

Milestone Events in Atypical Parkinsonian Syndromes: A Preliminary Observation

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Abstract

Background

Atypical parkinsonian syndromes (APS)—including progressive supranuclear palsy (PSP), multiple system atrophy (MSA), and dementia with Lewy bodies (DLB)—are rapidly progressive neurodegenerative disorders with distinct clinical trajectories. Milestone events such as recurrent falls, wheelchair dependence, dysphagia, and urinary dysfunction are critical for prognostic counseling and care planning, yet data on their timing across APS subtypes remain limited, particularly for DLB.

Methods

We retrospectively reviewed patients diagnosed with PSP, MSA, or DLB at the Department of Neurology, Aerospace Center Hospital, between September 2019 and June 2021. Six milestone events were assessed: severe urinary incontinence/retention, severe dysphagia, dysarthria, recurrent falls, need for walking assistance, and wheelchair dependence. The time origin was the date of disease onset; event timing was based on patient or caregiver recall. Given the small sample size, only descriptive statistics with exact 95% confidence intervals (Clopper-Pearson) were used.

Results

A total of 19 patients were included: 9 with PSP, 7 with MSA, and 3 with DLB. At least one milestone event occurred in 7/9 PSP (77.8%), 6/7 MSA (85.7%), and 3/3 DLB (100%) patients. The most common milestone was recurrent falls in PSP (66.7%) and DLB (100%), and need for walking assistance in MSA (85.7%). The median time to first milestone event was 2 years in PSP, 2.5 years in MSA, and 3 years in DLB. All three DLB patients experienced multiple milestones with recorded event times clustering at year 3.

Conclusions

These preliminary observations suggest distinct patterns of milestone events across APS subtypes, with DLB potentially characterized by a clustered onset of multiple functional milestones. Larger prospective studies are needed to validate these findings.

Background

Atypical parkinsonian syndromes (APS)—including progressive supranuclear palsy (PSP), multiple system atrophy (MSA), and dementia with Lewy bodies (DLB)—are a group of neurodegenerative disorders that share clinical features of parkinsonism but differ from Parkinson's disease (PD) in their underlying pathology, clinical course, and prognosis [1, 2]. While PD typically progresses slowly over

decades with a sustained response to dopaminergic therapy [3], APS are characterized by faster functional decline, poorer or transient response to levodopa, and significantly shorter survival [4]. PSP is characterized by early postural instability, vertical gaze palsy, and prominent bulbar dysfunction, with a median survival of 6–9 years after symptom onset [5]. A clinicopathological study of 24 patients with pathologically confirmed PSP reported that falls occurred early in the disease course and were a major contributor to morbidity [6]. MSA presents with autonomic failure, parkinsonism or cerebellar ataxia, and has a median survival of 7–10 years [7, 8]. Urinary dysfunction, particularly urinary retention and incontinence, is a hallmark of MSA and often precedes motor symptoms [9]. DLB is characterized by fluctuating cognition, visual hallucinations, and parkinsonism, with a highly variable prognosis and frequent falls [10]. Extrapyramidal signs, including rigidity and bradykinesia, are common in DLB and contribute to falls and functional decline [11].

Milestone events such as recurrent falls, need for walking assistance, wheelchair dependence, severe dysphagia, dysarthria, and severe urinary dysfunction mark critical transitions in the disease course and have profound implications for quality of life, caregiver burden, and healthcare resource utilization [12–14]. In PD, falls have been shown to be a major predictor of reduced quality of life and increased caregiver burden [15]. Understanding when these events occur is essential for prognostic counseling, care planning, and the design of clinical trials. While milestone events have been described in PSP and MSA [5, 7], data on DLB remain particularly scarce. Moreover, the temporal sequence of milestone events across APS subtypes has not been systematically compared.

To date, most studies on APS progression have been based on large prospective cohorts, such as the European MSA Study Group cohort for MSA and the Queen Square cohort for PSP [5, 7]. A meta-analysis of survival in pathologically proven MSA reported a median survival of 9.3 years from symptom onset [8]. These studies have provided valuable longitudinal data on survival and functional decline, but prospective studies require decades of follow-up, are costly, and may suffer from selection bias. Retrospective surveys, despite inherent limitations such as recall bias, can capture disease course information within a shorter timeframe and are particularly suitable for single-center settings with limited resources [16].

In PD, milestone events such as falls, dysphagia, and dementia have been systematically studied. The Sydney Multicenter Study reported that among 20-year survivors, 87% had experienced falls and 81% had moderate dysarthria [17]. A meta-analysis of six prospective studies reported that approximately 60% of PD patients experience at least one fall annually [18]. However, comparable data for APS are limited.

In this study, we report a preliminary observation of six milestone events in a single-center cohort of patients with PSP, MSA, and DLB. Our objectives were: (1) to characterize the incidence of six clinically meaningful milestone events across APS subtypes; (2) to estimate the timing of these events from disease onset; and (3) to generate hypotheses regarding differential progression patterns, particularly for DLB, that warrant validation in larger prospective cohorts.

Methods

Study design and participants

This was a single-center retrospective cohort study conducted at the Department of Neurology, Aerospace Center Hospital. Consecutive patients diagnosed with PSP, MSA, or DLB between September 2019 and June 2021 were reviewed. Diagnosis was based on established clinical criteria: PSP according to the NINDS-SPSP criteria [5], MSA according to the Gilman criteria [7], and DLB according to the McKeith criteria [10].

Data collection

Data were collected through medical record review and telephone or outpatient follow-up. The following variables were recorded: sex, age, education level (1 = primary or below, 2 = secondary, 3 = college or above), age at onset, disease duration, initial symptom (1 = tremor, 2 = bradykinesia/rigidity, 3 = mixed), affected body side (1 = left, 2 = right, 3 = bilateral, 4 = axial), Hoehn and Yahr (H-Y) stage (off-state), UPDRS-III score (on-state), UPDRS-IV score, MoCA, HAMA, HAMD, levodopa equivalent daily dose (LED) [19], and medication.

The UPDRS, MoCA, HAMA, and HAMD are previously published and widely validated instruments. The UPDRS was used as originally described [20]. Cognitive function was assessed using the MoCA [21]. Anxiety and depression were assessed using the HAMA [22] and HAMD [23], respectively. No new or adapted questionnaires were developed for this study.

Milestone events

Six milestone events were assessed

severe urinary incontinence/retention (defined as persistent urinary incontinence requiring pads or urinary retention requiring catheterization), severe dysphagia (defined as difficulty swallowing requiring dietary modification or tube feeding), dysarthria (defined as speech impairment affecting communication), recurrent falls (defined as ≥ 2 falls in the past year), need for walking assistance (defined as requiring a cane, walker, or assistance from another person for ambulation), and wheelchair dependence (defined as being unable to ambulate independently and requiring a wheelchair for mobility).

Time scale, event ascertainment, and censoring

The time origin was the date of disease onset. For each milestone event, the event time was defined as the interval from disease onset to the first occurrence of that event, as recalled by the patient or

caregiver. Patients who had not experienced the event at the time of survey were censored at the survey date.

Statistical analysis

Given the very small sample size, only descriptive statistics with exact 95% confidence intervals (Clopper-Pearson) were used. No formal comparisons were performed. All analyses were performed using R software version 4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

A total of 19 patients were included: 9 with PSP, 7 with MSA (3 MSA-P, 2 MSA-C, and 2 unspecified), and 3 with DLB. Baseline characteristics are summarized in Table 1. The median age at onset was 65 years (range 61–86) for PSP, 60 years (range 47–65) for MSA, and 74 years (range 73–82) for DLB. The median disease duration at survey was 5 years (range 3–7) for PSP, 3 years (range 2–5) for MSA, and 3 years for DLB. All patients presented with bradykinesia/rigidity as the initial symptom. The distribution of H-Y stages was: for PSP, 1 patient (11.1%) at stages 1–2.5 and 8 patients (88.9%) at stages 3–5; for MSA, 1 patient (14.3%) at stages 1–2.5 and 6 patients (85.7%) at stages 3–5; for DLB, all 3 patients (100%) at stages 3–5.

Table 1
Baseline characteristics of patients with PSP, MSA, and DLB.

Characteristic	PSP (n = 9)	MSA (n = 7)	DLB (n = 3)
Male, n (%)	4 (44.4%)	3 (42.9%)	1 (33.3%)
Age, years, median (range)	71 (67–90)	62 (47–70)	77 (76–85)
Age at onset, years, median (range)	65 (61–86)	60 (47–65)	74 (73–82)
Disease duration, years, median (range)	5 (3–7)	3 (2–5)	3 (3)
Education, n (%)			
Primary or below	1 (11.1%)	1 (14.3%)	1 (33.3%)
Secondary	5 (55.6%)	1 (14.3%)	1 (33.3%)
College or above	3 (33.3%)	5 (71.4%)	1 (33.3%)
Initial symptom, n (%)			
Bradykinesia/rigidity	9 (100%)	7 (100%)	3 (100%)
Affected body side, n (%)			
Right	1 (11.1%)	1 (14.3%)	0 (0%)
Bilateral	2 (22.2%)	2 (28.6%)	0 (0%)
Axial	1 (11.1%)	1 (14.3%)	1 (33.3%)
Missing	5 (55.6%)	3 (42.9%)	2 (66.7%)
H-Y stage, n (%)			
1–2.5	1 (11.1%)	1 (14.3%)	0 (0%)
3–5	8 (88.9%)	6 (85.7%)	3 (100%)
UPDRS-III, median (range)	46 (18–98)	48 (17–84)	65 (62–82)
MoCA, median (range)	16 (6–23)	19 (7–26)	3 (3–5)
HAMA, median (range)	7 (0–15)	14 (1–22)	4 (0–9)
HAMD, median (range)	6 (0–12)	12 (0–28)	5 (0–24)
LED, mg/day, median (range)	400 (200–800)	350 (100–691)	375 (200–550)
PSP, progressive supranuclear palsy; MSA, multiple system atrophy; DLB, dementia with Lewy bodies; H-Y, Hoehn and Yahr; UPDRS, Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment; HAMA, Hamilton Anxiety Rating Scale; HAMD, Hamilton Depression Rating Scale; LED, levodopa equivalent daily dose.			

Incidence of milestone events

At the time of survey, 7/9 PSP (77.8%, 95% CI 40.0–97.2), 6/7 MSA (85.7%, 95% CI 42.1–99.6), and 3/3 DLB (100%, 95% CI 29.2–100) patients had experienced at least one milestone event. Motor milestones (recurrent falls, need for walking assistance, or wheelchair dependence) occurred in 6/9 PSP (66.7%, 95% CI 29.9–92.5), 6/7 MSA (85.7%, 95% CI 42.1–99.6), and 3/3 DLB (100%, 95% CI 29.2–100). Non-motor milestones (urinary incontinence/retention, severe dysphagia, or dysarthria) occurred in 5/9 PSP (55.6%, 95% CI 21.2–86.3), 5/7 MSA (71.4%, 95% CI 29.0–96.3), and 2/3 DLB (66.7%, 95% CI 9.4–99.2).

The most common individual milestone was recurrent falls in PSP (6/9, 66.7%, 95% CI 29.9–92.5) and DLB (3/3, 100%, 95% CI 29.2–100), and need for walking assistance in MSA (6/7, 85.7%, 95% CI 42.1–99.6). Severe dysphagia occurred only in PSP (3/9, 33.3%, 95% CI 7.5–70.1) and was absent in MSA and DLB. Urinary incontinence/retention was present in 2/9 PSP (22.2%, 95% CI 2.8–60.0), 4/7 MSA (57.1%, 95% CI 18.4–90.1), and 2/3 DLB (66.7%, 95% CI 9.4–99.2). Wheelchair dependence occurred in 2/9 PSP (22.2%, 95% CI 2.8–60.0), 3/7 MSA (42.9%, 95% CI 9.9–81.6), and 2/3 DLB (66.7%, 95% CI 9.4–99.2). Detailed incidence and timing data are provided in Supplementary Table S1.

Time to milestone events

Median time from disease onset to each milestone event was calculated only for patients with complete timing data. In PSP, the median time to severe dysphagia was 4.5 years (range 4–5), to dysarthria 4.5 years (range 4–5), to recurrent falls 4 years (range 3–5), to walking assistance 3.5 years (range 2–6), and to wheelchair dependence 4.5 years (range 4–5). In MSA, the median time to walking assistance was 3.25 years (range 2–5), to recurrent falls 2 years (range 1.5–2), to urinary dysfunction 3.25 years (range 3–5), and to wheelchair dependence 4 years (range 4–5). In DLB, all recorded event times were at year 3: walking assistance in 3/3 patients and wheelchair dependence in 2/3 patients. Timing data were missing for some events despite documented occurrence (e.g., falls in all 3 DLB patients and 2/3 MSA patients), reflecting the inherent limitations of recall-based retrospective data collection.

DLB clustered progression

All three DLB patients experienced multiple milestones, with recorded event times clustering at year 3. Patient 1 developed walking assistance and wheelchair dependence at year 3, with urinary incontinence and falls also documented but without precise timing. Patient 2 developed walking assistance at year 3, with urinary incontinence and falls documented without timing. Patient 3 developed walking assistance and wheelchair dependence at year 3, with falls documented without timing. Although timing data were incomplete for some events, the available data suggest that DLB patients may experience a clustered onset of multiple functional milestones within a narrow time window, in contrast to the more gradual sequence observed in PSP and MSA (Fig. 1).

Composite endpoint analysis

When all six milestones were combined into a composite endpoint, the median time to first milestone event was 2 years (range 1–4) in PSP, 2.5 years (range 1.5–3) in MSA, and 3 years in DLB.

Event sequence analysis

The most common sequence in PSP was falls followed by walking assistance (3/9), whereas in MSA, urinary dysfunction preceded walking assistance in 3/7 patients. In DLB, all three patients experienced multiple events within the same year, precluding a clear sequential pattern.

Subgroup analysis of MSA

Among MSA patients, those with MSA-P ($n = 3$) more frequently experienced early falls (2/3), whereas MSA-C patients ($n = 2$) showed a higher burden of urinary dysfunction (2/2).

Discussion

In this small case series, we observed distinct patterns of milestone events across APS subtypes. PSP patients frequently experienced early falls and dysarthria, consistent with previous reports [5]. Litvan et al. reported that falls occurred early in the disease course and were a major contributor to morbidity in PSP [6]. In contrast, MSA patients showed a high burden of urinary dysfunction and walking assistance, with relatively preserved speech and swallowing. Sakakibara et al. reported that urinary dysfunction is a hallmark of MSA and often precedes motor symptoms [9]. DLB patients had a high rate of falls and walking assistance, but no dysphagia or dysarthria, which may reflect the shorter disease duration in this subgroup. Aarsland et al. reported that extrapyramidal signs, including rigidity and bradykinesia, are common in DLB and contribute to falls and functional decline [11]. The absence of dysphagia in our MSA and DLB patients contrasts with some prior studies [24], but may be due to the small sample size and short follow-up.

We hypothesize that DLB patients experience a clustered onset of multiple functional milestones, potentially reflecting a more widespread neuropathological burden. In contrast, PSP and MSA may follow a more sequential pattern. Future prospective studies should test whether the sequence of milestones differs between MSA-P and MSA-C and whether DLB has a distinct temporal profile.

Comparison with previous studies

Previous studies have reported milestone event timing in PSP and MSA, although direct comparisons are limited by differences in milestone definitions, follow-up duration, and study design. As shown in Table 2, our findings are broadly consistent with previously reported estimates. O'Sullivan et al. reported that falls occurred early in the course of PSP, with recurrent falls typically emerging within the first 2–3 years after disease onset, and dysphagia occurring in the advanced stage, approximately 4–5 years after onset [5]. In our PSP cohort, the median time to recurrent falls was 4 years (range 3–5), and to severe dysphagia 4.5 years (range 4–5), which is consistent with these observations. Nath et al. reported a median survival of 5.9 years from symptom onset in a clinical cohort of PSP, with falls and dysphagia being

major contributors to morbidity [25]. Our findings support the notion that falls and bulbar dysfunction are early and clinically significant milestones in PSP.

Table S1
Incidence and timing of milestone events in patients with PSP, MSA, and DLB.

Event	PSP (n = 9)	MSA (n = 7)	DLB (n = 3)
Urinary incontinence/retention			
n (%)	2 (22.2%)	4 (57.1%)	2 (66.7%)
Median time, years (range)	4.5 (4–5)	3.25 (3–5)	3 (3)
Severe dysphagia			
n (%)	3 (33.3%)	0 (0%)	0 (0%)
Median time, years (range)	4 (3–5)	—	—
Dysarthria			
n (%)	4 (44.4%)	2 (28.6%)	0 (0%)
Median time, years (range)	3.5 (1–5)	3.5 (3–4)	—
Recurrent falls			
n (%)	6 (66.7%)	3 (42.9%)	3 (100%)
Median time, years (range)	4 (3–5)	2 (1.5–2)	3 (3)
Need for walking assistance			
n (%)	6 (66.7%)	6 (85.7%)	3 (100%)
Median time, years (range)	3.5 (2–6)	3.25 (2–5)	3 (3)
Wheelchair dependence			
n (%)	2 (22.2%)	3 (42.9%)	2 (66.7%)
Median time, years (range)	4.5 (4–5)	4 (4–5)	3 (3)
Data are n (%) / median time from disease onset (years).			
PSP, progressive supranuclear palsy; MSA, multiple system atrophy; DLB, dementia with Lewy bodies. Timing data were missing for some events despite documented occurrence (e.g., falls in all 3 DLB patients and 2/3 MSA patients).			

Table 2
Comparison of milestone event timing with previous studies.

Event	Present study, median (range), years	O'Sullivan 2008 [5]	Wenning 2013 [7]
PSP recurrent falls	4 (3–5)	~ 2–3	—
PSP dysphagia	4.5 (4–5)	~ 4–5	—
MSA walking assistance	3.25 (2–5)	—	~ 3–4
MSA urinary dysfunction	3.25 (3–5)	—	~ 3–5
PSP, progressive supranuclear palsy; MSA, multiple system atrophy. Data are median time from disease onset in years. Dashes indicate data not reported. Approximate values (~) are estimated from published survival curves or reported ranges.			

In MSA, Wenning et al. reported that walking assistance was typically required approximately 3–4 years after disease onset, and urinary dysfunction occurred approximately 3–5 years after onset [7]. Our MSA cohort showed a median time to walking assistance of 3.25 years (range 2–5) and to urinary dysfunction of 3.25 years (range 3–5), which is consistent with these estimates. Ben-Shlomo et al. reported a median survival of 9.3 years from symptom onset in pathologically proven MSA, with autonomic failure and motor impairment being the predominant drivers of disability [8]. Sakakibara et al. further demonstrated that urinary dysfunction, particularly urinary retention and incontinence, is a hallmark of MSA and often precedes motor symptoms [9]. These observations are consistent with the high burden of urinary dysfunction observed in our MSA patients.

For DLB, comparable data on milestone event timing are scarce. To our knowledge, this is among the first reports describing the temporal sequence of functional milestones in DLB. Ballard et al. reported that psychiatric morbidity, including visual hallucinations and cognitive fluctuations, is common in DLB and may contribute to functional decline [26]. Aarsland et al. reported that extrapyramidal signs, including rigidity and bradykinesia, are common in DLB and contribute to falls and functional decline [11]. Our observation of clustered milestones at year 3 may represent a distinct progression pattern in DLB that warrants validation in larger prospective cohorts.

Comparison with Parkinson's disease

Compared with PD, APS patients in our cohort experienced milestone events much earlier. A recent study of 3,343 patients with PD reported that approximately 35% developed motor fluctuations and 18.5% developed dyskinesia at 4–6 years after disease onset [27]. Hely et al. reported that among 20-year survivors with PD, 87% had experienced falls and 81% had moderate dysarthria [17]. In contrast, our APS patients frequently experienced recurrent falls and walking assistance within 2–4 years of disease onset. Pickering et al. reported that approximately 60% of PD patients experience at least one fall

annually [18]. This difference is consistent with the more aggressive nature of APS and underscores the importance of early recognition and proactive care planning in these patients.

A recent study using the PPMI database identified two distinct progression subtypes in early PD: slow progression (83%) and rapid progression (17%), with the rapid subtype experiencing more and earlier-onset milestones within 6 years [28]. Our APS cohort experienced milestones even earlier than the rapid progression PD subtype, further highlighting the aggressive nature of APS. Zhao et al. reported that the median time from H-Y stage 1 to 2 was 20 months and from stage 2 to 2.5 was 62 months in PD [29]. These early-stage transitions occur within the first few years after disease onset, whereas the milestone events assessed in our study represent more advanced functional milestones and occurred much later in APS.

DLB clustered progression: possible mechanisms

The clustered onset of multiple milestones in our three DLB patients may reflect the widespread distribution of Lewy body pathology in this disorder. Unlike PSP, in which pathology predominantly involves the brainstem and basal ganglia, and MSA, in which pathology primarily affects the striatonigral and olivopontocerebellar systems, DLB is characterized by diffuse cortical and subcortical Lewy body deposition [10]. Ballard et al. reported that psychiatric morbidity, including visual hallucinations and cognitive fluctuations, is common in DLB and may contribute to functional decline [29]. This widespread neuropathological burden could lead to simultaneous impairment of multiple functional domains—motor, autonomic, and bulbar—resulting in a more compressed timeline of milestone events. However, given the very small number of DLB patients in our cohort, this hypothesis must be interpreted with caution and warrants validation in larger prospective studies.

In contrast to the gradual sequence observed in PSP and MSA, where milestone events tended to occur in a stepwise fashion over several years, the DLB patients in our cohort experienced multiple events within the same year (year 3). This difference may have clinical implications: whereas PSP and MSA patients may have time to adapt to each functional decline, DLB patients may require more rapid and comprehensive care planning.

Clinical implications

If confirmed, the clustered progression pattern in DLB would suggest that clinicians should consider early multidisciplinary assessment and proactive care planning immediately after diagnosis, rather than waiting for individual milestones to occur. For example, early involvement of physiotherapy, speech therapy, and occupational therapy may help mitigate the impact of simultaneous functional decline. Additionally, caregivers of DLB patients may need more intensive support during the period when multiple milestones occur.

The quantified incidence and timing of milestone events also has implications for prognostic counseling. For example, our data suggest that approximately 2 in 3 PSP patients may experience recurrent falls within 4 years of disease onset, and that approximately 1 in 4 patients with APS may require walking

assistance within 2–4 years. These estimates can help patients and families anticipate future care needs and make informed decisions about advance care planning. In PD, falls have been shown to be a major predictor of reduced quality of life and increased caregiver burden [15, 30]. Similar studies in APS are warranted to quantify the impact of milestone events on caregivers and healthcare systems.

Limitations

Our study has several limitations. First, the sample size is very small (19 patients), limiting statistical power and precluding formal comparisons. Second, the retrospective design is subject to recall bias. Third, the single-center setting limits generalizability. Fourth, the follow-up duration was short (median 3–5 years), which may underestimate the cumulative incidence of milestone events. Fifth, the absence of a control group (e.g., Parkinson's disease) limits interpretation. Sixth, DLB was represented by only 3 patients, and the clustered phenomenon may be coincidental. Seventh, timing data were missing for some events despite documented occurrence, further limiting the precision of our estimates. Eighth, the retrospective survey design could not capture patients who died before the survey, potentially introducing survival bias. These findings should be considered exploratory and hypothesis-generating. Larger prospective studies are needed to validate the differential timing of milestone events across APS subtypes.

Future directions

Future prospective, multicenter cohort studies with long-term follow-up are needed to validate our findings. Specifically, studies should aim to: (1) confirm whether DLB is characterized by a clustered onset of multiple functional milestones; (2) determine whether the sequence of milestones differs between MSA-P and MSA-C; (3) explore biomarkers that predict milestone event timing; and (4) develop clinical prediction models incorporating baseline characteristics to estimate individual-level milestone event timing.

Conclusions

These preliminary observations suggest distinct patterns of milestone events across APS subtypes, with DLB potentially characterized by a clustered onset of multiple functional milestones. Larger prospective studies are needed to validate these findings.

Abbreviations

APS

Atypical parkinsonian syndromes

PSP

Progressive supranuclear palsy

MSA

Multiple system atrophy

DLB

Dementia with Lewy bodies

CI

Confidence interval

H-Y

Hoehn and Yahr

UPDRS

Unified Parkinson's Disease Rating Scale

MoCA

Montreal Cognitive Assessment

HAMA

Hamilton Anxiety Rating Scale

HAMD

Hamilton Depression Rating Scale

LED

Levodopa equivalent daily dose

Declarations

Ethics approval and consent to participate:

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Aerospace Center Hospital (approval number: 20190614- SF- 06). Written informed consent was obtained from all participants or their legal guardians.

Consent for publication:

Not applicable. Not applicable. This manuscript does not contain any individual person's data in any form.

Consent to participate:

Written informed consent was obtained from all participants or their legal guardians.

Competing interests:

The authors declare that they have no competing interests.

Authors' contributions

LZ, ZW and JD conceived and designed the study. LZ, ZW, JL and JD acquired the data. LZ and JL performed the statistical analysis. LZ and ZW drafted the manuscript. JD and ZW critically revised the

manuscript for important intellectual content. All authors read and approved the final manuscript.

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Author Contribution

LZ, ZW and JD conceived and designed the study. LZ, ZW, JL and JD acquired the data. LZ and JL performed the statistical analysis. LZ and ZW drafted the manuscript. JD and ZW critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Not applicable.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

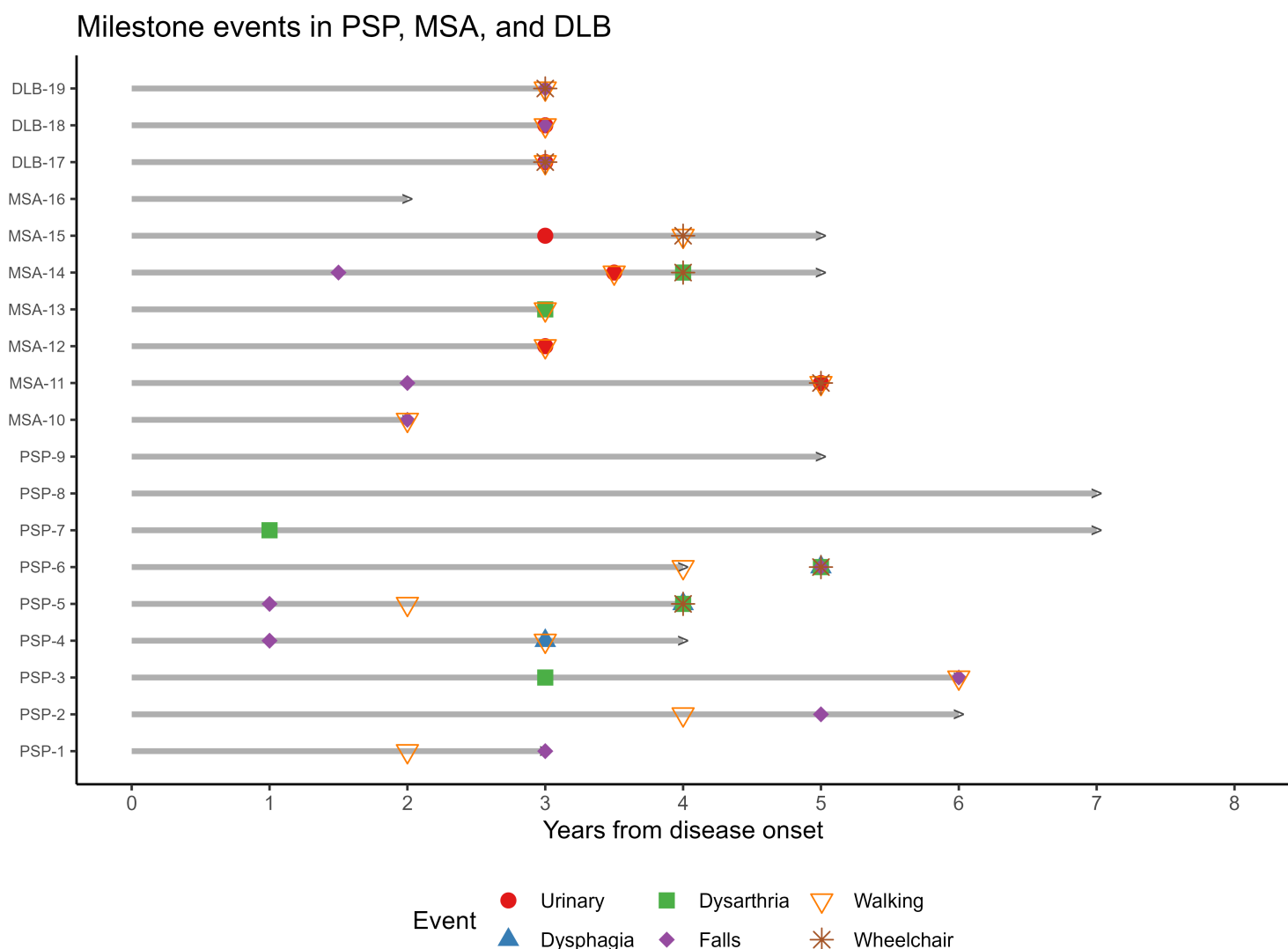


Figure 1

Swimmer plot of milestone events in patients with PSP, MSA, and DLB. Each horizontal bar represents one patient. Symbols indicate the time from disease onset to each milestone event: urinary incontinence/retention (red circle), severe dysphagia (blue triangle), dysarthria (green square), recurrent falls (purple diamond), need for walking assistance (orange inverted triangle), and wheelchair dependence (star). Arrows indicate censoring at the survey date. DLB patients showed a cluster of multiple events within the same year, whereas PSP and MSA patients exhibited a more gradual sequence.

Detailed incidence and timing data are reported in Supplementary Table S1.