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MOTOR PHENOTYPE TRANSITIONS IN PARKINSON'S DISEASE AND THEIR ASSOCIATION WITH COGNITIVE DECLINE: A NARRATIVE REVIEW

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Abstract. Parkinson's disease is clinically heterogeneous, with variation in motor manifestations and cognitive outcomes. This narrative review synthesises evidence on the classification of motor phenotypes, their longitudinal stability, factors associated with transitions between subtypes, and the potential relationship between such transitions and cognitive decline. The literature indicates that phenotype classification may change over time and that the postural instability and gait difficulty phenotype is associated with less favourable cognitive outcomes. However, evidence that subtype transition itself independently predicts cognitive decline remains limited and heterogeneous. Longitudinal studies with standardised repeated assessment of motor phenotypes and cognitive outcomes are needed to clarify its prognostic value.
Keywords: Parkinson's disease, motor phenotypes, tremor-dominant, postural instability and gait difficulty, cognitive decline, dementia.

Parkinson's disease (PD) is a progressive neurodegenerative disorder defined by motor dysfunction, including bradykinesia, rigidity, and resting tremor, which can impair daily functioning. In addition to motor manifestations, patients may experience a broad range of non-motor symptoms, including cognitive impairment, autonomic dysfunction, sleep disturbances, and neuropsychiatric symptoms (Postuma et al., 2015). However, the clinical course of PD is highly heterogeneous, with considerable interindividual variation in the onset, severity, and progression of both motor and non-motor manifestations (Greenland et al. (2019), Mestre et al. (2021)). This heterogeneity in symptom profiles and severity presents challenges for accurate prognostic assessment of disease progression (Greenland et al., 2019). Consequently, efforts to develop and refine subtyping methods to characterise clinical heterogeneity among patients with Parkinson's disease (PD) have become an important focus of research.

The most widely used clinical classification of Parkinson's disease (PD) motor phenotypes distinguishes tremor-dominant (TD) and postural instability and gait difficulty (PIGD) subtypes. Early work by Zetusky et al. (1985) described the clinical and prognostic heterogeneity of PD, while Jankovic et al. (1990) operationalised the classification using the relative scores of tremor and gait/balance items on the Unified Parkinson's Disease Rating Scale (UPDRS). Patients who meet neither the TD nor the PIGD criteria are classified as indeterminate.

Although motor subtypes in Parkinson's disease (PD) are defined primarily by motor symptom profiles, these classifications have also been used to investigate differences in disease progression and cognitive outcomes. Evidence suggests that the tremor-dominant (TD) subtype is associated with relatively preserved cognitive function, whereas postural instability and gait difficulty (PIGD) and related gait-predominant phenotypes are associated with greater cognitive impairment (Child et al., 2026). However, traditional motor subtypes show limited longitudinal stability, with patients frequently transitioning between categories as the disease progresses (von Coelln et al., 2021). These limitations have prompted interest in broader classification approaches that incorporate cognitive, autonomic, and sleep-related features alongside motor symptoms (Johansson et al., 2023).

An other limitation is that phenotype is typically assigned at baseline, and then treated as a stable characteristic. Yet the phenotype is computed from continuous scores that change as the disease progresses, with treatment, and with day-to-day variability. A patient classified as TD at one visit may meet PIGD criteria at a later visit (Alves et al., 2006; Simuni et al., 2016; Eisinger et al., 2017). It is unclear whether such change represents clinical progression, treatment effects, measurement variability, or a mixture of these. Treatment-related changes in tremor and gait/balance scores may also contribute to subtype transitions, particularly in moderate-to-advanced disease. Nevertheless, dopaminergic treatment does not appear to explain all observed transitions, suggesting that disease progression and classification variability may also contribute (Motor phenotype classification in moderate to advanced PD in BioFIND study, 2019; Simuni et al., 2016).

There may be a relationship between cognitive changes and subtype transitions, as recent studies have identified more rapid MMSE decline among patients who transitioned from TD to PIGD (D'Souza et al., 2025; Child et al., 2024).

The aim of this review is to critically synthesise the evidence on (i) how motor subtypes are defined, (ii) how stable they are over time, (iii) what patterns and correlates of transition have been described, and (iv) what is known about the relationship between transition and cognitive outcomes. We also identify the questions that a subsequent systematic review and meta-analysis would need to address.

2. Literature Search Approach

This is a narrative review and does not claim to be exhaustive or to follow a systematic review protocol. Literature was identified through searches of PubMed/MEDLINE, Scopus, and Web of Science, supplemented by reference-list searching of key articles and prior reviews. The final search was conducted on 10.10.2026. Representative search terms combined concepts for Parkinson's disease ("Parkinson disease"), motor phenotype ("tremor-dominant", "postural instability gait difficulty", "PIGD", "motor subtype", "phenotype"), change over time ("transition", "conversion", "stability", "longitudinal"), and cognitive outcomes ("cognitive decline", "mild cognitive impairment", "dementia").

The review drew on longitudinal cohort studies, cross-sectional studies where they informed classification or mechanisms, methodological papers on motor-subtype algorithms, and previous reviews. Findings were organised thematically and compared with attention to study design, classification method, follow-up duration, and cognitive endpoint. Study selection and data extraction were not performed in duplicate and no formal risk-of-bias assessment was undertaken; conclusions should therefore be read as an interpretive synthesis, not a pooled estimate.

3. Motor-Subtype Classification in Parkinson's Disease

3.1 Established phenotypes

The most common distinctions among Parkinson’s disease (PD) motor subtypes are tremor-dominant (TD) and postural instability and gait difficulty (PIGD). TD patients typically present with rest tremor as the primary feature, show slower disease progression, and demonstrate a more favorable response to levodopa. By contrast, PIGD patients exhibit axial symptoms such as gait disturbance, reduced arm swing, postural instability, and balance impairment early in the disease course. These symptoms are frequently accompanied by a higher non-motor burden, including autonomic dysfunction, depression, and cognitive impairment (Ren et al., 2020; Gong et al., 2023). A third phenotype, akinetic-rigid (AR), is characterized predominantly by bradykinesia and rigidity (Marras et al., 2020).

3.2 How subtypes are operationalised

Comparing PD subtypes and evaluating the effects of DBS require outcome measures that are both clinically valid and standardized. The most widely used tool is the Unified Parkinson's Disease Rating Scale (UPDRS), developed in the 1980s to comprehensively assess motor and non-motor symptoms in PD. The original UPDRS includes 42 items across four sections: Part I (Mentation, Behavior, and Mood; 4 items), Part II (Activities of Daily Living; 13 items), Part III (Motor Examination; 14 items scored bilaterally, yielding 27 ratings), and Part IV (Complications of Therapy; 11 items). Parts I–III employ a five-point ordinal scale (0 = normal, 4 = severe), while Part IV combines dichotomous and 0–4 item scales (Movement Disorder Society Task Force, 2003; Martinez-Martin et al., 2006). There is also a revised version, the MDS-UPDRS, designed to enhance sensitivity; however, most studies report results using the original scale (Goetz et al., 2008).

Part III is particularly relevant for motor subtype classification as it encompasses tremor, rigidity, bradykinesia, and axial symptoms. Several classification algorithms have been derived from these items. Lewis et al. (2005) first defined TD, AR, and mixed (MX) phenotypes, while Stebbins et al. (2013) refined this approach using a tremor/PIGD ratio derived from UPDRS Parts II and III. Patients with a ratio >1.15 are classified as TD, those with a ratio <0.90 as PIGD, and those in between as indeterminate. This algorithm has since been widely applied in both clinical and surgical research.

3.3 Factors influencing classification

Several factors affect which label a patient receives, independent of any underlying biological change. Medication state matters because tremor and axial signs respond differently to dopaminergic therapy, so ON and OFF assessments can yield different classifications. Disease duration and severity matter because axial features tend to accumulate with advancing disease. The timing of assessment relative to medication dose, interrater variability, missing items, and the particular algorithm and thresholds chosen also contribute (Stebbins et al., 2013; Vu et al., 2012).

3.4 Limitations of categorical phenotypes

One of the limitations is that categorical phenotypes can switch from one to another during longitudinal follow-up. For example, studies using the PPMI cohort have reported substantial changes in phenotype classification, with some patients initially classified as TD later meeting the criteria for PIGD or an indeterminate phenotype (Simuni et al., 2016; von Coelln et al., 2021). Secondly, medication may have a confounding effect, as phenotypes may look different during an "OFF" state compared with an "ON" state. Dopaminergic treatment can alter the motor scores used to assign phenotypes, potentially masking the natural progression of the disease (Mestre et al., 2019). However, treatment does not explain all transitions, as changes in phenotype have also been observed in untreated patients (Simuni et al., 2016). This suggests that subtype transitions may reflect a combination of disease progression, treatment effects, and variability in clinical assessment.

Another limitation is that these classifications rely mainly on motor features and may not fully capture the broader clinical heterogeneity of PD. Patients assigned to the same motor phenotype may differ considerably in their cognitive function, autonomic symptoms, sleep disturbances, and other non-motor manifestations. Consequently, motor phenotypes alone may not adequately represent the different clinical trajectories of patients (Tan et al., 2025; Rigon et al., 2026). Furthermore, traditional motor subtypes do not necessarily correspond to distinct underlying biological mechanisms. Recent reviews have therefore highlighted the need for classification approaches that integrate clinical features with imaging, genetic, and other biological markers to

improve prognostic accuracy and support more individualised treatment strategies (Tan et al., 2025; Rigon et al., 2026).

Table 1.

Common approaches to motor-subtype classification and key limitations

Approach	Basis	Main strengths	Main limitations
Original UPDRS tremor/PIGD ratio (Jankovic et al., 1990)	Ratio of mean tremor to mean PIGD items	Long history; most prior literature uses it	Classification depends on selected UPDRS items and may change over time
MDS-UPDRS-adapted ratio (Stebbins et al., 2013)	Re-derived items and cut-offs for MDS-UPDRS	Adapted and evaluated for use with the revised scale;	Not interchangeable with UPDRS results; ON/OFF dependence
Alternative categorical schemes (TD/AR/mixed) (e.g., Schiess et al., 2000; Eggers et al., 2011)	Clinical judgement or score patterns	Captures alternative motor presentations and allows comparisons using different operational definitions	Less standardized; AR and PIGD are related but not equivalent labels; classifications may disagree across algorithms
Data-driven and multidomain subtypes (e.g., Fereshtehnejad et al., 2017; Campbell et al., 2020)	Statistical clustering or composite motor and non-motor features	Incorporates non-motor burden	Requires large datasets; less transferable to routine clinics

4. Longitudinal Stability and Motor-Subtype Transitions

4.1 Evidence for stability and change

Longitudinal studies suggest that Parkinson's disease (PD) motor-subtype classifications are unstable over time, although the extent of change depends on the classification method and follow-up duration. In a Norwegian community-based cohort of 171 patients followed for eight years, Alves et al. (2006) found that transitions from tremor-dominant (TD) or indeterminate subtypes to postural instability and gait difficulty (PIGD) were associated with accelerated cognitive decline and substantially increased odds of incident dementia. In the Parkinson's Progression Markers Initiative (PPMI) cohort, Simuni et al. (2016) reported that, among patients with subtype data at baseline and 12 months, 18% initially classified as TD and 39% initially classified as PIGD changed subtype during follow-up. Longer-term evidence from von Coelln et al. (2021) further demonstrated algorithm-dependent instability: among 178 patients reassessed after a mean of 6.2 years, only 15–36% of those initially classified as TD retained this classification, while 46–50% transitioned to PIGD/akinetic-rigid. These findings indicate that motor-subtype assignments are not necessarily stable longitudinal characteristics. However, differences in classification algorithms, cohort characteristics, assessment schedules, and follow-up duration limit direct comparisons between studies.

4.2 Patterns of transition

The most frequently described movement is from TD or indeterminate towards PIGD as the disease advances, consistent with accumulating axial dysfunction (Alves et al., 2006; Eisinger et al., 2017). Transitions in the opposite direction, and from indeterminate to a defined subtype, are also reported, which is expected if part of the instability reflects measurement variability and medication effects. Pasquini et al. (2018) showed that tremor itself evolves in early PD, which complicates the interpretation of a decline in tremor-dominance as improvement. A longstanding clinicopathological study suggested that subtype can shift over very long disease courses (Rajput et al., 2009). Importantly, transitions should not be assumed to be equally common or equally meaningful; their frequency and direction must be established from the underlying studies.

4.3 Factors associated with transition

Reported correlates of transition include longer disease duration, older age, greater baseline motor severity, and treatment exposure, although much of the evidence is exploratory and some proposed predictors are authors' hypotheses rather than longitudinally demonstrated findings (Nutt, 2016; Eisinger et al., 2017). Distinguishing demonstrated predictors from speculative ones is an important task for future syntheses.

4.4 Biological progression versus measurement artefact

Genuine worsening of gait and postural stability is expected with disease progression, and axial features are relatively resistant to dopaminergic treatment (Vu et al., 2012). Nutt (2016) proposed that many patients move along a continuum from tremor-predominant to PIGD-predominant presentations. At the same time, artefacts arise from scale choice, cut-offs, medication state, and regression to the mean. These two explanations are not mutually exclusive, and studies rarely attempt to separate them, for example by modelling continuous scores alongside categorical transitions.

4.5 Implications for prognostic research

If phenotype changes, studies that use only a baseline label may misclassify patients' subsequent course, and the association between PIGD and poor outcomes could be partly attributable to patients who become PIGD later. Repeated phenotype assessment may therefore contain prognostic information not captured by baseline classification, but this requires direct empirical testing rather than assumption.

5. Motor-Subtype Transitions and Cognitive Progression

5.1 Baseline motor phenotype and cognition

A considerable body of work, both cross-sectional and longitudinal, links the PIGD phenotype with worse cognition and a higher risk of dementia. Burn et al. (2006) found that PIGD patients showed greater cognitive decline than TD patients, and the CamPaIGN cohort identified axial motor features and certain cognitive profiles as predictors of dementia (Williams-Gray et al., 2009). Kelly et al. (2015) reported associations between specific cognitive domains and PIGD features. Cross-sectional associations do not establish that a patient who later acquires PIGD features will subsequently decline cognitively, which is the distinct question of interest here.

5.2 Cognitive decline following phenotype transition

The most directly relevant evidence comes from Alves et al. (2006), who examined changes in motor subtype and the risk of incident dementia in a long-term cohort and reported an association between subtype change and dementia risk. Beyond this, studies that repeatedly classify subtype and then model later cognitive outcomes (global scores, incident PD-MCI, and dementia as separate endpoints) appear limited. Because different cognitive endpoints measure different

constructs, they should be analysed separately in future work (Litvan et al., 2012; Emre et al., 2007).

5.3 Temporal sequence and predictive value

Whether a transition precedes, coincides with, or follows cognitive decline determines whether it has prognostic value or is merely a concurrent marker. If both are driven by the same progressing pathology and are measured at the same visit, transition would be a correlate and not a predictor. Studies designed with a clear temporal ordering, in which transition is documented before the cognitive endpoint is ascertained, are needed.

5.4 Potential mechanisms

Several hypotheses link axial motor decline and cognition. Cholinergic denervation, including pedunculopontine and basal forebrain pathways, has been associated with falls, gait impairment, and attentional deficits (Bohnen & Albin, 2011; Yarnall et al., 2011; Bohnen et al., 2012). Gait control also depends on executive and attentional resources, producing gait-cognition interactions (Amboni et al., 2013). Kehagia et al. (2010) described distinct cognitive syndromes in PD, with frontostriatal (dopaminergic) and posterior cortical (more cholinergic/Lewy-body-related) contributions. These mechanisms are best regarded as hypotheses, as direct evidence that transition itself is mechanistically linked to cognitive decline is lacking.

5.5 Confounding and alternative explanations

Age, education, disease duration, baseline cognition, baseline motor severity, depression, medication exposure, and attrition may all influence both motor change and cognitive outcome. Older age and longer disease duration, for instance, increase the risk of both axial motor progression and dementia (Hely et al., 2008). Unadjusted associations may therefore exaggerate the contribution of transition, whereas overadjustment for motor severity may obscure it. Differential loss to follow-up, in which patients with the poorest outcomes drop out, is a further source of bias in long-term cohorts.

Table 2.

Illustrative studies of Parkinson's disease motor-subtype classification, longitudinal stability, and cognitive outcomes

Study	Design and population	Subtype assessment	Relevant finding
Jankovic et al. (1990)	Baseline analysis of 800 patients with early, untreated PD in the DATATOP cohort	Clinical motor heterogeneity and UPDRS-derived classification	Found substantial clinical heterogeneity in early PD; provides foundational context for motor-subtype classification but does not establish longitudinal stability.
Burn et al. (2006)	Two-year longitudinal study of PD (n = 40), PDD (n = 42), DLB (n = 41), and age-matched controls (n = 41)	Baseline motor subtype, with subsequent assessment of motor and cognitive changes	Among patients with PD, dementia developed in 4/16 initially classified as PIGD versus 0/18 initially classified as TD, supporting an association between baseline PIGD phenotype and cognitive deterioration.
Alves et al. (2006)	Community-based cohort of 171 initially	Repeated TD, indeterminate, and	Transition from TD or indeterminate to PIGD was

	nondemented patients with PD; assessments at baseline, 4 years, and 8 years	PIGD classification using UPDRS items	associated with more than threefold faster MMSE decline and increased odds of dementia; estimates were imprecise, with wide confidence intervals.
Williams-Gray et al. (2009)	Five-year follow-up of 126 incident PD cases in the CamPaIGN cohort	Baseline cognitive and neuropsychological measures; not a direct longitudinal motor-subtype transition analysis	Baseline age and specific cognitive deficits, including impaired semantic fluency and visuospatial performance, predicted dementia. Provides contextual evidence about cognitive prognosis rather than direct evidence of motor-subtype instability.
Simuni et al. (2016)	One-year longitudinal analysis of 320 participants with available baseline and 12-month subtype data from the PPMI de novo cohort	Repeated TD, PIGD, and indeterminate classification using an established UPDRS-derived algorithm	At 12 months, 39% of baseline PIGD and 18% of baseline TD participants changed subtype. Dopaminergic treatment did not explain the observed changes.
Eisinger et al. (2017)	Longitudinal analysis of 423 newly diagnosed PD participants from PPMI	Data-driven hierarchical clustering identifying five motor subtypes across repeated assessments	Demonstrated that motor-subtype assignments can change over disease duration, supporting the need to account for longitudinal instability and classification methodology.
Aleksovski et al. (2018)	Four-year longitudinal analysis of PPMI participants consistently classified as TD or PIGD at every assessment; 254 participants in the analysis	Repeated TD/PIGD classification, with inclusion restricted to patients retaining their subtype	PIGD patients showed faster progression in selected non-motor features, including cognitive impairment, hallucinations, and psychosis-related symptoms. Because unstable classifications were excluded, the study does not directly quantify subtype transitions.

Abbreviations: DATATOP, Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism; DLB, dementia with Lewy bodies; MMSE, Mini-Mental State Examination; PD, Parkinson's disease; PDD, Parkinson's disease dementia; PIGD, postural instability and gait difficulty; PPMI, Parkinson's Progression Markers Initiative; TD, tremor-dominant; UPDRS, Unified Parkinson's Disease Rating Scale.

6. Discussion

6.1 Principal findings

The available literature supports three main points. First, motor subtype is not fixed: classification changes over time in a meaningful proportion of patients, with a tendency towards PIGD as the disease advances. Second, baseline PIGD is consistently associated with worse cognitive outcomes. Third, evidence that change in motor subtype itself carries prognostic information for cognition is much thinner, resting largely on a small number of longitudinal cohorts.

6.2 Why findings may disagree

Differences between studies likely reflect heterogeneity in populations (de novo versus established PD, disease duration), classification algorithms and thresholds, medication state during assessment, follow-up length, cognitive instruments (screening tests versus full neuropsychological batteries), and statistical adjustment. Studies in early, untreated cohorts will observe different transition dynamics from those in advanced disease.

6.3 Methodological weaknesses

Recurring limitations include small cohorts, attrition, inconsistent subtype definitions, few repeated assessments, incomplete confounder adjustment, and limited domain-specific cognitive testing. Many analyses are descriptive and do not estimate adjusted prognostic effects.

6.4 The unresolved question

It remains uncertain whether longitudinal motor-subtype transition provides prognostic information about cognitive decline beyond baseline phenotype and established clinical risk factors. Existing evidence is suggestive but limited and heterogeneous. Before a research gap is formally declared, the relevant prior studies and reviews should be re-checked to ensure that recent publications have not already addressed this question.

6.5 Future research

Future longitudinal studies should use standardised classification at fixed intervals, report both categorical transitions and continuous score changes, document medication state, ensure that transition precedes ascertainment of cognitive outcomes, and adjust for key confounders. A subsequent systematic review and meta-analysis with a prespecified protocol could estimate transition rates, clarify temporal relationships, pool adjusted associations where data allow, and test whether repeated classification adds value over baseline subtype alone.

7. Conclusion

Motor phenotype in Parkinson's disease is better conceptualised as a dynamic clinical state than a permanent trait. Baseline PIGD is associated with worse cognitive outcomes, and subtype change has been linked to dementia risk in at least one long-term cohort, but whether transition independently predicts cognitive decline remains unresolved. Clarifying this question will require repeated, standardised motor assessment, careful handling of classification artefacts and confounding, and a rigorous systematic synthesis.

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