Primary Complex Motor Stereotypies in Older Children and Adolescents: Clinical Features and Longitudinal Follow-Up

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ABSTRACT

BACKGROUND: Complex motor stereotypies are rhythmic, repetitive, fixed, and purposeless movements that stop with distraction. Once believed to occur only in children with autism spectrum or other developmental disorders, their presence in otherwise typically developing children (primary) has been well-established. In primary complex motor stereotypies, little information is available about the long-term outcome of these movements or existing comorbidities. METHODS: Forty-nine healthy participants (31 boys), ages 9 to 20 years with primary complex motor stereotypies who were previously diagnosed at a pediatric movements disorder clinic, were identified from medical records. Parents or the young adult (if older than age 18), completed a telephone interview evaluating family history, outcome, and comorbidities including attention-deficit hyperactivity disorder, obsessive compulsive disorder, anxiety, and tics/Tourette syndrome. Standardized questionnaires assessing attention-deficit hyperactivity, obsessive compulsive disorder, and anxiety were used to validate parent report of comorbidities. RESULTS: Stereotypy onset occurred before age 3 years in 98%. In all but one individual, stereotypies persisted at the time of phone follow-up (follow-up range: 6.8-20.3 years). Positive family history of complex motor stereotypies was identified in 39%. Most participants (92%) had concern for at least one comorbid disorder, including parent-/patient-reported clinically elevated levels of anxiety (73%), attention-deficit hyperactivity (63%), obsessive compulsive disorder (35%), and tics/Tourette syndrome (22%). CONCLUSION: Primary motor stereotypies typically begin in early childhood and, although reduced in frequency and duration, persist at least through the teenage years. Repetitive movements are associated with a variety of comorbidities that often have a greater functional impact than the stereotypic behavior.

Keywords: movement disorder, ADHD, Tourette syndrome, obsessive compulsive disorder, pediatric, executive function, stereotypies

Introduction

Motor stereotypies are repetitive, involuntary, fixed, and rhythmic movements that are suppressible with distraction. They are predictable in pattern, amplitude, and location, and seem purposeful yet are really purposeless.\textsuperscript{1} Movements are generally noted before 3 years of age, last for seconds to minutes, tend to occur in clusters, and may appear many times throughout the day. They are often triggered by periods of excitement, being engrossed in activities, stress, fatigue, and/or boredom.\textsuperscript{2} The aforementioned criteria used in this study differs from that in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, which requires that the repetitive motor behavior interfere with social, academic, or other activities or possibly cause self-injury.\textsuperscript{3} Typical childhood examples of complex motor stereotypies (CMS) include hand/arm flapping and waving, hand rotating, and finger wiggling. Stereotypies have long been associated with children who have intellectual disabilities, including those with an autism...
spectrum disorder, but have also been noted to occur in otherwise typically developing healthy children, which is labeled as primary CMS.\textsuperscript{2,4–12}

Despite a postulated prevalence of 2\% to 4\%,\textsuperscript{9} there is a paucity of published data among individuals with primary CMS regarding the long-term clinical course of movements and associated comorbidities. Prior studies evaluating outcome and comorbidities have typically focused on children younger than 12 years. Outcomes reported in these younger cohorts suggested that movements resolved in 3\% to 20\%\textsuperscript{10–13}; those in whom the movements continued caused concern for the family and social disruption for the child. Comorbid conditions are common among individuals with primary CMS, and include attention-deficit hyperactivity disorder (ADHD) (25\%-50\%), tics (18\%-43\%), and obsessive compulsive disorder (OCD)/obsessive compulsive behavior (OCB; 10\%-12\%).\textsuperscript{10–13}

The purpose of our study was to extend the period of follow-up through adolescence and to focus on the course of the movement abnormality and the documentation of comorbidities. Where possible, those individuals participating in prior survey studies \textsuperscript{11,12} were included to allow for the analysis of serial data. Additional areas assessed included family history (given the previous suggestion of a possible genetic link), experiences with therapeutic approaches, and the comorbidity of anxiety, recognizing its prevalence in other childhood movement disorders.

Methods

Participants

Approval was granted for this study from the Johns Hopkins Institutional Review Board. Each child’s parent provided written consent, and participants provided verbal assent. Data from individuals who had been diagnosed with primary CMS in the Pediatric Movement Disorders Clinic at Johns Hopkins Hospital were extracted from an institutional review board–approved hospital database. Diagnosis of primary CMS was made based on the presence of: (1) repetitive, purposeless, rhythmic movements with a fixed pattern (bilateral flapping, waving, wiggling movements of the hands/arms); (2) movements not better characterized as mannerisms, compulsions, or complex motor tics; (3) no reported premonitory urge; (4) temporary suppression of movements by an external stimulus or distraction; and (5) presence for at least 4 weeks. As mannerisms, compulsions, or complex motor tics; (3) no reported premonitory urge; (4) temporary suppression of movements by an external stimulus or distraction; and (5) presence for at least 4 weeks. As part of clinic assessment, the majority of participants’ parents also provided a video of the child’s movements to assist with diagnosis. To be considered primary, individuals were required to be otherwise typically developing. Comorbid conditions included ADHD, OCB, and anxiety disorders were not exclusionary diagnoses. Participants were excluded if they had any of the following comorbid diagnoses at either the initial evaluation or on telephone follow-up: (1) severe psychiatric disorder requiring treatment (e.g., psychosis, bipolar disorder, major depression); (2) known neurological disorders (e.g., epilepsy, stroke, tumor, traumatic brain injury, encephalitis, central nervous system damage secondary to infection, inborn errors of metabolism); (3) history of intellectual disability, including Down syndrome; (4) autism or any diagnosis falling into the autism spectrum; or (5) a history of sensory impairment or deprivation. Participants were screened via parent interview for autism spectrum disorders using the Autism Spectrum Screening Questionnaire,\textsuperscript{13} with score \textgreater{}13 used as the exclusionary criterion. Following identification of a pool of participants who had received a prior diagnosis of primary CMS and were between the ages of 9.0 and 20.9 years, attempts were then made to contact the individual and/or family by telephone for a follow-up interview. A total of 56 individuals were identified from the database who met criteria for the study: 49 individuals/families were contacted by telephone, all of whom met criteria, agreed to participate, and completed a structured interview. The remaining seven individuals were never reached despite multiple phone calls.

Data collection

Structured telephone interviews (see Appendix 1) were conducted by trained personnel (C.O., T.K., and C.M.-B.) with either the parent or the individual with CMS. During the telephone interviews, the following information was obtained from the parent, or in adults from the patient: family history, age of onset of stereotypies, change to the individual’s stereotypy patterns over time, current frequency and duration of the stereotypies, school performance, required school accommodations, treatments and results of any pharmacological and nonpharmacological trials, and the presence of specific comorbidities including ADHD, OCB/OCD, tics/Tourette syndrome, and anxiety. Of note, a positive family history was recorded if there was a history of diagnosed disorders in the individual’s parents, siblings, grandparents, aunts, uncles, or first cousins, with the subclassification of first-degree relatives referring to specifically parents and siblings. Additionally, the Stereotypy Severity Scale, which assesses the number, frequency, and intensity of stereotypies as well as disruption in daily life and overall impairment,\textsuperscript{15} was used to assess the individual’s worst period as well as the present time. After approximately 30 telephone interviews, preliminary data suggested a higher than anticipated prevalence of reported comorbidities, and the structured telephone interview was expanded to include standardized questionnaires including the ADHD Rating Scale–IV, Children’s Yale-Brown Obsessive Compulsive Scale (CYBOCS), and the Multidimensional Anxiety Scale for Children (MASC). Families who had not previously completed these questionnaires were recontacted. At the conclusion of data collection, 40 of 49 participants completed all parts of the interview(s).

Data analyses

Summary statistics were generated for categorical variables for the entire sample (n = 49). Variables of interest included family history, age of onset, movement outcomes (i.e., worse, better, same, stopped), episode duration, movement frequency, movement triggers, and, when possible, the presence of comorbidities with confirmation.

Results

Clinical characteristics

The study group consisted of 49 individuals (31 males, 18 females) with a mean age (at time of follow-up contact) of 13.1 ± 3.2 years (range 9.0–20.8 years). Of these, 29 were between 9 and 12 years, 13 were between 13 and 17 years, and seven were between 18 and 20 years. Forty-eight participants were Caucasian (non-Hispanic) and one was Hispanic.

Family history (see Table 1)

A total of 19 participants (39\%) reported a positive family history of primary CMS, with 14 of the 19 affecting a first-degree relative, and seven participants reporting multiple family members with stereotypies.

Motor stereotypies (see Table 1)

The mean age of onset for motor stereotypies was 1.3 ± 0.9 years, with a median of 1.0 year (range 0.0–4.0 years). At the time of the telephone interview, 48 of 49 individuals (98\%) continued to have stereotypies. Among the 48 individuals with persisting stereotypies, the mean interval between onset and telephone interview was 11.8 ± 3.3 years (range 6.8–20.3 years). A total of 16 (33\%)
had persistence of stereotypies for less than 10 years, 23 (48%) had persistence of stereotypies for between 10 and 15 years, and nine (19%) had persistence of stereotypies for more than 15 years. Specific reported stereotypies at the time of the telephone interview included flapping/waving movements of the hands and arms and finger wiggling/repetitive fisting with or without head posturing/mouth opening, jumping, and leg movements. A total of nine (18%) reported new stereotypic movements compared with those that were initially noted at time of onset (specifics not obtained). Twenty-two (45%) reported that the original stereotypies had changed in appearance, generally noting the presence of less overt movements or that flapping was replaced by more subtle repetitive hand or finger movements.

Most individuals (37 of 48) noted an improvement (i.e., stereotypies were less severe, less frequent, or more manageable/controllable) at the time of the phone interview compared with their initial reporting. Conversely, in 10 of 48, symptoms remained the same, whereas only one participant noted a worsening/exacerbation of symptoms. At the time of the follow-up interview for those 48 individuals who reported continued stereotypies, 10 (21%) reported the stereotypies were occurring on average less than once per day, whereas nine (19%) reported stereotypies occurring greater than 10 times a day, with the remaining 29 (60%) noting their occurrence between one and 10 times a day. In terms of duration for those who were still having stereotypies, 19 (40%) reported their stereotypy lasted longer than 1 minute, whereas 12 (25%) reported their stereotypy lasted less than 10 seconds.

The results of Stereotypy Severity Scale are summarized in Table 2. Data are included for current symptoms (referring to the 2 weeks before the follow-up interview) and for the reported point in time during which each individual’s stereotypies were most severe. Changes for all subjects from worst ever to current for the total Stereotypy Severity Scale score were $30.2 \pm 12.3$ to $15.8 \pm 11.9$ (mean difference: $-14.4 \pm 13.7$) and for the global impairment score were $19.4 \pm 11.3$ to $8.4 \pm 9.9$ (mean difference: $-11.0 \pm 11.9$).

### Academic outcomes

Academically, all participants reported participating in age-appropriate, regular classroom settings throughout their educational career. In the present sample, 46 of 49 reported having current average class grades of C or above, and 41 of 49 reported having an A/B average and/or qualifying for the honor roll. Three individuals reported having a
speech/language disability, and nine had required either an individualized education plan or Section 504 plan at some point during their educational career. Overall, 29 (59%) individuals reported having some degree of trouble in school, with 23 noting problems with attention/focus, three with social concerns/teasing, and three not specified.

**Comorbid conditions (see Table 3)**

Structured interview data on ADHD, OCD, anxiety, and tics/Tourette syndrome were available for 49 participants, of whom 40 also completed standardized rating scales.

**ADHD.** A total of 31 (63%) individuals reported attention or focus problems of such severity that the diagnosis of ADHD was considered. Of these individuals, 27 completed the ADHD Rating Scale-IV, with 23 (85%) answering positively to at least six of nine questions about inattentiveness, hyperactivity/impulsivity, or both, suggesting a diagnosis of ADHD. Of the 18 individuals who denied a history of ADHD, 13 completed the ADHD Rating Scale-IV; all who completed this questionnaire answered positively to less than the minimum required to suggest a diagnosis of ADHD (i.e., reporting less than six of the nine symptoms required to suggest diagnosis).

**OCD/OCB.** In 17 participants (35%), a current concern for obsessive-compulsive symptoms was reported, of which 15 completed the CYBOCS. Of the 15 who completed the CYBOCS, 14 scored ≥8, suggesting a diagnosis of OCD (CYBOCS scoring: 0–7 subclinical, 8–15 mild, 16–23 moderate, 24–31 severe, 32–40 extreme). Of note: for those 14 individuals, 10 were mild, three were moderate, and one was extreme. The one that did not rate high enough for OCD had OCB and was noted to be in the subclinical category. For those who denied a history of obsessive-compulsive symptoms (n = 32), 25 completed the CYBOCS, with none meeting diagnostic criteria for OCD and only one qualifying as subclinical based on CYBOCS scores.

**Tics/Tourette syndrome.** A total of 11 participants (22%) reported a history of a tic disorder.

**Anxiety.** A total of 35 participants (71%) reported anxiety as a concern, and one (2%) had social concerns suggestive of anxiety. Of this subgroup, 32 of 36 completed the MASC questionnaire. Of the 32 participants who completed the MASC and reported a concern for anxiety, 20 (63%) had a total score greater than the gender-specific total MASC scores suggestive of general anxiety (boys = 48, girls = 56), as reported by Ivarsson in 2006.16 In the 13 who denied any history or concern for anxiety, eight completed the MASC, with all eight (100%) scoring below the suggested gender-specific MASC scores for general anxiety based on Ivarsson’s 2006 report.16 The mean MASC score in the group reporting anxiety was 51.0 ± 15.2 (range 15–76), and in those who denied a history of anxiety the mean score was 15.7 ± 9.3 (range 9–34).

**Prior treatments**

None of the participants reported receiving pharmacotherapy targeted at either motor stereotypes or comorbidities during initial visit to the Pediatric Movement Disorders Clinic at Johns Hopkins Hospital. At the time of follow-up, 17 participants (35%) had been prescribed pharmacological agents at some point in their lives, with 15 receiving medication (at least in part) to address attentional difficulties. The reported pharmacological agents that had been prescribed included: methylphenidate, atomoxetine, amphetamine mixed salts, lisdexamfetamine, dexamphetamine, guanfacine, fluoxetine, lamotrigine, topiramate, and escitalopram. At follow-up, only six participants were still taking medications. None of the individuals who had been prescribed pharmacological agents reported any effect on their motor stereotypes, either positively or negatively.

A total of 22 participants (45%) had tried some form of nonpharmacological therapy to treat the motor stereotypes. Of these, 13 (27%) had behavioral therapy (specific type not defined) only, three (6%) had other types of psychological therapy or counseling, and six (12%) had both behavioral therapy (specific type not defined) and psychological therapy or counseling. Behavioral therapy was sought out by the families independently, possibly from

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<th>TABLE 3. Comorbid Conditions (n = 49)</th>
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<td>ADHD Rating Scale-IV (n = 40)</td>
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Abbreviations:
ADD = Attention deficit disorder
ADHD = Attention deficit hyperactivity disorder
CYBOCS = Children’s Yale-Brown Obsessive Compulsive Scale
MASC = Multidimensional Anxiety Scale for Children
OCD = Obsessive compulsive behavior
OCB = Obsessive compulsive disorder

* Six of nine questions for either the ADD or ADHD screening questions answered 2 or higher needed to suggest diagnosis of ADD or ADHD (noted as positive in the table).
* CYBOCS positive could be subclinical, mild, moderate, severe, or extreme.
* One subclinical, 10 mild, three moderate, one extreme.
* MASC positive if score >48 for boys and >56 for girls.16
influence by prior studies from this institution showing a beneficial effect, but the exact reasoning for seeking behavioral therapy not ascertained. Of the 19 who tried behavioral therapy, 10 (53%) indicated that behavioral therapy had helped their stereotypies to some degree, and six (32%) noted no effect (three noted they had tried behavioral therapy but did not comment if it helped their stereotypies or not).

Discussion

Motor stereotypies have long been associated with underlying neurological and developmental disorders such as autism spectrum disorders and intellectual disabilities. In the past two decades, motor stereotypies have been increasingly reported in typically developing children (primary) and further characterized into three subcategories including: “common” (i.e., body rocking, tapping), head nodding, and complex (i.e., bilateral hand and arm flapping, waving, wiggling movements). The 49 individuals in the current follow-up study—all with primary complex motor stereotypies—represent the oldest cohort evaluated to date.

Clinical characteristics of our cohort, ranging in age from 9 to 20 years, were highly consistent with prior reports in younger groups with primary CMS. As in prior studies, the vast majority of individuals in the present cohort were Caucasian; the sample was predominantly male (with 2:1 ratio); and caregivers consistently reported an early age of onset (by age 3 years in all but one participant). Additionally, participants in the current cohort reported that their movements were aborted by auditory or physical distraction and they had an absence of movements during sleep. As expected, based on prior reports of formal neuropsychological testing in this population, most individuals were performing at or above average in their academic settings. Supporting a previously suggested Mendelian inheritance pattern, approximately 40% of participants reported a family history of stereotypies, which is higher than prior reports of 31% and 25%. In addition, 29% had an affected first-degree relative compared with 17% in a prior study.

Further studies into the genetics of primary motor stereotypies are being pursued. Prior studies in primary CMS have suggested a resolution of stereotypic movements in 3% to 20% of affected individuals. This report of long-term outcomes, which includes a cohort of older children, adolescents, and young adults, suggests a rate of resolution of 2%, such that movements persist in virtually all of the individuals. Although movements almost always continued, it should be emphasized that most individuals reported a reduction in frequency and duration and all denied any current functional impairment related specifically to their movements. Although the stereotypies themselves tend not to cause functional impairment as one progresses into adolescence and early adulthood, the associated comorbidities appear more prevalent and problematic than previously noted.

More specifically, the prevalence of comorbidities, including anxiety (73%), ADHD (63%), OCD (35%), and motor tics (22%), was greater in this older cohort than what has been reported in younger samples. More than 90% had a concern for at least one comorbidity, and 65% had concerns for at least two. Anxiety, which has not been assessed in prior studies, appears to be especially prevalent. Concerns that the numbers represented a possible overestimation by those who were participating in the telephone interview were in part negated by the use of standard questionnaires.

There is no evidence that pharmacotherapy has a beneficial role in suppressing movements among individuals with primary CMS. Although anecdotal, an extensive list of medications had been tried in this study population for a variety of issues, and none was reported to have had a positive effect on the stereotypic movements. In contrast, more than half of those who tried behavioral therapy reported a beneficial effect. This latter finding is supported by the results of a small study using a combination of two behavioral modifying techniques: awareness training and reinforcement of other behaviors. The effectiveness of behavioral training is also supported by results from a home-based DVD training program (H.S. Singer, unpublished observation).

The underlying pathophysiology for complex motor stereotypies is unknown. Existing parallel interacting cortical-striatal-thalamic-cortical circuits provide a framework for understanding this movement disorder. In particular, the habitual pathway that controls repetitive, non-goal behaviors and runs between the premotor cortex/supplemental motor area and putamen appears implicated. Supporting data indicate reductions in the volume of the putamen and diminished levels of the inhibitory neurotransmitter gamma aminobutyric acid in the striatum. As is the case in other childhood movement disorders such as Tourette syndrome, the underlying relationships between a movement abnormality and its comorbidities remains undetermined.

Our results provide updated data which may allow practitioners to better explain expectations and provide renewed anticipatory guidance to affected patients and families. Limitations of this study include potential referral bias because those included in the cohort sought care or were referred to a tertiary center in hopes of garnering a diagnosis, information, and potential treatment for their child’s movement disorder. Further limitations include the analysis of data based solely on parent or patient recall as well as a lack of video confirmation of the current reported movements. This holds for both the persisting stereotypic movements and characterization of comorbidities. Furthermore, screening questionnaires were used as a basis for suggesting a comorbidity diagnosis (ADHD, OCD/OCB, anxiety specifically) rather than a formal diagnosis evaluation. Future studies using formal longitudinal assessments, serial direct observations of movements including at the time of the study, additional performance-based assessments specifically targeted at the cognitive and behavioral phenotype of CMS, and formal neuropsychological evaluations and diagnostic techniques for comorbidities will further advance our understanding of primary CMS and their associated comorbidities.

References


Phone Calls to Stereotypy Patients

CHECK CLINIC NOTES/CHART BEFORE CALLING! GET CONTACT, NAME, HISTORY FIRST!

Date: __/__/____

I am calling from Johns Hopkins Hospital to follow-up on a previous visit that your child had with Dr. Singer. ___________ was diagnosed with having stereotypies when he/she came in to see Dr. Singer on ___.

He just wanted to see how _________ was doing at this point since we haven’t seen him/her for a while.

Gender: M F Race: ___________ (get from charts)

Basically, Dr. Singer wants to get some background information on all of the patients he has seen who have stereotypes. He wants to identify any current issues since their last visit and just see how they are doing at this point in time. In addition, we would like to invite you to participate in a research study in which we will ask you one questionnaire over the phone, and you can go online and complete some additional questionnaires about your child. Questionnaires will include: a qualitative LIC questionnaire, obsessive-compulsive/qualitative/quantitative questionnaire, medication history, repetitive behavior scale, stereotypy linear analog scale, and an ADHD rating scale. Online questions will take approximately one to two hours to complete. All data will be collected and stored electronically. Data obtained online will be confidential and coded. This new data is essential for the establishment of a longitudinal assessment of normal children with motor stereotypes. Though you will not benefit directly from participation in this study, you will contribute to our understanding of stereotypes, and may help others in the future. In addition to that questionnaire study, there are several other studies currently ongoing here at Hopkins investigating primary complex motor stereotypes. After our completing our follow-up clinical questions, would you like to hear more about these studies? (Y/N)

Now I will ask you some clinical follow-up questions:

1. Is ___________ still having stereotypes?

2. Have the movements changed at all?
   How so?

   (arm flapping, finger automatisms, body rocking, head nodding, facial movements, eye blinking)

   Stopped entirely ___________ continued but better ___________ continued and the same ___________ continued but worse

   Any new movements?

   When did they start?
   ≤24 months 25-36 months ≥37 months

3. How often is he/she having stereotypes?

4. How many times a day?
   <10 a day 1-10 a day Once a day Less than once a day

   How long does the movement last?
   ≤10 seconds 11-60 seconds >60 seconds

5. Is there anything that makes these movements stop or get better?
   Do they stop if you say his/her name? [tap, etc.] – (stop when cured: y/n)
   Anything that makes them worse?

   Triggers: Excited/happy Engrossed Anxious/stressed Tired/fatigue bored

   Are they present during sleep? Never Do not know Yes

6. Do these movements affect your child’s functioning – performance in school, socially, self esteem, cause self-injury or injury to others, etc?

7. Are the stereotypies getting worse?

COMPLETE STEREOTYPY SEVERITY SCALE (BOTH CURRENT AND WORST EVER)

5. How are things going in school for ___________?

6. Does ___________ receive any special services at this time?
   Special Ed IEP Tutoring Speech Tx

7. Does ___________ have any learning disabilities?
   Trouble in school? [Attention, etc.]

8. What kind of grades does he/she usually get?

(continued).