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Vestibular Stimulation for ADHD: Randomized Controlled Trial of Comprehensive Motion Apparatus

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Objective:

This research evaluates effects of vestibular stimulation by Comprehensive Motion Apparatus (CMA) in ADHD.

Method:

Children ages 6 to 12 (48 boys, 5 girls) with ADHD were randomized to thrice-weekly 30-min treatments for 12 weeks with CMA, stimulating otoliths and semicircular canals, or a single-blind control of equal duration and intensity, each treatment followed by a 20-min typing tutorial.

Results:

In intent-to-treat analysis (n = 50), primary outcome improved significantly in both groups (p = .0001, d = 1.09 to 1.30), but treatment difference not significant (p = .7). Control children regressed by follow-up (difference p = .034, d = 0.65), but overall difference was not significant (p = .13, d = .47). No measure showed significant treatment differences at treatment end, but one did at follow-up. Children with IQ-achievement discrepancy ≥ 1 *SD* showed significantly more CMA advantage on three measures.

Conclusion:

This study illustrates the importance of a credible control condition of equal duration and intensity in trials of novel treatments. CMA treatment cannot be recommended for combined-type ADHD without learning disorder. *(J. of Att. Dis. 2008; 11(5) 599-611)*

This report evaluates a device for providing motion stimulation to both the semicircular canals and the otolith structures (utricles and saccules) of the inner-ear vestibules as a treatment for ADHD. ADHD is a syndrome of age-inappropriate inattention, distractibility, impulsivity, and restless overactivity (American Psychiatric Association, 2000; National Institutes of Health, 1998). Almost half (30% to 50%) of children with ADHD exhibit poor balance and coordination (Blondis, 1999; Piek, Pitcher, & Hay, 1999; Sergeant, Piek, & Oosterlaan, 2006), suggesting vestibular and cerebellar involvement.

Imaging studies report that (a) the cerebellum, right prefrontal cortex, and striatum are significantly smaller in children with ADHD (Castellanos et al., 2002; Faraone & Biederman, 1998), (b) methylphenidate significantly increased brain metabolism in the cerebellum and frontal and temporal lobes (Volkow et al., 2004), and (c) caloric stimulation of the inner-ear vestibular labyrinth activates the limbic system and neocortex (Vitte et al., 1996), providing a neuroanatomical link between vestibular stimulation and the limbic dopaminergic system. Dysfunction of the ventral tegmental–limbic dopaminergic system is suspected in ADHD

(Nieoullon, 2002; Viggiano, Grammatikopoulos, & Sadile, 2003). The basal ganglia and cerebellum are important for not only motor control but also cognitive and emotional function (Anderson, Lowen, & Renshaw, 2006; Heath, Franklin, & Shraberg, 1979; Jacobsen, Giedd, Berquin, & Krain, 1997; Schmahmann, 1997). Andreasen, Paradiso, and O'Leary (1998) and Anderson et al. (2006) hypothesized that cerebellar connections with limbic structures and prefrontal cortex are important in normal attention and cognition.

Dysregulation of norepinephrine is associated with labile attention and poor task performance. The locus ceruleus and ventrolateral medulla provide norepinephrine stimulation to the entire brain, including cerebral and cerebellar cortex. Phasic discharge of the locus ceruleus in response to a specific task against a background of low tonic activity results in improved performance (Aston-Jones & Cohen, 2005). Thus, dysregulation of the central noradrenergic system may play a role in the pathophysiology of ADHD (Lasky-Su et al., 2006; Seidman et al., 2006), probably involving deficits in catecholamine inhibitory frontostriatal connections. Otolith projections provide excitatory input to sympathetic system nuclei, including locus ceruleus and subretrofacial nucleus of the ventrolateral medulla (Jian, Acernese, Lorenzo, Card, & Yates, 2005; Yates, 1992; Yates & Bronstein, 2005; Yates, Goto, & Bolton, 1992; Yates, Goto, Kerman, & Bolton, 1993). In contrast, semicircular canal connections are primarily associated with brain regions related to acetylcholine. An eighth nerve lesion severing input from both semicircular canals and otolith organs significantly increases hippocampal norepinephrine levels, probably through vestibular–locus–ceruleus connections (Smith et al., 2005; Zheng, Darlington, & Smith, 2004). Otolith stimulation increased the activity in locus ceruleus neurons (Marshburn, Kaufman, Purcell, & Perachio, 1997), whereas caloric stimulation of semicircular canals inhibited locus ceruleus activity (Nishiike, 2003; Nishiike, Takeda, Kubo, & Nakamura, 2001). Previc (1993) and Previc and Ercoline (2001) suggested that otolith input is important in the sympathetic norepinephrine system, whereas semicircular canal input is important in the parasympathetic system.

Among sensory inputs to the cerebellum, vestibular is unique. Most senses relay through synapses in thalamus or brainstem, but some vestibular input enters the cerebellum directly without crossing a synapse (Kotchabhakdi & Walberg, 1978a). Vestibular input to the vermis, especially inferior, is abundant (Kotchabhakdi & Walberg, 1978b; Zajonc & Roland, 2005). The two vestibular end organ components, the semicircular canals and the otolith organs (saccules and utricles), sense angular and linear acceleration, respectively. Their central projections differ: Semicircular canals target more superior vestibular nuclear regions, otolith projections more inferior. Both also project directly to most cerebellar regions (Brodal, 1974; Carpenter, 1988; Zajonc & Roland, 2005).

Previous Studies of Motion Stimulation in ADHD

In an exploratory crossover study, 18 children 4 to 14 years of age with a hyperkinetic reaction diagnosed according to the second edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-II*) experienced rotary stimulation of the semicircular canals twice weekly for 4 weeks and an equal-time sham condition, with random assignment to order. In a specially adapted swivel chair, the head was held in various planes to stimulate each pair of semicircular canals in turn by rapid acceleration to 33 rpm. Conners's scales showed significant improvement compared to the sham (Bhatara, Clark, Arnold, Gonsett, & Smeltzer, 1981). However, the sham consisted merely of sitting in the same chair used for the rotary treatment and talking with the assistant.

In a later study, 30 *DSM-III*-diagnosed children with attention deficit disorder with hyperactivity had the same rotary motion in a single-blind crossover design with random assignment to order (Arnold, Clark, Sachs, Jakim, & Smithies, 1985). All received eyes-open combined

vestibular and visual stimulation and a control condition. Half the sample also received visual rotational stimulation inside an optokinetic drum (visual alone), and the other half received semicircular canal stimulation while wearing opaque goggles (vestibular alone). The control condition, called tactile–auditory–visual, occupied the children for the same length of time looking through a stereoscopic projector (visual), listening to sounds (auditory), and feeling air "poofed" onto their skin with a bellows (tactile). The active treatments resulted in a significant improvement in behavior from baseline to end of treatment in blinded-teacher-rated behavior. The vestibular-alone condition showed the greatest effect, Cohen's *d* about 0.5 compared to the control condition.

Comprehensive Motion Apparatus (CMA)

The CMA differs from technology used in previous studies, which restricted stimulation to the semicircular canals. The CMA also stimulates the otolith system, which detects gravity and other linear acceleration. It was originally developed and used clinically for rehabilitation of neurological patients and treatment of learning disorder. It was always used with "engineered" white noise to the right ear. Ferrara et al. (1999) found encouraging open results. Learning-disordered children received 30-min treatments 3 times per week for 12 weeks. Significant improvements occurred in spelling (34%), word attack (31%), and motor tests. These remained improved 6 weeks later. A major criticism of this study was that it did not have a control group. Also, children received 20 min of a computerized typing tutorial immediately after each treatment, on the rationale that an immediate learning experience could help reorganize neurological function during the period of post-CMA plasticity. Therefore, it is unclear whether the improvements reported are a result of CMA treatment, the engineered white noise, the tutorial, the combination, or nonspecific effects such as statistical regression, history or maturation, and Hawthorne (placebo) effect. Furthermore, learning disorder was targeted, and it is not clear whether the results could generalize to ADHD without learning disorder.

Thus, previous work suggested benefit from rotary stimulation of semicircular canals in ADHD and from CMA combined stimulation of canals and otolith system in learning disorder, but there was no test of the combined stimulation in diagnosed ADHD and no placebo-controlled study of the CMA. The study reported here was designed to test these hypotheses:

Primary hypothesis:

The CMA shows a clinically and statistically significant benefit for ADHD symptoms compared to a credible control condition that includes non-CMA components of the usual CMA treatment package.

Secondary hypothesis:

The improvement persists for 6 weeks following treatment end. Neuropsychological tests also show treatment differences.

Exploratory questions:

Do internalizing symptoms or global impairment show a treatment difference? Is there any difference by ADHD subtype, suspected presence of learning disorder comorbidity, or prior medication?

Method

Sample

Participants were boys and girls ages 6 to 12 with *DSM-IV* ADHD diagnosed by a child psychiatrist assisted by the computerized Diagnostic Interview Schedule for Children, Parent Version (Shaffer et al., 1996). They were recruited by ads, by referral from pediatricians and school staff, and by a mailing to the patients with an ADHD diagnosis attending the Children's Hospital behavioral health clinics. Inclusion criteria stated that, in addition to *DSM-IV* diagnosis by child psychiatrist and structured interview, each participant was required to have a mean rating on the parent's or teacher's SNAP-IV (ADHD checklist of *DSM-IV* symptoms) of 1.7 or more on the 0 to 3 scale (Swanson, 1992). The child had to be unmedicated (for ADHD) for 2 weeks prior to randomization and stay unmedicated during treatment. Exclusion criteria included currently in the hospital, in another study, IQ below 75, bipolar disorder, psychosis, or neuroleptic drug in the previous 6 months. All parents gave written permission and children gave assent using consent forms approved by the university institutional review board. Details of sample characteristics are in Table 1.

Design

In a randomized, parallel-group design, an experimental group and control group were each treated 30 min thrice weekly for 12 weeks, with 6-week follow-up assessment.

Experimental treatment.

The CMA is a reclining chair in which the child rotates with programmed gradual acceleration to 4 rpm accompanied by rocking and tilting. The main axis of rotation is at waist level, offset from the vertical by about 5°, with head reclined about 2 ft. from the axis. The CMA provides some semicircular canal stimulation (muted from that in the previous studies, only 4 rpm) but also otolith system stimulation. The amplitude and direction of linear acceleration change as the CMA rotates, rocks, and tilts. The centrifugal force on the head provides gravity-like acceleration in the opposite direction (waist to head) from the usual perception of gravity. The axial rocking provides anterior–posterior motion; the lateral rocking provides additional lateral and some rotary motion. Thus motion is provided in at least six vectors.

Characteristic	Total Sample		Treatment		Control	
N	53		26		27	
	M	*SD*	*M*	*SD*	*M*	*SD*
Age, years	8.4	1.5	8.5	1.6	9.2	1.4
	n	%	*n*	%	*n*	%
Male	46	86.8	23	88.5	23	85.2
Caucasian	47	88.7	23	88.5	24	88.9
	M	*SD*	*M*	*SD*	*M*	*SD*
Height (in.)	53.3	3.6	52.9	3.6	53.9	3.4
Weight (lb.)	66.7	20.3	75.9	24.1	75.2	16.1
	n	%	*n*	%	*n*	%
ADHD						
Inattentive type	13	22.6	4	15.4	9	33.3
Combined type	40	75.5	22	84.6	18	66.7
Oppositional-defiant disorder	9	17	4	15.4	5	18.5
Other comorbidity	3	5.7	2	7.7	1	3.7

Previous ADHD medication or treatment	23	43.4	10	38.5	13	48.1
	M	*SD*	*M*	*SD*	*M*	*SD*
Wechsler Abbreviated IO	103.7	12.5	101.4	11.3	105.8	13.5
Wechsler Individual Achievement Test Screener composite	94.1	11.7	92.8	9.4	95.4	13.6
Reading	97.7	11.3	96.2	10.0	99.1	12.5
Math	95.8	13.0	95.7	12.5	95.8	13.7
Spelling	93.7	12.4	92.7	9.8	94.6	14.7
	n	%	*n*	%	*n*	%
% with 1.5 *SD* discrepancy from IO	17	32.1	8	30.8	9	33.3
Reading	3	5.7	2	7.7	1	3.7
Math	8	15.1	3	11.5	5	18.5
Spelling	10	18.9	4	15.4	6	22.2

Table 1 Sample Characteristics

The sensation is similar to a small boat yawing, pitching, and rocking. As used clinically by the developer, Passive Motion Therapeutics, it was always accompanied by specially engineered white noise into the right ear via headphones.

In a quiet darkened room children reclined in the CMA and experienced programmed movement for 30 min. Rotation (4 rpm) continued for 1 min and then changed to the opposite direction while gently rocking about the 2 axes providing lateral and sagittal motion. The participant wore opaque ophthalmic eye shields and an acoustic head set that blocked ambient sound and provided the low volume, broad-spectrum white noise engineered by the CMA developer. This is consistent with Ferrara et al. (1999).

Immediately following each session, treatment or control, each participant received a 20-min academic tutorial consisting of computer-assisted instruction using the Mavis-Beacon typing program, as in the Ferrara study, in case this component was necessary to consolidate the CMA benefit.

Control condition.

The control condition was designed to control for Hawthorne/placebo effect by matching factors other than actual CMA motion stimulation: number and duration of sessions, experience of reclining in the chair, accompanying engineered white noise, and postsession computer typing tutorial. While reclining in the CMA, which rotated 180° once over 30 s, the control participants listened to the same white noise, broken in the middle by a 10-min entertaining video. The same kind of eye shields were worn, except when viewing the video.

The control condition was single-blindly masked by presenting this as a study of eighth nerve stimulation, which involves both hearing and sense of balance and motion. A brief explanation of eighth nerve sensation or perception with equal emphasis on cochlear or auditory and canal-otolith vestibular function was given to study participants, with a rationale of why promoting better perception in both channels could help learning and behavior. Parents and children were told at the beginning that we were comparing different doses and combinations of the CMA movement with auditory and visual input. Children and parents were asked not to tell the teacher exactly what happened in the session as an extra precaution to maintain the blindness

of teacher ratings.

Outcome measures.

Outcome measures included clinical and neuropsychological measures at baseline, end of treatment (posttest, PT) and at 6-week follow-up (FU) and some clinical ratings more frequently during treatment.

Clinical assessments.

The primary outcome measure was *DSM-IV* ADHD symptoms rated by parent and teacher weekly on a 0 to 3 scale (e.g., SNAP-IV; Swanson, 1992). These 18 symptoms were also embedded in the monthly Conners's Rating Scales (parent and teacher versions; Conners, 2001) collected monthly. They have demonstrated validity and sensitivity in previous treatment studies (e.g., MTA Cooperative Group, 1999): The Multidimensional Anxiety Scale for Children (March, 1997) measured possible changes in internalizing pathology, and the Columbia Impairment Scale (Bird et al., 1993) measured possible changes in global impairment, both collected monthly and at FU.

Neuropsychological testing.

Neuropsychological examination on entry (baseline), after 12 weeks of treatment (PT), and 6 weeks after treatment end (FU) focused on measures of executive function, attention, vigilance, and impulsivity. All tests have normative data by age. The Continuous Performance Test (CPT; Conners, 2000) was the primary measure of attention and vigilance. Variables included number of omissions and commissions, response speed, variability, and change in response speed. The Wisconsin Card Sorting Test (Chelune & Baer, 1986) measures reasoning, concept formation, perseveration, and impulsivity (number of breaks in response set). Because the study budget did not allow for complete psychoeducational evaluation and clinical diagnosis of learning disorder, a proxy variable was constructed from brief achievement and IQ testing at screening by Wechsler Individual Achievement Test (Wechsler, 2001) screener and Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999). The threshold for the binary proxy variable for suspected learning disorder was a 1 standard deviation gap between achievement standard score and IQ. This threshold was selected over the more usual 1.5 standard deviations to balance group sizes better for the analysis.

Data analysis.

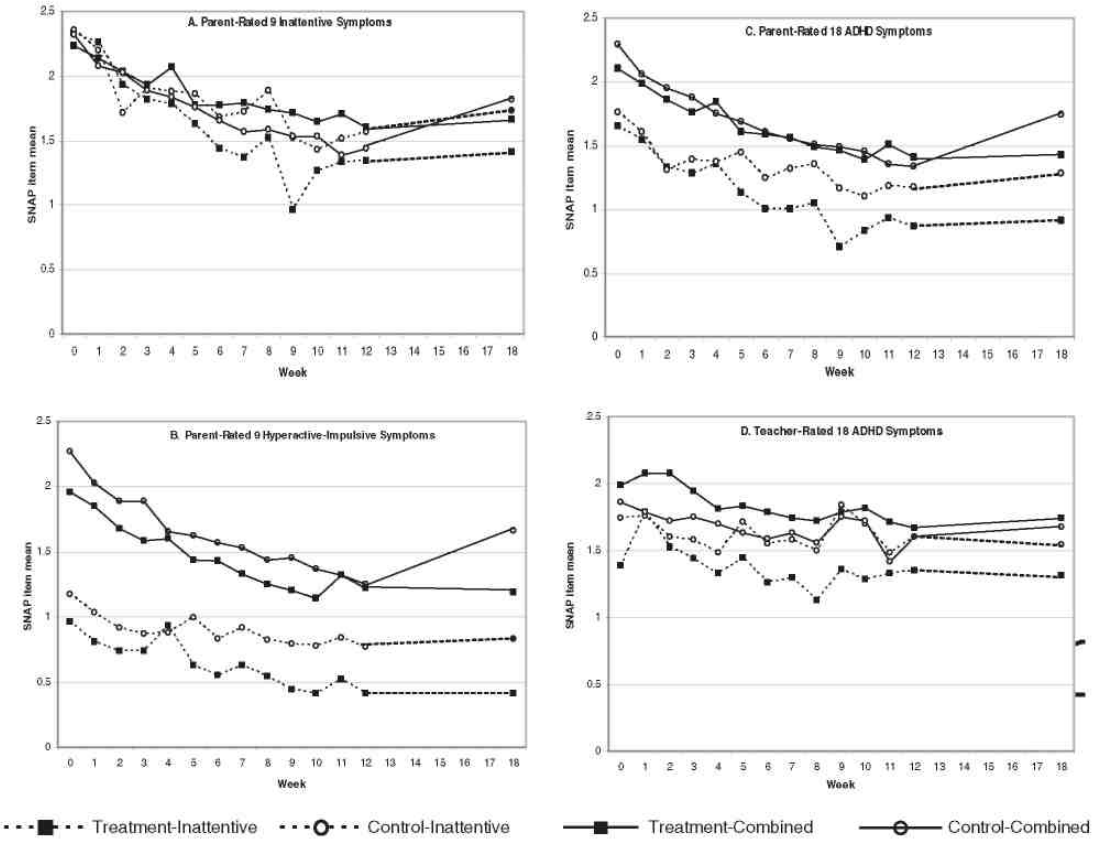
The main outcome measure, the average of all 18 ADHD symptoms rated by parent and teacher, was related to potential predictors via a linear mixed-effects model (Pinheiro & Bates, 2000) that included fixed-effects terms for two continuous predictors, time and time squared, and three dichotomous indicators—treatment (active vs. control), rater (parent vs. teacher), and diagnostic subtype (inattentive vs. combined)—and all possible two-way interactions except for time squared. The random effects included participant-specific intercepts and slopes for time and rater-specific intercepts within participant. We used the S-PLUS software (Insightful Corp) to fit the model. The use of both raters in the same analysis was recommended and used by Conners et al. (2001), Swanson et al. (2001), and MTA Cooperative Group (2004), based on Kraemer and Thiemann (1989). Alpha of .05 was used; the single primary outcome required no correction.

Secondary subgroup and follow-up analyses and analyses of secondary measures, including neuropsychological tests, were done by simpler repeated measures ANOVAs. Time (within participant) had two levels: baseline versus PT (last observation carried forward),

baseline versus FU, or PT versus FU. Assigned treatment was a between-subjects factor. Age, prior use of ADHD medication, IQ achievement discrepancy scores, and diagnostic subtype were included as covariates, and the interaction of covariate with treatment assignment was used to detect moderator effects, which, when significant, were further explored by subgroup analyses. Alpha of .05 was used for the secondary exploratory outcomes. For group comparisons on secondary measures, effect sizes (Cohen's *d*) were calculated by computing change scores for each child, then computing means and standard deviations for change scores of each treatment group, then dividing the difference in means by the pooled standard deviation of the means.

Results

Of 76 who were screened, 53 (26 active treatment and 27 control condition) were eligible and randomized. But 3 immediately dropped out, 2 active and 1 control, leaving 24 treatment and 26 control participants with usable data for intention-to-treat analyses (at least one weekly assessment after randomization). Sample characteristics are shown in Table 1 and did not differ significantly between randomly assigned groups. One participant in active treatment was terminated at 5 weeks because of protocol violation (starting behavioral treatment program at school). In all, 45 participants completed all 12 weeks of treatment, and of these, 43 (19 treatment and 24 control) returned for FU. Because FU occurred in the



Note: Treatment ended at Week 12 (posttest [PT]). For parent ratings, *N* = 24 active treatment and 26 control condition for PT, 19 active and 24 control for follow-up. For teacher ratings, *N* = 17 active and 21 control for PT, 8 active and 11 placebo for follow-up.

Fig. 1. ADHD Symptoms Rated 0 to 3 by Parents and Teachers, by Treatment and Subtype

summer for 20 participants, teacher FU ratings were incomplete. One control participant started atomoxetine during the follow-up interval. No other psychoactive drugs were reported during the study, although 43% stopped ADHD medication to be in the trial and all were free to start or restart medication after week 12 PT.

Test of Primary Hypothesis: Superiority of CMA at Posttest

The primary outcome measure, the average of all 18 ADHD symptoms rated by parent and teacher, showed significant improvement over time ($t = –7.826$, $p < .0001$ for time; $t = 7.273$, $p < .0001$ for time^2). This represented large improvement (Cohen's $d = 1.09$ to 1.30) by combination of parent and teacher rating, large improvement ($d = 1.37$ to 1.75) by parent rating, and medium improvement ($d = 0.40$ to 0.64) by teacher rating in both the treatment and control groups. However, the difference between groups in their linear improvement over time was not significant ($t = -0.386$, $p = .7$ for treatment x time interaction).

Secondary Hypothesis, Maintenance of Gains at Follow-Up

At FU, with 19 remaining in the treatment group and 24 in the control group (for parent ratings), the active-treatment group maintained its improvement, whereas the control group regressed on parent ratings ($df = 1$, $F = 4.173$, partial $\eta^2 = .094$, $p = .048$ for group difference). This resulted in a significant treatment difference ($df = 1$, $F = 4.824$, partial $\eta^2 = .108$, $p = .034$, $d = 0.65$) in the change PT to FU on the primary outcome (combined parent and teacher ratings), favoring the active treatment. However,

Table 2
Parent and Teacher Ratings of *DSM-IV* ADHD Symptoms at Baseline (Weeks 0 and 1), Posttest (Week 12), and Follow-Up (Week 18) by ADHD Subtype and Treatment Group

Measures	Assessment Point	*M* and *SD* by Treatment Group, ADHD Subtype								*M* and *SD* by Treatment Group				Effect Size (Cohen's *d*) of Difference in Change Score Between Conditions[a]		
	Week	Treatment–Inattentive		Control–Inattentive		Treatment–Combined		Control–Combined		Treatment		Control				
n		3		8		21		18		24		26		Baseline to Treatment End	Treatment End to Follow-Up	Baseline to Follow-Up
		M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*			
Parent rated, 9 inattentive symptoms	0	2.33	0.29	2.35	0.43	2.23	0.49	2.32	0.51	2.25	0.47	2.33	0.48	–0.21	0.47	0.35
	1	2.26	0.39	2.20	0.56	2.14	0.55	2.08	0.60	2.15	0.52	2.12	0.58			
	12	1.34	1.16	1.57	0.44	1.60	0.59	1.44	0.74	1.56	0.66	1.47	0.67			
	18[b]	1.41	1.10	1.73	0.82	1.66	0.76	1.82	0.87	1.62	0.79	1.80	0.84			
Parent rated, 9 hyperactive–impulsive symptoms	0	0.96	0.23	1.17	0.57	1.96	0.64	2.27	0.50	1.83	0.69	1.93	0.73	–0.25	0.67*	0.42
	1	0.81	0.55	1.03	0.55	1.85	0.62	2.03	0.60	1.72	0.69	1.72	0.74			
	12	0.41	0.36	0.77	0.47	1.22	0.70	1.25	0.54	1.10	0.71	1.11	0.56			
	18[b]	0.41	0.45	0.83	0.58	1.19	0.77	1.66	0.77	1.07	0.77	1.45	0.80			
Parent rated, all 18 ADHD symptoms	0	1.65	0.23	1.76	0.33	2.10	0.50	2.29	0.40	2.04	0.50	2.13	0.45	–0.26	0.60*	0.41
	1	1.54	0.34	1.61	0.37	1.99	0.49	2.06	0.52	1.94	0.49	1.92	0.52			
	12	0.87	0.71	1.17	0.37	1.41	0.53	1.34	0.57	1.33	0.58	1.29	0.52			
	18[b]	0.91	0.59	1.28	0.67	1.43	0.70	1.74	0.76	1.35	0.70	1.63	0.75			
Teacher rated, all 18 ADHD symptoms	0	1.39	0.17	1.74	0.73	1.99	0.49	1.86	0.62	1.91	0.50	1.82	0.65	0.13	–0.10[c]	0.28[c]
	1	1.79	0.24	1.76	0.83	2.08	0.53	1.79	0.72	2.04	0.51	1.78	0.65			
	12	1.35	0.81	1.60	0.68	1.67	0.60	1.60	0.71	1.58	0.70	1.60	0.59			
	18[c]	1.31	1.38	1.54	0.72	1.74	0.56	1.68	0.63	1.64	0.85	1.61	0.66			

a. Negatively signed effect size nominally favors control group.
b. *n* for follow-up parent rating: 19 treatment, 24 control.
c. *n* for follow-up teacher rating: 9 treatment, 15 control.
*$p < .05$.

Measure	Variable	Week	Treatment Group				Effect Size (Cohen's *d*)[a]	
			Treatment		Control		Baseline to Follow-Up	End of Treatment to Follow-Up
n			21[b]		24			
			M	*SD*	*M*	*SD*		
CPT	Number of omission errors ↓	0	22.59	17.70	20.96	19.40	–0.09	0.01
		12	32.47	58.66	28.50	26.83		
		18	25.65	24.89	22.04	15.81		
	Number of commission errors ↓	0	27.88	5.46	27.88	4.82	0.78*	0.56†
		12	25.47	6.42	26.96	6.82		
		18	21.94	7.78	25.96	6.73		
	Mean hit reaction time (overall) ↓	0	431.22	98.32	392.30	96.77	–0.04	–0.14
		12	451.21	156.33	423.81	71.93		
		18	470.06	62.34	427.46	65.79		
	Detectability (ability to discriminate signal and noise) ↑	0	0.21	0.22	0.10	0.23	–0.16	0.39
		12	0.14	0.59	0.25	0.29		
		18	0.35	0.34	0.30	0.33		
	Reaction time interstimulus interval change ↓	0	0.08	0.06	0.07	0.05	0.39	0.93**
		12	0.15	0.08	0.08	0.06		
		18	0.09	0.07	0.11	0.07		
	Standard error by interstimulus interval ↓	0	0.14	0.17	0.09	0.13	0.38	0.74*
		12	0.22	0.15	0.13	0.16		
		18	0.15	0.17	0.18	0.16		
WCST	Number of categories achieved ↑	0	4.62	1.83	4.29	2.14	0.47	0.52†
		12	4.81	1.69	4.17	2.24		
		18	5.19	1.60	4.13	2.31		
	Perseverative errors ↓	0	19.74	13.16	24.75	22.13	–0.01	–0.21
		12	14.16	10.20	21.00	16.51		
		18	13.63	10.52	18.46	19.80		
	Number of set breaks	0	1.32	1.60	1.00	1.22	0.18	0.36
		12	1.89	1.56	1.33	1.74		
		18	1.63	1.34	1.63	1.53		
MASC	Item mean ↓	0	1.39	0.49	1.11	0.36	0.16	0.24
		12	1.31	0.45	1.06	0.44		
		18	1.20	0.44	1.02	0.43		
CIS	Item mean ↓	0	1.51	0.62	1.71	0.85	–0.27	0.14
		4	1.45	0.73	1.50	0.86		
		8	1.12	0.54	1.39	0.81		
		12	1.27	0.78	1.22	0.72		
		18	1.25	0.72	1.40	0.84		
CPRS	Item mean ↓	0	1.37	0.39	1.49	0.49	0.06	0.48
		4	1.27	0.39	1.19	0.58		
		8	0.95	0.31	1.09	0.47		
		12	1.03	0.49	0.93	0.39		
		18	0.96	0.44	1.13	0.56		
CTRS	Item mean ↓	0	1.46	0.43	1.46	0.52	0.18	0.39
		4	1.35	0.49	1.29	0.59		
		8	1.25	0.55	1.23	0.60		
		12	1.31	0.57	1.23	0.50		
		18	1.26	0.82	1.25	0.54		

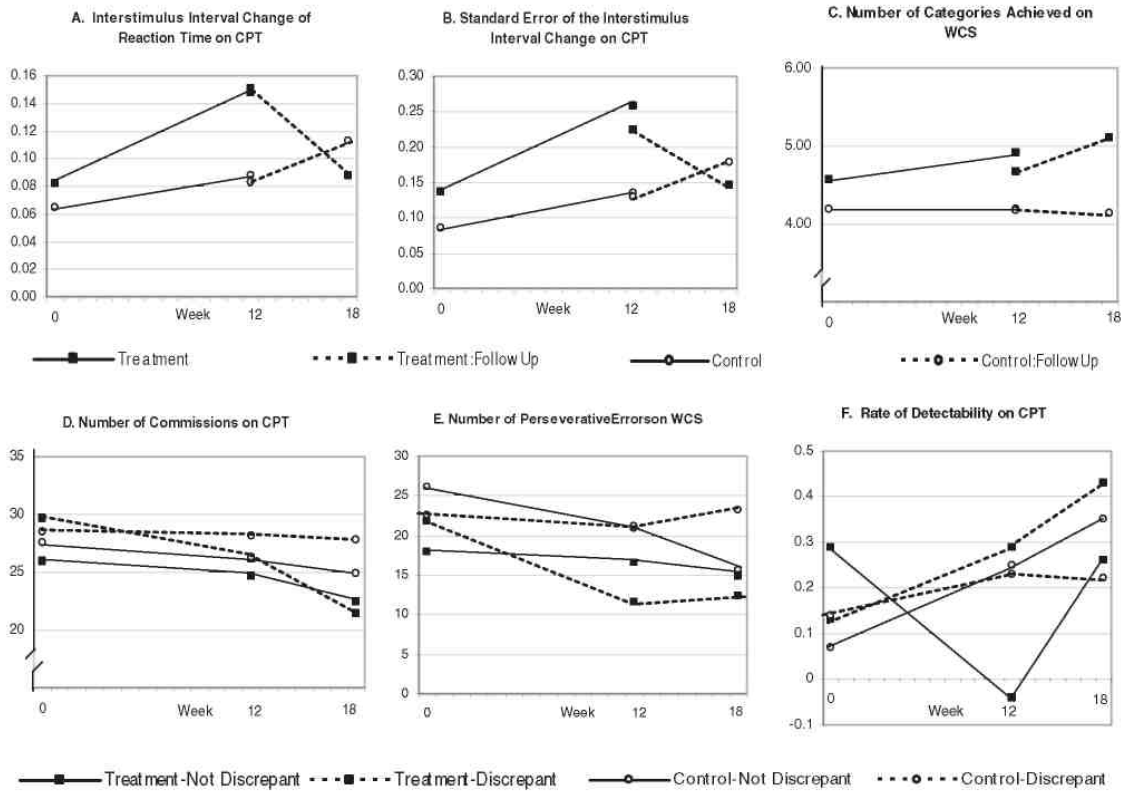
Note: Week 0 = baseline, Week 12 = posttest, Week 18 = follow-up. ↑ = Higher score favorable; ↓ = Lower score favorable. CPRS = Conners Parent Rating Scale long version, CTRS = Conners Teacher Rating Scale long version.

a. Negatively signed effect sizes favor control group.

b. CPT $n = 17$.

†$p = .05$ to .1. *$p < .05$. **$p < .01$.

Table 3 Outcomes for Secondary Measures: Continuous Performance Task (CPT), Wisconsin Card Sort Test (WCST), Multi-Axial Anxiety Scale for Children (MASC), Columbia Impairment Scale (CIS), and Conners's Scales



Note: A, B, and C are Week 12 posttest (PT) to Week 18 follow-up (FU) changes favoring active treatment. For the last segment of timeline, only participants with FU data are included (17 active, 24 control). From PT to FU, active treatment produced significantly more improvement on reaction time interstimulus interval change ($df = 1$, $F = 8.82$, partial $\eta^2 = .192$, $p = .005$, $d = 0.93$) and standard error by interstimulus interval ($df = 1$, $F = 5.48$, partial $\eta^2 = .129$, $p = .025$, $d = 0.74$) and a marginal trend on categories of the Wisconsin Card Sort (WCS; $p = .073$, $d = 0.52$). D, E, and F are baseline to FU changes with significant moderation by presence of IQ-achievement discrepancy greater than 1 standard deviation. $N = 23$ discrepant at PT, 18 discrepant at FU, 25 not discrepant. Discrepancy favors active treatment on CPT commission errors ($df = 1$, $F = 4.39$, partial $\eta^2 = .114$, $p = .044$), CPT detectability/d' ($df = 1$, $F = 6.26$, partial $\eta^2 = .156$, $p = .017$), and WCS perseveration errors ($p = .028$).

Fig. 2. Neuropsychological Test Changes

the overall advantage baseline to FU for active treatment was not significant, even by parent rating ($df = 1$, $F = 2.327$, partial $\eta^2 = .049$, $p = .13$, $d = 0.47$).

Covariates in Primary Analysis

Means of all 18 ADHD symptoms for children with different subtype diagnosis (inattentive vs. combined) did not change over time at a significantly different rate ($t = -0.692$, $p = .49$ for subtype x time interaction in the mixed effects linear analysis). Raters (parents vs. teachers) did not differ significantly in rating control versus treatment participants ($t = -1.098$, $p = .28$ for rater x treatment interaction) or in rating inattentive versus combined subtype ($t = -1.347$, $p < .18$ for rater x subtype interaction). However, parents reported more improvement over time ($t = 10.031$, $p < .0001$ for rater x time interaction). Therefore, we heuristically examined parent and teacher ratings separately (Table 2 and Figure 1). Because inattentive type was unevenly distributed, we also examined difference by diagnostic subtype (inattentive vs. combined) in Table 2 and Figure 1 and covaried subtype in secondary analyses, even though the uneven

distribution was not significant ($\chi^2 = 2.305$, *df* 1, $p = .13$).

Cognitive-neuropsychological objective test outcomes and secondary clinical outcomes are shown in Table 3 and Figure 2. From baseline to PT, there was no significant difference between treatment groups. However, from baseline to FU the active treatment ($n = 17$) was significantly superior to the control condition ($n = 24$) on commission errors of the CPT ($df = 1$, $F = 5.38$, partial $\eta^2 = .137$, $p = .027$, $d = 0.78$), apparently based mainly on medium-sized ($d = 0.56$) continued improvement in the active-treatment group following the PT, which in itself did not reach significance ($df = 1$, $F = 3.14$, partial $\eta^2 = .078$, $p = .085$). From PT to FU, the active treatment showed significantly more improvement on reaction time interstimulus interval change ($df = 1$, $F = 8.82$, partial $\eta^2 = .192$, $p = .005$, $d = 0.93$) and standard error by interstimulus interval ($df = 1$, $F = 5.48$, partial $\eta^2 = .129$, $p = .025$, $d = 0.74$) and showed a marginal trend on categories of the Wisconsin Card Sort ($p = .073$, $d = 0.52$).

In moderator analyses, a discrepancy of greater than 1 standard deviation between IQ and achievement standard score was used as a proxy for suspected mild learning disorder ($n = 18$ discrepant, 25 not discrepant available at FU). Discrepancy was associated with more benefit of CMA treatment compared to control from baseline to FU on CPT commission errors ($df = 1$, $F = 4.39$, partial $\eta^2 = .114$, $p = .044$), CPT detectability/d' ($df = 1$, $F = 6.26$, partial $\eta^2 = .156$, $p = .017$), and WCS perseveration errors ($p = .028$). Caregiver ratings showed no significant moderator effects. Parent ratings showed a significant time x previous medication interaction ($df = 1$, $F = 4.86$, partial $\eta^2 = .097$, $p = .033$ at endpoint, $p = .034$ at FU) on all 18 ADHD symptoms, mainly accounted for by the hyperactive-impulsive symptoms ($df = 1$, $F = 6.78$, partial $\eta^2 = .136$, $p = .013$ at PT, $p = .022$ at FU). Teacher ratings showed similar interaction at FU ($df = 1$, $F = 5.088$, partial $\eta^2 = .230$, $p = .038$), accounted for by hyperactive-impulsive symptoms ($df = 1$, $F = 9.09$, partial $\eta^2 = .348$, $p = .008$). Those with no previous medication improved more than did those who had previous medication, but the treatment difference between CMA and control condition was not significant.

Adverse events were unremarkable, totaling 30 for treatment and 34 for control group. Nausea occurred in 4 and 3, respectively. One active-treatment participant dropped out because of mild nausea on the first treatment; another developed evening headaches on treatment days toward the end of the 12 weeks. Vital signs, height, and weight showed no significant differences.

Discussion

This report illustrates the importance of control conditions in trials of intensive, unusual, or glamorous treatments for ADHD and the importance of blinding the raters. Without the control condition, the improvement on caregiver ratings shown in this study at treatment end would have been impressive. In fact, the standardized pre–post effect size (Cohen's *d*, the number of standard deviations difference, 1.34) and the improvement in the raw SNAP mean (from 2.04 to 1.35) over the 12-week treatment on parent ratings of symptoms was comparable to that shown at 3 months ($d = 1.32$, SNAP mean improvement 2.00 to 1.32) by the proven medication management algorithm of the MTA and nominally superior to the MTA multicomponent behavioral treatment ($d = 0.61$, SNAP mean improvement 1.96 to 1.56). However, the equally impressive improvement on the control condition showed that the improvement could not be credited to a specific effect of the CMA. Rather, it was mainly because of nonspecific effects (placebo expectation, maturation, etc.) or unintended specific effects of components shared by control and active treatments. Curiously, the improvement dissipated between PT and FU in the control group but not in the active-treatment group. The differential improvement in CPT commission errors from baseline at FU but not at PT could raise a question about possible sleeper effect, which could be compatible with the FU difference in primary outcome.

Two previous studies reported significant improvement in ADHD behavior compared to a control condition following 4 weeks of vestibular stimulation using teacher and parent rating scales similar to those used in the current study. Among possible reasons for the different results in this study could be that the control conditions in the previous studies were less credible so that they did not control for expectation (and the treatments in both studies were ineffective), that the control condition in this one was not ineffective, or that the treatment in this one was not as effective as in the previous studies.

The stimulation in both previous studies focused on the semicircular canals and attempted to isolate them from the otolith system. Head position was controlled to present a series of 10 stimuli to each of the paired horizontal semicircular canals and the two sets of paired vertical semicircular canals. The head was centered over the axis of rotation to minimize otolith stimulation. The stimulus to the semicircular canals was intense, with rapid acceleration to 33 rpm (100.0° per s), continuing for 60 s and then stopping impulsively, resulting in vertigo and nystagmus. The intensity was reflected in stomach awareness as reported by most participants; several reported nausea, and a few sessions were terminated prematurely to prevent vomiting. Participants often slept on the ride home.

In contrast, the CMA stimulus was mixed and milder. The CMA accelerated to only 4.0 rpm (12.1° per s). There was no impulsive stop but a gradual deceleration to 4.0 rpm in the opposite direction over 10 s. However, there was significant otolith stimulation, with axis of rotation through the hips. The head, located about 20 in. from the axis of rotation, was exposed to mild centrifugal force, linear rather than rotary. Although several participants reported stomach awareness, there was little nausea, and none were drowsy or slept on the way home.

Thus, there is a possibility that the combined otolith and semicircular canal stimulation, which we believed would be superior to semicircular canal stimulation alone, was actually inferior through some sort of interference or competition or that the intensity of semicircular canal stimulus was not adequate with the CMA.

Limitations

The size of this sample had power to detect only large effects. However, inspection of raw data (Table 2) up to treatment end at Week 12 suggests that there was not a Type II error from inadequate power for the primary analysis. Nevertheless, it is possible that a small to moderate baseline to FU effect was missed in view of the significant differential change from PT to FU favoring the CMA on the primary outcome and a few objective secondary measures. In fact, Cohen's *d* for baseline to FU on the primary outcome measure was 0.47, which would have required a sample of 130 to detect statistical significance with 80% power. On the other hand, the significant results on some secondary analyses could have resulted from experiment-wise error in the absence of correction for multiple tests. Another limitation is generalizability of the sample. Families able and willing to come for treatments thrice weekly for 12 weeks may not be representative of those with ADHD. Another limitation is lack of double blindness; single blinding (i.e., of patient, parent, and teacher but not treatment staff) was the best that could be done. However, the large improvement in parent ratings (the measure most susceptible to placebo effects) in the control group seems evidence that blinding was effective. In fact, the more objective neuropsychological measures favored the active treatment more than did parent ratings. A more severe limitation is that the complexity of the control condition, although good for the credibility of the blind, may have resulted in unintended therapeutic effects. The engineered white noise and the typing tutorial may have some benefit beyond the nonspecific effect of intense involvement in an unusual treatment three times a week with an interested adult. Therefore, the

failure of significance on the main outcome measure and most secondary measures cannot provide a firm basis for concluding that the whole treatment package is ineffective, only that the CMA is not an essential component of any therapeutic effect that may be involved. Furthermore, the lack of differential effect may not generalize to more intense vestibular stimulation or that focused on the semicircular canals.

Conclusion

On the basis of the current study, the CMA cannot be recommended for ADHD, at least combined type without comorbid learning disorder. It is not clear whether this conclusion applies to other forms of vestibular stimulation, more intense or focused on semicircular canals. It does appear that the treatment is a safe way of eliciting a strong placebo effect, a therapeutic tool recommended by Weintrob (2005). The improvement (presumably placebo) was impressive, enough so that of the 43 families returning for 6-week FU, only 1 (in the control group) had found it necessary to obtain medication posttreatment, even though 43% had been medicated prior to study entry.

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