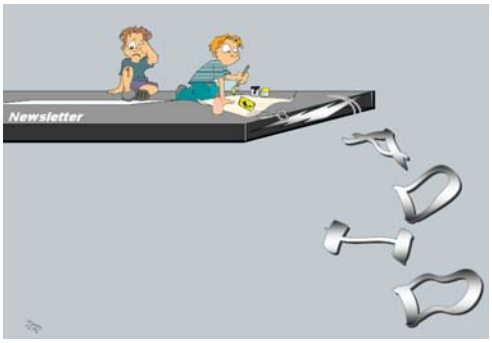


# ADHD

ATTENTION DEFICIT HYPERACTIVITY DISORDER

*Laboratorio per la Salute Materno Infantile*

MARIO NEGRI
ISTITUTO DI RICERCHE FARMACOLOGICHE

**NEWSLETTER** **N. 17 - anno II - Maggio 2009**

## INDICE



Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticles 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.

Milano, 17 aprile 2009

**COMUNICATO STAMPA**

# MOLTO MENO DI QUELLI PREVISTI I BAMBINI CON ADHD IN TERAPIA CON PSICOFARMACI

L'8 marzo 2007, veniva autorizzata l'immissione in commercio dell'atomoxetina e del metilfenidato per il trattamento della sindrome da Deficit di Attenzione e Iperattività (ADHD). Da giugno 2007 è attivo il "Registro Nazionale dell'ADHD nell'età evolutiva" per il monitoraggio dei percorsi diagnostico-terapeutici e assistenziali e per la valutazione degli effetti avversi dei due farmaci indicati per il trattamento della sindrome. La prescrizione del farmaco è vincolata alla registrazione del paziente nel Registro Nazionale.

In 20 mesi di attività sono stati iscritti nel registro 1090 pazienti che hanno ricevuto almeno una prescrizione di atomoxetina (639 pazienti pari al 57% dei registrati) o metilfenidato (451; 43%). Il 40% dei pazienti risiedono in Lombardia, Veneto o Sardegna e un quarto del totale risulta in carico a solo 3 degli 86 Centri di riferimento accreditati dalle Regioni e dalle Province autonome.

Solo il 30% dei pazienti ha ricevuto una terapia psicofarmacologica associata a counseling e ad una terapia cognitivo-comportamentale, come previsto dal protocollo del Registro e dalle linee guida nazionali e internazionali. Interventi di counseling sono stati effettuati al 59% dei pazienti, di parent training al 37% e di child training al 25%.

In 35 pazienti si sono verificati eventi avversi: 8 durante terapia con metilfenidato (1,8% dei casi) e 27 durante terapia con atomoxetina (4,2% dei casi). Per 12 dei 35 pazienti le reazioni sono state giudicate gravi (1 metilfenidato e 11 atomoxetina) ed è stata necessaria la sospensione della terapia. In 3 degli 11 casi in terapia con atomoxetina la reazione avversa è stata l'ideazione suicidaria.

Il Registro si è quindi rivelato uno strumento utile per monitorare l'uso dei farmaci per la terapia dell'ADHD, migliorandone l'appropriatezza e identificando in modo più accurato gli effetti avversi. La temuta (da alcuni) "epidemia" di prescrizioni di psicofarmaci ai bambini italiani con ADHD non si è verificata. Anche la prevalenza dell'ADHD in Italia sembra essere considerevolmente inferiore a quanto descritto in altri Paesi europei. Tuttavia, l'applicazione dell'intero percorso diagnostico e terapeutico riconosciuto come il più appropriato è ancora ampiamente disattesa sull'intero territorio nazionale e rimanda alla necessità di attivare adeguate risorse (umane e organizzative) a livello locale, nell'ambito dei servizi sanitari e sociali preposti alla salute per l'età evolutiva.

***Pietro Panei***
*Dipartimento del Farmaco*
*Istituto Superiore di Sanità*

***Maurizio Bonati***
*Capo, Dipartimento Salute Pubblica*
*IRFMN Milano*

NR/**166**

Editoriali

## IL REGISTRO DELL'ADHD: LO STATO DELL'ARTE

Da giugno 2007 è attivo il "Registro Nazionale dell'ADHD nell'età evolutiva" per il monitoraggio dei percorsi diagnostico-terapeutici e assistenziali e per la valutazione degli effetti avversi degli psicostimolanti (metilfenidato e amoxetina) indicati per il trattamento dell'ADHD[1]. La durata prevista era inizialmente di due anni; recentemente è stata prorogata di un ulteriore anno. È quindi tempo di fare alcune considerazioni sulla resa di uno strumento di grandi potenzialità per rispondere, in modo appropriato ed equo a livello nazionale, a bisogni di salute ancora largamente inevasi.

• Nel corso dei primi 20 mesi di attività sono stati inseriti i dati relativi a 1050 pazienti che hanno ricevuto almeno una prescrizione di uno psicostimolante: 618 (57%) atomoxetina, 432 (43%) metilfenidato.
*Dallo studio Prisma[2] e dalla stima riportata dall'Istituto Superiore di Sanità[3], la prevalenza dell'ADHD in Italia nella popolazione di 6-17 anni d'età dovrebbe essere dell'1-2%, quindi, almeno 68.000 casi. I risultati dello studio MTA[4] indicano che, per il 34% della popolazione affetta da ADHD, la terapia psico-sociale-educativa è efficace e rappresenta la terapia di pri-*

*ma scelta. Sarà quindi al rimanente 66% della popolazione non responder che andrà combinata la terapia farmacologica (che risulta efficace per un ulteriore 34%)[4]. La dimensione attesa della popolazione italiana affetta da ADHD da sottoporre a terapia farmacologica con psicostimolanti è, quindi, di circa 45.000 pazienti. L'aver arruolato nel Registro, sinora, solo 1050 pazienti induce a formulare alcune ipotesi: a) una possibile ampia sottostima della casistica reale imputabile alla scarsa compliance al Registro da parte dei Centri di Riferimento; b) l'efficacia dei trattamenti non farmacologici è maggiore di quanto documentato nella letteratura scientifica; c) la prevalenza del disturbo in Italia è considerevolmente inferiore a quanto stimato.*

• I pazienti risultano in carico a 86 dei 125 Centri di riferimento (69%), sebbene solo 18 Centri abbiano in carico più di 10 pazienti, per un totale di 924 (88%). Il 16% dei pazienti registrati risiede in Lombardia (218), il 15% in Veneto (199) e l'8% in Sardegna (104) e afferisce, in particolare, a 3 Centri: Garbagnate, Milano (60 pazienti), San Donà di Piave, Venezia (151), Cagliari (95).
*I Centri di riferimento sono stati indicati da ciascuna Regione previo accreditamento/accertamento della disponibilità e possibilità del Centro di garantire le procedure diagnostico-terapeutiche previste dal Registro. La constatazione che un terzo dei Centri individuati non abbia in carico pazienti in trattamento farmacologico con psicostimolanti e che il 40% dei pazienti inseriti nel Registro afferisca a solo 3 Centri può essere attribuibile: a) a una scarsa compliance al Registro da parte dei Centri; b) a una diversa attitudine terapeutica dei singoli Centri; c) al confluire/indirizzare i pazienti con ADHD verso i Centri con maggior tradizione alla cura del disturbo.*

• L'89% dei pazienti arruolati (953) sono maschi; la fascia di età prevalente è 10-13 anni (441, 42%); la scolarità 3ª elementare - 2ª media inferiore (665, 63%). La segnalazione del paziente al Centro di riferimento è stata fatta nella maggioranza dei casi dai genitori del bambino (48%) o da altri Servizi di Neuropsichiatria (26%); solo il 7% dei casi è stato segnalato dal pediatra di famiglia. Oltre ai 3 sintomi cardini (inattenzione, iperattività e impulsività), riscontrati nella quasi totalità dei pazienti, i sintomi più frequenti sono stati: i problemi scolastici (65% dei pazienti), il disturbo opposizionale (46%), i problemi dell'apprendimento (45%).
*Il profilo della popolazione risponde all'atteso, secondo quanto descritto, anche nel setting scolastico italiano[5]. Tuttavia, sebbene i problemi scolastici e quelli di apprendimento costituiscano i sintomi prevalenti, la mancata segnalazione dei pazienti al Centro di riferimento da parte della scuola suggerisce che l'interazione tra i vari attori, prevista dalle procedure del Registro, necessita di un'implementazione che deve, nella pratica, essere ancora costruita.*

• La diagnosi più frequente è stata di ADHD complessa (85%), rispetto al disturbo con prevalenza di inattenzione (11%) o iperattività (4%). Oltre alla terapia farmacologica, il 59% dei pazienti ha ricevuto anche interventi di *counselling*, il 37% di *parent training*, il 25% di *child training* e il 23% una terapia cognitivo-comportamentale. Altri interventi terapeutici sono stati effettuati ad almeno un quarto dei pazienti. Solo il 30% dei pazienti ha ricevuto una terapia psico-farmacologica associata a *counselling* e a una terapia cognitivo-comportamentale.
*La terapia non farmacologica, nella sua varietà di utilizzo, di tipologia e offerta, rappresenta la prima scelta di documentata efficacia per la maggioranza dei pazienti con ADHD, da complementarsi (e non sostituirsi), al bisogno, con quella farmacologica[6]. Lo scarso utilizzo di alcuni degli interventi non farmacologici e la loro variegata offerta che emergono da questa analisi preliminare suggeriscono che diverse sono le attitudini da parte delle strutture sanitarie locali preposte alle cure. Differenze riconducibili sia alle scarse risorse disponibili e, forse, anche a differenti approcci culturali. Sono questi elementi per una riflessione più ampia, nella consapevolezza che non è sufficiente introdurre uno strumento evidence based per modificare una pratica.*

• In corso di terapia farmacologica sono stati segnalati eventi avversi in 30 pazienti (8 per il metilfenidato, 2% dei casi, e 22 per l'atomoxetina, 4%), 9 dei quali gravi (1 metilfenidato e 8 atomoxetina). In 23 casi è stato necessario sospendere la terapia. In 3 casi, in terapia con atomoxetina, la diagnosi è stata di ideazione suicidaria.
*Il monitoraggio delle reazioni avverse in corso di terapia con psicostimolanti era uno dei mandati dell'Agenzia Nazionale sul Farmaco (AIFA), che ha voluto e sostenuto la creazione del Registro nell'ambito di una serie di iniziative volte a garantire un uso razionale dei farmaci per i bambini[7]. I dati sinora raccolti documentano effetti collaterali e reazioni avverse potenzialmente attesi e già descritti, ma consentono, per la prima volta, di quantificarne la prevalenza e la gravità e di consentire provvedimenti regolatori[8] basati su quanto riscontrato a livello nazionale e non mutuato da segnalazioni internazionali.*

Nonostante alcuni limiti, storture e difficoltà (strutturali e gestionali), dopo un necessario periodo di rodaggio, il Registro si è quindi rivelato uno strumento potenzialmente utile e appropriato a rispondere alle finalità che ne hanno determinato la sua costituzione. Strumento unico per la realtà neuropsichiatrica nazionale e internazionale, consente di individuare le criticità della gestione delle cure non solo associate all'ADHD ma, più in generale, dell'assistenza dei disturbi psichiatrici dell'età evolutiva nell'ambito del Servizio Sanitario Nazionale. In tale contesto, le risorse sinora investite e quelle ancora necessarie per un adeguato aggiornamento del Registro potranno essere foriere di un suo impiego anche per altre problematiche (p. es., autismo, uso degli psicofarmaci ecc.) che necessitano di sistematici interventi di monitoraggio complessivo (diagnosi, terapia, gestione delle cure). Infatti, l'esperienza acquisita e la rete degli operatori che si è costituita "attorno" al Registro rappresentano un risultato utile per la pianificazione di altre iniziative di risposta a quesiti che necessitano ancora di adeguate evidenze. Sarà compito delle istituzioni preposte (sia nazionali che locali), delle Società Scientifiche, delle Associazioni dei genitori e, più in generale, di tutti gli operatori coinvolti quotidianamente nella presa in carico dei bambini e degli adolescenti con disturbi psichiatrici, determinare la rilevanza dei bisogni e le possibili iniziative da intraprendere, in modo collegiale e partecipato, nel prossimo futuro. È questo il risultato generale, ma forse il più significativo, già raggiunto con il Registro Nazionale dell'ADHD.

Editoriali

**Bibliografia**

1. Bonati M. Disturbi mentali e farmaci: il caso dell'ADHD e degli psicostimolanti. Medico e Bambino 2007;26:76-7.
2. Frigerio A, Rucci P, Goodman R, et al. Prevalence and correlates of mental disorders among adolescents in Italy: the PrISMA study. Eur Child Adolesc Psychiatry 2009;18:217-26.
3. Knellwolf AL, Panei P, Arcieri R, Vella S. Failure to diagnose ADHD correctly puts children in danger. Ital J Pediatr 2006;32:136-7.
4. MTA Cooperative Group. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. Pediatrics 2004;113:754-61.
5. Mugnaini D, Masi G, Brovedani P, et al. Teacher reports of ADHD symptoms in Italian children at the end of first grade. Eur Psychiatry 2006;21:419-26.
6. National Institute for Health and Clinical Excellence. Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. NICE guideline 2008; www.nice.org.uk/nicemedia/pdf/CG072NiceGuidelineV2.pdf.
7. Bonati M. L'AIFA al servizio dei bambini. Medico e Bambino 2008; 27:551-2.
8. AIFA. Atomoxetina e idee suicidarie in pediatria. Reazioni 2009; 3:7.

**Maurizio Bonati**
**Laboratorio per la Salute Materno-Infantile, IRFMN, Milano**
**Pietro Panei**
**Dipartimento del Farmaco, ISS, Roma**

# 8-Year Follow-up of the MTA Sample

PHILIP L. HAZELL, PH.D., F.R.A.N.Z.C.P.

*A Dance to the Music of Time* is the collective title given to a 12-volume series of novels by English author Anthony Powell that spans the period 1914–1971 and involves more than 300 characters.[1] The work is notable for the way Powell advances the narrative while, at the same time, developing further background to the story through reminiscences of the narrator and conversations between the characters. Reporting of the NIMH Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder (MTA) is unfolding in a similar fashion. The MTA started with 579 children aged between 7 and 9.9 years who were randomized to receive one of 4 treatment conditions for 14 months. At the completion of the randomized phase of the trial, participating children and their families were free to resume or initiate treatment under the supervision of community clinicians. Their progress has been followed by the MTA study team. Eight primary articles have advanced the narrative by reporting the main findings of the study at successive waves of follow-up,[2] whereas supplementary articles have developed the background to these main findings. Overall, more than 70 articles have been published on the MTA data set to date, creating a challenge for those wishing to keep the myriad of findings from this study in focus. Readers are directed to two recent articles that seek to review and integrate the MTA literature.[2,3] This issue of the *Journal* includes a primary article reporting key outcomes at 6 and 8 years,[4] and a supplementary article on the level of agreement between parental accounts of their child's adherence to medication and objective assessment of adherence through salivary assay for methylphenidate.[5]

Less than 2 years have passed since the publication of the MTA 3-year follow-up data.[6] This was the first in the sequence of primary articles to show that differences in key outcomes attributable to treatment group assignment during the first 14 months of the trial had vanished. The authors were careful to point out that the study had not been designed to demonstrate benefits of the randomized treatments beyond 14 months.[6] After all, in the intervening 22 months, under the supervision of community clinicians, the treatment received by the participants available to follow-up had grown to look not identical but similar. Gradual extinction of the effect of assigned treatment as evaluated by intent-to-treat analyses was predicted after the 24-month follow-up.[7] Nevertheless, the authors of the article in this issue of the *Journal* tested the hypothesis that there may be a sleeper effect, with the benefits of assigned treatment emerging again later in development.[4] A betting person would give short odds against this being the case, and they are correct. There were no differences between the four assigned treatment groups after 6 and 8 years on repeated measures of psychiatric symptoms, academic function, and social functioning. Nor were there differences on new measures salient to adolescence such as grade point average, arrest by the police, or psychiatric hospitalization. The minority of participants who continued with medication at 8 years was at no clear advantage over those who did not, but as the study was no longer controlled, the finding should be interpreted with caution. Fresh attempts to elucidate the mechanism underlying the convergence in outcome of the four assigned treatment groups are unwarranted, given the effort already directed to the interpretation of the convergence at 3-year follow-up.[3] We accept that the absence of a sleeper effect is a reflection of the reality and not the consequence of bias in the study. The authors are correct in their statement that it is purely speculative whether persistence of intensive treatment beyond 14 months would have led to sustained differences between the assigned treatments.[4]

The article by Molina et al.[4] reports two secondary analyses. The first involved the grouping of participants not by assigned treatment but according to trends in attention-deficit/hyperactivity disorder (ADHD) symptoms from baseline through 14, 24, and 36 months, as described by Swanson et al.[8] Evaluable data were available for 485 participants. On first pass, it may seem that an initial large improvement in ADHD symptoms that then plateaus over

*Accepted January 27, 2009.*

*Dr. Hazell is with the Discipline of Psychological Medicine, Concord Clinical School, University of Sydney.*

*Correspondence to Philip Hazell, Ph.D., F.R.A.N.Z.C.P., Thomas Walker Hospital (Rivendell), Hospital Rd, Concord West, NSW 2138, Australia; e-mail: philip.hazell@sswahs.nsw.gov.au.*

0890-8567/09/4805-0461©2009 by the American Academy of Child and Adolescent Psychiatry

DOI: 10.1097/CHI.0b013e31819c242f

36 months is associated with more favorable clinical, academic, and social outcomes after 8 years than other trends in ADHD symptoms, such as slow gradual improvement or initial improvement followed by deterioration.[4] This, however, may be an artifact arising from the fact that participants with an initial and sustained improvement in ADHD symptoms had milder problems at baseline than other MTA participants. The mundane interpretation is that patients with milder problems in middle childhood are likely to continue to have milder problems in mid-adolescence. An additional analysis involved the comparison of MTA participants with a sample of local normal controls matched for age and sex distribution. Although the MTA participants showed improvement from baseline in clinical, academic, and social measures, their scores remained significantly different from those of the normal controls. The finding confirms previous research that has demonstrated symptomatic, if not syndromal, persistence of ADHD into late adolescence.[9] It also confirms that treatments for ADHD, like those for diabetes or asthma, even when highly structured and intense, provide symptomatic improvement, not a cure.

The second MTA article in this issue of the *Journal* reports that one quarter of participants in the two medication arms of the study were inadequately adherent with treatment during the 14-month randomized phase of the trial.[5] Furthermore, contemporaneous reports by parents substantially overestimated adherence. The reader should take these data with a grain of salt, as saliva samples were inconsistently obtained, making the definition of physiological adherence somewhat arbitrary. However, the data do point to unplanned variability in treatment, even in the intensive first 14 months of the study. Why was there a discrepancy in the estimates of adherence obtained by parental report and by analysis of the saliva samples? My guess is that parents were simply unaware that their children were not compliant. The participants themselves may have had a part to play. At age 10 years, if you had to make a choice between getting in trouble from your parents for not taking your medication, or running the risk of having your fib detected years later, what would you have done? We will never know, but one wonders whether there was even poorer adherence to medication in the nonexperimental community care arm of the study. Perhaps this contributed to the lower efficacy of treatment in the community care group, even in the face of higher prescribed (but not necessarily ingested) doses of medication.[10]

The fact that the 6- and 8-year follow-up article includes both primary and secondary analyses signals a departure from the pattern established in previous MTA articles. In the future, there will be less attention given to analyses based on the four assigned treatment groups. The emphasis will shift to the reporting of a high-quality cohort study involving subjects who met criteria for ADHD in middle childhood, shared a common experience of participation in the acute phase of the MTA, and have subsequently followed varying trajectories. We could liken them to the characters of *A Dance to the Music of Time*, who were exposed to a common and binding experience (in their case, the impact of World War II) and then moved on "through the vicissitudes of marriage, work, aging, and ultimately death."[1]

*Disclosure: Dr. Hazell has received support for research, consultancy, or speaker fees from Celltech, Janssen, Lilly, Novartis, Pfizer, and Shire.*

## REFERENCES


1. Selig RL. *Time and Anthony Powell: A Critical Study*. Madison: Fairleigh Dickinson; 1991.
2. Swanson J, Arnold LE, Kraemer H et al. Evidence, interpretation, and qualification from multiple reports of long-term outcomes in the Multimodal Treatment study of Children with ADHD (MTA): Part I: executive summary. *J Atten Disord*. 2008;12:4–14.
3. Swanson J, Arnold LE, Kraemer H et al. Evidence, interpretation, and qualification from multiple reports of long-term outcomes in the Multimodal Treatment Study of children with ADHD (MTA): Part II: supporting details. *J Atten Disord*. 2008;12:15–43.
4. Molina BSHS, Swanson JM, Arnold LE et al. The MTA at 8 years: prospective follow-up of children treated for combined type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry*. 2009;48:484–500.
5. Pappadopulos E, Jensen PS, Chait AR et al. Medication adherence in the MTA: saliva methylphenidate samples vs. parent report and mediating effect of concomitant behavioral treatment. *J Am Acad Child Adolesc Psychiatry*. 2009;48:501–510.
6. Jensen PS, Arnold LE, Swanson JM et al. 3-year follow-up of the NIMH MTA study. *J Am Acad Child Adolesc Psychiatry*. 2007;46:989–1002.
7. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics*. 2004;113:762–769.
8. Swanson JM, Hinshaw SP, Arnold LE et al. Secondary evaluations of MTA 36-month outcomes: propensity score and growth mixture model analyses. *J Am Acad Child Adolesc Psychiatry*. 2007;46:1003–1014.
9. Mick E, Faraone SV, Biederman J. Age-dependent expression of attention-deficit/hyperactivity disorder symptoms. *Psychiatr Clin North Am*. 2004;27:215–224.
10. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. *Arch Gen Psychiatry*. 1999;56:1073–1086.

# THE MTA AT 8 YEARS: PROSPECTIVE FOLLOW-UP OF CHILDREN TREATED FOR COMBINED- TYPE ADHD IN A MULTISITE STUDY

BROOKE S.G. MOLINA, PH.D., STEPHEN P. HINSHAW, PH.D., JAMES M. SWANSON, PH.D.,
L. EUGENE ARNOLD, M.D., M.ED., BENEDETTO VITIELLO, M.D.,
PETER S. JENSEN, M.D., JEFFERY N. EPSTEIN, PH.D., BETSY HOZA, PH.D.,
LILY HECHTMAN, M.D., HOWARD B. ABIKOFF, PH.D., GLEN R. ELLIOTT, PH.D., M.D.,
LAURENCE L. GREENHILL, M.D., JEFFREY H. NEWCORN, M.D., KAREN C. WELLS, PH.D.,
TIMOTHY WIGAL, PH.D., ROBERT D. GIBBONS, PH.D., KWAN HUR, PH.D.,
PATRICIA R. HOUCK, M.S., AND THEMTA COOPERATIVE GROUP

**ABSTRACT**

**Objectives**: To determine any long-term effects, 6 and 8 years after childhood enrollment, of the randomly assigned 14-month treatments in the NIMH Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder (MTA; N = 436); to test whether attention-deficit/hyperactivity disorder (ADHD) symptom trajectory through 3 years predicts outcome in subsequent years; and to examine functioning level of the MTA adolescents relative to their non-ADHD peers (local normative comparison group; N = 261).
**Method**: Mixed-effects regression models with planned contrasts at 6 and 8 years tested a wide range of symptom and impairment variables assessed by parent, teacher, and youth report.
**Results**: In nearly every analysis, the originally randomized treatment groups did not differ significantly on repeated measures or newly analyzed variables (e.g., grades earned in school, arrests, psychiatric hospitalizations, other clinically relevant outcomes). Medication use decreased by 62% after the 14-month controlled trial, but adjusting for this did not change the results. ADHD symptom trajectory in the first 3 years predicted 55% of the outcomes. The MTA participants fared worse than the local normative comparison group on 91% of the variables tested.
**Conclusions**: Type or intensity of 14 months of treatment for ADHD in childhood (at age 7.0Y9.9 years) does not predict functioning 6 to 8 years later. Rather, early ADHD symptom trajectory regardless of treatment type is prognostic. This finding implies that children with behavioral and sociodemographic advantage, with the best response to any treatment, will have the best long-term prognosis. As a group, however, despite initial symptom improvement during treatment that is largely maintained after treatment, children with combined-type ADHD exhibit significant impairment in adolescence. Innovative treatment approaches targeting specific areas of adolescent impairment are needed.

J. Am. Acad. Child Adolesc. Psychiatry, 2009;48(5):484-500.

# MEDICATION ADHERENCE IN THE MTA: SALIVA METHYLPHENIDATE SAMPLES VERSUS PARENT REPORT AND MEDIATING EFFECT OF CONCOMITANT BEHAVIORAL TREATMENT

ELIZABETH PAPPADOPULOS, PH.D., PETER S. JENSEN, M.D.,
ALANNA R. CHAIT, B.A., L. EUGENE ARNOLD, M.D., JAMES M. SWANSON, M.D.,
LAURENCE L. GREENHILL, M.D., LILY HECHTMAN, M.D., SHIRLEY CHUANG, M.S.,
KAREN C. WELLS, M.D., WILLIAM PELHAM, PH.D., THOMAS COOPER, M.S.,
GLENN ELLIOTT, M.D., PH.D., AND JEFFREY H. NEWCORN, M.D.

**ABSTRACT**

**Objective**: Although research supports the use of appropriately administered stimulant medication to treat children with ADHD, poor adherence and early termination undermine the efficacy of this treatment in real-world settings. Moreover, adherence measures often rely on parent report of medication use, and their validity and reliability are unknown.
**Method**: Drawing on data from 254 participants in the NIMH Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder, we examine the discrepancy between parents' verbal reports of medication adherence and physiological adherence measures determined via methylphenidate saliva assays collected at four time points during the 14-month treatment period. In addition, we examine the impact of physiologically documented medication adherence on parent- and teacher-reported outcomes through 14 months.
**Results**: Overall, nearly one fourth (24.5%) of the saliva samples indicated nonadherence. Among subjects, 63 (24.8%) of the 254 participants were nonadherent on 50% or more of their repeated saliva assays. Only 136 (53.5%) of the subjects were adherent at every time point at which saliva assays were taken, indicating that some degree of nonadherence characterized nearly half of all other NIMH Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity DisorderYtreated children. Findings also indicated that nonadherence produced greater deleterious effects in children in the medication-only condition compared with those receiving both medication and behavioral treatment.
**Conclusions**: Same-day saliva methylphenidate assays suggest that nearly half of the parents are inaccurate informants of their child's ADHD medication adherence and that parents may overestimate actual (physiological) adherence. This finding suggests the need for interventions to improve accuracy of parental report. Clinicians need to focus on adherence enhancement strategies to improve outcomes of children being treated with medication, particularly when benefits are suboptimal.

J. Am. Acad. Child Adolesc. Psychiatry, 2009;48(5):501-510.

## BIBLIOGRAFIA NEWSLETTER ADHD MESE DI MAGGIO

Acta Paediatrica. 2009 Apr;98:731-36.
**Effects of zinc supplementation on parent and teacher behaviour rating scores in low socioeconomic level Turkish primary school children**.
***Uçkardeş Y***, ***Ozmert EN***, ***Unal F***, ***Yurdakök K***.
**Objective**: To determine the effect of zinc supplementation on behaviour in low-income school aged children. Design: Double-blind randomized, placebo controlled trial.
**Setting**: Low-income district primary school in Turkey.
**Participants**: Third grade students in the school. Among 252 students, 226 participated and 218 completed the study.
**Intervention**: Children in each class were randomized either to the study group to receive 15 mg/day elemental zinc syrup or to placebo group to receive the syrup without zinc for 10 weeks. Main Outcome
**Measures**: The change in Conner's Rating Scales for Teachers and Parents scores after supplementation.
**Results**: The mean Conner's Rating Scale for Parents scores on attention deficit, hyperactivity, oppositional behaviour and conduct disorder decreased significantly in the study and placebo groups after supplementation ($p < 0.01$). The prevalence of children with clinically significant parent ratings on attention deficit ($p = 0.01$) and hyperactivity ($p = 0.004$) decreased in the study group while prevalence of oppositional behaviour ($p = 0.007$) decreased in the placebo group. In children of mothers with low education all mean Parents' scores decreased significantly ($p < 0.01$) in the study group while only hyperactivity scores decreased in the placebo group ($p < 0.01$). In this subgroup the prevalence of children with clinically significant scores for attention deficit, hyperactivity and oppositional behaviour decreased only in the study group ($p < 0.05$). There was no change in mean Teachers' scores.
**Conclusion**: In our study zinc supplementation decreased the prevalence of children with clinically significant scores for attention deficit and hyperactivity. The affect on behaviour was more evident in the children of low educated mothers.


Pediatrics. 2009 May;123:e770-e776.
**Controlled clinical trial of zolpidem for the treatment of insomnia associated with attention-deficit/ hyperactivity disorder in children 6 to 17 years of age**.
***Blumer JL, Findling RL, Shih WJ, et al***.
**OBJECTIVE**: The goal was to evaluate the hypnotic efficacy of zolpidem at 0.25 mg/kg per day (maximum of 10 mg/day), compared with placebo, in children 6 through 17 years of age who were experiencing insomnia associated with attention-deficit/hyperactivity disorder.
**METHODS**: An 8-week, North American, multicenter, double-blind, placebo-controlled, parallel-group study was conducted. Patients underwent stratification according to age (6-11 years [N = 111] or 12-17 years [N = 90]) and were assigned randomly to receive treatment with the study drug or placebo (in a 2:1 ratio). The primary efficacy variable was latency to persistent sleep between weeks 3 and 6. Secondary efficacy variables also were assessed, and behavioral and cognitive components of attention-deficit/hyperactivity disorder were monitored. Safety was assessed on the basis of reports of adverse events, abnormal laboratory data, vital signs, and physical examination findings. The potential for next-day residual effects also was assessed.
**RESULTS**: The baseline-adjusted mean change in latency to persistent sleep at week 4 did not differ significantly between the zolpidem and placebo groups (-20.28 vs -21.27 minutes). However, differences favoring zolpidem were observed for the older age group in Clinical Global Impression scores at weeks 4 and 8. No next-day residual effects of treatment were associated with zolpidem, and no rebound phenomena occurred after treatment discontinuation. Central nervous system and psychiatric disorders were the most-frequent treatment-emergent adverse events (>5%) that were observed more frequently with zolpidem than with placebo; these included dizziness, headache, and hallucinations. Ten (7.4%) patients discontinued zolpidem treatment because of adverse events.
**CONCLUSION**: Zolpidem at a dose of 0.25 mg/kg per day to a maximum of 10 mg failed to reduce the latency to persistent sleep on polysomnographic recordings after 4 weeks of treatment in children and adolescents 6 through 17 years of age who had attention-deficit/hyperactivity disorder-associated insomnia.

Am Fam Physician. 2009 Apr;79:640, 642.
**Multimodal treatment of attention-deficit/hyperactivity disorder in children** .
***Felt BT, Lumeng J, Christner J***.

J Voice. 2009 Mar;23:190-94.
**Vocal characteristics in children with attention deficit hyperactivity disorder**.
***Hamdan AL, Deeb R, Sibai A, et al***.
The aim of this study was to evaluate vocal changes in patients with attention deficit hyperactivity disorder (ADHD). Nineteen children diagnosed to have ADHD according to the Diagnostic and Statistical Manual of Mental Disorders criteria and 19 controls were enrolled in this study. They underwent vocal perceptual evaluation and acoustic analysis. Hoarseness, breathiness, strain, and loudness were graded on a scale of 0â€“3. The following acoustic parameters were recorded: Fundamental frequency, Shimmer, Relative average perturbation, Noise-to-Harmony ratio, Voice Turbulence Index, and Habitual pitch. Children with ADHD were perceived to have significantly more hoarseness, breathiness, and straining in their voice. They were also louder compared to controls. There were no significant changes in the acoustic parameters except for the Fundamental frequency, which was lower in the ADHD group. The vocal behavior in children with ADHD is different than controls. Early diagnosis of such behavior in this group of children is important.


Int J Psychophysiol. 2009 May;72:145-53.
**Response inhibition and interference control in children with AD/HD: A visual ERP investigation**.
***Johnstone SJ, Barry RJ, Markovska V, et al***.
Children with Attention-deficit Hyperactivity Disorder (AD/HD) show deficits in executive inhibitory functions such as behavioral inhibition and interference control, but investigations of both of these domains in the same groups of children is scarce, especially with concurrent consideration of ERP indices of inhibitory processes. Twenty children with AD/HD and 20 matched controls aged between 8 and 14 years performed visual Go's Nogo (30% Nogo) and Flanker tasks while EEG was recorded. Results indicated that children with AD/HD traded off speed for accuracy in the Go's Nogo task, resulting in similar levels of response inhibition accuracy; in the Flanker task response speed and errors were at control levels, while misses were increased and showed an enhanced interference effect. In the Goâ€“Nogo task, the AD/HD group showed reduced Go/ Nogo P2, a reduced central N2 Nogo>Go effect, and a more anterior Go/Nogo P3 compared to controls. For the Flanker task, the AD/HD group showed delayed N1 and P2, dramatically reduced N2 to Incongruent stimuli, enhanced N2 to Neutral stimuli, as well as increased P3 to Incongruent stimuli, compared to controls. These results indicate that Goâ€“Nogo behavioral inhibition and Flanker interference control were not equally impaired in children with AD/HD, and that factors such as effort, arousal and motivation require further investigation.


Infant Behavior & Development. 2009 Apr;32:173-82.
**Parenting of 7-month-old infants at familial risk for ADHD during infant's free play, with restrictions on interaction**.
***Landau R, Amiel-Laviad R, Berger A, et al***.
Patterns of interaction of 34 mothers and fathers with their 7-month-old boys at familial risk for ADHD and 25 comparison families were studied during infant play with blocks. The parents were instructed to refrain from intervening as much as possible. Infants in the risk group did not differ from those in the comparison group in frequency of needing help or involving parents in play. Nonetheless, they received adequate responsivity from their mothers less often than infants in the comparison group. Mothers in the risk group were also more likely not to respond to these needs at all. Mothers in the comparison group were more physically intrusive. No group difference was found for maternal rebuilding of the infant's play. No group differences were found for any of father's behaviors. However, fathers in both groups rebuilt their infant's play more frequently than mothers, infants looked at them more often, and a larger number of infants involved the father in their play.

Hong Kong Journal of Psychiatry. 2009 Mar;19:18-25.
**The ability of Hong Kong children with attention-deficit hyperactivity disorder to recognise facial emotion**.
***Lee YK, Hung SF, Lam WC, et al.***
**Objectives**: To evaluate the facial emotion recognition ability in local children with attention-deficit hyperactivity disorder (ADHD) and the effect of inattention and impulsivity on such ability. Participants and
**Methods**: Eight-seven Chinese children (45 controls and 42 with ADHD) of primary 1 to 3 were recruited. They were matched for age, sex, intelligence, and family income. The subjects were shown facial emotion pictures developed by Matsumoto and Ekman (1998) together with emotional story vignettes. Conners' Continuous Performance Test II was used to evaluate the attention/impulsivity level of the subjects.
**Results**: The difference in performance in facial emotion recognition between the 2 groups was not statistically significant. There was also no significant correlation between the accuracy of facial emotion recognition and the inattention/impulsivity level. Intelligence level correlated significantly with the facial emotion recognition ability.
**Conclusions**: The ability to recognise facial emotion is affected by multiple factors. A single diagnostic label is unlikely to be fully predictive. Further research on the influence of co-morbidities and presence of different ADHD subtypes should be considered.


Neuropsychology. 2009 May;23:367-80.
**Delay and reward choice in ADHD: An experimental test of the role of delay aversion**.
***Marco R, Miranda A, Schlotz W, et al.***
Children with attention deficit/hyperactivity disorder (ADHD) choose smaller sooner (SS) over larger later (LL) rewards more than controls. Here we assess the contributions of impulsive drive for immediate rewards (IDIR) and delay aversion (DAv) to this pattern. We also explore the characteristics of, and the degree of familiality in, ADHD SS responders. We had 360 ADHD probands; 349 siblings and 112 controls (aged between 6 to 17 years) chose between SS (1 point after 2 s) and LL reward (2 points after 30 s) outcomes on the Maudsley Index of Delay Aversion (Kuntsi, Oosterlaan, & Stevenson, 2001): Under one condition SS choice led to less overall trial delay under another it did not. ADHD participants chose SS more than controls under both conditions. This effect was larger when SS choice reduced trial delay. ADHD SS responders were younger, had lower IQ, more conduct disorder and had siblings who were more likely to be SS responders themselves. The results support a dual component model in which both IDIR and DAv contribute to SS choice in ADHD. SS choice may be a marker of an ADHD motivational subtype.


MMW Fortschr Med. 2009 Feb;151:16.
**[Therapy of ADHD. British institute recommends: drugs only in severe cases]**.
***Matthis M.***

Am Fam Physician. 2009 Apr;79:640, 642.
**Multimodal treatment of attention-deficit/hyperactivity disorder in children** .
***Felt BT, Lumeng J, Christner J.***

Pediatrics. 2009 May;123:e770-e776.
**Controlled clinical trial of zolpidem for the treatment of insomnia associated with attention-deficit/ hyperactivity disorder in children 6 to 17 years of age**.
***Blumer JL, Findling RL, Shih WJ, et al.***
**OBJECTIVE**: The goal was to evaluate the hypnotic efficacy of zolpidem at 0.25 mg/kg per day (maximum of 10 mg/day), compared with placebo, in children 6 through 17 years of age who were experiencing insomnia associated with attention-deficit/hyperactivity disorder.
**METHODS**: An 8-week, North American, multicenter, double-blind, placebo-controlled, parallel-group study was conducted. Patients underwent stratification according to age (6-11 years [N = 111] or 12-17 years [N = 90]) and were assigned randomly to receive treatment with the study drug or placebo (in a 2:1 ratio). The primary efficacy variable was latency to persistent sleep between weeks 3 and 6. Secondary efficacy variables also were assessed, and behavioral and cognitive components of attention-deficit/hyperactivity disorder were monitored. Safety was assessed on the basis of reports of adverse events, abnormal

laboratory data, vital signs, and physical examination findings. The potential for next-day residual effects also was assessed.
**RESULTS**: The baseline-adjusted mean change in latency to persistent sleep at week 4 did not differ significantly between the zolpidem and placebo groups (-20.28 vs -21.27 minutes). However, differences favoring zolpidem were observed for the older age group in Clinical Global Impression scores at weeks 4 and 8. No next-day residual effects of treatment were associated with zolpidem, and no rebound phenomena occurred after treatment discontinuation. Central nervous system and psychiatric disorders were the most-frequent treatment-emergent adverse events (>5%) that were observed more frequently with zolpidem than with placebo; these included dizziness, headache, and hallucinations. Ten (7.4%) patients discontinued zolpidem treatment because of adverse events.
**CONCLUSION**: Zolpidem at a dose of 0.25 mg/kg per day to a maximum of 10 mg failed to reduce the latency to persistent sleep on polysomnographic recordings after 4 weeks of treatment in children and adolescents 6 through 17 years of age who had attention-deficit/hyperactivity disorder-associated insomnia.

---

J Pediatr Psychol. 2009 Apr;34:328-37.
**ADHD subtypes and comorbid anxiety, depression, and oppositional-defiant disorder: Differences in sleep problems**.
**Mayes SD, Calhoun SL, Bixler EO, et al**.
**Objective**: Sleep problems were analyzed in children with ADHD (Attention-deficit hyperactivity disorder).
**Methods**: Scales were completed by parents of 135 control children and 681 children with ADHD combined type (ADHD-C) or inattentive type (ADHD-I) with or without comorbid oppositional defiant disorder (ODD), anxiety, or depression.
**Results**: Children with ADHD-I alone had the fewest sleep problems and did not differ from controls. Children with ADHD-C had more sleep problems than controls and children with ADHD-I. Comorbid anxiety/depression increased sleep problems, whereas ODD did not. Daytime sleepiness was greatest in ADHD-I and was associated with sleeping more (not less) than normal. Medicated children had greater difficulty falling asleep than unmedicated children.
**Conclusions**: Differences in sleep problems were found as a function of ADHD subtype, comorbidity, and medication.


---

Pediatrics. 2009 May;123:e857-e864.
**Short sleep duration and behavioral symptoms of attention-deficit/hyperactivity disorder in healthy 7- to 8-year-old children**.
***Paavonen EJ, Raikkonen K, Lahti J, et al***.
**OBJECTIVE**: It has been hypothesized that sleep deprivation may manifest in children as behavioral symptoms rather than as tiredness, but only a few studies have investigated this hypothesis. The objective of our study was to evaluate whether short sleep is associated with behavioral symptoms of attention-deficit/hyperactivity disorder in 7- to 8-year-old children.
**METHODS**: We performed a cross-sectional study of children born in 1998 in Helsinki, Finland. The participants included 280 (146 girls, 134 boys) children with a mean age of 8.1 years (SD: 0.3; range: 7.4-8.8). Sleep quality was measured by using actigraphs. The Sleep Disturbance Scale for Children and the Attention-Deficit/Hyperactivity Disorder Rating Scale IV were administered to parents.
**RESULTS**: Children whose average sleep duration as measured by actigraphs was short (<10th percentile, ie, <7.7 hours) and had a higher hyperactivity/impulsivity score (9.7 vs 7.8 or 7.5) and a higher attention-deficit/hyperactivity disorder total score (17.3 vs 14.5 or 13.1) but a similar inattention score (7.6 vs 6.7 or 5.6) compared with children sleeping 7.7 to 9.4 hours or >9.4 hours. In multivariate statistical models, short sleep duration remained a statistically significant predictor of hyperactivity/impulsivity, and sleeping difficulties were associated with hyperactivity/impulsivity, inattention, and the total score. There were no significant interactions between short sleep and sleeping difficulties.
**CONCLUSIONS**: Children's short sleep duration and sleeping difficulties increase the risk for behavioral symptoms of attention-deficit/hyperactivity disorder.

---

Sleep: Journal of Sleep and Sleep Disorders Research. 2009 Apr;32:530-35.

**Children show individual night-to-night variability of periodic limb movements in sleep**.

***Picchietti MA, Picchietti DL, England SJ, et al.***

**Study Objective**: Several studies have documented the occurrence of significant night-to-night variability of periodic limb movements in sleep (PLMS) in adults.The aim of this study was to investigate the night-to-night variability of PLMS in children.

**Design and Measurements**: Two to 4 nights of polysomnography were performed as part of a multisite, placebo-controlled study investigating the effects of carbidopa/levodopa on attention-deficit/hyperactivity disorder in children who were not taking other medications that impacted the central nervous system. Baseline polysomnograms from all children and endpoint polysomnograms from children who were randomly assigned to a placebo group were scored using International Restless Legs Syndrome Study Group criteria for PLMS. PLMS indexes from 101 sleep studies of 36 children, aged 7 to 12 years, were compared. Interventions: N/A.

**Results**: For all 36 children as a group, PLMS index on Night 1 was predictive of PLMS index on Night 2 (odds ratio 7.0,95% confidence interval 1.4-38.4), suggesting that overall diagnostic classification (PLMS index above or below 5/h) was accurate. In addition, for the 15 children with 5 or more PLMS per hour on either night, there was no significant group difference on Night 1 versus Night 2 for mean PLMS index (10.6 vs 8.5/h, P = 0.92) or chance of having 5 or more PLMS per hour, indicating no first-night effect. When looking at individual data, however, 9 of these 15 children (60%) had PLMS indexes over and under the 5 per hour cutoff on these 2 nights. Of these 15,10 had clinical diagnoses of restless legs syndrome and 5 of periodic limb movement disorder (PLMD). The PLMS indexes of all children who were medication free for a third and fourth night (n = 7) or just a third night (n = 2) and had not shown a PLMS index of 5 or greater on either of the first 2 nights remained under this threshold.

**Conclusions**: In this sample of children, considerable individual night-to-night variability of PLMS indexes was observed. This finding has important clinical relevance for the diagnosis of restless legs syndrome and PLMD and may have an impact on future studies that correlate individual PLMS severity with frequently associated symptoms, such as negative affect, fatigue, and inattention. Our data, however, also suggest that individual PLMS variability is random and not likely to skew the group-level analysis of treatment outcome studies.



---

Neuropsychology. 2009 May;23:381-91.

**Attention problems, inhibitory control, and intelligence index overlapping genetic factors: A study in 9-, 12-, and 18-year-old twins**.

***Polderman TJC, de Geus EJC, Hoekstra RA, et al.***

It is assumed that attention problems (AP) are related to impaired executive functioning. We investigated the association between AP and inhibitory control and tested to what extent the association was due to genetic factors shared with IQ. Data were available from 3 independent samples of 9-, 12-, and 18-year-old twins and their siblings (1,209 participants). AP were assessed with checklists completed by multiple informants. Inhibitory control was measured with the Stroop Color Word Task (Stroop, 1935), and IQ with the Wechsler Intelligence Scale for Children (Wechsler et al., 2002) or Wechsler Adult Intelligence Scale (Wechsler, 1997). AP and inhibitory control were only correlated in the 12-year-old cohort (r = .18), but appeared non-significant after controlling for IQ. Significant correlations existed between AP and IQ in 9- and 12-year olds (r = âˆ’.26/â€“.34). Inhibitory control and IQ were correlated in all cohorts (r = âˆ’.16, âˆ’.24 and âˆ’.35, respectively). Genetic factors that influenced IQ also influenced inhibitory control. We conclude that the association between AP and inhibitory control as reported in the literature may largely derive from genetic factors that are shared with IQ.



---

Ugeskr Laeger. 2009 Apr;171:1500-04.

**[Danish standardization of the attention deficit hyperactivity disorder rating scale]**.

***Poulsen L, Jorgensen SL, Dalsgaard S, et al.***

**INTRODUCTION**: Attention deficit hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity and impulsivity. The diagnostic classification is based on developmental anamnesis, objective examination, neuropsychological tests, observation of the child, and evaluation of the symptoms from rating scales.

**MATERIAL AND METHODS**: The internationally known ADHD rating scale (ADHD-RS) has been translated into Danish and representative norm data from teachers and parents were collected. A total of 1,718 ADHR-RS questionnaires were distributed to 859 anonymous school children, aged 6-17 years, and a total of 1,477 ADHD-RS questionnaires were returned. Analyses were made on 781 children, 420 boys and 361 girls.

**RESULTS**: The average participation rate was 99.5% for teachers and 72.4% for parents. The factor structure was supported and internal consistency was high. The normative scores were calculated for both girls and boys in three age-groups, for parent answers and teacher answers separately.
**CONCLUSION**: There were significant variations in ratings of ADHD and behavioural symptoms as a function of gender and age. It is crucial, during an evaluation of a child, to compare his or her scores to gender- and age-stratified normative data. Standardized normative ADHD-RS data from school children is now available and can be implemented in a national quality database within child and adolescent mental health services. The questionnaire can support the diagnostic classification, measure symptom-load and evaluate outcome of treatment of ADHD.

---

Am Fam Physician. 2009 Apr;79:657-65.
**Current strategies in the diagnosis and treatment of childhood attention-deficit/hyperactivity disorder**.
***Rader R, McCauley L, Callen EC***.
Symptoms of childhood attention-deficit/hyperactivity disorder affect cognitive, academic, behavioral, emotional, social, and developmental functioning. Attention-deficit/hyperactivity disorder is the most commonly diagnosed neurodevelopmental disorder in children and adolescents. An estimated 2 to 16 percent of school-aged children have been diagnosed with the disorder. The prevalence of attention-deficit/hyperactivity disorder in the primary care setting is similar to that in the general community, depending on the diagnostic criteria and population studied. The causality of attention-deficit/hyperactivity disorder is relatively unknown. Most recent studies focus on the role of dopamine; norepinephrine; and, most recently, serotonin neurotransmitters. The disorder is classified into three general subtypes: predominantly hyperactive-impulsive, predominantly inattentive, and combined. Screening tools and rating scales have been devised to assist with the diagnosis. Appropriate treatment can dramatically improve the function and quality of life of the patient and family. Pharmacologic treatment includes stimulants, such as methylphenidate and mixed amphetamine salts, or nonstimulants, such as atomoxetine. Behavioral approaches, particularly those that reward desirable behavior, are also effective. A combination of pharmacologic and behavioral therapies is recommended.

---

Journal of Child & Adolescent Substance Abuse. 2009 Apr;18:172-92.
**Drug use and psychosocial functioning of a community-derived sample of adolescents with childhood ADHD**.
***Realmuto GM, Winters KC, August GJ, et al***.
We describe the late adolescent psychosocial outcomes from a relatively large, community-identified sample of children with ADHD who have been assessed longitudinally from childhood through late adolescence. A range of outcomes were compared between ADHD (n = 119) and normal control (n = 93) groups, as well as ADHD subgroups that varied as a function of the course of externalizing predominantly ODD problems (persisters, desisters, escalaters, and resisters). ADHD youths that did not show externalizing problems during childhood (ADHD resisters) were associated with drug use outcomes generally comparable to the normal non-affected controls. All other ADHD groups with externalizing problems (ADHD persisters, ADHD escalaters, and ADHD desisters) consistently revealed worse drug use outcomes compared to controls/ADHD resisters. However, ADHD youths with or without externalizing problems showed worse outcomes compared to the control group on the non-drug, psychosocial functioning variables. The study highlights that ADHD with coexisting disruptiveness, whether the disruptiveness persists or remits before adolescence, is associated with an increased risk for drug involvement and that ADHD, regardless of the comorbid pattern, confers a poorer level of psychosocial functioning.


---

Pediatrics. 2009 May;123:1273-79.
**Positive association between attention-deficit/ hyperactivity disorder medication use and academic achievement during elementary school**.
***Scheffler RM, Brown TT, Fulton BD, et al***.
**OBJECTIVE**: Approximately 4.4 million (7.8%) children in the United States have been diagnosed with attention-deficit/hyperactivity disorder, and 56% of affected children take prescription medications to treat the disorder. Attention-deficit/hyperactivity disorder is strongly linked with low academic achievement, but the association between medication use and academic achievement in school settings is largely unknown. Our objective was to determine if reported medication use for attention-deficit/hyperactivity disorder is positively associated with academic achievement during elementary school.

**METHOD**: To estimate the association between reported medication use and standardized mathematics and reading achievement scores for a US sample of 594 children with attention-deficit/hyperactivity disorder, we used 5 survey waves between kindergarten and fifth grade from the nationally representative Early Childhood Longitudinal Study--Kindergarten Class of 1998-1999 to estimate a first-differenced regression model, which controlled for time-invariant confounding variables.
**RESULTS**: Medicated children had a mean mathematics score that was 2.9 points higher than the mean score of unmedicated peers with attention-deficit/hyperactivity disorder. Children who were medicated for a longer duration (at >2 waves) had a mean reading score that was 5.4 points higher than the mean score of unmedicated peers with attention-deficit/hyperactivity disorder. The medication-reading association was lower for children who had an individualized education program than for those without such educational accommodation.
**CONCLUSIONS**: The finding of a positive association between medication use and standardized mathematics and reading test scores is important, given the high prevalence of attention-deficit/hyperactivity disorder and its association with low academic achievement. The 2.9-point mathematics and 5.4-point reading score differences are comparable with score gains of 0.19 and 0.29 school years, respectively, but these gains are insufficient to eliminate the test-score gap between children with attention-deficit/hyperactivity disorder and those without the disorder. Long-term trials are needed to better understand the relationship between medication use and academic achievement

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://crc.marionegri.it/bonati/adhdnews/subscribe.html

Iniziativa nell'ambito del Progetto di ricerca indipendente AIFA
"*Sicurezza a lungo termine dei farmaci utilizzati nel trattamento di bambini in età scolare con sindrome da deficit di attenzione e iperattività ed epidemiologia della malattia nella popolazione italiana*".

**ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI**
***DIPARTIMENTO DI SALUTE PUBBLICA***
***Laboratorio per la Salute Materno Infantile***
*Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - www.marionegri.it*
*tel +39 02 39014.511 - fax +39 02 3550924 - mother_child@marionegri.it*