NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD aprile 2016

ADHD Atten Deficit Hyperact Disord. 2016;1-9.

FACTORS PREDICTING TREATMENT ADHERENCE IN PATIENTS WITH ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A PRELIMINARY STUDY.

Semerci B, Taskıran S, Tufan E, et al.

This study aimed to elicit patient- and treatment-related factors that can potentially predict treatment adherence in adult ADHD. Subjects who were over 18 and received a diagnosis of ADHD were included in the study. Chart review data of 102 subjects regarding demographics, medications, comorbidities, concomitant medications and domains of functional impairment were collected, and predictors were assessed using a binominal logistical regression model. One hundred and two patients (78.4 % male) with a mean age of 28.8 (SD = 9.8, range = 18-55) years were enrolled in the study. Childhood diagnosis of ADHD, agents used for treatment (MPH or atomoxetine), individual domains of dysfunction and use of additional psychotropic drugs were not found to be related to treatment adherence. Patients with a university education and those referred for family history of ADHD were more likely to adhere to treatment (p = 0.05 and 0.03, respectively). On the other hand, reasons for referral other than ADHD were significantly more frequently related to non-adherence (p = 0.02). Treatment noncompliance remains a significant problem despite therapeutic effects of medications. Identification of predictors of non-adherence can lead to heightened awareness of special populations at risk. We have found that prior awareness on ADHD (via past history/media/friends) leading to self/clinician referral to rule out ADHD and pervasiveness of symptoms across functional domains led to better compliance in our sample. Future research with prospective design utilizing objective tools for adherence is required

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

ADHD Atten Deficit Hyperact Disord. 2016;1-8.

OBSESSIVE-COMPULSIVE ADULTS WITH AND WITHOUT CHILDHOOD ADHD SYMPTOMS.

Tan O, Metin B, Metin S.

Obsessive-compulsive disorder (OCD) and attention-deficit and hyperactivity disorder (ADHD) frequently coexist. To understand whether childhood ADHD can increase the risk of OCD in adulthood and whether it influences the phenomenology of OCD, we investigated the symptoms of ADHD during childhood in obsessive-compulsive adults who had never been diagnosed as ADHD. Adults with OCD (n = 83) were given the Wender Utah Rating Scale (WURS), Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Barratt Impulsiveness Scale-11 (BIS-11), Hamilton Depression Rating Scale-17 (HDRS-17) and Beck Anxiety Inventory (BAI). The prevalence of childhood ADHD symptoms was 40.9 % (n = 34) and that of adult ADHD was 16.9 % (n = 14). Patients with childhood ADHD symptoms had an earlier onset of OCD, higher scores of the BAI and BIS-11. The scores of the Y-BOCS and HDRS-17 did not differ between those having and not having childhood ADHD symptoms. Childhood history of ADHD symptoms is common in adult OCD patients who have never been diagnosed as ADHD. Childhood ADHD symptoms are associated with an earlier age of OCD, more severe anxiety and higher impulsiveness. Even remitted ADHD may be a risk factor for OCD in later life

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Am J Med Genet Part B Neuropsychiatr Genet. 2016.

GENOME-WIDE ANALYSES OF AGGRESSIVENESS IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Brevik EJ, van Donkelaar MM, Weber H, et al.

Aggressiveness is a behavioral trait that has the potential to be harmful to individuals and society. With an estimated heritability of about 40%, genetics is important in its development. We performed an exploratory genome-wide association (GWA) analysis of childhood aggressiveness in attention deficit hyperactivity disorder (ADHD) to gain insight into the underlying biological processes associated with this trait. Our primary sample consisted of 1,060 adult ADHD patients (aADHD). To further explore the genetic architecture of childhood aggressiveness, we performed enrichment analyses of suggestive genome-wide associations observed in aADHD among GWA signals of dimensions of oppositionality (defiant/vindictive and irritable dimensions) in childhood ADHD (cADHD). No single polymorphism reached genome-wide significance (P<5.00E-08). The strongest signal in aADHD was observed at rs10826548, within a long noncoding RNA gene (beta=-1.66, standard error (SE)=0.34, P=1.07E-06), closely followed by rs35974940 in the neurotrimin gene (beta=3.23, SE=0.67, P=1.26E-06). The top GWA SNPs observed in aADHD showed significant enrichment of signals from both the defiant/vindictive dimension (Fisher's P-value=2.28E-06) and the irritable dimension in cADHD (Fisher's P-value=0.0061). In sum, our results identify a number of biologically interesting markers possibly underlying childhood aggressiveness and provide targets for further genetic exploration of aggressiveness across psychiatric disorders

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Andrology. 2016.

INCREASED RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ASSOCIATED WITH EXPOSURE TO ORGANOPHOSPHATE PESTICIDE IN TAIWANESE CHILDREN.

Yu CJ, Du JC, Chiou HC, et al.

Attention-deficit/hyperactivity disorder (ADHD) is male predominated, and the etiology of this disorder remains unclear. Past studies have assessed the association of low-level organophosphate pesticide exposure with childhood ADHD cross-sectionally and prospectively. However, the results have been inconsistent. A first case-control study was performed to investigate the relationship between organophosphate pesticide exposure and ADHD with adjusted covariates. We recruited 97 doctor-diagnosed ADHD cases and 110 non-ADHD controls who were 4-15 years of age. Exposure was assessed using urinary levels of dialkylphosphate metabolites, which are biomarkers of OP pesticide exposure. Blood lead levels and polymorphisms of two commonly verified dopaminergic-related genes (the D4 dopamine receptor gene DRD4 and the dopamine transporter gene DAT1) were also analyzed. The sociodemographics and lifestyles

of the children and of the mothers during pregnancy were collected using a questionnaire. The blood lead levels of both groups were similar (1.57 ± 0.73 vs. 1.73 ± 0.77 μg/dL, p = 0.15). Significant urinary concentration differences in one of the six dialkylphosphate metabolites, dimethylphosphate (DMP), were found between ADHD and control subjects (322.92 ± 315.68 vs. 224.37 ± 156.58 nmol/g cr., p < 0.01). A dose-response relationship was found between urinary concentrations of DMP and ADHD in both crude and adjusted analyses (p for trend<0.05). Children with higher urinary DMP concentrations may have a twofold to threefold increased risk of being diagnosed with ADHD. We report a dose-response relationship between child DMP levels and ADHD. Organophosphate pesticide exposure may have deleterious effects on children's neurodevelopment, particularly the development of ADHD

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Asian Biomedicine. 2015;9:803-07.

PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH EPILEPSY IN A THAI HOSPITAL.

Subchartanan J, Patharathitikul S, Chonchaiya W.

Background: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental and behavioral disorder commonly prevalent in school-aged children. ADHD can be a comorbid diagnosis in those with epilepsy. However, the relationship between ADHD and epilepsy is complex and not entirely known.
Objectives: To compare the prevalence of ADHD between children with epilepsy at Prapokklao Hospital and healthy children in Chantaburi province, Thailand.
Methods: We recruited 73 children with epilepsy at Prapokklao Hospital and 73 age- and sex-matched healthy children at a local school in Chantaburi. The parents of all children rated their child's behavior using ADHD rating scales. In those with higher scores, a child psychiatrist at Prapokklao Hospital then diagnosed ADHD based on the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5).
Results: Children with epilepsy appeared to be from families with a lower socioeconomic status than their counterparts. Furthermore, those with epilepsy tended to have a greater probability of diagnosis with ADHD than healthy controls (19% versus 3%, P < 0.001). However, this finding was not significant after data were controlled for the socioeconomic status of the children.
Conclusions: There was an interesting trend towards a greater probability of ADHD diagnosis in those children with epilepsy than in healthy children. As such, epilepsy may increase the risk of these children developing ADHD. To document the prevalence of ADHD in children with epilepsy and healthy controls, both groups of children should be matched not only based on age and sex, but also socioeconomic status

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Behavioral Interventions. 2016 Apr;31:210-18.

DISCRIMINATED FUNCTIONAL COMMUNICATION FOR ATTENTION: EVALUATING FIXED AND VARIED DURATIONS OF REINFORCER AVAILABILITY.

Balka KE, Hausman NL, Schaller E, et al.

Discriminated functional communication (DFC) training has been used to teach children to attend to naturally occurring discriminative stimuli when manding for attention. In this study, the participant was taught to only mand for attention during experimenter non-busy periods. The participant could only discriminate busy and non-busy activities during more naturalistic varied reinforcer availability periods following prior exposure to a fixed duration of availability. These data suggest that DFC may first have to be taught under more predictable conditions prior to transitioning to more naturalistic conditions.

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Behavioural Pharmacology. 2016.

THE RELATIONSHIP BETWEEN AGGRESSION, EMPATHY SKILLS AND SERUM OXYTOCIN LEVELS IN MALE CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Demirci E, Ozmen S, Kilic E, et al.

Although attention deficit and hyperactivity disorder (ADHD) are recognized as neurodevelopmental disorders characterized by impairment in executive functions, impairments in social functioning are often accompanied by ADHD. Oxytocin (OT) has been investigated in a number of psychiatric disorders owing to its effects on social interactions. The aim of this study was to determine the relationship between aggression, empathy and OT levels in children with ADHD. Forty male patients with ADHD, ranging in age from 7 to 18 years, and 40 healthy age-matched and sex-matched individuals were included in this study. The patients and healthy controls filled in the BussΓÇôPerry Aggression Questionnaire and BryantΓÇÖs Empathy Index for Children and Adolescents; the Reading the Mind in the Eyes test was then completed. Blood samples were collected for OT at the beginning of the study. Lower serum OT levels were observed in patients with ADHD compared with the healthy controls. Moreover, there was a negative correlation between serum OT level and aggression scores and a positive correlation between the serum OT level and empathy scores in patients with ADHD. We conclude that OT may play a role in aggression and empathy skills, affecting the social life of those with ADHD

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Brain Injury. 2016 Feb;30:311-17.

TREATMENT OF VERTICAL HETEROPHORIA AMELIORATES PERSISTENT POST-CONCUSSIVE SYMPTOMS: A RETROSPECTIVE ANALYSIS UTILIZING A MULTI-FACETED ASSESSMENT BATTERY.

Rosner MS, Feinberg DL, Doble JE, et al.

Primary objective: To examine the effectiveness of neutralizing prismatic lenses for reduction of headache, dizziness and anxiety in patients with persistent post-concussive symptoms and vertical heterophoria (VH). Background: Approximately 5–10% of patients with traumatic brain injury (TBI) develop persistent post-concussive symptoms. Many rehabilitation/treatment modalities are tried, but are largely unsuccessful, indicating a need for more effective treatment. Design and method: This retrospective study included 38 patients with persistent post-concussive symptoms, who were diagnosed by an optometric binocular vision sub-specialist with VH (a sub-set of binocular vision dysfunction [BVD] that manifests as vertical eye and image misalignment). Data was collected both before and after prism application and included validated survey instruments for headache, dizziness, anxiety and BVD symptom burden; subjective rating (0–10 scale) of headache, dizziness and anxiety severity; and a sub-analysis of the BVD survey instrument questions that pertain specifically to headache, dizziness and anxiety. Upon conclusion of treatment, subjective assessment of overall improvement of heterophoria symptoms was obtained utilizing a 10 cm visual analogue scale. Outcomes: Results demonstrated marked reduction in all measures of headache, dizziness and anxiety (19.1–60.8%) and an overall subjective improvement of VH symptoms of 80.2%. Conclusions: Neutralizing prismatic lenses are an effective treatment of headache, dizziness and anxiety in patients with persistent post-concussive symptoms and VH.

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Child Adolesc Ment Health. 2016.

A SCHOOL CONSULTATION INTERVENTION FOR ADOLESCENTS WITH ADHD: BARRIERS AND IMPLEMENTATION STRATEGIES.

Sibley MH, Olson S, Morley C, et al.

Background: Academic impairment is among the most troubling domains of impairment for adolescents with Attention Deficit/Hyperactivity Disorder (ADHD).

Method: This investigation presents results of a yearlong academic intervention delivered to adolescents with ADHD (N = 218) by engaging school staff as interventionists through behavioral consultation with an outside mental health professional.

Results: The intervention was coordinated successfully in some cases, but not in others. The principal challenge to intervention coordination was sustaining monthly contact between consultants and interventionists (38.5% success rate) and scheduling in-person consultation meetings with interventionists (40.0% success rate). Implementation of the intervention was enhanced when the student (a) attended a public (vs. private) school, (b) had an IEP or Section 504 plan in place, (c) was in middle school (vs. high school), (d) had a parent who communicated regularly with the school, and (e) had a special education support staff member or counselor (vs. teacher or administrator) as a school interventionist. **Conclusions**: Considering these data, recommendations are provided for effective coordination of academic interventions for adolescents with ADHD

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Child Adolesc Psychiatry Ment Health. 2016;10.

SUBSTANCE ABUSE AND PERSONALITY DISORDER COMORBIDITY IN ADOLESCENT OUTPATIENTS: ARE GIRLS MORE SEVERELY ILL THAN BOYS?

Korsgaard HO, Torgersen S, Wentzel-Larsen T, et al.

Background: Substance use disorders (SUDs) constitute a major health problem and are associated with an extensive psychiatric comorbidity. Personality disorders (PDs) and SUDs commonly co-occur. Comorbid PD is characterized by more severe addiction problems and by an unfavorable clinical outcome. The present study investigated the prevalence of SUDs, PDs and common Axis I disorders in a sample of adolescent outpatients. We also investigated the association between PDs and SUDs, and how this association was influenced by adjustment for other Axis I disorders, age and gender.
Methods: The sample consisted of 153 adolescents, aged 14-17 years, who were referred to a non-specialized mental health outpatient clinic with a defined catchment area. SUDs and other Axis I conditions were assessed using the mini international neuropsychiatric interview. PDs were assessed using the structured interview for DSM-IV personality.
Results: 18.3 % of the adolescents screened positive for a SUD, with no significant gender difference. There was a highly significant association between number of PD symptoms and having one or more SUDs; this relationship was practically unchanged by adjustment for gender, age and presence of Axis I disorders. For boys, no significant associations between SUDs and specific PDs, conduct disorder (CD) or attention deficit hyperactivity disorder (ADHD) were found. For girls, there were significant associations between SUD and BPD, negativistic PD, more than one PD, CD and ADHD.
Conclusions: We found no significant gender difference in the prevalence of SUD in a sample of adolescents referred to a general mental health outpatient clinic. The association between number of PD symptoms and having one or more SUDs was practically unchanged by adjustment for gender, age and presence of one or more Axis I disorders, which suggested that having an increased number of PD symptoms in itself may constitute a risk factor for developing SUDs in adolescence. The association in girls between SUDs and PDs, CD and ADHD raises the question if adolescent girls suffering from these conditions may be especially at risk for developing SUDs. In clinical settings, they should therefore be monitored with particular diligence with regard to their use of psychoactive substances. Trial registration The regional committee for medical research ethics for eastern Norway approved the study protocol in October 2004 (REK: 11395).

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Child Development. 2016 Mar;87:365-73.

PEER REJECTION AND ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS: RECIPROCAL RELATIONS THROUGH AGES 4, 6, AND 8.

Stenseng F, Belsky J, Skalicka V, et al.

Attention deficit hyperactivity disorder (ADHD) predicts poor peer relationships. What remains unclear is whether poor peer relationships affect ADHD symptomatology. Hence, reciprocal effects of peer rejection and ADHD symptoms were examined in a community sample of 962 Norwegian children at ages 4, 6, and 8. Results showed that ADHD symptoms at age 4 predicted more peer rejection at age 6, and that peer rejection at age 4 predicted more symptoms at age 6. However, when conducting analyses on ADHD

subtypes, hyperactivity–impulsivity and inattentiveness symptoms were adversely affected by peer rejection at ages 6 and 8, whereas peer rejection was unaffected by such symptoms, indicating that the effect of peer rejection on ADHD symptoms was most robust. Mediational relation were also identified.

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Child Neuropsychol. 2016;1-21.

TIME-BASED PROSPECTIVE MEMORY DIFFICULTIES IN CHILDREN WITH ADHD AND THE ROLE OF TIME PERCEPTION AND WORKING MEMORY.

Mioni G, Santon S, Stablum F, et al.

Time-based prospective memory (PM) is the ability to remember to perform an intended action at a given time in the future. It is a competence that is crucial for effective performance in everyday life and may be one of the main causes of problems for individuals who have difficulty in planning and organizing their life, such as children with attention deficit/hyperactivity disorder (ADHD). This study systematically examines different aspects of time-based PM performance in a task that involves taking an action at a given future time in a group of 23 children with ADHD who were compared with a matched group of typically-developing (TD) children. The children were asked to watch a cartoon and then answer a questionnaire about its content (ongoing task). They were also asked to press a key every 2-áminutes while watching the cartoon (PM task). The relationships of time perception and verbal working memory with PM performance were examined by administering appropriate tasks. The results showed that the children with ADHD were less accurate than the TD children in the PM task and exhibited less strategic time-monitoring behavior. Time perception was found to predict PM accuracy, whereas working memory was mainly involved in time-monitoring behavior, but this applied more to the TD group than to the ADHD group, suggesting that children with ADHD are less able to use their cognitive resources when meeting a PM request

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Child Psychiatry Hum Dev. 2016 Apr;47:259-69.

IRON DEFICIENCY PARAMETERS IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Percinel I, Yazici KU, Ustundag B.

The aim of this study is to compare iron deficiency parameters in patients with stimulant-naive attention-deficit/hyperactivity disorder (ADHD) and healthy controls, to investigate whether there are differences among the ADHD presentations, and to evaluate the relationship between ADHD symptom severity and serum ferritin levels. In addition, ADHD-Predominantly Inattentive (ADHD-PI) patients with restrictive hyperactivity/impulsivity symptoms were evaluated as a separate group with “restrictive inattention presentation” (ADHD-Rest) and were compared with other groups. Patients with ADHD-Rest are typically defined as having six or more symptoms of inattention and fewer than three symptoms of hyperactivity/impulsivity. A total of 200 ADHD cases consisting of 100 ADHD-Combine (ADHD-C) and 100 ADHD-PI and a total of 100 healthy control cases were included in the study. The Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version was performed in a semi-structured interview during the diagnosis. The Turgay DSM-IV-Based Child and Adolescent Behavior Disorders Screening and Rating Scale, the Conners’ Rating Scale-Revised: Long Form (Parent–Teacher) (CPRSR:L, CTRS-R:L) were used for clinical evaluation. Hemogram, serum iron, iron binding capacity and serum ferritin levels were assessed. There were no significant differences between the ADHD patients and the healthy control cases in terms of iron deficiency parameters. Further, there were no significant differences among the ADHD presentations in terms of the same parameters, nor were there any significant differences when the groups were examined after the identification of the ADHD-Rest. The CPRS-R:L Hyperactivity and the CTRS-R:L Hyperactivity scores were negatively correlated with serum ferritin level in the ADHD group. To our knowledge, our current study is the first to compare serum ferritin levels in ADHD-Rest with other

presentations of ADHD, and included the largest number of patients that were classified by ADHD presentations. Elucidation of these findings is important for both the etiology and treatment of ADHD.

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Emot Behav Difficulties. 2016;1-14.

THE ANTITHESIS OF INCLUSION? THE EMERGENCE AND FUNCTIONING OF ADHD SPECIAL EDUCATION CLASSES IN THE SWEDISH SCHOOL SYSTEM.

Malmqvist J, Nilholm C.

The neuropsychiatric paradigm has substantial impact on schools. The increase in the number of pupils being diagnosed with attention-deficit/hyperactivity disorder (ADHD) is an expression of the medicalisation of deviance. There is also an increase in educational classes specially designed to meet the needs of children with ADHD. This is contrary to the notion of inclusion and in conflict with the Swedish school law. Thus, it is important to obtain knowledge about Swedish ADHD classes. A questionnaire was sent to all Swedish municipalities (290, response rate 76%) regarding schooling for pupils with ADHD. As many as 40 Swedish municipalities have classes specifically designed for pupils with ADHD. Although the classes are said to be specifically designed for ADHD problems, they are not properly evaluated. Municipalities with ADHD classes also exhibit ambivalence towards these classes. The emergence, prevalence and functioning of the ADHD classes are discussed in light of the notion of inclusive education

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Eur Child Adolesc Psychiatry. 2016;25:351-60.

HOW 'CORE' ARE MOTOR TIMING DIFFICULTIES IN ADHD? A LATENT CLASS COMPARISON OF PURE AND COMORBID ADHD CLASSES.

Van Der Meer JMJ, Hartman CA, Thissen AJAM, et al.

Children with attention-deficit/hyperactivity disorder (ADHD) have motor timing difficulties. This study examined whether affected motor timing accuracy and variability are specific for ADHD, or that comorbidity with autism spectrum disorders (ASD) contributes to these motor timing difficulties. An 80-trial motor timing task measuring accuracy (μ), variability (s) and infrequent long response times (t) in estimating a 1-s interval was administered to 283 children and adolescents (8-17 years) from both a clinic and population based sample. They were divided into four latent classes based on the SCQ and CPRS-R:L data. These classes were: without behavioral problems 'Normal-class' (n = 154), with only ADHD symptoms 'ADHD-class' (n = 49), and two classes with both ASD and ADHD symptoms; ADHD(+ASD)-class (n = 39) and ASD(+ADHD)-class (n = 41). The pure ADHD-class did not deviate from the Normal class on any of the motor timing measures (mean RTs 916 and 925 ms, respectively). The comorbid ADHD(+ASD) and ASD(+ADHD) classes were significantly less accurate (more time underestimations) compared to the Normal class (mean RTs 847 and 870 ms, respectively). Variability in motor timing was reduced in the younger children in the ADHD(+ASD) class, which may reflect a tendency to rush the tedious task. Only patients with more severe behavioral symptoms show motor timing deficiencies. This cannot merely be explained by high ADHD severity with ASD playing no role, as ADHD symptom severity in the pure ADHD-class and the ASD(+ADHD) class was highly similar, with the former class showing no motor timing deficits

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Eur Child Adolesc Psychiatry. 2016;1-15.

THE IMPACT OF ADHD ON THE HEALTH AND WELL-BEING OF ADHD CHILDREN AND THEIR SIBLINGS.

Peasgood T, Bhardwaj A, Biggs K, et al.

Childhood attention-deficit/hyperactivity disorder (ADHD) has been associated with reduced health and well-being of patients and their families. The authors undertook a large UK survey-based observational study of the burden associated with childhood ADHD. The impact of ADHD on both the patient (N = 476) and their siblings (N = 337) on health-related quality of life (HRQoL) and happiness was quantified using multiple standard measures [e.g. child health utility-9D (CHU-9D), EuroQol-5D-Youth]. In the analysis, careful

statistical adjustments were made to ensure a like-for-like comparison of ADHD families with two different control groups. We controlled for carersΓÇÖ ADHD symptoms, their employment and relationship status and siblingsΓÇÖ ADHD symptoms. ADHD was associated with a significant deficit in the patientΓÇÖs HRQoL (with a CHU-9D score of around 6 % lower). Children with ADHD also have less sleep and were less happy with their family and their lives overall. No consistent decrement to the HRQoL of the siblings was identified across the models, except that related to their own conduct problems. The siblings do, however, report lower happiness with life overall and with their family, even when controlling for the siblings own ADHD symptoms. We also find evidence of elevated bullying between siblings in families with a child with ADHD. Overall, the current results suggest that the reduction in quality of life caused by ADHD is experienced both by the child with ADHD and their siblings

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Eur Neuropsychopharmacol. 2016.

CORTISOL AWAKENING RESPONSE IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: SUBTYPE DIFFERENCES AND ASSOCIATION WITH THE EMOTIONAL LABILITY.

Ramos-Quiroga JA, Corominas-Roso M, Palomar G, et al.

Cortisol awakening response (CAR) has been studied in children with ADHD, and some authors have reported morning cortisol differences among ADHD subtypes. Despite, only half of the children with ADHD continue to exhibit the disorder into adulthood, CAR has not been studied in adults so far. One hundred and nine adults with ADHD according to the DSM-IV criteria (46 inattentive and 63 combined) ranging in age from 18 to 55 years, and 27 healthy controls were included. Psychiatric and organic comorbidities were excluded. Salivary cortisol samples were obtained at 0, 30, 45 and 60 minutes after awakening. CAR was present in 84% of the healthy controls but in only 64% of the adults with ADHD (68% of the inattentive and 61% of the combined were CAR-positive). There were no significant differences in any of the morning cortisol measures between patients and controls or between the combined and inattentive subtypes of ADHD. Among the inattentive subtype but not in the combined patients, significant positive correlations were observed between the CAR and emotional lability (p=0.05), or self-concept (p=0.014) CAARS subscales, as well as with the cognitive impulsivity subscale of the Barratt impulsiveness scale (p=0.028). These results suggest that adults with ADHD exhibit normal cortisol responses upon awakening and thus cannot be defined in terms of hypo-arousal. Neurobiological differences between the combined and inattentive subtypes involving cortisol, are discussed

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Eur Psychiatry. 2016;35:47-54.

SIX-YEAR FOLLOW-UP STUDY OF COMBINED TYPE ADHD FROM CHILDHOOD TO YOUNG ADULTHOOD: PREDICTORS OF FUNCTIONAL IMPAIRMENT AND COMORBID SYMPTOMS.

Cadman T, Findon J, Eklund H, et al.

Background: ADHD in childhood is associated with development of negative psychosocial and behavioural outcomes in adults. Yet, relatively little is known about which childhood and adulthood factors are predictive of these outcomes and could be targets for effective interventions. To date follow-up studies have largely used clinical samples from the United States with children ascertained at baseline using broad criteria for ADHD including all clinical subtypes or the use of DSM III criteria. Aims: To identify child and adult predictors of comorbid and psychosocial comorbid outcomes in ADHD in a UK sample of children with DSM-IV combined type ADHD.

Method: One hundred and eighteen adolescents and young adults diagnosed with DSM-IV combined type ADHD in childhood were followed for an average of 6 years. Comorbid mental health problems, drug and alcohol use and police contact were compared for those with persistent ADHD, sub-threshold ADHD and population norms taken from the Adult Psychiatric Morbidity Study 2007. Predictors included ADHD symptomology and gender.

Results: Persistent ADHD was associated with greater levels of anger, fatigue, sleep problems and anxiety compared to sub-threshold ADHD. Comorbid mental health problems were predicted by current symptoms

of hyperactivity-impulsivity, but not by childhood ADHD severity. Both persistent and sub-threshold ADHD was associated with higher levels of drug use and police contact compared to population norms.
Conclusions: Young adults with a childhood diagnosis of ADHD showed increased rates of comorbid mental health problems, which were predicted by current levels of ADHD symptoms. This suggests the importance of the continuing treatment of ADHD throughout the transitional years and into adulthood. Drug use and police contact were more common in ADHD but were not predicted by ADHD severity in this sample

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Gene. 2016.

ASSOCIATION OF GLUTATHIONE S-TRANSFERASES M1, T1 AND P1 GENE POLYMORPHISMS WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER IN KOREAN CHILDREN.

Lee JY, Hwang IW, Lim MH, et al.

Attention deficit and hyperactivity disorder (ADHD) is highly heritable disorder and common in school-age children characterized by inattention, hyperactivity and impulsivity. Although its heritability was estimated at 80-90% from family, adoption and twin studies, the molecular etiology of this disorder has not elucidated. Meanwhile, an impaired balance of oxidant-antioxidant status and increased oxidative stress is observed in ADHD, and it may imply a possible relationship between oxidative stress and etiology of ADHD. Glutathione S-transferase (GST) is antioxidant enzymes that play a key role in the cellular detoxification. In the present study, we examined the association between the genetic polymorphisms of GSTM1, GSTP1 and GSTT1, and ADHD in Korean children. Case-control study was conducted with 243 ADHD children and 327 controls. There were no significant associations between the polymorphisms and the incidence of ADHD (p >. 0.05). However, significant associations were observed in the stratified analyses. The frequency of GSTP1 Ile/Ile genotype is reached to the significant level in the hyperactivity subtype (88.2%) compared to controls (64.8%) (p = 0.035) and the frequency of GSTT1-null genotype is significantly higher in the inattentive boys (p = 0.005). Similarly, GSTT1-null genotype showed significant associations in combined subtype (p = 0.016) and hyperactivity subtype (p = 0.036) of the ADHD girls. Thus our result imply that the polymorphisms in the GST genes may affect ADHD, however, replication study for larger sample set and functional studies are crucial to confirm these findings

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International Archives of Otorhinolaryngology. 2015.

AUDITORY PROCESSING ASSESSMENT IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: AN OPEN STUDY EXAMINING METHYLPHENIDATE EFFECTS .

Lanzetta-Valdo BP, Oliveira GAD, Ferreira JTC, et al.

Introduction Children with Attention Deficit Hyperactivity Disorder can present Auditory Processing (AP) Disorder.
Objective The study examined the AP in ADHD children compared with non-ADHD children, and before and after 3 and 6 months of methylphenidate (MPH) treatment in ADHD children.
Methods Drug-naive children diagnosed with ADHD combined subtype aging between 7 and 11 years, coming from public and private outpatient service or public and private school, and age-gender-matched non-ADHD children, participated in an open, non-randomized study from February 2013 to December 2013. They were submitted to a behavioral battery of AP tests comprising Speech with white Noise, Dichotic Digits (DD), and Pitch Pattern Sequence (PPS) and were compared with non-ADHD children. They were followed for 3 and 6 months of MPH treatment (0.5 mg/kg/day).
Results ADHD children presented larger number of errors in DD ($p < 0.01$), and less correct responses in the PPS ($p < 0.0001$) and in the SN ($p < 0.05$) tests when compared with non-ADHD children. The treatment with MPH, especially along 6 months, significantly decreased the mean errors in the DD ($p < 0.01$) and increased the correct response in the PPS ($p < 0.001$) and SN ($p < 0.01$) tests when compared with the performance before MPH treatment.
Conclusions ADHD children show inefficient AP in selected behavioral auditory battery suggesting impaired in auditory closure, binaural integration, and temporal ordering. Treatment with MPH gradually improved

these deficiencies and completely reversed them by reaching a performance similar to non-ADHD children at 6 months of treatment

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J Abnorm Child Psychol. 2016 Apr;44:561-74.

PARENTING STRESS OF PARENTS OF ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Wiener J, Biondic D, Grimbos T, et al.

This study examined parenting stress among parents of adolescents with Attention-Deficit Hyperactivity Disorder (ADHD). The sample comprised 138 adolescents (84 ADHD, 52 boys, 32 girls; 54 non-ADHD, 24 boys, 30 girls) age 13 to 18 and their parents. Mothers (n = 135) and fathers (n = 98) of participating teens completed the Stress Index for Parents of Adolescents. Mothers and fathers of adolescents with ADHD reported more stress than parents of adolescents without ADHD with regard to their children's challenging behaviors (Adolescent domain stress). Mothers of adolescents with ADHD also reported that they experienced elevated levels of stress in terms of role restrictions, feelings of social alienation, conflict with their partner, feelings of guilt and incompetence (Parent domain stress), and relationship with their children (Adolescent-Parent Relationship domain stress; APR). The extent to which clinical levels of adolescent Oppositional Defiant Disorder (ODD) symptoms or externalizing behavior in general were associated with parenting stress depended on the rater of these behaviors. Parenting stress was associated with higher levels of ODD and other externalizing behaviors when these behaviors were rated by parents but not when they were rated by teachers. In addition, over and above adolescent ADHD classification, mothers' self-reported ADHD symptoms were associated with higher parenting stress in the Adolescent and Parent domains, and fathers' self-reported ADHD symptoms were associated with lower APR stress. The results suggest directions that should be considered for addressing parenting stress when designing interventions for families of adolescents with ADHD.

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J Abnorm Child Psychol. 2016 Apr;44:575-86.

POSITIVELY BIASED SELF-PERCEPTIONS IN CHILDREN WITH ADHD: UNIQUE PREDICTOR OF FUTURE MALADJUSTMENT.

Jia M, Jiang Y, Mikami AY.

This study assessed children's overestimations of self-competence (positively biased self-perceptions or positive bias [PB]) relative to parent/teacher ratings of children's competence in predicting children's adjustment in a new setting. Eighty-five children (13 boys and 11 girls with Attention-Deficit/Hyperactivity Disorder [ADHD]; 30 boys and 31 girls who were typically developing [TD]), ages 6.8 to 9.8 years (M = 8.13; SD = 0.82), attended a 2-week summer day camp grouped into same-age, same-sex classrooms with previously unacquainted peers and counselors. Prior to camp, PB was assessed by creating standardized discrepancy scores between children's self-ratings relative to parent or teacher ratings of the children's social and behavioral competence. The relative ability of these discrepancy scores to predict peer preference and oppositionality at camp in relation to parent or teacher ratings alone was evaluated. For children with ADHD, both discrepancy scores and informant ratings of competence were uniquely predictive of peer preference and oppositionality assessed during camp. For TD children, only informant ratings of competence were predictive of outcomes at camp. These results suggest that PB may be a unique predictor of maladjustment within a novel environment for children with ADHD, but not TD children

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Journal of Child Psychology and Psychiatry. 2016 Apr;57:532-37.

THE RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN EXPOSED TO MATERNAL SMOKING DURING PREGNANCY—A RE-EXAMINATION USING A SIBLING DESIGN.

Obel C, Zhu JL, Olsen J, et al.

Background: Conventional cohort studies have consistently shown that exposure to maternal smoking in pregnancy is associated with about twice the risk of attention deficit hyperactivity disorder (ADHD) in the offspring. However, recent studies using alternative designs to disentangle the effect of social and genetic confounders have suggested that confounding may account for the association. In this study we aimed to estimate the association by a sibling design.

Methods: We used a design with half and full siblings in a Danish national register-based cohort on all singletons born between January 1991 and December 2006 and followed until January 2011. Data were available for 90% (N = 968,665) of the singleton live births in the period. We used the combination of the International Classification of Diseases (10th version) diagnosis of hyperkinetic disorder (HKD) and ADHD medication to identify children. We used sibling-matched (conditional) Cox regression to control social and genetic confounding.

Results: Using conventional cohort analyses, we found the expected association between pregnancy smoking and offspring ADHD (adjusted HR 2.01, 95% CI 1.94–2.07). In the sibling analysis, however, we did not detect such a strong association (adjusted HR 1.07, 95% CI 0.94–1.22). There was no difference between results for half- and full sibling analyses. The link between pregnancy smoking and low birth weight remained robust in the sibling design (adjusted OR 1.68, 95% CI 1.33–2.12).

Conclusions: We found no support for prenatal smoking as a strong causal factor in ADHD. Our findings suggest that the strong association found in most previous epidemiological studies is likely to be due to a strong link between maternal smoking and maternal ADHD genetics or shared family environment. Pregnant women should still be encouraged to stop smoking because of other risks, but we have no reason to believe that this would reduce the risk of ADHD in the offspring

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Journal of Child Psychology and Psychiatry. 2016 Apr;57:523-31.

THE OPPOSITE END OF THE ATTENTION DEFICIT HYPERACTIVITY DISORDER CONTINUUM: GENETIC AND ENVIRONMENTAL AETIOLOGIES OF EXTREMELY LOW ADHD TRAITS.

Greven CU, Merwood A, van der Meer JMJ, et al.

Background: Although attention deficit hyperactivity disorder (ADHD) is thought to reflect a continuously distributed quantitative trait, it is assessed through binary diagnosis or skewed measures biased towards its high, symptomatic extreme. A growing trend is to study the positive tail of normally distributed traits, a promising avenue, for example, to study high intelligence to increase power for gene-hunting for intelligence. However, the emergence of such a 'positive genetics' model has been tempered for ADHD due to poor phenotypic resolution at the low extreme. Overcoming this methodological limitation, we conduct the first study to assess the aetiologies of low extreme ADHD traits.

Methods: In a population-representative sample of 2,143 twins, the Strength and Weaknesses of ADHD Symptoms and Normal behaviour (SWAN) questionnaire was used to assess ADHD traits on a continuum from low to high. Aetiological influences on extreme ADHD traits were estimated using DeFries–Fulker extremes analysis. ADHD traits were related to behavioural, cognitive and home environmental outcomes using regression.

Results: Low extreme ADHD traits were significantly influenced by shared environmental factors (23–35%) but were not significantly heritable. In contrast, high-extreme ADHD traits showed significant heritability (39–51%) but no shared environmental influences. Compared to individuals with high extreme or with average levels of ADHD traits, individuals with low extreme ADHD traits showed fewer internalizing and externalizing behaviour problems, better cognitive performance and more positive behaviours and positive home environmental outcomes.

Conclusions: Shared environmental influences on low extreme ADHD traits may reflect passive gene-environment correlation, which arises because parents provide environments as well as passing on genes. Studying the low extreme opens new avenues to study mechanisms underlying previously neglected positive

behaviours. This is different from the current deficit-based model of intervention, but congruent with a population-level approach to improving youth wellbeing.

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Journal of Child Psychology and Psychiatry. 2016 Apr;57:540-48.

FEVER AND INFECTIONS IN PREGNANCY AND RISK OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN THE OFFSPRING.

Dreier JW, Andersen AMN, Hvolby A, et al.

Background: Fever and infections are common events during pregnancy, and have been shown to be associated with neurodevelopmental impairment in the offspring. The evidence in relation to attention deficit/hyperactivity disorder (ADHD) is, however, nonexistent for fever and limited for infections. The aim of this study was therefore to investigate the impact of these exposures on the occurrence of ADHD in the offspring, considering gestational timing as well as intensity of exposure.
Methods: The study was conducted within the Danish National Birth Cohort, using data on 89,146 pregnancies enrolled during 1996–2002. Exposure to fever and infections were assessed prospectively in two computer-assisted telephone interviews during pregnancy and ADHD status in the child was determined using registry information from three nation-wide patient and prescription registers. Stratified Cox regressions were used to calculate adjusted hazard ratios of ADHD occurrence.
Results: The analyses revealed no overall association between maternal exposure to fever or infections and ADHD in the offspring [adjusted hazard ratio (aHR): 1.03, 95% confidence interval (CI): 0.93–1.13 and aHR: 1.01, 95% CI: 0.92–1.11]. When the exposures were considered during specific gestational periods, increased rates of ADHD were observed following fever in gestational weeks 9–12 (aHR: 1.33, 95% CI: 1.12–1.58), and genitourinary infections in weeks 33–36 (aHR: 1.60, 95% CI: 1.13–2.26).
Conclusions: Although no overall adverse association between fever and infections in pregnancy and ADHD in the offspring was found, the analyses indicated that exposures during specific time windows of the pregnancy could be associated with increased ADHD occurrence.

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Journal of Child Psychology and Psychiatry. 2016 Apr;57:472-80.

IDENTIFYING MECHANISMS THAT UNDERLIE LINKS BETWEEN COMT GENOTYPE AND AGGRESSION IN MALE ADOLESCENTS WITH ADHD.

van Goozen SHM, Langley K, Northover C, et al.

Background: There is a known strong genetic contribution to aggression in those with ADHD. In a previous investigation of a large population cohort, impaired 'emotional/social cognitive' processing, assessed by questionnaire, was observed to mediate the link between COMT Val158Met and aggression in individuals with ADHD. We set out to replicate and extend this finding in a clinical sample, using task-based and physiological assessments of emotional and cognitive processing. Our aim was to test the hypothesis that directly assessed emotional processing mediates the link between COMT Val158Met and aggression in young people with ADHD.
Methods: Males aged 10–17 years with ADHD were recruited from UK community clinics (n = 194). Research diagnostic interviews (parent and child) were used to assess psychopathology and generate DSM-IV Conduct Disorder symptom scores. Participants completed tasks assessing executive function (response inhibition and set shifting), empathy for fear, sadness and happiness, and fear conditioning [measured using skin conductance responses (SCR) to aversive stimuli].
Results: COMT Val allele carriers showed poorer response inhibition ($F = 5.27$, $p = .02$) and set shifting abilities ($F = 6.45$, $p = .01$), reduced fear empathy ($F = 4.33$, $p = .04$) and reduced autonomic responsiveness (lower SCRs) to the conditioned aversive stimulus ($F = 11.74$, $p = .001$). COMT Val158Met did not predict impairments in recognising others' emotions or affective empathy for happiness or sadness. Mediation analysis revealed that impaired fear-related mechanisms indirectly mediated the link between COMT Val158Met and aggression.

Conclusion: Our findings suggest fear mechanisms as possible targets for psychological interventions to disrupt links between genetic risk and aggressive outcomes in ADHD. Our findings also reveal the potential of hypothesis-driven approaches for identifying neuropsychological mechanisms that mediate genetic risk effects on behaviour and psychopathology.

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Journal of Child Psychology and Psychiatry. 2016 Apr;57:502-09.

LINKS BETWEEN WITHIN-PERSON FLUCTUATIONS IN HYPERACTIVITY/ATTENTION PROBLEMS AND SUBSEQUENT CONDUCT PROBLEMS.

Arnett AB, Pennington BF, Young JF, et al.

Background: The onset of hyperactivity/impulsivity and attention problems (HAP) is typically younger than that of conduct problems (CP), and some research supports a directional relation wherein HAP precedes CP. Studies have tested this theory using between-person and between-group comparisons, with conflicting results. In contrast, prior research has not examined the effects of within-person fluctuations in HAP on CP.
Method: This study tested the hypothesis that within-person variation in HAP would positively predict subsequent within-person variation in CP, in two population samples of youth (N = 620) who participated in identical methods of assessment over the course of 30 months. Three-level, hierarchical models were used to test for within-person, longitudinal associations between HAP and CP, as well as moderating effects of between-person and between-family demographics.
Results: We found a small but significant association in the expected direction for older youth, but the opposite effect in younger and non-Caucasian youth. These results were replicated across both samples.
Conclusions: The process by which early HAP relates to later CP may vary by age and racial identity.

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J Nerv Ment Dis. 2016.

KNOWLEDGE AND ATTITUDES ABOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND SPECIFIC LEARNING DISORDER IN AN URBAN INDIAN POPULATION.

Mukherjee S, Shah HR, Ramanathan S, et al.

Attention-deficit/hyperactivity disorder (ADHD) and specific learning disorders (SLDs) are an important cause of scholastic backwardness among children and often go unrecognized. Few studies have examined knowledge and attitudes toward ADHD and SLD among school-aged children. To address this deficit, 120 school-aged children, attending a child guidance clinic in Mumbai, were interviewed using a questionnaire that examined children's knowledge and attitudes about ADHD and SLD. The results were compared both qualitatively and quantitatively with a frequently occurring medical illness, common cold. Approximately 80% to 100% of children were aware of their illness; however, a large variation was noted in the proportion of children (15%-80%) who could describe their symptoms, provide accurate attributions for their illness, and identify treatment modalities. Children with ADHD reported greater control over their illness. The study identified a significant lack of knowledge about ADHD and SLD among school-aged children in India and discusses implications of this finding

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J Neural Transm. 2016;1-7.

A CANDIDATE GENE INVESTIGATION OF METHYLPHENIDATE RESPONSE IN ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PATIENTS: RESULTS FROM A NATURALISTIC STUDY.

Hegvik TA, Jacobsen KK, Fredriksen M, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common childhood onset neuropsychiatric disorder with a complex and heterogeneous symptomatology. Persistence of ADHD symptoms into adulthood is common. Methylphenidate (MPH) is a widely prescribed stimulant compound that may be effective against ADHD symptoms in children and adults. However, MPH does not exert satisfactory effect in all patients. Several genetic variants have been proposed to predict either treatment response or adverse effects of stimulants.

We conducted a literature search to identify previously reported variants associated with MPH response and additional variants that were biologically plausible candidates for MPH response. The response to MPH was assessed by the treating clinicians in 564 adult ADHD patients and 20 genetic variants were successfully genotyped. Logistic regression was used to test for association between these polymorphisms and treatment response. Nominal associations ($p < 0.05$) were meta-analysed with published data from previous comparable studies. In our analyses, rs1800544 in the ADRA2A gene was associated with MPH response at a nominal significance level (OR 0.560, 95 % CI 0.329ΓÇô0.953, $p = 0.033$). However, this finding was not affirmed in the meta-analysis. No genetic variants revealed significant associations after correction for multiple testing ($p < 0.00125$). Our results suggest that none of the studied variants are strong predictors of MPH response in adult ADHD as judged by clinician ratings, potentially except for rs1800544. Consequently, pharmacogenetic testing in routine clinical care is not supported by our analyses. Further studies on the pharmacogenetics of adult ADHD are warranted

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J Psychiatr Pract. 2016;22:22-30.

COMORBIDITY OF ADHD AND HIGH-FUNCTIONING AUTISM: A PILOT STUDY ON THE UTILITY OF THE OVERFLOW MOVEMENTS MEASURE.

Pitzianti M, D'Agati E, Pontis M, et al.

Objectives: Children with attention-deficit/hyperactivity disorder (ADHD) and high-functioning autism (HFA) commonly show neurological soft signs (NSS) and impairment in executive functioning (EF). Many children with HFA may experience ADHD-like symptoms, and the 2 disorders may be comorbid. Evaluating NSS and EF in drug-naive subjects with ADHD, HFA, and ADHD+HFA compared with healthy children may be critical in understanding and differentiating the biological substrates and cognitive phenotypes associated with these disorders. The goal of this study was to evaluate possible differences among these groups in motor and EF and the effects of comorbidity.

Methods: Thirty-eight drug-naive patients (13 with ADHD, 13 with HFA, 12 with ADHD+HFA) and 13 healthy controls (HC) were evaluated on measures of planning, verbal working memory, and response inhibition. Evaluation of NSS involved 3 primary variables: overflow movements (OM), dysrhythmia, and speed of timed activities.

Results: The group with ADHD and the group with HFA both showed impairment on measures of planning, response inhibition, and verbal working memory compared with the HC group. Moreover, the group with ADHD showed a greater number of NSS compared with the HC group, whereas the group with HFA showed greater dysrhythmia and slowness compared with the HC group. The group with ADHD+HFA showed deficits of planning and response inhibition and a greater number of NSS compared with the HC group. The group with ADHD+HFA showed greater impairment of planning compared with the other clinical groups and greater dysrhythmia compared with the group with ADHD.

Conclusion: According to our data, the OM measure revealed a gradient in which ADHD was at one extreme (more OM) and HFA at the other extreme (less OM), whereas ADHD+HFA showed a number of OM that fell in the middle between the numbers for the ADHD and HFA groups

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J Sleep Res. 2016.

NO OBJECTIVELY MEASURED SLEEP DISTURBANCES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bergwerff CE, Luman M, Oosterlaan J.

The main goal of this study was to gain more insight into sleep disturbances in children with attention-deficit/hyperactivity disorder, using objective measures of sleep quality and quantity. The evidence for sleep problems in children with attention-deficit/hyperactivity disorder thus far is inconsistent, which might be explained by confounding influences of comorbid internalizing and externalizing problems and low socio-economic status. We therefore investigated the mediating and moderating role of these factors in the association between attention-deficit/hyperactivity disorder and sleep problems. To control for the effects of

stimulant medication use, all participants were tested free of medication. Sixty-three children with attention-deficit/hyperactivity disorder and 61 typically developing children, aged 6-13 years, participated. Sleep was monitored for one to three school nights using actigraphy. Parent and teacher questionnaires assessed symptoms of attention-deficit/hyperactivity disorder, internalizing behaviour, oppositional defiant disorder and conduct disorder. Results showed no differences between the attention-deficit/hyperactivity disorder and typically developing group in any sleep parameter. Within the attention-deficit/hyperactivity disorder group, severity of attention-deficit/hyperactivity disorder symptoms was not related to sleep quality or quantity. Moderation analyses in the attention-deficit/hyperactivity disorder group showed an interaction effect between attention-deficit/hyperactivity disorder symptoms and internalizing and externalizing behaviour on total sleep time, time in bed and average sleep bout duration. The results of our study suggest that having attention-deficit/hyperactivity disorder is not a risk factor for sleep problems. Internalizing and externalizing behaviour moderate the association between attention-deficit/hyperactivity disorder and sleep, indicating a complex interplay between psychiatric symptoms and sleep

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Medicina Clinica. 2015;145:471-76.

CHILDREN'S RELATIVE AGE IN CLASS AND MEDICATION FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER. A POPULATION-BASED STUDY IN A HEALTH DEPARTMENT IN SPAIN.

Librero J, Izquierdo-María R, García-Gil M, et al.

Background and objective Previous studies in various countries have shown that the youngest school children in the same class-grade are more likely to be treated for attention-deficit/hyperactivity disorder (ADHD) than their older classmates. The aim of this study is to determine in the Spanish setting whether younger relative age children in each grade have a higher prevalence of treatment for ADHD.

Subjects and methods Population, observational, cross-sectional study in a health department, using prevalence data (November 2013) of treatment for ADHD in children aged 6-12 years. Data was obtained from the information systems of the Valencia Ministry of Health and multivariate models were used to estimate the prevalence ratio of treatment according to the month of birth of children in each grade.

Results Twenty thousand two hundred and thirty-seven children were included of whom 1.73% were treated for ADHD (boys: 2.70%; girls: 0.71%) in October 2013. The prevalence of treatment increased with age, in males, and in youngest children (born in the last months of each year). In the multivariate analysis, the prevalence of treatment in the youngest children (born in the months of August to December) was 2.5 to 3 times higher than in their older classmates (born in January).

Conclusions The younger children relative to their classmates are more likely to be treated pharmacologically with methylphenidate and/or atomoxetine

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Neurology. 2016;86.

IDENTIFICATION OF ADHD IN YOUTH WITH EPILEPSY.

Kral M, Lally M, Boan A.

Objective. To determine the most efficient way to identify Attention-Deficit/Hyperactivity Disorder (ADHD) in a large, clinic-referred sample of youth with epilepsy.

Background. Children with epilepsy are at increased risk for ADHD. Historically, this comorbidity has been under-identified and undertreated.

Methods. Youth with epilepsy who were referred for comprehensive neuropsychological evaluation due to behavioral or learning problems comprised the sample. Data were obtained via archival record review. Youth with epilepsy were grouped according to ADHD diagnosis (no ADHD, ADHD - Combined Type, and ADHD - Predominantly Inattentive Type) and compared on a number of neurocognitive variables, seizure-related variables, and parent and teacher-completed behavior rating scales. Data were examined via generalized linear models with post hoc pairwise comparisons, employing Tukey procedure where appropriate.

Results. Youth in this clinical case series (N=204) demonstrated a significantly higher rate of ADHD diagnosis (65[percnt]) as compared to the general pediatric population (5[percnt]-9[percnt]). ADHD-

Combined Type was identified with slightly greater frequency than ADHD - Predominantly Inattentive Type. For all three groups (no ADHD, ADHD - Combined Type, and ADHD - Predominantly Inattentive Type), age of seizure onset, seizure classification, and seizure frequency did not differ significantly. The groups also did not differ on most neurocognitive variables examined (intellectual functioning, working memory, processing speed, and sustained attention). Significant group differences were found for parent and teacher-completed behavior rating scales assessing inattention, hyperactivity, and executive dysfunction. Specifically, the no ADHD group did not demonstrate clinically significant levels of inattention, hyperactivity, or executive dysfunction (BASC-2 and BRIEF T-scores<65). In contrast, the ADHD groups demonstrated clinically elevated levels of inattention, hyperactivity, and executive dysfunction (BASC-2 and BRIEF T-scores>65).
Conclusion. Inclusion of behavior rating scales as part of routine care in neurology clinics may be the most efficient and cost effective way to identify ADHD in youth with epilepsy

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Neuropsychiatr Dis Treat. 2016 Mar;12.

OCCURRENCE OF ADHD IN PARENTS OF ADHD CHILDREN IN A CLINICAL SAMPLE.

Starck M, Grünwald J, Schlarb AA.

Background: Despite the fact that there is a large amount of research on childhood attention deficit hyperactivity disorder (ADHD) treatment and an increasing amount of research on adult ADHD, little is known about the prevalence and influence of parental ADHD. Therefore, this study examined the frequency of parental ADHD in a clinical sample of German children suffering from ADHD. We also tried to find different levels of symptom severity for prognostic relevance. Furthermore, the association between subtypes of ADHD in children and their parents was investigated.
Method: In this study, parents of 79 ADHD children were screened for ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition and International Classification of Diseases, 10th edition. The Wender Utah Rating Scale and the ADHS-Self-Report were given to 75 mothers and 49 fathers for retrospective and current symptoms. Frequency of ADHD symptoms and severity groups was calculated and relationship between parental and children's ADHD was tested.
Results: ADHD occurrence for mothers of children with ADHD was 41.3%, for fathers 51.0%. About 16.0% of the mothers had a mixed type, 9.3% had a hyperactive-impulsive subtype, and 16.0% had an inattentive subtype. Of the fathers, 18.4% had a mixed type, 10.2% had a hyperactive-impulsive subtype, and 22.4% had an inattentive subtype; 61% of the mothers and 46.9% of the fathers had low symptom severity. Medium symptom severity was reported by 37.7% mothers and 46.9% fathers, while 1.3% of the mothers and 6.2% of the fathers showed severe symptoms. No significant correlation between parental and child diagnoses was observed.
Conclusion: As nearly half of the parents suffered from ADHD, these results are a matter of concern in families with ADHD children. Besides parent–child interactions, parental ADHD symptoms might influence parental education style and also effects parent training as well as the child's therapy outcome. In the future, parents should be screened for ADHD symptoms if they or their child receive treatment and to adjust processes and design of treatment to the symptoms

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Neuropsychobiology. 2016;131-38.

EVENT-RELATED POTENTIALS CORRELATE WITH THE SEVERITY OF CHILD AND ADOLESCENT PATIENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Yamamuro K, Ota T, Iida J, et al.

BACKGROUND: Attention deficit/hyperactivity disorder (ADHD) symptoms can continue through adolescence and adulthood, including difficulty in staying focused, paying attention, and controlling behavior, as well as hyperactivity. While children and adolescents with ADHD have functional impairments at multiple dimensions, there are no objective biological indicators to assess the severity of ADHD. Event-related potentials (ERPs) are widely used as a noninvasive method for evaluating sensory and cognitive processes involved in attention tasks. Previous studies have shown that P300 amplitude or latency, a main component

in ERPs, is altered in patients with ADHD. However, little is known about the relationship between P300 and the severity of ADHD symptoms.
METHOD: We sought to measure both P300 amplitude and latency in ERPs during auditory oddball tasks in 44 patients with ADHD (mean age ± SD 10.28 ± 3.43 years) and 15 age- and gender-matched normally developing children (11.40 ± 3.02 years). In ADHD patients, we also assessed symptom severity using the ADHD rating scale-IV-Japanese version.
RESULT: In ADHD groups, P300 amplitude and latency were attenuated and prolonged compared to controls at the frontocentral, centroparietal, and parietal positions. Furthermore, levels of P300 latency at these positions are positively correlated with the inattention subscale scores measured by the ADHD rating scale-IV-Japanese version.
CONCLUSIONS: The present study revealed that the degree of P300 latency might reflect the severity of ADHD symptoms with children and adolescents, suggesting that ERPs are a useful technique to evaluate the severity of ADHD symptoms

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Pharmacopsychiatry. 2015.
CYTOGENETIC EFFECTS OF CHRONIC METHYLPHENIDATE TREATMENT AND CHRONIC SOCIAL STRESS IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Kittel-Schneider S, Spiegel S, Renner T, et al.
Introduction: Methylphenidate (MPH) is widely used to treat childhood and adult attention-deficit/hyperactivity disorder (ADHD). However, there are still safety concerns about side effects in long-term treatment. The aim of this study was to assess cytogenetic effects of chronic MPH treatment in adult ADHD and to find out if chronic social stress is attenuated by medication and to investigate whether chronic psychosocial stress leads to mutagenic effects by itself.
Methods: Lymphocytes for micronucleus assay and saliva samples for cortisol measurement were collected from adult ADHD patients and healthy controls. Stress exposure of the last 3 months was assessed by TICS (Trier Inventory for Chronic Stress).
Results: We could not detect an influence of MPH treatment on cytogenetic markers. ADHD patients displayed significantly higher chronic stress levels measured by TICS compared to healthy controls which were influenced by duration of MPH treatment. ADHD patients also showed significantly lower basal cortisol levels.
Discussion: We could corroborate that there are neither cytogenetic effects of chronic stress nor of chronic MPH intake even after several years of treatment

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Psychiatry Res. 2015;230:227-32.
A FOUR-YEAR FOLLOW-UP CONTROLLED STUDY OF STRESS RESPONSE AND SYMPTOM PERSISTENCE IN BRAZILIAN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT DISORDER AND HYPERACTIVITY (ADHD).
Palma SMM, Natale ACMP, Maria Calil H.
This study evaluated children and adolescents with Attention Deficit Disorder andHyperactivity Disorder (ADHD), reassessing them at a four-year follow-up. Their cortisol response to a stress stimulus was measured twice. ADHD symptom persistence, development of comorbidities, and psychostimulant usage were also reassessed. The initial sample consisted of 38 ADHD patients and 38 healthy controls, age ranging 6-14. At the follow-up, there were 37 ADHD patients and 22 healthy controls, age ranging 10-18. ADHD was classified as persistent if the patients fulfilled all DSM IV criteria for syndromic or subthreshold or had functional impairment. Salivary cortisol samples were collected prior to the application of a cognitive stressor (Continuous Performance Test - CPT), and at three time intervals afterwards at baseline and at the follow-up. Their reassessment showed that 75% had persistent symptoms, psychiatric comorbidities (oppositional defiant and behavioral disorders), functional and academic impairement. Only seven patients were on medication. The ADHD group's cortisol levels were lower than those measured four years earlier, but cortisol

concentrations were similar for both ADHD and control groups at the four-year follow-up. The cortisol results suggest that HPA axis reactivity could be a marker differentiating ADHD from ADHD with comorbidities

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Psychiatry Res. 2016;240:1-3.
The prevalence of symptoms of attention-deficit/hyperactivity disorder in parents of children with autism spectrum disorder.
Bonatto SJ, Kerner M, Merelles S, et al.
This study aims to estimate the prevalence of symptoms of attention-deficit/hyperactivity disorder (ADHD) in parents of children with autism spectrum disorder (ASD). This is a cross-sectional study conducted with the parents of 89 children previously diagnosed with ASD. The research instrument used was the 18-item Adult ADHD Self-Report Scale (ASRS). Symptoms of ADHD were present in 10.4% of the mothers of children with a diagnosis of ASD and in 11.3% of the fathers. These results suggest that the prevalence of symptoms of ADHD in the parents of children with autism is higher than that found in the general adult population

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Reproductive Sciences. 2016;23:145A.
ASSOCIATION BETWEEN HYPEREMESIS GRAVIDARUM AND CHILDHOOD ATTENTION DEFICIT HYPERACTIVITY DISORDER BY GESTATIONAL AGE AND RACE/ETHNICITY.
Getahun D, Chiu V, Michael FJ.
INTRODUCTION: Hyperemesis gravidarum (HG) is associated with adverse perinatal outcomes. It may deprive the fetus of necessary nutrients and thereby impair fetal brain development. As little is known about the association between HG and attention deficit hyperactivity disorder (ADHD), we examined these associations and whether the risk varies by gestational age and maternal race/ethnicity.
METHODS: A retrospective cohort study of singleton born children age 3-17 years delivered at ΓëÑ28 weeks of gestation (n=393,535) in Kaiser Permanente Southern California (KPSC) hospitals (1991-2009) was performed using the Perinatal Service System, Hospital Inpatient, Outpatient physician encounter, and Pharmacy records. ICD-9 codes from hospitalizations during pregnancy and infant birth certificates as well as pharmacy records on medication specific for ADHD were used to ascertain the exposure and outcomes of interest. Adjusted hazard ratio (HR) and 95% confidence interval (CI) were used to quantify the associations.
RESULTS: Two percent of pregnancies were complicated by HG. Compared with exposed children, unexposed children were more likely to be male and of White or African-American race/ethnicity. Exposed children were more likely than unexposed children to be diagnosed with ADHD (HR 1.25, 95%CI 1.11-1.41). A stratified analysis by gestational age revealed that exposure during first, second, and third trimester were associated with significantly increased risk; 1.18-fold (95%CI 1.02, 1.36), 1.42-fold (95%CI 1.10, 1.84), and 1.84-fold (95%CI 1.07-3.17), respectively. PSD was associated with increased risk of ADHD for African American and White racial/ethnic groups.
CONCLUSIONS: The results suggest that HG is associated with increased risk of childhood ADHD. Identification of at-risk children may provide the opportunity for early diagnosis and initiate treatment when it is more effective

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Sleep Med. 2016;17:163.
WHAT IS THE ROLE OF ADHD SYMPTOMS IN OBESITY AFFECTING COGNITIVE OUTCOMES?
Yang R, Gao W, Li R, et al.

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CHILD NEUROPSYCHOLOGY, 2016
http://dx.doi.org/10.1080/09297049.2016.1172561

Routledge
Taylor & Francis Group

Time-based prospective memory difficulties in children with ADHD and the role of time perception and working memory

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ABSTRACT

Time-based prospective memory (PM) is the ability to remember to perform an intended action at a given time in the future. It is a competence that is crucial for effective performance in everyday life and may be one of the main causes of problems for individuals who have difficulty in planning and organizing their life, such as children with attention deficit/hyperactivity disorder (ADHD). This study systematically examines different aspects of time-based PM performance in a task that involves taking an action at a given future time in a group of 23 children with ADHD who were compared with a matched group of typically-developing (TD) children. The children were asked to watch a cartoon and then answer a questionnaire about its content (ongoing task). They were also asked to press a key every 2 minutes while watching the cartoon (PM task). The relationships of time perception and verbal working memory with PM performance were examined by administering appropriate tasks. The results showed that the children with ADHD were less accurate than the TD children in the PM task and exhibited less strategic time-monitoring behavior. Time perception was found to predict PM accuracy, whereas working memory was mainly involved in time-monitoring behavior, but this applied more to the TD group than to the ADHD group, suggesting that children with ADHD are less able to use their cognitive resources when meeting a PM request.

ARTICLE HISTORY
Received 10 August 2015
Accepted 27 March 2016
Published online
19 April 2016

KEYWORDS
Attention deficit/hyperactivity disorder; time-based prospective memory; time monitoring; time perception; working memory

Prospective memory (PM) is defined as the ability to remember to perform a planned action in the future (Kliegel, McDaniel, & Einstein, 2008; McDaniel & Einstein, 2000). PM is a complex construct that includes multiple phases (Ellis, 1996; Kliegel, Martin, McDaniel, & Einstein, 2002). The first phase (intention formation) concerns PM intention formation, i.e., the individual must plan which actions to perform at a future time. In the second phase (intention retention), this PM intention has to be kept in mind while performing other ongoing tasks. The third phase (intention initiation) begins when it is time to initiate the intended action, i.e., when the individual has to inhibit ongoing activities and execute the intended action. In the fourth and final phase (intention execution), the intended action has to be carried out, as previously planned, on the individual's own initiative. Depending on the cue that identifies the appropriate

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moment for initiating the intended action, the literature distinguishes between event- and time-based PM tasks (Kliegel et al., 2008; McDaniel & Einstein, 2000). When the PM cue is event-based, the intended action is initiated and executed in response to a given event that may help people recall their intention (e.g., they remember to mail a letter when they see a mail box). A condition that is usually more challenging is when no such priming cue is available and the PM request is time-based, i.e., the intended action has to be executed at a given time or after a given time interval (e.g., remembering to go to a music class at 3 p.m.; Einstein & McDaniel, 1996).

Focusing on time-based PM paradigms, in most laboratory studies participants are instructed to press a key at or after a given time interval while they are engaged in an ongoing task, and they are given the chance to check the time whenever they wish. Harris and Wilkins (1982) described a "test-wait-test-exit" process that seems to be involved in time-based PM tasks. To accomplish the time-based PM task successfully, participants check the time on a clock and then wait until another clock check seems appropriate. According to the authors, participants continue looping through this clock-checking and waiting cycle until they reach the "critical period" near the time when it becomes appropriate to take action.

Time-based PM performance can be assessed in terms of PM accuracy (i.e., accuracy in taking action at the target time), ongoing task accuracy, and time-monitoring behavior (Einstein, McDaniel, Richardson, Guynn, & Cunfer, 1995; Mäntylä & Carelli, 2006). Efficient time monitoring requires a strategic scheduling of the actions involved (i.e., when and how to check the time) and striking the right balance between the cost of monitoring and the cost of having inaccurate information about the environment (Mäntylä & Carelli, 2006). Previous studies found certain regularity in time-monitoring behavior that revealed a J-shaped curve, which remained flat or rose only slightly during the first part of the time interval, then clock-checking increased shortly before the target time (Einstein et al., 1995; Harris & Wilkins, 1982; Mäntylä & Carelli, 2006). A high amount of clock-checking has the advantage of providing more temporal information and therefore increasing the likelihood of accurately responding at the target time. Significant correlations have been reported between monitoring frequency and PM accuracy, i.e., participants who increased their clock-checking before the target time (efficient strategic monitoring) had a better PM performance (Einstein et al., 1995; Mäntylä & Carelli, 2006; Mioni & Stablum, 2014).

The present study focuses on time-based PM difficulties in children with attention deficit/hyperactivity disorder (ADHD), comparing them with a group of matched typically-developing (TD) children. PM seems to be a crucial issue in children with ADHD, as they often reportedly forget to execute their planned actions (Kerns & Price, 2001; Kliegel, Ropeter, & Mackinlay, 2006; Talbot & Kerns, 2014; Zinke et al., 2010).

Time-Based PM Performance in Children

Performance on PM tasks has consistently been shown to improve with age, in fact older children tend to carry out their intended actions more often than younger children (Kerns & Price, 2001; Mackinlay, Kliegel, & Mäntylä, 2009; Mahy et al., 2015; Mahy, Moses, & Kliegel, 2014). Time-based PM has been shown to develop between 7 and 12 years of age, as children become more proficient in the application

of time-checking strategies (Ceci & Bronfenbrenner, 1985; Kvavilashvili, Kyle, & Messer, 2008; Mahy et al., 2014, 2015) and as their working memory abilities improve, which may support their time-based PM performance (Kerns, 2000; Mahy et al., 2015; Voigt et al., 2014). Mäntylä, Carelli, and Forman (2007) showed that children between 8 and 12 years of age monitored the time more often than adults, and they were equally accurate at meeting the target time. Both the children and the adults provided more than 80% of the target responses within 10 s, but the children relied more on external timekeeping than the adults in order to obtain the same level of time-based PM performance. To further investigate developmental changes in time-monitoring behavior, Forman, Mäntylä, and Carelli (2011) retested the children involved in the Mäntylä et al. (2007) study four years later, when they were between 12 and 16 years of age. The results showed a clear change in the sample's monitoring strategy: their time-monitoring rate dropped from approximately nine instances of clock-checking to less than two during a task lasting 5 minutes. This less frequent time monitoring had a negative impact on their PM accuracy, and the authors concluded that the participants, now adolescents, overestimated their timekeeping capacity; in fact, the reduced monitoring had a large cost in timing accuracy. While monitoring the time usually has its benefits in terms of PM accuracy, it may impair ongoing task performance because it absorbs more cognitive resources that might otherwise be allocated elsewhere. Participants who engage in more clock-checking also have to switch more frequently between clock-checking and performing the ongoing task, and this also taxes their cognitive resources (Schnitzspahn, Stahl, Zeintl, Kaller, & Kliegel, 2012). Mahy et al. (2015) tested 5- to 11-year-old children with a time-based PM task and used the Dresden Cruiser (Kerns, 2000) as the ongoing task, a driving simulation game that requires children to drive a vehicle on a road without crashing into other cars and to refuel the car when the fuel is low. The authors manipulated the cognitive demand by adding a secondary task that requires divided attention between playing the Dresden Cruiser and concurrently executing a verbal labeling task in order to test the effect of reduced cognitive functions on time-based PM performance. In the ongoing task (baseline condition), the older children outperformed the younger children and the children generally performed better in the full-attention than in the divided-attention condition. Adding the secondary task had a greater impact on time-monitoring behavior than on PM accuracy; the older children increased their clock-checking frequency during the "critical period" more than the younger children, whereas no interaction between age and the secondary task was seen for PM accuracy. Clock-checking frequency during the "critical period" emerged as a significant predictor of PM performance.

Time Perception and Working Memory in Time-Based PM

It has been suggested that time-based PM relies partly on time perception, as well as on executive functions (Mahy et al., 2015; Voigt et al., 2014). In fact, the ability to perform the intended action at a precise time in the future is fundamental to time-based PM, so time perception should be a crucial component of time-based PM performance (Glicksohn & Myslobodsky, 2006). Very few studies have specifically investigated the relationships between PM accuracy, time-monitoring behavior and time perception. Only one study examined children's performance (Mackinlay et al., 2009), while the

others concerned students (Labelle, Graf, Grondin, & Gagné-Roy, 2009), older adults (McFarland & Glisky, 2009; Mioni & Stablum, 2014), or patients with a traumatic brain injury (TBI; Mioni, Stablum, McClintock, & Cantagallo, 2012).

Labelle et al. (2009) found no correlation between PM accuracy and performance in a temporal task, but time perception correlated significantly with monitoring frequency. McFarland and Glisky (2009) found no significant association between PM indices (accuracy and time-monitoring frequency) and time perception in older adults, whereas Mioni and Stablum (2014) found that time perception predicted time-monitoring behavior rather than PM accuracy. Mioni et al. (2012) with TBI patients also found a significant correlation between time perception and time-monitoring behavior. Finally, Mackinlay et al. (2009) found a significant correlation for time perception and PM accuracy, but not for time-monitoring frequency.

The different results may be due to methodological differences not only in the time-based PM tasks used but also in the time-perception tasks and the time intervals considered. The choice of temporal task and time interval is critical when investigating time perception: each temporal task and time interval (i.e., above or below one second) can highlight differences in temporal processing and require different cognitive processes (Grondin, 2010; Mioni et al., 2012). The temporal task adopted by Labelle et al. (2009) and McFarland and Glisky (2009) was a time-production task in which participants were asked to produce a time interval equivalent to a previously indicated duration (i.e., "produce 1 second"), therefore they had to translate an objectively labeled duration into a subjectively experienced duration (Grondin, 2010). Mioni et al. (2012) and Mioni, Stablum, McClintock, and Grondin (2014) used a time-reproduction task in which participants were asked to reproduce the duration of a previously presented stimulus (see also Grondin, 2010). Mackinlay et al. (2009) used four different temporal tasks that included a verbal estimation task, a production task (in filled and unfilled conditions), and a retrospective estimation task. As for the time intervals considered, both Labelle et al. (2009) and Mackinlay et al. (2009) asked participants to judge time intervals that corresponded directly to the target time of the time-based PM task (Labelle et al., 2009 used intervals of 30, 60, or 90 s, while Mackinlay et al., 2009 used intervals of 120 s). In the McFarland and Glisky (2009) study, participants were asked to press the target key every 5 minutes and produce 10 s in a time-production task. In Mioni et al. (2012, 2014), participants were asked to press the target key every 5 minutes and to reproduce three different time intervals (4, 9, and 14 s), chosen for their similarity to the monitoring frequency typically seen in these participants, particularly in the last minute before the target time.

As already mentioned, adequate executive functions are considered crucial for time-based PM performance (Kliegel et al., 2002; Kretschmer, Voigt, Friedrich, Pfeiffer, & Kliegel, 2014; Martin, Kliegel, & McDaniel, 2003). A particular function that seems to have a role in this setting is working memory, which has been identified as an important predictor of PM performance in both adults (Kliegel et al., 2002) and children (Mahy et al., 2015; Voigt et al., 2014). Working memory is needed to actively maintain the PM intention while working on the ongoing task. Kerns (2000) and Mackinlay et al. (2009) reported significant correlations between PM accuracy and working memory in children. Interestingly, Mäntylä et al. (2007) extended these results, demonstrating that working memory is also related to children's time-monitoring

behavior. The authors inferred that children and adults with better working-memory abilities are able to update and maintain temporal information in their working memory more efficiently. This would produce a continuous sense of time that would give rise to more strategic time-monitoring behavior.

Time-Based PM Performance in Children with ADHD

ADHD is a neuropsychological disorder characterized by a persistent and pervasive pattern of impulsiveness, inattention, and hyperactivity. Children with ADHD have trouble organizing and finishing activities (e.g., schoolwork, chores), and they often forget to perform daily activities (American Psychiatric Association, 2013). One of their difficulties stems from an impaired ability to plan ahead and carry out planned actions in an organized way. It has been suggested that the behavioral symptoms of ADHD are associated with impairments in executive functions (Biederman et al., 2004; Pennington & Ozonoff, 1996; Seidman, 2006), including response inhibition (Barkley, 1997; Geurts, Verté, Oosterlaan, Roeyers, & Sergeant, 2004), working memory (McInnes, Humphries, Hogg-Johnson, & Tannock, 2003), and planning (Clark, Prior, & Kinsella, 2000). Children with ADHD have also been attributed time-perception dysfunctions (Noreika, Falter, & Rubia, 2013). Given the resources needed in time-based PM tasks (Kretschmer et al., 2014), children with ADHD can be expected to have a time-based PM dysfunction, and there is some evidence to support this prediction. For example, Kerns and Price (2001) used a computer game developed by Kerns (2000) called CyberCruiser in which children were asked to drive a car in a busy street (ongoing task) and to remember to fill up the gas tank (time-based PM task). The primary purpose of the game was to score as many points as possible by avoiding other cars while driving faster around the course and passing other cars. The second task involved monitoring the fuel level by pressing a button on the joystick (the total number of button presses was recorded as a measure of the player's monitoring behavior). Children with ADHD were less accurate that the TD children and ran out of fuel more often. There was no difference between the children with ADHD and the TD children in the total number of times the fuel level was checked, which emerged as a significant predictor of PM performance only for the TD children; it was found that the TD children who checked more often were less likely to run out of fuel. Children with ADHD checked the fuel level just as often as the TD children, but they were less able to use this information to avoid running out of fuel. The children with ADHD may have been less able to encode their time-monitoring information, or they may have checked randomly and failed to foresee the "critical period" when it would be nearly time to fill up the gas tank. Zinke et al. (2010) extended the findings of Kerns and Price (2001) to include the analysis of time-monitoring behavior and ongoing task performance. Children first performed the ongoing task alone (a one-back picture task) then they performed the ongoing task together with the time-based PM task (pressing a target key every 2 minutes). The children with ADHD were less accurate than the TD children, but the two groups did not differ in the number of instances of clock-checking. Analyzing ongoing task performance showed that it was lower in the dual-task condition (ongoing task plus time-based PM task) than for the ongoing task alone, but with no differences between the children with ADHD and the TD children. Further analyses

suggested that some of the variance originated from differences in the appropriate use of the time-monitoring information before the target time, but that other mechanisms were involved too. The authors suggested that good candidates for explaining the lower PM accuracy of children with ADHD included deficits in time estimation (Noreika et al., 2013) and working memory (McInnes et al., 2003).

Finally, Talbot and Kerns (2014) used the CyberCruiser-II, a modification of the CyberCruiser used by Kerns and Price (2001), but this time children piloted a spaceship through space while avoiding obstacles. As in the previous version of the game, children were asked to remember to refuel the tank and they could check the fuel level during the game. The difficulty of the ongoing task was adjusted (by increasing or decreasing the number and frequency of the obstacles that appeared) based on the child's level of performance. A time-reproduction task (3–17 s) was also included to investigate time perception. The results showed that children with ADHD ran out of fuel more often than the TD children (lower PM accuracy). Performance in the ongoing task also differed between the two groups, but making the PM task more demanding seemed to have a more negative effect on the performance of the TD children than on the children with ADHD. This finding may seem counterintuitive, but it is not the first time that such patterns have been seen in children with ADHD. For example, children with ADHD performing simple sustained attention tasks may do better when the tasks are made slightly more challenging (Leung, Leung, & Tang, 2000). Contrary to expectations, the children's time perception was unrelated to their time-based PM performance (the number of times they ran out of fuel). The study did not measure the children's monitoring behavior however, so these results are difficult to interpret. Taken together, research suggests that children with ADHD are less accurate than TD children in time-based PM tasks (Kerns & Price, 2001; Talbot & Kerns, 2014; Zinke et al., 2010) and that they also benefit differently from strategic monitoring (Zinke et al., 2010). The picture is still not entirely clear, and further research is needed. For example, analyses on performance on ongoing tasks has generated mixed results; Zinke et al. (2010) found children with ADHD and TD children to be equally accurate, whereas Talbot and Kerns (2014) reported that the dual-task condition (ongoing task plus time-based PM) affected TD children more severely than children with ADHD. None of the previous studies investigated PM accuracy, ongoing task performance and time-monitoring behavior together with executive functions and time perception—all within the same study—in order to better elucidate the pattern and the source of time-based PM dysfunction in children with ADHD.

Aims of the Present Study

Considering the importance of adequate PM abilities in everyday life and the difficulties that children with ADHD have in remembering and completing future actions, it seems particularly crucial to examine the different aspects of these children's time-based PM abilities. The present study investigated time-based PM performance in children with and without ADHD using a PM task that enabled an assessment of their time-monitoring behavior.

The first aim was to investigate PM performance in children with and without ADHD, paying particular attention to PM accuracy, time-monitoring behavior, and accuracy in the ongoing task; all are considered important indicators of time-based PM

performance (Harris & Wilkins, 1982; Mäntylä & Carelli, 2006). In line with the results of previous studies (Kerns & Price, 2001; Talbot & Kerns, 2014; Zinke et al., 2010), we predicted that children with ADHD would perform less accurately than TD children in terms of both PM accuracy and accuracy on the ongoing task, and that they would also adopt less efficient time-monitoring strategies. To shed more light on the time-monitoring behavior of children with and without ADHD, we analyzed their clock-checking frequency for every 30-s interval. We also consider other measures of time-monitoring accuracy (objective and subjective accuracy, and accuracy score; see the Statistical Analyses section for more details) in order to further analyze the "critical period" between the last clock-checking action and the response at the target time.

We predicted correlations between different measures of PM performance, assuming that children adopting a more strategic time-monitoring behavior would also be more accurate at the target time (PM accuracy). Since a higher time-monitoring frequency might reduce the attentional resources available for performing the ongoing task (i.e., the cost and benefit of high-frequency clock-checking; Harris & Wilkins, 1982), we examined whether frequency of clock-checking correlated with success in the ongoing task. We assumed that children dedicating more attentional resources to clock-checking, or being more distracted by their time-monitoring actions, would pay less attention to the ongoing task and that their performance would suffer as a result.

The second aim of the study was to investigate the involvement of working memory and time-perception abilities in PM accuracy and time-monitoring behavior. Different paradigms can be used to investigate working memory (e.g., verbal vs. visuo-spatial, passive vs. active) and time perception (e.g., time discrimination, time production, verbal estimation and time reproduction; Grondin, 2010). In the present study, working memory was assessed with the categorization listening span task (De Beni, Palladino, Pazzaglia, & Cornoldi, 1998), which enables both recall and interference control to be measured and involves the verbal component, which is sometimes less impaired in ADHD than the corresponding visuo-spatial component (Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005). To assess time perception we used a time-reproduction task in which the children were asked to reproduce the duration of a previously-presented stimulus. The durations used in the task were chosen to be representative of the time intervals observed between the children's clock-checking (Mioni et al., 2012; Mioni & Stablum, 2014). We predicted a relationship between PM indices, working memory and time perception because an accurate time-based PM relies on the ability to manage information temporarily stored in memory (task requests, information about the ongoing task, and information about the time) and to represent time accurately. We also examined whether differences in time-based PM between the children with and without ADHD could be explained by a different involvement of working memory and time-perception abilities in their PM performance.

Method

Participants

The study involved 23 children with ADHD (females = 5; mean age = 10.89 years, standard deviation [*SD*] = 1.04) and 24 TD children (females = 7; mean age = 10.89 years,

SD = 0.91). Exclusion criteria were dyslexia, dyscalculia, other comorbid diagnoses (e.g., conduct disorder), and poor comprehension of the instructions. The children with ADHD had been diagnosed by local health professionals according to the *Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition* (*DSM-5*; American Psychiatric Association, 2013) criteria. As we were not allowed to administer intelligence tests, a general index of the children's cognitive abilities was obtained from teachers' and clinicians' ratings based on a four-point scale to investigate their level of cognitive abilities derived from a standardized battery and already validated for research purposes (Marzocchi, Re, & Cornoldi, 2010).

There was no difference between the groups in terms of age (p = .997, Cohen's d = .01) or level of cognitive abilities (p = .146, Cohen's d = .43; children with ADHD = 3.04, *SD* = 0.70; TD children = 3.33, *SD* = 0.64). All children were also assessed for inattention and hyperactivity by their parents with the Sindrome da Deficit Attentivo – Scala per Genitori (SDAG [Attention Deficit Syndrome – Scale for Parents]; Cornoldi, Gardinale, Masi, & Pettenò, 1996), a four-point scale (with a score range of 0–3) for scoring each of the 18 ADHD symptoms listed in the *DSM-5* manual. The children with ADHD had significantly higher total scores than the TD children on the SDAG subscales inattention, $t(45) = 14.18$, $p < .001$, Cohen's d = 4.13; children with ADHD = 16.83, *SD* = 3.39; TD children = 4.50, *SD* = 2.52, and hyperactivity, $t(45) = 7.98$, $p < .001$, Cohen's d = 2.31; children with ADHD = 13.00, *SD* = 5.24; TD children = 3.71, *SD* = 2.20.

Procedure

The children with ADHD were recruited at the Unità Operativa Complessa per l'Età Evolutiva (ULSS 10) in San Donà di Piave, near Venice, Italy, one of the few Italian units specifically recognized by the Italian Ministry of Public Health (Ministero della Salute) for the diagnosis and treatment of ADHD. The TD children were recruited at a public school in the same area (Enrico Mattei School in Fossalta di Piave, Venice, Italy). All the children were tested individually in a quiet room. All tasks were presented in the same order for all the children (time-reproduction, PM and working-memory tasks) on a 15-inch PC screen that the children viewed from a distance of approximately 60 cm. E-Prime 2.0 was used to program and run the experiments. Each task was preceded by a practice phase, and before starting the test phase all children were asked to repeat the task instructions to ensure that they had been understood. After completing each task, each child was again asked to repeat the task instructions to ensure that he or she had not forgotten the purpose of the tasks. None of the children failed to recite the task instructions accurately or exhibited any memory or comprehension dysfunctions. Informed consent was obtained from the parents of all the children who participated in the study, conducted in accordance with Padova University's Department of General Psychology guidelines and with the Helsinki Declaration (Fifty-ninth WMA General Assembly, Seoul, 2008).

Time-Based PM Task

The children watched a cartoon (*The Smurfs*) which lasted 11 minutes and were instructed to mark the passage of time every 2 minutes by pressing a key on a keyboard

(Mioni et al., 2012; Mioni & Stablum, 2014). The children had two keys on the keyboard, one red and one green, and they were told to press the red key every 2 minutes (at 2:00, 4:00, 6:00, 8:00 and 10:00 minutes). They were also told that they could press the green key at any time during the task to check the time; when they pressed the green key, the time appeared for 2 s in the bottom right-hand corner of the computer screen. None of the children had problems understanding the task instructions. It is important to mention that the children were advised to watch the cartoon carefully because they would be asked questions about its content. Soon after watching the cartoon, the children answered a questionnaire containing ten questions (e.g., "What party is going on in the Smurfs' village?"), scoring one point for each correct answer.

A practice phase was included at the beginning of the task to clarify the instructions and familiarize the children with the task. The experimenter showed that the clock would start at 00:00 and that, for example, 2:00 means 2 minutes.

Time-Perception Task

A time-reproduction task was used to assess time perception (Mioni & Stablum, 2014; Mioni et al., 2014). The children were instructed to reproduce the duration of a previously-seen stimulus (a "smiley" face) appearing on the computer screen for 4, 9 or 14 s. Each duration was randomly presented four times (for a total of 12 stimuli) and then after a 1-s inter-stimulus interval a question mark appeared on the screen and the children were asked to press and hold the spacebar for the same amount of time as the smiley face had been on the screen. The experimenter did not provide any specific feedback during the task. A practice phase was included at the beginning of the task, requiring children to reproduce each of the three durations once.

Working-Memory Task

A verbal dual task was used to assess working memory, adapted from the listening categorization working-memory task proposed by De Beni et al. (1998). Sets of lists of concrete familiar words, including a large number of animal nouns (25% of all the words) were presented to the children, each list consisting of four words presented at a rate of 1 s. The children were instructed: (1) to press the space bar every time they heard the name of an animal; and (2) to recall the last word on each list at the end of each set. The level of difficulty (the number of lists in each set) increased during the task from 2 to 6 word lists of words. The task was abandoned when a child was unable to recall the last word on each list in both sets of a given length.

Statistical Analyses

Time-based PM performance was assessed in terms of PM accuracy (response at the target time), clock-checking (time-monitoring frequency), and ongoing task performance (accuracy of answers about the cartoon's content).

PM accuracy was scored as correct if the children responded within 10 s of the target time (± 5 s of the target time).To further analyze PM performance at the target time, we

also calculated the PM relative score; based on the results of analyses often conducted in the temporal literature this provides more detailed information on performance at the target time (Mioni et al., 2014). The PM relative score is obtained by dividing the child's response at the target time by the expected PM target time. This provided an index of the direction of timing errors, with coefficients above and below 1.0 being indicative of over-estimation (the child presses the target key after the expected time, i.e., expected PM target time = 2 minutes, child's response = 2.2 minutes, PM relative score = 1.10) or under-estimation (the child presses the target key before the expected time; i.e., expected PM target time = 2 minutes, the child's response = 1.8 minutes, PM relative score = 0.90), respectively. Two separate *t*-tests were conducted on PM accuracy and PM relative score.

Time-monitoring frequency was analyzed in terms of the number of clock-checks. Each 2-minute interval was divided into four sub-intervals of 30 s each (1st interval = 0–30 s, 2nd interval = 31–60 s, 3rd interval = 61–90 s, 4th interval = 91–120 s). We calculated the number of clock-checks for each 30-s period during the 2-minute interval (for a similar procedure, see Zinke et al., 2010). A 2 × 4 mixed analysis of variance (ANOVA) was run on the time-monitoring frequency data, with group (children with ADHD, TD children) as the between-subject factor and interval (1st, 2nd, 3rd, 4th) as the within-subject factor. As in the work by Zinke et al. (2010), we also calculated the index of objective clock-monitoring accuracy, which is the mean time deviation between the last instance of clock-checking in the 4th interval and the target time. Moreover we also investigated the deviation between the last instances of clock-checking in the 4th interval and the actual time at which the child pressed the target time (subjective clock-monitoring accuracy). To evaluate the magnitude of the discrepancy between the objective and subjective clock-monitoring accuracy, we calculated the clock-monitoring accuracy score (subjective clock-monitoring accuracy /objective clock-monitoring accuracy). We included these indices to further elucidate the children's performance during the final monitoring period, which has been found to be crucial to accurate PM performance. The *t*-test was applied to these indices.

Ongoing task accuracy was measured from the number of correct answers in the questionnaire on the cartoon's content, using the *t*-test.

Correlational analyses between the time-based PM performance indices (PM accuracy, time-monitoring behavior estimated in term of numbers of clock-checking and ongoing accuracy) were conducted on the sample as a whole and then separately on the children with ADHD and the TD children. Correlations were also run between the PM performance indices and the symptoms of the children with ADHD.

Performance in the time-reproduction task was analyzed in terms of ratio and coefficient of variation (CV; Mioni et al., 2014). The ratio was obtained by dividing each child's time response by the time duration of the interval presented for that trial. For example, a response of 13.26 s for the 14-s interval implies a ratio of 0.94, whereas a response of 14.32 s for the 14-s interval of implies a ratio of 1.02. This index provided an index of the direction of errors, with coefficients above and below 1.0 being indicative of over-reproduction and under-reproduction, respectively. The CV index is a measure of timing variability that allowed us to assess how consistent children were in their temporal judgments of the same target interval. The CV index was calculated

for each child at each interval by dividing the *SD* of the reproduced intervals by the mean reproductions (Mioni et al, 2014).

Performance in the working-memory task was assessed, as suggested by De Beni et al. (1998), in terms of working-memory span (the length of the longest set of word lists accurately recalled). Working-memory accuracy (the proportion of times the children pressed the space bar for an animal noun) and intrusions (the proportion of non-final words incorrectly recalled as final words on the lists) were also considered. A *t*-test was carried out on the time perception and working memory indices.

Analyses of covariance (ANCOVAs) were conducted on the PM measures, with working memory (span) and time perception (CV) as covariates, in order to investigate the influence of time perception (CV) and working memory (span) on PM accuracy and time-monitoring behavior. These analyses were first conducted on the sample as a whole and then separately on the children with and without ADHD. Pearson's correlation analyses were conducted to investigate the relationship of time perception (CV) and working memory (span) on time-based PM performance (PM accuracy, time-monitoring behavior, and ongoing accuracy).

When necessary the significant analyses were followed by post hoc analyses with Bonferroni's correction to reduce the Type I error rate, and the effect size was estimated with partial eta squared (η^2_p) or Cohen's *d*.

Results

Table 1 shows the mean scores obtained by the two groups in the main dependent variables. The following paragraphs present a detailed statistical analysis of the two groups' performance in the PM task, followed by an analysis of their performance in the other two tasks, and the relationships between the three tasks.

Table 1. Mean Scores Obtained by the Children with ADHD and the TD Children on the Main Measures of Prospective Memory, Time Perception, and Working Memory.

	Children with ADHD	TD Children		
	M (*SD*)	*M* (*SD*)	*t*	*d*
PM Accuracy	0.63 (0.34)	0.84 (0.18)	2.57*	0.77
PM Relative Score	1.02 (0.01)	1.01 (0.01)	2.04*	1.00
Monitoring	27.71 (14.34)	27.39 (14.16)	0.07	0.02
Objective Monitoring Accuracy	12.28 (11.66)	10.18 (8.57)	1.60	0.20
Subjective Monitoring Accuracy	17.51 (17.19)	14.67 (12.04)	1.97*	0.19
Monitoring Accuracy Score	1.56 (0.48)	1.51 (0.35)	2.41*	0.12
Ongoing Accuracy	6.48 (2.11)	7.97 (1.83)	2.57*	0.75
Time-Reproduction Ratio	0.89 (0.09)	0.91 (0.15)	0.54	0.16
Time-Reproduction CV	0.15 (0.09)	0.09 (0.06)	2.59*	0.78
Working-Memory Detection Accuracy	0.83 (0.09)	0.85 (0.07)	0.73	0.24
Working-Memory Span	3.04 (0.84)	3.17 (1.15)	0.42	0.13
Working-Memory Intrusions	0.07 (0.07)	0.05 (0.10)	0.73	0.23

*$p < .05$. Cohen's d: Cohen (1992) defines effect sizes of 0.2 as small, 0.5 as medium, and 0.8 as large.

Time-Based PM Task

PM Accuracy

The analyses showed that the children with ADHD were less accurate than the TD children, $t(45) = 2.57$, $p = .013$, and had a greater tendency to respond after the correct target time, $t(45) = 2.04$, $p = .047$.

Time-Monitoring Frequency

The results showed a main effect of interval, $F(3, 126) = 47.91$, $p < .001$, $\eta^2_p = .533$, indicating that the frequency of clock-checking increased as the target time approached. There was no main effect of group, $p = .807$, $\eta^2_p = .001$, showing that there was no significant difference in the total number of clock-checking instances, but group significantly interacted with interval, $F(3, 126) = 6.56$, $p < .001$, $\eta^2_p = .135$ (Figure 1). Post hoc analyses showed that the children with ADHD checked the chock more often than the TD children in the 1st interval, $p = .032$, $\eta^2_p = .104$, while the TD children checked the time more often than the children with ADHD in the 4th interval, $p = .050$, $\eta^2_p = .088$; no differences between groups were observed during the other intervals, all $ps \geq .352$, all $\eta^2_p \leq .021$. The clock-checking frequency increased for all children as they neared the target time, but there was a greater increase in clock-checking frequency from the 1st interval to the 4th interval in the TD children, $p < .001$, $\eta^2_p = .658$, than in the children with ADHD, $p < .001$, $\eta^2_p = .440$.

Analyses of objective clock-monitoring accuracy showed no significant differences between groups, $t(45) = 1.60$, $p = .104$, but significant differences were found between groups for subjective clock-monitoring accuracy, $t(45) = 1.96$, $p = .050$. Interestingly, significant differences were observed between groups on clock-monitoring accuracy scores, $t(45) = 2.41$, $p = .020$, indicating that children with ADHD waited longer before the last instance of clock-checking and the target.

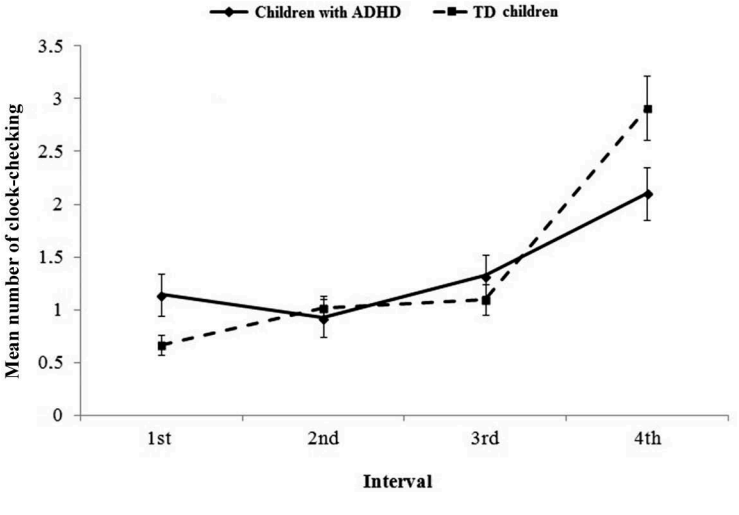

Figure 1. Frequency of clock-checking collapsed across 2-minute task intervals for children with ADHD and TD children. *Note*. Error bars indicate standard error. 1st interval = 0–30 s; 2nd interval = 31–60 s; 3rd interval = 61–90 s; 4th interval = 91–120 s.

Ongoing Task Performance

There was a significant difference between the groups' accuracy in the ongoing task, $t(45) = 2.57$, $p = .013$, with the children the ADHD being less accurate than the TD children.

Correlation Analyses between PM Indices

In the sample as a whole, a negative medium-size correlation (Cohen, 1992) emerged between PM accuracy and accuracy on the ongoing task, $r = -.401$. Medium- to large-size correlations were found between PM accuracy and monitoring frequencies for the last three intervals: 2nd interval $r = .350$; 3rd interval $r = .296$; 4th interval $r = .577$.

Pearson's correlation analyses were also conducted separately on the ADHD and TD groups. Large-size correlations (Cohen, 1992) were seen between PM accuracy and monitoring frequency at the 4th interval for both the children with ADHD, $r = .651$, and the TD children, $r = .493$. The TD children had medium- to large-size correlations between PM accuracy and monitoring frequency in the 2nd, $r = .365$, and 3rd, $r = .484$, intervals, indicating that the children who checked the clock more often closer to the target time were also more accurate. In both groups, a medium-size correlation was also found between frequency of clock-checking and ongoing task accuracy, indicating that children who monitored more often were also less accurate on the ongoing task, all rs $< -.291$.

Correlation Analyses between PM Indices and ADHD Symptoms

Correlation analyses were run on the ADHD group to control for any effects of the severity of their ADHD symptoms on PM performance. A medium-size correlation was found between SDAG inattention and PM accuracy, $r = -.352$, and a large-size correlation was found between SDAG inattention and accuracy on the ongoing task, $r = -.528$, indicating that more severe ADHD symptoms resulted in a lower PM performance. No significant correlations emerged between SDAG hyperactivity and indices of PM performance.

Time Perception and Working-Memory Performance

There were no differences between the groups in terms of the ratio, $t(45) = 0.54$, $p = .589$, indicating that both groups under-reproduced temporal intervals. Significant differences emerged between the groups in terms of the CV, $t(45) = 2.59$, $p = .029$, indicating that children with ADHD were more variable in their performance. No differences were observed between groups on working-memory accuracy, working-memory span, or intrusions, all ps $\geq .471$.

Relationships between PM Indices, Working Memory and Time Perception

To examine the contribution of time perception and working memory to PM performance, ANCOVAs were run with the main PM measures as dependent variables and working memory (span) and time perception (CV) as covariates.

Concerning PM accuracy, an ANCOVA was first conducted on the entire sample and showed that time perception influenced PM accuracy, $F(1, 45) = 5.60$, $p = .023$, $\eta^2_p = .118$, whereas there was no apparent involvement of working memory, $p = .692$, $\eta^2_p = .004$. When the analyses were conducted separately on the children with ADHD and the TD children, the involvement of time perception was only confirmed for the TD children, $F(1, 23) = 9.05$, $p = .007$, $\eta^2_p = .312$. No involvement of working memory emerged for either group, all ps $\geq .305$, $\eta^2_p = .019$.

An ANCOVA on monitoring behavior (number of instances of clock-checking) was first conducted on the whole sample and a significant main effect of working memory was found, $F(1, 39) = 6.06$, $p < .018$, $\eta^2_p = .134$. When the analyses were conducted separately on the two groups, a significant main effect of working memory, $F(1, 19) = 14.65$, $p < .001$, $\eta^2_p = .435$, was seen for the TD children as well as a significant interaction between intervals and working memory, $F(3, 57) = 3.14$, $p < .032$, $\eta^2_p = .142$. There was no involvement of time perception or working memory for the children with ADHD, all ps $\geq .185$, $\eta^2_p = .009$.

The different patterns in the two groups emerging from the ANCOVAs are supported by the main correlations identified when the two groups were considered separately. Correlational analyses showed a positive correlation between performance on the ongoing task and working-memory span in the children with ADHD, $r = .393$. Conversely, significant negative correlations emerged for the TD children between PM accuracy and time perception, $r = -.361$, and between working-memory span and the total number of instances of clock-checking, $r = -.672$.

Discussion

Previous studies have found a poorer PM performance in children with ADHD than in TD children (Kerns & Price, 2001; Kliegel et al., 2006; Zinke et al., 2010), and identified executive dysfunction as one the main reasons for this (Kretschmer et al., 2014; Mahy et al., 2014, 2015). The present study was conducted to investigate time-based PM performance in children with ADHD and TD children, paying particular attention to the relationship between PM accuracy and time-monitoring behavior, and to the contribution of temporal and working-memory abilities to time-based PM performance. A time-based PM task which allows the assessment of time-monitoring behavior was used and PM performance was analyzed in term of PM accuracy, time-monitoring behavior and accuracy on the ongoing task. A time-reproduction task and a verbal working-memory dual task were also administered.

Consistent with previous studies, our ADHD group was less accurate than the TD group in the time-based PM task (Kerns & Price, 2001; Kliegel et al., 2006; Zinke et al., 2010). The method adopted here also gave us the opportunity to examine in detail the characteristics of the performance of children with ADHD in the PM task. In fact, the children with ADHD were less accurate than the TD children on the time-based PM task when their performance was analyzed in terms of PM accuracy (proportion of hits), and a more detailed analysis showed that the children with ADHD pressed the key to indicate the target time later than TD children (PM relative score). Analyzing their performance in the ongoing task showed that children with ADHD again performed less accurately than TD children, i.e., the former were less accurate in reporting on the

content of the cartoon. Both these aspects are congruent with the often-reported observation that children with ADHD are late in carrying out the requests they receive and may have difficulty in organizing activities associated with more than one task request (American Psychiatric Association, 2013).

With the exception of the study by Zinke et al. (2010), no attention had been paid to the time-monitoring behavior of children with ADHD.[1] This is a crucial aspect of time-based PM tasks because it is essential to monitor the time elapsing often enough to ensure the successful initiation of the PM task (Ceci & Bronfenbrenner, 1985; Einstein et al., 1995; Harris & Wilkins, 1982; Mäntylä & Carelli, 2006). For a time-monitoring strategy to be efficient, the clock-checking actions must be scheduled appropriately and the right balance must be struck between the cost of monitoring and the cost of not having accurate information (Mäntylä & Carelli, 2006). Studies on time-based PM have suggested that successful PM performance relies on increasing the time-monitoring rate as the deadline approaches (Mäntylä & Carelli, 2006; Mäntylä et al., 2007). In the present study, all the children increased their time-monitoring frequency closer to the target time, but the children with ADHD had a higher frequency of clock-checking than the TD children in the 1st interval, while the TD children had a higher frequency of clock-checking than the children with ADHD in the 4th interval. More frequent time monitoring in the 1st interval can be interpreted as a "calibration" phase to synchronize the individual's internal clock with the real passage of time (Ceci & Bronfenbrenner, 1985), but this is less crucial than checking the clock closer to the target time. Ceci and Bronfenbrenner (1985) identified three phases of time-monitoring behavior: a "calibration phase", an "intermediate phase" (when clock-checking occurs less often), and a "scalloping phase", when the frequency of clock-checking increases as the deadline approaches. This use of strategic monitoring produces a typical distribution of clock-checking in both children (Mäntylä et al., 2007; Zinke et al., 2010) and adults (Einstein et al., 1995; Harris & Wilkins, 1982; Mioni & Stablum, 2014). The results of the present study suggest that children with ADHD have a less efficient strategy, with clock-checking occurring more often during the 1st interval, probably because they are more impulsive and have more difficulty in calibrating their internal clock. The TD children only occasionally checked the clock during the 1st interval and strategically increased their clock-checking frequency closer to the target time, thus obtaining a higher PM accuracy. When clock-monitoring accuracy was further analyzed, a different pattern emerged in the children's time-monitoring behavior. There was no difference between the groups in terms of the objective clock-monitoring accuracy index, confirming the data obtained by Zinke et al. (2010) in the mean time elapsed between the last instance of clock-checking before pressing the key at the target time. But when the subjective clock-monitoring accuracy index was analyzed, a difference between groups was found: the discrepancy (in seconds) between the last instance of clock-checking and the actual moment at which children pressed the target key was greater in children with ADHD than in TD children. This result was also confirmed by the analyses conducted on the clock-monitoring accuracy score, which also represents an index of discrepancy between subjective and objective clock-monitoring accuracy. Our results concerning time-monitoring accuracy further support the data obtained for PM accuracy, since the

[1]Kerns and Price (2001) reported the total number of times the children checked the fuel level.

children with ADHD were late in responding (PM relative score) more often than the TD children.

It is possible that the children with ADHD wrongly estimated the time between the last instance of clock-checking and the target time. In fact, the children with ADHD had a higher variability (CV) than the TD children in the time-reproduction task, indicating a weaker temporal ability. This hypothesis is also supported by the results obtained for PM accuracy when we covaried for time perception, and also by the temporal dysfunction often seen in children with ADHD (Barkley, 1997; Noreika et al., 2013). On the other hand, it may be that the children with ADHD had more difficulty with the dual effort of performing the PM task and processing ongoing information. It is worth noting that a higher frequency of clock-checking was negatively correlated with ongoing task performance in both groups.

Consistent with the study conducted by Mackinlay et al. (2009) on healthy children, and at odds with the study by Talbot and Kerns (2014) conducted on children with ADHD, we found a relationship between time perception and PM accuracy in the TD children. Our results indicated that time perception is involved in time-based PM performance, and that TD children with adequate temporal abilities can use them to perform time-based PM tasks efficiently. Only Mackinlay et al. (2009) analyzed the relationship between time perception and time-monitoring behavior, finding no relationship between the two variables. Our data confirmed their findings, and suggest that adequate temporal abilities are needed more for accuracy at the target time than for strategically monitoring the time, in TD children at least.

Consistent with other studies (Kretschmer et al., 2014; Mackinlay et al., 2009; Mäntylä et al., 2007; Voigt et al., 2014), we found a relationship between working memory and PM performance, particularly with time-monitoring behavior, suggesting that working memory is needed to succeed in a PM task. Mäntylä et al. (2007) found working memory to be related to time-monitoring behavior too, confirming their results in a longitudinal study (Forman et al., 2011) and showing that adolescents with greater relative gains in working-memory abilities were better calibrated than children with less well-developed working-memory abilities.

It is important to note, however, that the relationship between time perception, working-memory abilities and time-based PM performance was evident in the TD children but not in the children with ADHD, suggesting that the latter are less able to use their cognitive resources in an integrated manner when performing complex tasks. Concerning working memory, this effect seems particularly interesting because it cannot be attributed to a weakness in working memory per se. The children with ADHD did not differ significantly from the TD children in the working memory measures, as others have observed, especially with regard to verbal working memory (Martinussen et al., 2005). This is also congruent with a previous observation (Cornoldi, Giofrè, Calgaro, & Stupiggia, 2013) indicating that working memory is more closely related to complex cognition in TD children than in children with ADHD.

Investigating time-based PM performance in children with ADHD can have interesting implications, also shedding further light on PM impairment in adults with ADHD. Cognitive dysfunction is reportedly more pronounced in the adult form of this disorder (Woods, Lovejoy, & Ball, 2002) and previous studies have confirmed PM dysfunction in adults with ADHD too. As far as we know, only two published studies

(Altgassen, Kretschmer, & Kliegel, 2014; Fuermaier et al., 2013) and one Ph.D. thesis (Karidi, 2013) have investigated PM performance in adults with ADHD. Fuermaier et al. (2013) used a complex PM task that did not include any time-based PM tasks, while Altgassen et al. (2014) used the Dresden Breakfast Task, which includes both event- and time-based PM tasks. Karidi (2013) used Virtual Week, which also includes both event- and time-based tasks, but the time-based task in Virtual Week represents not a "real time" but a "virtual time" relating to the number obtained by rolling a die (Rendell & Craik, 2000). Virtual Week also fails to measure ongoing task performance and time-monitoring behavior. A closer look at the study by Altgassen et al. (2014), who used a time-based PM task and measured PM accuracy, time-monitoring behavior and ongoing task performance, confirmed PM dysfunction in adults with ADHD. In particular, adults with ADHD were less accurate at the target time, despite monitoring the time as much as the controls, indicating that they were unable to put the information they obtained by checking the clock to good use (Kerns & Price, 2001; Zinke et al., 2010). Together with our findings in children with ADHD, these results suggest that their weaker performance persists into adulthood and that no compensatory strategy is acquired during their development. Altgassen et al. (2014) also found no differences in general ongoing task performance between their groups, but a deeper look at plan quality and plan adherence revealed a worse performance in adults with ADHD. Overall, the controls planned more accurately and followed their plans more closely than the adults with ADHD. With respect to our results, we found that the children with ADHD had a lower ongoing task performance than the TD children. These results confirm the lower time-based PM abilities in individuals with ADHD (both children and adults), and underscore the importance of further exploring different aspects of time-based PM performance and the cognitive functions potentially involved. Some studies found no relationship between time-monitoring behavior and PM accuracy, suggesting as a result that the deficit in time-based PM may manifest itself without the pathway of reduced strategic monitoring (Altgassen et al., 2014; Kerns & Price, 2001; Zinke et al., 2010), but our own results and those of others highlight this relationship (Kretschmer et al., 2014; Mackinlay et al., 2009; Mahy et al., 2015; Mäntylä et al., 2007). Future studies should improve our comprehension of the complex relationship between time-based PM, working memory and time perception. In particular, it would be interesting to see whether adults with ADHD show a better involvement of their working-memory and time-perception abilities in time-based PM performance than children with ADHD.

In conclusion, our results further support the hypothesis that the disorganized behavior of children with ADHD is associated with a basic difficulty in time-based PM. Importantly, this difficulty was detected with an experimental task conducted in a quiet, controlled environment. By thoroughly analyzing the characteristics of their time-based PM performance, we could see that the children with ADHD in the present study adopted less efficient clock-checking strategies and had difficulty in carrying out the time-based PM task. The concurrent involvement of time-perception and working-memory tasks gave us the opportunity to identify specific relationships between working memory, time perception, and different aspects of time-based PM performance. These relationships are more evident in the case of TD children than in children with ADHD however, suggesting that the latter do

not use their cognitive resources to the same extent. These results are important, not only for a better understanding of the difficulties of children with ADHD but also with a view to improving their ability to meet PM requests, as they could be taught to adopt strategies and use their available resources more effectively. The present findings suffer from a number of limitations, however, and further research is needed to collect more evidence and replicate our results. In particular, the present study should be replicated using larger samples and with other measures, including tasks that cover other aspects of time perception and working memory.

Acknowledgements

The authors gratefully acknowledge Dr Claudio Vio, all the children, and their families and friends who cooperated in the present study. The authors gratefully acknowledge Prof. Frances Coburn for assisting with editing. These data were presented at the XXIV National AIRIPA Conference (Associazione Italiana per la Ricerca e l'Intervento nella Psicopatologia dell'Apprendimento), Pesaro, Italy, 2015.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

Altgassen, M., Kretschmer, A., & Kliegel, M. (2014). Task dissociation in prospective memory performance in individuals with ADHD. *Journal of Attention Disorders*, *18*, 617–624. doi:10.1177/1087054712445484

American Psychiatric Association. (2013). *DSM-5. Diagnostic and statistical manual of mental disorders*. Washington, DC: Author.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, *121*(1), 65–94. doi:10.1037/0033-2909.121.1.65

Biederman, J., Monuteaux, M. C., Doyle, A. E., Seidman, L. J., Wilens, T. E., Ferrero, F., … Faraone, S. V. (2004). Impact of executive function deficits and attention deficit/hyperactivity disorder (ADHD) on academic outcomes in children. *Journal of Consulting & Clinical Psychology*, *72*(5), 757–766. doi:10.1037/0022-006X.72.5.757

Ceci, S. J., & Bronfenbrenner, U. (1985). "Don't forget to take the cupcakes out of the oven": Prospective memory, strategic time monitoring, and context. *Child Development*, *56*(1), 152–164. doi:10.2307/1130182

Clark, C., Prior, M., & Kinsella, G. J. (2000). Do executive function deficits differentiate between adolescents with ADHD and oppositional defiant/conduct disorder? A neuropsychological study using the Six Elements Test and Hayling Sentence Completion Test. *Journal of Abnormal Child Psychology*, *28*(5), 403–414. doi:10.1023/A:1005176320912

Cohen, J. (1992). A power primer. *Psychological Bulletin*, *112*(1), 155–159. doi:10.1037/0033-2909.112.1.155

Cornoldi, C., Gardinale, M., Masi, A., & Pettenò, L. (1996). *Impulsività e autocontrollo* [Impulsivity and self-control]. Trento: Erickson.

Cornoldi, C., Giofrè, D., Calgaro, G., & Stupiggia, C. (2013). Attentional WM is not necessarily specifically related with fluid intelligence: The case of smart children with ADHD symptoms. *Psychological Research*, *77*, 508–515. doi:10.1007/s00426-012-0446-8

De Beni, R., Palladino, P., Pazzaglia, F., & Cornoldi, C. (1998). Increases in intrusion errors and working memory deficit of poor comprehenders. *The Quarterly Journal of Experimental Psychology*, *51A*(2), 305–320. doi:10.1080/713755761

Einstein, G. O., & McDaniel, M. A. (1996). Retrieval processes in prospective memory: Theoretical approaches and some new empirical findings. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 1151–1124). Mahwah, NJ: Lawrence Erlbaum.

Einstein, G. O., McDaniel, M. A., Richardson, S. L., Guynn, M. J., & Cunfer, A. R. (1995). Aging and prospective memory: Examining the influences of self-initiated retrieval processes. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *21*(4), 996–1007. doi:10.1037/0278-7393.21.4.996

Ellis, J. A. (1996). Prospective memory or the realization of delayed intentions: A conceptual framework for research. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 1–22). Mahwah, NJ: Lawrence Erlbaum.

Forman, H., Mäntylä, T., & Carelli, M. G. (2011). Time keeping and working memory development in early adolescence: A 4-year follow-up. *Journal of Experimental Child Psychology*, *108*, 170–179. doi:10.1016/j.jecp.2010.07.004

Fuermaier, A. B. M., Tucha, L., Koerts, J., Aschenbrenner, S., Westermann, C., Weisbrod, M., … Tucha, O. (2013). Complex prospective memory in adults with attention deficit hyperactivity disorder. *PLoS ONE*, *8*(3), e58338. doi:10.1371/journal.pone.0058338

Geurts, H. M., Verté, S., Oosterlaan, J., Roeyers, H., & Sergeant, J. A. (2004). How specific are executive functioning deficits in attention deficit hyperactivity disorder and autism? *Journal of Child Psychology and Psychiatry*, *45*(4), 836–854. doi:10.1111/j.1469-7610.2004.00276.x

Glicksohn, J. E., & Myslobodsky, M. S. (2006). *Timing the future. The case for a time-based prospective memory*. New York, NY: World Scientific Publishing.

Grondin, S. (2010). Timing and time perception: A review of recent behavioral and neuroscience findings and theoretical directions. *Attention, Perception, & Psychophysics*, *72*(3), 561–582. doi:10.3758/APP.72.3.561

Harris, J. E., & Wilkins, A. J. (1982). Remember to do things: A theoretical framework and an illustrative experiment. *Human Learning*, *1*, 123–136.

Karidi, D. (2013). *The effects of task features and executive functioning on prospective memory performance of adults with ADHD* (PhD thesis). Retrieved from http://gateway.proquest.com/openurl?url_ver=Z39.882004&res_dat=xri:pqdiss&rft_val_fmt=info:ofi/fmt:kev:mtx:dissertation&rft_dat=xri:pqdiss:3563748

Kerns, K. A. (2000). The CyberCruiser: An investigation of development of prospective memory in children. *Journal of the International Neuropsychological Society*, *6*(1), 62–70. doi:10.1017/S1355617700611074

Kerns, K. A., & Price, K. J. (2001). An investigation of prospective memory in children with ADHD. *Child Neuropsychology*, *7*(3), 162–171. doi:10.1076/chin.7.3.162.8744

Kliegel, M., Martin, M., McDaniel, M. A., & Einstein, G. O. (2002). Complex prospective memory and executive control of working memory: A process model. *Psychologische Beitrage*, *44*, 303–318.

Kliegel, M., McDaniel, M. A., & Einstein, G. O. (2008). *Prospective memory: Cognitive, neuroscience, developmental, and applied perspective*. Mahwah, NJ: Lawrence Erlbaum.

Kliegel, M., Ropeter, A., & Mackinlay, R. (2006). Complex prospective memory in children with ADHD. *Child Neuropsychology*, *12*(6), 407–419. doi:10.1080/09297040600696040

Kretschmer, A., Voigt, B., Friedrich, S., Pfeiffer, K., & Kliegel, M. (2014). Time-based prospective memory in young children. Exploring executive functions as a developmental mechanism. *Child Neuropsychology*, *20*(6), 662–676. doi:10.1080/09297049.2013.841881

Kvavilashvili, L., Kyle, F., & Messer, D. J. (2008). The development of prospective memory in children: Methodological issues, empirical findings, and future directions. In M. Kliegel, M. A. McDaniel, & G. O. Einstein (Eds.), *Prospective memory: Cognitive, neuroscience, developmental, and applied perspectives* (pp. 115–140). Mahwah, NJ: Lawrence Erlbaum.

Labelle, M.-A., Graf, P., Grondin, S., & Gagné-Roy, L. (2009). Time-related processes in time-based prospective memory and in time-interval production. *European Journal of Cognitive Psychology*, *21*(4), 501–521. doi:10.1080/09541440802031000

Leung, J., Leung, P. W., & Tang, C. S. (2000). A vigilance study of ADHD and control children: Event rate and extra-task stimulation. *Journal of Developmental and Physical Disabilities*, *12*, 187–201. doi:10.1023/A:1009409720485

Mackinlay, R. J., Kliegel, M., & Mäntylä, T. (2009). Predictors of time-based prospective memory in children. *Journal of Experimental Child Psychology*, *102*(3), 251–264. doi:10.1016/j.jecp.2008.08.006

Mahy, C. E., Moses, L. J., & Kliegel, M. (2014). The impact of age, ongoing task difficulty, and cue salience on preschoolers' prospective memory performance: The role of executive function. *Journal of Experimental Child Psychology*, *127*, 52–64. doi:10.1016/j.jecp.2014.01.006

Mahy, C. E., Voigt, B., Ballhausen, N., Schnitzspahn, K., Ellis, J., & Kliegel, M. (2015). The impact of cognitive control on children's goal monitoring in time-based prospective memory task. *Child Neuropsychology*, *21*(6), 823–839. doi:10.1080/09297049.2014.967202

Mäntylä, T., & Carelli, M. G. (2006). Time monitoring and executive functioning: Individual and developmental differences. In J. Glicksohn & M. Myslobodsky (Eds.), *Timing the future. The case of time-based prospective memory* (pp. 191–211). New York, NY: World Scientific Publishing.

Mäntylä, T., Carelli, M. G., & Forman, H. (2007). Time monitoring and executive functioning in children and adults. *Journal of Experimental Child Psychology*, *96*(1), 1–19. doi:10.1016/j.jecp.2006.08.003

Martin, M., Kliegel, M., & McDaniel, M. A. (2003). The involvement of executive functions in prospective memory performance of adults. *International Journal of Psychology*, *38*(4), 195–206. doi:10.1080/00207590344000123

Martinussen, R., Hayden, J., Hogg-Johnson, S., & Tannock, R. (2005). A meta-analysis of working memory impairments in children with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *44*(4), 377–384. doi:10.1097/01.chi.0000153228.72591.73

Marzocchi, G. M., Re, A. M., & Cornoldi, C. (2010). *BIA: Batteria Italiana per l'ADHD [Italian Battery for ADHD]*. Trento: Centro Studi Erickson.

McDaniel, M. A., & Einstein, G. O. (2000). Strategic and automatic processes in prospective memory retrieval: A multiprocess framework. *Applied Cognitive Psychology*, *14*(7), 127–144. doi:10.1002/acp.775

McFarland, C. P., & Glisky, E. L. (2009). Frontal lobe involvement in a task of time-based prospective memory. *Neuropsychologia*, *47*(7), 1660–1669. doi:10.1016/j.neuropsychologia.2009.02.023

McInnes, A., Humphries, T., Hogg-Johnson, S., & Tannock, R. (2003). Listening comprehension and working memory are impaired in attention-deficit hyperactivity disorder irrespective of language impairment. *Journal of Abnormal Child Psychology*, *31*(4), 427–443. doi:10.1023/A:1023895602957

Mioni, G., & Stablum, F. (2014). Monitoring behaviour in a time-based prospective memory task: The involvement of executive functions and time perception. *Memory*, *22*(5), 536–552. doi:10.1080/09658211.2013.801987

Mioni, G., Stablum, F., McClintock, S. M., & Cantagallo, A. (2012). Time-based prospective memory in severe traumatic brain injury patients: The involvement of executive functions and time perception. *Journal of the International Neuropsychological Society*, *18*(4), 697–705. doi:10.1017/S1355617712000306

Mioni, G., Stablum, F., McClintock, S. M., & Grondin, S. (2014). Different methods for reproducing time, different results. *Attention, Perception, & Psychophysics*, *76*(3), 675–681. doi:10.3758/s13414-014-0625-3

Noreika, V., Falter, C. M., & Rubia, K. (2013). Timing deficits in attention-deficit/hyperactivity disorder (ADHD): Evidence from neurocognitive and neuroimaging studies. *Neuropsychologia*, *51*(2), 235–266. doi:10.1016/j.neuropsychologia.2012.09.036

Pennington, B. F., & Ozonoff, S. (1996). Executive functions and developmental psychopathology. *Journal of Child Psychology and Psychiatry*, *37*(1), 51–87. doi:10.1111/j.1469-7610.1996.tb01380.x

Rendell, P. G., & Craik, F. I. (2000). Virtual week and actual week: Age-related differences in prospective memory. *Applied Cognitive Psychology*, *14*(7), S43–S62. doi:10.1002/acp.770

Schnitzspahn, K. M., Stahl, C., Zeintl, M., Kaller, C. P., & Kliegel, M. (2012). The role of shifting, updating, and inhibition in prospective memory performance in young and older adults. *Developmental Psychology*, *49*(8), 1544–1553. doi:10.1037/a0030579

Seidman, L. J. (2006). Neuropsychological functioning in people with ADHD across the lifespan. *Clinical Psychology Review*, *26*(4), 466–485. doi:10.1016/j.cpr.2006.01.004

Talbot, K.-D. S., & Kerns, K. A. (2014). Event- and time-triggered remembering: The impact of attention deficit hyperactivity disorder on prospective memory performance in children. *Journal of Experimental Child Psychology*, *127*, 126–143. doi:10.1016/j.jecp.2014.02.011

Voigt, B., Mahy, C. E. V., Ellis, J., Schnitzspahn, K., Krause, I., Altgassen, M., & Kliegel, M. (2014). The development of time-based prospective memory in childhood: The role of working memory updating. *Developmental Psychology*, *50*(10), 2393–2404. doi:10.1037/a0037491

Woods, S. P., Lovejoy, D. W., & Ball, J. D. (2002). Neuropsychological characteristics of adults with ADHD: A comprehensive review of initial studies. *The Clinical Neuropsychologist*, *16*(1), 12–34. doi:10.1076/clin.16.1.12.8336

Zinke, K., Altgassen, M., Mackinlay, R. J., Rizzo, P., Drechsler, R., & Kliegel, M. (2010). Time-based prospective memory performance and time-monitoring in children with ADHD. *Child Neuropsychology*, *16*(4), 338–349. doi:10.1080/09297041003631451

Research Article

Comorbidity of ADHD and High-functioning Autism: A Pilot Study on the Utility of the Overflow Movements Measure

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Objectives: **Children with attention-deficit/hyperactivity disorder (ADHD) and high-functioning autism (HFA) commonly show neurological soft signs (NSS) and impairment in executive functioning (EF). Many children with HFA may experience ADHD-like symptoms, and the 2 disorders may be comorbid. Evaluating NSS and EF in drug-naive subjects with ADHD, HFA, and ADHD+HFA compared with healthy children may be critical in understanding and differentiating the biological substrates and cognitive phenotypes associated with these disorders. The goal of this study was to evaluate possible differences among these groups in motor and EF and the effects of comorbidity.**

Methods: **Thirty-eight drug-naive patients (13 with ADHD, 13 with HFA, 12 with ADHD+HFA) and 13 healthy controls (HC) were evaluated on measures of planning, verbal working memory, and response inhibition. Evaluation of NSS involved 3 primary variables: overflow movements (OM), dysrhythmia, and speed of timed activities.**

Results: **The group with ADHD and the group with HFA both showed impairment on measures of planning, response inhibition, and verbal working memory compared with the HC group. Moreover, the group with ADHD showed a greater number of NSS compared with the HC group, whereas the group with HFA showed greater dysrhythmia and slowness compared with the HC group. The group with ADHD+HFA showed deficits of planning and response inhibition and a greater number of NSS compared with the HC group. The group with ADHD+HFA showed greater impairment of planning compared with the other clinical groups and greater dysrhythmia compared with the group with ADHD.**

Conclusion: **According to our data, the OM measure revealed a gradient in which ADHD was at one extreme (more OM) and HFA at the other extreme (less OM), whereas ADHD+HFA showed a number of OM that fell in the middle between the numbers for the ADHD and HFA groups.**

(*Journal of Psychiatric Practice 2016;22;22–30*)

KEY WORDS: neurological soft signs, executive functioning, attention-deficit/hyperactivity disorder, high-functioning autism, comorbid attention-deficit/hyperactivity disorder+high-functioning autism

Neurological soft signs (NSS) are subtle motor, sensory, and integrative abnormalities that cannot be related to impairment of a specific brain region and result in considerable sociopsychological dysfunction.[1] NSS are mainly represented by overflow movements (OM) and dysrhythmia. OM are defined as comovements of body parts not specifically needed to efficiently complete a motor task.[2] OM may take a number of different forms: associated movements, contralateral motor irradiation, and mirror movements. Associated movements refer to involuntary movement in nonhomologous muscles, either contralaterally or ipsilaterally.[3] Contralateral motor irradiation and mirror movements are involuntary

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The authors declare no conflicts of interest.

DOI: 10.1097/PRA.0000000000000120

movements that occur in the homologous muscles contralateral to voluntary movements.[4] Dysrhythmia is defined as an improper timing and/or rhythm of movement that is otherwise normal.[5] NSS are commonly observed in children with typical development and reflect the immaturity of the central nervous system, but their persistence into later childhood and adolescence suggests motor dysfunction and could be a marker of atypical neurodevelopment. OM seem to be related to a delay or defect of maturation in the intracortical and intercortical systems that support automatic inhibition,[6] whereas dysrhythmia appears to be due to cerebellar dysfunction.[7] Executive functions (EF) are represented by mental control processes that enable physical, cognitive, and emotional self-control and are necessary to maintain effective goal-directed behavior.[8,9] EF generally include response inhibition, working memory, cognitive flexibility (set-shifting), planning, and fluency, and they are supported by the frontostriatal system, including frontal lobes and basal ganglia.[9] According to Barkley,[10] EF are those abilities that allow an individual to plan and organize information in working memory and develop/evaluate an appropriate action on the basis of this information. He conceptualized EF as a means of behavioral self-regulation that modulates behavior in a manner that is adaptive to the dynamic contexts of the situation at hand.[10,11] Attention-deficit/hyperactivity disorder (ADHD) and high-functioning autism (HFA) are 2 neurodevelopmental disorders with a multifactorial etiology and a high heritability. ADHD is characterized by varying degrees of inattention, impulsivity, and hyperactive behavior, whereas HFA is characterized by impairment in communication and reciprocal social interaction and a restricted repertoire of activities and interests.[12] ADHD affects 3% to 8% of children worldwide,[13] and autism spectrum disorder, including HFA, affects up to 1 in 88 to 110 children[14]; thus these disorders are a major public health concern. Moreover, ADHD and HFA may often be comorbid.[15] NSS and impairment in EF are commonly reported in children with ADHD and HFA in addition to the main symptoms of these disorders.[16,17] Motor problems, including OM, impaired timing of motor responses, and poor motor coordination, have been observed in children with ADHD. These could reflect dysfunctions of frontal-striatal-cerebellar networks involved in motor control and white matter abnormalities in motor and premotor circuits.[16] Similarly, motor impairments, such as difficulty with motor preparation and execution, dysrhythmia, and motor slowness, have been observed in children with HFA.[17] These could reflect functional deficits in the frontostriatal circuits, cerebellum, and basal ganglia.[17,18] A meta-analysis of the literature on ADHD has shown that the strongest and most consistent deficits in EF found across studies involved response inhibition, vigilance, working memory, and planning.[19] The significant areas of EF deficits in HFA appear to be cognitive flexibility or strategy selection and planning.[20–22] Children with comorbid ADHD +HFA have greater difficulty with vigilance and response inhibition.[23,24] Evaluating motor performance and EF in drug-naive subjects with ADHD, HFA, and comorbid ADHD+HFA compared with healthy controls (HC) may be critical in understanding and differentiating both the biological substrates and cognitive phenotypes associated with these neurodevelopmental disorders. The goal of this study was to evaluate possible differences among these clinical groups on measures of planning, verbal working memory, response inhibition, and NSS and the effects of comorbidity on all of the analyzed variables.

METHODS

Subjects

The study included 51 subjects divided into 3 clinical groups and a control group: 13 patients with ADHD (12 boys, 1 girl), 13 patients with HFA (all boys), 12 patients with comorbid ADHD+HFA (10 boys, 2 girls), and 13 HC (12 boys, 1 girl) aged 8 to 15 years with IQ≥85 (Table 1). Subjects of the 3 clinical groups were consecutive referrals at the Unit of Child Neurology and Psychiatry of "Tor Vergata" University of Rome, Italy. All patients in the 3 clinical groups were drug-naive at enrollment. In accordance with the criteria in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*,[12] the diagnoses of ADHD, HFA, and comorbid ADHD+HFA were based on clinical assessment, observations of children, and interviews with parents and children, which were carried out by an experienced child psychiatrist. Both the long version of the Conners' Parents Rating Scale-Revised (CPRS-R:L)[25] and the

TABLE 1. Demographic Variables

	ADHD	*HFA*	*ADHD+HFA*	*Controls*
No. subjects	12 boys, 1 girl	13 boys	10 boys, 2 girls	12 boys, 1 girl
Age (mean±SD)	10.15±1.9	10.69±2.1	10.25±2.0	11.85±2.7
IQ (mean±SD)	97.46±11.04	106.00±17.41	108.36±14.84	106.31±11.84

ADHD indicates attention-deficit/hyperactivity disorder; HFA, high-functioning autism; ADHD+HFA, comorbid ADHD and HFA.

Conners' Teachers Rating Scale-Revised (CTRS-R:L)[25] were used to make the diagnosis of ADHD. To keep the sample of children with ADHD as homogeneous as possible, only those who met the DSM-IV-TR criteria for ADHD/combined type were included in the study. The interview of the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL)[26] was used to exclude other psychiatric comorbidities in the groups with ADHD, HFA, and ADHD+HFA. The Autism Diagnostic Inventory-Revised (ADI-R),[27] the Autism Diagnostic Observation System (ADOS),[28] the K-SADS-PL,[26] and the CPRS-R:L[25] and CTRS-R:L[25] were used to make the diagnosis of HFA and comorbid ADHD+HFA. Both patients with ADHD and those with comorbid ADHD+HFA had inattention and hyperactivity and, for this reason, they met the criteria for the DSM-IV-TR ADHD/combined type. The healthy children were recruited in schools and selected from a pool of subjects who participated voluntarily in the study. None of them had a history of neurological or psychiatric disease or learning disability. The diagnoses of ADHD and HFA, according to the DSM-IV-TR criteria, were excluded in all healthy participants. All subjects included in the study had a normal IQ on the basis of the Wechsler Intelligence Scale for Children-III (WISC-III).[29] (Note that the WISC-IV was not available in an Italian translation when this study was conducted.) At the time of the study, no participants were taking medication known to affect the central nervous system. Before testing, every parent or legal guardian of the subjects included in the study signed a written informed consent.

Evaluation of Planning

The *Tower of London* (ToL) test was used to evaluate planning ability.[30,31] The task material includes 3 wooden pegs of different lengths mounted on a strip of wood and 3 colored balls (red, yellow, and blue). These balls are manipulated on the pegs to reproduce a picture. The same initial position is set for the practice problem and each of the 12 problems of graded difficulty. The demand for planning is changed by presenting problems whose solution requires a different number of minimum moves. For each problem, scores ranged from 0 (the problem was not solved after the third attempt) to 3 (the problem was solved at the first attempt). Performance is evaluated with 2 scores: the sum of the total scores and the total time spent to complete the 12 different patterns.

Evaluation of Verbal Working Memory

The *Backward Digit Span Test* (Digit Span Backward of the WISC-III)[29] was used to evaluate verbal working memory. Recall is in inverse order and the span is the length of the longest list that is correctly recalled.

Evaluation of Response Inhibition

The computerized task of *go/no-go* (Go/No-Go) was used to measure response inhibition. In this task, a sequence of stimuli is presented to the child in quick succession on the monitor. Two targets are chosen among the stimuli, and the child has to press a button when the target appears on the monitor. The child can make omission errors (failure to press the button upon the appearance of the target) or commission errors (pressing the button for a stimulus that is not the target).

Assessment of NSS

The Physical and Neurological Examination for Soft Signs (PANESS)[32] was used to assess motor function. It was evaluated by a child neurologist trained to reliability criteria using the PANESS. The

examiner was blind to the child's diagnostic status at the time of assessment and during scoring. The PANESS has been found to have adequate test-retest reliability,[33] interrater reliability, internal consistency,[34] and sensitivity to age-related changes[2] in diverse and more recently evaluated cohorts. The PANESS measures salient components of motor function, including lateral preference, gaits, balance, motor persistence, coordination, overflow, dysrhythmia, and timed movements. Three primary outcome variables were obtained: (1) total OM included the total number of abnormal movements for age observed during stressed gaits (ie, walking on heels, toes, or sides of feet), tandem gaitsm (walking in tandem forward and backward, touching heels to toes), and during timed movements; (2) total dysrhythmia included total number of timed motor examination trials in which the child failed to maintain a steady rhythm throughout the task; (3) total speed of timed activities of hands/feet included 3 repetitive movements and 3 sequenced movements performed bilaterally: toe tapping, alternating heel-toe tapping, repetitive hand patting, hand pronation/supination, repetitive finger tapping, and finger sequencing.

Statistical Analysis

The comparison of independent samples was performed with Mann-Whitney *U* tests. For the statistical analysis, an α-level of 0.05 was applied. All statistical analyses were carried out using the Statistical Package for Social Sciences SPSS software (version 17.0, Chicago, IL).

RESULTS

Table 2 summarizes neuropsychological and motor variables from the 3 clinical groups and the control group. The patients and HC did not differ in age or IQ. Table 3 summarizes the results of independent samples comparisons with Mann-Whitney *U* test, which are discussed below.

Planning

Significant differences were found between the ADHD group and the control group in ToL total scores and ToL total time, between the HFA group and the control group in ToL total scores and ToL total time, and between the comorbid ADHD+HFA group and the control group in ToL total scores and ToL total time. Significant differences were also found between the ADHD group and the HFA group in ToL total time but not in ToL total scores (P=0.534), between the ADHD group and the comorbid ADHD+HFA group in ToL total time but not in ToL total scores, and between the HFA group and the comorbid ADHD+HFA group in ToL total scores but not in ToL total time.

TABLE 2. Neuropsychological and Motor Variables

	Mean±SD			
	ADHD	***HFA***	***ADHD+HFA***	***Controls***
ToL total score	25.30±3.03	26.07±2.87	21.83±6.57	30.92±2.18
ToL total time	294.15±64.30	360.00±73.50	424.92±136.28	173.77±14.15
Digit span backward	2.61±0.65	3.38±1.04	3.58±1.16	4.07±0.07
Go/No-Go omission errors	1.61±2.98	0.53±0.77	2.25±4.59	0.07±0.27
Go/No-Go commission errors	3.00±2.79	4.23±5.38	5.83±4.50	0.76±1.23
Go/No-Go reaction time	685.92±136.04	609.62±124.72	683.67±133.66	549.69±84.50
Total overflow movements	8.30±2.13	4.41±1.66	4.61±2.06	2.23±1.88
Total dysrhythmia	7.46±1.80	7.23±4.39	9.41±2.57	2.07±1.98
Total speed of timed activities	189.54±52.57	157.62±47.73	152.92±56.15	115.07±6.51

ADHD indicates attention-deficit/hyperactivity disorder; HFA, high-functioning autism; ADHD+HFA, comorbid ADHD and HFA; ToL, Tower of London test.

TABLE 3. Results of Independent Samples Comparisons With Mann-Whitney *U* Tests

	ADHD Vs. Controls (P)	*HFA Vs. Controls (P)*	*ADHD+ HFA Vs. Controls (P)*	*ADHD Vs. HFA (P)*	*ADHD Vs. ADHD+ HFA (P)*	*HFA Vs. ADHD+ HFA (P)*
ToL total score	**0.001***	**0.001***	**0.001***	0.534	0.131	**0.040***
ToL total time	**0.001***	**0.001***	**0.001***	**0.038***	**0.009***	0.247
Digit span backward	**0.001***	**0.037***	0.170	**0.034***	**0.022***	0.626
Go/No-Go omission errors	**0.010***	0.060	**0.019***	0.311	0.770	0.180
Go/No-Go commission errors	**0.006***	**0.024***	**0.001***	0.897	0.088	0.544
Go/No-Go reaction time	**0.003***	0.248	**0.004***	0.158	0.870	0.242
Total overflow movements	**0.001***	0.060	**0.001***	**0.001***	**0.001***	0.700
Total dysrhythmia	**0.007***	**0.037***	**0.003***	0.877	**0.037***	0.253
Total speed of timed activities	**0.004***	**0.050***	**0.045***	0.124	0.064	0.624

**Level of significance P≤0.05.*
Statistical significance is indicated in bold.
7ADHD indicates attention-deficit/hyperactivity disorder; HFA, high-functioning autism; ADHD+HFA, comorbid ADHD and HFA; ToL, Tower of London test.

Verbal Working Memory

Significant differences on the Digit Span Backward test were found between the ADHD group and the control group and between the HFA group and the control group, whereas no significant differences on the Digit Span Backward test were found between the comorbid ADHD+HFA group and the control group. Significant differences on the Digit Span Backward test were also found between the ADHD group and the HFA group and between the ADHD group and the comorbid ADHD+HFA group, whereas no significant differences on the Digit Span Backward test were found between the HFA group and the comorbid ADHD+HFA group.

Response Inhibition

Significant differences were found between the ADHD group and the control group in omission errors, commission errors, and reaction time, between the HFA group and the control group in commission errors but not in omission errors and reaction time, and between the comorbid ADHD+HFA group and the control group in omission errors, commission errors, and reaction time.

No significant differences were found in omission errors, commission errors, and reaction time between the ADHD group and the HFA group, between the ADHD group and the comorbid ADHD+HFA group, and between the HFA group and the comorbid ADHD+HFA group.

NSS

Significant differences were found between the ADHD group and the control group in total OM, total dysrhythmia, and total speed of timed activities, between the HFA group and the control group in total dysrhythmia and total speed of timed activities but not in total OM, and between the comorbid ADHD+HFA group and the control group in total OM, total dysrhythmia, and total speed of timed activities. Significant differences were found between the ADHD group and the HFA group in total OM but not in total dysrhythmia and total speed of timed activities, between the ADHD group and the comorbid ADHD+HFA group in total OM and total dysrhythmia but not in total speed of timed activities. No significant differences between the HFA group and the comorbid ADHD+HFA

group were found in total OM, total dysrhythmia, and total speed of timed activities.

DISCUSSION

ADHD and HFA, 2 of the most common neurodevelopmental disorders with onset in early childhood, are highly heritable conditions associated with documented brain abnormalities, the symptoms of which cause academic and social dysfunction, and skills deficits.[35,36] Moreover, many children with HFA may experience ADHD-like symptoms and the 2 disorders are often comorbid.[15] Structural and functional neuroimaging studies point to multiple abnormalities in the frontalstriatal system (including frontal lobes and basal ganglia) and in motor and premotor circuits and cerebellum in children with ADHD[37] and HFA.[36] These brain regions are important in motor control and EF, and dysfunction in these areas may explain the deficits in EF, and motor impairment found in ADHD, HFA, and in comorbid ADHD+HFA. In this study, possible differences on measures of planning, verbal working memory, response inhibition, and NSS were evaluated in a well-defined sample of drug-naive patients with ADHD, HFA, and comorbid ADHD+HFA. We also analyzed the effects of comorbidity on all of the considered variables.

In our study, the ADHD group showed an impairment on measures of planning, response inhibition, and verbal working memory when compared with the HC group. These findings support previous studies: indeed, planning difficulties have been found in children with ADHD[38,39] and response inhibition and working memory have consistently been identified as problematic for children with ADHD.[40,41] In addition, impairment of verbal and spatial working memory has been proposed as a possible neurocognitive trait of ADHD.[42] Deficits in EF are strongly related to dysfunction of the prefrontal cortex, and neuroimaging studies have shown involvement of prefrontal and connected structures in children with ADHD.[33,37]

Moreover, in our study, the ADHD group showed a great number of NSS, such as increased OM, increased dysrhythmia, and lower speed of timed activities when compared with the HC group. An increased number of NSS, such as increased OM,[6,43] impaired timing of motor responses,[44] and deficits in motor coordination[45] and fine motor abilities,[46] has been reported in children with ADHD. The presence of NSS in children with ADHD may reflect immaturity and/or dysfunction of the frontal-striatal-cerebellar networks involved in motor control.[16,47]

In our study, the HFA group showed executive dysfunction when compared with the HC group, in particular planning difficulties and impairment in response inhibition and verbal working memory. Thus, these findings support previous studies that showed deficits across most measures of EF.[23,41,48] As in children with ADHD, EF deficits in those with HFA also seem to be due to disruption of the frontostriatal system, including prefrontal cortex, lateral orbitofrontal cortex, anterior cingulate, supplementary motor area, and basal ganglia.[36] Consistent with findings from our previous study,[18] this study found that the HFA group had increased dysrhythmia and lower speed of timed activities when compared with the HC group. These findings also support the results of other studies that have used the PANESS, in which greater dysrhythmia and slowness of timed movements of hands and feet were documented in patients with HFA compared with healthy children.[17,49] Dysrhythmia may reflect cerebellar dysfunction,[7] and slowness of timed activities may be due to functional deficits of the frontostriatal system,[49] cerebellum, and basal ganglia.[47]

Although few studies have examined the effects of comorbidity on EF, it appears that children with comorbid ADHD and autism spectrum disorders exhibit greater deficits and, in particular, a greater impairment of vigilance and response inhibition.[15,23,24] The ADHD+HFA group in our study was impaired on measures of planning and response inhibition when compared with the HC group. To our knowledge, no studies have examined the effects of comorbidity on motor function. The ADHD+HFA group in our study showed a great number of NSS, such as increased OM, increased dysrhythmia, and lower speed of timed activities, when compared with the HC group. Comparative studies have generally found EF deficits and motor impairment across clinical groups with ADHD and those with autism spectrum disorders. Children with ADHD have been found to show more difficulty in response inhibition[38] and verbal working memory[50] compared with those with HFA, whereas

children with HFA have been found to show more impairment in planning and fluid reasoning compared with those with ADHD.[51] On the basis of the data in our study, the ADHD group showed deficits of planning and working memory when compared with the HFA group. Moreover, we have found that planning difficulties were even more serious in the ADHD+HFA group when compared with the other clinical groups. Children with ADHD showed a greater number of OM compared with the HFA group. OM likely reflect dysfunction within motor and premotor circuits that are important for the execution and preparation of motor responses.[52] A functional neuroimaging study showed a smaller extent of activation in the contralateral primary motor cortex in subjects with ADHD while performing a simple motor task, which may represent insufficient recruitment of neuronal activity necessary to mobilize transcallosal interhemispheric inhibition.[53] This finding may explain the increased prevalence of OM in children with ADHD.[6] Dysfunctions in motor and premotor circuits, responsible for OM in patients with ADHD, may be due to abnormalities in white matter tracts, including the corpus callosum.[16] In a recent study, Ferrin and Vance[54] found that NSS are associated with difficulties in spatial working memory and may be used as a possible "sign" of ADHD. These findings support the proposal to use the examination of NSS as a diagnostic tool for neurodevelopmental disorders and ADHD in particular. In our study, greater dysrhythmia distinguished the ADHD+HFA group from the ADHD group, and we hypothesized that this may reflect a more severe cerebellar dysfunction in the case of comorbidity. In conclusion, on the basis of our investigation, deficits in EF and a greater number of NSS differentiated the ADHD and HFA groups from the HC group. Moreover, a more serious impairment on measures of planning and verbal working memory and increased OM differentiated the ADHD group from the HFA group. Finally, the ADHD+HFA group showed a more serious deficit in planning than the other clinical groups.

The strength of the current study is the inclusion of a well-defined group of drug-naive children with ADHD, HFA, and comorbid ADHD+HFA, who were carefully screened for other comorbid psychiatric conditions. Another strong point of our investigation was that it evaluated the effects of comorbidity on motor and executive functioning. It is interesting to note that, on the basis of our data, measures of NSS appear to show stronger power to differentiate ADHD and HFA compared with other clinical variables, although this result needs to be confirmed in a larger sample of patients. In particular, the OM measure revealed a gradient in which ADHD was at one extreme (more OM) and HFA at the other extreme (less OM), whereas ADHD+HFA showed a number of OM that was positioned in the middle between ADHD and HFA. Therefore, our findings suggest that ADHD and HFA may be distinguished in terms of neurological impairment. Moreover, they are consistent with the results of other researchers who have shown the usefulness of NSS in the diagnostic work-up of other neuropsychiatric diseases such as schizophrenia and bipolar disorder.[55] Note that the patients recruited in this study were all drug naive and therefore we could not investigate the impact of medication on NSS. However, future research evaluating the utility of NSS examination as a diagnostic tool should keep in mind that a marked improvement or complete resolution of NSS following treatment with methylphenidate has been reported in patients with ADHD.[56] On the basis of this scientific evidence, we suggest that evaluation of NSS before and after methylphenidate treatment would be useful to monitor the effectiveness of pharmacological treatment in patients with ADHD.

The main limitation of our study was the small sample of subjects, which constrains the interpretation of our findings. Future studies involving a larger sample size will help expand our knowledge about the effects of comorbidity on motor and EF and possible correlations between motor problems and executive dysfunction. Moreover, additional studies with a larger sample size will help clarify the different motor and executive dysfunctions related to the subtypes of ADHD. Finally, it would be useful to assess executive dysfunction with an ecologically valid parent/self-report measure of EF, which would provide a measure of planning, working memory, and response inhibition in a less structured setting.

REFERENCES

1. Shafer SQ, Shaffer D, O'Connor PA, et al. Hard thoughts on neurological soft signs. In: Rutter M, editor.

Developmental Neuropsychiatry. New York: Guilford Press; 1983:pp. 133–143.
2. Larson JC, Mostofsky SH, Goldberg MC, et al. Effects of gender and age on motor exam in typically developing children. Dev Neuropsychol. 2007;32:543–562.
3. Abercrombie ML, Lindon RL, Tyson MC. Associated movements in normal and physically handicapped children. Dev Med Child Neurol. 1964;6:573–580.
4. Armatas CA, Summers JJ, Bradshaw JL. Mirror movements in normal adult subjects. J Clin Exp Neuropsychol. 1994;16:405–413.
5. Cole WR, Mostofsky SH, Larson JC, et al. Age-related changes in motor subtle signs among girls and boys with ADHD. Neurology. 2008;71:1514–1520.
6. Mostofsky SH, Newschaffer CJ, Denckla MB. Overflow movements predict impaired response inhibition in children with ADHD. Percept Mot Skills. 2003;97: 1315–1331.
7. Schmahmann JD. Disorders of the cerebellum: ataxia, dysmetria of thought, and the cerebellar cognitive affective syndrome. J Neuropsychiatry Clin Neurosci. 2004;16:367–378.
8. Denckla MB. Biological correlates of learning and attention: what is relevant to learning disability and attention deficit hyperactivity disorder? J Dev Behav Pediatr. 1996;17:114–119.
9. Pennington BF, Ozonoff S. Executive functions and developmental psychopathology. J Child Psychol Psychiatry. 1996;37:51–87.
10. Barkley RA. "Executive function and ADHD": reply. J Am Acad Child Adolesc Psychiatry. 2001;40:501–502.
11. Barkley RA. ADHD and the Nature of Self-control. New York: Guilford Press; 2005.
12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR). Washington, DC: American Psychiatric Association; 2000.
13. Steinhausen HC. The heterogeneity of causes and courses of attention-deficit/hyperactivity disorder. Acta Psychiatr Scand. 2009;120:392–399.
14. Kogan MD, Blumberg SJ, Schieve LA, et al. Prevalence of parent-reported diagnosis of autism spectrum disorder among children in the US 2007. Pediatrics. 2009;124: 1395–1403.
15. Goldstein S, Schwebach AJ. The comorbidity of pervasive developmental disorder and attention deficit hyperactivity disorder: results of a retrospective chart review. J Autism Dev Disord. 2004;34:329–339.
16. D'Agati E, Casarelli L, Pitzianti MB, et al. Overflow movements and white matter abnormalities in ADHD. Prog Neuropsychopharmacol Biol Psychiatry. 2010;34: 441–445.
17. Jansiewicz EM, Goldberg MC, Newschaffer CJ, et al. Motor signs distinguish children with high functioning autism and Asperger's syndrome from controls. J Autism Dev Disord. 2006;36:613–621.
18. Pasini A, D'Agati E, Pitzianti M, et al. Motor examination in children with attention-deficit/hyperactivity disorder and Asperger syndrome. Acta Paediatr. 2012;101: e15–e18.
19. Wilcutt EG, Doyle AE, Nigg JT, et al. Validity of the executive function theory of ADHD: a meta-analysis review. Biol Psychiatry. 2005;57:1336–1346.
20. Kenworthy LE, Black DO, Wallace GL, et al. Disorganization: the forgotten executive dysfunction in high-functioning autism (HFA) spectrum disorders. Dev Neuropsychol. 2005;28:809–827.
21. Hill EL. Evaluating the theory of EF deficits in autism. Dev Rev. 2004;24:189–233.
22. Ozonoff S, Cook I, Coon H, et al. Performance on Cambridge neuropsychological test automated battery subtests sensitive to frontal lobe function in people with autistic disorder: evidence from collaborative programs of excellence in autism network. J Autism Dev Disord. 2004;34:139–150.
23. Corbett BA, Constantine LJ, Hendren RL, et al. Examining executive functioning in children with autism spectrum disorder, attention deficit hyperactivity disorder and typical development. Psychiatry Res. 2008;166: 210–222.
24. Sinzig J, Walter D, Dopfner M. Inhibition, flexibility, working memory and planning in autism spectrum disorder with and without comorbid ADHD-symptoms. Child Adolesc Psychiatry Ment Health. 2008;2:1–12.
25. Nobile M, Alberti B, Zuddas A, et al. Conners' Rating Scales Revised Adattamento italiano. Firenze: Giunti Organizzazioni Speciali; 2007.
26. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997;36:980–988.
27. Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J Autism Dev Disord. 1994;24:659–685.
28. Lord C, Rutter M, Goode S, et al. Autism Diagnostic Observation Schedule: a standardized observation of communicative and social behavior. J Autism Dev Disord. 1989;19:185–212.
29. Wechsler D. Wechsler Intelligence Scale for Children, 3rd ed. San Antonio: The Psychological Corporation; 1991.
30. Shallice T. Specific impairments of planning. Philosophical Transcripts of the Royal Society of London B. 1982; 298:199–209.
31. Krikorian R, Bartok J, Gay N. Tower of London procedure: a standard method and developmental data. J Clin Exp Neuropsychol. 1994;16:840–850.
32. Denckla MB. Revised neurological examination for subtle signs (1985). Psychopharmacol Bull. 1985;21:773–800.
33. Holden EW, Tarnowski KJ, Prinz RJ. Reliability of neurological soft signs in children: reevaluation of the PANESS. J Abnorm Child Psychol. 1982;10:163–172.
34. Vitiello B, Ricciuti AJ, Stoff DM, et al. Reliability of subtle (soft) neurological signs in children. J Am Acad Child Adolesc Psychiatry. 1989;28:749–753.
35. Curatolo P, Paloscia C, D'Agati E, et al. The neurobiology of attention deficit/hyperactivity disorder. Eur J Paediatr Neurol. 2009;13:299–304.
36. Zachor DA, Curatolo P. Recommendations for early diagnosis and intervention in autism spectrum disorders: an Italian-Israeli consensus conference. Eur J Paediatr Neurol. 2014;18:107–118.
37. Chandan JV. Neurodevelopmental abnormalities in ADHD. Curr Top Behav Neurosci. 2012;9:49–66.
38. Bramham J, Ambery F, Young S, et al. Executive functioning differences between adults with attention deficit hyperactivity disorder and autistic spectrum disorder in initiation, planning and strategy formation. Autism. 2009;13:245–264.

39. Marzocchi GM, Oosterlaan J, Zuddas A, et al. Contrasting deficits on executive function between ADHD and reading disabled children. J Child Psychol Psychiatry. 2008;49:543–552.
40. Scheres A, Oosterlaan J, Geurts H, et al. Executive functioning in boys with ADHD: primarily an inhibition deficit? Arch Clin Neuropsychol. 2004;19:569–594.
41. Goldberg MC, Mostofsky SH, Cutting LE, et al. Subtle executive impairment in children with autism and children with ADHD. J Autism Dev Disord. 2005;35: 279–293.
42. Pasini A, Paloscia C, Alessandrelli R, et al. Attention and executive functions profile in drug naive ADHD subtype. Brain Dev. 2007;29:400–408.
43. Uslu R, Kapci EG, Oztop D. Neurological soft signs in comorbid learning and attention deficit hyperactivity disorder. Turk J Pediatr. 2007;49:263–269.
44. Rubia K, Overmeyer S, Taylor E, et al. Hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: a study with functional MRI. Am J Psychiatry. 1999;156:891–896.
45. Watemberg N, Waiserberg N, Zuk L, et al. Developmental coordination disorder in children with attention deficit hyperactivity disorder and physical therapy intervention. Dev Med Child Neurol. 2007;49:920–925.
46. Pitcher TM, Piek JP, Hay DA. Fine and gross motor ability in males with ADHD. Dev Med Child Neurol. 2003;45:525–535.
47. Pasini A, D'Agati E. Phatophysiology of NSS in ADHD. World J Biol Psychiatry. 2009;10:495–502.
48. Geurst HM, Verte S, Oosterlaan J, et al. How specific are executive functioning deficits in attention deficit hyperactivity disorder and autism? J Child Psychol. 2004;45: 836–854.
49. Rinehart NJ, Bradshaw JK, Brereton AV, et al. Movement preparation in high-functioning autism and Asperger disorder: a serial choice reaction time task involving motor reprogramming. J Autism Dev Disord. 2001;31:79–88.
50. Ozonoff S, Strayer DL. Further evidence of intact working memory in autism. J Autism Dev Disord. 2001;31: 257–263.
51. Clikeman-Semrud M, Walkowiak J, Wilkinson A, et al. Executive functioning in children with Asperger syndrome, ADHD-combined type, ADHD-predominately inattentive type, and controls. J Autism Dev Disord. 2010;40:1017–1027.
52. Cincotta M, Borgheresi A, Boffi P, et al. Bilateral motor cortex output with intended unimanual contraction in congenital mirror movements. Neurology. 2002;58: 1290–1293.
53. Mostofsky SH, Rimrodt SL, Schafer JG, et al. Atypical motor and sensory cortex activation in attention-deficit/hyperactivity disorder: a functional magnetic resonance imaging study of simple sequential finger tapping. Biol Psychiatry. 2006;59:48–56.
54. Ferrin M, Vance A. Examination of neurological subtle signs in ADHD as a clinical tool for the diagnosis and their relationship to spatial working memory. J Child Psychol Psychiatry. 2012;53:390–400.
55. Ruggini S, Dimitri-Valente G, Mandarelli G, et al. Neurological soft signs discriminate schizophrenia from bipolar disorder. J Psychiatr Pract. 2014;20:147–153.
56. Lerer RJ, Lerer MP. The effects of methylphenidate on the soft neurological signs of hyperactive children. Pediatrics. 1976;57:521–525.

L'IRCCS – Istituto di Ricerche Farmacologiche Mario Negri si trova a Milano in zona Bovisa nelle vicinanze del Campus Politecnico (Ingegneria di fronte al padiglione B23) e della Triennale Bovisa. E' facilmente raggiungibile con il passante ferroviario, scendendo alle fermate di Bovisa (FNM) o Villapizzone (FS).

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La partecipazione è gratuita e prevede l'assegnazione di 5.60 crediti ECM. L'iscrizione al Convegno è obbligatoria e deve essere effettuata accedendo al link:

www.ADHD.marionegri.it

Con il patrocinio:

SINPIA Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza

ACP Associazione Culturale Pediatri

CONVEGNO

Uso razionale degli psicofarmaci in età evolutiva

(per il trattamento dell'ADHD)

Milano, 21 giugno 2016
Ore 9.00-17.30 - AULA GUASTI

IRCCS
Istituto di Ricerche Farmacologiche Mario Negri
Via G. La Masa 19 - 20156 Milano

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

Azienda Ospedaliera
SPEDALI CIVILI BRESCIA

SEBBENE SIANO POCHI QUELLI APPROVATI PER L'USO IN ETÀ PEDIATRICA, GLI PSICOFARMACI SONO PRESCRITTI AL BAMBINO E, IN PARTICOLARE, ALL'ADOLESCENTE SPESSO IN MODO INAPPROPRIATO.

LA PRESCRIZIONE DI UN FARMACO, E IN PARTICOLARE DI UNO PSICOFARMACO, DOVREBBE ESSERE PARTE DI UN DISEGNO STRATEGICO MULTIMODALE NON STATICO MA IN CONTINUA E NECESSARIA RIVALUTAZIONE.

COME PARTE DEL PERCORSO ATTIVATO CON IL PROGETTO REGIONALE "CONDIVISIONE DEI PERCORSI DIAGNOSTICO-TERAPEUTICI PER L'ADHD IN LOMBARDIA" L'INCONTRO È INTESO COME MOMENTO DI RIFLESSIONE COLLEGIALE PER UN USO PIÙ APPROPRIATO (CONDIVISO E PARTECIPATO) DEGLI PSICOFARMACI IN ETÀ EVOLUTIVA.

RELATORI

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Il Progetto: "Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia" è stato in parte finanziato dalla Regione Lombardia con Decreto DG Salute n 3798 del 08.05.2014 e n 778 del 05.02.2015. Il progetto coinvolge 18 Centri di Riferimento per l'ADHD e il Laboratorio per la Salute Materno Infantile dell'IRCCS - Istituto di Ricerche Farmacologiche Mario Negri. Coordinatore del Progetto è la UONPIA degli Spedali Civili di Brescia.

9.15-11.00 **Introduzione**
Silvio Garattini

Principi di psicofarmacologia clinica
(efficacia e sicurezza, uso off-label, schemi terapeutici, …)
Maurizio Bonati, Antonio Clavenna

Coordina: *Edda Zanetti*

DISCUSSIONE

CASI A CONFRONTO

Commentatori: *Serafino Corti, Rocco Farruggia, Luigi Mazzone*

Coordina: *Ottaviano Martinelli*

11.00-11.45 **Non sempre il farmaco**
Claudio Bissoli

11.45-12.30 **Il farmaco dopo**
Paola Morosini

Pausa Pranzo

Coordina: *Massimo Molteni*

14.00-14.45 **Il farmaco prima**
Stefano Conte

14.45-15.30 **Più farmaci**
Matteo Chiappedi

TAVOLA ROTONDA

16.00-17.30 **INFORMAZIONE, FORMAZIONE E AGGIORNAMENTI PER UN USO RAZIONALE DEGLI PSICOFARMACI**
Antonella Costantino, Corrado Barbui
Elisa Fazzi, Francesca Neri, Umberto Balottin

Coordina: *Maurizio Bonati*

DISCUSSIONE

Dal 2016 “Disturbi di Attenzione e Iperattività” ha referee nazionali ed è indicizzata nel JournalTOCS (http://rivistedigitali.erickson.it/disturbi-di-attenzione-iperattivita/) aumenta quindi l’interesse e l’opportunità di pubblicare lavori scientifici su questa rivista.

Gian Marco Marzocchi
Direttore scientifico

WebCenter

Questionario per la valutazione della Newsletter ADHD

Gent.mi lettori,

questo è un invito alla compilazione del questionario on-line sulla Newsletter ADHD.

Tale operazione Vi impegnerà per 2 minuti al massimo accedendo al seguente link:

http://www.adhd.marionegri.it/index.php/newsletter/valutazione-newsletter

Si confida nella Vs preziosa collaborazione.

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://www.adhd.marionegri.it/index.php/newsletter/iscrizione-newsletter

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3798 del 08/05/2014 e n. 778 del 05/02/2015)
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia" "*Percorsi diagnostico-terapeutici per l'ADHD*".

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