

January 20, 2000

The following two tables supplement our review, "The challenge of predicting which children with ADHD respond positively to methylphenidate", in press, *Journal of Applied Developmental Psychology*.

-- Jeremy R. Gray, Ph.D., and Jerome Kagan, Ph.D.

Table 1. Reviews of Predicting MPH Response

<u>Barkley, 1976</u>	<u># studies</u>	<u>Predictive value</u>
psychophysiological (mainly attentional)	18	EEG equivocal, other measures show some promise
neurological "soft" signs	12	mixed evidence, some correlation?
familial	4	mixed evidence, unclear causality
demographic/sociological	8	none
diagnostic category	5	mixed evidence, anxious worse?
rating scales: teacher	8	inconsistent
parent	7	equivocal
clinician	7	inconsistent
psychological	15	attentional measures are best
Conners' profile types	2	attentional measures predict response within clusters
<u>Taylor, 1983</u>		
overactivity ratings	10	not always predictive
attentiveness	15	mixed evidence

Table 2. Studies Predicting MPH Response (1976-1998)

<u>Study</u>	<u>Participants</u>	<u>Predictor Variables</u>	<u>Response Measures</u>	<u>Relationship</u>
Aman & Turbott, 1991	n = 26 (22 boys) age 5.5-12.7 ADD-H	age, memory distraction task, behavioral inhibition task	parent and teacher ratings (global change, inattention change, motor excess change)	multiple R's = .67 to .71
Aman et al., 1991	n = 30 (IQ's below 90) age 4.1-16 ADHD	high or low functioning (based on breadth of attention, mental age, IQ level)	teacher ratings of problem behavior	higher functioning (esp. IQ > 46) and cognitive maturity predicted improvement
Aman et al., 1993	n = 28, low IQ age 5-13 ADHD	mental age, IQ	parent & teacher ratings	mental age not predictive, IQ > 45 predicts better response

Aman et al., 1997	n = 30 (IQ 36-84) age 5-14 ADHD	age, mental age, IQ, breadth of attention		mental age not predictive, IQ > 50 suggests better response
Barkley & Cunningham, 1979	n = 20 boys age 5-12 hyperkinetic	maternal - child interaction coding	actometers, interaction coding, parental questionnaire	better mother-child relation weakly predicts a better resp.
Barkley & Jackson, 1977	n = 12 boys (known to be MPH resp.), 12 controls age 5-12 hyperkinetic	5 psychophys. measures of autonomic arousal	drug - placebo change scores on 11 behavioral measures	degree of resp. unrelated to initial levels of autonomic arousal
Barkley et al., 1989	n = 70, 37 with comorbid aggression age 6-13 ADHD	aggression group	parent & teacher ratings, MFFT, SRT, CPT, restricted academic situation test	aggression group did not predict MPH response, except as assessed by conduct test
Beery, 1994	n = 66 boys age 7-13 ADHD	disinhibition (= mother and teacher reports of impulsivity & hyperactivity)	10 behavioral measures	disinhibition predicted improvement on interrupting others, verbal abuse to staff
Buitelaar et al., 1995	n = 46 (41 boys) age = 6-13 DSM-III-R	neuropsych- ological tests (?), parent & teacher ratings, demographics	improvement at home or school (from Conners' ratings, clinical rating)	not predictive
		above, plus acute resp. to the first 10mg dose	(same as above)	response to first dose helps predicts later response, D's = 60- 82%
		WISC-R, inattentive at school, age, severity, home anxiety	strong response (= improved at home <u>and</u> school, n = 8) or not	D = 100% of strong resp., 78% of others.

Carlson et al., 1995	n = 16 boys in psychiatric hospital  age 7.7-12.8  ADHD + mood disorder + ODD, CD, or both	multiple psychiatric diagnoses (only this group of 16 was assessed, no controls)	school and hospital staff ratings	changes on externalizing but not internalizing symptoms  little to no clinical efficacy
Castellanos et al., 1996	n = 45 boys  age 6-12  DSM-III-R	monoamine metabolites (HVA, MHPG, 5- HIAA) in CSF fluid	Conners Teacher Rating Scale	baseline severity + HVA accounted for 73% of variance (higher HVA - better response)
Conte & Kinsbourne, 1988	n = 32 boys  age 8.2-12  ADD+H	Electrodermal lability (high, medium, low)	paired associate learning (fast or slow rate)	lability group interacted with task rate; MPH improvement depended on group and rate
de Sonneville et al., 1994	n = 58 boys (30 resp., 28 non- resp.); 27 controls  age = 8-11  ADD-H	memory search rate, memory efficiency, impulsivity, RT following incorrect	ratings by parents & others	D = 92% (resp. & non- resp.)
		WISC-R & subtests	(as above)	D = 54%
		neurological exam	(as above)	D = 75%
		psychological tests	(as above)	D = 75%
Denney, 1997	n = 76 (66 boys); same group as in Rapport et al., 1994  age 6-11  ADHD	hyperactivity, attention, initial scores,  daily school performance (APRS)	gain scores  dose response curves  responder status based on confidence intervals  optimal dose	multivariate analyses did not support many previous models  academic performance is most useful
Douglas et al., 1988	n = 19 (17 boys)  age 7.0-13  ADD-H	ratings (9 d.v.), academic tasks (14 d.v.), and cognitive tasks (22 d.v.)	(same as predictors)	all children improved on at least several measures

DuPaul et al., 1994	n = 40 age 6-12  ADHD (n=23) or ADD	internalizing groups: high, med., low	behavior home school, lab; sustained attention, arithmetic	high int. group showed worse resp. in school and lab, but not on cognitive measures
Effron et al., 1997	n = 125 (114 boys) age 5-14.9  ADHD (80% combined type, DSM-IV)	baseline parent and teacher ratings, aggressive- delinquent behavior	?	severity of baseline measures predicts better response  age, gender, socioeconomic status, and anxiety- depression not predictive
Elia et al., 1990	n = 31 boys age 6-12  ADDH	urinary epinephrine and metanephrine	parent, teacher, and physician assessments	urinary epinephrine and metanephrine increases with MPH did not correlate with resp.
Ferguson et al., 1976	n = "small" age 7-12  hyperactive	heart rate, skin conductance during baseline, reaction time task, and white noise	retrospective, from parent or physician comments in files	no consistent pattern between resp. & non- resp. groups
Ferguson & Trites, 1980	n = 79 boys age 7.5-12.5  hyperactive	neuropsych. exam, patient history and characteristics	attentional measures  Conners' ratings  global ratings	resp. were younger, lower IQ, less attentive, more physical abnormalities
	n = 25	EEG	(same as above)	abnormal EEG group had higher resp.
Gualtieri et al., 1982	n = 44 age 6-13  DSM-III	serum level of MPH, 2 dose levels	resp. & non- resp. group, as based on clinical impression	serum levels not different between resp. & non- resp. groups
Halliday et al., 1976	n = 42 (37 boys) age mean 9.5, SD 1.5  physician, teacher, and parent report	evoked potential variability and amplitude indices	pediatrician's evaluation (responder = greatly improved)	classified 32 of 42 correctly (76%)

Halliday et al., 1980	n = 15  age = 7.3 - 13.3	age, initial severity	parent and teacher ratings	older and higher initial severity predicts better dose response
	hyperactive			
Halliday et al., 1984	n = 20  age 7-13	visual ERP amplitude & latency	parent, teacher, & physician blind ratings	predicted resp. 91-100%, non- resp. 44-56%
	hyperactive			
Halperin et al., 1986	n = 80  age 6-12  pervasively hyperactive	behavior ratings, clinical EEG, neurological exam	change in Conners' scores, psychiatric global improvement	controlling for age and severity, neurological soft signs and EEG not predictive
Handen et al., 1994	n = 47 (31 boys), with IQ = 48 to 77  age 6-13  ADHD	sex, IQ, mental age, impulsivity-hyperactivity ratings, on-task behavior	school response (Conners' teacher rating scale, # of problems completed, % correct)	multiple R's .45 to .53
		hyperactivity ratings, race, impulsivity ratings, SES, conduct	laboratory response (task, Conners' scale, CPT)	multiple R's .47 to .67
Hicks et al., 1985	n = 44 (36 boys)  age mean 8.4 (SD 1.75)	placebo responding on 52 non-orthogonal measures	responding on the same 52 measures	placebo responses predict drug resp. for 47 of 52 measures
	ADD			
Hinshaw et al., 1989	n = 25 boys, 15 controls  age 6-12  ADHD	aggressive, non-aggressive	observations of social behavior	aggression group did not predict response
Jonkman et al., 1998	n = 12 (8 resp., 4 non- resp.)  age 10.3 (2.0)  ADHD	plasma conc. of MPH enantiomers	mean P3 ERP amplitude increased from placebo to MPH	non- resp. had higher plasma conc. of both D- and L- <u>threo</u> enantiomers

Kidder, 1990	n = 107 boys age 6-16  suspected ADHD	WISC-R, full scale IQ & subtests	paired associate learning	D = 52%
Kimball, 1986	n = 17 boys age 6.6-11  DSM-II or DSM-III	clinical observations, tests of tactile sensory integration & vestibular function	paired associate learning	4 of 22 measures correlated with drug response, r's = .57, -.50, .65, and .69
Kinsbourne, 1985	n = 55 (29 responders)  age ?  ADD ?	SCR, heart rate, and MFFT	responding on the same measures	baselines affect amount of change
Klorman et al., 1988	n = 63 (19 aggressive, 20 borderline ADHD)  age 6 - 12  ADHD cross- situational	3 groups: aggressive, non- aggr., and non- aggr. / borderline ADHD	parent / teacher ratings, EEG & behavioral measures during CPT-X and CPT-double	groups did not reliably differ
Klorman et al., 1994	n = 78 (34 ADD + aggression), 29 controls  age 5.6-11.9  ADD	aggression group	Sternberg's memory scanning task, ERP measures	aggression group not predictive of response
Klorman et al., 1989	n = 43 (24 low, 19 high on aggression)  age 6-12  ADHD cross- situational	high vs. low- aggression group (parent & teacher ratings)	CPT, ERPs during CPT, parent and teacher ratings	aggression group did not predict MPH response
Klorman et al., 1987	n = 12 age 12-19  ADD in adolescence & childhood	2 groups based on whether had stimulant therapy in childhood (n = 6) or not	parent, teacher, and self-report	childhood stimulant therapy did not predict adolescent resp.

Livingstone et al., 1992	n = 109 boys (internalizers, externalizers, both, or neither)	4 groups: ADD, ADD+int, ADD+ext, ADD+int + ext	teacher ratings	no effect of group, except that "both" shows worse response to low dose only
	age 7-11			
	ADD			
Loney, Prinz, et al., 1978	n = 84 boys age 6-12 hyperkinetic/MBD	age at referral, hyperactivity, & degree of perinatal complications	clinically rated improvement	multiple R = .50
Matier et al., 1992	n = 25 (14 aggressive), 13 controls age = 6.5 - 12	physically aggressive or not (DSM-III-R symptoms for conduct disorder)	CPT (impulsivity, inattention, dyscontrol errors), and activity	dyscontrol errors and activity level decreased only in the non-aggressive group
	ADHD			
McBride, 1988	n = 73 (53 boys) age 6-17 ADD (77% ADD-H)	Conners' ratings, sex, family history, physical exam, EEG, WISC-R	written comments and Conners' parent and teacher ratings, the child's own observations	younger age, male gender, higher IQ, and greater distractibility predicted better resp.
Nolan & Gadow, 1994	n = 34 (31 boys) age 5-13	school behavior coded by trained observers	rating scales	r's .37 to .55
	ADHD			
Pelham & Milich, 1991	n = 26 boys age mean 8.1	CPT, learning task, and teacher ratings	17 behavior measures, recreational and classroom	not predictive, either singly or in combination
	DSM-III-R			
Pelham et al., 1989	n = 24 (equal #'s boys and girls, matched for age and IQ) age = 5.5-11.3	sex	daily conduct, classroom behav., math, reading, seatwork, spelling, counselor & teacher ratings, peer interaction	no overall effect of sex or interaction of sex with drug on outcome measures
	ADD, ADD-H			
Pliszka, 1989	n = 43, 13 w/ anxiety age ? (similar across groups)	anxiety, conduct disorder, and oppositional/defiant disorder	teacher ratings	only comorbid anxiety predicted a poor resp. to MPH
	ADHD			

Prichep & John, 1990	n = 28 (16 resp.) age 6-12  learning disabled with or without ADHD	EEG neurometric profiles	Conners' ratings, global ratings, paired associate learning, & academic test	D = 82% (resp. 81%, non-resp. 83%)
Rappoport et al., 1989	n = 45 boys age 5-12  ADHD	three weight groups: low 22-26 kg, med. 27-31 kg, high 32-36 kg	classroom observations, teacher ratings, academic measures	body weight did not predict drug response
Rappoport et al., 1994	n = 76 (66 boys), 25 controls  age 6-11  ADHD	placebo and 4 dose levels	attentional, academic, and behavioral ratings	failure to respond at lower dose predicts favorable response at higher dose
Rappoport & Denney, 1997	n = 76 age  ADHD	body weight	dose response curves, optimal dose by statistical analysis of change scores	body weight did not affect response
Shen & Wang, 1984	n = 78 (62 boys); 57 controls  age 7-12  DSM-III	urinary MHPG	Conners' rating scales	decrease in MHPG excretion predicts positive resp.
Suffin & Emory, 1995	n = 46 (34 boys) age mean 12.4  DSM-III-R	EEG subgroups (frontal alpha excess, theta excess, hyper- coherent, other)	moderate or better Clinical Global Improvement (2 or 3), not always MPH	resp. and non-resp. groups were not differentiable
Sunohara et al., 1997	n = 13 resp, 13 non-resp, 13 controls  age 11.4 +/- 1.2  ADHD	paired associate learning, errors on placebo; ERP	psychoeducational assessments and cognitive tasks (?)	paired associate and placebo not predictive;  no ERP differences while off MPH  on MPH, longer latencies in P3b and N2 ERP for non- resp.
Swanson et al., 1978	n = 53 (50 boys) age > 5, mean 10.2  hyperactive	anxiety	paired associate learning	anxiety predicts a worse response

Tannock et al., 1995	n = 40 (18 with anxiety)  age 7-11  ADHD	anxiety group	activity level, working memory	comorbid anxiety but not learning disorder predicts worse response
Taylor et al., 1987	n = 38 boys  age 6-10  referred; 26 found to meet DSM-III criteria	age, IQ, hyperactive home behavior and attentional measures, neurological exam	6 measures of behavior (ratings) and attention	clinical rating: D = 70% resp., 73% non- resp.  hyperactivity: D = 81% resp., 68% non- resp.
Thomson, 1992	n = 336 (278 boys), much missing data  age 3-16, mean 8.6  ADHD, ADD	neurological diagnosis, age, child behavior checklist (CBCL), WISC-R	based on Conners' parent and teacher ratings	D = 72% (75% resp., 59% non- resp.)
	n = 61, with complete data (?)	neurological diagnosis, CBCL, family structure	(same as above)	D = 89% (97% resp., 86% non- resp.)
	n = 36, with complete data (?)	WISC-R subtests, CBCL	(same as above)	multiple R = .59
Tirosh et al, 1993	n = 20 (16 boys)  age 7-12  DSM-III	digit, word, visual tests derived from WISC-R, motor control, maze drawing	teacher ratings, parent ratings	placebo - drug r's .44-.71 (teacher) .20-.54 (parent)  baseline-drug r's .30-.52 (teacher) .29-.42 (parent)
Varley & Trupin, 1982	n = 10 (7 boys), IQ's 48-77  age 4.5-15  DSM-III	IQ, sex, social class, ratings	Conners' parent & teacher ratings	5 of 10 responded, no predictors identified
Voelker et al., 1983	n = 46 (36 boys); 46 controls  age 5-15  hyperkinetic	Personality Inventory for Children	home behavior ratings; retrospectively	D = 74% (78% resp., 68% non- resp.)

Young et al., 1995	n = 35 (21 boys) age 12.3 +/- 2.57	ERP measures of acute response (P3b amplitude)	physicians' clinical assessment (global ratings)	acute response above threshold or not predicted 81% of outcomes
<u>DSM-III-R</u>				

Notes. CPT = continuous performance test; ext = externalizer; int = internalizer; MFFT = Kagan's (1966) Matching Familiar Figures Test; resp. = responders; SCR = skin conductance response; SRT = Selective Reminding Test; WISC = Weschler Intelligence Scale for Children; ? = information missing or unclear.

Participants = number & characteristics, age in years, and diagnosis.

Predictor Variables = independent variables used to discriminate between responders and non-responders (e.g., entered into the discriminant function)

Response measures = outcome measure(s) used to assess drug response.

Relationship = prediction effectiveness: D = percentage of correct classification of responders and nonresponders by a discriminant function (chance = 50%);  $r$  = simple or partial correlation with MPH response,  $R$  = multiple correlation.

## References

- Aman, M. G., Kern, R. A., McGhee, D. E., & Arnold, L. E. (1993). Fenfluramine and methylphenidate in children with mental retardation and ADHD: Clinical and side effects. Journal of the American Academy of Child and Adolescent Psychiatry, *32*(4), 851-859.
- Aman, M. G., Kern, R. A., Osborne, P., Yumuluru, R., Rojahn, J., & del Medico, V. (1997). Fenfluramine and methylphenidate in children with mental retardation and borderline IQ: Clinical effects. American Journal of Mental Retardation, *101*, 521-534.
- Aman, M. G., Marks, R. E., Turbott, S. H., Wilsher, C. P., & Merry, S. N. (1991). Clinical effect of methylphenidate and thioridazine in intellectually subaverage children. Journal of the American Academy of Child and Adolescent Psychiatry, *30*(2), 246-256.
- Aman, M. G., & Turbott, S. H. (1991). Prediction of clinical response in children taking methylphenidate. Journal of Autism and Developmental Disorders, *21*, 211-228.
- American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: Author.
- Anderson, J. C., Williams, S., McGee, R., & Silva, P. A. (1987). DSM-III-R disorders in preadolescent children: Prevalence in a large sample from the general population. Archives of General Psychiatry, *44*, 69-76.
- Anderson, K. J., & Revelle, W. (1994). Impulsivity and time of day: Is rate of change in arousal a function of impulsivity? Journal of Personality and Social Psychology, *67*(2), 334-344.
- Arnold, L. E. (1996). Sex differences in ADHD: Conference summary. Journal of Abnormal Child Psychology, *24*(5), 555-569.
- Arnold, L. E., Votolato, N. A., Kleykamp, D., Baker, G. B., & Bornstein, R. A. (1990). Does hair zinc predict amphetamine improvement of ADD/hyperactivity? International Journal of Neuroscience, *50*(1-2), 103-107.
- Barkley, R. A. (1976). Predicting the response of hyperactive children to stimulant drugs: A review. Journal of Abnormal Child Psychology, *4*(4), 327-348.
- Barkley, R. A. (1977). A review of stimulant drug research with hyperactive children. Journal Child Psychology and Psychiatry, *18*, 137-165.
- Barkley, R. A. (1990). Attention deficit hyperactivity disorder: A handbook for diagnosis and treatment. New York: Guilford.
- Barkley, R. A. (1991). The ecological validity of laboratory and analogue assessment methods of ADHD symptoms. Journal of Abnormal Child Psychology, *19*, 149-178.
- Barkley, R. A. (1994). Impaired delayed responding: A unified theory of attention deficit hyperactivity disorder. In D. K. Routh (Ed.), Disruptive behavior disorders: Essays in honor of Herbert Quay (pp. 11-57). New York: Plenum.
- Barkley, R. A. (1997a). ADHD and the nature of self-control. New York: Guilford.
- Barkley, R. A. (1997b). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. Psychological Bulletin, *121*, 65-94.
- Barkley, R. A., & Cunningham, C. E. (1979). The effects of methylphenidate on the mother-child interactions of hyperactive children. Archives of General Psychiatry, *36*, 201-208.
- Barkley, R. A., Grodzinsky, G., & DuPaul, G. J. (1992). Frontal lobe functions in attention deficit disorder with and without hyperactivity: A review and research report. Journal of Abnormal Child Psychology, *20*(2), 163-188.
- Barkley, R. A., & Jackson, T. L. (1977). Hyperkinesis, autonomic nervous system activity and stimulant drug effects. Journal of Child Psychology and Psychiatry, *18*, 347-357.

Barkley, R. A., McMurray, M. B., Edelbrock, C. S., & Robbins, K. (1989). The response of aggressive and nonaggressive ADHD children to two doses of methylphenidate. Journal of the American Academy of Child and Adolescent Psychiatry, 28(6), 873-881.

Bawden, D. (1993). Predicting methylphenidate response with neurometric testing: Case studies. In L. F. Koziol, C. E. Stout, & D. H. Ruben (Eds.), Handbook of childhood impulse disorders and ADHD: Theory and practice (pp. 60-77). Springfield, IL: Charles C. Thomas.

Bedi, G. C., Halperin, J. M., & Sharma, V. (1994). Investigation of modality-specific distractibility in children. International Journal of Neuroscience, 74, 79-85.

Beery, S. H. (1994). Behavioral disinhibition, anxiety and response to methylphenidate and behavior intervention in children with attention deficit hyperactivity disorder. Unpublished doctoral dissertation, University of Miami, Coral Gables, FL.

Bekaroglu, M., Aslan, Y., Gedik, Y., Deger, O., Mocan, H., Erduran, E., & Karahan, C. (1996). Relationships between serum free fatty acids and zinc, and attention deficit hyperactivity disorder: A research note. Journal of Child Psychology and Psychiatry, 37(2), 225-227.

Biederman, J., Faraone, S. V., Keenan, K., Benjamin, J., Krifcher, B., Moore, C., Sprich-Buckminster, S., Ugalia, K., Jellinek, M. S., Steingard, R., Spencer, T., Norman, D., Kolodny, R., Kraus, I., Perrin, J., Keller, M. B., & Tsuang, M. (1992). Further evidence for family-genetic risk factors in attention deficit hyperactivity disorder. Archives of General Psychiatry, 49, 728-738.

Biederman, J., Lapey, K., Milberger, S., Faraone, S. V., Reed, E. D., & Seidman, L. J. (1994). Motor preference, major depression and psychosocial dysfunction among children with attention deficit hyperactivity disorder. Journal of Psychiatry Research, 28(2), 171-184.

Biederman, J., Milberger, S., Faraone, S. V., Kiely, K., Guite, J., Mick, E., Ablon, S., Warburton, R., & Reed, E. (1995). Family-environment risk factors for attention-deficit hyperactivity disorder. Archives of General Psychiatry, 52, 464-470.

Buitelarr, J. K., Van der Gaag, R. J., Swaab-Barneveld, H. & Kuiper, M. (1995). Prediction of clinical response to methylphenidate in children with attention-deficit hyperactivity disorder. Journal of the American Academy of Child and Adolescent Psychiatry, 34(8), 1025-1032.

Carlson, G. A., Rapport, M. D., Kelly, K. L., & Pataki, C. S. (1995). Methylphenidate and desipramine in hospitalized children with comorbid behavior and mood disorders: Separate and combined effects on behavior and mood. Journal of Child and Adolescent Psychopharmacology, 5(3), 191-204.

Casey, B. J., Castellanos, F. X., Giedd, J. N., Marsh, W. L., Hamburger, S. D., Schubert, A. B., Vauss, Y. C., Vaituzis, A. C., Dickstein, D. P., Sarfatti, S. E., & Rapoport, J. L. (1997). Implication of right frontostriatal circuitry in response inhibition and attention-deficit/hyperactivity disorder. Journal of the American Academy of Child and Adolescent Psychiatry, 36(3), 374-383.

Castellanos, F. X., Elia, J., Kruesi, M. J. P., Marsh, W. L., Gulotta, C. S., Potter, W. Z., Ritchie, G. F., Hamburger, S. D., & Rapoport, J. L. (1996). Cerebrospinal fluid homovanillic acid predicts behavioral response to stimulants in 45 boys with Attention Deficit / Hyperactivity Disorder. Neuropsychopharmacology, 14, 125-137.

Castellanos, F. X., Giedd, J. N., Eckburg, P., Marsh, W. L., Vaituzis, A. C., Kaysen, D., Hamburger, S. D., & Rapoport, J. L. (1994). Quantitative morphology of the caudate nucleus in attention deficit hyperactivity disorder. American Journal of Psychiatry, 151, 1791-1796.

Conners, C. K. (1971). The effect of stimulant drugs on human figure drawings in children with minimal brain dysfunction. Psychopharmacologia, *126*, 329-333.

Conners, C. K. (1972). Psychological effects of stimulant drugs in children with minimal brain dysfunction. Pediatrics, *49*, 702-708.

Conte, R., & Kinsbourne, M. (1988). Electrodermal lability predicts presentation rate effects and stimulant drug effects on paired associate learning in hyperactive children. Psychophysiology, *25*(1), 64-70.

Cook, E. H., Stein, M. A., & Leventhal, B. L. (1997). Family-based association of attention-deficit/hyperactivity disorder and the dopamine transporter. In K. Blum & E. P. Noble (Eds.), Handbook of psychiatric genetics (pp. 297-310). Boca Raton, FL: CRC Press.

de Sonneville, L. M. J., Njokitjien, C., & Bos, H. (1994). Methylphenidate and information processing. Part I: Differentiation between responders and nonresponders; Part II: Efficacy in responders. Journal of Clinical and Experimental Neuropsychology, *16*(6), 877-897.

Denckla, M. B. (1996). Biological correlates of learning and attention: What is relevant to Learning Disability and Attention-Deficit Hyperactivity Disorder? Developmental and Behavioral Pediatrics, *17*, 114-119.

Denney, C. B. (1997). Predictive models of methylphenidate response in children with Attention-Deficit Hyperactivity Disorder: Premises, implications, and an empirical evaluation. Unpublished Ph.D. Dissertation, University of Hawaii, Honolulu, HI.

Douglas, V. I., Barr, R. G., Amin, K., O'Neill, M. E., & Britton, B. G. (1988). Dosage effects and individual responsivity to methylphenidate in attention deficit disorder. Journal of Child Psychology and Psychiatry, *29*(4), 453-475.

DuPaul, G. J., Barkley, R. A., & McMurray, M. B. (1994). Response of children with ADHD to methylphenidate: Interaction with internalizing symptoms. Journal of the American Academy of Child Psychiatry, *33*, 894-903.

Effron, D., Jarman, F., & Barker, M. (1997). Methylphenidate versus dextroamphetamine in children with attention deficit hyperactivity disorder: A double-blind, crossover trial. Pediatrics, *100*(6), E6.

Elia, J., Borcharding, B. G., Rapoport, J. L., & Keysor, C. S. (1991). Methylphenidate and dextroamphetamine treatments of hyperactivity: Are there true nonresponders? Psychiatry Research, *36*, 141-155.

Elia, J., Breck, G., Borcharding, B. G., Potter, W. Z., Mefford, I. N., Rapoport, J. L., & Keysor, C. S. (1990). Stimulant drug treatment of hyperactivity: Biochemical correlates. Clinical Pharmacology & Therapy, *48*, 57-66.

Ferguson, H. B., Simpson, S., & Trites, R. L. (1976). Psychophysiological study of methylphenidate responders and nonresponders. In R. M. Knights & D. J. Bakker (Eds.), Neuropsychology of learning disorders. Baltimore: University Park Press.

Ferguson, H. B., & Trites, R. L. (1980). Predicting the response of hyperactive children to Ritalin: An empirical study. In R. M. Knights & D. J. Bakker (Eds.), Treatment of hyperactive and learning disordered children. Baltimore: University Park Press.

Fischer, M., Barkley, R. A., Fletcher, K. E., & Smallish, L. (1993). The stability of dimensions of behavior in ADHD and normal children over an 8-year followup. Journal of Abnormal Child Psychiatry, *21*(3), 315-337.

Gray, J. A. (1982). The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system. Oxford: Oxford University Press.

Gualtieri, C. T., Hicks, R. E., Evans, R. W., & Patrick, K. (1988). The clinical importance of methylphenidate blood level determinations. In L. M. Bloomingdale (Ed.), Attention deficit disorder (Vol. 3, pp. 81-100). New York: Pergamon Press.

Gualtieri, C. T., Wargin, W., Kanoy, R., Patrick, K., Shen, C. D., Youngblood, W., Mueller, R. A., & Breese, G. R. (1982). Clinical studies of MPH serum levels in children and adults. Journal of the American Academy of Child Psychiatry, *21*(1), 19-26.

Halliday, R., Callaway, E., & Rosenthal, J. H. (1984). The visual ERP predicts clinical response to methylphenidate in hyperactive children. Psychophysiology, *21*(1), 114-121.

Halliday, R., Gnauck, K., Rosenthal, J. R., McKibben, J. L., & Callaway, E. (1980). The effects of methylphenidate on school and home behavior of the hyperactive child. In R. M. Knights & D. J. Bakker (Eds.), Treatment of hyperactive and learning disordered children. Baltimore, MD: University Park Press.

Halliday, R., Rosenthal, J. H., Naylor, H., & Callaway, E. (1976). Averaged evoked potential predictors of clinical improvement in hyperactive children treated with methylphenidate: An initial study and replication. Psychophysiology, *13*(5), 429-440.

Halperin, J. M., Gittelman, R., Katz, S., & Struve, F. A. (1986). Relationship between stimulant effect, electroencephalogram, and clinical neurological findings in hyperactive children. Journal of the American Academy of Child and Adolescent Psychiatry, *25*(6), 820-825.

Handen, B. L., Breaux, A. M., Gosling, A., Ploof, D. L., & Feldman, H. (1990). Efficacy of methylphenidate among mentally retarded children with attention deficit hyperactivity disorder. Pediatrics, *86*(6), 922-930.

Handen, B. L., Feldman, H., Gosling, A., Breaux, A. M., & McAuliffe, S. (1991). Adverse side effects of methylphenidate among mentally retarded children with ADHD. Journal of the American Academy of Child and Adolescent Psychiatry, *30*, 241-245.

Handen, B. L., Janosky, J., McAuliffe, S., Breaux, A. M., & Feldman, H. (1994). Prediction of response to methylphenidate among children with ADHD and mental retardation. Journal of the American Academy of Child and Adolescent Psychiatry, *33*(8), 1185-1193.

Heiligenstein, E., & Anders, J. (1997). Pemoline in adult attention deficit hyperactivity disorder: Predictors of nonresponse. Journal of American College Health, *45*, 225-229.

Heilman, K. M., Voeller, L. L., & Nadeau, S. E. (1991). A possible pathophysiological substrate of attention deficit hyperactivity disorder. Journal of Child Neurology, *6*(Suppl.), S76-S81.

Hicks, E., Gualtieri, C. T., Mayo, J. P., Schroeder, S. R., & Lipton, M. A. (1985). Methylphenidate and homeostasis: Drug effects on the cognitive performance of hyperactive children. In L. M. Bloomingdale (Ed.), Attention deficit disorder: Identification, course and treatment rationale (pp. 131-141). New York: Spectrum.

Hinshaw, S. P., Hencker, B., Whalen, C. K., Erdhardt, D., & Dunnington, R. E. (1989). Aggressive, prosocial, and nonsocial behavior in hyperactive boys: Dose effects of methylphenidate in naturalistic settings. Journal of Consulting and Clinical Psychology, *57*, 636-643.

Janowsky, J. S., & Carper, R. (1996). Is there a neural basis for cognitive transitions in school-age children? In A. J. Sameroff & M. M. Haith (Eds.), The five to seven year shift (pp. 33-60). Chicago, IL: University of Chicago Press.

John, E. R., Prichep, L. S., & Almas, M. (1992). Subtyping of psychiatric patients by cluster analysis of QEEG. Brain Topography, *4*(4), 321-326.

Jonkman, L. M., Verbaten, M. N., de Boer, D., Maes, R. A. A., Buitelaar, J. K., Kemner, C., van Engeland, H., & Koelega, H. S. (1998). Difference in plasma concentrations of the D- and L-threo methylphenidate enantiomers in responding and non-responding children with attention deficit hyperactivity disorder. Psychiatry Research, *78*, 115-118.

Kagan, J. (1966). Reflection-impulsivity: The generality and dynamics of conceptual tempo. Journal of Abnormal Psychology, *71*, 17-24.

Kaplan, S. L., Busner, J., Kupietz, S., Wasserman, E., & Segal, B. (1990). Effects of methylphenidate on adolescents with aggressive conduct disorder and ADDH: A preliminary report. Journal of the American Academy of Child and Adolescent Psychiatry, *29*, 719-723.

Kaufman, A. S. (1976). A new approach to the interpretation of test scatter on the WISC-R. Journal of Learning Disabilities, *9*, 160-168.

Khan, A. U., & Dekirmenjian, H. (1981). Urinary excretion of catecholamine metabolites in hyperkinetic child syndrome. American Journal of Psychiatry, *138*(1), 108-110.

Kidder, K. R. (1990). Factorial analysis of WISC-R subtest scatter scores of attention deficit hyperactivity disordered children and adolescents: A predictor of positive Ritalin responders? Unpublished Ph.D. dissertation, George Washington University.

Kimball, J. G. (1986). Prediction of methylphenidate (MPH) responsiveness through sensory integrative testing. American Journal of Occupational Therapy, *40*(4), 241-248.

Kinsbourne, M. (1985). Base-state dependency of stimulant effects on the cognitive performance of hyperactive children. In L. M. Bloomingdale (Ed.), Attention deficit disorder: Identification, course, and treatment rationale (pp. 143-154). New York: Spectrum.

Klein, R. G., & Wender, P. (1995). The role of methylphenidate in psychiatry. Archives of General Psychiatry, *52*, 429-433,

Klorman, R., Brumaghim, J. T., Fitzpatrick, P. A., Borgstedt, A. D., & Strauss, J. (1994). Clinical and cognitive effects of methylphenidate on children with attention deficit disorder as a function of aggression/oppositionality and age. Journal of Abnormal Psychology, *103*(2), 206-221.

Klorman, R., Brumaghim, J. T., Salzman, L. F., Strauss, J., Borgstedt, A. D., McBride, M. C., & Loeb, S. (1988). Effects of methylphenidate on children with attention-deficit hyperactivity disorder with and without aggression/non-compliant features. Journal of Abnormal Psychology, *97*, 413-422.

Klorman, R., Brumaghim, J. T., Salzman, L. F., Strauss, J., Borgstedt, A. D., McBride, M. C., & Loeb, S. (1989). Comparative effects of methylphenidate on attention-deficit hyperactivity disorder with and without aggressive noncompliant features. Psychopharmacology Bulletin, *25*(1), 109-113.

Klorman, R., Coons, H. W., & Borgstedt, A. D. (1987). Effects of methylphenidate on adolescents with a childhood history of attention deficit disorder: I. Clinical findings. Journal of the American Academy of Child and Adolescent Psychiatry, *26*(3), 363-367.

Knopp, W., Arnold, E., Andras, R., & Smeltzer, D. (1973). Predicting amphetamine response in hyperkinetic children by electronic pupillography. Pharmacopsychiatry, *6*, 158-166.

Livingstone, R. L., Dykman, R. A., & Ackerman, P. T. (1992). Psychiatric comorbidity and two doses of methylphenidate in children with attention deficit disorder. Journal of Child and Adolescent Psychopharmacology, *2*, 115-122.

Loney, J. (1986). Predicting stimulant response among hyperactive children. Psychiatric Annals, *16*, 16-19.

Loney, J., Langhorne, J. E., & Paternite, C. E. (1978). An empirical basis for subgrouping the hyperkinetic / minimal brain dysfunction syndrome. Journal of Abnormal Psychology, *87*(4), 431-441.

Loney, J., Prinz, R., Mishalow, J., & Joad, J. (1978). Hyperkinetic / aggressive boys in treatment: Predictors of clinical response to methylphenidate. American Journal of Psychiatry, *135*, 1487-1491.

Matier, K., Halperin, J. M., Sharma, V., Newcorn, J. H., & Sathaye, N. (1992). Methylphenidate response in aggressive and nonaggressive ADHD children: Distinctions on laboratory measures of symptoms. Journal of the American Academy of Child and Adolescent Psychiatry, *31*, 219-225.

McBride, M. C. (1988). An individual double-blind crossover trial for assessing methylphenidate response in children with attention deficit disorder. Journal of Pediatrics, *113*, 137-145.

Mick, E., Biederman, J., & Faraone, S. V. (1996). Is season of birth a risk factor for attention-deficit hyperactivity disorder? Journal of the American Academy of Child and Adolescent Psychiatry, *35*(11), 1470-1476.

Milberger, S., Biederman, J., Faraone, S. V., Chen, L., & Jones, J. (1996). Is maternal smoking during pregnancy a risk factor for attention-deficit hyperactivity disorder in children? American Journal of Psychiatry, *153*(9), 1138-1142.

Nolan, E. E., & Gadow, K. D. (1994). Relation between ratings and observations of stimulant drug response in hyperactive children. Journal of Clinical Child Psychology, *23*(1), 78-90.

Pelham, W. E., & Milich, R. (1991). Individual differences in response to methylphenidate in classwork and social behavior. In L. L. Greenhill & B. B. Osman (Eds.), Ritalin: Theory and patient management (pp. 203-221). New York: Mary Ann Liebert.

Pelham, W. E., Walker, J. L., Sturges, J., & Hoza, J. (1989). Comparative effects of methylphenidate on ADD girls and ADD boys. Journal of the American Academy of Child and Adolescent Psychiatry, *28*, 773-776.

Peloquin, L. J., & Klorman, R. (1992). Effects of methylphenidate on normal children's mood, event-related potentials, and performance in memory scanning and vigilance. Journal of Abnormal Psychology, *95*(1), 88-98.

Pliszka, S. R. (1989). The effects of anxiety on cognition, behavior, and stimulant response in ADHD. Journal of the American Academy of Child and Adolescent Psychiatry, *28*(6), 882-887.

Prichep, L. S., & John, E. R. (1990). II. Neurometric studies of methylphenidate responders and non-responders. In G. T. Pavlidis (Ed.), Perspective on dyslexia Volume I Neurology, Neurophysiology and Genetics (pp. 133-139). New York: Wiley.

Quay, H. C. (1988). Attention deficit disorder and the behavioral inhibition system: The relevance of the neuropsychological theory of Jeffrey A. Gray. In L. M. Bloomingdale & J. Sergeant (Eds.), Attention deficit disorder: Criteria, cognition, intervention (pp. 117-126). New York: Pergamon.

Quay, H. C. (1997). Inhibition and attention deficit hyperactivity disorder. Journal of Abnormal Child Psychology, *25*(1) 7-13.

Rapoport, J. L., Buchsbaum, M., Weingartner, H., Zahn, T., Ludlow, C., & Mikkelsen, E. (1980). Dextroamphetamine: Cognitive and behavioral effects in normal and hyperactive boys and normal men. Archives of General Psychiatry, *37*, 933-943.

Rapoport, J. L., Buchsbaum, M., Zahn, T., Weingartner, H., Ludlow, C., & Mikkelsen, E. (1978). Dextroamphetamine: Cognitive and behavioral effects in normal prepubertal boys. Science, *199*, 560-562.

Rapoport, M. D., & Denney, C. (1997). Titrating methylphenidate in children with Attention-Deficit / Hyperactivity Disorder: Is body mass predictive of clinical response? Journal of the American Academy of Child & Adolescent Psychiatry, *36*, 523-530.

Rapoport, M. D., Denney, C., DuPaul, G. J., & Gardner, M. J. (1994). Attention deficit disorder and methylphenidate: Normalization rates, clinical effectiveness, and response prediction in 76 children. Journal of the American Academy of Child & Adolescent Psychiatry, *33*(6), 882-893.

Rapoport, M. D., DuPaul, G. J., & Kelly, K. L. (1989). Attention deficit hyperactivity disorder and methylphenidate: The relationship between gross body weight and drug response in children. Psychopharmacology Bulletin, *25*, 285-290.

Rapoport, M. D., DuPaul, G. J., Stoner, G., & Jones, J. T. (1986). Comparing classroom and clinic measures of attention deficit disorder: Differential, idiosyncratic, and dose-response effects of methylphenidate. Journal of Consulting and Clinical Psychology, *54*(3), 334-341.

Rapoport, M. D., Jones, J. T., DuPaul, G. J., Kelly, K. L., Gardner, M. J., Tucker, S. B., & Shea, M. S. (1987). Attention deficit disorder and methylphenidate: Group and single-subject analyses of dose effects on attention in clinic and classroom settings. Journal of Clinical Child Psychology, *16*, 329-338.

Safer, D. J., Zito, J. M., Fine, E. M. (1996). Increased methylphenidate usage for attention deficit disorder in the 1990s. Pediatrics, *98*(6 Pt 1), 1084-1088.

Sameroff, A. J., & Haith, M. M. (Eds.) (1996). The five to seven year shift: The age of reason and responsibility. Chicago, IL: University of Chicago Press.

Schachar, R. J., Tannock, R., & Logan, G. (1993). Inhibitory control, impulsiveness, and attention deficit hyperactivity disorder. Clinical Psychology Review, *13*, 721-739.

Schachar, R. J., Tannock, R., Marriott, M. & Logan, G. (1995). Deficient inhibitory control in attention deficit hyperactivity disorder. Journal of Abnormal Child Psychology, *23*, 411-438.

Sergeant, J. A., & Van der Meere, J. (1988). What happens after a hyperactive child commits an error? Psychiatry Research, *24*(2) 157-164.

Sergeant, J., & Van der Meere, J. (1990). Convergence of approaches in localizing the hyperactivity deficit. In B. B. Lahey & A. E. Kazdin (Eds.), Advances in clinical child psychology (Vol. 13, pp. 207-240). New York: Elsevier.

Shekim, W. O., Dekirmenjian, H., & Chapel, J. L. (1979). Urinary MHPG excretion in minimal brain dysfunction and its modifications by d-amphetamine. American Journal of Psychiatry, *136*, 667-671.

Shekim, W. O., Javaid, J., Davis, J. M., & Bylund, D. B. (1983). Urinary MHPG and HVA excretion in boys with attention deficit disorder and hyperactivity treated with d-amphetamine. Biological Psychiatry, *18*, 707-714.

Shen Y., & Wang Y. (1984). Urinary 3-methoxy-4-hydroxyphenylglycol sulfate excretion in seventy-three schoolchildren with minimal brain dysfunction syndrome. Biological Psychiatry, *19*(6), 861-870.

Sprague, R. L., & Sletator, E. K. (1977). Methylphenidate in hyperkinetic children: Differences in dose effects on learning and social behavior. Science, *198*, 1274-1276.

Suffin, S. C., & Emory, W. H. (1995). Neurometric subgroups in attentional and affective disorders and their association with pharmacotherapeutic outcome. Clinical Electroencephalography, *26*(2), 76-83.

Sunohara, G. A., Voros, J. G., Malone, M. A., & Taylor, M. J. (1997). Effects of methylphenidate in children with attention deficit hyperactivity disorder: a comparison of event-related potentials between medication responders and non-responders. International Journal of Psychophysiology, *27*, 9-14.

Swanson, J. M. (1988). Measurement of serum concentration and behavioral responses in ADHD children to acute doses of methylphenidate. In L. M. Bloomingdale (Ed.), Attention deficit disorder (Vol. 3, pp. 107-126). New York: Pergamon Press.

Swanson, J. M., Kinsbourne, M., Roberts, W., & Zucker, K. (1978). Time-response analysis of stimulant medication on the learning ability of children referred for hyperactivity. Pediatrics, *61*, 21-29.

Tannock, R., Ickowicz, A., & Schachar, R. (1995). Differential effects of methylphenidate on working memory in ADHD children with and without comorbid anxiety. Journal of the American Academy of Child and Adolescent Psychiatry, *34*(7), 886-896.

Taylor, E. (1983). Drug response and diagnostic validation. In M. Rutter (Ed.), Developmental neuropsychiatry (pp. 348-368). New York: Guilford.

Taylor, E., Schachar, R., Thorley, G., Wieselberg, H. M., Everitt, B., & Rutter, M. (1987). Which boys respond to stimulant medication? A controlled trial of methylphenidate in boys with disruptive behavior. Psychological Medicine, *17*, 121-143.

Thomson, J. B. (1992). Prediction of stimulant response in children with ADHD. Unpublished Ph.D. Dissertation, University of Victoria.

Tirosh, E., Elhasid, R., Cohen-Bar Kamah, S., & Cohen, A. (1993). Predictive value of placebo methylphenidate. Pediatric Neurology, *9*, 131-133.

Varley, C. K., & Trupin, E. W. (1982). Double-blind administration of methylphenidate to mentally retarded children with attention deficit disorder: A preliminary study. American Journal of Mental Deficiency, *86*(6), 560-566.

Voelker, S., Lachar, D., & Gdowski, C. L. (1983). The Personality Inventory for Children and response to methylphenidate: Preliminary evidence for predictive utility. Journal of Pediatric Psychology, *8*(2), 161-169.

Waldrop, M. F., Bell, R. Q., McLaughlin, B., & Halverson, C. F., Jr. (1978). Newborn minor physical abnormalities predict short attention span, peer aggression, and impulsivity at age 3. Science, *199*, 563-564.

Werry, J. S., & Sprague, R. (1974). Methylphenidate in children: Effects of dosage. Australian and New Zealand Journal of Psychiatry, *8*, 9-19.

Whalen, C. K., Henker, B., Swanson, J. M., Granger, D., Kliewer, W., & Spencer, J. (1987). Natural social behaviors in hyperactive children: Dose effects of methylphenidate. Journal of Consulting and Clinical Psychology, *55*, 187-193.

Young, E. S., Perros, P., Price, G. W., & Sadler, T. (1995). Acute challenge ERP as a prognostic of stimulant therapy outcome in Attention Deficit Hyperactivity Disorder. Biological Psychiatry, *37*, 25-33.

Zahn, T. P., Rapoport, J. L., & Thompson, C. L. (1980). Autonomic and behavioral effects of dextroamphetamines and placebo in normal and hyperactive prepubertal boys. Journal of Abnormal Child Psychology, *8*, 145-160.

Zametkin, A. J., & Rapoport, J. L. (1987). Neurobiology of attention deficit disorder with hyperactivity: Where have we come in 50 years? Journal of the American Academy of Child and Adolescent Psychiatry, 26(5), 676-686.