Post-Stroke Movement Disorders: The Clinical, Neuroanatomic, and Demographic Portrait of 284 Published Cases

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ABSTRACT

Post-stroke movement disorders represent a frequent cause of secondary movement disorders even if abnormal movements are a relatively uncommon complication of strokes. Besides the known correlation between stroke location and certain movement disorders, there remain uncertainties about the collective effects of age and stroke mechanism on phenomenology, onset latency, and outcome of abnormal movements. In order to address these gaps, we systematically reviewed all published cases and case-series with adequate clinical-imaging correlations. A total of 284 cases were analyzed to evaluate the distribution of different movement disorders and their association with important cofactors. Posterolateral thalamus was the most common region affected (22.5%) and dystonia the most commonly reported movement disorder (23.2%). According to stroke type, the most common disorders were parkinsonism (17.4%) and chorea (17.4%) after ischemic strokes and dystonia (45.5%) and tremor (19.7%) after hemorrhagic strokes. Strokes in the caudate and putamen were complicated by dystonia in one third of the cases; strokes in the globus pallidus were followed by parkinsonism in nearly 40%. Chorea was the earliest post-stroke movement disorder, appearing within hours, whereas dystonia and tremor manifested several months after stroke. Hemorrhagic strokes were responsible for most delayed-onset movement disorders (> 6 months) and were particularly overrepresented among younger individuals affected by dystonia. We hypothesize that selective network vulnerability and resilience explain the differences observed in movement phenomenology and outcome after stroke. A prospective epidemiologic study would be desirable to determine which elements of this evidence-mapping portrait may be accurate and which embellished or misleading.

Keywords: Movement disorders, Stroke, Ischemic Stroke, Hemorrhage, Dystonia.

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Author Roles

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INTRODUCTION

Post-stroke movement disorders (PSMD) represent up to 22% of all secondary movement disorders. However, PSMD are only observed in 1-4% of all strokes.[1,2] [1, 2] Despite the fact that the basal ganglia, thalamus, and cerebellum are commonly affected, the vast majority of strokes in these regions do not complicate their course with a movement disorder.[1,3] [1, 3] This remains an intriguing phenomenon, considering the role of these structures in the pathophysiology of idiopathic and degenerative movement disorders. Furthermore, while selected movement disorders may emerge after lesions in distinct parts of the brain, the topographical specificity for many movements may be poor and there remains uncertainty about the effects of age and stroke type on phenomenology, onset latency and outcome of abnormal movements. The reasons for these discrepancies remain unclear.

In this study, we sought to elucidate the role of type of stroke (ischemic vs. hemorrhagic), location, and age on the phenomenology, latency to onset, and outcome of PSMD based on a review of published cases.

METHODS

We conducted a systematic review of the literature to identify cases of PSMD reported between 1986 and 2016. We performed a PubMed search with the following terms: (stroke or infarct or hemorrhage or ischemia) AND (movement disorders or hyperkinetic or dystonia or myoclonus or chorea or Parkinson's or parkinsonism or tremor or restless legs syndrome or periodic limb movements or stereotypy or akathisia or alien hand syndrome or tics). Search results, titles and abstracts were reviewed to include case reports and case series pertinent to our research

objectives. Among the identified articles, we included in the review those which contained (1) well documented patients with movement disorders developing after a stroke; (2) characterization of the stroke type (e.g., ischemic, hemorrhagic) and location; (3) report of the latency between the stroke and onset of the movement disorder; and (4) patients did not present alternative causes for the emergence of the movement disorder (e.g., metabolic abnormalities, medications). Additional articles were identified by screening secondary research articles (reviews, commentaries, and letters) yielded by the initial PubMed search. We excluded articles with incomplete characterization of the movement disorder or the imaging data regarding localization. Subjects from criteria-meeting articles were included in a database, which included demographics (e.g., age and gender), type and location of stroke, reported movement disorder, latency to onset and, if available, outcome (e.g., improvement or persistence).

Statistical Analysis: A total of 74 articles yielding 284 patients were found suitable for the analysis.[4-77] Since the majority were case reports each subject from each study was considered to be a unit of analysis and thus no weight was assigned to any studies. Type of stroke (ischemic versus hemorrhagic), average age, gender distribution, type and location of movement disorders, latency period between stroke and movement disorder, and outcomes were extracted from each report. All the data were described using frequencies and proportions. All data were compared according to type of stroke, gender, and age groups using Fisher's exact tests. Comparison of latency period according to different factors was assessed using Chi square test. All the statistical analyses were carried out using STATA 13.

RESULTS

General features of PSMD. Of a total of 323 qualifying cases, 39 were excluded due to insufficient data. In total, 284 cases fulfilled our research criteria and were used for analyses. Reported PSMD were more common in men (58%) with a mean age at presentation of 62 years (range 18-93). Ischemic strokes preceded more than three-quarters of PSMD. Posterolateral thalamus (23%) was the region most frequently affected, followed by the putamen (19%) and caudate (14%). Dystonia was the most common PSMD (23%), followed by chorea (16%) and myoclonus (15%) (**Table 1**).

Basic demographics and PSMD. In those between 50-70 years (51.4%), the posterolateral thalamus was the most common location (29%) while myoclonus and dystonia the most common PSMD (27% and 24% respectively). In those younger than age 50, the putamen and caudate (28% and 19%) were the most common locations, and dystonia the most common PSMD (40%). In those older than 70 years, the putamen was most frequently affected (25%) and chorea the most common PSMD (24%) (**Supplementary table 1**). Women showed greater putaminal involvement than men (26% vs. 14.0%) but similar frequency of stroke involvement in other localizations. While dystonia and myoclonus were of relatively similar frequency in men and women (~23% and ~15%, respectively), parkinsonism was among the top three disorders in men (16%) and chorea among the top three in women (18%) (**Supplementary table 2**).

Type of stroke and PSMD. Ischemia was the most common mechanism of stroke in those older than 70, while hemorrhage was more common between the ages of 50 and 70. The distribution of ischemic and hemorrhagic strokes was similar between men and women. Ischemic strokes complicated with PSMD were more frequently located in the putamen (22%), followed by

frontal lobe (16%), midbrain (16%), and caudate (15%), while hemorrhagic strokes in the posterolateral thalamus (42%), midbrain (15%) and pons (9%). Parkinsonism, chorea, and dystonia (17% each) were the most commonly observed movement disorders in patients with ischemic strokes while dystonia (46%), tremor (20%), and myoclonus (15%) in hemorrhagic stroke. Compared to hemorrhagic strokes, parkinsonism and restless leg syndrome were significantly more frequent PSMD after ischemic strokes (6% vs. 17% and 0% vs. 9% respectively); compared to ischemic strokes, dystonia (46%) and tremor (20%) were significantly more frequent after hemorrhagic strokes, complicating almost two thirds of such cases ($p < 0.001$) (**Table 2 and supplementary table 3**).

Stroke location and type of PSMD. PSMD varied depending on the location of the stroke. While caudate and putaminal strokes were complicated by dystonia in one third of the cases, those selectively affecting the globus pallidus exhibited parkinsonism in nearly 40%. Thalamic strokes yielded distinct phenotypes depending on the region affected (**Figure 1**).

Latency to PSMD after stroke. Most PSMD (46%) manifested within the first seven days after a stroke. Chorea was the earliest PSMD, appearing within 24 hours, whereas dystonia and tremor had a post-stroke latency measured in several months (**Figure 2**). Ischemia remained the most common mechanism of stroke for movement disorders manifesting in less than a month. Hemorrhagic strokes were responsible for most cases of delayed onset of movement disorders (> 6 months) (**Figure 3**). The latency period varied depending on stroke location. For patients who manifested PSMDs within the first week, the posterolateral thalamus was the most common location. The putamen was the most common location involved in patients presenting with

symptoms within a day, and the caudate was most commonly involved in patients presenting with symptoms within 6 months.

Outcome of PSMD. Outcome data were reported in 64% of cases reviewed. Over seventy percent of these patients exhibited spontaneous improvement or resolution. Of those with persistent symptoms only half experienced benefit from symptomatic treatment. The most common movement disorder to improve or resolve spontaneously was myoclonus (84%), while tremor the most to persist (38%) and parkinsonism the most common to improve with treatment (36%) (**Figure 4**). The frontal lobe was the most common location involved in cases that spontaneously improved/resolved, the putamen in cases that persisted despite treatment, and the midbrain in cases that responded to treatment. There was no difference in outcome among the different age groups. There was no statistical difference in the outcomes of PSMD manifesting from ischemic or hemorrhagic strokes, though there was a trend for movement disorders resulting from ischemic strokes to improve on their own or resolve with treatment compared to movement disorders resulting from hemorrhagic strokes.

In summary, an interesting portrait emerged from the analysis of these 284 cases. The most common PSMD was dystonia (both in men and women) and most of them were in those younger than age 50 years and after hemorrhagic strokes. The second most common PSMD was chorea, with slightly higher frequency among those older than 70 years with ischemic strokes. Myoclonus was the third most common PSMD and most of these cases were observed in the 50-70 age bracket, and were equally distributed among hemorrhagic and ischemic strokes. The frequency of dystonia and tremor were significantly higher in patients with hemorrhagic strokes

while the frequency of parkinsonism and restless leg syndrome were significantly higher in patients with ischemic strokes. Delayed onset of movement disorders was mostly observed in patients with hemorrhagic strokes associated with dystonia and tremor while earlier onset of movement disorders was due to ischemic strokes leading to chorea (over one third persisted), parkinsonism (over half improved with treatment/resolved), and restless leg syndrome (over two third improved/resolved).

DISCUSSION

With the inherent biases of published case reports and case series, the collective data suggests a relatively small but significant burden of post-stroke movement-related complications. As with other studies, the type of stroke and location provided only a rough estimate of the associated movement disorder.[1, 2] Posterolateral thalamus, putamen, and caudate emerged as the most commonly reported regions affected by stroke and dystonia as the most common movement disorder. Ischemia remained the most common mechanism of stroke across all PSMD. The type of stroke was important in predicting the phenomenology, with parkinsonism and restless legs syndrome being more prevalent after ischemic strokes while dystonia and tremor after hemorrhagic strokes (more than 2/3 of hemorrhagic cases exhibited dystonia). Finally, age was also a variable affecting location and movement phenomenology, with putamen and caudate appearing more frequently affected in those under 50.

Three studies have examined the clinical characteristics of post-stroke movement disorders and reported chorea, including hemiballism (the most severe form) as the most common PSMD, followed by dystonia.[1, 2, 78] Our literature reappraisal showed that chorea, parkinsonism, dystonia,

and myoclonus were most commonly disorders among patients with ischemic strokes. Dystonia was disproportionately more prevalent (accounting for 2/3 of the cohort) in hemorrhaging cases. Ischemia was the most common stroke mechanism, with thalamus and basal ganglia the most common stroke localizations. Prior studies underscore the inconsistencies between stroke localization and phenomenology. Mehanna and Jankovic's study sought to correlate movement phenomenology with other stroke features. Similar to our study, they uncovered a higher incidence of dystonia in younger patients and chorea in older patients. Our review is the first to assess differences in gender, latency, and outcome according to the type of stroke, localization, type of movement disorder, and age, assisted by the high number of cases retrieved compared to the three studies mentioned above.

The relatively poor association between stroke localization and movement phenomenology (most associations were under 30%) may be explained by the inability to discern the different motor networks involved in the pathophysiology of movement disorders. These networks represent the interaction between multiple regions of the brain and can be analyzed at different levels, from neurons and synapses to anatomical regions and fiber tracts.[79] Therefore, the focal damage caused by a stroke may affect one or multiple neural networks within a single structure. Thus, patients with strokes involving a given region (e.g., the thalamus) may suffer damage to one or more varying neuronal networks resulting in a spectrum of motor deficits. In addition, the disruption of the network architecture may trigger different adaptive responses to ensure the maintenance of motor function which stand to alter the movement disorder phenomenology.[80, 81] In particular, maladaptive mechanisms like diaschisis, dedifferentiation, and abnormal axonal regeneration may lead to an aberrant network function potentially manifesting as PSMD.[79]

We found that patients with PSMD after hemorrhagic strokes were younger compared to those presenting after ischemic stroke. In addition, younger age and hemorrhagic type of stroke were independently associated with a later onset of PSMD, beyond at least one month. We speculate that the differences between these groups may be due to the higher degree of resilience and neuroplasticity in younger subjects and their decline with age.[82-83] While diminished neuroplasticity results in limb paresis in some cases, the ability of the neural networks to reorganize itself may lead to an aberrant network regeneration, manifesting as abnormal movements.[84-85] In addition, the ability of the neural networks to reorganize themselves depends on the severity of the initial insult.[86] We suggest that PSMD are more likely to emerge after hemorrhagic strokes in younger patients due to their higher degree of resilience (and at a longer latency due to stroke severity), whereas older patients with hemorrhagic strokes are more likely to have more severe outcomes, including death or paresis (precluding later documentation of abnormal movements). Similar reasoning may apply to ischemic strokes, where younger patients may be left with a lower prevalence of residual deficits compared with older patients.

There are several limitations to this literature reappraisal. First, it was based on reported cases which includes a marked selection bias: while most PSMD remain a small fraction of all strokes, it is likely that only a fraction of this fraction has ever been reported, with more common cases of post-stroke chorea or dystonia becoming unlikely to be reported in the modern era. As a result, our findings are not suitable to estimate prevalence assumptions after stroke types and localization in the general population (e.g., it is uncertain whether the higher percentages of movement disorders occurring in the first week after strokes in patients older than 70 compared

to those younger than 50 are due to the shorter survival of the former group). Relatedly, a number of cases may have been unique rather than representative of phenomena seen during routine clinical practice. Moreover, most of these case reports were not accompanied by video material and the determination of the movement phenomenology may have been made by clinicians without specialized training in movement disorders, potentially leading to a percentage of mischaracterized phenotypes. Also, the aggregated level of data from different studies did not allow the use of multivariable analysis. Due to mixed study designs with small number of cases, the analysis could not account for weighting structure of each study. Finally, we did not include abnormalities not considered "classic" movement disorders, such as spasticity and apraxia, even though these may complicate strokes far more commonly and we lacked neuropathologic data to exclude comorbidities that may at least partially account for a given phenotype (e.g., potential for Lewy bodies and nigra degeneration in individuals with presumed post-stroke parkinsonism). Despite these imitations, this is the first comprehensive systematic review study to evaluate the distribution of PSMD and their outcomes based on all of the published cases (which may not be accrued from a single medical center) for which sufficient clinico-imaging data are available.

CONCLUSION

PSMD remain an uncommon but important source of disability in neurology with differences in phenomenology and outcome which may result from selective network vulnerability and resilience. A prospective epidemiologic study would be desirable to determine which elements of this evidence-mapping portrait may be accurate and which embellished or misleading, further refining the variables that may affect the frequency, type, and outcome of these secondary post-stroke motor disorders.

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Table and Figure Legends

Table 1: General characteristics of post-stroke movement disorders.

Table 2: Type of stroke and movement disorders.

Figure 1: Frequency of post-stroke movement disorders according to stroke localization.

Figure 2: Latency for most common post-stroke movement disorders.

Figure 3: Latency according to type of stroke. * indicates significant difference ($p < 0.05$)

Figure 4: Outcome of post-stroke movement disorders and locations involved for each.

Supplementary Material

Supplementary Table 1: Age at stroke and movement disorders.

Supplementary Table 2: Gender and post-stroke movement disorders

Supplementary Table 3: Type of stroke and movement disorders

Figure 1

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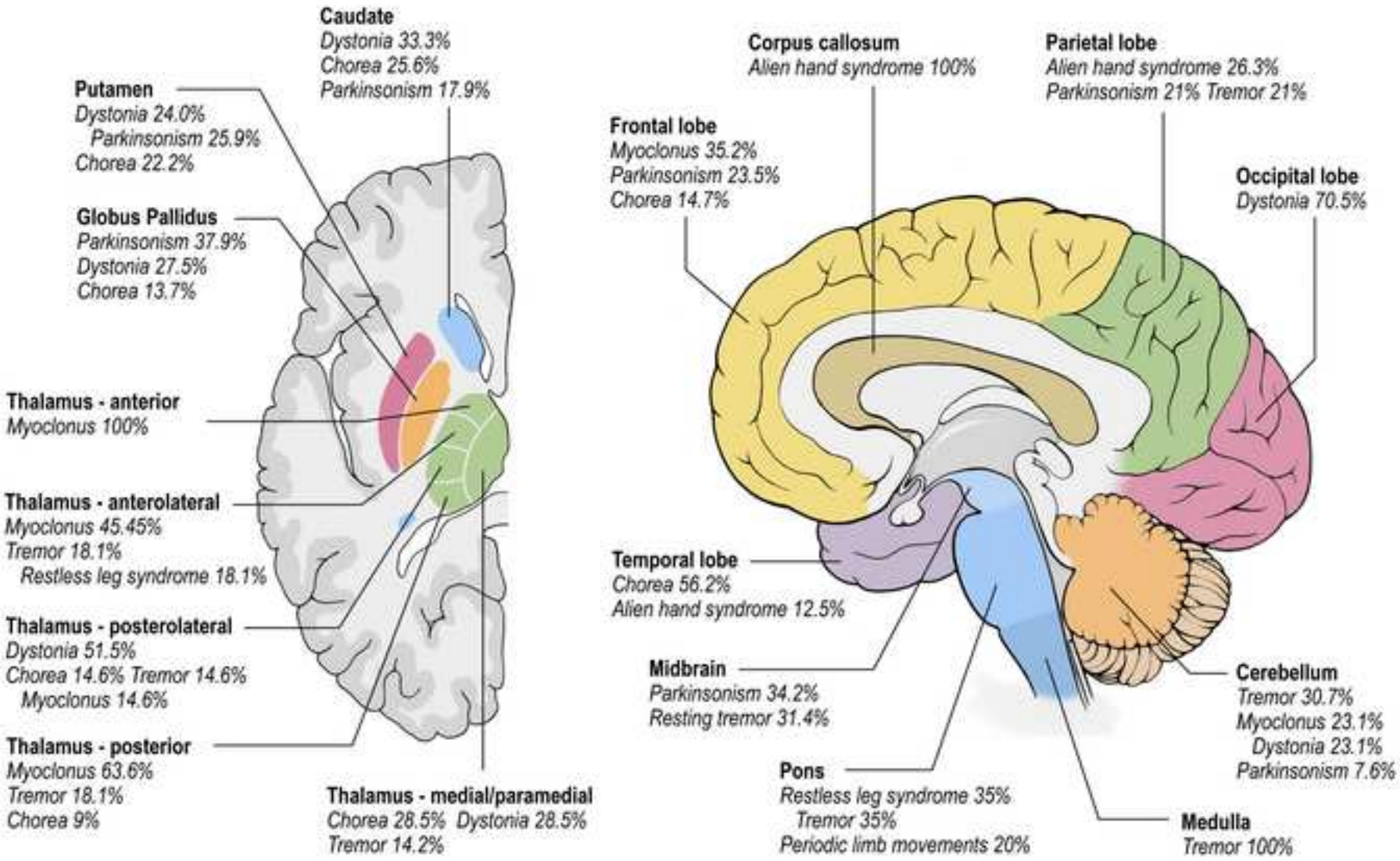

Figure 2

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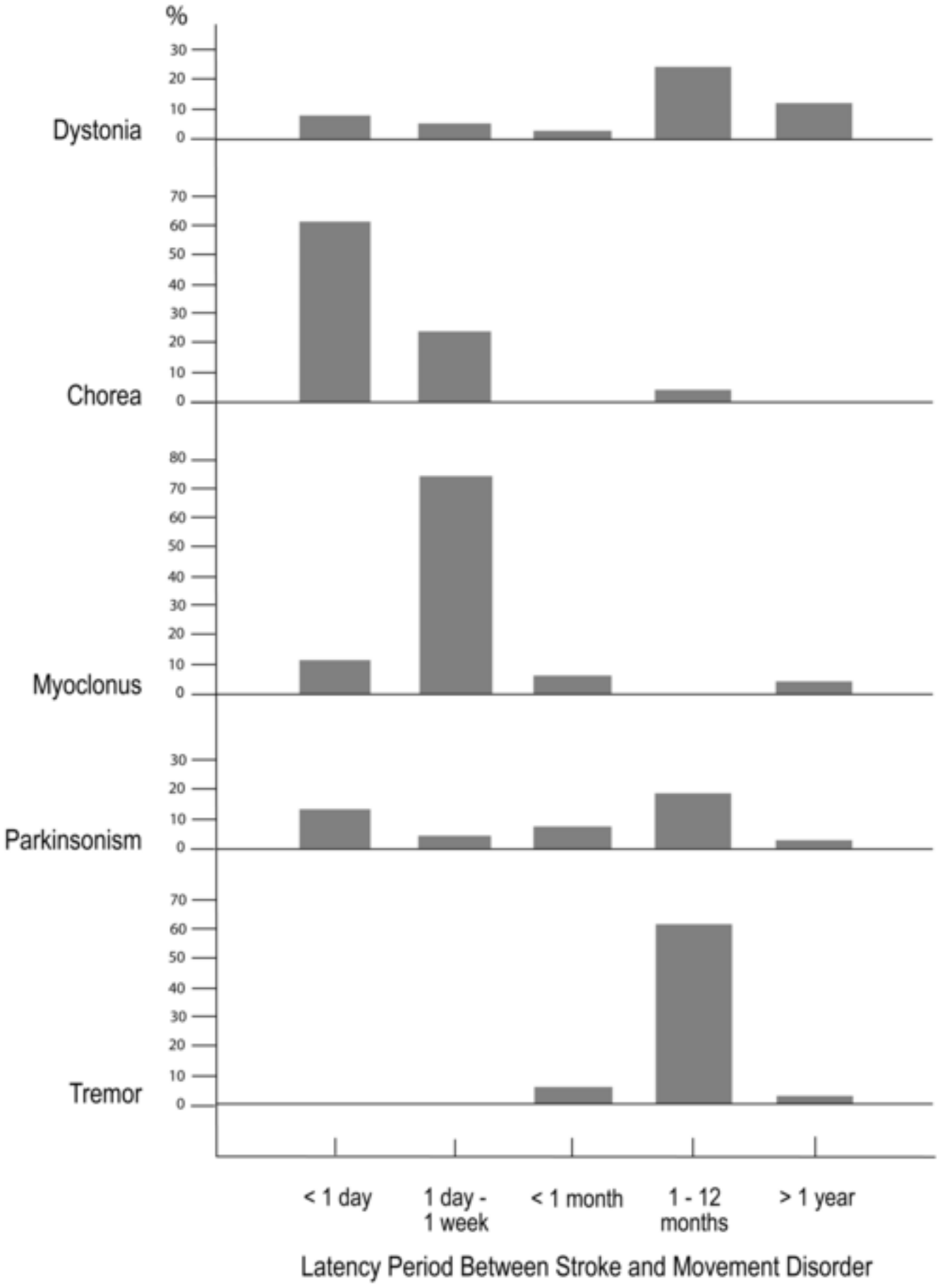

Figure 3

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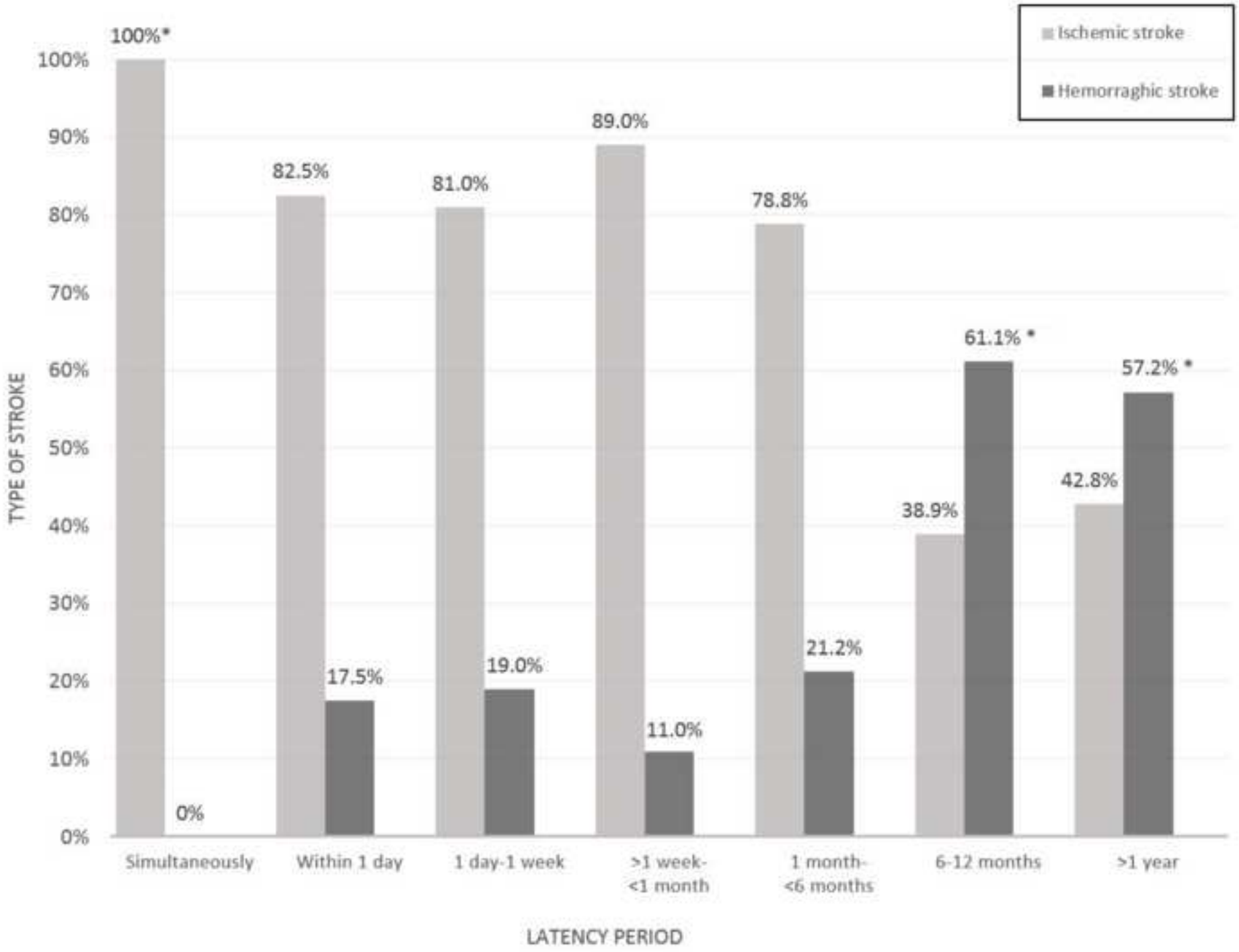

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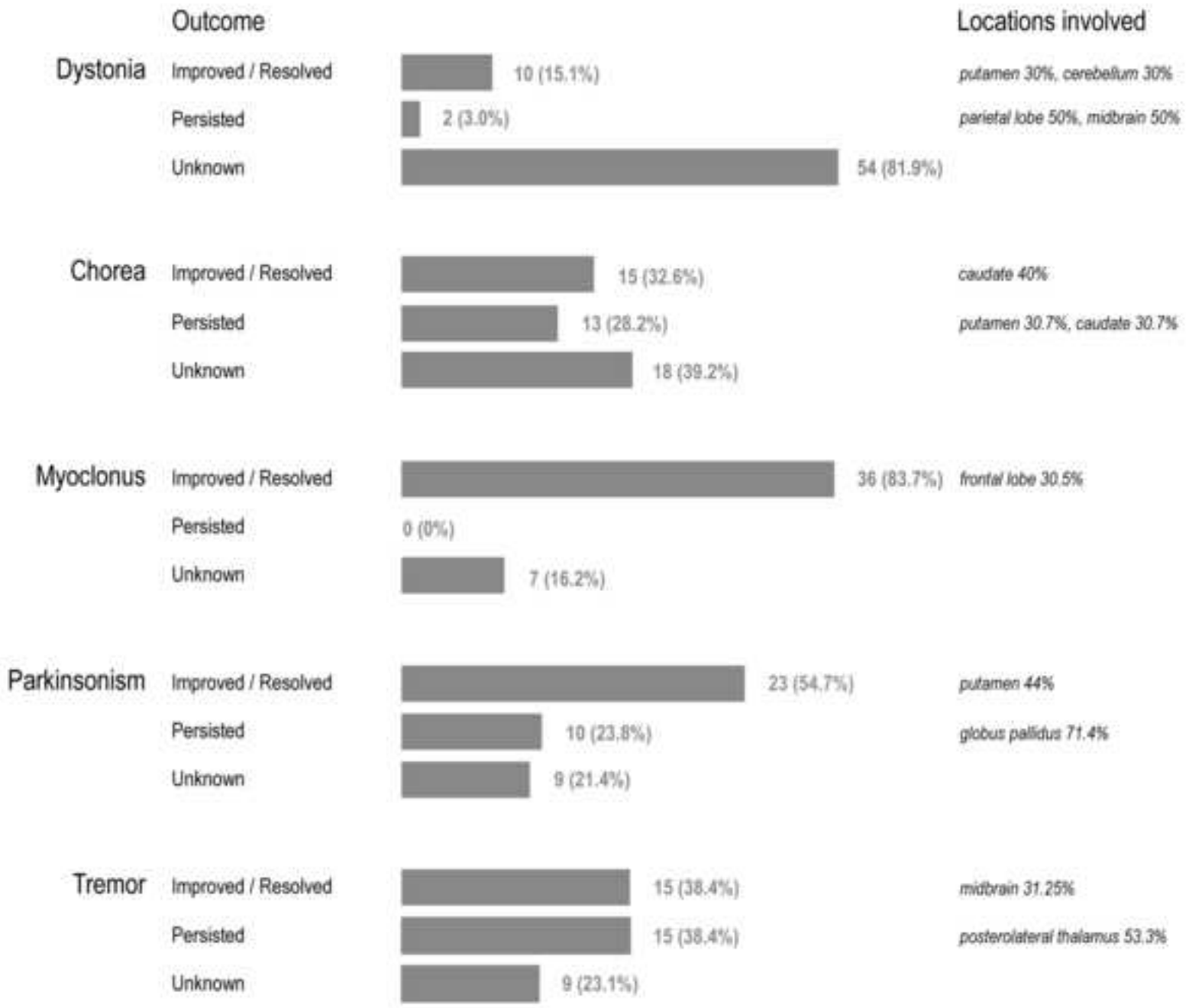

Table 1. General Characteristics of Post Stroke Movement Disorders

Movement Disorder	N (%)	Men affected, N (%)	Age Years (range)	Ischemic Cases N (%)	Hemorrhagic Cases N (%)	Most common Location N (%)
All	284	164 (57.7)	61.8 (18-93)	218 (76.7)	66 (23.2)	Posterolateral thalamus: 64 (22.5)
Dystonia	66 (23.2)	39 (40.9)	61.7 (37-76)	19 (28.7)	20 (30.3)	Posterolateral thalamus: 22 (66.6)
Chorea	46 (16.1)	25 (54.3)	61.72 (42-85)	19 (41.3)	6 (13.0)	Caudate: 5 (50)
Myoclonus	43 (15.1)	25 (58.1)	66.6 (47-83)	20 (46.5)	5 (11.6)	Frontal lobe: 9 (75)
Parkinsonism	42 (14.7)	26 (61.9)	60.7 (18-80)	25 (59.5)	1 (2.4)	Putamen: 9 (64.2)
Tremor	39 (13.7)	24 (61.5)	53.3 (18-76)	16 (41)	8 (20.5)	Midbrain: 6 (54.5)
Restless legs syndrome	20 (7.04)	7 (35.0)	65.2 (46-83)	7 (35)	0 (0)	Pons: 2 (28.5) Putamen: 1 (14.2)
Alien Hand syndrome	9 (3.1)	4 (44.4)	62.9 (25-83)	4 (44.4)	0 (0)	Parietal lobe: 2 (40)
Periodic Limb Movements	9 (3.1)	4 (44.4)	60.5 (53-75)	4 (44.4)	0 (0)	Pons: 3 (50)
Stereotypy	8 (2.8)	6 (75)	63.8 (40-93)	6 (75)	0 (0)	Putamen: 3 (37.5)
Akathisia	1 (0.35)	1 (100)	60 (N/A)	1 (100)	0 (0)	Posterior thalamus: 1 (100)
Tics	1 (0.35)	1 (100)	71 (N/A)	1 (100)	0 (0)	Caudate: 1 (100)

Table 2: Type of Stroke and Movement Disorders

Characteristics	**Entire Cohort**	**Ischemic**	**Hemorrhagic**	**p-value**
	N (%)	**N (%)**	**N (%)**	
Age (years)				**0.002**
<50	58(20.4)	42(19.3)	16(24.2)	
50-70	146(51.4)	104(47.7)	42(63.6)	
>70	80 (28.2)	72(33)	8(12.1)	
Gender				0.478
Male	164(57.7)	123(56.4)	41(62.1)	
Female	120(42.3)	95(43.6)	25(37.9)	
Movement disorders				
Dystonia	66(23.2)	36(16.5)	30(45.5)	**<0.001**
Tremor	39(13.7)	26(11.9)	13(19.7)	**<0.001**
Chorea	46(16.2)	38(17.4)	8(12.1)	0.346
Myoclonus	43(15.1)	33(15.1)	10(15.2)	1.000
Parkinsonism	42(14.8)	38(17.4)	4(6.1)	**0.028**
Restless leg syndrome	20(7)	20(9.2)	0(0)	**0.005**
Alien hand syndrome	9(3.2)	8(3.7)	1(1.5)	0.690
Periodic limb movements	9(3.2)	9(4.1)	0(0)	0.123
Stereotypy	8(2.8)	8(3.7)	0(0)	0.205
Akathisia	1(0.4)	1(0.5)	0(0)	1.000
Tics	1(0.4)	1(0.5)	0(0)	1.000
Latency				**<0.001**
Simultaneously	18(6.3)	18(8.3)	0(0)	
Within 1 day	40(14.1)	33(15.1)	7(10.6)	
1 day- 1 week	74(26.1)	60(27.5)	14(21.2)	
>1 week-< 1 month	18(6.3)	16(7.3)	2(3)	
1 month-< 6 months	33(11.6)	26(11.9)	7(10.6)	
6-12 months	18(6.3)	7(3.2)	11(16.7)	
>1 year	14(4.9)	6(2.8)	8(12.1)	
Unknown	69(24.3)	52(23.9)	17(25.8)	
Outcome				0.124
Spontaneously resolved or improved	85(29.9)	71(32.6)	14(21.2)	
improved with treatment	48(16.9)	39(17.9)	9(13.6)	
persisted	50(17.6)	38(17.4)	12(18.2)	
unknown	101(35.6)	70(32.1)	31(47)	

Supplementary table 1

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Supplementary table 2

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Supplementary table 3

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