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Nonautistic Motor Stereotypies: Clinical Features and Longitudinal Follow-Up

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To characterize further the clinical features and long-term outcomes among children with motor stereotypies who do not manifest mental retardation or pervasive developmental disorders, a review of clinical records and semistructured telephone interviews were undertaken. The identified clinical cohort consisted of 100 typically developing children with motor stereotypies. The mean length of follow-up was 6.8 ± 4.6 years. At most recent follow-up, movements had continued in 94% of the sample (62% for >5 years). Only six children reported complete cessation of movements, with four (3 of 4 with head nodding) doing so >1 year after their initial diagnosis. Thus the course of motor stereotypies, especially in children with arm/hand movements, appears chronic. Nearly half the children in this cohort exhibit other comorbidities, including attention-deficit-hyperactivity disorder (30%), tics (18%), and obsessive-compulsive behaviors/obsessive-compulsive disorder (10%). Twenty-five percent of children with motor stereotypies reported positive family histories of motor stereotypies, suggesting an underlying genetic abnormality. Finally, evidence is emerging that the clinical course of children who exhibit head nodding may differ from those whose motor stereotypy predominantly involves the hands and arms.

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Introduction

Movements are considered stereotyped when they are involuntary, repetitive, rhythmic, suppressible with distraction, seemingly purposeful in character but unusual in form, and possessed of a pattern, amplitude, and location that are predictable [1]. Common examples include arm flapping, hand waving/rotating, finger wiggling, head nodding, and body rocking. They occur in a wide spectrum of children, i.e., those with autism, mental retardation, sensory deprivation, and a variety of syndromes, as well as in otherwise healthy individuals [2-11]. Unfortunately, the specific movement itself does not permit differentiation into a pathologic or physiologic etiologic category, often leading to incorrect diagnoses.

In the literature, there is a relative paucity of information describing the clinical course of motor stereotypies in typically developing children. Several small studies commented on their characteristics and suggested that children with motor stereotypies and average intelligence demonstrate an early age of onset, a common prevalence of neurobehavioral problems, poor response to pharmacotherapy, and a chronic course [11-15]. Recognizing that the largest study to date described clinical features and outcomes in only 40 typically developing children with motor stereotypies, further evaluation with additional subjects and a longer follow-up period is clearly warranted. In addition, a suggestion that this disorder may be inherited in some individuals [13] requires confirmation.

The goal of this study was to expand our knowledge of otherwise normal, nonautistic children with motor stereotypies by obtaining additional longitudinal data on the 40 cases previously reported [13] as well as 60 new subjects. A conscious effort was made to include children with motor stereotypies beyond those with repetitive arm and hand movements, i.e., head nodding, to assess whether different movement categories have varying comorbidities and outcomes. Statistical analyses were used to determine those clinical variables with the greatest value in predicting outcomes. We also sought to explore in greater depth the strong familial component suggested in previous studies. The results of the present study provide an expanded

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evaluation of clinical outcomes in typical children with motor stereotypies.

Methods

Study Patients

Charts of children seen between 1993-2007 in a referral-based pediatric neurology movement-disorders clinic specializing in tic disorders at Johns Hopkins Hospital (Baltimore, MD) were reviewed. Records were identified for otherwise typically developing children referred for the evaluation and treatment of persistent repetitive movements. One hundred and seventeen individuals were identified from approximately 1500 new patient visits. This group included 40 patients identified in the initial study cohort [13] and 76 patients subsequently evaluated. A senior pediatric neurologist (H.S.S.), with expertise in childhood movement disorders, made the diagnosis of motor stereotypies, using the study diagnostic criteria described below. The movements of all children diagnosed with motor stereotypies were directly observed in person or on videotape.

Patients were excluded if they had any of the following comorbid diagnoses at initial presentation or on telephone follow-up: (1) severe psychiatric disorder requiring treatment (e.g., psychosis, bipolar disorder, or major depression); (2) known neurologic disorders (e.g., epilepsy, stroke, tumor, traumatic brain injury, encephalitis, central nervous system damage secondary to infection, or inborn errors of metabolism); (3) a history of mental retardation, including Down syndrome; (4) marked developmental delay; (5) autism or any diagnosis falling into the spectrum of pervasive developmental disorder-not otherwise specified; or (6) a history of sensory impairment or deprivation. Comorbid tic disorders, attention-deficit-hyperactivity disorder, obsessive-compulsive disorder or behaviors, and anxiety disorders were not exclusionary diagnoses. Using these criteria, 17 children were removed from the dataset: 4 had mood disorders requiring pharmacotherapy, 4 had received diagnoses of autism or pervasive developmental disorder-not otherwise specified, 3 had seizure histories requiring medication, 2 had a history of stroke/paralysis, 3 were excluded because of hearing loss/central deafness, and one was excluded because of Down syndrome. During the course of previous workups at outside institutions, a small number of children underwent electroencephalography or magnetic resonance imaging studies, the results of which were always normal.

Data Collection

For children whose last visit was after January 2006 (n = 19), information was abstracted directly from their most recent clinic note. For the 40 subjects in our initial clinical cohort and the 41 children who had not been seen at a clinic after January 2006, trained personnel (Kendra M. Harris and Kristy Yuan) obtained semistructured telephone interviews to assess the status of the children. Approval for data acquisition via the chart review and the semistructured telephone interviews was obtained from the Johns Hopkins Institutional Review Board. Of the 81 families who required additional follow-up, 70 were successfully contacted by telephone. During telephone interviews, the following information was updated: clinical features (movement description, context, and triggers), associated comorbidities, and school performance. The interviewers also obtained information regarding whether the child received special educational services, an expanded family history, attempts at and outcomes of any treatment directed at diminishing motor stereotypies, and clinical outcomes (focused primarily on whether the motor stereotypies stopped, persisted at the same level, or became better or worse). For the 11 children whose families were unreachable by telephone, information from their most recent clinic visit was used in data analysis. Data were examined and categorized with a focus on movement onset, associated behavioral disorders, family history, treatments, related assessment information, and outcome information.

Diagnostic Criteria for Motor Stereotypies

Motor stereotypies were defined as involuntary, patterned, coordinated, repetitive, fixed, rhythmic, nonreflexive, seemingly purposeful, suppressible, and bilateral (when possible) movements present for at least 4 weeks. Such movements included but were not limited to combinations of waving or flapping of the hands or arms, wiggling or fluttering of the fingers, shoulder movements, and a nodding or bobbing of the head from side to side. Moreover, a subset of children exhibited movements that could be described as patterned, volitional, purposeful behaviors, such as bending over, rocking, or pacing. None of the evaluated children had vocalizations accompanying their stereotypies. Clinical characteristics used to distinguish stereotypies from tics included a more constant/fixed pattern, rhythmic movements that were of continuous or prolonged duration, an absence of premonitory urges (in those old enough to describe such symptoms), and easy suppression with distraction. Children were grouped according to the body part involved in their predominant movement: hands/arms, shoulders, head, or whole body.

Associated Disorders

Associated disorders and behaviors were determined by a review of the patient's history during the clinic visit or the follow-up interview (e.g., the diagnosis had been performed by another provider using Diagnostic and Statistical Manual of Mental Disorders 4th edition criteria) or identified at the time of their movement-disorders clinic visit. Diagnoses of attention-deficit hyperactivity disorder were confirmed using the Attention-Deficit Hyperactivity Disorder Rating Scale IV and the Conners' Parent Rating Scale. Other neuropsychiatric diagnoses reported by parents were not confirmed by formal assessments.

Family History

A family history was considered positive if there was a reported history of diagnosed disorders in the patient's parents, siblings, grandparents, aunts, uncles, or first cousins. Disorders in first-degree relatives (i.e., the patient's parents and siblings only) were confirmed by evaluation of movement description, features, clinical course, and when possible, observations in the clinic or on videotape.

Analyses

Summary statistics were generated for categorical variables for the entire sample (n = 100) and in a subgroup of patients aged ≥7 years (n = 61; these latter to assure an age range that would include the diagnoses of interest, e.g., attention-deficit hyperactivity disorder, and tics). Chi-square tests were used to compare differences in the rates for categorical variables. Mean values (*t* tests) were examined for continuous variables. Variables of interest included age of onset, episode duration, movement frequency, movement triggers, family history, clinical outcome, and (for the subgroup of patients aged ≥7 years) the presence of comorbidities. In addition, for those aged ≥7 years, stepwise discriminant function analysis was used to explore which variables had the greatest prognostic value in terms of motor stereotypy outcome.

Results

Total Study Population

Clinical characteristics The final dataset was composed of 100 children (62 boys and 38 girls). At most recent evaluation, the mean age was 8.3 ± 4.5 years (median age, 8.5 years; range, 8 months to 27 years). Twenty-four children were <5 years of age, 42 were

between ages 5-10 years, and 34 were aged ≥11 years. Ninety-seven children in the sample were white (non-Hispanic), one was African-American, and one was of Near-East Indian descent. Although no formal data on socioeconomic status were available, the sample was identified to be at least middle class on the basis of referral source, parental profession, and health insurance. All children of school age were in a regular classroom at their expected grade level at either a public school or a private religious or magnet school, and were achieving at least grade C work. Nine (9%) children had some form of early motor delay (3 were late walkers, 2 exhibited hypotonia, 3 demonstrated delayed fine motor skills, and one manifested an unknown specific deficit). Six (6%) children had a history of early language delay in the form of "late speech." In terms of services among those children with delays, seven received private occupational therapy, and one received speech therapy.

Ninety children experienced one or a combination of the following movements: bilateral wiggling of the fingers, flapping/shaking of the hands or arms, and bilateral flexion or extension of the arms or hands. Eight children described head nodding as their primary movement, one child exhibited repetitive "hunching" of both shoulders, and one child experienced whole-body rocking. Twenty children exhibited a facial grimace that accompanied movement episodes.

Table 1. Characteristics of motor stereotypies†

Characteristic	Total (n = 100) (%)	Hands/Arms (n = 90), n (%)	Head (n = 8), n (%)
Age at onset			
≤24 mo	81	71 (79)	8 (100)
25-36 mo	11	11 (12)	0 (0)
≥37 mo	8	8 (9)	0 (0)
Typical duration of episode			
<10 seconds	37	33 (37)	4 (50)
11-60 seconds	25	24 (27)	0 (0)
>60 seconds	38	33 (37)	4 (50)
Frequency			
Once a day or more	90	70 (78)	8 (100)
Less than once a day	10	30 (22)	0 (0)
Trigger identified*			
Excited/happy	80	77 (86)	3 (38)
Engrossed	33	31 (34)	2 (25)
Anxious/stressed	26	24 (27)	2 (25)
Tired/fatigued	21	19 (21)	2 (25)
Present in sleep			
Never	88	81 (90)	5 (63)
Do not know	12	9 (10)	3 (37)
Stop when cued			
Yes	99	89 (99)	8 (100)
No	1	1 (1)	0 (0)

* A number of children identified more than one trigger.
† Two additional children, included in the summary analysis, who exhibited shoulder movements and body rocking are discussed in the text only.

Table 2. Family histories of disorders

	Disorders Affecting First-Degree Relatives* (n = 100) (%)	Disorders Affecting Any Relatives† (n = 100) (%)
Motor stereotypies	17	25
Tic disorder/TS	4	22
ADHD	10	13
OCD/OCB	12	14

* Limited to proband's parents and siblings.
† Limited to proband's parents, siblings, grandparents, aunts, uncles, or first cousins.

Abbreviations:
ADHD = Attention-deficit-hyperactivity disorder
OCB = Obsessive-compulsive behaviors
OCD = Obsessive-compulsive disorder
TS = Tourette syndrome

Key features of the natural history of motor stereotypies and their clinical course are summarized in Table 1. The mean age of motor stereotypy onset was 1.5 ± 1.1 years, with a median age at onset of 1 year. No significant difference in age of onset was observed between boys and girls ($t_{(97)} = 0.06$, $P = 0.96$). Overall, more than a third of the children reported a mean episode duration in excess of 1 minute, and 90% demonstrated more than one episode of motor stereotypies per day. Triggers were defined as conditions that typically led to the onset or exacerbation (prolonged, more frequent, or more intense) of motor stereotypy episodes. Fifty-four children had more than one reported trigger; excitement/happiness was the trigger most frequently cited. No subject exhibited motor stereotypies during sleep, and all but one (99%) typically stopped the behavior when cued (e.g., upon hearing his or her name called). Eighteen children, at a mean age of 10.2 years (range, 4-21 years), were teased because of their stereotypies or were inhibited such that the movements impaired participation in group activities. Children with motor stereotypies of the head demonstrated an earlier onset than those exhibiting movements of the hands/arms ($t_{(97)} = 4.73$, $P = 0.03$), and were more likely to experience movements more than once a day.

Family history Table 2 summarizes selected disorders present in relatives of subjects. Seventeen children with motor stereotypies had first-degree relatives with similar movements, and 25 had at least one relative with motor stereotypies. All children in the sample with a positive family history of motor stereotypies exhibited flapping/waving movements of the hands/arms. In contrast, none of the children with head nodding, shoulder movements, or body rocking had positive family histories. The relatively equal distribution of motor-stereotypy family history between maternal (n = 10) and paternal (n = 12) lines (three families had positive family histories because of siblings with motor stereotypies) discourages the suggestion of sex linkage, despite the clear sex asymmetry among children

in the present study. In all cases, family history was confined to the maternal or the paternal side of the family.

Treatment approaches Twenty children had been prescribed psychotropic medications at some point in the past. Although no pharmacologic therapy for the treatment of motor stereotypies was initiated at Johns Hopkins Hospital, pharmacotherapies prescribed elsewhere to these patients included clonidine, risperidone, oxcarbazepine, fluoxetine, topiramate, pimozide, levetiracetam, divalproex, carbamazapine, clonazepam, phenytoin, and acetazolamide. None of the patients, or any of their caregivers, reported that any of the sampled medications helped reduce movement frequency, duration, or amplitude. Fourteen patients were referred for behavioral modification therapy [16] of motor stereotypies. Five parents felt that the behavioral therapy resulted in modest reductions in the frequency of their child's movements, and five parents reported stopping the behavioral therapy after their child expressed reluctance or frustration. There are no data regarding the outcomes of therapy for the last four children.

Follow-up and outcomes Six of 100 children experienced complete cessation of their motor stereotypies. Of those 6 (3 boys and 3 girls), 4 stopped their movements spontaneously <1 year after onset. Three of these four children exhibited head nodding, and the fourth wiggled her fingers bilaterally. The final two children, i.e., boys with flapping of the hands, experienced complete resolution after durations of 11 and 12 years, respectively. None of these six children received pharmacotherapy or behavioral therapy for their movements, and all exhibited onset at <24 months of age.

In the 94 children with persisting motor stereotypies, the mean time interval from reported onset to most recent follow-up was 6.8 ± 4.6 years (the length of follow-up ranged from 2 months to 26 years, with a median of 6 years). Of those with persistent movements, 21 (22%) exhibited movements for >10 years, 41 (44%) exhibited movements for 6-10 years, 20 (21%) exhibited movements for 3-5 years, 8 (9%) for 1-2 years, and 10 (11%) exhibited movements for <1 year.

Among those with continued movements, the outcomes varied (Table 3). Ten children experienced a worsening of motor stereotypies (defined as an increase in the frequency, duration, or intensity of movements), 57 experienced no change, and 27 reported an improvement. A significantly greater proportion (one third) of the children with head nodding or bobbing subsequently stopped their movements, compared with only 3% of children with hand/arm movements ($\chi^2 = 25.4$, $P = 0.001$).

Table 3. Stereotypy outcomes according to predominant movement*

Outcomes	Hands/Arms (n = 90), n (%)	Head (n = 8), n (%)
Stopped entirely	3 (3)	3 (38)
Continued	87 (97)	5 (62)
Better	24 (28)	2 (40)
Same	53 (61)	3 (60)
Worse	10 (11)	0 (0)

* The difference between hand/arm compared with head motor stereotypies in terms of the proportion stopping entirely was statistically significant ($P = 0.05$).

Table 4. Associated conditions*

Comorbidity	Total (n = 61), n (%)	Hands/Arms† (n = 57), n (%)	Head (n = 2), n (%)
None	33 (54)	31 (54)	1 (50)
ADHD	18 (30)	18 (32)	0 (0)
Tics/TS	11 (18)	9 (16)	1 (50)
OCD/OCB	6 (10)	5 (9)	1 (50)

* Among those children aged ≥7 years.
† Two additional children, included in the summary analysis, who exhibited shoulder movements and body rocking are discussed in the text only.

Abbreviations:
ADHD = Attention-deficit-hyperactivity disorder
OCB = Obsessive-compulsive behaviors
OCD = Obsessive-compulsive disorder
TS = Tourette syndrome

Subgroup Analysis: Children Aged ≥7 Years

Clinical characteristics Among the 61 children (39 boys and 22 girls) aged ≥7 years with motor stereotypies, the mean time interval from reported onset to most recent follow-up was 9.4 ± 3.8 years. The mean age of onset was 1.6 ± 1.1 years, and at most recent visit, the mean age was 11 ± 3.4 years.

Associated conditions Twenty-eight (46%) of those children aged ≥7 years had received at least one comorbid diagnosis (Table 4). Eighteen children (30%) met the criteria for attention-deficit hyperactivity disorder, 2 (3%) received a diagnosis of obsessive-compulsive disorder from a psychiatrist, and 4 (7%) exhibited obsessive-compulsive behaviors, although not at a sufficient level to warrant a formal diagnosis of obsessive-compulsive disorder. Eleven children (18%) had a history of chronic motor or vocal tics that were distinct from the observed stereotypies. Of these, 3 (7%) were formally diagnosed with Tourette syndrome. Among the head nodders, only two were aged ≥7 years: one had comorbid tics and obsessive-compulsive behaviors, and the other was without additional diagnoses.

Predicting outcomes To assess which clinical features best predicted outcomes in children aged ≥7 years, a stepwise discriminant function analysis was used to compare those who became better (i.e., stereotypies became less frequent or stopped; n = 26) with those who did not improve (i.e., stereotypies remained unchanged or became more frequent or disruptive; n = 35). Predictor variables included sex, age of motor-stereotypy onset,

duration of illness, patient history of tics, patient history of attention-deficit hyperactivity disorder, patient history of obsessive-compulsive disorder/obsessive-compulsive behaviors, first-degree family history of tics, first-degree family history of attention-deficit hyperactivity disorder, first-degree family history of obsessive-compulsive disorder/obsessive-compulsive behaviors, and first-degree family history of motor stereotypies. Using the criteria of an F value of 3.84 to enter and 2.71 to remove, the analysis produced a significant function (Wilks' lambda = 0.91, $P = 0.02$). Of the multiple variables tested, only duration of illness achieved statistical significance in predicting stereotypy outcome. However, it correctly classified only 64% of the sample.

Discussion

Motor stereotypies have been categorized into pathologic and physiologic forms. Movements observed in the setting of neurologic impairment or dysfunction (e.g., autism or mental retardation) are representative of the pathologic group [2-10]. Physiologic motor stereotypies occurring in typical children are subdivided into common (e.g., body-rocking, thumb-sucking, and nail-biting), head nodding, and complex arm and hand movements [11-15]. However, as illustrated by the variety of stereotyped movements described in this study, the number of physiologic subgroups needs to be revised. Findings in the 100 typically developing children with motor stereotypies in this report are similar in several aspects to data previously described in the literature [12-15]. The disorder is more common in boys than girls, at a ratio of about 3 to 2. Nearly all affected children demonstrate an onset of stereotypic movements by age 3 years. Movements can last for minutes, can occur multiple times throughout the day, and tend to be associated with periods of excitement, stress/anxiety, or fatigue, or when the child is engrossed. Sensory stimuli or distractions, such as calling out the child's name, typically suppress the movements [12-15]. Movements are also absent during sleep. Despite the concerns of caregivers, the behaviors appear to be of little concern to the affected child, whose daily activities are rarely affected.

Consistent with previous reports, longer longitudinal follow-ups confirm that most motor stereotypies are persistent. Hence, suggestions to parents that motor stereotypies are a brief and transient problem appear to be erroneous. Nevertheless, although the numbers are small, it appears that outcome differences vary, based on the type of movement, i.e., head nodding compared with more complex arm and hand movements. Of the 6 children who demonstrated a complete resolution of their stereotypies, 3 were head nodders, and represented 3 of 8 (38%) in this group. Moreover, 4 of the 6 children (3 head nodders and 1 arm/hand waver) whose movements resolved before age 7 years did so after exhibiting signs for <6 months. Thus, children who do not exhibit head nodding, or those in whom movements persist for >1 year, are likely to manifest persistent signs.

Associated conditions are common in the nonautistic motor stereotypy population, with nearly 50% of children receiving at least one comorbid diagnosis. In subjects aged ≥ 7 years, i.e., beyond the expected age for the appearance of signs, 30% demonstrated attention-deficit hyperactivity disorder, and 18% demonstrated tics. Obsessive-compulsive behaviors are also common in this population. Because of the small number of head nodders aged >7 years in this study, the ability to distinguish the rates of comorbidities among different subgroups of physiologic motor stereotypies was limited. Nevertheless, children with stereotypies involving the hands and arms exhibit associated signs that are intriguingly similar to those of individuals with Tourette syndrome [17,18]. This finding suggests that motor behaviors may result from a dysfunction within the same structures associated with tic disorders. The prevalence of physiologic stereotypies is unknown, and cannot be extrapolated from this tertiary-care sample.

The underlying pathophysiologic mechanism of motor stereotypies in typically developing children remains unknown. Hypotheses range from psychological concerns to neurobiological abnormalities [19-26]. In animal models, stereotypic behaviors can be induced in response to both directly and indirectly acting dopamine receptor agonists, and may require a combination of both D1 and D2 receptors [22-27], although this approach is controversial. Volumetric reductions in frontal white matter in a small group of boys with stereotypies imply that the defect may reside in the fronto-striatal circuitry [28]. The predominance of affected first-degree relatives suggests a pattern of Mendelian inheritance, perhaps in an autosomal-dominant fashion. Future work using parametric linkage analysis may help identify movement-related genes.

Several small studies attempted to compare stereotypic movements of children in the general population to those in autistic children. MacDonald et al. [6] scored the number and types of repetitive movements in videotaped play sessions, and found that children with autism or pervasive developmental disorder-not otherwise specified had somewhat higher levels of stereotypic behavior than their typically developing peers. Smith and Van Houten [29], using a similar approach, suggested that those with developmental delay exhibited movements described as "more bizarre" than those in "nonhandicapped children." Although the present study was not designed to address direct comparisons between pathologic and physiologic stereotypies, it is evident that behaviors in nonautistic children can be prolonged, and may include complex motor patterns.

This study presented a historical review of motor stereotypies in typical children, and was greatly dependent on information obtained from parents or caregivers, subject enrollment in a regular classroom, and the presence of normal socialization skills. The possibility exists that

information on early development, the frequency of movements, the presence of comorbidity, family history, and the lack of response to pharmacotherapy could all be influenced by differential parental expectations or poor memory. Clearly, the ideal study in this population would involve a prospective analysis containing formal assessments designed to characterize stereotypies longitudinally, assess developmental milestones, cognitive capabilities, and comorbid diagnoses, and screen for mild autistic features. Unfortunately, until funding becomes available, this will remain a laudable but unrealized goal.

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