Pergamon

CLINICAL PSYCHOLOGY REVIEW

Clinical Psychology Review 22 (2002) 1107–1131

Review

Attention deficit/hyperactivity disorder and methylphenidate A review of height/weight, cardiovascular, and somatic complaint side effects

Mark D. Rapport[a,*], Catherine Moffitt[b]

[a]*Department of Psychology, University of Central Florida, P.O. Box 161390, Orlando, FL 32816, USA*
[b]*Department of Psychology, University of Hawaii, USA*

Received 15 February 2002; accepted 7 March 2002

Abstract

Three classes (height/weight, cardiovascular, and somatic complaints) of treatment emergent symptoms (side effects) associated with methylphenidate (MPH) therapy for children with attention deficit/hyperactivity disorder (ADHD) are reviewed. The more easily quantifiable side effects (e.g., blood pressure [BP], heart rate [HR], height/weight) are mostly transient, dose-dependent, easily rectified with dosage adjustments, and considered minor from a clinical perspective considering the breadth and level of improvement in behavior and cognitive functioning observed in most children. Previously reported somatic complaints associated with psychostimulant therapy may reflect symptoms occurring prior to initiation of treatment and require additional study.

1. Introduction

The short- and intermediate-term therapeutic efficacy of psychostimulants for treating children with attention deficit/hyperactivity disorder (ADHD) is well-established (MTA Cooperative Group, 1999). Beneficial effects are observed across multiple domains of functioning based on direct observations of children's attention, behavior, and academic

* Corresponding author. Tel.: +1-401-823-2216; fax: +1-401-823-5862.
E-mail address: mrapport@pegasus.cc.ucf.edu (M.D. Rapport).

0272-7358/02/$ – see front matter
PII: S0272-7358(02)00129-0

Table 1
Emergent symptom studies of MPH in children with ADHD

Citation	*N*	Diagnosis criteria	Measurement instruments (DVs)	Drug conditions	Source	Design	Results
Height and weight studies							
Safer et al. (1972)	29 (NR)	NFDC hyperactive receiving medication or referred for medication but not receiving any	height weight	MPH (20, 30, and 40 mg/day) DEX (10 and 15 mg/day)	Ph	naturalistic, longitudinal	weight gain: 20 mg MPH > 30–40 mg MPH 10 and 15 mg DEX: NS Ss continued on stimulants through summer < Ss d/c Ss continued on DEX through summer < Ss d/c Ss continued vs. d/c on MPH through summer: NS Ss continued on stimulants through summer: average of 60% expected weight gain Ss continued on stimulants for 2 years: sign less weight gain than expected Height: Stimulants: sign decline in height percentile vs. controls
Greenberg and Yellin (1975)	40 males and 7 females	NFDC hyperactive	weight	PL and MPH (40 mg/day) IMI (100 mg/day)	Ph	randomized, double-blind, placebo controlled, crossover	weight: PL > MPH

Millichap (1978)	36 males	NFDC hyperactive MBD LD	height growth rate	BL and MPH (5–20 mg/day)	Ph	longitudinal	height percentile: BL vs. end of treatment: NS annual growth rate: sign less than normal, for two patients; sign greater than normal for six patients
Satterfield et al. (1979)	72 males (1 year) and 48 males (2 years)	NFDC hyperactive hyperexitability, impulsivity, and inattention reported by P/T	height weight	MPH (mean = 24.2 mg/day)	Ph	longitudinal	Height gain: 1 year: MPH < expected 2 years: NS Ss continued vs. Ss d/c on MPH through summers: NS Weight gain: 1 year: MPH < expected 2 years: MPH < expected Ss continued on MPH through summers < Ss d/c for summers
Conners and Taylor (1980)	57 males and 3 females	NFDC hyperkinesis	weight	PL, MPH (mean = 0.82 mg/kg/day) PEM (2.25 mg/kg/day)	Ph	randomized, double-blind, placebo-controlled	weight: PL>MPH, PEM
Winsberg et al. (1982)	25 males	DSM-III ADHD CTRS	weight	BL, PL, and MPH (0.25, 0.5, and 1.0 mg/kg bid)	Ph, O	double-blind, placebo-controlled, crossover	weight: NS

(continued on next page)

Table 1 (*continued*)

Citation	*N*	Diagnosis criteria	Measurement instruments (DVs)	Drug conditions	Source	Design	Results
Height and weight studies							
Mattes and Gittleman (1983)	86 (NR)	NFDC CTRS Classroom observation	height percentile Weight percentile	BL and MPH (up to 80 mg/day)	Ph	longitudinal	height percentile: MPH < BL after 2–4 years (dose-related). weight percentile: MPH < BL after 1–4 years (dose-related)
Greenhill et al. (1984)	8 males	DSM-III ADHD Item #94 of CPRS CTRS ACRS	height, weight, prolactin, and human growth hormone sleep patterns	BL, MPH (10–60 mg/day; mean = 39 mg/day)	Ph	longitudinal	height velocity and percentile: BL vs. MPH: NS weight velocity and percentile: MPH < BL sleep stage shifts: MPH > BL mean REM activity: MPH > BL mean REM fragmentation: MPH > BL number of REM periods: MPH > BL prolactin concentration: NS human growth hormone concentration: NS
Klein et al. (1988)	53 males (1 year), 5 females (1 year), and 36 (NR; 2 years)	DSM-II criteria (hyperkinetic)	height weight	MPH (doses NR)	Ph	longitudinal	height: 1 year: MPH continued through summer vs. d/c for summer: NS 2 years: MPH d/c for summers > MPH continued through summer weight:

							1 year: MPH d/c for summer > MPH continued through summer 2 years: NS
Klein and Manuzza (1988)	61 males and 99 (NR)	DSM-II criteria (hyperkinetic)	height	MPH (mean = 45 mg/day)	Ph SR	longitudinal	height: MPH vs. controls: NS
Zeiner (1995)	23 males ADHD medicated and 23 males ADHD unmedicated	DSM-III-R ADHD ADHD Rating Scale CBCL Semistructured interview	height weight	MPH (mean = 23 mg/day)	Ph	longitudinal	height: NS weight: NS
Spencer et al. (1996)	124 males ADHD (110 pharmacologically treated and 12 pharmacologically untreated) and 109 control males	DSM-III-R ADHD K-SADS	height and weight (child and parent)	45% of ADHD treated with stimulant, equivalent to 38 mg/day (mean) of MPH	Ph	naturalistic, longitudinal	height: children: ADHD vs. control: NS adolescents: ADHD < control young adults: ADHD vs. control: NS early pubertal children: ADHD < control late pubertal children: ADHD vs. control: NS pharmacologically treated ADHD vs. pharmacologically untreated ADHD: NS

(continued on next page)

Table 1 (*continued*)

Citation	*N*	Diagnosis criteria	Measurement instruments (DVs)	Drug conditions	Source	Design	Results
Height and weight studies							
							ADHD treated with stimulants in last 2 years vs. not: NS weight: ADHD vs. controls: NS pharmacologically treated ADHD < pharmacologically untreated ADHD ADHD treated with stimulants in last 2 years vs. not: NS
Schachar et al. (1997)	50 males and 16 females (37 ADHD MPH and 29 ADHD unmedicated)	DSM-III-R PICS teacher telephone interview RCMAS SPPC WRAT-R	height weight	BL, PL, and MPH (0.7 mg/kg bid)	P T	randomized, double-blind, placebo controlled	height: PL vs. MPH: NS at 4 months weight: PL>MPH at 4 months
Cardiovascular studies							
Aman and Werry (1975)	10 males	NFDC hyperkinetic or aggressive	HR respiration rate	PL and MPH (0.5 mg/kg/day)	Ph	randomized, double-blind, placebo controlled, crossover	HR: MPH>PL respiration: NS

Greenberg and Yellin (1975)	40 males and 7 females	NFDC hyperactive	HR BP	PL, MPH (40 mg/day) IMI (100 mg/day)	Ph	randomized, double-blind, placebo controlled, crossover	HR: NS SBP: NS vs. PL; IMI>MPH DBP: NS vs. PL; IMI>MPH
Ballard et al. (1976)	24 males and 3 females	NFDC, hyperactive, ACTRS	HR BP	PL and MPH (mean = 0.48 mg/kg/day)	Ph	randomized, double-blind, placebo controlled, crossover	HR: MPH>PL SBP: MPH>PL DBP: MPH>PL
Barkley and Jackson (1977)	12 males	NFDC hyperkinetic	HR	PL and MPH (10 mg/day)	Ph	randomized, double-blind, placebo controlled	HR: NS respiration: NS
Sprague and Sleator (1977)	18 males and 2 females	NFDC CTRS	HR	PL and MPH (0.3 and 1.0 mg/kg/day)	Ph	randomized, double-blind, placebo controlled, crossover	HR: MPH>PL
Conners and Taylor (1980)	57 males and 3 females	NFDC hyperkinesis	HR BP	PL and MPH (mean = 0.82 mg/kg/day) PEM (2.25 mg/kg/day)	Ph	randomized, double-blind, placebo-controlled	HR: NS SBP: NS DBP: MPH>PEM, PL
Solanto and Conners (1982)	8 males and 2 females	NFDC hyperactive CPRS CTRS	HR	PL and MPH (0.3, 0.6, and 1.0 mg/kg bid)	Ph	double-blind, placebo-controlled, crossover	HR: 0.6 mg, 1.0 mg>PL; 0.6 mg>0.3 mg

(continued on next page)

Table 1 (*continued*)

Citation	*N*	Diagnosis criteria	Measurement instruments (DVs)	Drug conditions	Source	Design	Results
Cardiovascular studies							
Winsberg et al. (1982)	25 males	DSM-III ADHD CTRS	BP	BL, PL, and MPH (0.25, 0.5, and 1.0 mg/kg bid)	Ph	double-blind, placebo-controlled, crossover	DBP: NS SBP: 1.0 mg>BL, PL, 0.25 mg
Garfinkel et al. (1983)	12 males	DSM-III ADD	HR BP	PL and MPH (mean = 18 mg/day) DMI (mean = 85 mg/day) CMI (mean = 85 mg/day)	P O Ph	randomized, double-blind, placebo controlled, crossover	morning HR: MPH, CMI, DMI>PL DBP: MPH, CMI, DMI>PL
Brown et al. (1984)	11 males	NFDC parent and school report	HR BP	PL and MPH (0.3 mg/kg bid)	Ph	randomized, double-blind, placebo controlled, crossover	HR: NS BP: NS
Kelly et al. (1988)	44 males and 3 females	DSM-III ADHD HSQ WWP ACTRS	HR	BL, PL, and MPH (5, 10, 15, and 20 mg/day)	Ph	randomized, double-blind, placebo controlled, crossover	HR: 120 min: 15 and 20 mg MPH >PL; 180 min: 10, 15, and 20 mg MPH >PL; 15 and 20 mg MPH>5 mg MPH; with BL and initial values as covariates: HR: 10, 15, and 20 mg MPH>PL

							Decrease in HR 120 min: PL; 180 min: PL, 5 mg With BL as covariate: decrease in HR 120 and 180 min: PL; increase in HR 120 min and 180 mm: 20 mg MPH
Brown and Sexson (1989)	11 males	DSM-III ADHD ACTRS	HR BP	PL and MPH (0.15, 0.3, and 0.5 mg/kg bid)	Ph	randomized, double-blind, placebo-controlled, crossover	HR: NS SBP: MPH>PL; no between-dose differences DBP: 0.15, 0.3, and 0.5 mg>PL; 0.5 mg>0.15 and 0.3 mg
Satterfield et al. (1989)	70 males (1 year), 44 males (2 years), 15 males (3 years), and 7 males (4 years)	NFDC hyperactive hyperexitability, impulsivity, and inattention reported by P/T	BP HR	BL and MPH (first year mean = 0.47 mg/kg/day; second year mean = 0.52 mg/kg/day)	Ph	longitudinal	HR: 1 year MPH>BL 3 years BL>MPH SBP: 2 and 3 years MPH>BL DBP: 2 and 3 years MPH>BL
Tannock et al. (1989)	10 males 2 females	DSM-III ADHD criteria PICS ACTRS Rutter-B questionnaire SNAP	HR BP	PL and MPH (0.3 and 1.0 mg/kg bid)	Ph O	randomized, double-blind, placebo-controlled, crossover	HR: 1.0 mg>PL, 0.3 mg SBP: 1.0 mg>PL, 0.3 mg DBP: 1.0 mg>PL, 0.3 mg

(continued on next page)

Table 1 (*continued*)

Citation	*N*	Diagnosis criteria	Measurement instruments (DVs)	Drug conditions	Source	Design	Results
Cardiovascular studies							
Zeiner (1995)	23 males ADHD medicated and 23 males ADHD unmedicated	DSM-III-R ADHD ADHD Rating Scale CBCL Semistructured interview	HR BP	MPH (mean = 23 mg/day)	Ph	longitudinal	HR: NS BP: NS
Side effect questionnaire studies							
Garfinkel et al. (1983)	12 males	DSM-III ADD criteria	WWP	PL and MPH (mean = 18 mg/day) DMI (mean = 85 mg/day) CMI (mean = 85 mg/day)	P O Ph	randomized, double-blind, placebo controlled, crossover	WWP: sleep disturbance: MPH>CMI, DMI, and PL
Whalen, Henker, Buhrmester, et al. (1989) and Whalen, Henker, and Granger (1989)	Study 1: 22 males and 2 females Study 2: 24 males and 12 males	NFDC hyperactivity, ADD or ADHD ACRS	UC-CCBS	Study 1: PL, MPH (0.3 mg/kg bid) Study 2: PL, MPH (0.6 mg/kg bid)	O	randomized, double-blind, placebo controlled, crossover	Study 1: dysphoria: MPH>placebo Study 2: dysphoria: hyper/ADHD: MPH >placebo
Barkley et al. (1990)	71 males and 12 females	NFDC PPVT CBCL	SEQ	PL and MPH (0.3 and 0.5 mg/kg bid)	P T	randomized, double-blind, placebo controlled, crossover	parent ratings: mean severity insomnia and headache: MPH 0.3 and 0.5>PL. decreased appetite and

							stomachache: MPH 0.3, 0.5>PL; MPH 0.5>MPH 0.3 percent of severe occurrence: decreased appetite and insomnia: MPH 0.5>PL Teacher ratings: mean severity staring: PL>MPH 0.3, 0.5 sadness: PL, MPH 0.3>MPH 0.5 anxiety: PL>MPH 0.5 paresthesias: pindolol>PL or MPH MPH vs. PL: NS
Buitelaar et al. (1996)	46 males and 6 females	DSM-III-R ADHD CBCL CTRS deficits on RT task or CPT	SEQ	PL and MPH (10 mg bid) pindolol (20 mg bid)	P	randomized, double-blind, placebo controlled, incomplete crossover	
Ahman et al. (1993)	117 males and 30 females	DSM-III-R ACTRS CTRS	SEQ	PL and MPH (0.3 and 0.5 mg/kg tid)	P	randomized, double-blind, placebo controlled, crossover	insomnia, appetite disturbance, stomachache, headache, and dizziness: MPH>PL staring and daydreaming, irritability, anxiety, and nail-biting: PL>MPH odds ratios: shown in parenthesis insomnia: 0.5 mg MPH>Pl (3.13); 0.3 mg, MPH>PL (5.40)

(continued on next page)

Table 1 (*continued*)

Citation	*N*	Diagnosis criteria	Measurement instruments (DVs)	Drug conditions	Source	Design	Results
Side effect questionaire studies							appetite disturbance: 0.5 mg MPH>PL (19.00); 0.3 mg MPH (7.10) stomachache: 0.5 mg MPH>PL (7.00); 0.3 mg MPH (4.10) headache: 0.5 mg MPH>PL (5.29) dizziness: 0.5 mg MPH>PL (7.50); 0.3 mg MPH>PL (4.20) irritability: PL>0.5 mg MPH (0.33) anxiety: PL>0.5 mg MPH (0.42) nail-biting: PL>0.5 mg MPH (0.19); 0.3 mg MPH>0.5 mg MPH
Fine and Johnston (1993)	24 (NR)	NFDC P/T ratings: 8/14 DSM-III-R ADHD symptoms	SEQ	PL and MPH (0.3 and 0.6 mg/kg bid)	P	randomized, double-blind, placebo-controlled	trouble sleeping, decreased appetite, nail-biting: MPH>PL
Fischer and Newby (1991)	141 males and 20 females	NFDC CPRS CBCL	SEQ	PL and MPH (0.2 and 0.4 mg/kg bid)	P T	randomized, double-blind, placebo controlled,	parent: number of SEs: NS mean severity rating: NS

		CTRS CBCL TRF				crossover	Teacher: number of SEs: NS mean severity rating: PL>MPH
DuPaul et al. (1996)	19 males and 5 females	DSM-III-R ADHD CBCL	SEQ	PL and MPH: (mean = 0.16, 0.29, and 0.42 mg/kg)	P T SR	randomized, double-blind, placebo controlled, crossover	mean teacher SE severity rating: PL >MPH; MPH 5–15 mg>MPH 5–20 mg nail-biting: MPH 5–10 mg>MPH 10–15 mg tics: PL>MPH 10–20 mg insomnia, appetite, drowsiness, and euphoria: SR>T ratings drowsiness, euphoria, and dizziness: SR >P ratings stares/daydreams: T>P insomnia: P>T nightmares: SR: PL>MPH
Musten et al. (1997)	26 males and 5 females	DSM-III-R criteria DICA-P SNAP PPVT CPRS-R parent-supervised attention task	SEQ	PL and MPH (0.3 and 0.5 mg/kg bid)	P	randomized, double-blind, placebo controlled crossover	total number of symptoms: 0.5 mg>0.3 mg, PL symptom severity: 0.5 mg>0.3 mg, PL

(continued on next page)

Table 1 (*continued*)

Citation	*N*	Diagnosis criteria	Measurement instruments (DVs)	Drug conditions	Source	Design	Results
Side effect questionaire studies							
Schachar et al. (1997)	50 males and 16 females (37 ADHD MPH and 29 ADHD unmedicated)	DSM-III-R PICS teacher telephone interview RCMAS SPPC WRAT-R	SEQ (modified)	BL, PL, and MPH (0.7 mg/kg bid)	P T	randomized, double-blind, placebo controlled	SEQ: parent: SEs: MPH>BL physiologic: MPH at 3–4 weeks, MPH at 4 months>BL affective: MPH at 4 months>BL, MPH at 3–4 weeks tics: MPH at 4 months vs. MPH at 3–4 weeks vs. BL: NS teacher: MPH at 4 months vs. MPH at 3–4 weeks vs. BL: NS
Smith et al. (1998)	41 males and 5 females	DSM-III-R	Side effects rating form (Name NR)	PL and MPH (25, 50, and 75 mg qd)	P O	randomized, double-blind, placebo-controlled	tired: 75 mg>PL, 25 mg withdrawn: 50 and 75 mg>PL picking at skin: 75 mg>PL decreased appetite: 50 and 75 mg>PL, 25 mg

Manos et al. (1999)	66 males 18 females	DSM-IV criteria CDISC ACRS ARS	SE/BMS	PL and MPH (5, 10, and 15 mg bid) ADD (5, 10, and 15 mg qd)	P	randomized, double-blind, placebo-controlled	number of SEs: NS

ACRS = Abbreviated Conners Rating Scale; ACTRS = Abbreviated Conners Teacher Rating Scale; ARS = ADHD Rating Scale; bid = twice daily; BL = baseline; CBCL = Child Behavior Checklist; CBCL TRF = Child Behavior Checklist Teacher Report Form; CMI = clomipramine; CPRS = Conners Parent Rating Scale; CPT = Continuous Performance Test; CTRS = Conners' Teachers' Rating Scale; DBP = diastolic BP; d/c = discontinued; DEX = dextroamphetamine; DICA-P = Diagnostic Interview for Children and Adolescents—Parent Version; DMI = desipramine; HR = heart rate; HSQ = Home Situations Questionnaire; K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children—Epidemiologic version; LD = learning disabled; MBD = minimal brain damage; MPH = methylphenidate; NFDC = no formal diagnostic criteria; NR = not reported; NS = not significant; O = other; P = parent report; PEM = pemoline; Ph = physical or physiological measurement; PICS = Parent Interview for Child Symptoms; PL = placebo; PPVT = Peabody Picture Vocabulary Test; RCMAS = Revised Children's Manifest Anxiety Scale; RT = reaction time; SEs = side effects; SBP = systolic BP; SE/BMS = Side Effects Behavior Monitoring Scale; SEQ = Side Effects Questionnaire; SNAP = Swanson, Nolan, and Pelham Checklist; SR = self-report; SPPC = Self-Perception Profile for Children; Ss = subjects; T = teacher report; UC-CCBS = University of California—Conners Child Behavior Scale; WRAT-R = Wide Range Achievement Test—Revised; WWP = Werry–Weiss–Peters Activity Rating Scale.

performance (Barkley, 1977b; Cunningham, Siegel, & Offord, 1985; Douglas, Barr, O'Neill, & Britton, 1985; DuPaul & Rapport, 1993; Rapport, Denney, DuPaul, & Gardner, 1994), parent/teacher ratings of social deportment (DuPaul & Rapport, 1993; Fischer & Newby, 1991; MTA Cooperative Group, 1999; Musten, Firestone, Pisterman, Bennett, & Mercer, 1997), and objective performance indices associated with a wide range of clinic-based neurocognitive tests, tasks, and paradigms (for reviews, see Denney & Rapport, 2001; Losier, McGrath, & Klein, 1996; Rapport & Kelly, 1991). Peer relationships and interpersonal behavior (Barkley, Karlsson, Pollard, & Murphy, 1985; Cunningham, Seigel, & Offord, 1991; Cunningham et al., 1985; Humphries, Kinsbourne, & Swanson, 1978; Smith et al., 1998; Whalen, Henker, Buhrmester, et al., 1989), and even performance during extracurricular activities such as playing baseball (Pelham et al., 1990) may improve as a function of treatment.

Psychostimulant treatment response rates are equally impressive, with positive effects ascertained in an estimated 50–96% of children with ADHD, depending on the stringency with which positive response is defined and the nature of the targeted outcome variable. For example, positive treatment response is estimated to occur in 70% of children undergoing psychostimulant therapy (Barkley, 1977a), whereas an overall 96% improvement rate in behavior problems is demonstrated when response is defined as improvement on any one of several alternative psychostimulants (Elia, Borcherding, Rapoport, & Keyser, 1991). Conversely, others have shown response rates to vary between 53% and 94% for academic efficiency and teacher-rated classroom behavior, respectively, when positive response is evaluated using psychometric indices such as statistically derived normative comparison scores (Rapport et al., 1994).

As with all medications and most other interventions, side effects can and do occur. These effects warrant consideration because of their relevance to children's health and potential impact on treatment continuity. For example, significant cardiovascular effects (Kelly, Rapport, & DuPaul, 1988; Solanto & Conners, 1982; Tannock, Schachar, Carr, & Logan, 1989) and reductions in growth velocity (Mattes & Gittleman, 1983) are associated with psychostimulant treatment in children with ADHD. These and more commonly reported emergent symptoms (e.g., insomnia, reduced appetite, stomachaches) may contribute to poor treatment compliance and are complicated by methodological issues that merit discussion. To this end, extant literature investigating both short- and long-term emergent symptoms associated with methylphenidate (MPH) treatment was reviewed using front- (e.g., PsycLit, MedScape) and back-search methodology. Articles published since 1970 and reporting inferential statistics were selected for review. Earlier studies included children described as hyperactive, whereas those published after 1980 included children meeting DSM criteria for ADHD (American Psychiatric Association, 1980, 1987, 1994).

A total of 34 studies was located (see Table 1). As shown in the table, three classes of dependent variables are emphasized in the studies and the focus of this review. These include effects on height and weight, cardiovascular effects (heart rate [HR] and blood pressure [BP]), and somatic complaints—the latter of which are assessed using questionnaire data derived from parent, teacher, and occasionally self-ratings. Studies are listed

under the three classes of dependent variables with additional study details noted under adjoining column headings. These include sample size, basic diagnostic criteria, primary instruments used to assess outcome, drug conditions, measurement source (e.g., physiological, self-report, parent report), experimental design employed, and a summary of obtained results.

2. Weight and height effects

Eight of 11 studies investigating MPH effects on children's weight reported significant differences in expected levels of weight gain (Safer, Allen, & Barr, 1972; Satterfield, Cantwell, Schell, & Blashke, 1979), less comparable weight gain between treated and untreated children (Klein, Landa, Mattes, & Klein, 1988), between placebo and active medication conditions (Conners & Taylor, 1980; Greenberg & Yellin, 1975; Schachar, Tannock, Cunningham, & Corkum, 1997), or between baseline and active medication (Greenhill et al., 1984; Mattes & Gittleman, 1983). The remaining studies reported no significant MPH effect on children's weight compared to baseline (Winsberg, Kupietz, Sverd, Hungund, & Young, 1982) or to untreated control children (Spencer et al., 1996; Zeiner, 1995). One of the eight studies reporting reduced weight gain initially found no significant difference in weight at 2-year follow-up (Klein et al., 1988).

MPH effects on height were examined in 10 studies (see Table 1). Four reported significant findings. These included reductions in expected levels of height gain (Satterfield et al., 1979), less comparable height gain relative to control children (Safer et al., 1972), lower height percentile under active medication contrasted to baseline (Mattes & Gittleman, 1983), and greater expected gains in height percentiles at 2-year follow-up in children discontinued from medication during summer months (Klein et al., 1988). The initial reductions in children's height reported in two of the four investigations were no longer significant at long-term follow-up assessment (Klein & Manuzza, 1988; Satterfield et al., 1979).

3. Cardiovascular effects

Extant studies of psychostimulant effects on children's cardiovascular function traditionally examine indices of HR and BP. Seven of 14 studies examining MPH on HR reported significant effects (see Table 1). These include significant differences between placebo and active drug (Aman & Werry, 1975; Ballard, Boileau, Sleator, Massey, & Sprague, 1976; Garfinkel, Wender, Sloman, & O'Neil, 1983; Kelly et al., 1988; Solanto & Conners, 1982; Sprague & Sleator, 1977; Tannock et al., 1989) and high- vs. low-dose contrast effects (Kelly et al., 1988; Solanto & Conners, 1982; Tannock et al., 1989). The remaining seven studies failed to find HR changes under active drug compared to placebo (Barkley & Jackson, 1977; Brown & Sexson, 1989; Brown, Wynne, & Slimmer, 1984; Conners & Taylor, 1980; Greenberg & Yellin, 1975) or nonmedicated ADHD control children (Zeiner, 1995) or found that initial changes dissipated with time (Satterfield, Schell, & Barb, 1989).

Five of 10 studies examining MPH effects on children's BP reported significantly elevated systolic BP compared to placebo (Ballard et al., 1976; Brown & Sexson, 1989; Tannock et al., 1989; Winsberg et al., 1982) or baseline conditions (Satterfield et al., 1989), whereas six reported significantly elevated diastolic BP compared to placebo (Ballard et al., 1976; Brown & Sexson, 1989; Conners & Taylor, 1980; Garfinkel et al., 1983; Tannock et al., 1989) or baseline conditions (Satterfield et al., 1989). Four studies failed to find significant elevations in BP between drug and placebo (Brown et al., 1984; Greenberg & Yellin, 1975; Winsberg et al., 1982) or between treated and untreated children with ADHD (Zeiner, 1995).

4. Somatic complaints (side effects questionnaires/ratings)

Eight of 12 studies examining somatic complaints derived from questionnaire data reported significantly more complaints under MPH than placebo conditions. Common complaints associated with MPH therapy included appetite reduction (Ahman et al., 1993; Barkley, McMurray, Edelbrock, & Robbins, 1990; Fine & Johnston, 1993), sleep disturbance (Ahman et al., 1993; Barkley et al., 1990; Fine & Johnston, 1993; Garfinkel et al., 1983), headaches (Ahman et al., 1993; Barkley et al., 1990), dizziness (Ahman et al., 1993), and stomachache (Ahman et al., 1993; Barkley et al., 1990). Two studies failed to find significant differences in somatic complaints between MPH and placebo conditions (Buitelaar, van der Gaag, Swaab-Barneveld, & Kuiper, 1996; Manos, Short, & Findling, 1999), whereas four reported paradoxical findings—that is, a significantly greater number of somatic complaints under placebo compared to MPH conditions.

Three of the four studies reporting paradoxical findings were based on teacher reports of more severe somatic complaints under placebo than MPH (Barkley et al., 1990; DuPaul, Anastopoulos, Kwasnick, Barkley, & McMurray, 1996; Fischer & Newby, 1991). The fourth study relied on parent ratings and reported significantly fewer somatic complaints such as staring, daydreaming, irritability, anxiety, and nail biting under MPH than placebo (Ahman et al., 1993).

5. Discussion

Our review of potential side effects associated with MPH therapy in children with ADHD focused on the three most frequently reported classes of outcome variables reported in the literature: weight and height, cardiovascular effects, and somatic complaints.

5.1. Weight and height

Studies investigating weight change suggest that MPH is associated with reduced levels of weight gain in some children at least initially and that this association may be dose-dependent. These effects appear to be transient and readily resolved by discontinuation of

stimulant therapy during summer months, dosage adjustment, and parent education concerning timing of medication (e.g., administration after meals; see Swanson, Sandman, Deutsch, & Baren, 1983). With respect to height, extant findings indicate initial reductions in expected height percentiles in some children treated with psychostimulants. These effects appear to be dose related (Mattes & Gittleman, 1983), mitigated in some children by discontinuing drug administration during summer months (Klein et al., 1988), and fail to remain significant in longer-term follow-up studies exceeding 4 years (Klein & Manuzza, 1988).

5.2. Cardiovascular effects

A review of studies investigating cardiovascular effects indicates that elevated HR occurs in some children undergoing MPH therapy. Increases are generally reported to range from 3 to 10 bpm, which are considered minor from a clinical perspective (Safer, 1992), and appear to be linearly related to dose.

Systolic and diastolic BP is also elevated in some children as a function of MPH therapy. Reported changes for systolic BP ranged from 3.3 to 8 mmHg, while those for diastolic pressure ranged from 1.5 to 14 mmHg.

5.3. Somatic complaints

Explanations offered to account for the paradoxical findings associated with a decreased frequency of somatic complaints as a function of increasing MPH dose include the possibility that (a) adult raters (parents, teachers) confuse some symptoms of the disorder such as daydreaming and staring with drug-related side effects (Fine & Johnston, 1993) and (b) children with ADHD exhibit high rates of somatic complaints without treatment owing to the disabling nature of the disorder. In the latter case, reductions in somatic complaints may coincide with drug-related improved functioning at home and school, but would require both baseline-placebo and baseline-active drug statistical contrasts to differentiate everyday complaints from those due to expectancy or drug effects. Despite the abundance of published MPH side effects studies, only one included both baseline-placebo and baseline-active drug statistical contrasts (Schachar et al., 1997). This study, however, cannot address whether decreased side effects under MPH are associated with higher baseline rates of somatic complaints because of its design (between group), use of a single, predetermined target dose, and titration procedure (designed to "minimize side effects," p. 756).

5.4. Methodological considerations

Assessment of physical changes (weight, height) in children is relatively straightforward aside from potential measurement error associated with instrument scales or human recording of obtained values. Assessment of physiological functioning (BP and HR), in contrast, is subject to an additional potential confound based on predictions derived from the

law of initial value (LIV; Wilder, 1967). The LIV posits that the magnitude of autonomic response to a stimulus is related to the prestimulus level of response (i.e., the initial value). For function raising agents such as psychostimulants, a higher initial level of responding (e.g., a relatively high resting HR or BP recording prior to medication ingestion) should be followed by a proportionally lower poststimulus response level. Conversely, a lower prestimulus response level should result in a correspondingly higher poststimulus level of responding. At more extreme initial values, the effect should be negligible or even to reverse the direction of response.

The hour-to-hour periodicity in children's HR and BP under no-medication conditions and the potential contribution of prestimulus response levels (i.e., the initial value of the response) have been virtually ignored in previous investigations. Past reports of significant increases in ADHD children's cardiovascular functioning with increasing dosage may thus be an artifact owing to expected fluctuations in HR and BP across days and even hours, as well as possible dependence on the initial value.

It is equally plausible that physiological effects reported in the literature may underestimate children's response to psychostimulants (particularly at high doses) if HR or BP normally decreases over time. For example, if decreases in resting HR normally occur in children over a 3-h interval, then increases associated with MPH may raise HR levels to initial baseline recording levels and be misinterpreted as showing minimum or no change in HR for recordings taken later than the initial time interval (e.g., HR assessed initially at 12 noon and again at 3 p.m.). To address these issues, examination of LIV phenomenon as they apply to children's cardiovascular functioning is warranted and should incorporate multiple, standardized time intervals for recording physiological function under no medication and active (multiple dose) medication conditions.

Two methodological considerations applicable to studying somatic complaints in children warrant discussion. As noted earlier, additional research involving careful replication and inclusion of necessary contrast conditions is needed to clarify whether the frequency of somatic complaints reported by children and by adults monitoring children exceed baseline levels in both acute and extended trials with psychostimulants across a broad range of doses. The importance of this issue is exemplified by studies of somatic complaints in the general child population and the interplay between somatic complaints and child psychopathology. Past studies, for example, reveal that somatic complaints such as headaches, stomachaches, musculoskeletal pain, back pain, dizziness, and fatigue are common in children (Campo & Fritsch, 1994; Garber, Walker, & Zeman, 1991), with 10–30% of children reporting weekly or frequent headaches (Egger, Angold, & Costello, l998), 10–25% reporting recurrent abdominal pain (Alfven, 1993; Garber et al., 1991), and 5–20% complaining of musculoskeletal pain (Abu-Arafeh & Russell, 1996; Kristjansdottir, 1997). Psychiatric disability appears to accentuate the incidence of somatic complaints in children with internalizing (depression, anxiety disorders) and externalizing disorders (oppositional defiant disorder, conduct disorder, ADHD), and stomachaches in particular in children with ADHD (odds ratio = 3.5) compared to those without the disorder (Egger, Costello, Erkanli, & Angold, 1999). These findings suggest that the "paradoxical" reports of fewer side effects associated with MPH contrasted with placebo reported

previously may be a function of normally occurring base rates and associated emotional–behavioral problems. For example, children with ADHD are known to experience significant problems and associated distress at home and in school owing to inherent difficulties associated with the disorder, and may internalize these difficulties as physical complaints. In such cases, improved behavior and school performance associated with MPH therapy may correspond with reductions in somatic complaints consistent with previous reports of reductions in side effects ratings as a function of MPH therapy (Ahman et al., 1993; Barkley et al., 1990; DuPaul et al., 1996; Fischer & Newby, 1991). Further research can elucidate this issue by establishing whether the breadth and severity of general physical complaints reported by children with ADHD vary as a function of school and/or home difficulties over time.

A different issue concerns the questions asked on side effect rating scales. Many of the scale items on commonly used side effect questionnaires inquire about internal states (e.g., stomach discomfort, headaches, mood, anxiety) that are not readily observed by others in the child's environment. In these cases, children, as opposed to external observers, must be relied upon to accurately report occurrence, severity, and possible changes over time. Additional study in needed, however, to assess the temporal stability of these ratings (e.g., by assessing within- and between-day complaints) and to cross-validate their occurrence with observational data whenever possible. Parent–child agreement on side effect occurrence must also be addressed to determine whether agreement varies across internal–external states. Calculations using conventional statistics (e.g., correlation coefficients) typically rely exclusively on total score agreement but may need to be complemented by item level analysis. For example, recent investigations reveal no significant differences between parent and child side effect total scores across placebo and MPH doses, but minimal agreement on individual scale items (Rapport, Randall, & Moffitt, 2002).

6. Summary and conclusions

Extant literature indicates that side effects associated with MPH may include transient weight loss, initial reductions in height velocity, elevated HR, increased BP, and somatic complaints (i.e., reduced appetite, sleep disturbance, headaches, dizziness, and stomachaches). The more easily quantifiable side effects (e.g., BP, HR, and weight) are mostly transient, dose-dependent, easily rectified with dosage adjustments, and considered minor from a clinical perspective considering the breadth and level of improvement in behavior and cognitive functioning observed in most children. Previously reported somatic complaints associated with psychostimulant therapy may reflect symptoms occurring prior to the initiation of treatment (at least to some degree) and require additional study. Careful monitoring of emergent symptoms in children undergoing MPH therapy remains the sine qua non of professional care and should be supplemented with prudent baseline assessment to disentangle normally occurring somatic complaints from changes associated with active treatment.

References

Abu-Arafeh, I., & Russell, G. (1996). Recurrent limb pain in school. *Archives of Disability in Children*, *74*, 336–339.

Ahman, P. A., Waltonen, S. J., Olson, K. A., Theye, F. W., Van Erem, A. J., & LaPlant, R. J. (1993). Placebo-controlled evaluation of Ritalin side effects. *Pediatrics*, *91*, 1101–1106.

Alfven, G. (1993). The covariation of common psychosomatic symptoms among children from socio-economically differing residential areas: an epidemiological study. *Acta Paediatrica Scandinavica*, *82*, 484–487.

Aman, M. G., & Werry, J. S. (1975). Methylphenidate in children: effects upon cardiorespiratory function on exertion. *International Journal of Mental Health*, *4*, 119–131.

American Psychiatric Association (1980). *Diagnostic and statistical manual of mental disorders* (3rd edn.). Washington, DC: Author.

American Psychiatric Association (1987). *Diagnostic and statistical manual of mental disorders* (3rd edn., revised). Washington, DC: Author.

American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders* (4th edn.). Washington, DC: Author.

Ballard, J. E., Boileau, R. A., Sleator, E. K., Massey, B. H., & Sprague, R. L. (1976). Cardiovascular responses of hyperactive children to methylphenidate. *JAMA, the Journal of the American Medical Association*, *236*, 2870–2874.

Barkley, R. A. (1977a). A review of stimulant drug research with hyperactive children. *Journal of Child Psychology and Psychiatry*, *18*, 137–165.

Barkley, R. A. (1977b). The effects of methylphenidate on various types of activity level and attention in hyperkinetic children. *Journal of Abnormal Child Psychology*, *5*, 351–369.

Barkley, R. A., & Jackson, T. L. (1977). Hyperkinesis, automatic nervous system activity and stimulant drug effects. *Journal of Child Psychology and Psychiatry*, *18*, 347–357.

Barkley, R. A., Karlsson, J., Pollard, S., & Murphy, J. V. (1985). Developmental changes in the mother–child interactions of hyperactive boys: effects of two dose levels of Ritalin. *Journal of Child Psychology and Psychiatry*, *26*, 705–715.

Barkley, R. A., McMurray, M. B., Edelbrock, C. S., & Robbins, K. (1990). Side effects of methylphenidate in children with attention deficit hyperactivity disorder: a systematic, placebo-controlled evaluation. *Pediatrics*, *86*, 184–192.

Brown, R. T., & Sexson, S. B. (1989). Effects of methylphenidate on cardiovascular responses in attention deficit hyperactivity disordered adolescents. *Journal of Adolescent Health Care*, *10*, 179–183.

Brown, R. T., Wynne, M. E., & Slimmer, L. W. (1984). Attention deficit disorder and the effect of methylphenidate on attention, behavioral and cardiovascular functioning. *Journal of Clinical Psychiatry*, *45*, 473–476.

Buitelaar, J. K., van der Gaag, R. J., Swaab-Barnveld, H., & Kuiper, M. (1996). Pindolol and methylphenidate in children with attention deficit hyperactivity disorder, clinical efficacy and side-effects. *Journal of Child Psychology and Psychiatry*, *37*, 587–595.

Campo, J. V., & Fritsch, S. L. (1994). Somatization in children and adolescent. *Journal of the American Academy of Child and Adolescent Psychiatry*, *33*, 1223–1235.

Conners, C. K., & Taylor, E. (1980). Pemoline, methylphenidate and placebo in children with minimal brain dysfunction. *Archives of General Psychiatry*, *37*, 922–932.

Cunningham, C. E., Siegel, L. S., & Offord, D. R. (1985). A developmental dose–response analysis of the effects of methylphenidate on the peer interactions of attention deficit disordered boys. *Journal of Child Psychology and Psychiatry*, *26*, 705–715.

Cunningham, C. E., Seigel, L. S., & Offord, D. R. (1991). A dose–response analysis of the effects of methylphenidate on the peer interactions and simulated classroom performance of ADD children with and without conduct problems. *Journal of Child Psychology and Psychiatry*, *32*, 439–452.

Denney, C. B., & Rapport, M. D. (2001). Cognitive pharmacology of stimulants in children with ADHD. In M. V.

Solanto, & A. F. T. Arnsten (Eds.), *Stimulant drugs and ADHD: basic and clinical neuroscience* (pp. 283–302). New York: Oxford University Press.

Douglas, V. I., Barr, R. G., O'Neill, M. E., & Britton, B. G. (1985). Short term effects of methylphenidate on the cognitive, learning and academic performance of children with attention deficit disorder in the classroom. *Journal of Child Psychiatry and Psychology*, *27*, 191–211.

DuPaul, G. J., Anastopoulos, A. D., Kwasnick, D., Barkley, R. A., & McMurray, M. B. (1996). Methylphenidate effects on children with attention deficit hyperactivity disorder: self-report of symptoms, side-effects and self-esteem. *Journal of Attention Disorders*, *1*, 3–15.

DuPaul, G. J., & Rapport, M. D. (1993). Does methylphenidate normalize the classroom performance of children with attention deficit disorder? *Journal of the American Academy of Child and Adolescent Psychiatry*, *32*, 190–198.

Egger, J. L., Angold, A., & Costello, E. J. (1998). Headaches and psychopathology in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, *37*, 951–958.

Egger, J. L., Costello, E. J., Erkanli, A., & Angold, A. (1999). Somatic complaints and psychopathology in children and adolescents: stomach aches, musculoskeletal pains, and headaches. *Journal of the American Academy of Child and Adolescent Psychiatry*, *38*, 852–860.

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

Fine, S., & Johnston, C. (1993). Drug and placebo side effects in methylphenidate–placebo trial for attention deficit hyperactivity disorder. *Child Psychiatry and Human Development*, *24*, 25–30.

Fischer, M., & Newby, R. F. (1991). Assessment of stimulant response in ADHD children using a refined multimethod clinical protocol. *Journal of Child Clinical Psychology*, *20*, 232–244.

Garber, J., Walker, L. S., & Zeman, J. (1991). Somatization symptoms in a community sample of children and adolescents: further validation of the children's somatization inventory. *Psychological Assessment*, *3*, 588–595.

Garfinkel, B. D., Wender, P. H., Sloman, L., & O'Neill, I. (1983). Tricyclic antidepressant and methylphenidate treatment of attention deficit disorder in children. *Journal of the American Academy of Child Psychiatry*, *22*, 343–348.

Greenberg, L. M., & Yellin, A. M. (1975). Blood pressure and pulse changes in hyperactive children treated with imipramine and methylphenidate. *American Journal of Psychiatry*, *132*, 1325–1326.

Greenhill, L. L., Puig-Antich, J., Novacenko, H., Solomon, M., Anghern, C., Florea, J., Goetz, R., Fiscina, B., & Sachar, E. (1984). *Journal of the American Academy of Child Psychiatry*, *23*, 58–67.

Humphries, T., Kinsbourne, M., & Swanson, J. (1978). Stimulant effects on cooperation and social interaction between hyperactive children and their mothers. *Journal of Child Psychology and Psychiatry*, *19*, 13–22.

Kelly, K. L., Rapport, M. D., & DuPaul, G. J. (1988). Attention deficit disorder and methylphenidate: a multi-step analysis of dose–response effects on children's cardiovascular functioning. *International Clinical Psychopharmacology*, *3*, 167–181.

Klein, R. G., Landa, B., Mattes, J. A., & Klein, D. F. (1988). Methylphenidate and growth in hyperactive children: a controlled withdrawal study. *Archives of General Psychiatry*, *45*, 1127–1130.

Klein, R. G., & Manuzza, S. (1988). Hyperactive boys almost grown up. *Archives of General Psychiatry*, *45*, 1131–1134.

Kristjansdottir, G. (1997). Prevalence of pain combinations and overall pain: a study of headache, stomach pain and back pain among schoolchildren. *Scandinavian Journal of Social Medicine*, *25*, 58–63.

Losier, B. J., McGrath, P. J., & Klein, R. M. (1996). Error patterns on the continuous performance test in non-medicated and medicated samples of children with and without ADHD: a meta-analytic review. *Journal of Child Psychology, Psychiatry and Allied Disciplines*, *37*, 971–987.

Manos, M. J., Short, E. J., & Findling, R. L. (1999). Differential effectiveness of methylphenidate and Adderall in school-age youths with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *38*, 813–819.

Mattes, J. A., & Gittleman, R. (1983). Growth of hyperactive children on maintenance regimen of methylphenidate. *Archives of General Psychiatry*, *40*, 317–321.

Millichap, J. G. (1978). Growth of hyperactive children treated with methylphenidate. *Journal of Learning Disabilities*, *11*, 40–43.

MTA Cooperative Group (1999). 14-month randomized clinical trial of treatment strategies for attention deficit hyperactivity disorder. *Archives of General Psychiatry*, *56*, 1073–1086.

Musten, L. M., Firestone, P., Pisterman, S., Bennett, S., & Mercer, J. (1997). Effects of methylphenidate on preschool children with ADHD: cognitive and behavioral functions. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 1407–1415.

Pelham, W. E., McBurnett, K., Harper, G. W., Milich, R., Murphy, D. A., Clinton, J., & Thiele, C. (1990). Methylphenidate and baseball playing in ADHD children: who's on first? *Journal of Consulting and Clinical Psychology*, *58*, 130–133.

Rapport, 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 and Adolescent Psychiatry*, *33*, 882–893.

Rapport, M. D., & Kelly, K. L. (1991). Psychostimulant effects on learning and cognitive function: findings and implications for children with attention deficit hyperactivity disorder. *Clinical Psychology Review*, *11*, 61–92.

Rapport, M. D., Randall, R., & Moffitt, C. (2002). Attention-deficit/hyperactivity disorder and methylphenidate: a dose-response analysis and parent-child comparison of somatic complaints. *Journal of Attention Didorders*, *6*, 15–24.

Safer, D. J. (1992). Relative cardiovascular safety of stimulants used to treat attention-deficit hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology*, *2*, 279–290.

Safer, D. J., Allen, R., & Barr, E. (1972). Depression of growth in hyperactive children on stimulant drugs. *New England Journal of Medicine*, *287*, 217–220.

Satterfield, J. H., Cantwell, D. P., Schell, A., & Blaschke, T. (1979). Growth of hyperactive children treated with methylphenidate. *Archives of General Psychiatry*, *36*, 212–217.

Satterfield, J. H., Schell, A. M., & Barb, S. D. (1989). Potential risk of prolonged administration of stimulant medication for hyperactive children. *Developmental and Behavioral Pediatrics*, *1*, 102–107.

Schachar, R. J., Tannock, R., Cunningham, C., & Corkum, P. V. (1997). Behavioral, situational and temporal effects of treatment of ADHD with methylphenidate. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 754–763.

Smith, B. H., Pelham, W. E., Evans, S., Gnagy, E., Molina, B., Bukstein, O., Greiner, A., Myak, C., Presnell, M., & Willoughby, M. (1998). Dosage effects of methylphenidate on the social behavior of adolescents diagnosed with attention-deficit hyperactivity behavior. *Experimental and Clinical Psychology*, *6*, 187–204.

Solanto, M. V., & Conners, C. K. (1982). A dose–response and time–action analysis of autonomic and behavioral effects of methylphenidate in attention deficit disorder with hyperactivity. *Psychophysiology*, *19*, 658–667.

Spencer, T. J., Biederman, J., Harding, M., O'Donnell, D., Faraone, S. V., & Wilens, T. E. (1996). Growth deficits in ADHD children revisited: evidence for disorder-associated growth delays? *Journal of the American Academy of Child and Adolescent Psychiatry*, *35*, 1460–1469.

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

Swanson, J. M., Sandman, C. A., Deutsch, C., & Baren, M. (1983). Methylphenidate hydrochloride given with or before breakfast: I. Behavioral, cognitive, and electrophysiological effects. *Pediatrics*, *72*, 49–55.

Tannock, R., Schachar, R. J., Carr, R. P., & Logan, G. D. (1989). Dose–response effects of methylphenidate on academic performance and overt behavior in hyperactive children. *Pediatrics*, *84*, 648–657.

Whalen, C. K., Henker, B., Buhrmester, D., Hinshaw, S. P., Huber, A., & Laski, K. (1989). Does stimulant medication improve the peer status of hyperactive children? *Journal of Consulting and Clinical Psychology*, *57*, 545–549.

Whalen, C. K., Henker, B., & Granger, D. A. (1989). Ratings of medication effects in hyperactive children: viable or vulnerable? *Behavioral Assessment*, *11*, 179–199.

Wilder, J. (1967). *Stimulus and response. The law of initial value*. Bristol: John Wright and Sons.

Winsberg, B. G., Kupietz, S. S., Sverd, J., Hungund, B. L., & Young, N. L. (1982). Methylphenidate oral dose plasma concentrations and behavioral response in children. *Psychopharmacology*, *76*, 329–332.

Zeiner, P. (1995). Body growth and cardiovascular function after extended treatment (1.75 years) with methylphenidate in boys with attention-deficit hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology*, *5*, 129–138.