



Study results from confirm effectiveness of combined treatments and medication management in reducing children’s Attention Deficit/Hyperactivity Disorder (ADHD) symptoms

CITATION: MTA Cooperative Group. (1999b). Moderators and mediators of treatment response for children with attention-deficit/hyperactivity disorder: The multimodal treatment study of children with attention-deficit/hyperactivity disorder. *Archives of General Psychiatry*, 56,1088–1096..

LEVEL OF EVIDENCE: IA1a

RESEARCH OBJECTIVE/QUESTION

To examine response patterns in subgroups of participating children, defined by baseline variables (moderators) or variables related to treatment implementation (mediators)

The “moderators” were 5 baseline variables: (1) gender of the child, (2) whether the child had previously received medication, (3) whether the child had another disruptive disorder, (4) whether the child had a anxiety disorder, and (5) whether the family was receiving public assistance. Analysis of moderators reveals the types of participants who respond best to each intervention. The “mediators” were 2 variables related to treatment implementation: (1) family’s acceptance of child’s treatment assignment and (2) family’s attendance at treatment sessions. Analysis of mediators helps identify links between different treatments and particular outcomes.

DESIGN

X	RCT		Single case		Case control
	Cohort		Before–after		Cross-sectional

RCT = randomized control trial
4-group parallel design

SAMPLING PROCEDURE

	Random		Consecutive
X	Controlled		Convenience

4-phase entry procedure screened potential participants, determined ADHD diagnostic status, and assessed each recruit before randomization

SAMPLE

N = 579	M age = 8.5 years (SD = 0.8 years)	Male = 465	Ethnicity: White = 351, African American = 115, Hispanic = 48	Female = 114
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PARTICIPANT CHARACTERISTICS

Children (of either gender) were between ages 7 and 9.9 years, in Grades 1–4, and in residence with the same primary caretakers for the past 6 months or longer. All met the DSM-IV criteria for ADHD combined type.

MEDICAL DIAGNOSIS/CLINICAL DISORDER

ADHD (combined type)

OT TREATMENT DIAGNOSIS

N/A

OUTCOMES

Measures	Reliability	Validity
ADHD symptoms	-Y, but NR	-Y, but NR
SNAP	NR	NR
Social Skills Rating System (SSRS)	NR	NR
Classroom Observation Code	NR	NR
SNAP Oppositional Defiant Disorder Scale	NR	NR
Multidimensional Anxiety Scale for Children	NR	NR
Parent–Child Relationship Questionnaire	NR	NR

NR = Not reported

Outcome—OT terminology

Performance components:

- Cognitive integration and components
- Psychosocial skills and psychological components

Outcome—ICIDH-2 terminology

Impairments

INTERVENTION

- Behavioral treatment

- Medication management
- Combined treatment
- Community care

Description

Behavioral treatment:

Included parent training, child-focused treatment (summer camp), and school-based intervention

Medication management:

Began with a 28-day, double-blind, daily-switch titration of methylphenidate hydrochloride using 5 randomly ordered repeats each of placebo, 5 mg, 10 mg, and 15 or 20 mg (higher doses for children >25 kg); doses given at breakfast and lunch with a half-dose in the afternoon. For participants not obtaining an adequate response, alternate medications were used.

Combined treatment:

Medication management + behavioral treatment

Community care:

Participants received none of the above treatments (instead were provided with a list of community mental health resources).

Who delivered

- Same therapist–consultant (not specified) conducted parent training and teacher consultation
- Pharmacotherapist
- Paraprofessional aid (behavioral intervention)

• Setting

- School
- Clinical settings (different sites)

Frequency

Behavioral treatment:

Parent training: 8 individual sessions per family; began weekly on randomization concurrent with biweekly teacher consultation

Child-focused treatment:

8-week, 5 days per week, 9 hours per day

School-based treatment:

10–16 sessions of biweekly teacher consultation and 12 weeks of a part-time paraprofessional aid working directly with the child

Medication management:

3 times a day

Combined treatment:

By treatment end-point combined treatment, participants received lower daily doses of methylphenidate (31.2 mg) than did participants in medication management (37.7 mg).

Community care:

Most participants received medication averaging 2.3 doses per day.

Follow-up

N/A

RESULTS

- Because they are present before, proposed moderator variables in clinical trials should be uncorrelated with treatment assignment, but proposed mediator variables, occurring after treatment, may be associated with treatment condition.
- Interactions for all 14 dependent variables were tested (5 moderators + acceptance/attendance mediator) with treatment condition, yielding 84 (6×14) random-effects regression analyses. In 11 of these, the interaction was significant.
- For each of the first 3 moderators (gender, prior medication, and comorbid oppositional defiant disorder/conduct disorder) only 1 of the 14 core dependent measures yielded a significant overall interaction.
- For comorbid anxiety disorder, relevant interaction was significant for 3 outcome variables. Behavioral treatment showed unexpectedly strong benefit for children with ADHD and anxiety in contrast to those without the comorbidity.
- In SNAP Hyperactivity–Impulsivity measure, the contrast of combined treatment X medication management, was significant, suggesting that combined treatment showed relatively greater improvement over medication management for participants with anxiety than for those without anxiety.
- For familial receipt of public assistance, 2 outcome measures showed significant interactions: Teacher SSRS Total Social Skills and Parent–Child Relationship Questionnaire closeness.
- In SSRS Families Receiving Public Assistance measure, combined treatment seemed superior to all other conditions, whereas for those without assistance, there was no difference.
- In Parent–Child Relationship Questionnaire, all 4 treatments were equivalent in families without public assistance. For those receiving assistance, medication management was the only condition for which parent-reported positive interchanges decreased across the 14-month treatment; for all other conditions, positive interchanges increased or stayed level.

Mediator Analyses:

- Only 13 (9%) of 144 of participants given medication management and 5 (3%) of 145 participants given combined treatment refused medication throughout the study. None of the 144 given behavioral treatment and only 1 (<1%) of the 145 participants given combined treatment refused behavioral treatment.
- Overall acceptance/attendance differ across treatment groups [$\chi^2 = 16.6, p < .001$] confirming that this potential mediator was associated with treatment condition.

CONCLUSIONS

- Results were consistent across boys and girls, participants with and without prior medication treatment, and subgroups with and without comorbid oppositional defiant

disorder or conduct disorder; results were generalizable across these important variables.

- Lack of moderator effects for comorbid disruptive behavior disorder is striking; given the multiple impairments and poor prognosis of children with the combination of ADHD and aggression, lack of clearly demonstrated superiority for combined treatment regarding this subgroup is noteworthy.
- There were differences in treatment results for participants with and without comorbid anxiety; 34% of them showed an enhanced response for parent-reported ADHD and internalizing symptoms (after behavioral treatment). Behavioral treatment was superior to community care. Combined treatment was better than medication management.
- Contrary to the hypothesis, comorbid anxiety disorder status was not associated with a pattern of worse response to medication management.

LIMITATIONS

Biases

X	Attention		Masking/blinding	X	Drop outs
	Contamination		Co-intervention		

- Terminology used in this document is based on two systems of classification current at the time the evidence-based literature reviews were completed: *Uniform Terminology for Occupational Therapy Practice—Third Edition* (AOTA, 1994) and *International Classification of Functioning, Disability and Health (ICIDH-2)* (World Health Organization [WHO], 1999). More recently, the *Uniform Terminology* document was replaced by *Occupational Therapy Practice Framework: Domain and Process* (AOTA, 2002), and modifications to *ICIDH-2* were finalized in the *International Classification of Functioning, Disability and Health* (WHO, 2001).

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For more information about the Evidence-Based Literature Review Project, contact the Practice Department at the American Occupational Therapy Association, 301-652-6611, x 2040.

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