Disentangling Deficits in Adults With Attention-Deficit/Hyperactivity Disorder

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Context: A lack of inhibitory control has been suggested to be the core deficit in attention-deficit/hyperactivity disorder (ADHD), especially in adults. This means that a primary deficit in inhibition mediates a cascade of secondary deficits in other executive functions, such as attention. Impaired stopping has been claimed to support the inhibition hypothesis. However, executive functions such as inhibition and attention are hard to disentangle.

Objective: To use event-related potentials in adult patients with ADHD to show that impaired stopping is associated with abnormalities of attention.

Design: The stop signal task was presented to 24 adults with ADHD combined subtype and 24 controls. Stop event-related potentials are distorted by overlap from event-related potentials to other stimuli in close temporal proximity, but we applied a method (Adjar level 2) to effectively remove this overlap.

Results: In line with an inhibitory control deficit, the stop signal reaction time was longer in adults with ADHD ($F_{1,46}=7.12$, $P<.01$) whereas there was no significant difference for go stimulus reaction time. Overlap-free stop event-related potentials revealed smaller stop P3s in adults with ADHD ($F_{1,44}=4.20$, $P<.05$). In children with ADHD, this has been interpreted to reflect deficient inhibitory control. However, controls were also found to have larger early responses in the auditory cortex (N1) when stop signals resulted in successful stops, relative to failed stops, signifying increased attention ($F_{1,23}=11.88$, $P<.01$). This difference was completely absent in adults with ADHD.

Conclusions: Disturbed attentional processing of the stop signal contributed to impaired stopping in adults with ADHD. This finding may have implications for treatment.

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EXECUTIVE FUNCTIONS THAT govern everyday human behavior are manifold in nature. They range from being able to maintain a certain focus of attention, to switching attention from one source of information to another, to the ability to suppress inadequate but prepotent or ongoing response tendencies (response inhibition). These subfunctions have to be combined to achieve one's daily goals.[1] At an operational level, the relative contributions of these subfunctions are hard to distinguish. Behavioral measures such as speed and accuracy that are generally used as indices of executive functions by definition reflect the compound contributions of different subfunctions. Their distinction becomes particularly urgent when identifying core deficits underlying psychiatric disorders. A prime example is attention-deficit/hyperactivity disorder (ADHD).

The most prevalent subtype of ADHD (combined type) is characterized by symptoms of inattention, impulsivity, and hyperactivity.[2] Since its first clinical descriptions, researchers have focused on identifying the core deficit underlying all other symptoms in ADHD. Deficits of response inhibition[3,4] or attention[5,6] have been claimed to play a critical role. Nigg[7] reviewed the literature on ADHD and concluded that in children with the combined subtype, impaired performance was most consistently found for tasks measuring response inhibition. However, this does not settle the controversy surrounding the core nature of a response inhibition deficit.

Results from the stop signal task, which is generally accepted as the best behavioral approximation of response inhibition,[8] seem to support the notion that poor inhibitory control is central to ADHD in children[9] and especially in adults.[10,11] In the stop signal task, subjects are instructed to withhold their responses in a visual choice reaction time task when a stop signal, usually a tone, is presented. The probability of successful stops is thought to depend on the relative speeds of 2 independently operating processes: the

go process and the stop process. The speed of the stop process, the stop signal reaction time (SSRT), can be estimated by weighting the distribution of choice reaction times (RTs) associated with the go process with the proportion of successful stops (Ps). Relative to controls, children and adults with ADHD have been found to display slower SSRTs.[9-15]

The increase in SSRT found in patients with ADHD might be taken as evidence in favor of a core deficit in response inhibition. However, SSRTs reflect other aspects of stop signal processing as well, among which are attention to the set of task stimuli as a whole and the ability to switch attention from go stimuli to the occasional stop signal. Indeed, several authors have argued that the slower SSRTs in children with ADHD can be explained by a more general deficit of attention that is also manifest in the reaction to go stimuli.[5,10] Recently, it has become clear that in adults with ADHD, slowing is specifically related to the processing of the stop signal.[10,11] However, even then, the possibility that the primary deficit lies in the ability to switch attention to the stop signal is still open.[11]

Event-related brain potentials (ERPs) provide an online measure of cortical processing and allow for a separation of processing related to attention vs inhibition. The interpretation of ERPs to stop signals is, however, problematic. Because go stimuli generally lead stop signals by only a few hundred milliseconds, ERPs to stop signals are strongly overlapped by ERPs to go stimuli. Hence, confounding overlap has plagued the interpretation of previously reported stop signal ERPs in healthy subjects[16-18] and children with ADHD.[19-22] In children with ADHD, smaller N1s to go stimuli preceding stop failures[19] as well as smaller N2s[20,21] and P3s[22] to stop signals have been reported. Inconsistencies across studies might reflect differential dealing with overlap distortion. In our opinion, the only method that validly addresses overlap problems is the Adjacent Response filter method (Adjar level 2) developed by Woldorff.[23] In a previous study with healthy subjects, we demonstrated the efficacy of Adjar in the stop signal task.[24] After correction, successful stops were associated with a larger positivity over frontocentral areas as from 140-milliseconds post–stop signal than failed stops. This stop P3 has been reported before and has been interpreted to reflect response inhibition,[16,18] but previous studies could not exclude an interpretation in terms of overlap from ERPs to other stimuli (eg, motor potentials with a negative polarity that are smaller for successful stops than for failed stops).

Even with the overlap problem being resolved for the stop P3, the interpretation in terms of inhibition remains somewhat arbitrary. A completely new finding after Adjar correction was that successful stops were associated with a larger negative peak at about 100 milliseconds post-stimulus. This N1 almost certainly originates in auditory cortex and is very sensitive to selective attention.[25] More generally, it reflects the trial-to-trial varying impact a stimulus has in auditory cortex, which is an essential ingredient of the amount of attention that is switched to the stimulus on its presentation. This prompts the intriguing possibility that impaired stopping at least partly depends on the inability to switch attention to the stop signal.

In the present study, Adjar-corrected stop signal ERPs obtained from adults with ADHD (n=24) were com-

pared with those obtained from matched controls (n=24). Three hypotheses were tested. First, in the present sample of controls, successful stops are associated with larger N1s and stop P3s than failed stops. Second, the stop P3 effect is reduced in adults with ADHD, suggesting a deficient inhibitory mechanism. Third, the N1 effect is reduced in the ADHD group, suggesting that deficient attentional switching to the stop signal is the precursor of deficient inhibitory control.

METHODS

SUBJECTS

Twenty-four outpatient adults with ADHD diagnosed with the combined subtype (mean±SD age, 34.3±11.68 years; range, 18-57 years; 12 men; 3 left-handed) were matched on age and gender with 24 controls (mean age, 34.9 years; range, 18-57 years; 12 men; 1 left-handed). The vocabulary and block design subtests of the Wechsler Adult Intelligence Scale III[26] were administered to ensure comparable IQ across groups (mean±SD age-scaled scores were 10.3±3.6 and 10.0±3.0 for adults with ADHD and 11.1±3.2 and 10.5±3.9 for controls, respectively; $F_{1,46}$=0.79, P=.38, and $F_{1,46}$=0.21, P=.65). All subjects claimed to have normal hearing and normal or corrected-to-normal vision. Prior to participation, the use of psychoactive medication (at least 6 times the half-life concerned); drugs (at least 3 weeks); alcohol (at least 24 hours); and nicotine, caffeine, and cacao (at least 12 hours) was prohibited. All subjects signed informed-consent forms. The ethics committee of the Utrecht University Medical Center (Utrecht, the Netherlands) approved this study.

RECRUITMENT AND SCREENING

Patients were recruited when first seeking clinical help and had no former experience with psychostimulant medication, which is common among newly referred patients with ADHD in the Netherlands. Controls were recruited with advertisements in local newspapers and received €90.00 each for their participation. All subjects were first screened with a telephone interview addressing past and current ADHD symptoms; psychiatric, neurological, and medical disorders; physical impairments; use of medication; and substance abuse. Then, subjects filled out translated versions of the Brown ADD Scale,[27] the Conners' Adult ADHD Rating Scales,[28] and the *DSM-IV* ADHD-rating scale for current and past ADHD symptoms.[29] Finally, we administered 2 structured interviews: a translated version of the Diagnostic Interview Schedule assessing ADHD symptoms (DIS-L)[30] and the computerized Composite International Diagnostic Interview,[31] assessing comorbid *DSM-IV* disorders. In contrast with controls, patients scored above ADHD cut-off values on the 3 self-report questionnaires (details described elsewhere[11]) and the DIS-L.

EXCLUSION

Subjects who reported clinically unstable conditions (ie, suicidal behaviors, psychosis, mania, or physical aggression), organic brain disorder, epilepsy, or past concussions were excluded.

Regarding controls, subjects were additionally excluded if they were currently suspected of having ADHD, other psychiatric disorders, or substance abuse; if they were diagnosed with a developmental disorder in childhood; or if they reported ADHD among relatives. This decision was based on the telephone interview, the self-report questionnaires,[27-29] and the DIS-L.[30]

Regarding the ADHD group, patients were additionally excluded if an experienced physician stated that the severity of a

comorbid disorder was such that it required treatment first or that abstinence from previously prescribed medication was inadvisable. Comorbid Axis I disorders included current depression (n=2, both dysthymic), lifetime depression (n=13), current anxiety disorders (n=8), bipolar disorder (n=1, lifetime), tic disorder (n=1, lifetime), substance abuse (n=3, ie, alcohol, cannabis, and amphetamine), and alcohol dependence (n=1, lifetime). Two subjects ceased the use of a selective serotonin reuptake inhibitor prior to participation.

DIAGNOSTIC PROCEDURE

A psychiatrist who specializes in adult ADHD supervised each diagnostic evaluation performed by an experienced physician. If needed, they met the patient together (n=2). Only if both agreed was the patient allowed to participate. To be diagnosed with ADHD, subjects must have (1) met 6 of 9 *DSM-IV* criteria for inattention and hyperactivity/impulsivity for a diagnosis in childhood and at least 5 of 9 criteria in adulthood,[32] (2) described persistent ADHD symptoms from childhood to adulthood, and (3) experienced a moderate to severe level of impairment attributable to the ADHD symptoms. Current and childhood symptoms were evaluated with a semistructured diagnostic interview for ADHD and comorbid disorders (the SGIK)[33] and the DIS-L.[30] Other childhood disruptive disorders were assessed with a translated version of the structured diagnostic interview for retrospective diagnosis of ADHD and other disruptive disorders, the sections N (oppositional defiant disorder), O (conduct disorder), and P (antisocial personality disorder) of the DIS-IV.[30] If possible, school reports were examined, and 17 parents (70.8%) or 7 siblings (29.2%) were interviewed with a semistructured interview on childhood ADHD symptoms. Twenty-one (87.5%) partners attended all interviews with the patients and were asked for their opinions on the presence, severity, and duration of current ADHD symptoms as well as the level of dysfunction caused by these symptoms. Finally, the physician filled out the *DSM-IV* rating scale[29] and based the diagnosis of childhood-onset and current ADHD on all of this information.

TASKS AND PROCEDURES

The use of drugs (amphetamine, barbiturates, benzodiazepines, cocaine, morphine, and tetrahydrocannabinol) was tested with a urinal drug-detection device (Instant-View Drug Screen; Rapid Detect, Poteau, Okla), and the use of alcohol was tested with a breath device (Alcotest; Dräger Medical, Lübeck, Germany). Electroencephalographic data were recorded while subjects performed the stop signal task, the stop change task, and the continuous performance task. Only the stop signal task is discussed here.

Stimuli were presented on a computer screen in a sound-attenuating cabin at a distance of 100 cm. On each trial, a square-wave, black-on-white grating (750 milliseconds) immediately succeeded a white plus symbol (500 milliseconds). Intertrial intervals varied from 1000 to 1250 milliseconds. Subjects were instructed to press a button with the right index finger when a grating with a high (4.8 cycles per degree) spatial frequency appeared and to press another button with the left index finger when a grating with a low (0.6-cpd) spatial frequency appeared. The mapping of the response hand reversed after half of the blocks. Unpredictably, on 40% of the trials, a tone (1000 Hz, 80 dB, 400 milliseconds) was presented binaurally through earplugs (higher than usual [25%] presentation rates[19,22] were not expected to affect SSRT[34] but might yield stop P3s with relatively small amplitudes and short latencies[35]). The tone indicated that the planned response to the grating should be withheld. The delay between go stimuli and stop signals (stimulus onset asynchrony, or SOA) was jittered in a range of 240 milli-

seconds (with steps of 10 milliseconds) surrounding its mean value.[23] In the first block, the mean SOA was always set on 250 milliseconds. After each block, the mean SOA was adjusted with a tracking algorithm[36] to yield a performance of 50% successful inhibitions, corrected for the estimated number of omissions.[37]

The sequence of task presentation and the mapping of the response hand (ie, right-hand response to high spatial frequencies or to low spatial frequencies first) were balanced across subjects. Subjects received a practice block without tones and a practice block consisting of the stop signal task. Before we reversed the response hand, we presented a practice block without tones. We presented 6 experimental blocks that contained 126 trials: 76 trials without a tone and 50 trials with a tone. Within each block, the sequence of trials was pseudorandomized with the restriction of a maximum of 3 successive stop trials. We stressed the speed of responding so that the subjects would not develop waiting strategies. If reaction times increased more than 10% compared with the practice block without tones, subjects were urged to speed up their responses.

ELECTROPHYSIOLOGICAL RECORDINGS

Electroencephalographic data were recorded using an elastic cap with 62 tin electrodes arranged according to the International 10-10 system.[38] Tin electrodes were also used for bipolar recording of the vertical electro-oculogram from above and below the left eye and the horizontal electro-oculogram from the outer canthi of each eye. Electroencephalographic signals were referenced to the left mastoid. The AFz electrode functioned as ground. Impedances were kept below 5 kΩ. Data acquisition was continuous with a sampling rate of 1000 Hz. Signals were cut off below 0.05 Hz and above 50 Hz. Offline, signals were down-sampled to 250 Hz and cut off above 30 Hz.

DATA ANALYSIS

Performance measures were calculated separately for each subject and each block. Mean RTs were computed out of a response window of 150 to 1250 milliseconds poststimulus. Furthermore, we calculated the SSRT,[8] the corrected percentage of successful inhibitions,[37] and the mean SOA. All measures were averaged across blocks (individual data) and subjects (grand-average data).

We computed ERPs separately for successful stops and failed stops from −100 to 1552 milliseconds relative to the onset of the S1 (go stimulus) and S2 (stop stimulus). The 100 milliseconds preceding S1 served as a baseline. Trials with artifacts or analogue-to-digital–converter saturation were rejected from further analysis (discarded stop trials, 6.28% for controls and 7.35% for adults with ADHD). Ocular artifacts were estimated and subtracted by time domain regression.[39] Data were merged across 6 experimental blocks. Stop ERPs were filtered with Adjar level 2 in the interval from −100 to 700 milliseconds. Subsequently, a 100-millisecond pre-S2 baseline was applied.

TOPOGRAPHICAL MAPPING
AND SOURCE ANALYSIS

We used BESA 2.2[40] (MEGIS Software GmbH, Grafelfing, Germany) to derive maps and source models for the grand-average, average-referenced ERPs elicited by successful and failed stops. Models were derived for each group and each trial type (successful and failed stops) separately. The N1 was analyzed at the first negative peak after 80 milliseconds at FCz. The stop P3 was analyzed at the first positive peak after 150 milliseconds at Cz. The default 3-shell head model was used to model intracranial generators as a single bilateral dipole source. Digitized elec-
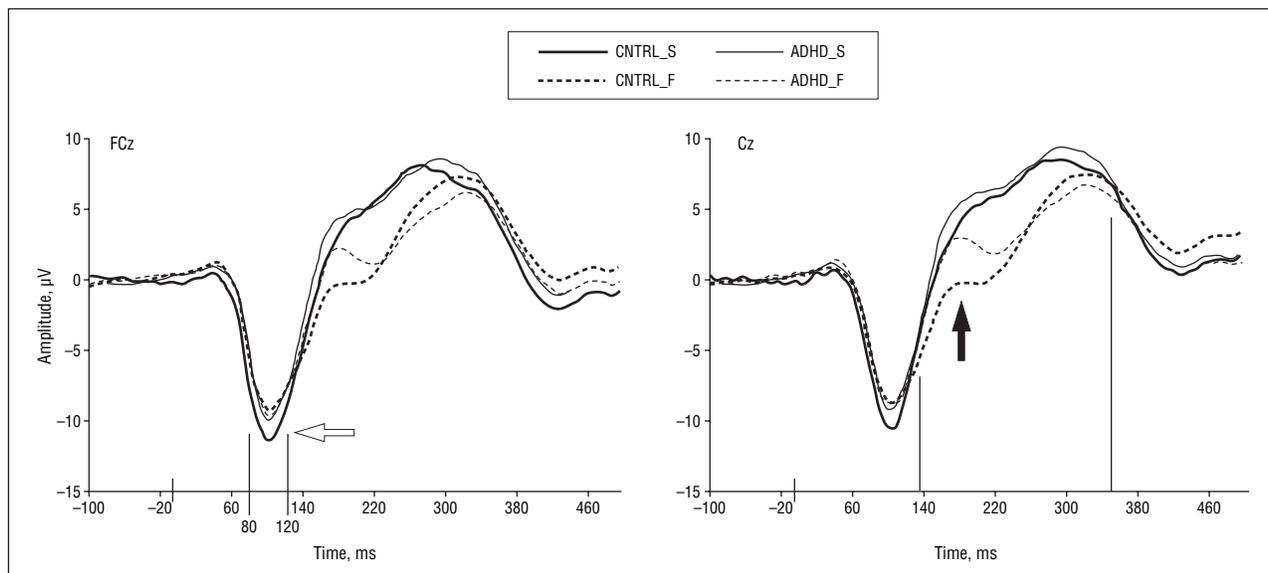
Figure 1. Stop signal event-related potentials associated with successful (solid lines) and failed stops (dotted lines) at leads FCz and Cz, separately for the control group and the attention-deficit/hyperactivity disorder group. The white and black arrows indicate the N1 and stop P3 effect, respectively. The 2 vertical lines refer to the window of statistical analysis. ADHD_F indicates the ADHD group failed stop; ADHD_S, the ADHD group successful stop; CNTRL_F, the control group failed stop; CNTRL_S, the control group successful stop.

trode locations were projected on a least-square-fitted sphere, which was rotated with respect to mastoid and nasion locations. The resulting coordinates were averaged across subjects within each group. These averaged coordinates were used as a representation of recording sites. Each dipole was characterized by 7 parameters: 3 for location, 3 for orientation, and 1 for strength or dipole moment. To limit the number of parameters to be estimated, we applied symmetry constraints with respect to location and orientation to each bilateral dipole pair. The possibility of interacting dipoles was reduced by preferring solutions with relatively low dipole moments with the aid of an "energy" constraint (weighted 20% in the compound cost function, as opposed to 80% for the residual variance). We found the optimal set of parameters in an iterative manner by searching for a minimum in the compound cost function. Reported dipole solutions were stable across randomly varying starting positions.

STATISTICAL ANALYSIS

All dependent measures were subjected to repeated measures of variances (Wilks λ) containing the between-factor group (ADHD vs control) and the within-factor trial type (successful vs failed stops) with a critical α level of .05. Sample wise testing (4 milliseconds) of ERP amplitudes was restricted to leads and time windows for which the effects were expected to be largest, a choice based on a previous study.[24] The N1 was analyzed from 80 to 124 milliseconds at FCz, and the stop P3 was analyzed from 136 to 352 milliseconds at Cz. Because this analysis involved many tests, the probability of making type I errors was minimized by considering effects significant only if they extended over at least 5 time points.[41]

RESULTS

PERFORMANCE

Performance data have been described in detail elsewhere.[11] Briefly, SSRT was longer in patients with ADHD (mean±SD, 185.2±38.9 milliseconds for controls and

237.3±87.2 milliseconds for adults with ADHD: $F_{1,46}=7.12$, $P<.01$) whereas there was no significant difference regarding RT (mean±SD, 463.3±68.8 milliseconds for controls and 467.9±87.6 milliseconds for adults with ADHD: $F_{1,46}=0.04$, $P=.84$). We adjusted the SOA individually (mean±SD, 267.6±58.4 milliseconds for controls and 230.3±78.1 milliseconds for adults with ADHD: $F_{1,46}=3.51$, $P=.07$) to yield a probability of successful stops of around 50% in both groups[36] (46.4±6.5% for controls and 42.8±10.6% for adults with ADHD: $F_{1,46}=2.08$, $P=.16$).

EVENT-RELATED POTENTIALS

Figure 1 displays ERPs elicited by stop signals associated with successful and failed stops at FCz and Cz. As for the N1, stop signals elicited a pronounced negative peak around 100 milliseconds latency. At FCz, the N1 was larger for successful than for failed stops, but only for the control group (interaction with group, 92-124 milliseconds: $F_{1,46}=4.77$, $P<.05$; effect of trial type in the control group, 80-124 milliseconds: $F_{1,23}=11.88$, $P<.01$). This is particularly visible in **Figure 2**, which displays difference waves obtained by subtracting ERPs for failed stops from those for successful stops. Mean amplitudes and standard deviations are summarized in the **Table**.

Regarding the stop P3, Figure 1 shows a larger positivity for successful than for failed stops, particularly at Cz (140-352 milliseconds: $F_{1,46}=4.21$, $P<.05$). Especially the difference waves in Figure 2 suggest that the stop P3 was smaller for the ADHD group. However, we did not find the expected interaction with group. Closer inspection revealed that the distribution across individuals of trial-type differences in amplitude deviated from normality in the ADHD group. Removal of 1 outlier (and the matched counterpart) yielded an interaction with group (172-200 milliseconds: $F_{1,44}=4.20$, $P<.05$), indicating smaller stop P3s in adults with ADHD (see also
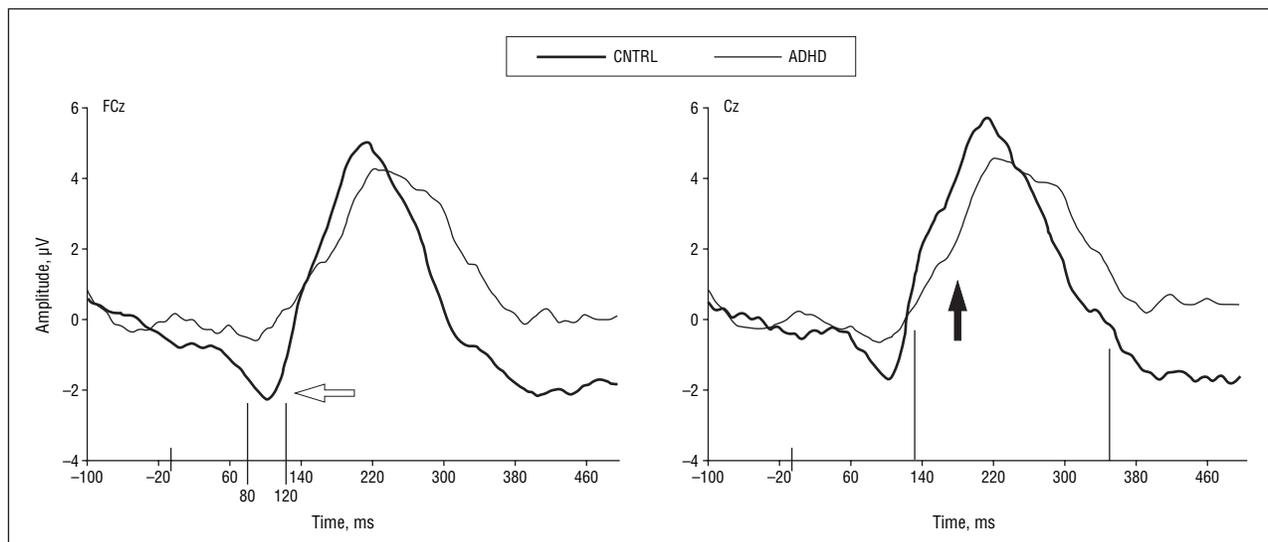
Figure 2. Difference waves obtained by subtracting event-related potentials (ERPs) for failed stops from ERPs for successful stops at leads FCz and Cz, separately for the control group (dark lines) and the attention-deficit/hyperactivity disorder (ADHD) group (gray lines). See legend of Figure 1. CNTRL indicates the control group; ADHD, the ADHD group.

Table. Mean Event-Related Potential Amplitudes for ADHD and Control Groups*

ERP	ADHD		Controls	
	Successful	**Failed**	**Successful**	**Failed**
N1 (92-124 ms at FCz)	−9.25 ± 5.14	−9.06 ± 4.43	−10.67 ± 3.62	−8.67 ± 3.16
Stop P3 (n = 24; 172-200 ms at Cz)	5.45 ± 3.74	2.87 ± 3.86	4.24 ± 5.33	−0.22 ± 7.04
Stop P3 (n = 23; 172-200 ms at Cz)	5.28 ± 3.73	3.22 ± 3.52	4.56 ± 5.21	0.02 ± 7.10

Abbreviation: ADHD, attention-deficit/hyperactivity disorder.
*All values are means and standard deviations in µV, calculated in the interval for which significant differences between the ADHD and control groups were found.

Table). However, Figure 1 suggests that the interaction with group reflects longer latencies rather than smaller amplitudes of the stop P3 in the ADHD group, which would be consistent with the increase in SSRT. This alternative interpretation was only partly confirmed: sample-wise testing for each group separately yielded an effect of trial type in the interval of 140 to 300 milliseconds for the control group ($F_{1,22}=11.29$, $P<.01$) and in the interval of 152 to 352 milliseconds for the ADHD group ($F_{1,22}=15.83$, $P<.01$).

To confirm the contribution of auditory cortex to the N1, we conducted coarse source localization using BESA 2.2.[40] **Figure 3** shows that the resulting source models and associated scalp topographies are consistent with generators in auditory cortex.[42] Analogous source modeling for the stop P3 suggested bilateral dipole pairs in more medial frontocentral regions (Figure 3). Importantly, statistical analysis using the latency-of-best-fit method to estimate individual source models[43] confirmed that the locations of stop P3 sources were more medial than those of N1 sources ($F_{1,46}=52.55$, $P<.01$; after removal of the outlier mentioned earlier in the article, $F_{1,44}=48.47$, $P<.01$).

Post hoc correlations between the difference in N1 as well as P3 amplitude (successful minus failed) and SSRT were assessed. No significant correlations were found. This might be due to uncontrolled sources of variance,

such as interindividual variability in N1 and P3 effects reflecting global neurophysiological differences, or to an indirect relation between SSRT and successful vs failed stopping. Furthermore, the amplitude measures were not found to correlate with self-report scales reflecting attention and impulsivity, respectively. This might additionally be due to conceptualization differences between experimental and clinical measures or to low validity of self-report scales.

COMMENT

The present study revealed that successfully stopping an ongoing response process is associated with a sequence of cortical activations elicited by the stop signal. Successful stops were associated with enhanced short-latency (100 milliseconds) activation in sensory cortex, followed by a longer-latency (as from 140 milliseconds) enhancement of activity in more medial frontocentral areas. These N1 and stop P3 effects were smaller in adults with ADHD, who also manifested impaired stopping as reflected in the behavioral index of stopping speed, the SSRT.

Our first hypothesis, that successful stops are associated with larger N1s and stop P3s than failed stops in the control group, was confirmed. Around 100 milliseconds,
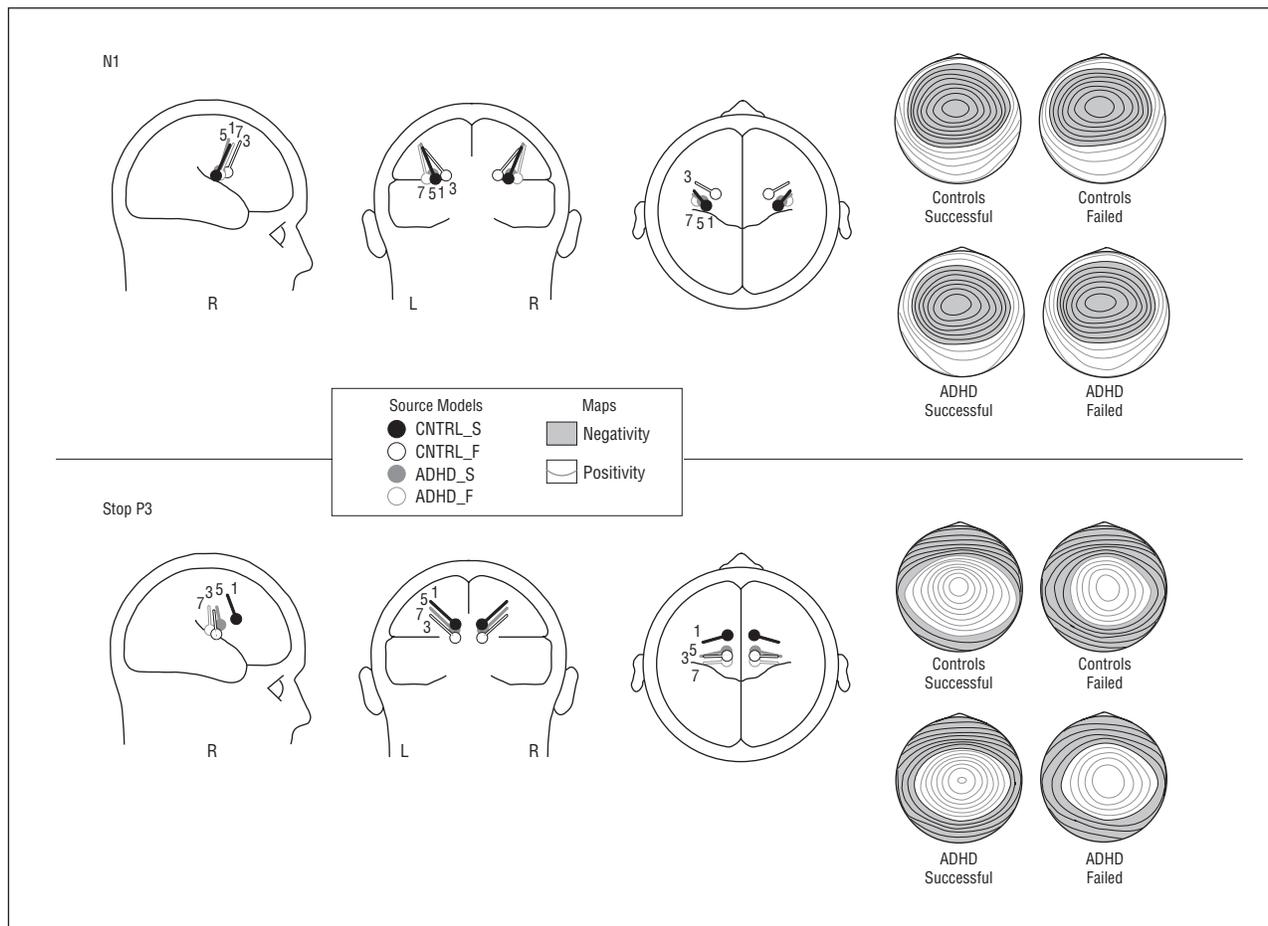
Figure 3. Source models and isocontour maps derived for the grand-average, average-reference data at the peak latency of the N1 (top panel) and the stop P3 (bottom panel) for each group and each trial type separately. For the control group, filled, black dipole pairs (1) correspond to successful stops and open, white dipole pairs (3) correspond to failed stops. For the ADHD group, filled, gray dipole pairs (5) correspond to successful stops and open, gray dipole pairs (7) correspond to failed stops. Dots indicate the location of the dipole source; the direction of the line represents its axis of orientation. Isocontour maps show the potential distribution of the average-referenced data. The dark shaded areas reflect negative activity; the nonshaded areas reflect positive activity. Spacing is 0.8 μV. Regarding the N1, in the control group, source models were derived at 99 milliseconds for successful stops (percentage variance not explained by the model (RV, 1.52%) and 116 milliseconds for failed stops (RV, 1.52%). In the ADHD group, source models were derived at 99 milliseconds for successful stops (RV, 2.06%) and 99 milliseconds for failed stops (RV, 1.26%). Regarding the stop P3, in the control group, source models were derived at 266 milliseconds for successful stops (RV, 3.62%) and 316 milliseconds for failed stops (RV, 3.78%). In the ADHD group, source models were derived at 283 milliseconds for successful stops (RV, 2.59%) and 316 milliseconds for failed stops (RV, 4.39%). ADHD_F indicates the ADHD group failed stop; ADHD_S, the ADHD group successful stop; CNTRL_F, the control group failed stop; CNTRL_S, the control group successful stop.

stop signals elicited a negative deflection over frontocentral scalp sites. In the control group, successful stops were associated with a larger N1 than failed stops. Similar results were found in a previous study with healthy subjects[24] after overlap removal with Adjar level 2.[23] Because the N1 has been shown to be very sensitive to manipulations of selective attention to auditory stimuli,[25] these findings imply that whether an auditory stop signal results in a successful or a failed stop at least partly depends on the amount of attention that is paid or switched to the stop signal. Further analysis of overlap-free stop ERPs revealed larger positive amplitudes for successful than for failed stops over central scalp sites as from 140 milliseconds. This stop P3 has previously been claimed to reflect response inhibition.[16,18] Replication after overlap removal excludes the possibility that this effect merely reflects differences in motor-related potentials[24] (see the introduction).

Coarse source localization of the N1 yielded models consistent with generators in auditory cortex. The stop P3 was modeled in more medial regions. This is in line with source models reported for the no-go P3 elicited in go/no-go tasks[44,45] and might reflect a generator in anterior cingulate cortex, which is thought to be involved in response inhibition, either directly or by the detection of conflict that signals other brain areas to exert inhibitory control.[46] Previous source localization of the stop P3 revealed generators in more posterior regions.[18] These probably reflect overlapping activity related to the processing of the go stimulus, underlining the importance of applying Adjar level 2 to validly isolate cortical processing of the stop signal. It should be noted that dipoles reflect an oversimplification of actually activated brain areas. Previous studies using functional magnetic resonance imaging have suggested right lateralized frontostriatal involvement in response inhibition.[47,48]

Consistent with earlier findings in children,[22] the stop P3 effect was smaller in adults with ADHD. Previous results indicating smaller N2s to stop signals[20,21] or smaller N1s to go stimuli[19] (not reported) could not be replicated. The reduced stop P3 can be interpreted by assum-

ing that, although individuals with ADHD can generate an inhibitory response to stop signals with a probability similar to that found for controls (around 50%, if stimulus conditions are appropriately adjusted), stopping was less efficient or the activation of the inhibition system was weaker in individuals with ADHD, as was also indicated by the increase in SSRT. Because the difference in onset of the stop P3 effect (140 milliseconds for controls, 152 milliseconds for ADHD) was smaller than the difference in SSRT (185 milliseconds for controls, 237 milliseconds for ADHD), which is thought to reflect the finishing time of the internal stop response,[8] this component might not be directly related to inhibition of ongoing responses. Furthermore, it should be noted that because of the transmission delay, inhibitory processes reflected in the stop P3 are not likely to exert an effect on behavioral measures until around 100 milliseconds after its onset.[16] Therefore, at least on some part of the trials, processes other than those reflected in the stop P3 are associated with (impaired) response inhibition.

The increase in N1 amplitude for successful stops relative to failed stops was absent in adults with ADHD. Given that the difference in N1 for successful vs failed stops reflects attentional modulation of auditory-cortex activation elicited by the stop signal, it can be concluded that such attentional modulation is absent in adult ADHD. A number of reports on children with ADHD have revealed significantly reduced enhancement of auditory-cortex activation by stimuli that are deemed relevant by task.[49-51] The present lack of N1 modulation, however, must reflect a more subtle mechanism. Internally generated trial-to-trial variation in N1 amplitude reflects fluctuations in the impact that stop signals have in auditory cortex, or, in other words, the amount of attention that is switched to the stimulus on its presentation. In healthy controls, these varying amounts of attention are directly related to the probability that subsequent stopping is successful. In adults with ADHD, this link between attention and stopping is lacking. Stated differently, no matter what the impact of the stop signal is in auditory cortex, it does not determine the probability of subsequent stopping: only a weakly activated inhibitory mechanism (reflected in a smaller stop P3 effect) was used for stopping. Because attention to go stimuli was unimpaired (there was no group effect on RT), the attentional deficit in adults with ADHD seems specifically related to the inability to switch attention to the stop signal. Accordingly, task-set switching deficits have been demonstrated in children with ADHD.[52] The present study reveals that in adults with ADHD, at least on part of the trials, deficits in attentional switching might be the precursor of deficient inhibitory control, which is reflected in a disproportional elongation in SSRT (relative to RT).

One could argue that in controls, failed stopping was related to failed attention as well as failed inhibition whereas in adults with ADHD, failed stopping was related to failed inhibition only. However, the mean amplitudes provided in the Table suggest that the N1 associated with failed stops in the control group was comparable with the N1 associated with both successful and failed stops in the ADHD group (difference, 0.58 and 0.39 μV, respectively), whereas the N1 associated with

successful stops in the control group was enlarged (difference, 1.42 and 1.61 μV, respectively). Following this line of reasoning, enhanced attention contributes to better stopping in controls, but not in ADHD.

A possible limitation of this study is the inclusion of patients with comorbid disorders. Because at least 75% of adults with ADHD suffer from additional *DSM-IV* disorders,[53] isolating ADHD is difficult and might not yield a representative sample. The nonsystematic presence of comorbidity is expected to increase error variance, which would reduce the likelihood of finding significant group effects. Furthermore, comorbidity mainly consisted of depression and anxiety. As for depression, symptoms were mild or currently absent. As for anxiety, in children, SSRTs have been found to be comparable with those measured in controls.[9]

In sum, the increase in SSRT found in patients with ADHD has often been interpreted to support a core deficit in inhibitory control rather than in attention. However, behavioral measures used as indices of executive functions merely reflect the compound contribution of different underlying subfunctions, which are hard to distinguish. Event-related potentials enable the disentangling of the relative contribution of inhibitory and attentional deficits eventuating in an increased SSRT. The present ERP study revealed that although general attention to task stimuli seemed undisturbed in adults with ADHD (no effect on RT), impaired stopping may still be related to deficiencies in other aspects of attention, in particular the ability to switch attention to the stop signal. This throws doubt on response inhibition as the primary deficit in ADHD and may have important implications for treatment.

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