Quantifying excessive mirror overflow in children with attention-deficit/hyperactivity disorder

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ABSTRACT

Objectives: Qualitative observations have revealed that children with attention-deficit/hyperactivity disorder (ADHD) show increased overflow movements, a motor sign thought to reflect impaired inhibitory control. The goal of this study was to develop and implement methods for quantifying excessive mirror overflow movements in children with ADHD.

Methods: Fifty right-handed children aged 8.2–13.3 years, 25 with ADHD (12 girls) and 25 typically developing (TD) control children (10 girls), performed a sequential finger-tapping task, completing both left-handed (LHFS) and right-handed finger sequencing (RHFS). Phasic overflow of the index and ring fingers was assessed in 34 children with video recording, and total overflow in 48 children was measured by calculating the total angular displacement of the index and ring fingers with electrogoniometer recordings.

Results: Phasic overflow and total overflow across both hands were greater in children with ADHD than in TD children, particularly during LHFS. Separate gender analyses revealed that boys, but not girls, with ADHD showed significantly more total phasic overflow and total overflow than did their gender-matched control children.

Conclusions: The quantitative overflow measures used in this study support past qualitative findings that motor overflow persists to a greater degree in children with ADHD than in age-matched TD peers. The quantitative findings further suggest that persistence of mirror overflow is more prominent during task execution of the nondominant hand and reveal gender-based differences in developmental neural systems critical to motor control. These quantitative measures will assist future physiologic investigation of the brain basis of motor control in ADHD. *Neurology*® 2011;76:622–628

GLOSSARY

ADHD = attention-deficit/hyperactivity disorder; **ADHD-RS-IV** = ADHD Rating Scale-IV; **CPRS** = Conners' Parent Rating Scales-Revised; **LHFS** = left-handed finger sequencing; **MCP** = metacarpophalangeal; **PANESS** = Physical and Neurological Examination for Subtle Signs; **RHFS** = right-handed finger sequencing; **TD** = typically developing; **TMS** = transcranial magnetic stimulation.

Anomalous motor development is a consistent, but understudied, characteristic of children with attention-deficit/hyperactivity disorder (ADHD). A consistent motor finding in children with ADHD is excessive overflow,^{1–3} which refers to unintentional and unnecessary movements^{3,4} that accompany voluntary activity. Motor overflow that occurs in homologous muscles on the opposite side of the body is referred to as mirror overflow.⁵ Abnormal persistence of mirror overflow beyond the first decade of life has been most commonly observed in developmental disorders associated with CNS dysfunction, including autism and ADHD,^{1–3,6,7} and may reflect delayed motor development.⁸ Furthermore, excessive mirror overflow in boys with ADHD is correlated with impaired response inhibition,³ a finding that has been implicated as a core deficit of the disorder.⁹

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Studies of motor overflow in children with ADHD have thus far relied on qualitative scales that have either been a simple account of the presence or absence of mirror overflow^{1,3,8} or a semiquantitative scale.^{2,6,10} Although these scales have proved to differentiate between children with ADHD and control children, the qualitative nature of the scoring limits the precision of these assessments. More quantitative measurement would allow detection of variations in the occurrence and amplitude of mirror movements, which would be important for understanding the neurophysiologic basis of excessive overflow in ADHD and other disorders.

The aim of this study was to quantify excessive mirror overflow movements in children with ADHD. We hypothesized that children with ADHD, particularly boys, would show greater mirror overflow than typically developing (TD) children.

METHODS Participants. Fifty right-handed children, aged 8.23–13.28 years, participated. Twenty-five (mean age = 10.49 years, SD = 1.26; 12 girls) had a diagnosis of ADHD and 25 were TD children (mean age = 10.73 years, SD = 1.27; 10 girls). The initial subjects had video data with insufficient resolution; therefore, of the 50 participants, video data were analyzed for phasic overflow in 34 subjects, whereas goniometer data, used to assess total overflow, was analyzed for 48 subjects (2 subjects were excluded to maintain age-matching). Consequently, we used separate age- and gender-matched groups for the phasic overflow and total overflow analyses.

Participants were of at least average intelligence, and participants displaying evidence of psychiatric disorders were excluded, except for those with oppositional defiant disorder and simple phobias (appendix e-1 on the *Neurology*® Web site at www.neurology.org).

Standard protocol approvals, registrations, and patient consents. This study was approved by the Cincinnati Children's Hospital and Johns Hopkins Medicine institutional review boards. Written consent was obtained from a parent or guardian; assent was obtained from every child.

Physical and Neurological Examination for Subtle Signs. The Physical and Neurological Examination for Subtle Signs (PANESS), a standardized childhood assessment, was used to assess basic motor skills.¹¹ Relevant to the current study, a section of the PANESS provided a qualitative measure for the presence or absence of overflow across several gait maneuvers, timed tapping maneuvers, and tongue movements. A PANESS total overflow score was generated by summing the number of maneuvers during which overflow was present.

Finger sequencing procedure. Each subject completed 5 blocks of sequential finger tapping on each hand, where the tapping hand alternated between left-handed finger sequencing

(LHFS) and right-handed finger sequencing (RHFS). During each block, subjects were asked to successively tap each finger to the thumb in a fixed sequence (index-middle-ring-little), which was repeated at least 10 times. Subjects were videotaped, and angle-calibrated electrogoniometers recorded the positions of the index and ring fingers. Baseline data were collected for 10 seconds before each block of finger sequencing where subjects remained stationary (appendix e-2).

Data acquisition. Phasic overflow: Video. A single phasic overflow movement was defined as any bidirectional movement occurring in the nontapping hand within 1.5 seconds or less. These movements were primarily extension-flexion or flexion-extension movements but also included side-to-side movements.

During video playback, a rater counted the number of phasic overflow movements in the nontask hand during LHFS and RHFS (appendix e-3). Protocol reliability was calculated using interclass correlation coefficients: intrarater LHFS = 0.95 and RHFS = 0.94 (L.K.M.); interrater LHFS = 0.95 and RHFS = 0.92 (2 raters: S.H.M. and L.K.M.).

Total overflow: Goniometer. Total overflow was defined as any deviation of the fingers from their resting baseline position, including sustained posturing (tonic) and phasic movements. It was quantified, using goniometer data tracings, as the summed angular displacement of each index and ring finger from the stationary baseline averages. To allow natural, unrestricted movement, we used modified MRI-compatible TSD131 finger electrogoniometers (Biopac Systems Inc., Goleta, CA). We chose to quantify movements on index and ring fingers because movement of the index finger is the most independent of other fingers, whereas movement of the ring finger is the most dependent on other fingers.¹² The goniometers were positioned and secured to measure angular deviations around the metacarpophalangeal (MCP) joints of the index and ring fingers (figure 1). The data file for each block of finger tapping, viewed in AcqKnowledge software 3.9.1v (Biopac Systems Inc.), had 4 signal channels representing the angular position in degrees of each index and ring finger about the MCP joint (figure 1, appendix e-4).

Definition of summed overflow: Phasic and total. Phasic and total overflow analyses were performed independently on the 10 blocks of finger sequencing. The overflow of the nontapping hand was recorded separately for the ring and index fingers during each block; these values for each hand were then summed across all 5 blocks to attain a total amount of overflow during LHFS and RHFS. We further added overflow for LHFS and RHFS to obtain the summed overflow across both hands.

Statistical analysis. Statistical analyses were completed with Statistical Package for the Social Sciences 17.0 (SPSS, Chicago, IL). Group demographics were compared using univariate analysis of variance and χ^2 tests. Pearson correlations were used to evaluate associations between measures of phasic and total overflow and between these measures and the PANESS measure of overflow.

The primary aim was to characterize the relationship between ADHD and phasic and total overflow occurring during finger sequencing. Because gender and age did not differ between groups, these comparisons were univariate. Separate analyses were conducted for RHFS/left hand overflow and vice versa. The relationship between ADHD and motor overflow was investigated in the whole group (boys and girls combined) and within each gender. Linear regression was used to examine for effects of gender and gender by diagnosis interaction on each measure of overflow. Pearson correlations were used to investigate associations of overflow with ADHD severity (ADHD Rating Scale–IV

Figure 1 Goniometers

(A) Goniometers attached with tape and Velcro to index and ring fingers. (B) Goniometer angle measurement of the metacarpophalangeal (MCP) joint. (C) Goniometer data recorded in AcqKnowledge Software during right-handed finger sequencing.

[ADHD-RS-IV] and Conners' Parent Rating Scales–Revised (CPRS)) and age.

RESULTS Demographic information. The phasic overflow analysis involved 34 children, aged 8.62–12.90 years: 17 children with ADHD (7 girls) and 17 TD control children (7 girls). The total overflow analysis involved 48 children, aged 8.23–13.28 years: 24 children with ADHD (11 girls) and 24 TD control children (9 girls). ADHD and TD control groups were matched on age and gender for the phasic and total overflow analyses (appendix e-5).

Correlations between phasic overflow and total overflow and PANESS. Considering both diagnostic groups together, there was a robust correlation between phasic overflow and total overflow summed across LHFS and RHFS ($r = 0.80, p \leq 0.001$). We also found a correla-

tion in children with ADHD between the qualitative PANESS total overflow measure and our quantitative measures of phasic overflow ($r = 0.59, p = 0.02$) and total overflow ($r = 0.53, p = 0.04$) summed across both hands.

Comparison of overflow measures by diagnosis. Children with ADHD showed greater phasic overflow ($F_{1,32} = 6.71, p = 0.01$) and total overflow ($F_{1,46} = 4.81, p = 0.03$) summed across both hands than TD children.

Dominant and nondominant hand effects. Phasic overflow during LHFS was greater in children with ADHD than in TD children ($F_{1,32} = 8.77, p = 0.006$); no effect of diagnosis was observed for RHFS. Likewise, total overflow was greater in children with ADHD than in TD children during LHFS ($F_{1,46} = 6.98, p = 0.01$) but not during RHFS (tables 1 and 2, figure 2).

Correlations between overflow and ADHD severity. For children with ADHD, parent-rated ADHD-RS-IV hyperactivity/impulsivity scores correlated with phasic overflow during RHFS ($r = 0.51, p = 0.04$), and there was a trend for a correlation between the ADHD-RS-IV total score and phasic overflow during RHFS ($r = 0.47, p = 0.07$). No significant correlations were observed with total overflow and ADHD-RS-IV or with phasic or total overflow and CPRS.

Comparison of overflow measures by diagnosis within gender groups. In boys with ADHD, phasic overflow ($F_{1,18} = 8.33, p = 0.01$) and total overflow ($F_{1,26} = 6.42, p = 0.02$) summed across both hands was greater than those in TD boys (tables 1 and 2, figure 3). As in the total cohort, phasic overflow during LHFS was greater in boys with ADHD ($F_{1,18} = 9.65, p = 0.006$). This approached significance during RHFS ($F_{1,18} = 3.27, p = 0.09$). Total overflow was greater in boys with ADHD during LHFS ($F_{1,26} = 4.48, p = 0.04$) and RHFS ($F_{1,26} = 9.69,$

Table 1 Analysis of variance of phasic overflow measures

Finger sequence	Mirror overflow	ADHD ^a	TD ^a	F	p
Boys + girls, n		17	17		
LHFS + RHFS	R + L total	65.41 (42.54)	32.91 (29.48)	6.71	0.01 ^b
LHFS	R total	35.12 (28.27)	12.53 (13.80)	8.77	0.006 ^b
RHFS	L total	30.29 (19.42)	20.38 (21.08)	2.03	0.16
Boys, n		10	10		
LHFS + RHFS	R + L total	80.30 (46.61)	30.25 (28.91)	8.33	0.01 ^b
LHFS	R total	44.50 (30.87)	11.60 (13.01)	9.65	0.006 ^b
RHFS	L total	35.80 (19.01)	18.65 (23.22)	3.27	0.09 ^c
Girls, n		7	7		
LHFS + RHFS	R + L total	44.14 (25.87)	36.71 (32.17)	0.23	0.64
LHFS	R total	21.71 (18.58)	13.86 (15.84)	0.73	0.41
RHFS	L total	22.43 (18.45)	22.86 (19.09)	0.002	0.97

Abbreviations: ADHD = attention-deficit/hyperactivity disorder group; LHFS = left-handed finger sequencing; RHFS = right-handed finger sequencing; TD = typically developing group; total = index + ring.

^a Mean (SD).

^b Significant findings.

^c Trends.

Table 2 Analysis of variance of total overflow measures

Finger sequence	Mirror overflow	ADHD ^a	TD ^a	<i>F</i>	<i>p</i>
Boys + girls, <i>n</i>		24	24		
LHFS + RHFS	R + L total	18.87 (14.89)	10.73 (10.44)	4.81	0.03 ^b
LHFS	R total	12.03 (11.41)	5.04 (6.16)	6.98	0.01 ^b
RHFS	L total	7.84 (5.48)	5.69 (6.80)	1.45	0.24
Boys, <i>n</i>		13	15		
LHFS + RHFS	R + L total	19.19 (11.81)	8.96 (9.54)	6.42	0.02 ^b
LHFS	R total	11.98 (9.14)	5.33 (7.49)	4.48	0.04 ^b
RHFS	L total	9.04 (5.31)	3.63 (3.85)	9.69	0.004 ^b
Girls, <i>n</i>		11	9		
LHFS + RHFS	R + L total	18.50 (18.50)	13.66 (11.79)	0.46	0.51
LHFS	R total	12.08 (14.11)	4.55 (3.24)	2.44	0.14
RHFS	L total	6.41 (5.59)	9.12 (9.26)	0.65	0.43

Abbreviations: ADHD = attention-deficit/hyperactivity disorder group; LHFS = left-handed finger sequencing; RHFS = right-handed finger sequencing; TD = typically developing group; total = index + ring.

^a Values are reported as mean (SD) degrees of angular displacement $\times 10^4$.

^b Significant findings.

$p = 0.004$) (tables 1 and 2). For girls with ADHD, there were no significant differences from TD girls in phasic overflow or total overflow, summed or separately by hand (tables 1 and 2, figure 3).

Examination of diagnosis by gender interactions.

There was no effect of gender on any of the overflow measures. There was, however, a gender by diagnosis interaction effect for total overflow during RHFS ($F = 5.42$, $p = 0.03$) and a trend for phasic overflow summed across both hands ($F = 3.01$, $p = 0.09$). For both measures, boys, but not girls, with ADHD showed more overflow than their gender-matched control children.

Correlations between overflow and age within gender groups.

There was a correlation between age of TD boys and total overflow during LHFS ($r = -0.57$, $p = 0.03$) and total overflow across both hands ($r = -0.63$, $p = 0.01$). The directions of these correlations were as expected: as age increased, overflow decreased. There were no correlations found between age of TD boys and phasic overflow, age of boys with ADHD and either overflow measure, or age of girls with ADHD or TD girls and either overflow measure.

DISCUSSION In this study, quantifiable measures were used to evaluate mirror overflow in children with ADHD and compare them with TD children. We were able to quantify phasic mirror movements, using video analysis, and total mirror movements, using electronic

Figure 2 Laterality of overflow measures

Means and SE for phasic overflow (typically developing [TD] group, $n = 17$; attention-deficit/hyperactivity disorder [ADHD] group, $n = 17$) during left-handed finger sequencing (LHFS) (A) and right-handed finger sequencing (RHFS) (B) and total overflow (TD, $n = 24$; ADHD, $n = 24$) during LHFS (C) and RHFS (D). Children with ADHD exhibited more phasic (A, $**p = 0.006$) and total (C, $*p = 0.01$) overflow than TD children during LHFS, but not during RHFS (B, D).

Figure 3 Overflow measures by diagnosis within gender groups

Means and SE for phasic overflow (typically developing [TD] group, $n = 17$, 7 girls; attention-deficit/hyperactivity disorder [ADHD] group, $n = 17$, 7 girls) across both hands and total overflow (TD group, $n = 24$, 9 girls; ADHD group, $n = 24$, 11 girls) across both hands. Boys with ADHD exhibited more phasic ($p = 0.01$) and total ($p = 0.02$) overflow than TD boys, but there were no differences between girls with ADHD and TD girls.

goniometer analysis. We found that children with ADHD exhibit significantly more mirror overflow than age-matched TD control children. The methodologies we used to measure phasic and total mirror overflow produced consistent and reliable results that were in agreement with those from prior studies.

Previously, studies have used qualitative^{1,3,8} or semi-quantitative assessments,^{2,6,10} force transducers,¹³⁻¹⁵ or EMG¹⁶ to evaluate mirror overflow. Force transducers have been used to quantify mirror movements in prior studies of adults; however, the validity of these measures may be limited because they allow only isometric movements, not naturally occurring open-ended movements involved in classic descriptions of mirror overflow. In this study, we defined a systematic means to quantify variations in the occurrence and amplitude of mirror overflow during naturalistic finger movements. Confidence in the quality of the methodology was provided

by the correlation between both types of quantified mirror overflow and the PANESS total overflow, the predominant qualitative assessment of overflow in past studies. In addition, the internal consistency between the phasic and total overflow results provides further assurance in our methodology. This strong correlation also suggests that the less expensive video analysis method may be sufficient. Nevertheless, the goniometers offer a more quantitative measure that could prove useful in correlations examining the physiologic basis of overflow.

The quantification of motor overflow is vital, because evidence from various studies indicates that the motor manifestations of ADHD may provide a window into the neuropathophysiology of the disorder.³ Mirror overflow is thought to result from impaired inhibition of involuntary synkinetic movements. Impairment of voluntary response inhibition has been hypothesized to contribute to the core diagnostic features of excessive hyperactivity, impulsivity, and off-task behavior.^{9,17} It has been shown that the presence of overflow movements in children with ADHD occurs in parallel to impairments in voluntary response inhibition^{9,18-21}; one study found a direct correlation between these variables.³ The association between motor overflow and response inhibition in ADHD highlights the importance of quantitative investigations of overflow.

Transcallosal inhibition is considered necessary for suppressing motor overflow. The 2 prevailing theories explaining the presence of motor overflow, bilateral activation theory, and ipsilateral activation theory, although through different mechanisms, both reflect the notion that a lack of inhibition via the corpus callosum results in overflow.²² It has been reported that there is an improvement with age in the ipsilateral silent period latency, a marker of callosal inhibition, in control boys but not in boys with ADHD. This result was suggested to be due to a delay in the development of interhemispheric connections important for transcallosal inhibition.²³ Detailed examination of the association between impairments in response inhibition and the persistence of motor overflow could provide important insights into the brain basis of ADHD and related developmental disorders.

The differences between right-handed children with ADHD and TD children were more prominent during LHFS. This finding suggests that for children aged 8–12 years, ADHD-associated differences in motor control are more noticeable in the later developing nondominant system. Nevertheless, we found phasic overflow during RHFS (but not LHFS) to be predictive of ADHD symptom severity. It may be that delayed development of the dominant motor control circuits more closely reflects a maturational delay or abnormality of the parallel higher-order systems that are

necessary to control impulsive, hyperactive, and distractible behavior. Analysis in larger populations across a broader age range would help to test these hypotheses.

Consistent with our hypothesis, we found that excessive mirror overflow in children with ADHD, aged 8–12 years, is specific to boys. Only boys with ADHD, not girls with ADHD, exhibited significantly more phasic and total overflow than did their age-matched TD control children. This result was supported by our findings of gender by diagnosis interactions for total overflow during RHFS and for phasic overflow across LHFS and RHFS. Studies in ADHD populations have largely focused on motor overflow in populations that were either completely or predominantly boys.^{1,3} A recent study of the difference in overflow measures across gender in children aged 8 through 12 years reported that girls with ADHD showed a steady age-related maturation similar to TD girls, whereas boys with ADHD, unlike TD boys, showed persistence of overflow across this age range.⁸ Our age correlations support this interpretation that there are differences in the maturation of 8- to 12-year-old TD boys and boys with ADHD. Group differences between girls with ADHD and TD girls and age correlations may not have been found in this study because of a smaller group size than that for the boys or because their trajectory of maturation is earlier than that of boys.²⁴ Thus, it is important to further study girls, especially earlier in their developmental process, to confirm that no difference in mirror overflow exists between girls with ADHD and TD girls.

In addition, we found laterality in the group effects of mirror overflow. In the combined group of boys and girls (all right-handed), there was significantly more phasic and total overflow in the right hands of children with ADHD than in those of TD children during LHFS. However, we found that boys with ADHD also had more total overflow in the left hand during RHFS than did TD children. Greater overflow during nondominant side task performance than during dominant side task performance has been reported in TD children and adults^{4,25-29} and has been proposed to be due to the development of more refined patterns of neural control because of the differential use of the dominant hand.²⁸ Because the left hand is used less than the right hand, movements made with this hand would be associated with less efficient networks of cortical control, thus inducing greater motor overflow.²⁸ There was one conflicting study that showed greater overflow during dominant side task performance. In this study, subjects had to successively perform finger flexions, extensions, and forced flexions. Because the muscle contraction of the dominant hand was stronger, the increased overflow could be attributed to strength differences between the hands.³⁰ Because, in our study, there was only a limited role of strength, this

finding lends support to the notion that boys with ADHD are likely to have impaired cortical tracts, which are necessary for inhibition of excitatory neural activity, thus leading to overflow in the left hand even during voluntary movement of the dominant right hand.

A major strength of this study is the ability to use the methods in conjunction with additional techniques to investigate the neurologic underpinnings of ADHD. The electrogoniometers and video camera are transcranial magnetic stimulation (TMS) and MRI-compatible, allowing for integrative studies involving motor manifestations of the disorder, inhibitory mechanisms, and anatomic and functional imaging data to investigate structural differences and cortical origins. Of particular interest would be impairments in the white matter tracts, specifically those of the corpus callosum. Additional strengths of the current methodologies are their ease of use and accessibility to investigators. The equipment is easy to use with a variety of hand sizes, and children find it easy to move with the goniometers attached to their hands. The equipment is also cost-effective; particularly for the phasic analysis, which only requires access to a video camera and computer. Overall, the consistency, versatility, and ease of use of the electrogoniometers and video recording make them valuable tools for quantifying mirror overflow.

Several limitations in this study are worth consideration. Phasic overflow was measured as the number of times a bidirectional movement occurred; therefore, there are no data on the amplitude of these movements. In the total overflow measure, we were not able to distinguish small amplitude overflow movements occurring for a long period of time from a large amplitude movement sustained for a short period of time, because total overflow was measured as the total angular displacement from a baseline. A goal of future goniometer analyses is to develop either an automated algorithm or manual protocol to classify short vs long duration and small vs large amplitude overflow on the data tracings. These identifying data could be used in statistical analyses to account for average time and average amplitude. A future study investigating the subtypes of ADHD would help to better pinpoint the neurologic basis of various behaviors associated with the disorder. Furthermore, a larger sample size would have provided more statistical power.

Continued study of motor overflow in ADHD is essential to provide greater insight into the neuropathophysiology of the disorder. Future integrated studies will allow more precise analyses of how these anomalous movements correlate with neurophysiologic measures obtained using TMS and neuroimaging, as well as the opportunity to further investigate gender effects and subtypes of the ADHD diagnosis.

AUTHOR CONTRIBUTIONS

Statistical analysis was conducted by L.K. MacNeil.

DISCLOSURE

L.K. MacNeil, P. Xavier, and Dr. Garvey report no disclosures. Dr. Gilbert has received honoraria from the Tourette Syndrome Association/Centers for Disease Control and Prevention, the Movement Disorder Society, the American Academy of Neurology, and the American Academy of Pediatrics; serves on the medical advisory board for the Tourette Syndrome Association; writes board review questions for PREP SA (American Academy of Pediatrics); and has received research support from the NIH (NIMH R01 MH078160 [coinvestigator], NIMH R01 MH08185 [coinvestigator], and NINDS NS056276 [coinvestigator]), the Cincinnati Children's Hospital Research Foundation, the University of Cincinnati, and the Tourette Syndrome Association. M.E. Ranta reports no disclosures. Dr. Denckla receives royalties from the publication of *Rapid Automatized Naming & Rapid Alternating Stimulus Tests RAN/RAS* (Pro Education, 2005) and has received research support from the NIH (NINDS R01 NS043480-05 [PI] and NIMH R01 MH078160 [coinvestigator]). Dr. Mostofsky has served on a scientific advisory for Bristol-Myers Squibb; serves on the editorial board of *Neurocase*; and receives research support from the NIH (NIMH R01 MH085328 [PI], NINDS R01 NS048527 [PI], NIMH R01 MH078160 [PI], and NICHD P50 HD052121 [coinvestigator]) and Autism Speaks.

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