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Dipole source localization of event-related brain activity indicative of an early visual selective attention deficit in ADHD children

L.M. Jonkman[a,*], J.L. Kenemans[b,d], C. Kemner[c], M.N. Verbaten[b], H. van Engeland[c]

[a]*Department of Neurocognition, Faculty of Psychology, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands*
[b]*Department of Psychopharmacology, Utrecht University, Utrecht, The Netherlands*
[c]*Department of Child and Adolescent Psychiatry, University Medical Centre, Utrecht, The Netherlands*
[d]*Department of Psychonomics, Utrecht University, Utrecht, The Netherlands*

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Abstract

Objective: This study was aimed at investigating whether attention-deficit hyperactivity disorder (ADHD) children suffer from specific early selective attention deficits in the visual modality with the aid of event-related brain potentials (ERPs). Furthermore, brain source localization was applied to identify brain areas underlying possible deficits in selective visual processing in ADHD children.

Methods: A two-channel visual color selection task was administered to 18 ADHD and 18 control subjects in the age range of 7–13 years and ERP activity was derived from 30 electrodes.

Results: ADHD children exhibited lower perceptual sensitivity scores resulting in poorer target selection. The ERP data suggested an early selective-attention deficit as manifested in smaller frontal positive activity (frontal selection positivity; FSP) in ADHD children around 200 ms whereas later occipital and fronto-central negative activity (OSN and N2b; 200–400 ms latency) appeared to be unaffected. Source localization explained the FSP by posterior-medial equivalent dipoles in control subjects, which may reflect the contribution of numerous surrounding areas.

Conclusions: ADHD children have problems with selective visual processing that might be caused by a specific early filtering deficit (absent FSP) occurring around 200 ms. The neural sources underlying these problems have to be further identified. Source localization also suggested abnormalities in the 200–400 ms time range, pertaining to the distribution of attention-modulated activity in lateral frontal areas.

Keywords: Attention-deficit hyperactivity disorder; Event-related brain potentials; Visual selective attention; Source localization; Frontal selection positivity; N2b

1. Introduction

In the past 25 years a large amount of attention research has been conducted on children with attention-deficit hyperactivity disorder (ADHD). The conclusions regarding the type of attention deficits shown by these children are diverse. Barkley (1997) suggests that attention deficits are secondary to general executive function problems in ADHD children. In his theory executive functions include behavioral inhibition, working memory, internalization of self-directed speech, control of emotional arousal and motivation. Swanson et al. (1998) on the other hand, recently characterized ADHD as a combination of executive attention and alerting deficits, based on the attention network theory proposed by Posner (Posner and Petersen, 1990; Posner and Raichle, 1994). Executive attention processes involve functions like planning, error detection, resolution of conflict and responding to novel or difficult stimuli and have been localized in frontal areas (mainly anterior cingulate gyrus). Both (right) frontal and posterior (parietal) areas have been shown to be involved in the regulation of the state of alertness.

Although numerous attention studies have been performed in ADHD children there is still no consensus about the involved attention networks and underlying brain areas. Recently, however, based on neuroimaging results, several researchers have concluded to the main deficits of ADHD children being with executive functions, and deficits in frontal-striatal circuitry (Casey et al., 1997a; Vaidya et al.,

* Corresponding author. Tel.: +31-43-388-1956; fax: +31-43-388-4125.
E-mail address: l.jonkman@psychology.unimaas.nl (L.M. Jonkman).

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1998; for reviews see Castellanos, 1997; Filipek, 1999; Swanson, 1998; Tannock, 1998). Besides this focus on top-down executive, fronto-striatal problems, ADHD children have repeatedly been reported to display early, auditory attention deficits such as inefficient filtering of relevant information, as evidenced by smaller N1 or Nd amplitudes (Jonkman et al., 1997; Loiselle et al., 1980; Satterfield et al., 1988, 1990; Zambelli et al., 1977; for a review see Barry et al., 2003). Although in recent reviews (Tannock, 1998) it is often concluded that there is no evidence for such early filtering deficits in the visual modality, there are a number of ERP studies that do indicate the presence of specific attention problems in early filtering or in orientation processes in ADHD in the visual modality (Brandeis et al., 1998; Jonkman et al., 1997; Van der Stelt et al., 2001; Van Leeuwen et al., 1998). Whereas later executive attention processes have been localized in prefrontal areas in adults as well as children (Casey et al., 1997b; MacDonald et al., 2000; Tamm et al., 2002), the brain areas that are involved in deficient early attention processes (filtering, orienting) in children have not yet been elucidated. Such knowledge is, however, important with regard to pharmacological treatment, since different pharmacological agents exert effects via different neurotransmitter systems localized in different brain areas.

More knowledge about the temporal course of early visual selective attention processes and involved brain areas comes from adult ERP studies. In these studies early filtering processes are measured in two-channel selective attention tasks in which stimuli consist of a conjunction of two features, for instance color (red, blue) and gratings (vertical, horizontal). The instruction in such tasks is to attend only to one stimulus attribute, like, for example, the color red, and to generate a response only to a red stimulus that contains vertical bars (the target). To obtain ERP activity that is evoked by the investment of selective attention, so-called selection potentials are computed by subtracting ERPs to non-target *unattended* (blue) stimuli from ERPs to non-target *attended* (red) stimuli. The advantage of using ERPs to attended and unattended non-targets (also called standards) is that early attention processes can be studied independently of target evaluation/selection and motor preparation.

Adult studies, in which two-channel attention tasks were used, have shown that similar patterns of ERP activity are evoked when stimulus selection is based on non-spatial features such as color, spatial frequency, orientation or shape (Anllo-Vento and Hillyard, 1996; Anllo-Vento et al., 1998; Harter and Guido, 1980; Hillyard and Münte, 1984; Karayanidis and Michie, 1996, 1997; Kenemans et al., 1993, 1995, 2002; Lange et al., 1998; Smid et al., 1999). Three waves can be distinguished in the selection potential: the frontal selection positivity (FSP; Kenemans et al., 1993), in adults occurring between 100 and 300 ms; a temporal-occipital selection negativity (OSN; Harter and Aine, 1984) starting between 150 and 200 ms; and the so-called N2b, a negative wave that, in adults, occurs between 250 and 300 ms after stimulus presentation and has a central maximum (Wijers et al., 1989). Smid et al. (1999) suggested that FSP activity is associated with a 'selection-for-action mechanism, enabling selective coupling of relevant stimuli to relevant responses' (p. 277) that might be related to frontal and subcortical selective processing. Recently, Kenemans et al. (2002) suggested a similar role for the FSP on the basis of selection of spatial frequency features by stating that it is associated with an early filter that codes only the primary selection features. In different studies (Anllo-Vento et al., 1998; Kenemans et al., 2002; Lange et al., 1998) the sources of the OSN were localized in ventral occipital-temporal areas. Accordingly, Smid et al. (1999) associated the OSN with selective processing in the posterior visual system 'enabling selective analysis of the visual percept (e.g. perceptual analysis in short-term memory, feature integration)' (p. 277). The N2b is thought to index a more general, feature non-specific selection process. In two studies (Lange et al., 1998; Kenemans et al., 2002) the sources of the N2b that were active during color and spatial frequency selection, respectively, were localized in medial frontal brain areas. Lange et al. (1998) suggested that the N2b is associated with an 'integrative executive system located in the anterior cingulate gyrus and reflects processes such as stimulus evaluations in the light of task instructions and selection of responses'. Accordingly, Smid et al. (1999) suggested that the neural generators underlying the N2b might coordinate frontal and infero-temporal mechanisms.

To our knowledge, there are only 3 ERP studies in which a two-channel visual selective attention task involving non-spatial stimulus features was administered to ADHD children (Jonkman et al., 1997; Satterfield et al., 1994; Van der Stelt et al., 2001). In the study by Satterfield et al. (1994) selection potentials were only computed for attended and unattended deviants, and not for standard stimuli, and hence the reported effects do not reflect the above described selective attention processes (FSP, OSN, N2b). In the other two studies no differences in N2b amplitude between ADHD and control children were reported, whereas behavioral data were indicative of inefficient filtering in ADHD subjects. Van der Stelt et al. (2001) used a similar color selection task as in Jonkman et al. (1997) but besides the N2b, also measured the FSP and OSN waves. No statistically significant OSN was reported for either control or ADHD children, but FSP amplitudes were smaller or absent in the ADHD group as compared to controls. These findings also indicate that in the visual modality, ADHD children might suffer from a filtering deficit, but in a rather early time window. In adult color selection studies, sources of FSP activity were localized in posterior areas (Anllo-Vento et al., 1998; Lange et al., 1998). If the FSP deficit in ADHD children (as reported by Van der Stelt et al., 2001) could also be localized in posterior areas, this would indicate an early filtering deficit, in addition to, or in

interaction with, executive problems that are caused by inefficient fronto-striatal functioning. In a recent ERP study by Perchet et al. (2001) using the Posner paradigm, evidence for such an early posterior attention deficit in ADHD children was reported with regard to spatial selective attention. In this study control children showed enlarged P1 amplitudes in response to validly cued targets (as compared with invalidly cued targets), indicating enhanced priming of occipital sensory areas at the attended location, whereas ADHD children had equal P1 amplitudes to validly and invalidly cued targets. But note that in this study the amount of trials in the invalid category was rather low, increasing signal-to-noise ratios.

In the recent study by Van der Stelt et al. (2001), a dipole model with two bilateral sources was constructed for the activity in a latency window from 200 to 600 ms in ADHD and control children. The authors concluded that the difference in FSP between the two groups was mainly due to differences in the parameters of a relatively frontal dipole pair, not in those of a relatively posterior pair. However, since this dipole model was constructed for a latency window of 200–600 ms, it may not accurately reflect selective activity before 200 ms, and instead it probably reflects contributions from latencies way beyond 300 ms. Furthermore, differences in dipole parameters were not subjected to statistical evaluation. The present study attempted to (1) replicate the differences in FSP as reported by Van der Stelt et al.; (2) construct instantaneous dipole models at selected latencies between 100 and 300 ms; and (3) confirm possible differences in dipole parameters statistically by using the procedure described by Kenemans et al. (2002).

2. Methods

2.1. Subjects

The analyses described in the present paper concern the same subjects as in the Jonkman et al. (1997) study. The reader is referred to this paper for elaborate information about inclusion criteria, subjects selection and mean group scores on IQ, CBCL and TRF scales. The final control and clinical groups consisted of 18 subjects each. There was no significant difference in mean age between the groups, mean ages were 10.0 and 10.6 years for the control and clinical groups, respectively. All children had IQ scores higher than 80, ADHD subjects had a DSM-III-R diagnosis of ADHD and scores above the clinical range on the Child Behavior Checklist (CBCL) and a Teacher Rating Scale (Conners TRF). All subjects discontinued medication use for 3 days prior to the experimentation day and had normal or corrected to normal vision. The experiment was approved by the Medical Ethical Committee of Utrecht Medical Centre (UMC) and all parents signed an informed consent form.

2.2. Visual task and procedure

The task consisted of 300 rectangles subtending a length of 4.5° of arc and a width of 3.7° of arc. Half of these stimuli were relevant (to-be-attended) and half were irrelevant (to-be-ignored) as defined by their color (red or yellow). The stimulus feature used to define stimulus types (standard or deviant) was the orientation (left or right) of diagonal gratings within the rectangles; 80% of the stimuli were non-targets and 20% were deviants (40% non-targets and 10% deviants in relevant and irrelevant conditions).

Each subject performed two tasks, one in which yellow was the relevant channel and one in which red rectangles were relevant. The orientation that determined the deviance of stimuli was balanced across subjects. The duration of each task was about 10 min, stimulus duration was 50 ms, and ISIs were randomized between 1750 and 2150 ms. All stimuli were presented in the center of the visual field on a monitor positioned at approximately 70 cm from the subject's eyes. The instruction was to attend to rectangles of one color only and to press a hand-held button as fast as possible whenever the orientation of gratings within these rectangles was deviant (target).

On arrival in the laboratory, children were familiarized with the procedure. Before the task was started the electro-cap and EOG electrodes were attached. After this, each child underwent a practice task of about 2 min, until the experimenter was convinced that task requirements were met. In most cases a parent or caretaker sat behind the child during experimentation in a soundproof and electrically shielded room. After completion of the experiment subjects were rewarded with a toy present (for a more elaborate procedure description see Jonkman et al. (1997)).

2.3. Recording and analysis

The behavioral data on percentage hits, false alarms and reaction time are reported in the Jonkman et al. (1997) paper. In the present paper, an additional signal detection analysis was performed on the behavioral data to be able to dissociate signal sensitivity from response bias. Since the distribution of false alarms was skewed we performed a non-parametric signal detection analysis (see Boice and Gardner, 1988) on the response bias parameter B''. Group effects for d' and B'' were tested by performing independent samples t tests.

The midline (Fz, Cz, Oz) ERP results that are reported in the present study are based on the same data as presented in the Jonkman et al. (1997) study. The analyses and the reported ERP activity are, however, different in that now a window analysis was performed based on mean area measurements. This procedure enables the study of early occurring FSP and OSN activity that was not reported in the earlier study in which only peak scoring procedures were applied on other ERP waves. Furthermore, the present topographical and source dipole localization analyses are

based on the whole set of electrodes. Electroencephalographic (EEG) activity was recorded from 31 tin electrodes by means of an electrocap (AFz, F7, F3, Fz, F4, F8, FC1, FC2, T7, C3′, C4′,C3, Cz, C4, T8, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8, PO7, PO1 (between Pz and O1), PO2 (between Pz and O2), PO8, O1, Oz, O1), nomenclature according to the American Electroencephalographic Society guidelines (1991). Linked earlobes, each connected with a 150 kΩ resistor, were used as reference. Horizontal electrooculogram (EOG) was recorded using tin electrodes attached to the outer canthus of each eye by means of adhesive rings. Similarly, vertical EOG was recorded from infraorbital and supraorbital electrodes placed in line with the pupil of the eye. A ground electrode was attached to the middle of the forehead. Electrode impedance was kept below 10 kΩ. All EEG signals were amplified with a time constant of 10 s by a set of purpose-built amplifiers. EOG signals were amplified with a time constant of 36 s. Sampling rate was 256 Hz. Sampling started 100 ms before stimulus onset and lasted 1 s.

EEG and EOG data were analyzed using Neuroscan software. First EEG and EOG epochs were baseline-corrected and filtered off-line with a 30 Hz, 24 dB/octave digital low-pass filter. Then, the EEG was corrected for vertical EOG artifacts by subtracting vertical EOG from EEG epochs by a regression method in the time domain (Semlitsch et al., 1986). Last, all EEG epochs containing artifacts (saturation of the A/D converter or an amplitude greater than −100 or 100 μV) were removed from the database. This amounted to, respectively, 4 and 6% rejected trials in control and ADHD groups.

For the purpose of the present study, ERPs were averaged across groups to relevant non-targets and irrelevant non-targets (false alarm trials were excluded). For dipole source analysis difference waves were also computed by subtracting the ERP to irrelevant non-targets from that to relevant non-targets. Since FSP and OSN waves are known to occur at, respectively, Fz and Oz leads, at these leads mean area scores were computed for each group and in each condition in a window from 120 to 280 ms at Fz and 200 to 280 ms at Oz. For the N2b mean area amplitudes were computed at Fz and Cz in a window from 320 to 400 ms. The choice of these windows was based on inspection of the grand average waveforms and on latency findings in other studies (Kenemans et al., 1993, 1995; Van der Stelt et al., 2001). Four separate ANOVAs were performed for mean area measures from 120 to 280 ms at Fz and 200 to 280 ms at Oz and from 320 to 400 ms at Fz and Cz. The ANOVAs included a between-factor group (ADHD, control) and a within-factor attention (relevant non-target, irrelevant non-target).

Iso-potential contour maps and source models were determined using the BESA program (V.2.2; Scherg, 1990). For source modeling the default 3 shell head model was used. Dipole pairs were fitted with locations and orientations constrained to be mirror-symmetrical.

Source models were computed at 3 different time points: 170, 240 and 375 ms, at which, respectively, FSP, OSN and N2b waves were largest. For each group separately, the best fitting source model on the grand average (difference) potential distribution was computed at the 3 time points. During the fitting process there was an energy constraint of 20% to reduce the probability of interacting dipoles. The procedure was as follows: first one symmetrical dipole pair was fitted; if the data could not adequately be explained by a one-pair model (residual variance (RV) above 5%), a second bilateral dipole pair was added. In almost all cases (except at 170 ms in the ADHD group) models with an RV below 5% were found and at 240 and 375 ms, in both groups, only a two-pair symmetrical dipole model could account for the data. In Van der Stelt et al. (2001) the need for a two-pair bilateral source model from 200 to 600 ms was already indicated. Additionally, to compare the time course and localization of exogenous processes not influenced by attention to the later attention-related activity, activity at 120 ms was also modeled in both groups. For this purpose ERPs were averaged over attended and unattended non-targets.

To enable statistical testing of group differences between the best-fitting models, the group models were fitted on the individual potential distributions of each group member. Again there was an energy restriction of 20%. Since at 170 ms no acceptable source solution could be found in the ADHD group, individual models were only computed in the control group. For each subject, time-varying residual-variance function waves between model and data were computed. The group model was then optimized at the time point at which the residual-variance curve was minimal (‘latency of best fit’, see Kenemans et al., 2002). With respect to the model at 120 ms, the lowest residual variances of all subjects occurred within a window from 100 to 145 ms. Due to larger variances, with regard to the models at 240 and 375 ms, the lowest residual variances were required to occur within predetermined windows from 190 to 300 ms for the 240 model and from 300 to 650 ms for the 375 model. Three location and three orientation parameters (x, y, and z values) of the two different dipole pairs and moment values of all 4 dipoles were determined for each subject. Group differences in dipole moments and location parameters were tested by performing t tests for independent groups. To compensate for the increased possibility of type 1 errors, due to the high amount of tests, a more conservative significance level of $P < 0.01$ was adopted for these tests.

To check for hemisphere differences in dipole moments extra ANOVAs were performed with a between-factor group (ADHD, control) and a within-factor hemisphere (left, right) for the different sources. For all tests a significance level of 5% was adopted.

3. Results

3.1. Behavioral results

ADHD children performed worse than control children in the sense that they had more omissions ($F(1,34) = 6.07$; $P < 0.05$) (33.8 versus 19.4%, respectively) and generated more false alarms to attended ($F(1,34) = -1.95$; $P < 0.05$) and unattended ($F(1,34) = -1.85$; $P < 0.05$) non-targets (7.5 versus 1.4% for attended non-targets and 0.3 versus 0% for unattended non-targets). Reaction times were 688 ms (SD 92 ms) in the control group and 722 ms (SD 91) in the ADHD group, but no significant group effect was found (see Jonkman et al., 1997).

To be able to distinguish between sensitivity and response bias, signal detection analysis was performed, which revealed that ADHD children had a lower sensitivity for detection of the target stimulus ($t(34) = -3.10$; $P < 0.005$); d' was 2.8 (SD 0.99) and 3.7 (SD 0.82) in ADHD and control groups, respectively. Also, non-parametric signal detection analysis revealed that the groups differed significantly in response bias ($t(34) = 12.34$; $P < 0.001$); B' was 0.86 (SD 0.18) in the ADHD group and 0.94 (SD 0.05) in the control group. Although both groups had a conservative response strategy, control subjects were more conservative than ADHD children. Correlation analysis on behavioral measures showed that

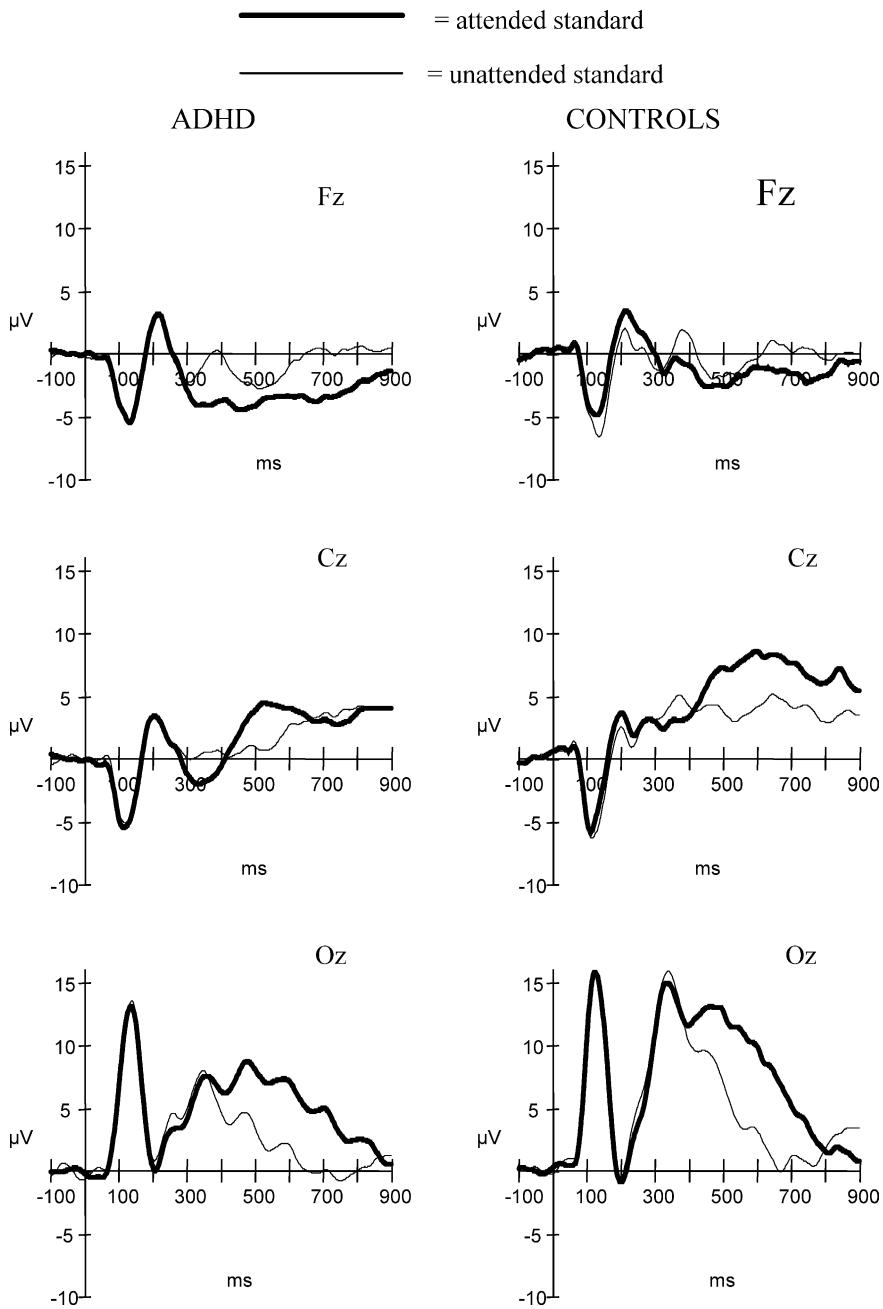

Fig. 1. Grand average ERPs at Fz, Cz and Oz in ADHD and control groups to attended and unattended non-targets.

there was a highly significant correlation ($r = 0.80$; $P < 0.0001$) between the percentage of omissions and d' but not with B'.

3.2. ERP results

Grand average ERPs at Fz, Cz and Oz to attended and unattended non-targets for both groups are shown in Fig. 1. Difference waves at all leads are presented in Fig. 2. Mean area amplitudes and SDs in the different time windows and for both groups are presented in Table 1.

3.2.1. FSP analysis

The ANOVA at Fz resulted in significant attention ($F(1, 34) = 7.27$; $P < 0.01$) and group × attention effects ($F(1, 34) = 4.26$; $P < 0.05$), indicating that the FSP was larger in controls (0.152 μV; SD 4.1) than in ADHD subjects (−0.72 μV; SD 2.19). Further testing of the attention × group interaction indicated a significant attention effect in the control group ($t(17) = 2.75$; $P = 0.01$), but not in the ADHD group ($t(17) = 0.63$; $P = 0.53$).

3.2.2. OSN analysis

At Oz, the ANOVA resulted in a significant attention effect ($F(1, 34) = 4.07$; $P = 0.05$) but no group × attention effect was found. Mean OSN activity in the 200–280 ms window was −1.0 μV in the ADHD and −1.2 μV in the control group.

3.2.3. N2b analysis

An attention effect was found from 320 to 400 ms at Fz ($F(1, 34) = 14.86$; $P < 0.0001$) and Cz ($F(1, 34) = 6.69$; $P < 0.05$). No group × attention effect was found, indicating that the groups did not differ in N2b amplitude. See Table 1 for mean amplitudes in the attended and unattended conditions.

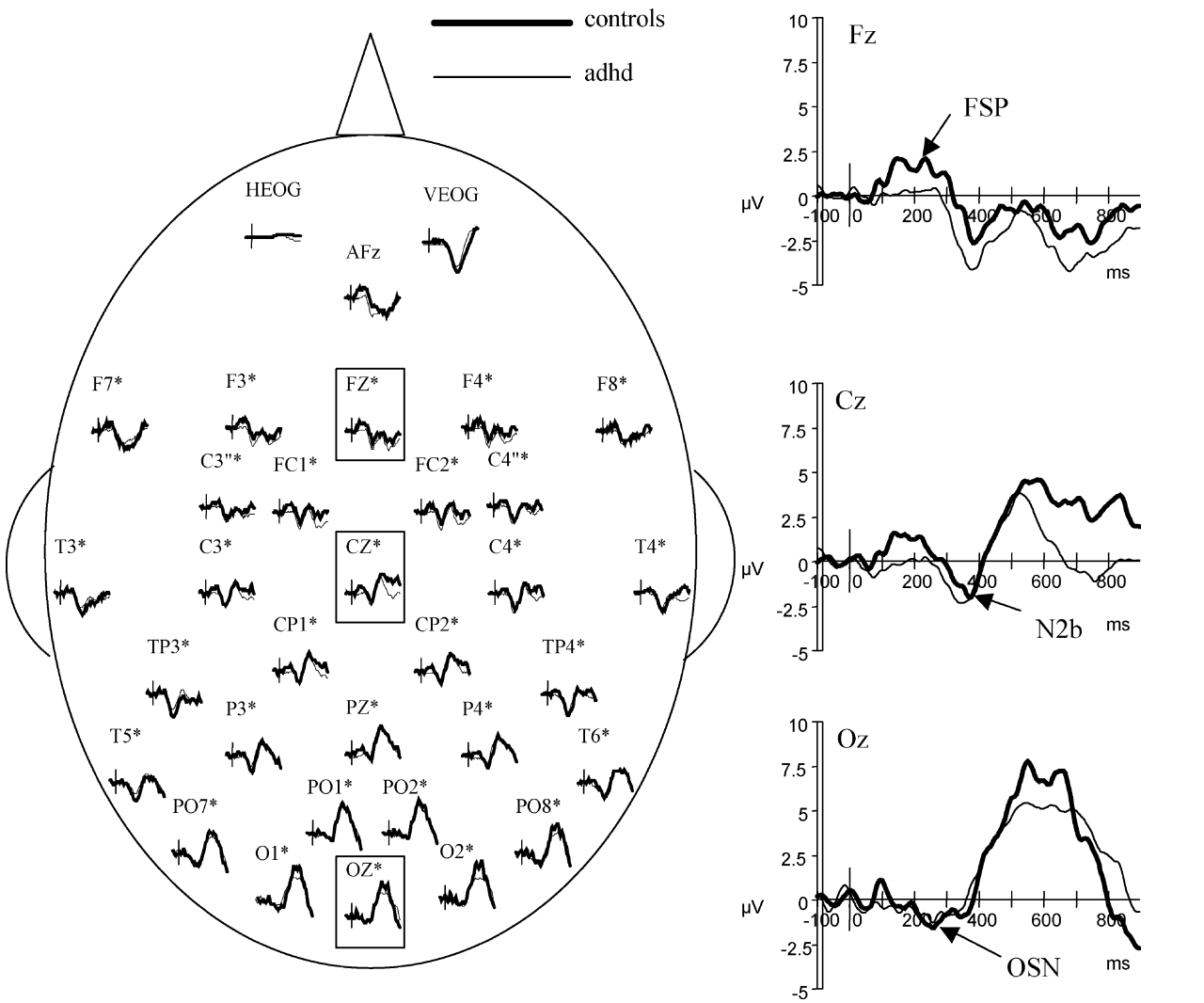

Fig. 2. Grand average difference waves (attended minus unattended non-targets) at all leads and enlarged for Fz, Cz and Oz positions where, respectively, FSP, N2b and OSN effects were reported. ADHD children only differed from controls in FSP activity at frontal locations.

Table 1
Mean area amplitudes and SDs (in parentheses) in μV to attended and unattended non-targets in 120–280 ms windows at Fz, from 200 to 280 ms at Oz and 320 to 400 ms time windows at Fz and Cz in control and ADHD groups. From 120–180 ms the asterisk refers to a significant group × attention interaction, from 320–400 ms asterisks refer to main attention, but not group, effects

	Attended non-targets	Unattended non-targets
120–280 ms Fz		
Controls	0.2 (5.0)	−1.5 (3.3)*
ADHD	−0.6 (2.3)	−0.8 (2.1)
200–280 ms Oz		
Controls	2.4 (8.0)	3.6 (7.8)
ADHD	2.0 (5.8)	3.0 (5.2)
320–400 ms Fz		
Controls	−0.9 (6.1)	0.5 (5.2)**
ADHD	−4.0 (4.6)	−0.7 (3.8)
320–400 ms Cz		
Controls	2.9 (5.2)	4.4 (4.9)*
ADHD	−1.6 (4.2)	0.4 (5.0)

$^{**}P < 0.0001$; $^{*}P < 0.05$.

3.3. Dipole source analysis

The values of the location x, y, z parameters and dipole moments of the different source models at 120, 170, 240 and 375 ms are given in Table 2.

Table 2
Overview of the (cartesian/US) x, y and z location (in mm) for the instantaneous dipole models fitted on the grand average difference waveforms (attended non-targets–unattended non-targets) from ADHD and control children at 120, 170, 240 and 375 ms

	Location x	Location y	Location z
120 ms			
ADHD-s1	0.35	−0.64	−0.00
Control-s1	0.28	−0.69	−0.06
170 ms			
Control-s1	0.10	−0.02	0.01
240 ms			
ADHD-s1	0.43	−0.74	0.13
ADHD-s3	0.58	0.35	−0.00
Control-s1	0.11	−0.61	0.21
Control-s3	0.53	0.13	0.01
375 ms			
ADHD-s1	0.44	−0.19	0.24
ADHD-s3	0.57	0.29	0.43
Control-s1	0.42	−0.24	0.12
Control-s3	0.39	0.22	0.57

s1, source 1 (right posterior source at 240 and 375 ms); s2, source 2 (left posterior source at 240 and 375 ms); s3, source 3 (right anterior source at 240 and 375 ms); s4, source 4 (left anterior source at 240 and 375 ms). Note that since symmetrical dipole constraints were used, only location and orientation parameters of one of the sources of a pair (right hemisphere; s1 and s3) are shown.

3.3.1. 120 ms

First, dipole models were computed for early exogenous activity at 120 ms that was not related to attention (as can be seen in Fig. 1 no attention effects were found from 0 to 120 ms in which P1 peaks were maximal; P values ranged between 0.30 and 0.96). Hereto, in both groups, dipole models were fitted on the grand average ERP signal averaged over attended and unattended non-targets. A single symmetrical dipole model fitted best with residual variances of 0.6 and 0.9 in ADHD and control groups, respectively. Conforming to findings reported in the literature concerning sources of the P1, in both groups, these sources were localized in the vicinity of primary visual areas (see Fig. 3). To test statistically whether location, orientation and dipole moments were different between the groups, individual source models were computed. Hence, the group model was fitted to individual data and the best fit was determined by taking the lowest point in the RV curve in a predetermined time window. For all individual models the residual variance was below 5.7% (mean RV 2.2; SD 1.3). No significant differences in location, orientation or strength of the dipoles were found between ADHD and control children. Also, there were no hemispheric differences between groups in the strength of the dipoles. These findings indicate intact early exogenous stimulus processing (independent of attention) in ADHD children in the visual modality.

3.3.2. 170 ms

Dipole models for the control group at 170 ms are shown in Fig. 4.

A symmetrical dipole pair fitted best in the control group and yielded an acceptable RV of 4.1%; the model was located medially and rather deep. Addition of a second dipole pair did not lead to a robust model. As can be expected on the basis of the reduced ERP activity in the ADHD group at this time point, no reliable model could be fitted here (RV 17.8%). Also, the ADHD model was located more posterior, probably due to the lack of positive activity at especially frontal locations (see spline map in Fig. 4). Because of the unreliability of the source model in the ADHD group it was not depicted in Fig. 4. Since no good solution was achieved in the ADHD group, individual source models at 170 ms were only computed in the control group. The residual variances of the individual models ranged from 44 to 3.7% (mean 15.7%; SD 10.7%). No statistically significant hemispheric difference in the strength of left and right dipoles were found. Averaging of the individually determined location parameters for the control children led to a more lateral and posterior model than when the source model was based on the grand average ERP (individually based model $x = 0.32$; $y = -0.26$; $z = 0.00$ versus grand average based model $x = 0.10$; $y = -0.02$ and $z = 0.01$; the grand average model is depicted in Fig. 4).

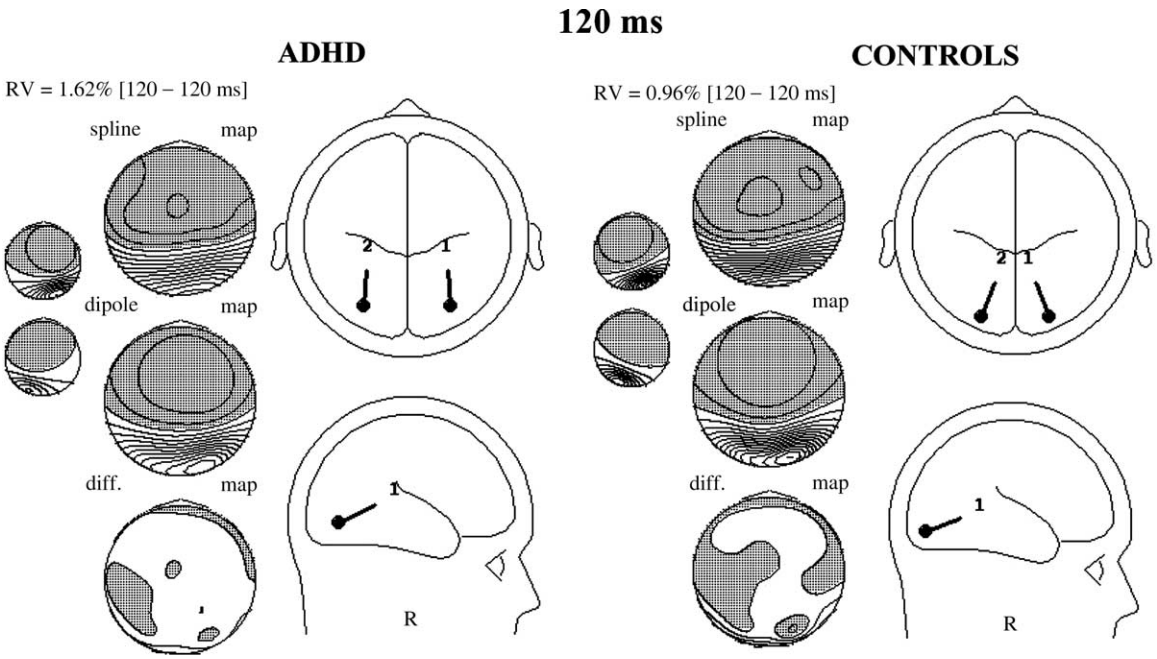

Fig. 3. Top and right lateral views of the instantaneous dipole models fitted at 120 ms The exogenous 120 ms model was determined by averaging activity from attended and unattended non-target ERPs. Left from the dipole model voltage maps of the ERP activity at this time point (spline maps) are presented (spacing is 0.5 μV) together with dipole maps and difference maps (negativity, shaded; positivity, unshaded). Also, the contributions of the two individual dipoles are visualized in the dipole maps most to the left. Source 1 is the source in the right hemisphere, source 2 in the left.

3.3.3. 240 ms

The best fitting model in both groups at 240 ms consisted of two symmetrical dipole pairs, one located more anterior and one located more posterior (see Fig. 5). In the ADHD group the RV of the model was 3.6 against 3.4% in the control group.

To test whether the differences in location and the dipole moments of the dipole pairs were statistically different between the groups, the group model was fitted to individual data as described above. RVs of the individual models ranged from 1.7 to 25.8% (mean RV 7.5%; SD 5.3%). The statistical analysis did not reveal any group differences in dipole moments. The only group differences that were found concerned the anterior dipole pair; the location at the *y*-axis was significantly different ($t = 9.59$; $P < 0.005$), more anterior in ADHD subjects, and the orientation was different at *x* and *y*-axis ($t = 7.96$; $P < 0.01$ and $t = 14.69$; $P < 0.001$, respectively). No hemisphere differences in dipole strength were found in control or ADHD groups.

3.3.4. 375 ms

The spline maps at 375 ms are depicted in Fig. 5. The best fitting model in both the control and ADHD groups consisted of two symmetrical dipole pairs (see Fig. 5). In control and ADHD groups the RV was, respectively, 6.2 and 5.6%. The RVs from the individually determined models ranged from 1.2 to 24.5% (mean RV 6.0; SD 4.1).

The statistical analysis on individually fitted data showed no significant group difference in the strength of the 4 dipoles. Significant group differences in location were only found for the anterior dipole pair; the location differed at the *x*-axis ($t = 7.5$; $P < 0.01$) and the *z*-axis ($t = 10.56$; $P < 0.004$), indicating that in ADHD subjects this dipole was located more lateral and deeper than in controls.

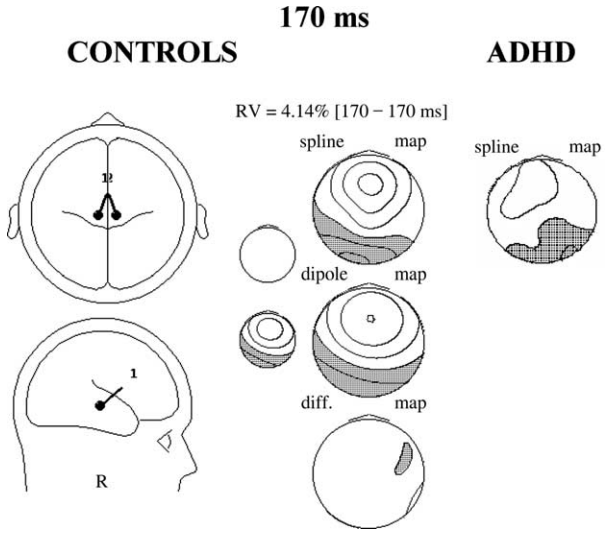

Fig. 4. The endogenous 170 ms model was based on the grand average difference waveforms (attended–unattended non-targets) of control children. Only the spline map of children in the ADHD group is shown because of the unreliable source model (RV of 17.8%). Right from the dipole model voltage maps of the ERP activity at this time point (spline maps) are presented (spacing is 0.5 μV) together with dipole maps and difference maps (negativity, shaded; positivity, unshaded). Also, the contributions of the two individual dipoles are visualized in the dipole maps most to the left. Source 1 is the source in the right hemisphere, source 2 in the left.

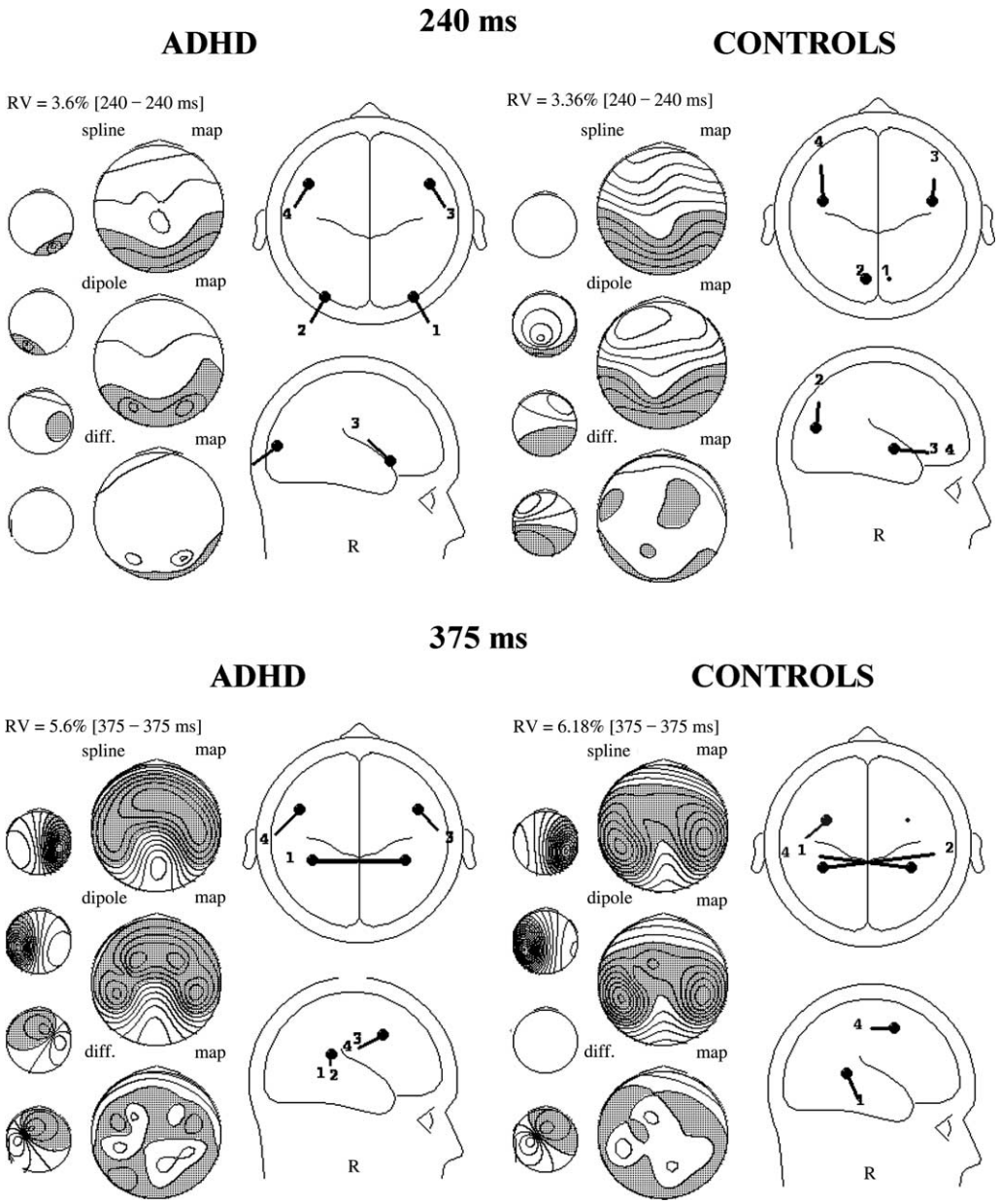

Fig. 5. Top and right lateral view of the instantaneous dipole models fitted at 240 and 375 ms in the grand average difference waveforms (attended–unattended non-targets) of ADHD and control children. Left from the dipole model voltage maps of the ERP activity at this time point (spline maps) are presented (spacing is 0.5 μV) together with dipole maps and difference maps (negativity is shaded, positivity is unshaded). Also, the contributions of the 4 individual dipoles are visualized in the dipole maps most to the left. Sources with odd numbers (1 and 3) are localized in the right hemisphere, sources 2 and 4 are left hemisphere sources.

3.3.5. Statistical comparison of 170 model with other models in control subjects

The availability of source location, orientation and moment parameters in individual subjects at the different time points created the possibility of testing differences between the parameters at different time points. The main aim of the following comparisons was to allow a more specific statement about the location of the source at 170 ms underlying the FSP activity in control children that was localized rather deep and medially. Comparison between source parameters of the source at 170 ms with earlier posterior (exogenous) models at 120 ms and later anterior and posterior models at 240 and 375 ms might give a better indication of the location of the source in the anterior or posterior half of the head.

Statistical comparison of the individually determined dipole models at 120 and 170 ms in the control group revealed that the models were different at y ($P < 0.0001$) and z ($P < 0.01$) location; the 120 model is more posterior and sources are located deeper. Also, the strength of the dipoles was weaker at 170 ms.

Statistical comparison of the individually determined 170 ms model with the model at 240 ms showed that the 170 ms model differed significantly from the anterior dipole pair at 240 ms in x and y location ($P < 0.001$), indicating that the model at 170 ms is less lateral and anterior than the anterior dipole pair at 240 ms. Statistically, the location and orientation of the dipole pair at 170 ms did not, however, differ from the posterior dipole pair at 240 ms. Finally, the 170 source differed from the anterior source at 375 ms in y and x locations ($P < 0.0001$), having a more posterior and medial location. In y and z coordinates there was no statistical difference between the posterior sources (1 + 2) at 375 ms and the 170 source, the sources did, however, differ in x location ($P < 0.01$); dipoles at 170 ms were less lateral (see Figs. 4 and 5).

4. Discussion

The aim of the present study was to investigate whether ADHD children show different visual selective processing compared to controls by using a two-channel color selection task. The focus was specifically on early attention-modulated ERP components (FSP, OSN and N2b). Like in the study by Van der Stelt et al. (2001), we found smaller or even absent FSPs (120–280 ms latency) in ADHD but a sizable FSP in controls, while there were no differences in OSN or N2b. Also, like Van der Stelt et al. (2001), ADHD children performed worse than controls; they missed more target stimuli and generated more false alarms to attended and unattended non-targets. The groups did, however, not differ in reaction time to targets. The signal detection analysis showed that ADHD subjects had lower sensitivity than controls but also had a less conservative response bias. The high positive correlation of 0.80 between perceptual sensitivity values and the amount of hits suggests that, instead of motor or motivation problems, the reduced perceptual sensitivity in ADHD children is the main cause for less efficient detection of targets. In several two-channel visual selective attention studies ADHD children were also reported to detect fewer target stimuli than normal children (Novak et al., 1995; Satterfield et al., 1994), but this was not accompanied by lower perceptual sensitivity as in the present color-selection task.

The FSP findings suggest that ADHD children have a deficit in an early stage of attention-modulated processing. It has been proposed that during this stage stimuli are filtered out on the basis of characteristics primarily relevant for the generation of a correct response (Kenemans et al., 2002; Smid et al., 1999). Since in both the Van der Stelt et al. (2001) and the present study color was the relevant filtering dimension it has to be further investigated whether this deficit is color-specific or also occurs in response to other features such as spatial frequency, shape or orientation.

No group differences were found for the occipital OSN and fronto-central N2b that were present in both groups. The attention effect at Oz (OSN activity) was significant from 200 to 280 ms. The later occurring N2b attention effect was significant in both groups at Fz and Cz from 320 to 400 ms. Van der Stelt et al. (2001) also reported normal N2b activity in ADHD children, the occipital OSN could not, however, be measured reliably in the latter study. Given the functional interpretations of the occipital OSN and central N2b in adult studies, one might suggest that ADHD subjects are as efficient as controls in later stages of selective color processing; that is, in further analysis of the visual percept (OSN) (Smid et al., 1999) and in higher-level 'executive' or 'controlling' processes (N2b) (Kenemans et al., 2002; Lange et al., 1998; Smid et al., 1999). It should be noted, however, that the FSP differences between ADHD and controls extended way over 280 ms latency, including the range of the OSN (Fig. 2). Thus, when taking into account complete distributions during the OSN time range, it must be concluded that groups differed profoundly with respect to attention-modulated processing also in the OSN time range. By all means, the present ERP findings do not agree with the generally adopted view that ADHD subjects do not suffer from abnormalities in early attention processes in the visual modality (Strandburg et al., 1996; Swanson et al., 1998; Tannock, 1998). The absence of early FSP activity in ADHD children in the present and the Van der Stelt et al. (2001) studies is clearly indicative of an early filtering deficit in the visual modality. Furthermore, if the N2b is indeed indicative of executive attention processes, the comparable N2b findings in both groups indicate that not all 'executive processes' have to be deficient in ADHD children.

4.1. Localization of FSP activity at 170 ms

In the topographic maps at 170 ms one can clearly see anteriorly distributed activity (and some posterior negativity) in the control group that is not present in the ADHD group. Source modeling of the anterior positive activity led to a medially located dipole pair in the control group while no reliable model could be fitted in the ADHD group due to the absence of FSP activity. More precise localization of the source underlying the activity at 170 ms in control children might give an indication of the area that is deficient in ADHD children. First, we computed a source model on the basis of the grand average ERP signal in the control group, the model thus acquired was located rather deep and medially (see Fig. 4). In an attempt to get more insight in the location of this early source, source models were also individually determined in control children to enable statistical comparison between the models at 170 ms and posterior and anterior source models in earlier (exogenous; 120 ms) and later (endogenous; 240 and 375 ms) time windows. First, in the average model (now obtained from the individually fitted parameters), the source shifted to a more posterior and lateral location. Second, statistical analysis showed that the 170 ms model in control children

was located anterior to the model at 120 ms, which presumably resides in primary visual areas, explaining exogenous activity that was not modulated by attention. In contrast, the 170 ms dipoles were located more posteriorly than the anterior sources associated with additional OSN and later N2b activity from 240 to 375 ms. Although precise localization is impossible regarding uncertainty associated with assumptions of the head model and dipole model, we might, on the basis of these analyses, conclude that the source explaining the activity at 170 ms (mainly FSP) in control children is located in the posterior half of the head, based on the individual analysis. Accordingly, in a study by Kenemans et al. (2002) in which spatial frequency was the selection feature, FSP activity was also localized in the posterior half of the head, but significantly more medial and dorsal than sources explaining later posterior activity. In two adult studies in which selection was based on color (Anllo-Vento et al., 1998; Lange et al., 1998) a selection positivity was found around 150 ms (with parietal and frontal maximum amplitudes, respectively) but in both studies the underlying source was localized in posterior-ventral areas. One explanation for the more medially located sources in children might be the involvement of more active sources because of more effortful processing at young age. In a study by Clark and Hillyard (1996), although concerning a spatial selective attention effect, a similar posterior-medial dipole as in the present study was reported, but for early negative frontal activity at 140 ms. According to the authors this dipole is caused by the activity of multiple generators that are located in ventral visual areas, although they do not rule out the contribution of active parietal or frontal sources. In this context, the absence of FSP and medial posterior source activity in ADHD children might also be explained by not properly functioning (attentional) control processes subsiding in frontal areas (Casey et al., 1997a; Liu et al., 2003; Vaidya et al., 1998). This possibility cannot, however, be properly investigated in the current paradigm.

4.2. Localization of attention-related activity from 240 to 375 ms

Two later source models were computed at 240 ms, where both occipital selection negativity and frontal selection positivity were present and at 375 ms, at which time point there was significant negativity at frontal and central leads.

At 240 ms, in both groups, a model consisting of two symmetrical dipole pairs, one with a more posterior and one with a more anterior location, was needed to adequately explain the data. For this time range, a similar model was reached by Van der Stelt et al. (2001). As mentioned, however, the present model was much more specific for the FSP/OSN time window, and group differences were subjected to statistical analysis. This analysis revealed that the difference in FSP during this time window is not due to differences in strength (moment) of the dipoles, but to the location of the anterior pair. This anterior dipole pair mainly explains the frontal positivity for this latency in controls (Fig. 5), and was located significantly more anterior in ADHD subjects. Speculating further on this finding, this more anterior location might reflect that the equivalent dipoles are actually located more eccentrically, possibly in (ventral) lateral frontal areas. This in turn might indicate that, in ADHD relative to controls, a smaller stretch of cortical tissue was activated in these areas, which would drive the equivalent dipoles to more eccentric areas. Lateral frontal areas are commonly associated with working memory (e.g. Smith et al., 1998); the present findings might indicate a reduced selective activation of these areas to relevant stimuli in ADHD. In accordance with this hypothesis, recently, Schweitzer et al. (2000) reported reduced regional cerebral blood flow (rCBF) in temporal and frontal areas during a working memory task in adult ADHD subjects when compared to controls. Also in children with ADHD working memory deficits have been reported as being one of the main executive function deficits (Denckla, 1996; Silberstein et al., 1998). But this is just speculation and has to be further investigated.

Also at 375 ms, in both groups, a model consisting of two symmetrical dipole pairs, one with a more posterior and one with a more anterior location, was needed to adequately explain the data. The only group significant difference concerned again the anterior dipole pair, which was located more laterally and inferiorly in ADHD. This pair predominantly explains the medial negativity termed N2b (compare Figs. 2 and 5). In both groups, scalp distributions are considerably complicated by the additional presence of strongly lateral negative foci (Fig. 5). If anything, the statistical dipole analysis also suggests that in this time range the distribution of frontal activity is different for ADHD versus controls.

5. Conclusion

The main conclusion from the present study is that children with ADHD, besides the more often reported attention deficits in the auditory modality (Jonkman et al., 1997; Loiselle et al., 1980; Satterfield et al., 1988, 1990; Zambelli et al., 1977), also show a deficit in early visual selective attention processing. In their behavior this deficit was expressed as a lower perceptual sensitivity that caused ADHD children to miss more targets and make more false alarms. In the ERP, deficient selection processes were marked by an absence of early frontal positivity in a 120–280 ms poststimulus window. Dipole source localization of attention-related ERP activity indicated that in control children a medial posterior source explained most of the FSP activity. This activity may function as an early selective filter, which is deficient in ADHD. Dipole analysis of longer-latency attention-modulated activity suggested

abnormal selective activation of lateral frontal areas in ADHD, which could be related to abnormal working-memory function.

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