et al.* (2007): Psychiatric comorbidity and functional impairment in a clinically referred sample of adults with attention-deficit/hyperactivity disorder (ADHD). *Eur Arch Psychiatry Clin Neurosci* 257:371–377.
51. American Electroencephalographic Society. (1994): *Guideline thirteen: Guideline for standard electrode position nomenclature*. American Electroencephalographic Society. *J Clin Neurophysiol* 11:111–113.
52. Ulrich R, Miller J (2001): Using the jackknife-based scoring method for measuring LRP onset effects in factorial designs. *Psychophysiology* 38:816–827.
53. Thomas MS, Annaz D, Ansari D, Serif G, Jarrold C, Karmiloff-Smith A (2009): Using developmental trajectories to understand developmental disorders. *J Speech Lang Hear Res* 52:336–358.
54. Stahl J, Gibbons H (2004): The application of jackknife-based onset detection of lateralized readiness potential in correlative approaches. *Psychophysiology* 41:845–860.
55. Hazell PL, Carr VJ, Lewin TJ, Dewis SA, Heathcote DM, Brucki BM (1999): Effortful and automatic information processing in boys with ADHD and specific learning disorders. *J Child Psychol Psychiatry* 40:275–286.

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56. Karatekin C, Asarnow RF (1998): Components of visual search in childhood-onset schizophrenia and attention-deficit/hyperactivity disorder. *J Abnorm Child Psychol* 26:367–380.
57. Töllner T, Zehetleitner M, Gramann K, Müller HJ (2011): Stimulus saliency modulates pre-attentive processing speed in human visual cortex. *PLoS One* 6:e16276.
58. Töllner T, Zehetleitner M, Krummenacher J, Müller HJ (2011): Perceptual basis of redundancy gains in visual pop-out search. *J Cogn Neurosci* 23:137–150.
59. Töllner T, Conci M, Rusch T, Müller HJ (2013): Selective manipulation of target identification demands in visual search: The role of stimulus contrast in CDA activations. *J Vis* 13:23.
60. Booth JR, Burman DD, Meyer JR, Lei Z, Trommer BL, Davenport ND, *et al.* (2005): Larger deficits in brain networks for response inhibition than for visual selective attention in attention deficit hyperactivity disorder (ADHD). *J Child Psychol Psychiatry* 46:94–111.
61. Karayanidis F, Robaey P, Bourassa M, De Koning D, Geoffroy G, Pelletier G (2000): ERP differences in visual attention processing between attention-deficit hyperactivity disorder and control boys in the absence of performance differences. *Psychophysiology* 37: 319–333.
62. Luck SJ, Fuller RL, Braun EL, Robinson B, Summerfelt A, Gold JM (2006): The speed of visual attention in schizophrenia: Electrophysiological and behavioral evidence. *Schizophr Res* 85: 174–195.
63. Verleger R, Talamo S, Simmer J, Śmigajewicz K, Lencer R (2013): Neurophysiological sensitivity to attentional overload in patients with psychotic disorders. *Clin Neurophysiol* 124:881–892.