Electrophysiological and behavioral indices of distractibility in school-age children

Doctoral dissertation

Valentina Gumenyuk Cognitive Brain Research Unit Department of Psychology University of Helsinki

To be presented, with the permission of the Faculty of Behavioral Sciences, Department of Psychology, University of Helsinki, for public criticism in Lecture Hall 1, at the Department of Psychology, on March 11th, 2005, at 12 noon.

Helsinki 2005

Supervised by:

Professor *Kimmo Alho* Department of Psychology University of Helsinki

and

Academy Professor *Risto Näätänen* Cognitive Brain Research Unit Department of Psychology University of Helsinki

ISBN 952-91-8324-0 ISBN 952-10-2348-1 (PDF) Yliopistopaino Helsinki 2005

To my Family

CONTENTS:

ABSTRACT	5
ACKNOWLEDLEDGEMENTS	6
LIST OF ORIGINAL PUBLICATIONS	8
INTRODUCTION	9
Brain indices of distraction	11
Developmental changes in exogenous (obligatory) auditory ERPs	13
Developmental changes in endogenous auditory ERPs	15
ERPs affected by attention deficit hyperactivity disorder	20
AIMS OF THE STUDY	22
METHODS	22
Subjects	22
Tasks and Stimuli	24
ERP recording	26
Data analysis	27
RESULTS AND DISCUSSION OF STUDIES I-IV	28
Study I. Electric brain responses indicate preattentive processing	
of abstract acoustic regularities in children	28
Study II. Brain activity index of distractibility in normal	
school-age children	30
Study III. Effects of auditory distraction on electrophysiological brain	
activity and performance in children aged 8 – 13 years	32
Study IV. Electrophysiological evidence of enhanced distractibility in	
children with ADHD	36
GENERAL DISCUSSION	40
Developmental changes in preattentive processing of auditory abstract	
regularities in school-age children	40
Developmental changes in brain indices of distractibility	
in school-age children	42
Effect of ADHD on brain index of distractibility in school-age children	45
Conclusions	46
REFERENCES	48

Electrophysiological and behavioral indices of distractibility in school-age children.

Valentina Gumenyuk, Cognitive Brain Research Unit, Department of Psychology, University of Helsinki, Finland.

Unraveling the intricacies of how the human central nervous system matures is crucial for understanding the mechanisms of development of both normal and abnormal perceptual and cognitive skills. Auditory event–related potentials (ERPs) provide a complex but rich source of information about the processing of sounds in the brain. By thoroughly characterizing ERP maturation, it may be possible to determine whether a relationship exists between age-related physiological changes reflected by ERPs and the development of perception and cognition.

The mismatch negativity (MMN) is an ERP component elicited by infrequent changes within a repeating sound or sound pattern. MMN may be used as an index of auditory processing discrimination abilities, for example, the ability to perceive preattentively changes in some abstract feature in the to-be-ignored sounds, e.g., ascending vs. descending pitch within a tone pair. In the present Study I, MMN to such changes was recorded in 8-14-year-old children (n=12). Unlike the findings in adults, increasing complexity of auditory stimulation led to a decrease in children's MMN amplitudes over frontal recording sites. Since the MMN subcomponent originating from the auditory cortex appeared to be unaffected by complexity of stimulation in adults, this finding suggests immaturity of prefrontal brain functions in the studied age group.

Owing to their relatively immature attentional skills, children, compared with adults, are easily distracted by unexpected sounds even during intensive task performance. In the present Studies II and III (*n*=20 and *n*=26, respectively), distractibility was observed as a deterioration of children's visual-motor task performance after the occurrence of a novel task-irrelevant sound (e.g., telephone ringing). Such sounds resulted in prolonged reaction times and decreased percentage of correct responses to visual target stimuli. Electrophysiologically, distraction caused by novel sounds was associated with the positive-polarity P3a ERP component elicited around 200-400 ms from novel-sound onset. The P3a consisted of two subcomponents, an earlier subcomponent (eP3a) with a centrally dominant scalp distribution and a later one (IP3a) with a frontal maximum, and it was followed by a frontally distributed late negative (LN) wave. P3a and LN showed age-related amplitude and scalp-distribution changes in children of 7-13 years. These findings suggest developmental changes in attentional brain functions in normally developing children.

Study (IV) comparing children with attention deficit hyperactivity disorder (ADHD, n=10) with normally developing children (n=10), showed higher behavioral distractibility indicated by increased percentage of response omissions after novel sounds. Moreover, the ERPs of children with ADHD to distracting novel sounds showed a negative-polarity ERP displacement at the P3a latency, an enhanced IP3a, and an attenuated LN compared with the ERPs of normally developing children. The ERP and behavioral effects caused by the processing of novel sounds reveal deficient control of involuntary attention in children with ADHD, which might underlie their abnormal distractibility.

ACKNOWLEDGEMENTS

The present study was carried out in the Cognitive Brain Research Unit, Department of Psychology, University of Helsinki. I express my warmest thanks to my supervisors, Professor Kimmo Alho and Academy Professor Risto Näätänen for providing me with the opportunity and encouragement for this research. It has been a great honor and a pleasure to work under the guidance of Professor Näätänen, one of the world's leading scientists in the field of cognitive brain research.

I want to thank my other co-authors Professor Carles Escera, Professor Erich Schröger, Professor István Winkler, Docent Petri Paavilainen, Docent Risto Ilmoniemi, Docent Minna Huotilainen, Dr. Oleg Korzyukov, Professor Lennart von Wendt, Docent Mirja Hämäläinen, Ms. Taru Häyrinen, LicPsych, and Ms. Henna Oksanen, M.A., for pleasant, successful collaboration.

Ms. Marja Riistama and Ms. Piiu Lehmus deserve my special warmest thanks, for their great help and support in my work. I also wish to thank Ms. Kirsi Järvinen (English school teacher) and Mr. Hannu Rantala (HPM, painikoulu, head coach) for their great help in recruiting the control children, as well as Ms. Leena Wallendahr and Mr. Timo Saarinen for their assistance in collecting data from the children who participated in these studies. I am grateful to Docent Teija Kujala, Docent Mari Tervaniemi, Dr. Elena Kushnerenko, Dr. Rika Takegata, Dr. Rita Čeponienė, and Dr. Teemu Rinne for their invaluable scientific suggestions. Mr. Markus Kalske and Mr. Pasi Piiparinen provided technical help that has been very valuable. Dr. Anna Shestakova, Ms. Sari Nenonen, M.A., Ms. Titta Ilvonen, M.A., Ms. Elvira Brattico, M.A., Ms. Marieke Saher, M.A., Ms. Anu Kujala, M.A., Ms. Titia van Zuijen, M.A., Ms. Tuulia Lepistö, M.A., and Mr. Teemu Peltonen aided me so much during my study. I am also very grateful to Professor Nash Boutros (Psychiatric Department, Yale University) for the opportunity to reanalyze the ERP data (Study IV) with his invaluable assistance.

I would like to express my warmest thanks to Professor Diane Kurtzberg and Docent Paavo Leppänen for acting as pre-examiners of my PhD thesis and their great efforts in reading, correcting and providing constructive comments to my work. I also wish to thank my thesis opponent Professor Judith M. Ford who committed her time and efforts to review and comment this thesis. The financial support for the present work was provided by the Academy of Finland, the Graduate School of Psychology, and the Centre for International Mobility (CIMO). This work would not exist without the encouragement, and great support of my collaborator, teacher, and lifetime best friend: my husband Oleg Korzyukov. Last but not least, my special warmest thanks to my dearest parents, Marija and Ivan Gumenyuk, and my loving sons, Yegor and Kirill for their support, great inspiration and understanding during my work.

Valentina Gumenyuk

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred to with Roman numerals in the text:

I. Gumenyuk V, Korzyukov O, Alho K, Winkler I, Paavilainen P, & Näätänen R. Electric brain responses indicate preattentive processing of abstract acoustic regularities in children. *NeuroReport*, 2003, 14, 1411-1415.

II. Gumenyuk V, Korzyukov O, Alho K, Escera C, Schröger E, Ilmoniemi R J, & Näätänen R. Brain activity index of distractibility in normal school-age children. *Neuroscience Letters*, 2001, 314, 147-150.

III. Gumenyuk V, Korzyukov O, Alho K, Escera C, & Näätänen R. Effects of auditory distraction on electrophysiological brain activity and performance in children aged 8 – 13 years. *Psychophysiology*, 2004, 41, 30-36.

IV. Gumenyuk V, Korzyukov O, Hämäläinen M, Huotilainen M, Häyrinen T, Escera C, Oksanen H, Näätänen R, von Wendt L, & Alho K. Electrophysiological evidence of enhanced distractibility in children with ADHD. *Neuroscience Letters*, 2005, 374, 212-217.

INTRODUCTION

Event-related brain potentials (ERP) are excellent tools for the study of cognitive brain functions in humans and the developmental time course of these functions in childhood (Courchesne, 1990; Eggermont, 1995). ERP is an electrical change generated in the brain and in association with something that occurs either in the external world or within the brain itself. ERPs recorded from the scalp can provide a non-invasive means to evaluate the activity in the human brain associated with perception, decision making, and control of behavior.

ERPs consist of positive and negative polarity deflections and one or more temporally and spatially summating negative and/or positive ERP *components*. According to Näätänen and Picton (1987), "[ERP] component is the contribution to the recorded waveform of a particular generator process, such as the activation of a localized area of cerebral cortex by a specific pattern input.... Whereas...[ERP] deflections ... can be directly measured from the average waveform, the components contributing to these peaks can usually be inferred only from the results of the experimental manipulation" (Näätänen & Picton, 1987, p.376). Deflections and components are often labeled with letter-number combinations. The letter N or P indicates the negative or positive polarity of the component. The number represents either the serial order of the deflection (e.g., the N1 deflection is the first late negative ERP deflection elicited by a sound and it consists of several components including N1a, N1b, and N1c as discussed below,) or the temporal interval, in milliseconds, from the eliciting event to the peak of the component (e.g., N1 is sometimes called N100 as its peak latency from sound onset is about 100 ms; Donchin et al., 1983; Näätänen & Picton, 1987).

Each ERP component has its own complex developmental time course (Courchesne, 1990). Thus, just as different neuronal structures may differ in the timing of neurogenesis, neuromigration, or dendritc arborization, so, too, may different ERP components differ in the developmental time course governing their emergence, waveform changes, latency changes, amplitude changes, topography distributions, and changes in the circumstances eliciting them. Developmental changes in ERPs may be related to both structural maturation of the brain and to the emergence of new

9

organizational patterns that depend to a large extent on the individual's interaction with the environment (Kurtzberg et al., 1984; Morr et al., 2002; Leppänen et al., 2004).

ERPs may provide valuable information on the developmental aspects of cognitive function that could not be obtained from behavioral measures only. With ERPs it is possible, to make a distinction between delayed and abnormal cognitive development (Courchesne, 1990), because ERPs provide information on the timing of brain activity related to maturation or to differences in tasks. Finally, ERPs show both quantitative and qualitative differences between children and adults (Figure 1), and the transition from childhood ERP waveforms to adulthood waveforms is gradual.



Developmental changes in ERPs elicited by auditory stimuli

Figure 1. ERPs obtained from children (n=15, 8-11 yrs) and adults (n=15; 22-45 yrs) representing development-related changes in the processing of simple tones (Morr et al. submitted; reprinted with permission. Note that negative voltages scale presented

downward). These ERPs were elicited by frequent repetitive tones (standards, 1000 Hz) and infrequent higher in frequency tones (deviants, 1200 Hz) presented with interstimulus-interval (ISI) of 600 ms. Unlike the obligatory potentials P1-N1(N100; adult) or P100-N200/N250 (children), which primarily reflect onset responses, the MMN is a neurophysiological correlate of perceptual and short-term memory processes that are important for auditory discrimination (Näätänen, 1990; Ponton et al., 2000) and is present as early as in newborns (Alho et al., 1990; Kurtzberg et al., 1995; Cheour et al., 1998).

Obligatory ERP components to auditory stimuli, such as the P1, are readily elicited in young children but show a larger amplitude than in adults, whereas some other components, like the N1components do not emerge until 9 years of age (see Ponton et al., 2000). The high temporal resolution of ERPs allows one to identify and study cognitive functions, for example, the timing and order of activations in the brain regions caused by attention-catching events (see, e.g., Giard et al., 1990; Näätänen, 1992; Knight & Scabini, 1998; Rinne et al., 2000; Escera et al., 2000, 2003).

Brain indices of distraction

Attentional processes may be either voluntary or involuntary (James, 1890; Broadbent, 1958). This dual-engagement system has an obvious adaptive advantage in that the voluntary engagement of attention enables a person to accomplish a goal-directed task. For instance, one is able to selectively focus attention, without much difficulty on a given conversation in a noisy environment. But sometimes, stimuli outside of one's attentional sphere or focus may occasionally break through to consciousness, thus causing an involuntary switch of attention to previously unattended events (Broadbent, 1982; Kahneman & Treisman, 1984). In fact, involuntary switching of attention may have essential survival value, since changes in the environment that initiate involuntary shift of attention often convey information of potential significance for biological systems (Pavlov, 1927; Näätänen, 1990, 1992).

Children are easily distracted by unexpected environmental sounds even during intensive task performance, but in the course of the normal development, they learn to control their attention to some extent (Courchesne, 1990). Dysfunction in resistance to distraction might result in learning difficulties and significant adjustment problems at school and in other social settings (Barkley, 1998). Increased distractibility may also be

related to a more severe neurobehavioral disorder, such as the attention deficit hyperactivity disorder (ADHD; Morgan et al., 1996).

At the behavioral level, auditory distraction is usually observed as a deterioration of performance in the current task caused by stimuli extraneous to the task (Escera et al., 1998; Escera, Yago, & Alho, 2001; Grillon, Courchesne, Ameli, Geyer, & Braff, 1990; Woods, 1992). For example, novel sounds have specific attention-capturing effects, and seem to offer a powerful way to investigate *distraction*.

Electrophysiologically such distraction appears to be indicated by the elicitation of the P3a response, presumably reflecting involuntary engagement of attention. Recent studies (Escera et al., 1998, 2000) showed that P3a consists of two subcomponents: an early P3a (eP3a) component with its peak latency at around 200 ms with a centrally dominant amplitude distribution over the scalp, and a late P3a (IP3a) component, peaking at around 300 ms with a frontal scalp maximum.

The association of the P3a with involuntary attention is suggested by results showing that a large P3a is elicited by behaviorally distracting novel sounds, such as a telephone ringing or a dog barking occurring among monotonously repeating tones (Woods, 1992; Knight, 1990). Studies in adults (Knight, 1984; Friedman & Simpson, 1994; Alho et al., 1998; Escera et al, 1998) showed a P3a response that might be associated with Pavlov's (1927) "what-is-it" or orienting/investigative response (Ruff & Rothbart, 1996; Sokolov et al., 2002).

The eP3a component onset may overlap with the P2 component (with peak latency around 200 ms) of the auditory ERP and therefore eP3a might be argued that it was caused by an enhanced (non-refractory) P2 in response to the new physical features of novel sounds (Näätänen & Picton, 1987). However, in combined recordings of ERPs and their magnetoencephalographic (MEG) counterparts, Alho et al. (1998) were able to separate the auditory-cortex generator sources of the P2 and eP3a.

Recent studies (Schröger & Wolff, 1998; Escera et al., 2001) of the distraction effect in adults indicate that the P3a is followed by a negative ERP component called the reorienting negativity (RON; Schröger & Wolff, 1998). RON has a maximal amplitude

over fronto-central scalp areas at 400–700 ms after the onset of a distracting sound and was suggested (Escera et al., 2001; Schröger at al., 2000) to be associated with the reorienting of attention back to task performance after distraction caused by an attention-catching, task-irrelevant event.

Developmental changes in exogenous (obligatory) auditory ERPs

The ERP responses that are mainly determined by physical features of stimulation and, within a wide range of variation in the organism's state, are elicited by appropriate stimulation are characterized as *exogenous* (Donchin et al., 1978) or *obligatory* (Näätänen, 1990). They represent an obligatory response of the brain to sensory input.

A series of small-amplitude ERP components can be recorded immediately following an auditory stimulus. These components seem to represent activity in the brainstem stations of the auditory pathway (Starr, Sohmer, & Celesia, 1978). For example in an ERP, elicited by a click, the first five components occur in the first 10 ms after the click. They represent activity of auditory nerve and auditory brainstem structures (Scherg & Von Cramon, 1985). The brainstem potentials have proved to be resistant robust to changes in the subject's state. No matter how aroused, alert, asleep, relaxed, or attentive the subject is, the brainstem evoked responses maintain their amplitude and, generally, their latencies. These responses can be recorded in premature newborns whose gestational age is as young as 30 weeks and their latencies and amplitudes change rapidly during the two postnatal years due to maturation of the auditory pathway (for review, see Galambos, 1982).

The early brainstem responses components are followed by later sensory components, including Na and Pa (Kraus et al., 1985). These "middle latency components" occur at 18-40 ms from stimulus. Current evidence suggests that the Na and Pa are generated in the thalamus and auditory cortex. They are absent or too small to be reliably detected during early childhood, and they do not show the reliable adult pattern until preadolescence (Kraus, Smith, Reed, Stein, & Cartee, 1985).

In adults, the middle latency components are followed by long-latency responses N1 and P2 that are maximal in amplitude at fronto-central scalp sites, with peak latencies at about 100 and 200 ms, respectively, and are usually preceded by a small positive peak at about 50 ms (P1; Picton, Hillyard, Krausz, & Galambos, 1974). Vaughan and Ritter (1970) found that the N1 to brief 1000 Hz tones presented every 2 s, recorded along a coronal chain of electrodes using the nose as a reference, reversed its polarity over the Sylvian fissure. Therefore, it was proposed that the auditory N1 is generated in primary auditory cortex on the superior aspect of the temporal lobe.

The N1 wave is the sum of at least three functionally distinct temporally overlapping sub-components (see, e.g., Näätänen & Picton, 1987) : 1) The supratemporal N1 (N1b) component is generated by bilateral, approximately vertically oriented dipolar sources in the auditory cortex areas on the superior temporal plane with its largest amplitudes over the front-central scalp areas; 2) a 'non-specific' component, maximally recorded at the vertex, presumed to reflect the activation of a relatively widespread neural network related to a general arousal response of the brain (Hari et al., 1982); and 3) the so-called T-complex, i.e., N1a-N1c with amplitude maxima over the temporal scalp areas and generators most likely in the auditory association areas on the lateral aspect of the superior temporal gyrus (Wolpaw & Penry, 1975).

The N1 response increases in amplitude with increasing stimulus intensity, when long ISIs are used (Picton et al., 1976; Gille, Böttcher, &Ullsperger, 1986). Moreover, the N1 wave is very sensitive to the stimulus rate. The N1 obtained with a relatively longer ISI is much larger in amplitude than that obtained in response to frequent sounds (e.g., Hari et al., 1982), this effect probably being explained by the refractoriness of the neurons generating N1 (Näätänen & Picton, 1987).

Children's long-latency obligatory auditory ERPs are dominated by the P1 (peak latency at around 100 ms) and N200 or N250 peaks (peak latencies at 200 or 250 ms; see Figure 1). During early childhood (1-4 yrs), the P1 is the most predominant peak (Kushnerenko et al., 2002; Morr et al., 2002), while during mid-childhood (3-6 yrs), the negativity with peak latency at around 200-250 ms (N2) becomes increasingly robust (Courchesne, 1978). Thereafter, the N2 dominates auditory ERPs until adolescence (Pang & Taylor, 2000; Ponton et al., 2000). Moreover, Ponton et al. (2000) found that

14

the N2 amplitude increases from age 4 to 10 and thereafter decreases to reach adult values by the age of 17. Furthermore, unlike the N1, the children's N2 is insensitive to stimulus rate (Čeponienė et al., 1998). The scalp predominance of the N2 shifts from frontal to fronto-central from 7-9 to 10-12 years of age (Bruneau & Gomot, 1998).

Karhu et al. (1997) compared ERPs to non-attended frequent and infrequent auditory input in school-aged children (9 yrs.) and young adults. In adults, they found that both inputs elicited N100 responses at Cz (vertex) electrode. While in children, infrequent stimuli evoked vertex responses with similar latency and refractoriness, whereas frequently delivered tones evoked responses on average at 240 ms. Their finding suggests that infrequent stimulation in children activated a separate neuronal population that is reflected by ERPs at latency range 260-300 ms. This "dual behavior", simultaneous refractoriness of one neuronal population (during frequent stimulus presentation) and "sensitization" of another (intermittent stimulation) was suggested as reflecting the redirecting of the attention in children (Karhu et al., 1997).

For the N1 elicitation in children (4-8 yrs), sounds have to be presented with an ISI of 1 s or longer (Bruneau & Gomot, 1998, Čeponienė et al., 1998). Most likely, this is due to the longer N1 refractory cycle in children than in adults. However, Tonquist-Uhlen (1995) found that in 8- to 16-year-old children the topography of the N1b (with the largest fronto-centrally amplitude) was similar to that in adults.

In sum, it appears that the N1/N2 distinction shares some commonalities in children and adults, e.g., sensitivity to stimulus rates. However, their maturational trajectories are different, with the N1/N2 amplitude ratio increasing with age. Moreover, the scalp distribution of both the N1 and N2 changed with maturation, which indicates a different component structure and function of children's and adults' N1 and N2 (Čeponienė et al., 1998).

Developmental changes in endogenous auditory ERPs

The *endogenous* components are often related to cognitive processes although some of them may be partially related to the physical parameters of the eliciting stimulus. However, some endogenous components can be elicited even in the absence of an

15

external stimulus. "The variance of endogenous components normally is accounted for by variation in the tasks assigned to the subject" (Donchin et al., 1978, p. 355). These components are usually rather late and slow, but may in some cases commence at a very short latency, and hence may overlap and summate with the relatively early exogenous components (Näätänen, 1990). Age-related differences have been observed in a wide variety of paradigms and are well documented in the behavioral development literature (for reviews, see Hagen & Hale, 1973; Lane & Pearson, 1982; Plude et al., 1994).

The so-called *passive oddball paradigm* is used to study the electrophysiological manifestation of discrimination of, and orienting of attention to deviant or novel stimuli in the condition where the subject's attention is directed away form the eliciting stimuli (e.g., the subject is instructed to concentrate on reading a book or watching a silent movie). For example, deviant auditory stimuli in a to-be-ignored stream of repeating standard sounds elicit an ERP component called the mismatch negativity (MMN; Näätänen, 1992) that is not elicited by the repetitive standard stimuli. The MMN typically reaches its maximum amplitude over the frontal scalp and it has generator sources in the auditory (e.g., Hari et al., 1984; Scherg et al., 1989) and frontal cortices (e.g., Giard et al., 1990; Rinne et al., 2000). The MMN peak latency and duration are shorter, and usually its amplitude is larger, the larger the stimulus difference (Gaillard, 1983; Sams et al., 1985; Alho et al., 1992; Näätänen & Tiitinen et al., 1994). MMN appears to be one of the early developing responses, which can be observed in newborns a (Alho et al., 1990a, b; Kurtzberg et al., 1995; Kushnerenko et al., 2002, Leppänen et al., 2004) and even in fetuses (Huotilainen et al., 2005).

Most of the child-MMN studies postulate that the MMN is developmentally a rather stable response in terms of its latency and amplitude (Kraus et al., 1993; Csépe, 1995). However, some studies (Martin et al., 1995, Shafer et al., 2000) report that peak latency and maturational changes in topography of the MMN decreases with age in school-age children. Gomes et al. (2000) found that the amplitude of the MMN elicited by frequency change was more sensitive to the amount of frequency deviation in 8–12 year old children than in adults. These differences suggest that the observed pattern of MMN maturation may be stimulus contrast dependent.

Näätänen and his colleagues (Näätänen, 1990; Ecsera et al., 2000; Schröger at al., 2000) proposed two main characteristics of the MMN: its connection to the neuronal basis of auditory sensory memory mechanisms and its automatic (preattentive) nature. A further suggestion is that the MMN generator mechanism might also be related to orienting functions, diverting the organism's attention to potentially significant stimulus changes in the environment. The frontal MMN generator has been associated with triggering of the involuntary switching of attention to stimulus deviance (Giard et al., 1990; Escera et al., 2000).

The MMN is often followed by a relatively sharp fronto-central positive wave that peaks at about 250 ms from stimulus onset and is apparently the P3a ERP component (Squires et al., 1975). For large stimulus deviations, the P3a may be preceded by the N2b (Näätänen et al., 1982). The P3a seems to be more easily elicited by the deviant stimuli when the magnitude of stimulus deviation is great and the primary task is not demanding. Findings showing prolonged reaction times (RTs) to a stimulus that is preceded by a P3a-eliciting stimulus strongly support the notion that the P3a reflects involuntary attention switching (Woods, 1992; Escera et al., 2000).

In infants, a P3a-like potential has been observed with much longer latencies than in adults; at 513 ms in 1-year-old (Fushigami et al., 1995) and at 600 ms in 10-month-old infants (McIsaac & Polich, 1992). However, in studies that focused on the MMN, a positive component at the same latency as in adults (i.e., at 250-350 ms) was observed in 2- to 7-month-old infants in response to deviant stimuli (Alho et al., 1990; Trainor et al., 2001). It was suggested by Alho et al. (1990) that this might represent the analogue of the adult P3a, reflecting orientation to the deviant stimuli. However, in several studies (Leppänen et al. 1997, 2004) a prominent positive response instead of the MMN was elicited in infants even in quiet sleep, indicating that at least during early developmental phase the maturational changes in the infant brain (myelination, changes in the anatomy, the architecture of the brain, axonal connectivity and synaptogenesis) could affect the polarity of ERP waveforms, resulting the mismatch response with a positive polarity.

As in adults, the P3a in older children has a peak latency of 250-350 ms from stimulus onset and maximal amplitude over the fronto-central scalp (Courchesne, 1990;

Čeponiene et al., 2004). In adults, the eP3a is maximal fronto-centrally and inverts in polarity at temporal and posterior scalp sites, whereas the IP3a is maximal frontally, is distributed anteriorly to the eP3a, and does not invert in polarity (Escera et al., 1998). According to scalp-current density mapping, the eP3a has its sources in the auditory and parietal cortices, whereas the IP3a gets a major contribution from the frontal cortex (Yago et al., 2003). The eP3a response is relatively insensitive to attentional manipulations (Escera et al., 2000) and therefore was suggested to reflect automatic detection of the violation of a multimodal neural model of the external world (Yamaguchi & Knight, 1991). The IP3 response, in turn, is enhanced by attention and habituates upon the repetition of the eliciting (novel) stimulus (Cycowicz & Friedman, 1997, Escera et al., 1998). The amplitude of IP3a increases as a function of the magnitude of stimulus change (Yago et al., 2001). Therefore, the IP3a was suggested to index a genuine attention switch. In a recent review, Friedman et al. (2001) discussed the frontal and posterior aspects of the novelty-P3 response, and suggested that the frontal aspect of P3a might reflect orienting, whereas the posterior aspect might reflect stimulus categorization processes related with memory.

In studies of children (Čeponienė et al 2004), novel sounds elicited a fronto-centrally predominant, biphasic P3a response at latencies similar to those in adults. The eP3a was distributed very similarly to that in adults (Escera et al., 1998; Yago et al., 2003) and in 7-10-year-old children (Čeponienė et al 2004). However, the IP3a in children was robust posteriorly relative to the eP3a, whereas in adults, the opposite was observed (Escera et al., 1998). This pattern of the children's P3a suggests that the processes involved in the orientation of attention (as indexed by the eP3a), are mature by the age of 7 years, but those underlying the relocation (switch) of attention (indexed by IP3a) are not. This might be explained by the slow maturation of the prefrontal cortices (Luria, 1973; Huttenlocher, 1979; Bunge et al., 2002), known to be critical for attention control (Knight, 1984; Daffner et al., 2000).

The P3a can be distinguished from the P300 or P3b component to target stimuli by its shorter latency and more frontal scalp distribution (Squires et al., 1975; Ford, Roth, & Kopell, 1976). The P3b is the best known of all endogenous ERP components; it is sometimes also referred to as the P3 or P300. By now, it has been observed and measured in hundreds of investigations (Sutton & Ruchkin, 1984; for review see

Polich, 2002). The P3b is triggered by events that are of importance to the person being recorded and depends upon controlled, conscious processing (Woods et al., 1980). Perhaps therefore clear evidence for the P3b in infants has not been found so far (Courchesne et al., 1981). However, a P3b-like component was observed in a 20-month-old and clear evidence of the P3b was found in children of 3 years and older (Courchesne, 1977, 1983). The P3b amplitude increases dramatically from 3 to 6 years of age (Courchesne, 1987). Thereafter the P3b amplitude and duration decrease with age. These age-changes in amplitude might reflect the gradual loss of synapses during this phase of development as by the end of the first decade of life there are roughly half as many synapses in all cortical and limbic areas as there were during late infancy and early childhood (Huttenlocher, 1979; Huttenlocher et al., 1982; Rakic et al., 1986).

Courchesne (1977, 1978) was the first to examine age-related ERP changes using a visual novelty oddball paradigm. His subject groups included 6-8-year-olds, 10-13year-olds, 14-17-year-olds, and 24-36-year-olds. They were presented with target (12%) and non-target stimuli (76%); while the rest of the stimuli were unrecognizable, "novel" stimuli in one condition or easily recognizable stimuli in another. The author reported that both non-target and target stimuli elicited posteriorly distributed P3b-like waves in children and adults. The ERPs elicited by the novel stimuli in adults were characterized by a centro-frontally maximal P3, whereas in children, this type of stimulus elicited large amplitude negative (peak latency 410 ms) and positive (900 ms) waves, labeled Nc and Pc, respectively. The amplitudes of these frontally maximal Nc and Pc components were found to be largest in young children and decreased dramatically with increasing age. Further, the Nc has been observed in response to both visual and auditory novel stimuli with a more frontal topography in the auditory modality than in the visual modality (Courchesne, 1990). Thus, the Nc and Nc-like potentials could be elicited by surprising, interesting, and important pictures and sounds in the classic "oddball" task (Kurtzberg & Vaughan, 1985). As with the P3b, Nc has a complex and long developmental time course. It is possible, that changes in the number of cortical synapses that occur during early development could affect the neuronal mechanisms generating the Nc (Huttenlocher, 1979; Huttenlocher et al., 1982; Rakic et al., 1986).

Other researches have reported a "negativity" referred to as the late discriminative negativity (LDN; Cheour, et al., 2001; Čeponienė et al., 1998) or the late MMN (IMMN; Korpilahti et al., 2001) that followed the MMN in children. Some adult studies have also found a late negativity following MMN in ERPs to deviant sounds in an unattended auditory input (for a review see, Alho, 1995). Näätänen et al. (1982) have suggested that in adults, such later activity might be associated with "sensitization processes" after a stimulus change and may serve as an automatic preparatory process for the detection of any additional changes. However, the exact nature of this late negativity following MMN and age-related changes in it are still unclear.

Schröger and Wolff (1998) observed a long-latency (approx. 400-600 ms after sound onset) frontally distributed negative ERP wave in adults also in response to distracting sound changes labeled it as the *reorienting negativity* (RON). The RON was suggested to be generated by processes involved in reorienting attention back to task performance after distraction caused by a distracting auditory event (Schröger & Wolff, 1998; Escera et al., 2000). In some studies, a so-called late negativity (LN) or RON has been observed in response to novel or deviant sounds in children of kindergarten and school age (Shestakova et al., 2003; Čeponienė et al 2004; Wetzel et al., 2004). However, developmental changes in the RON/LN and its relation to the other late negative waves elicited in children by deviant sounds, i.e., Nc, LDN, and IMMN (Kurtzberg & Vaughan, 1985; Courchesne, 1990; Čeponienė et al., 1998; Cheour, et al., 2001; Korpilahti et al., 2001) are still poorly understood.

ERPs affected by Attention Deficit Hyperactivity Disorder (ADHD)

One of the aims of present research was to determine, by using the ERPs and behavioral measures, whether children with ADHD tend to orient their attention more strongly to distracting task-irrelevant sounds and how effectively they are able to reorient their attention back to task-relevant stimuli. Therefore some main findings from the ERP studies on children with ADHD will be reviewed below.

ADHD is a multidimensional disorder that has its onset in childhood and is characterized by persistent problems of inattention, impulsivity, and hyperactivity (Morgan et al., 1996; American Psychiatric Association, 1994). Difficulties with sustained attention task (Kemner et al., 1996) in children with ADHD can be caused by different alternatives, one being abnormal distractibility.

In previous studies on children with ADHD, ERPs to target stimuli in an auditory oddball task have shown that children with ADHD are consistently differentiated from age-matched controls by a smaller amplitude of the auditory N1 deflection (Näätänen & Picton, 1987) at the age of 7–9 years (Satterfield et al., 1984; 1994), by a smaller N2 amplitude (peak around 200 ms) at the age of 6–8 years (Satterfield et al., 1990), and by a smaller P3b amplitude up to the age of approximately 12-13 years (Holcomb et al., 1986; Johnstone & Barry, 1996; Kemner et al., 1996; Kuperman et al., 1996; Jonkman et al., 1997, 2000). These findings suggest insufficient processing of target events in children with ADHD.

However, the findings on the effects of ADHD on the P3a response (or the novelty-P3) are not as consistent. For example, Jonkman et al. (2000) found no differences between 7-13-year-old children with ADHD and age-matched controls in P3 responses to task-irrelevant novel visual stimuli. Consistent with this, Kemner et al (1996) observed similar P3 responses to task-irrelevant auditory and visual novel stimuli ADHD and control children of 9-10 years. However, Loiselle et al. (1980) reported that the amplitude of the P3 response, possibly consisting of both P3a and P3b responses, to attended target stimuli in auditory or visual selective attention tasks is attenuated in 13-year-old children with ADHD in comparison with age-matched control children. Consistent with that, Liotti et al. (in press) observed an attenuated P3a response in 9-11-year-old children with ADHD in comparison with age-matched controls. Their P3a was recorded in a visual discrimination task in response to a visual stop signal that appeared at unpredictable intervals after the stimulus and informed that the children were to inhibit their response. Thus, it is not clear whether or not P3a is affected by ADHD and, further, whether it could be used to study the distractibility in children with ADHD.

AIMS OF THE PRESENT STUDY

The aims of the present study were:

(1) to evaluate with MMN and P3a ERP responses the ability of school-age children (8-14 yrs) to pre-attentively extract the abstract features from to-be-ignored sounds, i.e., ascending vs. descending frequency within standard and deviant tone pairs (Study I);

(2) to evaluate the P3a and LN ERP responses elicited by task-irrelevant novel sounds and the distracting effects of these sounds on visual task performance in two age groups of normally developing children: in 7-10-olds and 11-13-year-olds (Study II);

(3) to assess maturational changes in distractibility by measuring the P3a and LN responses to novel sounds and the distracting effects of these sounds on visual task performance in children of three more narrowly aged groups (8–9, 10–11, and 12–13 years) (Study III);

(4) to compare distractibility, as indicated by ERPs to task-irrelevant novel sounds and the distracting effects of these sounds on visual task performance, between children with ADHD and age-matched normally developing controls of 8-10 years (Study IV).

METHODS

A brief description of the methods used in the experimental work of the present doctoral dissertation based on Studies I-IV is presented in the following.

Subjects

Study I. Fourteen normally developing children with normal hearing, normal or corrected-to-normal vision, and no history of speech, language, learning, psychiatric or neurological problems participated in the experiment. All of them were in the age-appropriate grade level at school. Data from two children were excluded from the set due to low signal-to-noise ratio in their ERPs. Thus, data from twelve 8–14-year-old children (M= 10.2 yrs., SD= 1.8 yrs; 5 girls) were included in the analyses.

22

Study II. Twenty normally developing children fulfilling the same criteria as the children participating in Study I were divided into equal-size groups according to their ages (7-10 and 11-13 years of age): younger (M= 9.8 yrs., SD= 1.5 yrs.; 3 girls) and older (M= 12 .5 yrs., SD= 7 mo; 4 girls).

Study III. Twenty-six normally developing 8-13-year-old children (12 girls) from primary and secondary schools participated in the experiment. All children fulfilled the same criteria as the children participating in Studies I and II. Two children's data were excluded from the set due to a low percentage of correct responses (less than 50 %) in the visual task. The remaining 24 children were divided into three equal-size groups according to their ages: Young, 8–9 years (*M*= 8.0 yrs., SD= 0.6 mo), Middle, 10–11 years (*M*= 11.0 yrs., SD= 0.7 mo) and Old, 12–13 years (*M*= 12.5 yrs., SD= 0.8 mo).

Study IV. ERPs to the auditory stimuli and performance in the visual task distracted by auditory stimulation were measured in eleven 8-10-year-old children with ADHD and in ten age-matched normally developing control children (a subgroup of children participating in Study III selected to match the age and gender distributions of the ADHD group). The data of one ADHD child were excluded from further analyses due to a very poor performance in the visual task (less than 50% correct responses). The remaining ADHD group and the control group consisted of 10 subjects each (mean ages 8.7 and 8.6 yrs., respectively; one girl in each group).

The children with ADHD were recruited from the Department of Child Neurology of the Helsinki University Central Hospital. All of them had a thorough multidisciplinary diagnostic assessment and only children fulfilling the DSM-IV (1994) criteria for ADHD and having no other comorbidity disorder were accepted. Those children with ADHD who were on medication were withdrawn from it at least a day before the experiment. All children with ADHD had impulsivity and hyperactivity as critical symptoms of the disorder. The general intellectual ability of the clinical group was assessed with either the Wechsler Intelligence Scale for Children, Revised or Third Edition (WISC-R or WISC-III) or Wechsler Preschool and Primary Scale of Intelligence, Revised Edition (WPPSI-R; Wechsler, 1984; 1995; 1999).

In all studies, written informed consents were obtained from all parents of children participating in the studies. The Ethics Committee of the Children and Adolescents Hospital approved the protocol of the Study IV for the children with ADHD and The Ethics Committee of the Department of Psychology, University of Helsinki, approved the protocol of Studies I-IV for the normally developing children.

Tasks and Stimuli

In *Study I*, children were presented with pure sinusoidal tones with a duration of 50 ms (including 10 ms rise and fall times) and an intensity of 50 dB above the subjective hearing threshold at the frequencies of the sounds used in the tone pairs (see below). The tones were presented in pairs, which were delivered in a random order (Figure 2). 87.5% of the pairs were standard pairs "ascending" in frequency (the second tone having a higher frequency than the first tone) and 12.5% deviant tone pairs "descending" in frequency (the second tone having a lower frequency than the first tone).



Figure 2. A schematic illustration of stimuli used in Easy and Hard conditions of Study I. The frequencies of the tones presented in pairs varied randomly in the 523–1397-Hz range in steps corresponding to the fundamental frequencies of the notes in the C major scale. In the Easy condition, the frequency of the second tone of the pair was always one step higher (standard pairs, St.) or lower (deviant pairs, Dev.) than that of

the first tone. In the Hard condition, the frequency of the second tone was, randomly, 1–10 steps higher (standard pairs) or lower (deviant pairs) than that of the first tone.

The within-pair stimulus onset asynchrony (SOA) was 90 ms and the between-pair SOA was 490 ms. Eleven tone frequencies (523, 587, 659, 698, 784, 880, 937, 1046, 1174, 1318, and 1397 Hz) were used. These frequencies correspond to the fundamental frequencies of the notes on the C major scale. The frequency separation between the two tones within each pair was always one step on the C major scale in the Easy condition and varied from 1 to 10 steps in the Hard condition.

During the experiment, the children watched a self-chosen video with the sound turned off. They were instructed to attend to the movie and to ignore the sounds that were delivered binaurally through headphones. Each child was presented with a total of 6 stimulus blocks, each block lasting approximately 6 min.

In *Studies II-IV*, the experiment consisted of a visual RT task in which ERPs to the auditory stimuli preceding the visual stimuli were recorded. Auditory-visual stimulus pairs were presented at a constant rate of 1 pair in every 1.7 s (Figure 3). Each sound had a duration of 200 ms and was delivered binaurally through headphones at 50 dB above each child's subjective hearing threshold. The sound was either a sinusoidal tone of 600 Hz (p= .80) or a complex novel sound presented randomly (p= .20) with the exception that at least 3 tones occurred between any two successive novel sounds. The novel sounds were drawn from a pool of 160 different environmental sounds, such as those produced by a hammer, rain, door, or car horn. Their maximal intensities were approximately matched with those of the tones. Each novel sound was presented only once during the experiment. The visual stimuli were 32 different white-line drawings (16 animals and 16 non-animals) extending 9 cm horizontally and 9 cm vertically, presented for 300 ms and starting at 300 ms after the onset of the preceding sound. The visual stimuli were displayed in a random order in the center of a black computer screen located approximately 130 cm from the subject's eyes.



Figure 3. A schematic illustration of the auditory-visual distraction paradigm used in Studies II-IV. Auditory-visual pairs, starting with a tone or novel sound, were presented to children who performed a forced-choice visual (animal/non-animal) discrimination task.

Children were instructed to ignore sounds, to focus their gaze on a white fixation cross (1 cm x 1 cm) continuously presented in the center of the screen, and to respond in the visual discrimination task as accurately as possible by pressing one response button with their right thumb to an animal image appearing on the screen and another button with their left thumb to a non-animal image. Before the main experiment, each child participated in one or two practice blocks in the visual task without auditory stimuli. The main experiment consisted of eight 3-min experimental blocks with 1–2 min pauses between the blocks.

ERP Recordings

Study I. The electroencephalogram (EEG) was recorded with Ag/AgCl electrodes from 13 scalp locations (F7, F3, Fz, F4, F8, C3, Cz, C4, P3, Pz, and P4, according to the International 10–20 System, and the left and right mastoids, LM and RM, respectively) and digitized (SynAmps amplifiers and Scan software, NeuroScan, Inc.) at 250 Hz sampling rate with 0.1–40 Hz filter limits. The reference electrode was placed on the tip of the nose. The horizontal and vertical electrooculograms (EOGs) were recorded with a pair of electrodes placed lateral at the outer canthi of the two eyes and another electrode pair placed above and below the left eye, respectively. EEG and EOG signals were filtered off-line with a bandpass of 1–20 Hz. Epochs of 600–ms duration starting 100 ms before the tone-pair onset were extracted from the continuous EEG records. The epochs were baseline corrected by using the mean voltage level in the pre-stimulus period. Epochs during which extracerebral artifacts caused the EEG or

EOG signal to exceed $\pm 100 \ \mu$ V at any electrode were excluded from further processing. Responses to standard pairs that immediately followed a deviant pair were also omitted. For each child, ERPs were separately averaged for the standard and deviant pairs for a minimum of 300 and 150 acceptable epochs, respectively.

Studies II-IV. The EEG (0.1–100 Hz, sampling rate 250 Hz) was recorded from frontal (Fp1, Fp2, F7, F3, Fz, F4, and F8), central (C3, Cz, C4), temporal (T3, T4, T5, T6), parietal (P3, Pz, P4), and occipital (O1, O2) scalp sites and from the left and right mastoids (LM and RM, respectively). Voltage changes caused by eye movements and blinks were monitored with recordings from the forehead sites (Fp1, Fp2) and from additional electrodes placed at the left and right canthi. The common reference electrode was placed at the tip of the nose. ERPs were obtained separately for the tones and novel sounds by averaging EEG epochs over an 800-ms period (over a 1000-ms period for ERPs to visual target stimuli) starting 100-ms before each sound onset. These EEG epochs were digitally band-pass filtered at 1-30 Hz. The epochs were baseline -corrected by using the mean voltage level in the pre-stimulus period. Epochs during which extracerebral artifacts caused the EEG to exceed $\pm 100 \ \mu V$ at any electrode were excluded from further processing. In addition, the epochs for the first 4 stimuli of each block and the epochs for tones occurring right after a novel sound were excluded. For each child, averaged ERPs for the tones and novel sounds consisted of at least 300 and 100 acceptable EEG epochs, respectively.

Data Analysis

To determine the peak or mean amplitude of the ERP components, the electrodes with the largest amplitudes for the given waveforms were used in all studies, i.e., F3, Fz, and F4 for the MMN (Study I), P3a (Studies I-IV), F7, F3, Fz, F4, and F8 for LN (Studies II-IV), and C3, Cz, C4 for P3a (Studies II-IV).

In *Study I*, repeated-measures analyses of variance (ANOVAs) were conducted with factors Stimulus Type (standard vs. deviant) and Electrode (F3 vs. Fz vs. F4) to determine whether an MMN was elicited in the two (Easy and Hard) conditions.

27

In Studies II-IV, in order to remove the effects of visual ERPs from the auditory responses to novel sounds, the P3a and LN amplitudes were measured from ERP difference waves obtained by subtracting ERPs to repeating tones from those to novel sounds. As in previous adult studies (Escera et al., 2000; Escera & Corral, 2003), the P3a had two consecutive phases: the early P3a (peak around 250 ms from novelsound onset) and late P3a (peak around 350 ms novel-sound onset). Between-group differences in the P3a and LN amplitudes were tested with ANOVAs and Newman-Keuls post hoc tests. Greenhouse-Geisser corrections were used in reporting the Pvalues when appropriate. However, the original, non-corrected degrees of freedom are reported for all F-values. The scalp distributions of the P3a and LN responses were statistically analyzed with ANOVAs after voltage normalization performed by dividing the amplitude of the analyzed response at each electrode by the square root of the sum of the squared amplitudes of this response at all electrodes included in the analysis (McCarthy & Wood, 1985; see also Alho et al., 1994). The normalized ERP amplitudes were compared with four-way ANOVAs including the following factors: Group, Phase (early vs. late P3a or LN), Frontality (frontal electrodes F3, Fz, and F4 vs. central electrodes C3, Cz, and C4 vs. parietal electrodes P3, Pz, and P4) and Laterality (left-hemisphere electrodes F3, C3, and P3 vs. midline electrodes Fz, Cz, and Pz vs. right-hemisphere electrodes F4, C4, and P4).

In *Studies II-IV*, a correct button press occurring between 200–1500 ms after visual stimulus onset was classified as a hit. Mean hit RTs, and rates of hits, wrong responses, and missed responses were determined for each child separately for visual stimuli following tones and for those following novel sounds. ANOVAs with factors for Group and Preceding Sound (Tone vs. Novel) were used in the statistical analyses of these performance data.

RESULTS AND DISCUSSION OF STUDIES I-IV

The main results of Studies I-IV are presented below.

Study I

The preattentive processing of abstract acoustic regularities was investigated in children aged 8–14 years concentrating on watching a silent video film. ERPs elicited

28

by frequent (standard) pairs ascending in pitch and by infrequent (deviant) pairs descending in pitch. The frequency of the first tone in each pair was randomly chosen to be one of the fundamental frequencies between 523-1397 Hz of notes on the C major scale. In the Easy condition, the second tone of the pair was always one step (on the C major scale) higher (standard pairs) or lower (deviant pairs) than the first tone; while in Hard condition, the second tone was randomly 1–10 steps higher (standard pairs) or lower (deviant pairs) or lower (deviant pairs) or lower (standard pairs) or lower (deviant pairs) than the first tone.



Grand-average ERPs and difference wave

Figure 4. Nose-referenced group-averaged ERPs to deviant (broken lines) and standard (thin solid lines) tone pairs and the deviant-minus-standard ERP difference waves (thick solid lines) in children (n=12; 8-14 years) at frontal electrode sites (F3, Fz, F4) and at the left and right mastoid sites (LM and RM, respectively). The frontal MMN component peaked between 180 and 220 ms, whereas the temporal MMN (polarity-inverted at LM and RM inferior to the auditory cortex) peaked between 160 and 190 ms. ERPs and ERP difference waves are shown for the Easy and Hard condition. In the Easy condition, the MMN was followed by a small P3a-like deflection.

In the Easy condition, the MMN amplitude, measured from the deviant-minus-standard difference waves, was significantly different from 0 μ V at Fz (t(11) = -3.24, P<0.008) and at RM (t(11) = 3.95, P<0.002; see Fig. 4), where a polarity-inverted (positive) MMN was observed. The polarity-inverted MMN at the mastoid sites was also significant in the Hard condition (t(11) = 3.04, P < 0.01 and t(11) = 3.5, P < 0.005, for LM and RM, respectively). In contrast, no significant differences between standard and deviant ERPs were found at the frontal electrodes in the Hard condition. ANOVA for the frontal (F7, F3, Fz, F4, and F8) MMN amplitudes showed a significant main effect of Condition (F(1,22) = 4.19; P < 0.05), indicating that the amplitude of the frontal MMN was larger in the Easy than in the Hard condition (the mean amplitude over the frontal sites $-1 \mu V vs. -0.22 \mu V$, respectively). The same comparison for the inverted temporal MMN measured at LM and RM showed no significant amplitude differences between Easy and Hard conditions. In the Easy condition, deviant pairs elicited a prominent MMN followed by a small but significant P3a deflection (F4 electrode: *t*(11) = 2.50, P<0.03; Cz electrode: t(11) = 2.50, P<0.03). In the Hard condition, no P3a was observed.

These results suggest that the complexity of auditory stimulation affects preattentive detection of changes in abstract auditory regularities in children. The frontal MMN component has been suggested to be associated with initiation of involuntary attention to auditory changes (Giard et al., 1990; Näätänen, 1992) and the P3a with the resulting attention switching (Escera et al., 2000). Therefore, these results also suggest that children's attention was automatically captured more easily by stimulus changes in the Easy than Hard condition.

Study II

Children's attention is easily diverted from current activity to a new event in the environment. This was indexed in school-age children by diminished performance speed and accuracy in a visual discrimination task caused by task-irrelevant novel sounds.

Involuntary attention to novel sounds resulted in significantly longer RTs (F(1,18) = 9.99, P < 0.006), lower number of correct responses (F(1,18) = 14.94, P < 0.001), and higher number of wrong responses (F(1,18) = 16.50, P < 0.0007) to visual stimuli

preceded by a novel sound (mean \pm SD for RT was 605 \pm 89 ms; for hits 90 \pm 9%, for wrong responses 6 \pm 7%) than to those preceded by a tone (mean \pm SD was for RT 589 \pm 96 ms, hits 92 \pm 8%, wrong responses 8 \pm 7%). There were no significant differences between the younger and older children. However, the younger children showed a non-significant tendency for longer RTs to the visual stimuli preceded by a novel sound than those in the older group (younger group: 617 \pm 103 ms; older group: 593 \pm 76 ms, respectively).

The ERPs elicited by these distracting sounds showed a prominent P3a deflection that consisted of early and late phases, and a subsequent LN component (Figure 5). In both groups, the early phase of the P3a (mean amplitude measured over 150–250 ms) was largest over the central scalp with positive amplitudes over the frontal scalp and inverted, negative amplitudes over the inferior temporal and posterior scalp, whereas the later phase of the P3a (250-350 ms) showed a significantly different distribution (Phase × Frontality interaction, F(2,36) = 25.49, P < 0.001). As seen in Figure 5, in the 11–13-year-olds, the late phase of the P3a was distributed anteriorly to that in the 7– 10-year-olds (Age × Phase × Frontality F(2,36) = 6.24, P < 0.005). Moreover, the younger group showed a significant positive correlation (Spearman r = 0.75, P < 0.01) between the prolonging effect of a preceding novel sound on the visual RT and the amplitude of the eP3a over Cz. This positive correlation supports the involvement of the eP3a generator processes in the orienting of attention away from the visual task to the distracting novel sound. Finally, the LN (measured as a mean voltage over 450-550 and 600–700 ms) was larger (more negative) in the younger children than in the older ones (F(1,18) = 6.28, P < 0.02).

Differences in the P3a and LN amplitudes and in the correlation of P3a amplitude with RTs between the younger (7-10 years) and older (11-13 years) children indicated developmental changes in brain function associated with attention. The ability of the older children to control their attention with prefrontal executive control processes (Näätänen, 1992) might be indicated by shorter RTs after a novel sound and by the more frontally distributed late P3a in this age group than in the younger children.



Grand-average ERP difference waves to novel sounds

Figure 5. Grand-average ERP difference waves in 7-10-year-olds and 11-13-year-olds (10 children in each age group) obtained by subtracting ERPs to repetitive tones from those to novel sounds at frontal (Fz), central, Cz, parietal (Pz) and left and right temporal (T5 and T6 respectively) electrode sites. The P3a response followed by the late negativity (LN) is composed of two phases: early (eP3a) and late (IP3a). The circles on the schematic scalp show the electrode locations.

Study III

Although Study II showed a tendency to decreasing amount of distraction of visual task performance caused by novel sounds with increasing age, the between-group differences did not reach statistical significance. However, the observed tendency might be associated with maturational changes in attentional abilities in the age range of 8-13 years. Therefore, a more detailed investigation of distraction effect caused by novel sounds and ERPs to these sounds was conducted in children from three more homogeneous age groups (8–9, 10–11, and 12–13 years; Young, Middle, and Old group, respectively). The distractibility in these age groups was assessed with the same ERP and performance measures as in Study II.

Comparison of the hit rate between the age groups yielded significant group differences (F(2,21)=6.49, P<.006). Subsequent Newman–Keuls tests revealed that while Middle and Old groups did not differ significantly from each other, the Young group showed fewer correct responses (P<.006) to visual stimuli following novel sounds than the two older groups.

In the Young group, comparisons of the novel-minus-tone RT and hit-rate differences with zero revealed significant (F(1,7)=5.52, P<.05) prolongations of RT and a significant decrease in performance accuracy in the visual task (F(1,7)=34.36, P<.006) following novel sounds (see Table 1). In Middle and Old groups, such comparisons showed only significant decreases in the hit rate (F(1,7)=7.00, P<.03; F(1,7)=13.88, P<.007, respectively). The percentages of wrong responses and omissions were low and no significant within-group or between-group differences were found.

Table 1. Mean RTs and mean rates of hits, wrong responses, and missed responses in Young, Middle, and Old groups of children in the visual discrimination task after an occurrence of a task-irrelevant tone *vs.* novel sound.

Visual-task Performance	Preceding sound	Young	Middle	Old
Measure		Mean (SD)	Mean (SD)	Mean (SD)
RT (ms)	Novel	530 (162)	546 (150)	515 (114)
	Tone	497 (134)	493 (96)	458 (110)
Hit rate (%)	Novel	77 (11)	88 (9)	89 (7)
	Tone	81 (9)	91 (8)	92 (6)
Wrong-response rate (%)	Novel	9 (5)	5 (3)	4 (2)
	Tone	7 (9)	4 (4)	3 (1)
Miss rate (%)	Novel	14 (11)	7 (14)	7 (8)
	Tone	12 (10)	5 (13)	5 (6)

As seen in Figures 6 and 7, the IP3a amplitude for novel sounds was largest for the youngest group and showed a centrally dominant scalp distribution and smallest for the middle and oldest groups with a frontally dominant scalp distribution (at Cz electrode: 9.4 μ V vs. 8.7 μ V vs. 5.4 μ V, respectively; *F*(2,21)=3.59, *P*< .04) and

subsequent Newman-Keuls tests revealed that the IP3a amplitude was significantly smaller (P< .05) in Old than Young or Middle groups, whereas there was no significant difference in the IP3a amplitude between Young and Middle groups (see Figure 7).

A frontally dominant Late Negativity (LN) was larger in the Young group than in the Middle and Old groups (mean amplitude measured over the F3, Fz, and F4 electrodes at 450–650 ms: -6.6μ V, -3.6μ V, -2.7μ V, respectively; *F*(2,21)=6.26, *P*< .007). Subsequent Newman-Keuls tests revealed significantly larger LN amplitude over the frontal scalp (electrodes F3, Fz, and F4) in the Young group than in Middle and Old groups (*P*< .01), whereas there was no significant difference between Middle and Old groups.

ERPs to novel sounds and tones in three age groups of normaldevelopment children



Figure 6. Grand-average ERPs in Young (8-9 yrs.), Middle (10-11 yrs.), and Old (12-13 yrs.) groups of children (8 children is each group) elicited at frontal (Fz), central (Cz), and parietal (Pz) midline scalp sites by the auditory-visual stimulus pairs starting with a tone (thin lines) or with a novel sound (thick line). The auditory stimulus was always task-irrelevant, and the visual stimulus was always a target stimulus to be

discriminated with a button press as an animal or non-animal image. In the Middle and Old groups, both tones and novel sounds elicited an auditory N1 component peaking around 100 ms from sound onset. The Young group showed a very small auditory N1, presumably due to immaturity of the auditory cortex (Courchesne, 1990; Ponton et al., 2002). However, the N1 response to visual stimuli was quite prominent in all age groups. The P3a and LN responses to the novel sounds explain the differences between ERPs to pairs starting with a tone and those starting with a novel sound (see Figure 7).

These ERP results suggest age-related differences in orienting and reorienting processes caused by novel sounds: the late P3a and LN component was largest in Young group and smallest in Old one suggesting more efficient orienting/reorienting brain mechanism in oldest children compared with the youngest



The P3a and LN difference waveforms in children

Figure 7. Grand-average novel-minus-tone ERP difference waves in Young (solid line), Middle (dashed line) and Old (heavy line) groups of children at the frontal (Fz) and central (Cz) midline electrodes. The P3a elicited by novel sounds consists of two

phases: the early P3a (eP3a) and the late P3a (IP3a) that was followed by the Late Negativity (LN).

Moreover, our data suggest that activity of orienting system caused by environmental novel sounds develops at least until 13 years of age in children with normal developmental course of attentional functions.

Study IV

This study compared distractibility in children with ADHD with that in control children, as indicated by the same performance and those ERP measures as in Studies II and III. The children participating in Study IV apparently were at the same developmental stages suggested by similar obligatory P1 and N1 responses to auditory stimuli (Figure 8).



Figure 8. Grand-average ERPs to tones and novel sounds elicited in ADHD and control groups of 8-10-year-olds (10 children in each group) at the frontal (Fz), central (Cz), and parietal (Pz) midline electrode sites. Auditory P1 and N1 components suggest similar developmental stage in both groups. Vertical dashed bar indicates

visual-stimulus onset. N1 to the visual stimuli marked as N1vis. For the novel-minustone ERP difference waves, see Figure 9.

Because children were instructed to perform the visual discrimination task with an "accuracy instruction" (stress on performance accuracy, not on speed; cf. Pfefferbaum et al., 1983), changes in the rates of correct responses ("hits") and incorrect responses (wrong button presses and response omissions) caused by the task-irrelevant novel sounds were used as major behavioral indices distractibility.

The distraction effect in the visual task caused by novel sounds was significant for the hit rate in the ADHD and control groups (t(9) = 2.54, P < 0.03; t(9) = 2.96, P < 0.01, respectively) the hit rates in ach group being lower after an occurrence of a novel sound than after a tone (Table 2). Both groups showed longer RTs after novel sounds than after tones, but this effect reached significance only in the controls (t(9) = -3.79, P < 0.004).

A Mann-Whitney U test for the hit rates yielded significant between-group differences in the visual-task accuracy both for the visual stimuli preceded by a tone (U(11) = -2.9, P < 0.002) and for those preceded by a novel sound (U(14) = -2.7, P < 0.005), the children with ADHD making a smaller percentage of correct responses than the controls. Moreover, a Mann-Whitney U test for the rate of missed responses indicated that an occurrence of a novel sound (in comparison with the occurrence of a tone) significantly increased the number of response omissions in children with ADHD than those in controls (U(17) = 2.49, P < 0.01), this effect of the preceding sound on the number of omissions being 4% in the ADHD group but only 1% in the control group. No significant group difference or effect of preceding stimulus was found for the number of the wrong responses.

In both groups, these sounds elicited a biphasic P3a response and a frontally maximal LN (Figure 9). However, the early phase of the P3a had a significantly smaller amplitude over the left hemisphere in the children with ADHD than in the control children (Group × Frontality × Laterality interaction Group × Frontality × Laterality interaction: F(4,72)=4.64, P < 0.01). As seen in Figure 10 (e.g., at the F3 electrode), this effect might be caused by an overlapping negative component peaking around 240 ms in children with ADHD, which possibly reduced their eP3a amplitudes over the

left frontal scalp. The left-frontal scalp distribution of this possible negative component is seen in Figure 10 showing a distribution map for the amplitude difference between the grand- average novel-minus-tone ERP difference waves of the ADHD and control groups at 200-250 ms from sound onset. Moreover, as seen in Figures 9 and 10, the children with ADHD had significantly larger IP3a amplitudes at the left and midline parietal scalp sites than control children (Group × Frontality × Laterality interaction: F(4,72)=2.56, P< 0.04; mean amplitudes 4.8 vs. 3 µV at P3, Newman-Keuls test: P< 0.03; 6.7 vs. 4.6 µV at Pz, P< 0.01).

Table 2. Mean (standard deviations in parentheses) RTs and mean rates of hits, wrong responses, and missed responses in children with ADHD and in control children in the visual discrimination task after an occurrence of a task-irrelevant tone vs. novel sound.

Visual-task Performance Preceding Measure sound	Preceding	ADHD	Controls
	sound	Mean (SD)	Mean (SD)
RT (ms)	Tone	476 (78)	498 (122)
	Novel	488 (86)	553 (142)
Hit rate (%)	Tone	65 (13)	81 (8)
	Novel	62 (12)	78 (10)
Wrong-response rate (%)	Tone	13 (5)	6 (3)
	Novel	12 (6)	9 (3)
Miss rate (%)	Tone	22 (9)	12 (10)
	Novel	26 (9)	13 (10)

The LN appeared to be smaller in amplitude and to peak earlier in the ADHD group than that in the controls. An ANOVA for the frontal LN amplitudes including factors Group, Laterality (F8 vs. F4 vs. Fz vs. F3 vs. F7), and Time Window (420-490 ms vs. 490-560 ms) revealed a significant Group × Laterality × Time Window interaction (*F*(4,72)=6.18, *P* < 0.002) caused by the fact that over the frontal midline, the LN was larger in amplitude in the ADHD group than in the controls during the earlier time window (mean amplitudes -2.8 μ V vs. -1.2 μ V, respectively; Newman-Keuls test: *P*<0.001), but smaller in the ADHD group than in the controls during the later time window (mean amplitude 0.01 μ V vs. -1.7 μ V, respectively; *P*<0.001).



Novel – Tone ERP difference waves for children with ADHD and Controls

Figure 9. Novel-minus-tone grand-average ERP difference waves in the ADHD (thick line) and control groups (thin line) at frontal (F3, Fz, F4), central (C3, Cz, C4), and parietal (P3, Pz, P4) electrode sites. The P3a elicited by novel sounds consists of two phases: the early P3a (eP3a) and the late P3a (IP3a), which are followed by the Late Negativity (LN).



The P3a and LN difference-wave scalp distributions

а

-3.0 0 +3.0 μV

Figure 10. (a) P3a and LN scalp-distribution maps for each group of children. The maps show average voltages of novel-minus-tone ERP difference waves (see Figure 9) at the latency ranges of the eP3a, IP3a, and the earlier and later phases of LN.

(b) Topographic maps of the amplitude differences between the novel-minus-tone difference waves of the ADHD group and those of the control group (these maps suggest abnormal brain activity in the left hemisphere of the children with ADHD peaking around 240 ms. In Figure 9, this group difference is seen especially at the left frontal (F3) and central (C3) electrode sites.

In conclusion, the present performance data are in accordance with previous adult studies (Escera et al., 1998, 2000) by showing that novel sounds distract children's performance in a visual discrimination task as indicated by decreased hit rates and increased RTs after an occurrence of a novel sound in comparison with occurrence of a repeating tone. Moreover, larger number of response omissions after a novel sound in the ADHD group than in the control group revealed higher distractibility in the ADHD group. The shorter RTs of the ADHD group compared with controls might be related with abnormal (more sensitive) reaction to the novel sounds, which could be explained by behavior impulsivity of children with ADHD. Abnormal involuntary attention in the children with ADHD was also supported by the ERPs to the distracting novel sounds.

GENERAL DISCUSSION

Developmental changes in preattentive processing of auditory abstract regularities in school-age children

Findings from the developmental auditory ERP literature suggest that differences in ERP component morphology, amplitude and latency are found with age (Friedman et al., 1984, 1985; Martin et al., 1988; Courchesne, 1990; Polich et al., 1990; Ponton et al., 2000). Moreover, several auditory perceptual skills, such as the ability to recognize degraded speech (Palva & Jokinen, 1975) or to accurately understand speech presented in background noise (Elliott, 1979), do not become adult-like until adolescence. Maturational changes in other basic auditory processing skills including gap detection (Trehub et al., 1995), masked thresholds (Schneider & Trehub, 1995), and minimum audible angle (Litovsky, 1977) also have extended maturational time courses. The prolonged maturational time course of these perceptual skills cannot be attributed to immaturity in either cochlear functions, which are essentially adult-like already at the term birth (Eggermont et al., 1996), or in the auditory brainstem pathway generating adult-like ERP responses by the age of 2 years (Eggermont et al., 1988).

However, developmental changes range from physical differences, e.g., in the size of the ear canal and immature sensory processing, to differences in cognitive processes such as memory, and in executive functions such as attention and task strategies (Elfenbein et al., 1993) might contribute to delayed development of cognitive and behavioral auditory skills. Yet, it seems that prolonged development of at least some auditory perceptual skills is related to ongoing maturational changes in the central auditory system (Ponton et al., 2000). The maturation of the central auditory stimulation.

The MMN is thought to reflect an *automatic* (preattentive) processing of auditory stimulus changes even when the listener's attention is directed elsewhere. Due to the automatic nature of the MMN, there has been a great deal of interest in determining whether it can be used as an objective and accurate index of maturation of auditory processing and cortical auditory functions and dysfunctions in children (e.g., Kurtzberg et al., 1995; Kraus et al., 1999; Shafer et al., 2000; Morr et al., 2002). However, inconsistent results have been reported in the literature concerning the maturational time course of the MMN. A possible factor contributing to these inconsistencies is that different ISIs were used in different studies as the rate of stimulus presentation strongly affects the children's ERPs (Gomes et al., 1999; Morr et al., submitted).

The results of the Easy condition of the present Study I showing an MMN to descending deviant tone pairs occurring among ascending standard tone pairs are accord with previous findings in adults (Saarinen et al., 1992; Paavilainen et al., 1999) by showing that changes in abstract auditory features may elicit an MMN. Moreover, these results demonstrate that school-age children are able to preattentively extract abstract auditory features: the MMN elicited in children in the Easy condition was morphologically similar to that elicited by deviations in simple acoustic features in children (e..g., Oades et al., 1997) and in adults (e.g., Giard et al., 1995; Alain et al., 1998). The comparisons of the MMNs elicited in the Easy and Hard conditions in children indicated an effect of the complexity of the abstract regularity only on the frontally recorded MMN response, whereas the amplitudes of the polarity-inverted MMNs measured at the mastoid leads showed no condition effect. Assuming that the polarity-inverted MMN at the mastoids reflects specifically MMN component generating by neurons of temporal cortex, but the MMN recorder over frontal scalp

41

sites is a composition of responses generating frontal and temporal cortices (Giard et al., 1990; Rinne et al., 2000) these results may be explained by later maturation of the prefrontal than temporal cortex in childhood (Bunge et al., 2002).

The prefrontal MMN generator has also been proposed to be associated with triggering the involuntary switching of attention to stimulus deviance (Giard et al., 1990; Escera et al., 2000). Our results are compatible with this suggestion. Thus, in the Easy condition, MMN was followed by a P3a-like wave, which is regarded as the ERP correlate of the actual involuntary attention switching (Escera et al., 2000; Friedman et al., 2001; see also Studies II-IV), whereas in the Hard condition, where no frontal MMN could be observed, no P3a –like was elicited by deviant pairs. Thus, as in adults, the frontal MMN and the P3a responses in children might index the chain of cerebral events leading to orienting of attention towards changes detected in a regular sound sequence.

However, it should be noted that further ERP recordings with an electrode array covering the whole scalp and subsequent source modelling would be needed to ascertain the contributions of prefrontal and temporal MMN components to the children's ERPs to deviant tone pairs in the Easy and Hard conditions suggested above.

Developmental changes in brain indices of distractibility in school-age children

Studies II and III in normally developing 7–13-year-olds showed a P3a response to the novel sounds (e.g. telephone ringing), which might be associated with Pavlov's "what – is-it" orienting response (Pavlov, 1927; Ruff & Rothbart, 1996; Sokolov et al., 2002).

The orienting response that underlies distraction is a reflexive shift of attention thought to involve prefrontal brain functions (Luria, 1973) and to facilitate information processing by enhancing perceptual sensitivity to environmental stimuli (Sokolov, 1963). It is manifested as a complex pattern of physiological and behavioral changes that are elicited by a variety of different factors such as intensity, stimulus modality, novelty, a priori and sequential probability and significance of the eliciting stimuli

42

(Graham, 1979). This involuntary attention switching mechanism is also manifested in various ERP components, each of which probably represents a different aspect of orienting (for a review, see Rohrbaugh, 1984). In adults, ERP manifestations of orienting to the "deviant" stimuli that are embedded in train of frequently presented stimuli are the N1, MMN, N2b, P3a, and P3b (Näätänen, 1992). While the early components are assumed to primarily reflect *exogenous* or sensory aspect of "distractor", the P3 deflection is assumed to index the *endogenous* or cognitive aspects of distracting stimulus (Donchin et al., 1991).

Orienting has been described as including a passive shift of attention away from the current task (Öhman, 1979). As in adults, the children's shift of attention was caused by novel sounds, as indicated by the prolongation of RT and decrease in the performance accuracy in the visual task following novel sounds that corroborates the recent studies in adults (Alho et al., 1998; Escera et al., 1998; Yago et al., 2003). ERPs obtained from adults in these studies demonstrated a train of components such as an enhanced N1 and the MMN and P3a responses elicited by novel sounds relative to ERPs elicited by a repeating simple tone. According to this line of thought, although the brain processes generating the N1 and MMN preattentive, they may trigger the involuntary attention switching reflected by the P3a to distracting sounds extraneous to the current task (see also Näätänen, 1992; Lyytinen et al., 1992).

In contrast to the previous studies in adults (e.g., Escera et al., 1998; Yago et al., 2003), the children in our studies showed no MMN to novel sounds, suggesting a different, probably related with development, path of processing the novel sounds. This developmental-related aspect of the "absence" of MMN to novel sounds in children of school-age could be explained by a number of factors based on MMN developmental research. The MMN in children seems to be less stable and reliable than in adults (Unwer & Suchodolets von, 2000). Moreover, there is increasing evidence that in infants (Leppänen et al., 1997, 2004; Winkler et al., 2003) and in at least some children of 6-7 years (Maurer et al., 2003), deviant sounds may elicit a genuine mismatch "positivity" reflecting the processing of auditory stimulus changes instead of a mismatch negativity. Instability of MMN in children caused by different factors (e.g. ISI, maturation effect) could be one possible explanation for the lacking MMN in all our studies using auditory-visual distraction task.

Moreover, the lack of MMN but biphasic P3a response to randomly present novel sounds was observed in children of 9-13 years when speech sounds (/ka/ as a standard and /ta/ as a deviant) were applied by Čeponienė et al. (2004). The ISI in their study was 1.7 s which is similar to that used in the present Studies II-IV, suggesting that the relatively long ISI in these studies are close to the temporal limits of children's auditory sensory memory as reflected by the MMN. Consistent with this, Gomes et al. (1999) reported an absence of MMN in 6-12-year-olds when the sounds were separated by an intertrain interval of 8 s, whereas an interval of 1 s did not abolish MMN response. The absence of children's MMN at relatively slow stimulation rates is consistent with the findings that also in adults MMNs are smaller at very long ISIs (Cowan, Winkler, Teder, & Näätänen, 1993; Mäntysalo & Näätänen, 1987; Näätänen, Paavilainen, Alho, Reinikainen, & Sams, 1987; Schröger, 1996; Schröger & Winkler, 1995), but this pattern of results suggests that children's sensory memory decays than that of adults.

According to several authors (e.g., Squires et al., 1975; Snyder & Hillyard, 1976; Näätänen, 1990), the P3a is a sign of the activation of an attention-switching mechanism. In some studies (Alho et al., 1990; Knight et al., 1989), the P3a response was suggested as providing an index of distraction caused by irrelevant novel sounds and sound changes. In children, P3a to novel and deviant sounds has been reported several studies (Shestakova et al., 2003; Čeponienė et al., 2004; Morr et al., submitted) even in children with major depression (Lepistö et al., 2004). As in adults (cf. Escera et al., 1998; Yago et al., 2003), the P3a in children is, according to the present Studies II-IV, a composite response with two different phases: eP3a with a fronto-central scalp maximum and inverted polarity over posterior and inferior temporal scalp sites, and IP3a that decreases in amplitude and becomes more frontally distributed over the scalp with increasing age. The eP3a is elicited at the same latencies as the P2. In adults, the auditory-cortex generator sources of the temporally overlapping P2 and eP3a components have been separated spatially with MEG (Alho et al., 1998). However, further studies are needed to determine whether an enhanced P2 component to widely deviant novel sounds contributes to the eP3a in children.

The frontally distributed LN (latency approx. 400–700 ms from sound onset; see also Shestakova et al., 2003) observed in Studies II-IV, could be an index of reorienting the

44

diverted attention back to the task-relevant stimuli after a temporary distraction and therefore an analogue of the RON observed in adults (Schröger & Wolff, 1998; Berti & Schröger, 2001; Escera et al., 2001). According to Wetzel et al.'s (2004) study, the RON can be observed as early as in kindergarten children of 5-6 years, and as in adults, it is largest in amplitude in children over fronto-central scalp sites. However, the LN or RON elicited in the present Studies II and III in the youngest children who were only slightly older than Wetzel et al.'s subject, was spread over central and parietal areas, suggesting developmental changes in the scalp distribution of this response.

In conclusion, studies on normally developing children suggest that the brain responses related to the processing of distracting novel information might reflect an age-related ability to resist switching of attention to distracting events and to keep attention focused on the main task in a distracting environment. In the present studies, ERP components associated with orienting and reorienting responses showed age-related amplitude and topography changes. By the age of 13 years they appeared to become similar to the adults' corresponding responses, but possibly continue to mature even further.

Effect of ADHD on brain index of distractibility in school-age children

The children with ADHD who participated in Study IV performed less accurately in the visual discrimination task than did the control children, as indicated by the larger number of missed responses and smaller number of hit responses in the ADHD group than in the control group. Also theERPs indicated aberrant covert processing of the distracting novel sounds in the children with ADHD. These sounds elicited a biphasic P3a response with an early phase (eP3a) that had significantly smaller amplitudes over the left hemisphere in the children with ADHD than in the control group. The reduced eP3a amplitudes in the ADHD group appeared to be caused by a left-hemisphere dominant negative ERP component evoked by novel sounds in the ADHD group but not or evoked with much smaller amplitudes in the children with ADHD around 240 ms from novel-sound onset might be caused by a genuine reduction in the activity of one of the left-hemisphere generator sources contributing to the P3a response at the latencies between the eP3a and IP3a peaks (cf. Yago et al., 2003). For example,

45

this reduction might be associated with an aberrant processing of these distracting environmental sounds on early stages of encoding that may be based on automatic stimulus identification and classification (Escera et al., 2003). Moreover, the IP3a showed enhanced amplitude in the ADHD group in comparison with the controls in parietal electrode sites especially over the left hemisphere. These findings are in agreement with previous ones showing differences in the left-hemisphere sensitivity to auditory stimulus changes in ADHD patients compared with control subjects (Oades, 1998).

Finally, the smaller LN amplitudes in the children with ADHD than in the controls might be associated with a prefrontal cortical dysfunction in ADHD (Bush et al., 1999). This dysfunction might emerge as a deficit in the control of attention or as improper inhibition of irrelevant sensory inputs in children with ADHD (Plizka et al., 2000).

Conclusions

Taken together, the present studies on children's ERPs (Studies I-IV) and performance (Studies II-IV) suggest that as early as the age of 7 years, children do have an ability to resist distraction caused by unexpected auditory events, but this process requires more effort and concentration in young children than in the older ones or adults. Moreover, the present studies indicate that school-age children between 7-13 years are undergoing maturational changes in different perceptual and attentional functions.

The present studies also show that ERPs can provide information on development of the brain, e.g., on development of the prefrontal cortex. First, in Study I, the frontal MMN was larger for the smaller degree of complexity than for the higher degree of complexity in the regularity that had to be extracted from the standard tone pairs in order to discriminate the deviant pairs, whereas an adult study (Paavilainen et al., 1998) found no difference in MMNs between conditions. In Studies II and III, the P3a was more frontally dominant in the older children than in the younger ones and the LN amplitude was significantly larger for the younger children suggesting developmental changes in the orienting/reorienting processes.

Finally, in Study IV, ERPs recorded to task-irrelevant novel stimuli distracting the children's performance provided us with evidence supporting the observations of attentional and behavioral deficits in ADHD.

In conclusion, the present results indicate that the ERPs to to-be-ignored deviant and novel sounds may be powerful tools in evaluating development of attentional processes, as well as in assessing attentional deficits, in childhood. However, it should be noted that the present results were obtained at a group level and that the ERP methods used in the present studies need to be developed further if we want to use them to assess normal and deficient development in individual children.

REFERENCES:

Alho, K. (1995). "Cerebral generators of mismatch negativity (MMN) and its magnetic counterpart (MMNm) elicited by sound changes." *Ear Hear*, 16, 38-51.

Alho, K., Sainio, K., Sajaniemi, N., Reinikainen, K., Näätänen, R. (1990a). "Event-related brain potential of human newborns to pitch change of an acoustic stimulus." *Electroencephalogr Clin Neurophysiol*, 77, 151-155.

Alho, K., Sajaniemi, N., Niittyvuopio, T., Sainio, K., Näätänen, R. (1990b). "ERPs to an auditory stimulus change in pre-term and full-term infants." In: C.H.M. Brunia, A.W.K. Gaillard & A. Kok (Eds.), *Psychophysiological Brain Research,* vol 2. (p. 139-142).Tilburg University Press, Tilburg, The Netherlands.

Alho, K., Winkler, I., Escera, C., Huotilainen, M., Virtanen, J., Jääskeläinen, I., Pekkonen, E., Ilmoniemi, R.J. (1998). "Processing of novel sounds and frequency changes in the human auditory cortex: magnetoencephalographic recordings." *Psychophysiology*, 35, 211–224.

Alho, K., Woods, D.L., Algazi, A., Näätänen, R. (1992). "Intermodal selective attention. II. Effects of attentional load on processing of auditory and visual stimuli in central space." *Electroencephalogr Clin Neurophysiol*, 82, 356-368.

American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders, 4th ed. (DSM-IV). Washington, DC: American Psychiatric Association.

Baudena, P., Halgren, E., Heit, G., Clarke, J.M. (1995). "Intracerebral potentials to rare target and distractor auditory and visual stimuli. III Frontal cortex." *Electroencephalogr Clin Neurophysiol*, 94, 251–264.

Berti, S., Schröger, E. (2001). "A comparison of auditory and visual distraction effects of behavioral and event-related indices." *Cogn Brain Res, 10*, 265–273.

Bunge, S.A., Dudukovic, N.M., Thomason, M.E., Vaidya, C.J., Gabrieli, J.D.E. (2002). "Immature frontal lobe contributions to cognitive control in children evidence from fMRI." *Neuron*, 33, 301–311.

Broadbent, D.E. (1952)."Listening to one of two synchronous messages." *J Exp Psychol*, 44, 51-55.

Broadbent, D.E., (1958). Perception and Communication. London: Pergamon.

Bruneau, N., Gomot, M. (1998). "Auditory evoked potentials (N1 wave) as indices of cortical development throughout childhood." In: B. Garreau (Ed.) *Neuroimaging Child Neuropsychiatric Disorderds* (pp. 113-124). Springer Verlag. Buchsbaum, M. (1976). "Self-regulation of stimulus intensity, Augmenting/ reducing and the average evoked response." In: G.E. Schwartz & D. Shapiro (Eds.) *Consciousness and Self -regulation* (pp.101-135). New York: Plenum.

Casey, B.J., Giedd, J.N., Thomas, K.M. (2000). "Structural and functional brain development and its relation to cognitive development." *Biol Psychol, 54,* 241–257.

Cowan, N., Kail, R. (1996). "Covert processes and their development in short-term memory." In: S. Gathercole (Ed.), *Models of short –term memory* (pp.29-50). Hove, England: Erlbaum.

Cheour, M., Alho, K., Čeponienė, R., Reinikainen, K., Sainio, K., Pohjavuori, M., Aaltonen, O., Näätänen, R. (1998). "Maturation of mismatch negativity in infants." *Int J Psychophysiol*, 29, 217-226.

Cheour, M., Korpilahti, P., Martynova, O., Lang, A.H. (2001)." Mismatch negativity and late discriminative negativity in investigating speech perception and learning in children and infants." *Audiol Neurootol*, 6, 2-11.

Cowan, N., Winkler, I., Teder, W., Näätänen R. (1993). "Memory prerequisites of mismatch negativity in the auditory event-related potential (ERP)." *J Exp Psychol: Learn Mem Cogn*, 19, 909-921.

Čeponienė, R., Cheour, M., Näätänen, R. (1998). "Interstimulus interval and auditory event-related potentials in children: evidence for multiple generators." *Electroencephalogr Clin Neurophysiol*, 108, 345-354.

Čeponienė, R., Lepistö, T., Soininen, M., Aronen, E., Alku, P., Näätänen, R. (2004)." Event-related potentials associated with sound discrimination versus novelty detection in children." *Psychophysiology*, 41, 130-141.

Čeponienė, R., Rinne, T., Näätänen, R. (2002). "Maturation of cortical sound processing as indexed by event-related potentials." *Electroencephalogr Clin Neurophysiol*, 113, 870-882.

Courchesne, E. (1990). "Chronology of postnatal human brain development: event–related potential, positron emission tomography, myelinogenesis, and synaptogenesis studies." In: J.W. Rohrbaugh, R. Parasuraman, & R. Johnson, Jr. (Eds.), *Event–Related Brain Potentials. Basic Issue and Applications* (pp. 210–241). New York: Oxford University Press.

Courchesne, E., Courchesne, R.Y., Hillyard, S.A. (1978). "The effect of stimulus deviation on P3 waves to easily recognized stimuli." *Neuropsychologia*, 16, 189-199.

Courchesne, E., Hillyard, S.A., Courchesne, R.Y. (1977). "P3 waves to the discrimination of targets in homogeneous and heterogeneous stimulus sequences." *Psychophysiology*, 14, 590-597.

Galambos, R. (1982). "Maturation of auditory evoked potentials." In: G. A. Chiarenza & D. Papakostopoulos (Eds.), *Clinical Application of Cerebral Evoked Potentials in Pediatric Medicine* (pp. 323-343). Amsterdam: Excerpta Medica.

Giard, M.H., Perrin, F., Pernier, J., Bouchet, P. (1990). "Brain generators implicated in the processing of auditory stimulus deviance: a topographic event-related potential study." *Psychophysiology*, 27, 627-640.

Csépe, V. (1995). "On the origin and development of the mismatch negativity." *Ear Hear*, 16, 91-104.

Cycowicz, Y.M., Friedman, D., Rothstein, M. (1996). "An ERP developmental study of repetition priming by auditory novel stimuli." *Psychophysiology*, 33, 680–690.

Cycowicz, Y.M., Friedman, D. (1997). "A developmental study of the effect of temporal order on the ERPs elicited by novel environmental sounds." *Electroencephalogr Clin Neurophysiol*, 103, 304–318.

Daffner, K.R., Mesulam, M.M., Scinto, L.F., Calvo, V., Faust, R., Holcomb, P.J. (2000). "An electrophysiological index of stimulus unfamiliarity." *Psychophysiology*, 7, 737-747.

Donchin, E., McCarthy, G., Kutas, M., Ritter, W. (1983). "Event -related brain potentials in the study of consciousness." In: R.J. Davidson, G.E. Schwarts, & D. Shapiro (Eds.) *Consciousness and self-regulation*, Vol.3 (pp.81-121). New York: Plenum.

Donchin, E., Spencer, K.M., Wijesinghe, R. (2000). "The mental prosthesis: assessing the speed of a P300-based brain-computer interface." *IEEE Trans Neural Syst Rehabil Eng*, 8, 174-179.

Eggermont, J.J. (1995). "Evoked potentials as indicators of auditory development." *Int J Pediatr Otorhinolaryngol*, Suppl: 183-186.

Escera, C., Alho, K., Schröger, E., Winkler, I. (2000). "Involuntary attention and distractibility as evaluated with Event-related brain potentials." *Audiol Neurootol*, 5, 151–166.

Escera, C., Alho, K., Winkler, I., Näätänen, R. (1998). "Neural mechanisms of involuntary attention to acoustic novelty and change." *J Cogn Neurosci*, 10, 590-604.

Escera, C., Corral, M.J., Yago, E. (2002). "An electrophysiological and behavioral investigation of involuntary attention towards auditory frequency, duration and intensity changes." *Cogn Brain Res*, 14, 325-332.

Escera, C., Yago, E., Alho, K. (2001). "Electrical responses reveal the temporal dynamics of brain events during involuntary attention switching." *Eur J Neurosci*, 14, 877-883.

Escera, C., Yago, E., Corral, M.J., Corbera, S., Nunez, M.I. (2003). "Attention capture by auditory significant stimuli: semantic analysis follows attention switching." *Eur J Neurosci*, 18, 2408-2012.

Ford, J.M., Mathalon, D.H., White, P.M., Pfefferbaum, A. (2000). "Left temporal deficit of P300 in patients with schizophrenia: effects of task." *Int J Psychophysiol*, 38, 71-79.

Ford, J.M., Roth, W.T., Kopell, B.S. (1976a). "Auditory evoked potentials to unpredictable shifts in pitch." *Psychophysiology*, *13*, 32–39.

Ford, J.M., Roth, W.T., Kopell, B.S. (1976b). "Attention effects on auditory evoked potentials to infrequent events." *Biol Psychol*, 4, 65-77.

Freeseman, L.J., Colombo, J., Coldren, J.T. (1993). "Individual differences in infant visual attention: four-month-olds' discrimination and generalization of global and local stimulus properties." *Child Dev*, 64, 1191-1203.

Friedman, D., Cycowicz, Y.M., Gaeta, H. (2001). "The novelty P3:an event-related potential (ERP) sign of the brain's evaluation of novelty." *Neurosci Biobehav Rev, 25,* 355–373.

Friedman, D., Simpson, G.V. (1994)." ERP Amplitude and scalp distribution to target and novel events: Effect of temporal order in young, middle-aged and older adults." *Cogn Brain Res, 2,* 49–63.

Fuchigami, T., Okubo, O., Ejiri, K., Fujita, Y., Kohira, R., Noguchi, Y., Fuchigami, S., Hiyoshi, K., Nishimura, A., Harada, K. (1995). "Developmental changes in P300 wave elicited during two different experimental conditions." *Pediatr Neurol*, 13, 25-28.

Giard, M.H., Perrin, F., Pernier, J., Bouchet, P. (1990). "Brain generators implicated in the processing of auditory stimulus deviance: a topographic event-related potential study." *Psychophysiology*, 27, 627-640.

Gille, H.G., Böttcher, C., Ullsperger, P. (1986). "[.Influence of the intensity of disturbing auditory events during mental tasks on the P300 wave of the auditory event-related brain potential.]" Zeitschrift Gesamte Hygienie, 32, 566-568.

Gomes, H., Molholm, S., Ritter, W., Kurtzberg, D., Cowan, N., Vaughan, H.G. Jr. (2000). "Mismatch negativity in children and adults, and effects of an attended task." *Psychophysiology*, 37, 807-816.

Gomes, H., Sussman, E., Ritter, W., Kurtzberg, D., Cowan, N., Vaughan, H.G.Jr. (1999). "Electrophysiological evidence of developmental changes in the duration of auditory sensory memory." *Dev Psychol*, 35, 294-302.

Grillon, C., Courchesne, E., Ameli, R., Geyer, M., Braff, D.L. (1990). "Increased distractibility in schizophrenic patients." *Arch Gen Psychiatry, 4,* 171–179.

Hagen, J.W., Hale, G.H. (1973). "The development of attention in children." In: Pick, AD (Ed.), *Minnesota Symposia on Child Psychology*, vol. 7 (pp.117-141). Minneapolis: University of Minnesota Press.

Hari, R., Hämäläinen, M., Ilmoniemi, R., Kaukoranta, E., Reinikainen, K., Salminen, J., Alho, K., Näätänen, R. Sams, M. (1984). "Responses of the primary auditory cortex to pitch changes in a sequence of tone pips: Neuromagnetic recordings in man." *Neurosci Lett*, 50, 127-132.

Hari, R., Kaila, K., Katila, T., Tuomisto, T., Varpula, T. (1982). "Interstimulus interval dependence of the auditory vertex response and its magnetic counterpart: implications for their neural generation." *Electroencephalogr Clin Neurophysiol*, 54, 561-569.

Holcomb, P.J, Ackerman, P.T., Dykman, R.A. (1986). "Auditory event-related potentials in attention and reading disabled boys." *Int J Psychophysiol*, 3, 263-273.

Huotilainen, M., Kujala, A., Hotakainen, M., Parkkonen, L., Taulu, S., Simola, J., Nenonen, J., Karjalainen, M., Näätänen, R. (2005). "Short-term memory functions of the human fetus recorded with magnetoencephalography." *Neuroreport,* 16, 81-84.

Huttenlocher, P.R. (1979). "Synaptic density in human frontal cortex -

developmental changes and effects of aging." Brain Research, 163, 195-205.

Huttenlocher, P.R., Dabholkar, A.S. (1997). "Regional differences in

synaptogenesis in human cerebral cortex." *J Comp Neurol*, 387, 167-178.

Huttenlocher, P.R., De Courten, C., Garey, L.J., van der Loos, H. (1982-1983).

"Synaptic development in human cerebral cortex." Int J Neurol, 16-17, 144-154.

James, W. (1890). Principles of Psychology. New York: Holt.

Jonkman, L.M., Kemner, C., Verbaten, M.N., Van Engeland, H., Camfferman, G., Buitelaar, J.K., Koelega, H.S. (2000). "Attentional capacity, a probe ERP study: differences between children with attention-deficit hyperactivity disorder and normal control children and effects of methylphenidate." *Psychophysiology*, 37, 334-346.

Karhu, J., Herrgard, E., Pääkkönen, A., Luoma, L., Airaksinen, E., Partanen, J. (1997). "Dual cerebral processing of elementary auditory input in children." *Neurorepot*, 14, 1327-1330.

Keller, T.A., Cowan, N. (1994). "Developmental increase in the duration of memory for tone pitch." *Dev Psychol,* 30, 855–863.

Kemner, C., Verbaten, M.N., Koelega, H.S., Buitelaar, J.K., van der Gaag, R.J., Camfferman, G., van Engeland, H. (1996). "Event-related brain potentials in children with attention-deficit and hyperactivity disorder: effects of stimulus deviancy and task relevance in the visual and auditory modality." *Biol Psychiatry*, 40, 522-534.

Kilpeläinen, R., Luoma, L., Herrgard, E., Yppärila, H., Partanen, J., Karhu, J. (1999). "Persistent frontal P300 brain potential suggests abnormal processing of auditory information in distractible children." *Neuroreport*, 10, 3405-3410.

Knight, R.T. (1990). "Neuronal mechanisms of event-related potentials: Evidence from human lesion studies." In: J.W. Rohrbaugh, R. Parasuraman, R. Johnson, Jr. (Eds.), *Event-Related Brain Potentials: Basic Issues and Applications* (pp.3–18). New York: Oxford University Press.

Knight, R.T. (1984). "Decreased response to novel stimuli after prefrontal lesions in man." *Clin. Neurophysiol*, 59, 9–20.

Knight, R.T. (1996). "Contribution of human hippocampal region to novelty detection." *Nature*, 383, 256-259.

Knight, R.T., Scabini, D. (1998). "Anatomical bases of event-related potentials and their relationship to novelty detection in humans." *Clin Neurophysiol, 15*, 3–13.

Knight, R.T., Scabini, D., Woods, D.L., Clayworth, C. (1988). "The effects of lesions of superior temporal gyrus and inferior parietal lobe on temporal and vertex components of the human AEP." *Electroencephalogr Clin Neurophysiol*, 70, 499-509.

Knight, R.T., Scabini, D., Woods, D.L., Clayworth, C. (1989). "Contributions of temporal-parietal junction to the human auditory P3." *Brain Res*, *502*,109–116.

Korpilahti, P., Krause, C.M., Holopainen, I., Lang, A.H. (2001). "Early and late mismatch negativity elicited by words and speech-like stimuli in children." *Brain Lang*, 76, 332-339.

Korzyukov, O.A., Winkler, I., Gumenyuk, V.I., Alho, K. (2003) "Processing abstract auditory features in the human auditory cortex." *Neuroimage*, 20, 2245-2258.

Kraus, N., Smith, D.I., Reed, N.L., Stein, L.K., Cartee, C. (1985). "Auditory middle latency responses in children: effects of age and diagnostic category." *Electroencephalogr Clin Neurophysiol*, 62, 343-351.

Kraus, N., McGee, T., Micco, A., Sharma, A., Carrell, T., Nicol, T. (1993). "Mismatch negativity in school-age children to speech stimuli that are just perceptibly different." *Electroencephalogr Clin Neurophysiol*, 88, 123-130.

Kujala, T., Kallio, J., Tervaniemi, M., Näätänen, R. (2001). "The mismatch negativity as an index of temporal processing in audition." *Clin Neurophysiol*, 112, 1712-1719.

Kuperman, S., Johnson, B., Arndt, S., Lindgren, S., Wolraich, M. (1996). "Quantitative EEG differences in a nonclinical sample of children with ADHD and undifferentiated ADD." *J Am Acad Child Adolesc Psychiatry*, 35, 1009-1017.

Kurtzberg, D., Vaughan, H.G. Jr. (1985). "Electrophysiologic assessment of auditory and visual function in the newborn." *Clin Perinatol*, 12, 277-299.

Kurtzberg, D., Vaughan, H.G. Jr, Courchesne, E., Friedman, D., Harter, M.R., Putnam, L.E. (1984). "Developmental aspects of event-related potentials." *Ann N Y Acad Sci.*, 425, 300-318.

Kurtzberg, D., Vaughan, H.G. Jr., Kreuzer, J.A., Fliegler, K.Z. (1995). "Developmental studies and clinical application of mismatch negativity: problems and prospects." *Ear Hear*, 16, 105-117.

Kushnerenko, E., Čeponienė, R., Balan, P., Fellman, V., Huotilainen, M., Näätänen, R. (2002). "Maturation of the auditory event-related potentials during the first year of life." *Neuroreport*, 13, 47-51.

Lepistö, T., Soininen, M., Čeponienė, R., Almqvist, F., Näätänen, R., Aronen, E.T. (2004). "Auditory event-related potential indices of increased distractibility in children with major depression." *Clin Neurophysiol*, 115, 620-627.

Leppänen, P.H-T., Eklund, K.M-, Lyytinen, H. (1997). "Event-related brain potentials to change in rapidly presented acoustic stimuli in newborns." *Dev Neuropsychology*, 13, 175-204.

Leppänen, P.H-T., Guttorm, T.K., Pihko, E., Takkinen, S., Eklund, K.M., Lyytinen, H. (2004). "Maturational effects on newborn ERPs measured in the mismatch negativity paradigm." *Clin Exp Neurol*, 190, 91-101.

Liotti, M., Pliszka, S.R., Perez, R., Kothmann, D., Woldorff, M.G. (in press) Abnormal brain activity to perfromance monitoring and error detection in children with ADHD. *Cortex.*

Loiselle, D.L., Stamm, J.S., Maitinsky, S., Whipple, S.C. (1980). "Evoked potential and behavioral signs of attentive dysfunctions in hyperactive boys." *Psychophysiology*, 17,193-201.

Lou, H.C., Henriksen, L., Bruhn, P. (1990). "Focal cerebral dysfunction in developmental learning disabilities." *Lancet,* 335, 8-11.

Luria, A.R. (1973). "The Working Brain." *An Introduction to Neuropsychology*. New York: Basic Books.

Lyytinen, H., Blomberg, A.P., Näätänen, R. (1992). "Event-related potentials and autonomic responses to a change in unattended auditory stimuli." *Psychophysiology,* 29, 523-534.

Martin, B.A., Shafer, V.L., Morr, M.L., Kreuzer, J.A., Kurtzberg, D. (2003). "Maturation of Mismatch Negativity: A scalp current density analysis." *Ear Hear*, 24, 463-471.

Mäntysalo, S., Näätänen, R. (1987). "The duration of a neuronal trace of an auditory stimulus as indicated by event-related potentials." *Biol Psychol*, 24, 183-195.

McCarthy, G., Wood, C.C. (1985). "Scalp distributions of event-related potentials: An ambiguity associated with analysis of variance models." *Electroencephalogr Clin Neurophysiol, 62,* 203–208.

McIsaac, H., Polich, J. (1992). "Comparison of infant and adult P300 from auditory stimuli." *J Exp Child Psychol*, 53, 115-128.

Morgan, A.E., Hynd, G.W., Riccio, C.A., Hall, J. (1996). "Validity of DSM-IV ADHD predominantly inattentive and combined types: relationship to previous DSM diagnoses/subtype differences." *J. Am. Acad. Child Adolesc. Psychiatry*, 35, 325-333.

Morr, M.L., Shafer, V.L., Davidson, C., Kreuzer, J.A., Kurtzberg, D. "The effects of short ISIs on Mismatch Negativity in children and adults." (submitted).

Morr, M.L., Shafer, V.L., Kreuzer, J.A., Kurtzberg, D. (2002). "Maturation of mismatch negativity in typically developing infants and preschool children." *Ear Hear*, 23, 118-136.

Näätänen, R. (1990). "The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function." *Behav Brain Sci*, 13, 201-288.

Näätänen, R. (1992). Attention and Brain Function. Hillsdale, N.J.: Erlbaum.

Näätänen, R., Gaillard, A.W., Varey, C.A. (1981). "Attention effects on auditory EPs as a function of inter-stimulus interval." *Biol Psychol*, 13, 173-187.

Näätänen, R., Paavilainen ,P., Alho, K., Reinikainen, K., Sams, M. (1987a). "The mismatch negativity to intensity changes in an auditory stimulus sequence." *Electroencephalogr Clin Neurophysiol Suppl*, 40, 125-131.

Näätänen, R., Paavilainen, P., Tiitinen ,H., Jiang, D., Alho, K. (1993). "Attention and mismatch negativity." *Psychophysiology*, 30, 436-450.

Näätänen, R., Picton, T. (1987b). "The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure." *Psychophysiology*, 24, 375-425.

Näätänen, R., Simpson, M., Loveless, N.E. (1982). "Stimulus deviance and evoked potentials." *Biol Psychol, 14,* 53–98.

Oades, R.D., Dittmann-Balcar, A., Zerbin, D. (1997). "Development and topography of auditory event-related potentials (ERPs): Mismatch and processing negativity in individuals 8–22 years of age." *Psychophysiology, 34,* 677–693.

Öhman, A. (1979). "The orienting response, attention and learning: An information-processing perspective." In: H.D. Kimmel, E.H. van Olst, & J.F. Orlebeke (Eds.), *The Orienting Reflex in Humans* (pp. 443–471). Hillsdale, NJ: Erlbaum.

Paavilainen, P., Degerman, A., Takegata ,R., Winkler, I. (2003). "Spectral and temporal stimulus characteristics in the processing of abstract auditory features." *Neuroreport*, 15, 715-718.

Paavilainen, P., Jaramillo, M., Näätänen, R., Winkler, I. (1999). "Neuronal populations in the human brain extracting invariant relationships from acoustic variance." *Neurosci Lett*, 265, 179-182.

Pang, E.W., Taylor, M.J. (2000). "Tracking the development of the N1 from age 3 to adulthood: an examination of speech and non-speech stimuli." *Clin Neurophysiol*, 111, 388-397.

Pavlov, I.P. (1927). Condition reflexes, 121 pp. Oxford, New York.

Pearson, D.A., Lane, D.M. (1990). "Reorientation in Hyperactive and Non-Hyperactive children: Evidence for Developmentally Immature Attention." In: J. T. Enns (Ed.), *The Development of Attention: Research and Theory,* (pp. 347–350). Elsevier Science Publishers B.V. North-Holland. Amsterdam. Pfefferbaum, A., Ford, J.M., Johnson, R.Jr., Wenegrat, B., Kopell, B.S. (1983). "Manipulation of P3 latency: speed vs. accuracy instructions." *Clin. Neurophysiol*, 55, 188-197.

Picton, T.W. (1995). "The neurophysiological evaluation of auditory discrimination." *Ear Hear*, 16, 1-5.

Picton, T.W., Alain, C., Otten, L., Ritter, W., Achim, A. (2000). "Mismatch negativity: different water in the same river." *Audiol Neurootol.*, *5*, 111-139.

Picton, T.W., Hillyard, S.A. (1974b). "Human auditory evoked potentials. II. Effects of attention." *Electroencephalogr Clin Neurophysiol*, 36, 191-199.

Picton, T.W., Hillyard, S.A., Krausz, H.I., Galambos, R. (1974a). "Human auditory evoked potentials. I. Evaluation of components." *Electroencephalogr Clin Neurophysiol*, 36, 179-190.

Picton, T.W., Woods, D.L., Baribeau-Braun, J., Healey, T.M. (1976). "Evoked potential audiometry." *J Otolaryngol*, 6, 90-119.

Plude, D., Enns, J.T., Brodeur, D. (1994). "The development of selective attention: A life-span overview." *Acta Psychol*, 86, 227-272.

Polich, J. (2002). "Neuropsychology of P3a and P3b: A theoretical overview."

In :K. Arikan and N. Moore (Eds.), *Advances in Electrophysiology in clinical practice and research*. : Wheaton, IL: Kjellberg.

Ponton, C.W., Eggermont, J.J., Don, M., Waring, M.D., Kwong, B., Cunningham, J., Trautwein, P. (2000a). "Maturation of the Mismatch Negativity: Effects of profound deafness and cochlear implant use." *Audiol Neurootol*, 5, 167-185.

Ponton, C.W., Eggermont, J.J., Khosla, D., Kwong, B., Don, M. (2002). "Maturation of human central auditory system activity: separating auditory evoked potentials by dipole source modeling." *Clin Neurophysiol, 113,* 407–420.

Ponton, C.W., Eggermont, J.J., Kwong, B., Don, M. (2000b). "Maturation of human central auditory system activity: evidence from multi-channel evoked potentials." *Clin Neurophysiol*, 111, 220-236.

Rakic, P., Bourgeois, J.P., Eckenhoff, M.F., Zecevic, N., Goldman-Rakic, P.S. (1986). "Concurrent overproduction of synapses in diverse regions of the primate cerebral cortex." *Science*, 232, 232-235.

Richards, J.E. (1988). "Heart rate responses and heart rate rhythms, and infant visual sustained attention." *Adv Psychobiol, 3,* 189–221.

Rinne, T., Alho, K., Ilmoniemi, R.J., Virtanen, J., Näätänen, R. (2000). "Separate time behaviors of the temporal and frontal mismatch negativity sources." *NeuroImage*, 12, 14-19.

Ruff, H.A., Rothbart, M.K. (1996). "*Attention in Early Development*." Oxford, Oxford University Press.

Sams, M., Paavilainen, P., Alho, K., Näätänen, R. (1985). "Auditory frequency discrimination and event-related potentials." *Electroencephalogr Clin Neurophysiol*, 62, 437-448.

Satterfield, J.H., Schell, A.M., Nicholas, T., Backs, R.W. (1988). "Topographic study of auditory event-related potentials in normal boys and boys with attention deficit disorder with hyperactivity." *Psychophysiology*, 25, 591-606.

Satterfield, J.H., Schell, A.M., Nicholas, T.W., Satterfield, B.T., Freese, T.E. (1990). "Ontogeny of selective attention effects on event-related potentials in attentiondeficit hyperactivity disorder and normal boys." *Biol Psychiatry*, 28, 879-903.

Satterfield, J.H., Schell, A.M., Nicholas, T. (1994). "Preferential neural processing of attended stimuli in attention-deficit hyperactivity disorder and normal boys." *Psychophysiology*, 31, 1-10.

Scherg, M., von Cramon, D. (1985). "A new interpretation of the generators of BAEP waves I-V: results of a spatio-temporal dipole model." *Electroencephalogr Clin Neurophysiol*, 62, 290-299.

Schröger, E. (1996). "The influence of stimulus intensity and inter-stimulus interval on the detection of pitch and loudness changes." *Electroencephalogr Clin Neurophysiol,* 100, 517-526.

Schröger, E., Giard, M.H., Wolff, C. (2000). "Auditory distraction: event-related potential and behavioral indices." *Clin Neurophysiol, 111,* 1450–1460.

Schröger, E., Winkler, I. (1995). "Presentation rate and magnitude of stimulus deviance effects on human pre-attentive change detection." *Neurosci Lett*, 193, 185-188.

Schröger, E., Wolff, C. (1998). "Attentional orienting and reorienting is indicated by human event–related brain potentials." *NeuroReport, 9,* 3355–3358.

Shestakova, A., Huotilainen, M., Ceponiene, R., Cheour, M. (2003). "Event-related potentials associated with second language learning in children." *Clin Neurophysiol*, 114, 1507-1512.

Sokolov, E.N., Sprinks, J.A., Näätänen, R., Lyytinen, H. (2002). "*The Orienting Response in Information Processing*. "London, NJ: Lawrence Erlbaum Associates.

Squires, N.K., Squires, K.C., Hillyard, S.A. (1975). "Two varieties of long–latency positive waves evoked by unpredictable auditory stimuli." *Electroencephalogr Clin Neurophysiol, 38,* 387–401.

Starr, A., Sohmer, H., Celesia, G.G. (1978). "Some applications of evoked potentials to patients with neurological and sensory impairment." In: E. Callaway, P.Tueting, S.H. Koslow (Eds.) *Event-related potentials in man.* (pp. 345-407) New York: Academic Press.

Stuss, D.T. (1992). "Biological and psychological development of executive functions." *Brain Cogn, 20,* 8–23.

Sutton, S., Ruchkin, D.S. (1984). "The late positive complex. Advances and new problems." *Ann N Y Acad Sci*, 425, 1-23.

Sussman, E., Winkler, I., Schröger, E. (2003). "Top-down control over involuntary attention switching in the auditory modality." *Psychon Bull Rev*, 10, 630-637.

Tecce, J.J., Savignano-Bowman, J., Meinbresse, D. (1976). "Contingent negative variation and the distraction-arousal hypothesis." *Electroencephalogr Clin Neurophysiol*, *41*, 227–286.

Tiitinen, H., May, P., Reinikainen, K., Näätänen, R. (1994). "Attentive novelty detection in humans is governed by pre-attentive sensory memory." *Nature*, 372, 90-92.

Tonquist-Uhlen, I. (1995). "Topography of auditory evoked long-latency potentials in normal children, with particular reference to the N1 component." *Electroencephalogr Clin Neurophysiol*, 95, 34-41.

Trainor, L.J., Samuel, S.S., Desjardins, R.N., Sonnadara, R.R. (2001). "Measuring temporal resolution in infants using mismatch negativity." *Neuroreport*, 12, 2443-2448.

Vaughan, J.H.G., Kurtzberg, D. (1991). "Electrophysiologic indices of human brain maturation and cognitive development." In M.R. Guunar, C.A.Nelson (Eds.), *Minnesota Symposia on Child Psychology* (Vol.24, pp.1-36). Hillsdale, NJ: Erlbaum.

Vaughan, H.G. Jr., Ritter, W. (1970). "The sources of auditory evoked responses recorded from the human scalp." *Electroencephalogr Clin Neurophysiol*, 28, 360-367.

Wechsler, D. (1984). "Wechsler Intelligence Scale for Children" - Revised. In Finnish. Helsinki: Psykologien kustannus.

Wechsler, D. (1999). "Wechsler Intelligence Scale for Children "– Third Edition. In Finnish. Helsinki: Psykologien kustannus.

Wetzel, N., Berti, S., Widmann, A., Schröger, E. (2004). "Distraction and reorientation in children: a behavioral and ERP study." *Neuroreport,* 15, 1355-1358.

Winkler, I., Kushnerenko, E., Horvath, J., Čeponienė, R., Fellman, V., Huotilainen, M., Näätänen, R., Sussman, E. (2003). "Newborn infants can organize the auditory world." *Proc Natl Acad Sci U S A*, 100, 11812-11815.

Winkler, I., Schröger, E. (1995). "Neural representation for the temporal structure of sound patterns." *Neuroreport*, 6, 690-694.

Wolpaw, J.R., Penry, J.K. (1975). "A temporal component of the auditory evoked response." *Electroencephalogr Clin Neurophysiol*, 39, 609-620.

Woods, D.L. (1992). "Auditory selective attention in middle-age and elderly subjects: An event-related brain potential study." *Electroencephalogr Clin Neurophysiol, 84*, 456–458.

Yabe, H., Tervaniemi, M., Reinikainen, K., Naatanen, R. (1997). "Temporal window of integration revealed by MMN to sound omission." *Neuroreport*, 8, 1971-1974.

Yago, E., Escera, C., Alho, K., Giard, M.-H., Serra-Grabulosa, J.M. (2003). "Spatiotemporal dynamics of the auditory novelty-P3 event-related brain potential." *Cogn Brain Res*, 16, 383-390.

Yakovlev, P., Lecours, A. (1967). "The myelinogenetic cycles of regional maturation of the brain." In: A. Minkowski (Ed.), *Regional Development of the Brain Early in Life* (pp. 3–70). Oxford, England: Blackwell.

Yamaguchi, S., Knight, R.T. (1991). "Anterior and posterior association cortex contributions to the somatosensory P300." *J Neurosci*, 11, 2039-2054.