

Time processing in children and adults with ADHD

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Abstract A time-processing deficit has been proposed as a neuropsychological candidate endophenotype for Attention Deficit Hyperactivity Disorder (ADHD), but its developmental trajectory still needs to be explored. In the present study, children ($N = 33$) and adults ($N = 22$) with ADHD were compared to normal controls on two time-processing tasks. For time reproduction, ADHD-related impairment was found in the full group, but not when adults were analyzed separately. For the discrimination of brief intervals, children and adults with ADHD showed different patterns of deficit. We conclude that in ADHD

some time-processing deficits are still present in adults, but may take on age-related different forms.

Keywords ADHD · Time processing · Neuropsychological endophenotype · Time reproduction · Time discrimination · Development

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common mental disorders of children and adolescents. A sizable number of ADHD patients continue to be affected with impaired psychosocial behavior in later life. The strong familial and genetic component of ADHD (Rhee et al. 1999; Sherman et al. 1997), its links to an imbalance of specific neurotransmitter systems such as dopamine (Faraone et al. 2001; Lowe et al. 2004) and noradrenaline (Biederman and Spencer 1999; Gainetdinov et al. 1999) and the presence of neuropsychological (Barkley 1997; Klimkeit et al. 2005) as well as neurophysiological (Brandeis et al. 2002; van Leeuwen et al. 1998) markers of ADHD is well established.

Numerous studies have investigated aspects of time processing in ADHD such as time estimation, duration discrimination, temporal (re-)production and motor timing (Barkley et al. 1997; McInerney and Kerns 2003; Smith et al. 2002, 2008). They provide overwhelming evidence that individuals with ADHD have problems with temporal processing, though results are inconsistent for some specific aspects like verbal estimation or anticipation (Barkley et al. 2001a, b; Meaux and Chelonis 2003; Radonovich and Mostofsky 2004; Rubia et al. 2003).

Different theoretical approaches have provided explanations for time-processing deficits in ADHD. According

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to Barkley et al. (1997), impaired time processing in ADHD subjects is a consequence of impaired response inhibition and executive function deficits. The reproduction of time intervals with durations greater than a few seconds requires higher level cognitive processes such as working memory (Barkley et al. 2001b; Ivry 1996) which is often impaired in ADHD. The characteristic under-production of intervals observed in ADHD with increasing interval length has been linked to inhibitory control deficits. In his dual pathway model, Sonuga-Barke proposed motivational impairment due to delay aversion as an additional explanatory hypothesis. This model accounts for the heterogeneity of neuropsychological impairment associated with ADHD, as only a subgroup of children present clinically relevant problems in the executive function domain (Sonuga-Barke 2002). In an interval estimation study, Sonuga-Barke et al. (1998) found ADHD children to significantly underestimate these time intervals. They propose that children with ADHD have an internal clock running too fast during waiting periods, leading to an aversion to delay. Recently, Sonuga-Barke et al. (2010) have reported new results supporting a triple pathway model in which temporal processing constitutes an independent third dissociable neuropsychological component of ADHD.

A third theory, the cognitive energetic approach (see Sergeant 2000; van der Meere 2005), holds that deficient time processing is a consequence of impaired state regulation. This deficit can be conceptualized as a mismatch between the individuals' arousal and the stimulation provided by the task (van der Meere et al. 2009). Timing-related aspects such as the rate of stimulus presentation and the length of interstimulus intervals may thus be crucial for performance in ADHD. Also, the speed of internal pacemakers is influenced by the level of arousal (Mangels and Ivry 2001). Finally, increased response time variability—which can be interpreted as an irregularity of timing—has been found to be the most robust neuropsychological marker of ADHD (Castellanos et al. 2005, but for limitations, see Geurts et al. 2008). Lapses of attention as well as impaired response preparation seem both to contribute to this phenomenon (Vaurio et al. 2009), which has been linked to spontaneous fluctuations in brain activity (see Di Martino et al. 2008; Rothenberger 2009) or to dysfunctional premotor circuits (Suskauer et al. 2008a, b).

Impaired temporal processing has also been proposed as a distinct neuropsychological candidate endophenotype for ADHD (Castellanos et al. 2002). Rommelse et al. (2007) report that children with ADHD as well as their non-affected siblings are impaired on a time reproduction task. They conclude that time reproduction should be considered a candidate endophenotype. In a recent study contrasting duration discrimination in the milliseconds and seconds range, children with ADHD proved impaired in discriminating both brief and longer intervals, but non-affected

siblings only in discriminating brief intervals. Accordingly, the authors propose impaired discrimination of brief intervals as a marker of vulnerability or endophenotype for ADHD (Himpel et al. 2009).

There is agreement on the existence of two distinct systems of temporal processing. The more “automatic” system for timing in the milliseconds range computed by the cerebellum and basal ganglia is also considered important for motor coordination (Harrington et al. 1998). The more “cognitive” system for timing in the seconds to minutes range computed by frontal-striatal circuits (which also support working memory functions) is supposed to be important for temporal estimation and reproduction (Karmarkar and Buonomano 2007; Lewis and Miall 2003a, b, 2006; Madison 2001). Thus, temporal processing in the range of milliseconds should not primarily depend on working memory and attentional allocation abilities nor on motivational aspects, in contrast to temporal processing of time intervals longer than 1 s (Mangels et al. 1998). So far, impairments of either system in ADHD are compatible with experimental findings, neurobiological models and imaging studies (see Valera et al. 2010; Vloet et al. 2010, for recent imaging studies on timing in ADHD; for reviews, see Durston et al. 2009; Giedd et al. 2001; Kelly et al. 2007; Kieling et al. 2008; Willis and Weiler 2005).

Only few studies have investigated temporal processing in young adults with ADHD. These studies largely replicated findings from childhood samples for time reproduction (Barkley et al. 2001b; Seri et al. 2002). A recent investigation of rhythmic performance in young adults with ADHD revealed difficulties only at a medium speed (Gilden and Marusich 2009), suggesting that internal clock mechanism continues to be partly compromised in adulthood. Marx et al. (2010) compared time processing in children, adolescents and young adults with ADHD and controls. They found a general impairment in time discrimination and time reproduction in all three ADHD age groups, along with significant developmental effects. While reproduction errors generally decreased with maturation, only adolescents and adults with ADHD significantly under-reproduced the longest intervals of 36 and 48 s compared to controls. In a time production task, ADHD subjects under-produced time intervals although the absolute error did not differ between diagnostic and age groups.

To our knowledge, no study so far included ADHD groups with a mean age above 30 years. Therefore, the developmental course of temporal processing deficits in ADHD in later adulthood still needs to be explored. In addition, neuropsychological studies on adult ADHD usually include clinically referred adults who may not be representative of the typical course of childhood ADHD into adulthood in the general population. While a majority of these studies report heterogeneous neuropsychological impairment similar to that of childhood ADHD (Balint

et al. 2009; Boonstra et al. 2005; Hervey et al. 2004; Schoechlin and Engel 2005; Seidman 2006), some studies find age-related changes (Tucha et al. 2008). According to follow-up studies, executive function deficits seem to persist into adulthood, but only in those with full ADHD status and under the premise that EF deficits were already present in childhood (Biederman et al. 2007; Halperin et al. 2008). Halperin and Schulz (2006) claim that with maturation, frontally mediated executive functions increasingly compensate for primary and enduring subcortical deficits in many individuals with ADHD. This should lead to a reduction of ADHD symptoms in adulthood. Thus, one might expect differential developmental trajectories for tasks such as time reproduction taxing more executive aspects of time processing, and tasks tapping more basal internal clock mechanisms. Similarly, developmental studies of time processing in children have shown that the internal clock system seems to be functional at a relatively early age, whereas time encoding ability and associated attentional processes develop and improve with maturation (Droit-Volet et al. 2006).

The purpose of the current study was to examine the performance of both children and adults with ADHD in a time reproduction and a time discrimination task in order to investigate the stability of the deficits across different age groups. We hypothesized that children as well as adults with ADHD would show deficits in temporal processing compared to matched controls. However, we expected different patterns of impairment for the two employed task paradigms. Both children and adults should show significant impairment in a time discrimination task where target intervals are in the range of milliseconds. Here, the performance is supposed to be largely independent of inhibitory control and motor components and representative of basal timing mechanisms. On the time reproduction task, with durations up to several seconds, one would expect adults with ADHD to show minor deficits if at all when compared to matched controls. Children with ADHD, in contrast, should show a clear under-production of durations, especially with longer intervals. In line with this argument, we expect time reproduction performance to be correlated with inhibitory control measures and time discrimination performance with neuropsychological measures of arousal or sustained attention.

Methods

Subjects/participants

Children and adults with ADHD

Children and adults with ADHD were participants of the Zurich Multimodal Family Assessment Study on ADHD

(MFAA). For this study, families with at least one child suffering from ADHD (DSM-IV combined type) were recruited in the Department of Child and Adolescent Psychiatry in Zurich or via a Swiss organization for parents of children with ADHD. The study also had some benefits from interactions with the International Multi-centre ADHD Gene (IMAGE) project (see Brookes et al. 2006), which aims at investigating the genetic transmission of ADHD.

Children with ADHD

33 children with ADHD (20 boys, 13 girls, age range 8–15 years) were included in the study. Inclusion criteria were the diagnosis of ADHD combined subtype (DSM-IV), IQ of at least 80, and the absence of known neurological or other psychiatric diseases. The German versions of the Conners' Parent Rating Scale (CPRS-R:L; Conners et al. 1998a) and the Conners' Teacher Rating Scale (CTRS-R:L; Conners et al. 1998b) were used as screening instruments at the first stage. For children scoring above the clinical threshold for ADHD of the combined subtype on one of these questionnaires, the Parental Account of Children's Symptoms (PACS) interview (Taylor et al. 1986) was administered by a trained interviewer. PACS is a semi-structured, standardized, investigator-based clinical interview. DSM-IV diagnosis was derived by an algorithm combining PACS interview and CTRS-R:L data, adopted from the HYPEScheme procedure of the IMAGE study (Brookes et al. 2006). Twenty-three percent of the initially screened ADHD children did not meet the criteria of ADHD combined type according to HYPEScheme and had to be excluded. For a description of the study sample, see Table 1. According to PACS interview, 11 children with ADHD fulfilled research criteria for probable comorbid oppositional defiant disorder, 3 for comorbid depression and 2 for anxiety disorder. Three of the children had previously received a diagnosis of dyslexia; eight children with ADHD presented reading difficulties without a formal diagnosis according to information by their parents.

Adults with ADHD

22 adults (11 male, 11 female, age range 32–52 years) with ADHD participating in this study were identified among the parents of children with ADHD. Inclusion criteria were scores within the clinical range on an ADHD self-rating questionnaire for adults on current ADHD symptoms (ADHS-SB, Roesler et al. 2004) as well as on a retrospective self-rating questionnaire on ADHD childhood symptoms (German short form of the Wender-Utah Rating Scale, WURS-k, Retz-Junginger et al. 2003). To check for additional clinical symptoms, adults completed the Symptom

Table 1 Sample characteristics

	ADHD [<i>N</i> = 33 (children); <i>N</i> = 22 (adults)]		Controls [<i>N</i> = 33 (children); <i>N</i> = 22 (adults)]		<i>p</i>
	Mean	SD	Mean	SD	
Children					
Age (years)	11.0	2.1	11.0	2.1	.992
Sex (male/female)	20/13		20/13		
Estimated IQ	119.6	15.4	120.7	16.3	.783
Conners Teacher (<i>T</i> scores)					
Attention (DSM-IV)	65.4	10.6	51.0	7.3	<.001
H/I (DSM-IV)	68.5	12.6	49.3	8.7	<.001
Total (DSM-IV)	68.9	11.0	50.1	6.7	<.001
Conners Parents (<i>T</i> scores)					
Attention (DSM-IV)	72.3	12.3	47.3	5	<.001
H/I (DSM-IV)	77.4	11.8	46.3	3.7	<.001
Total (DSM-IV)	76.4	10.4	46.7	4.2	<.001
SDQ teacher hyperactivity	6.6	2.5	2.2	1.8	<.001
SDQ parents hyperactivity	7.5	2.3	1.6	1.4	<.001
Adults					
Age (years)	42.2	4.4	43.5	4.5	.304
Sex (male/female)	11/11		11/11		
Estimated IQ	111.1	11.4	111.6	12.4	.880
ADHS-SB (sum score)	23.0	6.9	6.2	4.2	<.001
WURS-k (sum score)	35.7	7.4	7.2	5.9	<.001

Checklist-90-Revised (SCL-90-R; Derogatis 1994): Twelve adults with ADHD reported psychopathological symptoms above the clinical cut-off (>60). Ten adults from the ADHD group reported reading disabilities on a reading questionnaire for adults (Lefly and Pennington 2000).

All participants taking stimulants (15 children, 4 adults) had interrupted medication at least 48 h before testing. Participants were free from other psychotropic medication.

Control subjects

33 control children and 22 control adults volunteered for the study. They were recruited from various sources, including regional elementary school, and local sport clubs. Control subjects who scored above the (sub-)clinical cut-off on the questionnaires used for ADHD screening in children or adults (i.e. CPRS for children, ADHS-SB and WURS-k for adults, $T > 60$) were excluded (1 child, no adult). None of the control children was diagnosed with conduct problems according to research criteria [based on Strengths and Difficulties Questionnaire (SDQ) and CPRS, see Christiansen et al. 2008, for the procedure]. Among the adult control subjects, three reported reading disabilities on a reading questionnaire for adults (Lefly and Pennington 2000). No adult control participant scored above the clinical cut-off on the SCL-90-R (Derogatis 1994).

Controls and ADHD subjects were matched pairwise according to sex, age, and IQ (see Table 1). Before entering the study, all children and adults gave their informed consent. The study was approved by the local ethics committee.

Instruments

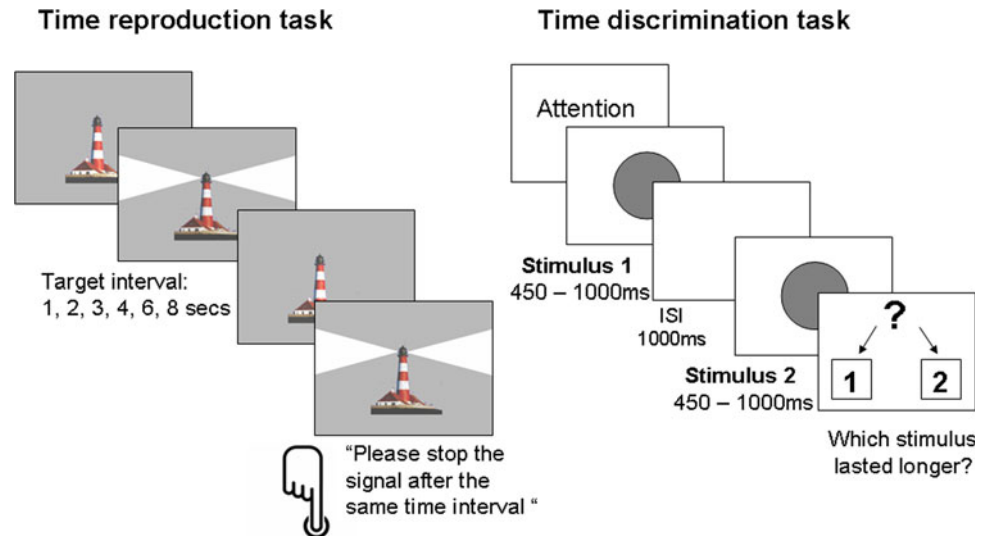
Time reproduction task

In the time reproduction task, participants were instructed to remember the duration of a visually presented beacon from a lighthouse and to stop an immediately following beacon after exactly the same time period by pressing the left mouse button. The presented beacons varied in their durations and lasted either 1, 2, 3, 4, 6, or 8 s (Fig. 1). Standardized verbal and visual instructions were used. Testing started following a practice block of five trials with feedback after each response. Thereafter, 60 experimental trials were administered. Each of the six interval lengths was randomly presented ten times. Participants did not receive feedback during the test block.

Time discrimination task

The performance on duration discrimination was assessed by presenting consecutively two visual stimuli which

Fig. 1 Time reproduction task: Presented beacons of the light house lasted 1, 2, 3, 4, 6 or 8 s. These intervals had to be reproduced by the participants by pressing the mouse button after the corresponding amount of time. Time discrimination task: Participants had to decide which one of two subsequently presented stimuli lasted longer. Stimulus 1 and stimulus 2 differed in their duration between 50 and 500 ms. Differences of duration were ≤ 100 ms in half of the trials, ≥ 200 ms in the other half



differed in their presentation time by 50–500 ms. Half of the total of 72 stimulus pairs differed by 100 ms or less (difficult condition), while the other half differed by 200 ms or more (easy condition). Presentation time of stimuli varied from 450 to 1,000 ms. Participants were asked to press the left mouse button if the first, and the right mouse button if the second stimulus had lasted longer. Standardized verbal and visual instructions were used. Testing started following a practice block where individuals received feedback whether their answers were right or wrong. During the test block, no feedback was given (Fig. 1).

Further neuropsychological tests

In addition, participants performed several classical neuropsychological tasks: a simple motor response task (Alertness), an inhibition task (Go/Nogo) and a cued continuous performance task (CPT O-X). The alertness and inhibition task were taken from the Test for Attentional Performance (TAP, Zimmermann and Fimm 2002), which is a standardized computerized instrument that has been evaluated for the assessment of children and adults with ADHD (Földenyi et al. 2000; Tucha et al. 2008).

In the Alertness task, participants responded as quickly as possible to a visually presented stimulus (presentation of a cross in the centre of a computer screen) that remained visible until the response was collected. Half of these trials also contained an acoustic warning signal preceding the target stimulus by 600–1,500 ms. The task was divided into four blocks of 20 stimuli: two blocks with and two blocks without acoustic warning signal.

In the Go/Nogo task, participants had to respond as quickly as possible to a Go-stimulus as represented by an “x”, and had to ignore the Nogo-stimulus as represented by

a “+”, both presented in the centre of the screen for 200 ms. From a total of 40 trials, 50% were Go and 50% Nogo trials. The cued CPT (Rosvold et al. 1956; Doehner et al. 2008; van Leeuwen et al. 1998) was part of the neurophysiological investigation which is described in detail in Valko et al. (2009). It consists of 400 black letters which are presented for 150 ms every 1,650 ms between two permanently visible vertical fixation bars. Participants had to press a button as quickly as possible whenever “O” (cue) was followed by “X” (target). This cue-target sequence or Go-condition occurred 40 times (10%). The other 40 cues initiated cue-nontarget sequences (“O” followed by a letter other than “X”: Nogo-condition).

Questionnaires and IQ

Assessment tools used to quantify ADHD symptoms in children included the German version of the CPRS-R:L (Conners et al. 1998a), the CTRS-R:L (Conners et al. 1998b), the SDQ, parent and teacher version (Goodman 1997), and the PACS Interview (PACS, Chen and Taylor 2006). Adults completed the ADHD Self-Report Scale (ADHS-SB, Roesler et al. 2004) and the German short form of the WURS-k (Retz-Junginger et al. 2003). In children, IQ was estimated by four subtests of the German version of the Wechsler Intelligence Scale for Children III: Vocabulary, Block design, Arithmetic, and Picture Arrangement (Schallberger 2005). In adults, IQ estimation was calculated by taking the arithmetic mean of the German WAIS subtests Vocabulary and Block design (Tewes 1991).

Procedure

The neuropsychological testing of the subjects with ADHD took place at the Department of Child and Adolescent

Psychiatry in Zurich. Neuropsychological testing of controls took place either at the department, at school, or at their home. Except for the CPT, all tests were administered on the same day.

Statistical analyses

The results were analyzed using SPSS version 14. For the time reproduction task, mean reproduction times (MRPTs) were converted into absolute discrepancy scores, which is the absolute value of the magnitude of discrepancy between target interval length and the participant's time reproduction. Discrepancy scores of MRPT and standard deviations of mean reproduction times (RPT-SDs) were log-transformed in order to meet distributional assumptions and z -transformed. Discrepancy scores of MRPT and RPT-SD were analyzed using a multivariate general linear model (MANOVA), with group (ADHD vs. controls) and age (children vs. adults) as between-subjects factors, and discrepancy of MRPT and RPT-SD as multivariate within-subjects measures. The interval lengths (six intervals: 1, 2, 3, 4, 6, 8 s) were treated as repeated measures. ANOVAs and post hoc t tests were calculated. Subsequently, separate MANOVAs for the children group and for the adults group were carried out with univariate tests and post hoc t tests. Additional ANOVAs were carried out with composite scores from the time reproduction task (total MRPT = sum of all MRPTs and the total RPT-SD = sum of all RPT-SDs) for the full group, and for children and adults separately.

For the time discrimination task, the same between-subjects factors were used, duration difference (DIFF = trials with a difference of less than 100 ms vs. trials with a difference of 200 ms or more) was used as repeated measure, and the mean reaction time (MRT), standard deviation of reaction time (RT-SD), and number of correct responses (hits) were entered as within-subjects measures. Data were first z -transformed. Post hoc t tests for group and age effects were calculated. Again, separate MANOVAs for the children and adults were carried out followed by univariate tests and post hoc t tests.

Neuropsychological tests were analyzed by MANOVA or ANOVA. Again, multiple models were run for the full group and for children and adults separately. For the Alertness task, group and age were entered as between-subjects factors, median reaction time (MD) and RT-SDs as within-subjects measures, and trials with or without warning tone (condition) as repeated measures. For the Go/Nogo task, MRT, RT-SD and errors were entered as dependent variables. For the CPT, an ANOVA was calculated with group (ADHD vs. controls) and age (children vs. adults) as between-subjects factor, and hits, commission errors, MRTs, and RT-SDs as dependent variables. A z -transformation was applied to all three tasks.

Scores from questionnaires were compared by t tests. In an exploratory analysis, composite scores from the time reproduction task (total MRPT = sum of all MRPTs, total RPT-SD = sum of RPT-SDs of 1, 2, 3, 4, 6, 8 s interval duration, z -transformed) and the time discrimination task (total hits, total MRT) were correlated separately for children and adults with parameters from Alertness, Go/Nogo and the CPT in partial correlations controlling for age.

Results

Time reproduction

Effects of ADHD across age groups

The MANOVA revealed a significant main effect of ADHD ($F_{(2,105)} = 5.844$, part. $\eta^2 = .100$, $p = .004$) for the full group, but no significant interaction of ADHD by age ($F_{(2,105)} = .284$, part. $\eta^2 = .005$, $p = .753$). There was no significant interaction between ADHD and interval length ($F_{(10,97)} = .317$, part. $\eta^2 = .032$, $p = .975$). A three-way interaction (ADHD by age, by interval length) was not significant ($F_{(10,97)} = .957$, $\eta^2 = .090$, $p = .485$). Univariate tests revealed that the main effect of ADHD was caused both by larger discrepancies between MRPT and target intervals ($F_{(1,106)} = 8.359$, part. $\eta^2 = .073$, $p = .005$) and by increased RPT-SD ($F_{(1,106)} = 7.842$, part. $\eta^2 = .069$, $p = .005$) in the ADHD group. Post hoc t tests showed that ADHD subjects differed significantly more from target intervals than control subjects by reproducing the time intervals of 2, 4 and 8 s (2 s: $t_{(108)} = 2.083$, $p = .040$; 4 s: $t_{(108)} = 2.686$, $p = .008$; 8 s: $t_{(108)} = 2.384$, $p = .024$) and by responding more variably when reproducing intervals of 2 s ($t_{(108)} = 2.261$, $p = .026$), 4 s ($t_{(108)} = 2.151$, $p = .034$) and 8 s ($t_{(108)} = 2.558$, $p = .012$) (Table 2). However, with Bonferroni–Holmes correction, only the 4-s discrepancy and 8-s RPT-SD remained significant.

Total MRPT was significantly smaller in the ADHD group compared to controls, total RPT-SD was significantly larger (ANOVA: $F = 6.958$, $p = .010$; total MRPT: ADHD 21,689 ms, controls 22,617 ms, $p = .006$; total RPT-SD: ADHD 6,083 ms, controls 5,397 ms, $p = .031$).

Age effects

The MANOVA of the full group revealed a significant main effect for age (children vs. adults: $F_{(2,105)} = 18.733$, part. $\eta^2 = .263$, $p < .001$), which was caused by both discrepancies of MRPT ($F_{(1,106)} = 4.861$, part. $\eta^2 = .044$, $p = .030$) and RPT-SD ($F_{(1,106)} = 37.840$, part. $\eta^2 = .263$, $p < .001$). Children, compared to adults, showed significantly larger RPT-SDs in the reproduction of all six time

Table 2 Time reproduction task

Target interval	Children (N = 33/33)				Adults (N = 22/22)				ANOVA	MANOVA
	M (SD)		p (t)		M (SD)		p (t)			
	ADHD	Controls	Children (33/33)	Controls	ADHD	Controls	Adults (22/22)	All (55/55)		
Absolute discrepancies between MRPT and target interval (ms)										
1 s	178 (104)	184 (130)	.401		177 (113)	165 (761)	.295		All: ADHD**, AGE*, ADHD × IN n.s., Children: ADHD**, ADHD × IN n.s., Adults: ADHD n.s., ADHD × IN n.s.	All: ADHD**, AGE**, IN n.s., ADHD × AGE n.s., ADHD × IN*, Children: ADHD**, IN n.s., ADHD × IN n.s., Adults: ADHD n.s., ADHD × IN n.s., ADHD × IN n.s.
2 s	253 (164)	196 (150)	.094		226 (16)	179 (154)	.179		.040	
3 s	379 (330)	288 (246)	.239		355 (28)	260 (218)	.322		.122	
4 s	506 (416)	270 (207)	.043		427 (365)	270 (202)	.097		.008	
6 s	713 (720)	412 (262)	.050		605 (606)	409 (273)	.833		.151	
8 s	968 (902)	502 (476)	.004		809 (786)	504 (430)	.837		.024	
RPT-SD (ms)										
1 s	488 (307)	391 (281)	.237		320 (305)	247 (242)	.172		.089	
2 s	585 (354)	404 (265)	.015		309 (148)	291 (102)	.703		.026	
3 s	559 (271)	522 (295)	.440		409 (245)	338 (122)	.423		.301	
4 s	786 (492)	610 (330)	.091		437 (228)	339 (150)	.079		.034	
6 s	968 (609)	739 (451)	.062		502 (280)	421 (133)	.357		.063	
8 s	1,248 (821)	885 (696)	.017		797 (674)	556 (235)	.241		.012	

Bold values represent $p < .05$. The table displays nontransformed data

All ADHD versus controls, MRPT mean reproduction time, RPT-SDs standard deviation of mean reproduction time, (t) = post hoc t test

MANOVA/ANOVA: ADHD ADHD effect, AGE age effect, IN interval length effect, ADHD × AGE interaction ADHD by age, ADHD × IN interaction interval by ADHD

* $p < .05$, ** $p < .01$, *** $p < .001$, n.s. non-significant

intervals (for 1 s: $t_{(108)} = 3.616$, $p < .001$; for 2 s: $t_{(108)} = 3.596$, $p < .001$; for 3 s: $t_{(108)} = 4.220$, $p < .001$; for 4 s: $t_{(108)} = 5.261$, $p < .001$; for 6 s: $t_{(108)} = 5.338$, $p < .001$; for 8 s: $t_{(108)} = 3.345$, $p < .001$) and a larger discrepancy from the target interval at 2 s ($t_{(108)} = 2.806$, $p = .006$). There was also a significant interaction of interval length by age ($F_{(10,97)} = 2.002$, part. $\eta^2 = .044$, $p = .041$), which in univariate analyses did not result in significant effects.

Separate analyses of children and adults

When analyzing children and adults separately, the ADHD effect remained solely in the children group (children: $F_{(2,63)} = 5.488$, part. $\eta^2 = .148$, $p = .006$) (Table 2). Children with ADHD showed larger discrepancies between MRPT and target interval ($F_{(1,64)} = 8.173$, part. $\eta^2 = .113$, $p = .005$) compared to control children which in post hoc t test were significant for interval lengths from 4 to 8 s (4 s: $t_{(64)} = -2.065$, $p = .043$; 6 s: $t_{(64)} = -2.002$, $p = .050$; 8 s: $t_{(64)} = -2.071$, $p = .004$). According to univariate tests, children with ADHD also showed larger variability in their reproduction times (RPT-SD: $F_{(1,64)} = 6.448$, part. $\eta^2 = .092$, $p = .014$) which was significant for 2- and 8-s intervals (RPT-SD 2 s: $t_{(64)} = -2.498$, $p = .015$; 8 s: $t_{(64)} = -2.446$, $p = .017$). When Bonferroni–Holmes was applied, differences at the 8-s interval and RPT-SD at 2 and 8 s remained significant. The time reproduction task did not discriminate between the subgroup of adults with and without ADHD (adults: $F_{(2,41)} = 1.523$, part. $\eta^2 = .069$, $p = .230$).

Time discrimination

Effects of ADHD across age groups

The results of the MANOVA showed a main effect of ADHD ($F_{(3,104)} = 2.9$, part. $\eta^2 = .077$, $p = .040$) and a significant interaction of ADHD by age (children vs. adults: $F_{(3,104)} = 2.8$, part. $\eta^2 = .074$, $p = .045$). There was only a trend for the interaction of duration difference (DIFF) by age ($F_{(3,104)} = 2.4$, part. $\eta^2 = .066$, $p = .068$) (Table 3). Univariate tests revealed that the ADHD subjects (both children and adults) produced fewer hits than control subjects (hits: $F_{(1,106)} = 7.3$, part. $\eta^2 = .064$, $p = .008$), and post hoc t tests made clear that this was the case for both differences of duration longer than 200 ms ($t_{(108)} = -2.4$, $p = .018$) and shorter than 100 ms ($t_{(108)} = -2.1$, $p = .035$). The interaction of ADHD by age was due to univariate effects of MRT (ADHD by age: $F_{(1,106)} = 7.7$, part. $\eta^2 = .067$, $p = .007$). Univariate effects for RT-SD only showed a trend ($F_{(1,106)} = 3.5$, part. $\eta^2 = .032$, $p = .065$).

Age effects

The main effect of age was significant (children vs. adults: $F_{(3,104)} = 15.7$, part. $\eta^2 = .312$, $p < .001$). Children compared to adults had fewer hits ($F_{(1,106)} = 26.3$, part. $\eta^2 = .199$, $p < .001$), increased MRTs ($F_{(1,106)} = 21.8$, part. $\eta^2 = .171$, $p < .001$) and responded more variably (RT-SD: $F_{(1,106)} = 38.3$, part. $\eta^2 = .265$, $p < .001$). Post hoc t tests showed that children had fewer hits than adults in both differences of duration (≥ 200 ms: $t_{(108)} = -4.0$, $p < .001$; ≤ 100 ms: $t_{(108)} = -4.9$, $p < .0010$). Age effects were also found at both duration differences for MRT (≥ 200 ms: $t_{(108)} = 5.6$, $p < .001$; ≤ 100 ms: $t_{(108)} = 3.2$, $p = .002$) and RT-SD (≥ 200 ms: $t_{(108)} = 5.6$, $p < .001$; ≤ 100 ms: $t_{(108)} = 5.6$, $p < .001$).

Separate analyses of children and adults

When children and adults were analyzed separately, the ADHD main effect remained significant both for children ($F_{(3,62)} = 3.4$, part. $\eta^2 = .142$, $p = .023$) and for adults ($F_{(3,40)} = 3.2$, part. $\eta^2 = .195$, $p = .033$). ADHD children significantly differed from control children in the number of hits ($F_{(1,64)} = 5.8$, part. $\eta^2 = .083$, $p = .019$). Post hoc t tests revealed that children with ADHD produced fewer hits than control children only in the condition with differences of duration ≥ 200 ms ($t_{(64)} = 2.7$, $p = .008$). Adults with ADHD could be discriminated from controls by slower (MRT: $F_{(1,42)} = 7.6$, part. $\eta^2 = .153$, $p = .009$) and more variable response times (RT-SD: $F_{(1,42)} = 4.9$, part. $\eta^2 = .105$, $p = .032$). Post hoc tests showed that adults responded more slowly in both differences of duration conditions (MRT ≥ 200 ms: $t_{(42)} = -3.0$, $p = .005$; MRT ≤ 100 ms: $t_{(42)} = -2.4$, $p = .023$). In addition, in the condition with differences of duration ≤ 100 ms, adults with ADHD showed larger RT-SD ($t_{(42)} = -2.3$, $p = .028$).

Further neuropsychological tests

Results of further neuropsychological tests are shown in Table 4. In the *Alertness* task, neither an ADHD effect nor a significant interaction of ADHD by age was found. There was a significant age effect (children vs. adults) ($F_{(2,105)} = 20.6$, part. $\eta^2 = .282$, $p \leq .001$), and a significant interaction for condition by age ($F_{(2,105)} = 22.3$, part. $\eta^2 = .298$, $p < .001$). Univariate tests revealed that children responded more slowly and more variably than adults (median RT: $F_{(1,106)} = 9.2$, part. $\eta^2 = .080$, $p = .003$; RT-SD: $F_{(1,106)} = 40.2$, part. $\eta^2 = .275$, $p < .001$), and that the condition by age interaction was caused by differences in median RT ($F_{(1,106)} = 32.7$, part. $\eta^2 = .236$, $p < .001$). Further investigation with post hoc t tests

Table 3 Time discrimination task

	Children (N = 33/33)				Adults (N = 22/22)				ANOVA		MANOVA
	M (SD)		p (t)		M (SD)		p (t)				
	ADHD	Controls	ADHD	Controls	ADHD	Controls	ADHD	Controls	Adults (22/22)	All (55/55)	
Hits											
Difference ≤ 100 ms	20.9 (4.2)	22.2 (2.9)	1.56	.156	24.0 (3.5)	26.0 (3.5)	.054	.035	.035	.035	All: ADHD*, AGE***, DIFF*, ADHD × AGE*, DIFF × ADHD n.s., DIFF × Age n.s.; Children: ADHD*;
Difference ≥ 200 ms	27.0 (5.3)	30.2 (4.4)	.008	.008	32.0 (6.6)	33.6 (5.0)	.386	.018	.018	.018	Adults: ADHD n.s., Children: ADHD*;
Mean of reaction times, MRT (ms)											
Difference ≤ 100 ms	1,322 (424)	1,453 (364)	.182	.182	1,281 (583)	951 (284)	.023	.541	.541	.541	All: ADHD n.s., AGE***, ADHD × AGE*, Children: ADHD*;
Difference ≥ 200 ms	1,105 (394)	1,168 (362)	.506	.506	906 (314)	682 (145)	.005	.470	.470	.470	Adults: ADHD n.s.; Children: ADHD*;
SD of reaction times, RT-SD (ms)											
Difference ≤ 100 ms	911 (422)	984 (404)	.474	.474	640 (414)	399 (268)	.027	.539	.539	.539	All: ADHD n.s., AGE**;
Difference ≥ 200 ms	871 (478)	923 (498)	.662	.662	551 (345)	401 (254)	.108	.752	.752	.752	Children: ADHD n.s.; Adults: ADHD*

The table displays nontransformed data. Bold values represent $p < .05$

All ADHD versus controls, M mean, MRT mean of reaction times, RT-SD standard deviation RT, (t) = post hoc t test

MANOVA/ANOVA: ADHD ADHD effect, AGE age effect, ADHD × AGE interaction ADHD by age, DIFF difference of duration length effect (≥200 vs. ≤100 ms)

* $p < .05$, ** $p < .01$, *** $p < .001$, n.s. non-significant

Table 4 Neuropsychological test results

	Children (N = 33/33)		Adults (N = 22/22)		MANOVA/ANOVA
	M (SD)		M (SD)		
	Controls	t tests, p	ADHD	Controls	
Alertness					
Median of reaction times (ms)					
Warning signal	271 (52)	.615	246 (45)	258 (62)	.922
No warning signal	312 (73)	.207	252 (49)	254 (52)	.363
RT-SD (ms)					
Warning signal	92 (43)	.977	52 (27)	42 (15)	.631
No warning signal	92 (53)	.032	42 (20)	42 (17)	.077
Go/NoGo					
Median of reaction times (ms)	450 (93)	.212	417 (64)	397 (66)	.601
RT-SD (ms)	127 (37)	.373	86 (35)	65 (16)	.090
Errors	4.0 (3.5)	.693	.7 (.8)	1.0 (1.1)	.895
CPT					
MRTs for hits (ms)	460 (91)	.672	399 (90)	350 (37)	.131
RT-SD for hits (ms)	168 (61)	.261	100 (50)	61 (24)	.041
Hits	36.5 (3.6)	.032	38.5 (1.8)	39.5 (.7)	.007
Commission errors	2.4 (2.8)	.442	1.0 (1.6)	.6 (1.0)	.291

The table shows nontransformed data. Bold values represent $p < .05$

Post hoc t tests: All ADHD versus controls (N = 55/55, df = 108), Children children with ADHD versus controls (N = 33/33, df = 64), Adults adults with ADHD versus controls (N = 22/22, df = 42), M mean, SD standard deviation, MRTs mean reaction times, RT-SDs standard deviation of reaction times

* $p < .05$, ** $p < .01$, n.s. not significant

Table 5 Correlations between time processing and neuropsychological tasks in children and adults

	Time discrimination						Time reproduction			
	Total hits		Total MRT		Total RT-SD		Total MRPT		Total RPT-SD	
	Children (<i>N</i> = 66)	Adults (<i>N</i> = 44)	Children (<i>N</i> = 66)	Adults (<i>N</i> = 44)	Children (<i>N</i> = 66)	Adults (<i>N</i> = 44)	Children (<i>N</i> = 66)	Adults (<i>N</i> = 44)	Children (<i>N</i> = 66)	Adults (<i>N</i> = 44)
Alertness										
MD no W	-.331**	-.038	.095	.062	.329*	.115	.071	-.172	.165	.493**
MD with W	-.248*	-.040	.096	.073	.358*	.133	.024	-.047	.032	.410**
RT-SD no W	-.351**	-.072	-.106	.169	.146	.240	-.060	-.279	.088	.342*
RT-SD with W	-.172	-.142	.072	.494**	.138	.482**	.064	-.124	-.051	.442**
Go-Nogo										
MD	-.096	-.051	.137	.297	.336*	.313*	.383**	-.112	.123	.229
RT-SD	-.12	-.514**	.145	.203	.322*	.177	.243	-.303*	.030	.370*
Errors	-.126	-.349*	-.208	-.005	.134	-.020	-.291*	-.078	.090	.054
CPT										
MRT	-.415**	-.153	.243*	.128	.205	.058	.085	-.201	.314*	.362*
RT-SD	-.417**	-.134	.214	.336*	.202	.274	-.058	-.262	.251*	.236
Hits	.296*	-.006	-.050	-.155	-.257*	-.191	.222	.250	-.138	-.104
Commission errors	-.021	-.001	.137	.417**	.009	.330*	-.046	-.005	.123	.111

W warning signal, MD median reaction time, MRTs mean reaction time, RT-SDs standard deviation of reaction time, MRPT mean reproduction time, RPT-SDs standard deviation of mean reproduction time

* $p < .05$, ** $p < .01$

revealed that in both conditions children's RT-SDs were more variable (with warning: $t_{(108)} = 5.4$, $p = .000$; without warning: $t_{(108)} = 5.3$, $p < .001$), and in the condition without warning signal median RT was slower compared to adults ($t_{(108)} = 4.2$, $p < .001$). When children and adults were analyzed separately, no significant main effect of ADHD emerged. In adults, a significant interaction of ADHD by condition was found ($F_{(2,41)} = 4.067$, part. $\eta^2 = .166$, $p = .024$), but did not reach statistical significance in univariate tests.

In the *Go/Nogo* task, only a trend for ADHD-related effects ($F_{(3,104)} = 2.6$, part. $\eta^2 = .070$, $p = .057$) was found in the full group, which was obviously due to RT-SDs ($F_{(1,106)} = 4.7$, part. $\eta^2 = .043$, $p = .032$). The main effect for age (children vs. adults) ($F_{(3,104)} = 22.1$, part. $\eta^2 = .389$, $p < .001$) indicated that children responded more slowly ($F_{(1,106)} = 13.0$, part. $\eta^2 = .109$, $p < .001$), more variably ($F_{(1,106)} = 46.2$, part. $\eta^2 = .303$, $p < .001$) and committed more errors than adults ($F_{(1,106)} = 39.1$, part. $\eta^2 = .270$, $p < .001$). When age groups were analyzed separately, no significant main effect for ADHD was found, neither in children ($F_{(3,62)} = 1.469$, part. $\eta^2 = .066$, $p = .232$) nor in adults. The latter presented at least a trend ($F_{(3,40)} = 2.730$, part. $\eta^2 = .170$, $p = .057$), which was related to RT-SD (RT-SD: $F_{(1,42)} = 6.7$, part. $\eta^2 = .137$, $p = .013$).

In the *cued CPT*, a significant main effect of ADHD was found in the full group ($F_{(4,103)} = 2.9$, part. $\eta^2 = .100$, $p = .027$). Univariate tests demonstrated that ADHD subjects detected fewer hits ($F_{(1,106)} = 7.0$, part. $\eta^2 = .062$, $p = .010$) and responded more variably (RT-SD: $F_{(1,106)} = 7.9$, part. $\eta^2 = .069$, $p = .006$) than controls. The effect for age (children vs. adults) was significant ($F_{(4,103)} = 18.5$, part. $\eta^2 = .418$, $p < .001$). Univariate tests showed that children scored fewer hits ($F_{(1,106)} = 9.2$, part. $\eta^2 = .080$, $p = .003$), committed more errors ($F_{(1,106)} = 9.7$, part. $\eta^2 = .084$, $p = .002$), and responded more slowly ($F_{(1,106)} = 27.7$, part. $\eta^2 = .207$, $p = .000$) and variably ($F_{(1,106)} = 66.3$, part. $\eta^2 = .385$, $p < .001$) than adults. Separate analyses for children and adults resulted in a significant main effect of ADHD in adults ($F_{(4,39)} = 3.5$, part. $\eta^2 = .266$, $p = .015$), but no significant ADHD effect in the children's group. Affected adults responded with fewer hits ($F_{(1,43)} = 5.7$, part. $\eta^2 = .120$, $p = .021$), and more slowly ($F_{(1,43)} = 5.7$, part. $\eta^2 = .120$, $p = .021$) and variably ($F_{(1,43)} = 11.1$, part. $\eta^2 = .209$, $p = .002$) than controls.

Exploratory correlational analysis

Although these analyses were exploratory, only correlations reaching $p < .01$ will be reported and commented

because of multiple comparisons. In children, the produced interval length from the time reproduction task was correlated with median RT in the Go/Nogo task (see Table 5). Time discrimination total hits were inversely correlated in the children's group with Alertness median RT and RT-SD in the conditions without warning, as well as with CPT MRT and RT-SD.

In the adult group, total RPT-SD of the time reproduction task showed moderate correlations with three parameters from the Alertness task. Time discrimination hits in the adult group were inversely correlated with Go/Nogo RT-SD. MRT of time discrimination was correlated in adults with Alertness RT-SD with warning as well as with commission errors of the CPT. Time discrimination RT-SD was correlated in adults with Alertness RT-SD with warning.

Discussion

This study compared neuropsychological performance on time reproduction of seconds and time discrimination of milliseconds in children and adults with ADHD and matched controls. ADHD-related differences in temporal processing were found both in children and adults, indicating that some deficits in this domain are present in both age groups. However, differences in ADHD-related deficits in children compared to adults point to a developmental change of certain weaknesses related to temporal processing.

In the time reproduction task, individuals with ADHD were significantly impaired compared to controls, and there was no interaction between ADHD and age effects when analyzing the full group. This result points toward a certain continuity of difficulties in time reproduction from childhood into adulthood. This is in contrast to our initial hypothesis which had predicted a decrease of time reproduction deficits associated with diminished problems of inhibitory control in adults. However, when analyzed separately, only children presented the characteristic under-reproduction of longer time intervals compared to controls which has been reported in the literature (Barkley et al. 2001a; McInerney and Kerns 2003; Rommelse et al. 2007). In addition, they showed significantly larger RPT-SD. Adults with ADHD were not significantly impaired on this task compared to controls. This lack of statistically significant group differences when adults were analyzed separately may be partly explained by the smaller subsample. In addition, several studies reporting significant under-reproduction in ADHD patients used time intervals considerably longer (up to 60 s, e.g. Barkley et al. 2001b). In the study by Marx et al. (2010), significant ADHD effects were found for the longest intervals (36 and 48 s, i.e. well above the maximum duration of 8 s used in the

present study) in adults and adolescents but not in children. One might speculate that more pronounced deficits in time reproduction might have emerged in the adult ADHD subgroup with longer intervals and thus enhanced demands on strategic control, and with a larger sample size.

In the time discrimination task, ADHD-related impairment was found in the full group of individuals with ADHD compared to controls. In this task, different patterns of deficit emerged in children and adults. In children, the ADHD effect was exclusively confined to an increased number of errors. An in-depth analysis showed that this was due to an increased number of errors in the condition with duration differences of 200 ms or more. This may be related to the greater difficulty of the short duration condition (<100 ms), which presented problems for both groups of children, independent of their ADHD status (floor effect; accuracy of both groups below 62%). Reaction time differences did not differentiate between the ADHD and control children in either condition. In adults, we found the opposite pattern: Response times were slower in adults with ADHD compared to controls, whereas the number of errors did not discriminate between the groups. There was only a trend for adults with ADHD to make more errors which was confined to the difficult condition (i.e. duration differences < 100 ms). In this type of task, increased response time is to be interpreted as the additional time needed for comparison processes and decision-making in a cognitively demanding task. This is illustrated by the fact that all subgroups hesitated longer when differences of duration were small. Longer hesitation discriminated between the adult groups in general, but more clearly in the easy condition (duration differences \geq 200 ms). Obviously, cognitive demands of the easy condition were so low for healthy individuals that they responded without hesitation. Individuals with ADHD, in contrast, needed more time to make their decision even though task demands seemed relatively low. As both groups took more time to respond in the difficult condition, group differences appeared more distinctly in the easy condition. The longer hesitation observed in adults with ADHD may reflect an attempt to cope with the difficulties encountered in this task and seems to indicate a basic weakness of processing in this domain. Standard deviation of response time (RT-SD) discriminated ADHD only in the adults group. Taken all together, impaired time discrimination of short durations seems to be a stable marker of ADHD, but with different manifestations in children and adults: whereas in children with ADHD deficits are reflected by the number of errors, deficits in adults are reflected by response time measures. The presence of impairment in both age groups argues for an enduring vulnerability and coincides with recent findings on timing deficits in ADHD across age groups (Marx et al. 2010).

This conclusion is also in line with findings by Himpel et al. (2009), suggesting that impaired time discrimination within the millisecond range may represent an endophenotype for ADHD. However, one cannot exclude that the results do not only reflect a specific weakness in time perception or internal clock mechanisms in ADHD but are also related to general task difficulty.

None of the standardized neuropsychological test procedures discriminated between the children with ADHD and their controls. This may be explained by their closely matched high IQ estimates, and is not an unusual finding (see Koschack et al. 2003; Scheres et al. 2004; Sonuga-Barke et al. 2008), even though IQ scores may be somewhat overestimated here by the algorithm used (Schallberger 2005). These tests tapping basic processes seem appropriate for correlational analyses, but are probably not specific enough to discriminate between groups of children, especially when the age range and, thus, the range of normal performance are large (Drechsler et al. 2005, 2009). Adults with ADHD could be discriminated from controls on the CPT by MRTs, increased RT-SDs and also error-related differences.

The exploratory correlational analysis showed the expected associations of performance, but only in children: The produced interval length in the time reproduction task was correlated with measures of an inhibitory control task, i.e. longer and more accurate time reproduction correlated positively with median RT of the Go/Nogo task. Also in line with predictions, children's hits in the time discrimination task were correlated with measures of alertness, i.e. simple motor timing as well as with sustained attention (CPT). Measures from the Alertness condition with warning, however, did not correlate with time discrimination MRT. This can be explained by the fact that typically developing children often have to fight the impulse to respond to the warning signal instead of to the target stimulus: for children this task may act as an inhibitory control task (Drechsler et al. 2005). Thus for children, the presumed associations between response inhibition and time reproduction on one side, and state regulation processes and time discrimination on the other side could be demonstrated.

The correlational pattern observed in the adult group was different: Standard deviation of time reproduction (RPT-SD) was correlated with reaction time measures of the Alertness subtasks, i.e. with measures of arousal rather than with inhibitory control, as suggested by Halperin et al. (Halperin and Schulz 2006; Halperin et al. 2008). In the time discrimination task, hits were inversely related to RT-SD in the Go/Nogo Task. This indicates that in adults, errors in the time discrimination task resulted from inhibitory control problems and not from impaired time discrimination as in children. Unexpectedly, adult time discrimination MRT was associated with commission

errors and standard deviation on the CPT and with the alertness condition with warning, i.e. with inhibitory control aspects of tests related to state regulation. This may be interpreted as an association between state regulation and executive aspects of time processing in adults. The result replicates difficulties in disentangling the impact of bottom up versus top down processes on performance in adult ADHD (see King et al. 2007), suggesting that attentional deficits may contribute to executive deficits (Bekker et al. 2005).

Limitations

Adults with ADHD were selected among the parents of children with ADHD if they scored above the cut-offs on two self-rating scales including a retrospective assessment for ADHD symptoms. Therefore, the diagnosis of adults meets research but not clinical criteria. It may be argued that at least some of these adult ADHD participants only showed subclinical impairment. They were probably also better integrated into society than a clinical adult ADHD clientele in need for professional help. Thus, it is uncertain to which extent the results may be generalized to clinical samples of adult ADHD patients. On the other hand, this sample seems to be more representative of the true developmental course of ADHD in the adult population than clinically referred ADHD patients. Furthermore, the presence of neuropsychological endophenotypes should not depend on the current ADHD status. Some of the ADHD adults were related to members of the ADHD children group. Whether or not family relationships constitute a potential confounder will be addressed in detail in a future study. Another limitation is the relatively small sample size of the adult group. We cannot exclude that additional group differences might have emerged with larger sample sizes.

Conclusion

This is the first study which directly compared time-processing performance in ADHD between children and adults with a mean age above 30 years. ADHD-related deficits in time processing were present both in children and adults with ADHD, but seemed to take different forms in childhood compared to adulthood. There is some evidence that in childhood ADHD effects due to executive function deficits on one side, and more basal time-processing problems on the other side coexist and can be distinguished relatively well. In the adult sample, manifestations of time-processing deficits seemed to be related more clearly to basic processes, such as arousal or time perception in the millisecond range, but they could not be completely separated from executive functions and inhibitory control

which seem to interact on a more subtle level in adults than in children.

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