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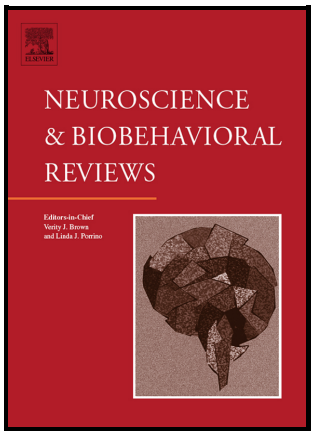

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Cognition and Freezing of Gait in Parkinson's Disease: A Systematic Review and Meta-Analysis

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Abstract

Freezing of gait (FOG) is a common and disabling symptom in people with Parkinson's Disease (PwPD). Although cognition is thought to be worse in PwPD who freeze, a comprehensive analysis of this relationship will inform future research and clinical care. This systematic review and meta-analysis compared cognition between PwPD who do and do not exhibit FOG across a range of cognitive domains and assessed the impact of disease severity and medication status on this relationship. 145 papers (n=9010 participants) were included in the analysis, with 144 and 138 articles meeting the criteria to assess moderating effects of disease severity and medication status, respectively. PwPD who freeze exhibited worse cognition than PwPD without FOG across global cognition, executive function/attention, language, memory, and visuospatial domains. Greater disease severity and "ON" levodopa medication status moderated the FOG status-cognition relationship in global cognitive performance but not in other cognitive domains. This meta-analysis confirmed that cognition is worse in PwPD with FOG and highlights the importance of disease severity and medication status in this relationship.

Keywords: Parkinson's disease, cognition, freezing of gait, non-freezers, people with Parkinson's Disease, cognitive impairment

1. Introduction

Freezing of gait (FOG) is a brief, episodic symptom of Parkinson's disease (PD) that leads to an inability to generate effective stepping (Giladi and Nieuwboer, 2008; Nutt et al., 2011). The incidence of FOG increases as the disease progresses, affecting approximately 50% of patients with advanced Parkinson's (Giladi and Nieuwboer, 2008). FOG increases the likelihood of falls and injurious falls, as well as anxiety, caregiver burden, and reduces the quality of life (Lieberman et al., 2019; Perez-Lloret et al., 2014). Despite this, optimal treatment strategies for FOG are limited by a poor understanding of the pathogenesis that underlies this complex symptom (Nutt et al., 2011). Non-motor symptoms (NMS) are more prevalent in those who experience FOG (Ehgoetz Martens et al., 2018), with prevalence increasing as the severity of FOG advances (Amboni et al., 2010; Giladi et al., 2001). Cognition is one of several NMS suggested to be related to FOG (Heremans et al., 2013; Peterson et al., 2015). To further understand the relationship between cognition and FOG, several studies have compared cognition in those with FOG (FOG+) to those without FOG (FOG-). However, results to date have been mixed. For instance, numerous studies have demonstrated worse cognition in FOG across several domains, such as executive function, attention, and visuospatial functioning (Amboni et al., 2008; Factor et al., 2014; Jha et al., 2015a; Morris et al., 2020; Raffo De Ferrari et al., 2015a). On the contrary, other studies have found no differences in executive function (Vitorio et al., 2020), working memory (Morris et al., 2020), or visuospatial function (Morris et al., 2020) between freezers and non-freezers. However, most studies to date are within small cohorts and do not account for confounders such as disease severity and medication status. Therefore, a comprehensive examination of cognitive differences between freezers and non-freezers is warranted. Furthermore, FOG and cognitive deficits are directly associated with

disease severity (Giladi et al., 2001), as both become more pronounced as the disease progresses. However, studies do not often control for PD disease severity when determining cognitive differences between freezers and non-freezers. Therefore, findings from some studies that freezers may exhibit worse cognition could be due, at least in part, to freezers having longer disease duration and greater disease severity compared to non-freezers. The associations between FOG and cognition are further complicated by medication status. Dopamine-based medications impact motor and NMS, with cognitive processes susceptible to the dopaminergic medication state (Costa et al., 2014). It has been postulated that dopamine may have both positive and negative effects on cognition, depending on the cognitive domain (Lange et al., 1995; Schaeffer and Berg, 2017). Previous studies investigating FOG and cognition are inconsistent with medication status (ON, OFF, or not reported), potentially adding confusion to the interpretation of results.

The primary objective of this systematic review and meta-analysis is to determine the effect of FOG on cognition across comprehensive cognitive domains (global cognition, attention/executive function, language, memory, and visuospatial) between freezers and non-freezers. Secondary analyses aimed to determine whether across-group differences were maintained after accounting for 1) disease severity between freezers and non-freezers and 2) dopaminergic medication state (e.g., whether tested ON or OFF medications).

2. Methods

A systematic review and meta-analyses were conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009). The study protocol was prospectively registered and published online on PROSPERO (CRD42022313249).

2.1 Literature search strategy

A computerized literature search in the following electronic databases was completed by three authors (AM, DSP, RM) in May 2022: PubMed, Scopus, CINAHL, and PsycInfo. Separate searches were undertaken for the three general focuses of the review: 1) Parkinson's disease, 2) Freezing of Gait, and 3) Cognition. Key terms were mapped to relevant medical subject headings (MeSH). The full search criteria are provided in **Supplementary Material 1**.

2.2 Eligibility Criteria

Original research articles of cross-sectional design comparing cognitive function between FOG+ and FOG- published between January 2000 and June 2022 were considered for inclusion in the review. Studies were included if they met the following criteria; 1) an assessment of FOG had been undertaken, either by participant recall (e.g., the Freezing of Gait Questionnaire (FOG-Q) (Giladi et al., 2000) or the New Freezing of Gait Questionnaire (N-FOG-Q) (Nieuwboer et al., 2009), or via direct clinical observation **(Table 1)**, 2) a minimum of one cognitive test was administered, 3) cognitive results were reported in PD with and without FOG and 4) cross-sectional studies. Where studies included an intervention, only baseline cognitive assessments were included. Full research articles, studies published in English, and articles published in peer-reviewed scientific journals were included.

2.3 Article screening and data extraction

First, non-duplicate articles were uploaded to an electronic systematic review software package (Ouzzani et al., 2016). All titles and abstracts obtained from the search were independently screened by two reviewers (DSP and RM). Articles were excluded if the title or abstract clearly indicated that the article 1) did not include human participants (e.g., animal- or in-vitro studies) or 2) was not an original research article (e.g., a review of the literature). The reviewers were then unblinded to the title and abstract screen inclusions and exclusions. Any discrepancies between the two reviewers were resolved with an online discussion and the

inclusion of a third reviewer (AM) where necessary. The three reviewers (AM, DSP, RM) then divided the remaining articles and conducted a full paper screen considering the inclusion and exclusion criteria. Discussions were held with other reviewers if the reviewer was uncertain on inclusion or exclusion. The review team then discussed the final decisions on inclusion and exclusion. Data extraction was then performed on all full-text articles. Missing data that was required for meta-analysis was requested via email. A list of excluded studies is provided in **Supplementary Material 2.**

2.4 Methodological Qualities

The methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for analytical cross-sectional studies, which is a valid and reliable tool for methodological assessment (Munn *et al.*, 2014). See **Supplementary Material 3** for details.

2.5 Statistical Analysis

Meta-Analyses assessing differences in cognition between FOG+ and FOG- were performed using RevMan (v5.4.1). A total of 5 distinct meta-analyses were performed for the following cognitive domains; 1) global cognition, 2) attention/executive function, 3) language, 4) memory, and 5) visuospatial. Cognitive domains were defined according to the guidelines developed by the Movement Disorder Society Task Force (Litvan et al., 2012) (**Table 1**). Cognitive data from FOG+ and FOG- were standardized and pooled using inverse-variance random-effects meta-analyses to compute effect sizes. Negative effect sizes reflect poorer cognitive performance in FOG+ compared to FOG-. For all analyses, heterogeneity between the studies in effect measures was explored using the χ^2 and I^2 statistics, whereby a significant χ^2 statistic ($p < 0.05$) and/or an I^2 value >50% was considered representative of substantial heterogeneity. In the event of considerable heterogeneity, sensitivity analyses were conducted.

Funnel plots were computed to evaluate potential bias. Studies were considered outliers if their effect estimates fell outside the 95% confidence interval (CI) of the pooled effect estimates, visualized as dotted lines on the funnel plots. These are presented in **Supplementary Material 5**.

Two additional analyses were then run to determine whether differences in cognition across groups were maintained after accounting for 1) disease severity across FOG+ and FOG- and 2) dopaminergic state (e.g., whether tested ON or OFF medications). For the first analysis, data on disease severity were obtained using a combination of the UPDRS part-III, the MDS-UPDRS part-III, and the total scores of each version depending on what was available for the study in question. The UPDRS/MDS-UPDRS was selected as the measure of disease severity for this analysis as it is the most widely used and valid measure of disease severity in PD. UPDRS score was chosen over disease duration as disease severity can be variable in relation to disease duration due to the heterogenous nature of PD. Studies were dichotomized into those where there was or was not a significant difference in disease severity across FOG+ and FOG- groups ("unmatched" and "matched, for disease severity, respectively) **(Table 1)**. Exploratory moderation analyses were also conducted to investigate differences in cognition between FOG+ and FOG- using Meta-Essentials (Suurmond et al., 2017). Cohen's D effect sizes for group (FOG+ and FOG-) differences in disease severity were calculated and used as the moderator in the weighted regression. As such, for both matched/unmatched and continuous analyses, although different metrics were used for disease severity across studies, these outcomes were standardized before across-study analyses. For the secondary, medication-based analysis, studies were dichotomized by whether cognitive outcomes were collected ON or OFF levodopa. Those studies where medication status was not reported were excluded from this secondary analysis.

Finally, to assess the potential effect of varying test-use within domains, we tabulate and present across-group effect sizes for each of the tests most frequently used within each sub-domain (Supplementary Material 4). When multiple assessments within the same cognitive domain were reported in studies, the data from the most frequently reported assessment was extracted and analyzed.

3. Results

3.1 Search yield

The search strategy generated a total of 1647 articles **(Figure 1)**. After the duplicates were removed, a total of 911 articles remained. 720 articles were removed during the abstract screening, with 191 remaining for the full paper screening. After the full paper screen, 44 additional articles were removed (see **Supplemental Material 2** for exclusion reasons), and 145 were eligible for data extraction. Disease severity status was not reported in 1 article (Myers et al., 2017) **(Table 1).** Medication status during cognitive assessment was unclear in 7 articles (Brugger et al., 2015; Hall et al., 2018; Jha et al., 2015; McKay et al., 2018; Shine et al., 2013; Sunwoo et al., 2013; Zhou et al., 2019) **(Table 1)**. The search result is summarized in **Figure 1**.

INSERT FIGURE 1

3.2 Participant characteristics

A summary of characteristics for each study and included participants are reported in **Table 1**. The search strategy identified 145 eligible studies, including a total sample size of 9010, comprised of 4240 FOG+ and 4770 FOG-. The mean reported age was similar for both groups (FOG+, 65.82 years ± 7.33; FOG-, 65.71 years ± 3.82). FOG status was determined using the following assessments: the FOG Questionnaire (FOG-Q) (n = 38), the New FOG Questionnaire (N-FOG-Q) (n = 50), direct observation (n = 10), self-report of freezing history (n

= 1), and the UPDRS/MDS-UPDRS (n = 2). Many studies (n = 45) used a combination of the above assessments to determine freezing status. FOG+ had greater disease severity as measured by Hoehn & Yahr Scale (FOG+, 2.49 ± 0.34; FOG-, 2.15 ± 0.31) along with longer average disease duration (FOG+, 8.92 years ± 2.49; FOG-, 6.28 years ± 1.97). Cognition was assessed in the ON state in 86 studies and the OFF state in 52 studies (see **Table 1**).

INSERT TABLE 1

3.3. Global Cognition

A total of 139 studies (n = 8796) assessed global cognition between FOG+ (n = 4123) and FOG- (n = 4673). 68 studies used the Montreal Cognitive Assessment (MoCA), 70 used the Mini-Mental State Examination (MMSE), and 1 study used the Mattis Dementia Rating Scale (MDRS). Global cognition was significantly worse in FOG+ than in FOG- (Z = 7.55, P < 0.00001; ES = -0.36 [-0.45, -0.27]) **(Figure 2),** but with large statistical heterogeneity across study effects ($\chi^2(138) = 535.96$, $p < 0.000001$ and $I^2 = 74\%$). The sensitivity analysis identified 8 outlier studies (Belluscio et al., 2019; Killane et al., 2015; Mi et al., 2020; Nanhoe-Mahabier et al., 2013; Singh et al., 2020; Vandenbossche et al., 2011, 2013; Zhou et al., 2019). After excluding these outliers, 131 studies (FOG+ = 4010, FOG- = 4573) were included, and the overall effect of worse global cognition in FOG+ than FOG- remained significant (Z = 7.75, p < 0.00001, ES = -0.34 (-0.43, -0.26]), with less statistical heterogeneity between the study effects ($\chi^2(130) = 421.91$, $p = 0.0007$ and $I^2 = 69\%$). Funnel plots are provided in **Supplementary Material 6**. Subgroup analysis examining the impact of disease severity revealed 82 studies were matched (FOG+; n = 1605; FOG-; n = 1677) and 57 were unmatched (FOG+; n = 2518; FOG-; n = 2996) on disease severity. Global cognition was worse in FOG+ in both the matched (ES, [95% CIs] = -0.23 [-0.32, -0.14]) and unmatched groups (ES, [95% CIs] = -0.53 [-0.69, -0.36]), however, this effect was greater in the unmatched studies

($\chi^2(1) = 9.62$, $p = 0.002$ and $I^2 = 89.6\%$) (**Figure 2**). The effect of worse global cognition in unmatched than matched studies remained significant after removing the outliers identified above ($\chi^2(1) = 9.82$, $p = 0.002$), but with similar heterogeneity ($I^2 = 89.8\%$). Given the remaining high heterogeneity, this result should be taken with caution. The exploratory moderation analysis confirmed that the severity of the disease, when continuously assessed, may influence the global cognition differences identified between FOG- and FOG+ ($\beta = 0.39$, SE = 0.07, 95% CI: [0.26, 0.53], $p < 0.001$) **(Supplementary Material 6)**.

INSERT FIGURE 2

Global cognition was assessed during the ON state in 85 studies (FOG+; n = 3082; FOG-; n = 3080) and the OFF state in 47 studies (FOG+; n = 908; FOG-; n = 1302). Global cognition was worse in FOG+ in both the ON (ES, [95% CIs] = -0.39 [-0.48, -0.30]) and OFF state (ES, [95% CIs] = -0.15 [-0.27, -0.02]). However, this effect was significantly greater in the ON state ($\chi^2(1) = 9.44$, $p = 0.002$) albeit with substantial heterogeneity ($I^2 = 89.4\%$; **Supplementary Material 7**). The sensitivity analysis removed 8 outlier studies (Belluscio et al., 2019; de Almeida et al., 2021; Killane et al., 2015; Mi et al., 2020; Nanhoe-Mahabier et al., 2013; Singh et al., 2020; Vandenbossche et al., 2011, 2013). After the removal of outlier studies, the effect of worse global cognition in the ON studies than the OFF studies remained significant ($\chi^2(1) = 4.96$, $p = 0.03$; ON meds ES, [95% CI] = -0.33 [-0.38, -0.27]); OFF meds = -0.18 [-0.29, -0.06]). However, given the high heterogeneity ($I^2 = 79.8\%$), this result should be taken with caution.

3.4 Executive Function/Attention

A total of 69 studies (n = 4294) assessed executive function/attention between FOG+ (n = 2038) and FOG- (n = 2256). 32 studies used the frontal assessment battery (FAB), 15 used the Trail Making Test B-A, 5 used the Trail Making Test B Score, 4 used the Stroop Test, 2 used

the MDRS Attention Subscale, 1 used the Go-No-Go Task, 1 used the Tower of London Test, 2 used the Dimensional Change Card Sort, 1 used a Shifting Task, 1 used a Simple Reaction Time Task, 1 used a Stop Signal Task, 1 used a Choice Reaction Time Task, ad 1 used the Brixton Executive Function Task. Executive function/attention was significantly worse in FOG+ than FOG- (Z = 7.42, P < 0.00001; ES = -0.50 [-0.63, -0.37]) **(Figure 3)** but with large statistical heterogeneity across study effects ($\chi^2(68) = 251.39$, p < 00001 and $I^2 = 73\%$). The sensitivity analysis identified 6 outlier studies (Belluscio et al., 2019; Bissett et al., 2015; Bosch et al., 2022; S. A. Factor et al., 2014; Killane et al., 2015; Pietracupa et al., 2018). After excluding these studies, 63 studies (FOG+ = 1926, FOG- = 2060) remained, and the overall effect was still significant (Z = 9.82, p < 00001, ES = -0.44 (-0.53, -0.35]), but with less heterogeneity ($\chi^2(62) = 93.76$, p = 0.006 and $I^2 = 34\%$). Funnel plots are provided in **Supplementary Material 5**.

Subgroup analysis examining the impact of disease severity revealed that 38 studies were matched (FOG+; n = 711; FOG-; n = 700), and 31 were unmatched (FOG+; n = 1327; FOG-; n = 1556). Executive function/attention was worse in FOG+ in both the matched (ES, [95% CIs] = -0.40 [-0.56, -0.25]) and unmatched groups (ES, [95% CIs] = -0.60 [-0.81, -0.39]), and, this effect was not significantly different between the matched and unmatched studies ($\chi^2(1) = 2.21$, p = 0.14 and $I^2 = 54.7\%$) **(Figure 3)**. The lack of difference in executive function/attention between matched and unmatched studies remained non-significant after removing the outliers identified above ($\chi^2(1) = 2.10$, p = 0.16) with slight reductions in heterogeneity ($I^2 = 50.3\%$). The exploratory moderation analysis revealed that disease severity, when assessed in a continuous manner, may influence the executive function/attention differences identified between FOG- and FOG+ (β = 0.28, SE = 0.11, 95% CI: [0.05, 0.51], p = 0.01) **(Supplementary Material 8)**.

INSERT FIGURE 3

Executive function/attention was assessed during the ON state in 44 studies (FOG+; n = 1550; FOG-; n = 1699) and the OFF state in 23 studies (FOG+; n = 446; FOG-; n = 508). Medication status was not reported or unclear in 3 studies (Hall et al., 2018; Jha et al., 2015b; McKay et al., 2018). Executive function/attention was worse in FOG+ in both the ON (ES, [95% CIs] = -0.59 [-0.77, -0.41]) and OFF states (ES, [95% CIs] = -0.41 [-0.59, -0.22]), and, no difference in executive function/attention was observed between ON and OFF studies ($\square^2(1)$ = 1.96, p = 0.16 and I^2 = 48.9%) **(Supplementary Material 9)**. Although no significant heterogeneity was observed (I^2 < 50%), an inspection of the funnel plot **(Supplementary Material 5)** revealed numerous outliers (Bosch et al., 2022; S. A. Factor et al., 2014; Killane et al., 2015; Mandal and Khan, 2021; Myers et al., 2017; Pieruccini-Faria et al., 2014; Tessitore et al., 2012). After the removal of outlier studies, the lack of difference in executive function/attention between ON and OFF studies remained ($\square^2(1)$ = 0.49, p = 0.48 and I^2 = 0%; ON meds ES, [95% CIs] = -0.41 [-0.51, -0.31]; OFF meds = -0.35 [-0.49, -0.21])).

3.5. Language

16 studies (n = 1228) assessed language between FOG+ (n= 624) and FOG- (n= 604). 10 studies used Word Fluency Tasks, 2 used Phonemic Fluency Tasks, 1 used the Controlled Oral Word Association Test (COWAT), and 3 used a Semantic Fluency Task. Language was significantly worse in FOG+ than FOG- (Z = 2.27, P = 0.02; ES = -0.21 [-0.39, -0.03]) **(Figure 4)** without substantial heterogeneity across study effects ($\square^2(15)$ = 26.58, p = 0.03 and I^2 = 44%). Inspection of the funnel plot revealed no significant outliers **(Supplementary Material 5)**.

Examination of the subgroup analysis investigating the impact on the matching of disease severity revealed 9 studies that were matched and 7 that were unmatched for disease severity. One study did not provide information concerning disease severity (Myers et al., 2017). For FOG+, language was not significantly different than FOG- within both the matched (ES, [95% CIs] = -0.25 [-0.57, 0.06]) and unmatched groups (ES, [95% CIs] = -0.18 [-0.39, 0.04]),

and no significant differences in language was observed between matched and unmatched studies ($\chi^2(1) = 0.16$, $p = 0.69$ and $I^2 = 0\%$) (Fig 4). The exploratory moderation analysis confirmed that disease severity did not seem to influence the language differences identified between FOG- and FOG+ ($\beta = -0.03$, SE = 0.27, 95% CI: [-0.61, 0.56], $p = 0.92$) **(Supplementary Material 10)**.

INSERT FIGURE 4

Language was assessed during the ON state in 12 studies (FOG+; n = 513; FOG-; n = 441) and during the OFF state in 4 studies (FOG+; n = 119; FOG-; n = 180). Language was worse in FOG+ in the ON state (ES, [95% CIs] = -0.23 [-0.45, -0.01]) but not in the OFF state (ES, [95% CIs] = -0.40 [-1.11, 0.30]) **(Supplementary Material 11)**. However, there was no significant difference in language between ON and OFF studies ($\chi^2(1) = 0.22$, $p = 0.64$ and $I^2 = 0\%$). Although no heterogeneity was observed, an inspection of the funnel plot **(Supplementary Material 6)** revealed one outlier (Myers et al., 2017). After the removal of outlier studies, the lack of difference in language between ON and OFF studies remained non-significant ($\chi^2(1) = 1.67$, $p = 0.20$ and $I^2 = 40.1\%$; ON meds ES, [95% CIs] = -0.23 [-0.45, -0.01]; OFF meds = 0.00 [-0.27, 0.27]).

3.6 Memory

A total of 25 studies (n = 2110) assessed memory between FOG+ (n = 1075) and FOG- (n = 1035). 14 studies used the backward Digit Span, 2 used the Rey Auditory Verbal Learning Test, 2 used the Corsi Block Tapping Test, 1 used a Digit Memory Task, 1 used the Hopkins Verbal Learning and Memory Test, 1 used the Fuld Object Memory Evaluation Test, 1 used a Dot Counting Task, 1 used Rey's Complex Figure Test (Recall), 1 used a Picture Sequence Memory Task, and 1 used a Letter Memory Task. Memory was significantly worse in FOG+ than FOG- (Z = 3.02, P = 0.003; ES = -0.30 [-0.49, -0.10]) **(Figure 5)**, but with large statistical

heterogeneity across study effects ($\square^2(24) = 90.07$, $p < 00001$ and $I^2 = 73\%$). The sensitivity analysis identified 5 outlier studies (Banks et al., 2019; Beck et al., 2015; Factor et al., 2014; Hall et al., 2015; Morris et al., 2020). After excluding these studies, 20 studies (FOG+ = 770, FOG- = 794) remained, which revealed that that the overall effect was still significant (Z = 5.12, p < 00001, ES = -0.32 [-0.44, -0.20]), but with less statistical heterogeneity across study effects ($\square^2(19) = 22.49$, p = 0.0.26 and $I^2 = 34\%$).

Subgroup analysis investigating the impact of disease severity showed that 13 studies were matched and 12 were unmatched. While memory in FOG+ was significantly worse in both the matched (ES, [95% CIs] = -0.27 [-0.49, -0.05]) and unmatched groups (ES, [95% CIs] = -0.27 [-0.49, -0.05]), no differences were observed between the matched and unmatched studies ($\square^2(1) = 0.32$, p = 0.57 and $I^2 = 73\%$) **(Figure 5)**. The lack of difference in memory between matched and unmatched studies remained with the removal of the outliers identified above ($\square^2(1) = 0.02$, p = 0.90 and $I^2 = 0\%$). The exploratory moderation analysis confirmed that disease severity had little influence on the memory differences identified between FOG- and FOG+ (β = -0.04, SE = 0.27, 95% CI: [-0.60, 0.51], p = 0.87) **(Supplementary Material 12)**.

INSERT FIGURE 5

Memory was assessed during the ON state in 18 studies (FOG+; n = 860; FOG-; n = 809) and during the OFF state in 5 studies (FOG+; n = 172; FOG-; n = 181). Two studies did not clarify medication status during memory assessment (Hall et al., 2018; Jha et al., 2015). Memory was worse in FOG+ than FOG- in the ON state (ES, [95% CIs] = -0.43 [-0.65, -0.22]) but trended better in FOG+ in the OFF state ((ES, [95% CIs] = 0.20 [-0.01, 0.42]), and this effect of worse memory in FOG+ in the ON studies than OFF studies was significant ($\chi^2(1) = 17.17$, p < 0001), albeit with substantial heterogeneity ($I^2 = 94.2\%$; **Supplementary Material 13**). Sensitivity analyses identified 5 outlier studies (Banks et al., 2019; Beck et al., 2015; Factor et

al., 2014; Hall et al., 2015; Morris et al., 2020). After the removal of outlier studies, no differences in memory were observed between ON and OFF studies ($\square^2(1) = 3.09$, $p = 0.08$ and $I^2 = 67.6\%$; (ON-meds ES, [95% CIs] = -0.36 [-0.50, -0.23]; OFF-meds: 0.02 [-0.39, 0.43]). However, given the high heterogeneity, this result should be taken with caution.

3.7 Visuospatial

A total of 17 studies (n = 1096) assessed visuospatial function between FOG+ (n = 583) and FOG- (n = 513). 7 studies used the Judgement of Line Orientation Test, 3 used the Block Design Test, 4 used Rey's Complex Figure Test, 1 used the Brixton Spatial Anticipation Test, 1 used the Visual Object and Space Perception Battery, and 1 used a Design Construction Task. Visuospatial functioning was significantly worse in FOG+ than FOG- ($Z = 3.22$, $P = 0.001$; ES = -0.38 [-0.62, -0.15]) **(Figure 6)**, but with substantial statistical heterogeneity ($\square^2(16) = 44.71$, $p = 0002$ and $I^2 = 64\%$). The sensitivity analysis identified 2 outlier studies (S. A. Factor et al., 2014; Raffo De Ferrari et al., 2015b). After excluding these studies, 15 studies (FOG+ = 469, FOG- = 483) remained, which revealed that that the overall effect was still significant ($Z = 2.29$, $p = 0.02$, ES = -0.15 (-0.28, -0.02]), but now with less statistical heterogeneity across study effects ($\square^2(14) = 13.03$, $p = 0.52$ and $I^2 = 0\%$).

Subgroup analysis investigating the impact of disease severity showed that 10 studies were matched while 7 were unmatched. Visuospatial functioning was significantly worse in FOG+ in the matched group (ES, [95% CIs] = -0.38 [-0.63, -0.13]) with a similar trending effect in the unmatched group (ES, [95% CIs] = -0.39 [-0.79, 0.01]). No significant differences in visuospatial function were observed ($\square^2(1) = 0.00$, $p = 0.97$ and $I^2 = 0\%$) between the matched and unmatched studies **(Figure 6)**. The lack of difference in visuospatial function between matched and unmatched studies remained with the removal of the two outliers identified above ($\square^2(1) = 1.07$, $p = 0.30$ and $I^2 = 6.7\%$). The exploratory moderation analysis confirmed that

disease severity has little influence on the memory differences identified between FOG- and FOG+ (β = -0.22, SE = 0.34, 95% CI: [-0.95, 0.52], p = 0.53) **(Supplementary Material 14)**.

INSERT FIGURE 6

Visuospatial function was assessed during the ON state in 12 studies (FOG+; n = 392; FOG-; n = 333) and during the OFF state in 4 studies (FOG+; n = 174; FOG-; n = 159). Medication status during visuospatial assessment was unclear in one study (Jha et al., 2015b). Visuospatial functioning was worse in FOG+ during both the ON (ES, [95% CIs] = -0.40 [-0.75, -0.06]) and OFF (ES, [95% CIs] = -0.22 [-0.44, -0.00]) state, but no significant difference in visuospatial function was observed between the ON and OFF studies ($\square^2(1) = 0.74$, p = 0.39 and I^2 = 0%) **(Supplementary Material 15)**. After the removal of outlier studies, the lack of difference in visuospatial function between ON and OFF studies remained ($\square^2(1) = 1.22$, p = 0.27 and I^2 = 17.7%).

INSERT FIGURE 7

3.8 Effect of Cognitive Assessment

Finally, as seen in Supplementary Material 4, a range of cognitive tests were used and included in this analysis. We provide information regarding the effect of FOG on each test included for all sub-domains. As can be noted from the effect sizes for the most frequently used tests, the result was, descriptively, largely consistent across assessments in that FOG+ demonstrated worse cognitive performance than FOG-.

3.9 Methodological Quality

The JBI critical appraisal checklist for analytical cross-sectional studies was used to assess the methodological quality of included studies, and a comprehensive summary is provided in **Supplementary Material 3**. In summary, inclusion criteria were provided in 137/145 (94.5%) studies. The study participants and settings were described in detail in 127 studies (87.6%), and FOG status was measured using valid and reliable measures in 139 studies (95.6%). Parkinson's Disease was measured according to objective, standard criteria in 134 studies (92.4%), and most studies (142; 97.9%) identified possible confounders such as age and disease severity. Thirteen studies explicitly described strategies to deal with potential cofounders. However, since the scope of this meta-analysis focused on descriptive demographic data (i.e., cognition), controlling for confounds was mostly non-applicable. Finally, 145 studies (100%) measured cognition validly and reliably, and 101 (69.7%) compared cognition between FOG+ and FOG- using appropriate analysis.

4. Discussion

To our knowledge, this is the first review and meta-analysis to comprehensively assess cognitive function across comprehensive cognitive domains in those with and without FOG. We identified that, overall, those with FOG have worse cognitive function than people without FOG and that this occurs across a range of cognitive domains. Disease severity and medication status may moderate the degree to which cognition varies in FOG+ and FOG- in global cognition, as cognitive deficits were more pronounced when FOG+ exhibited worse disease severity than FOG-or when participants were tested ON levodopa. Our findings suggest a potentially bi-directional relationship between FOG and cognition and that this relationship may be impacted by disease severity and medication state. These findings may have implications for future research and clinical practice.

4.1 Differences Across and Within Cognitive Domains

Although this systematic review and meta-analysis is novel in synthesizing the literature on cognition and FOG, previous literature has suggested cognitive impairment in FOG+ compared to FOG-. Inspection of the forest plots **(Figures 2-6)** and the summary plot (**Figure 7A**) indicates that FOG+ demonstrated worse cognition in each of the cognitive domains, with effects ranging from small (-0.21 for language) to medium (-0.50 for executive function/attention). The relatively large effect in the executive function/attention domain is consistent with converging evidence in the field outlining FOG-related attentional deficits (Ehgoetz Martens et al., 2020; Heremans et al., 2013; Nutt et al., 2011). However, despite the total combined effect highlighting worse cognition across domains in FOG+, not all studies within this review identified poorer cognitive function in FOG+. For example, within the executive function/attention domain, 59 of 69 studies (86%) indicated any degree of worse cognition in the FOG+ group (ignoring statistical significance). Of these, 28 of 59 studies (47%) reported a statistical difference between the groups. Therefore, while most studies indicated descriptively worse cognition in FOG+ vs. FOG-, the finding that almost half of the studies did not find statistically significant worse executive function/attention in freezers may point to the vast between-study variability in participant characteristics, including factors such as age, disease duration, cognition, and moderating factors that we have tested within this review such as disease severity and medication status. It is also important to note that not all cognitive domains were equally assessed across studies. Global cognition was the most frequently evaluated domain, followed by executive function (**Figure 7B**). This is expected due to the wide use of global cognitive and executive function measures as screening tools and ease of use. Language, memory, and visuospatial function measures were much less frequently assessed. Therefore, across-domain comparisons in this meta-analysis should be made with caution.

We observed substantial variability of tests used to asses cognition within each domain. This variability was most extensive in the executive function/attention, memory, and visuospatial domains. As noted below, this calls for the development of standardized tests (or a battery of tests) to assess cognition in people with PD who freeze. Interestingly, however, the relative effects of FOG on different cognitive were, descriptively, somewhat similar across tests within each domain (Supplementary Material 4). Freezers consistently demonstrated worse cognitive performance on each domain's most frequently used assessments. Contrary findings were often observed when cognitive assessments were infrequently performed across studies.

4.2 Effect of Disease Severity and Medication on the FOG-Cognition relationship

Disease severity is related to both FOG and cognition (Factor et al., 2014). As such, a secondary aim of this meta-analysis was to investigate whether disease severity moderated the FOG status/cognition effect. Our results indicated that the impact of FOG status on global cognition was more pronounced in studies that did *not* match participants on disease severity. This was confirmed by exploratory moderation analyses **(Supplementary Material 6)**. This indicates that for global cognition, it is relevant to control for disease severity when exploring the relationship between FOG and cognition. Notably, however, when disease severity is controlled for (i.e., in the "matched" subgroup), FOG+ still exhibited worse global cognitive function than FOG-, albeit with a smaller effect size (Matched EF= -0.24 vs. Unmatched EF= -0.53). Therefore, while disease severity likely contributes meaningfully to cognitive impairments observed in FOG+, there may be an independent relationship in which cognitive impairments exacerbate FOG or vice versa.

These findings were also observed in the executive function/attention domain analysis, although differences in matched-unmatched studies did not reach statistical significance. Notably, the exploratory moderation analysis, which assessed whether the inclusion of a continuous disease severity outcome (rather than binary as with the matched/unmatched

analysis) moderated the across-freezing status group affected cognition was statistically significant (p=0.01; **Supplementary Material 8**). The observed significant moderating effect of disease severity on the FOG+/FOG- cognitive difference may be due to the increased power of the continuous disease state variable. However, this moderation analysis was exploratory and should be treated with caution, especially given the large degree of heterogeneity across studies.

A surprising result was that disease severity seemed to moderate the FOG+/FOG- cognitive effect *less* in other cognitive domains, especially for language, visuospatial function, and memory. There were relatively few studies included in the meta-analysis, requiring cautious interpretation, and future work is needed to determine the impact of disease severity on these cognitive domains. However, these preliminary results indicate that the moderating effect of disease severity on FOG-cognition relationships may not be consistent across cognitive domains.

Our meta-analysis also investigated whether dopamine moderated the association between FOG and cognition. Results showed that dopamine only moderated the FOG-cognition effect for global cognition. Specifically, freezing status impacted global cognition *more* when measured during the ON state (effect size= -0.35) than when measured in the OFF state (effect size= -0.13). Similar, but smaller (and non-statistically significant) moderating effects were observed for executive function/attention and memory domain comparisons. The impact of dopaminergic medication on cognitive function is complex, varying depending on the cognitive domain tested and the type of medication (e.g., levodopa vs. dopamine agonists) (Gul and Yousaf, 2018; Moustafa et al., 2013). For example, several studies have demonstrated a subtle, positive effect of dopamine on executive function (Gotham et al., 1988; Gul and Yousaf, 2018; Lange et al., 2003) and stimulus-response learning (for review, see (Moustafa et al., 2013)), but not for other cognitive domains, including attention and memory (Lange et al., 2003; Lewis et al., 2003). Similarly, there is substantial variability in the effects of dopamine on domains such

as reinforcement learning (van Nuland et al., 2020). Given the lack of consistency in the impact of dopamine medication on cognition generally and the lack of studies directly assessing the effects of dopamine on cognition in FOG+ and FOG- groups, interpretation of the current results is challenging. However, findings of this meta-analysis *may* indicate that less severe (e.g., FOG-) participants receive more global cognition improvement via dopaminergic medication than FOG+. This is partially consistent with data from Morrison & colleagues, indicating that individuals with more severe PD may receive less cognitive benefit from levodopa than mild patients (Morrison et al., 2004). Notably, the current analysis does not allow a direct comparison of the effects of levodopa on cognition in those with and without FOG. Further, the FOG-disease severity relationship muddies this relationship. As such, this interpretation is speculative and requires additional work to clarify the impact of dopamine on cognitive functions in FOG+ and FOG-. However, regardless of the specific effects of dopamine on cognitive function, results from the current study underscore the importance of assessing and reporting dopamine status when reporting across-group (e.g., FOG+, FOG-) cognitive effects.

INSERT TABLE 2

4.3 Neural Framework

This meta-analysis suggests that people with PD and FOG exhibit worse cognitive function than FOG-. Considerable research has provided a deeper understanding of how these two behaviors are related. From our work we cannot determine the direction of causality between FOG and cognition and as to whether poorer cognitive function (and underlying pathology) causes and/or exacerbates FOG or whether the incidence of FOG worsens cognitive function. Recent evidence suggests there is likely a shared neuropathology between FOG and cognition. Specifically, acetylcholine is associated with executive function and attention, with sources both in the prefrontal cortex and pedunculopontine (PPN) (Morris et al., 2019). It is, therefore, plausible that cholinergic dysfunction underpins both cognitive deficits and FOG. In

support of this, Bohnen and colleagues showed that levels of acetylcholine are reduced in those with FOG, compared to those without, in the striatum, temporal, and mesiofrontal limbic regions(Bohnen et al., 2019). In the same study, those with FOG had significantly worse cognition, indicating that FOG pathophysiology may result from deficits of both dopamine and acetylcholine (Bohnen et al., 2019). Further, it is notable that cholinergic dysfunction typically occurs later in the disease course, and, like dopaminergic dysfunction, it may worsen through the course of the disease. This potentially shared, degenerative course of FOG and cognition across the course of PD further underscores the importance of controlling for factors such as disease severity (discussed further below).

In addition to cholinergic functioning, previous imaging studies help explain the neural underpinning of cognitive deficits, particularly within the executive function/attention domain. Structural (Canu et al., 2015; Droby et al., 2021; Fling et al., 2013; Hall et al., 2018) and functional (Belluscio et al., 2019; Bharti et al., 2020; Bosch et al., 2022; Canu et al., 2015; Droby et al., 2021; Gallardo et al., 2018; Guo et al., 2020) imaging techniques have implicated frontal-executive regions with FOG. Furthermore, impaired connectivity with this frontal region has been associated with cognitive deficits (assessed by MoCA (Droby et al., 2021) and Stroop (Fling et al., 2013), disease severity measured via the UPDRS (Canu et al., 2015; Droby et al., 2021), and severity of FOG (Belluscio et al., 2019; Bharti et al., 2020). Future work should build on the earlier research examining the effect on FOG and cognition to characterize the interlinked regions associated with frontostriatal FOG deficits for FOG ON and OFF medication.

Regardless of whether cognitive deficits and FOG have the same neural root cause, cognitive deficits may be directly linked to FOG events. In fact, executive function and attention may be causally related to FOG events. Instances of high cognitive load (Dual-Task (Nutt et al., 2011; Vandenbossche et al., 2013)), anxiety (Ehgoetz Martens et al., 2016), or complex gait tasks (e.g., turning, gait initiation (Peterson et al., 2014; Plotnik et al., 2014)) disproportionately result in FOG events. Therefore, individuals with poorer executive function are less able to

simultaneously attend to multiple tasks, leading to an overload of descending signals onto brainstem regions and ultimately a freezing event. This FOG model is known as the "interference model" and has become an important framework for understanding FOG (Lewis and Barker, 2009; Lewis and Shine, 2014; Nieuwboer and Giladi, 2013). This model describes the convergence of cortical input from various regions (e.g., cognitive, motor, and limbic) to the striatum in response to FOG triggers. This overload of neural input on the striatum, coupled with nigrostriatal and PPN degeneration (Hirsch et al., 1987), is hypothesized to result in dysfunctional over-inhibition of both thalamus, brainstem, and spinal regions, leading to FOG events (Lewis and Barker, 2009; Lewis and Shine, 2014).

Deficits in visuospatial processing have also specifically been implicated in FOG. Visuospatial processing forms an essential component of sensorimotor integration and motor planning (Culham et al., 2006; Marigold and Drew, 2017). Moreover, FOG+ have a greater dependence on visual feedback and visuospatial preprocessing for effective postural control and gait (Almeida and Lebold, 2010; Cowie et al., 2010). Unfortunately, deficits in visuospatial perception and processing are common in FOG+ compared to FOG-, both during validated visuospatial assessments (e.g., Block Design Test or Matrix Reasoning) (Nantel et al., 2012) and functional walking tasks (Almeida and Lebold, 2010; Cohen et al., 2011; Cowie et al., 2010). In the latter experiments, FOG+ had greater difficulty identifying door width and demonstrated exaggerated motor slowing and more variable gait through narrow doorways than FOG- and controls (Almeida and Lebold, 2010; Cohen et al., 2011; Cowie et al., 2010). These results suggest impaired visuospatial functioning could disrupt online sensorimotor integration and motor planning and be implicated in FOG+. Evidence from neuroimaging studies proposes that the PPC is involved in visuospatial dysfunction and FOG. For example, studies show altered structural (Hall et al., 2018; Herman et al., 2014; Jha et al., 2015; Pietracupa et al., 2018; Rubino et al., 2014) and functional (Bartels et al., 2006; Canu et al., 2015; Gilat et al.,

2015; Mi et al., 2017; Mitchell et al., 2019; Piramide et al., 2020; Shine et al., 2014; Tard et al., 2015) properties of the PPC in FOG+ but not in FOG-.

Language and memory deficits observed in FOG are poorly understood and require further study. The temporal lobe has been implicated in semantic processing (Jackson, 2021). Semantic deficits may be mediated by abnormal activations within the temporal and middle frontal gyrus, as Hu and colleagues discovered elevated activation in both the anterior ITG and MTG in FOG+ patients compared to either FOG- patients or healthy controls (Hu et al., 2020). The memory deficits observed in this study encompass various memory domains **(Supplementary Material 6)**. Still, evidence shows that deterioration in working memory may be more evident in FOG (Martens et al., 2016; Scholl et al., 2021), perhaps mediated by altered frontostriatal pathways (Amboni et al., 2008; Lewis and Shine, 2014). Future research should rigorously examine the association between language and memory with FOG.

4.4. Implications for Treatment

FOG is a complex symptom of PD and is challenging to treat. Characterizing cognitive deficits in FOG+ may inform future pharmacological and non-pharmacological intervention targets and improve the quality of life in those who experience FOG. Non-invasive brain stimulation (NIBS) includes techniques such as repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), and vagus nerve stimulation may indirectly improve FOG via cognitive function. Recent work using these techniques has demonstrated improvements in FOG (Chang et al., 2017; Kim et al., 2019) and cognition, including executive function (Chang et al., 2017; Doruk et al., 2014) and working memory (Boggio et al., 2006). However, refinement on stimulation sites and targets is required (for more, see (Potvin-Desrochers and Paquette, 2021)). Further, less is known regarding stimulation of other cognitive targets, including the posterior parietal cortex and the temporal gyrus, and

should be investigated in future NIBS protocols to enhance visuospatial and semantic processing. Other types of non-pharmacological interventions for FOG also promise (King et al., 2020; Walton et al., 2018). A computerized-based cognitive intervention demonstrated a positive effect on the percentage of time spent in a FOG episode during a gait task (Walton et al., 2018), while a dual-task exercise program found improvements in dual-task walking and moderate improvements for balance in FOG (King et al., 2020). Further work exploring the effects of cognitive interventions on FOG will help improve the understanding of the bi-directional link, or lack thereof, between cognition and FOG, as well as inform clinical guidelines to reduce FOG.

4.5 Implications for Future Work

The meta-analyses show an interplay between cognition in FOG and that level of disease severity and dopaminergic medication status could moderate this relationship. In addition, several gaps were noted in the current literature. Together, these findings lead to recommendations for future research when researching cognition and FOG. First, the use of comprehensive (exploring all domains of cognition) and standardized cognitive batteries should be implemented to facilitate comparison across studies. While it is outside of the scope of the current manuscript to make specific recommendations regarding which tests should be used, we provide information regarding the most frequently used tests (e.g., FAB for executive function, word fluency for language, digit span for memory, etc.), which may serve as a starting point for such discussions. Second, we need to ensure that FOG+ and FOG- cohorts are well characterized for clinical demographics- this includes disease severity and disease duration so that findings can be interpreted in relation to the cohort. Third, all studies should clearly report medication status and define how this was determined so that the impact of dopamine can be interpreted. Fourth, where possible, cohorts of FOG+ and FOG- should be matched for disease severity, or this measure should be accounted for in statistical analysis if the sample size allows.

Future research should aim to determine the impact of cognitive interventions on FOG severity, taking the above recommendations into account. Finally, there should be wide recognition within clinical practice that cognitive deficits in those with FOG should routinely be assessed. This raises the question of which assessments should be used. See **Table 2** for a full list of recommendations.

INSERT TABLE 2 HERE

4.6 Limitations

Several limitations should be noted. First, cognitive domains are not independent but were grouped for this review to structure the data extraction and reporting. Although we did use criteria to guide our analysis, this may challenge the interpretation of our findings. Second, dual-tasking provides a good proxy for cognitive performance in PD. However, we did not include dual-task studies within this review as dual-task protocols vary widely and findings are commonly inconsistent (Kelly et al., 2012). Third, generalizability was adversely affected by FOG assessment which is a subjective report of symptoms. Although routinely used to classify FOG, it is exclusively based on patients' impressions, and consequently, recall bias was inadvertently facilitated. Although this is the current gold standard, it is unreliable to detect small effect sizes (Hulzinga et al., 2020). Therefore, objective and quantified measures of FOG may improve the accuracy of FOG for observational and intervention studies (Lewis et al., 2022).literature. Fourth, there was heterogeneity in some of the analyses, which could partially impede interpretability, particularly for sub-group effects across disease severity and medication status. Despite efforts to reduce such variability through sensitivity analyses, the heterogeneity underlies the multifaceted nature of FOG. Finally, it is possible that some duplicate datasets have been included. If duplicity in datasets was suspected, the authors were contacted to confirm this, and the articles removed. When no response was received, sensitivity analyses

were performed with suspected duplicate reports removed the statistical inferences remained unchanged.

5. Conclusions

This review provides a comprehensive overview of cognitive function between those with and without FOG, indicating that people with Parkinson's Disease with FOG demonstrate cognitive impairments across various domains compared to non-freezers. Our findings also highlight that disease severity and medication may contribute to cognitive deficits observed between freezers and non-freezers in global cognition. Therefore, care should be taken to control for disease severity and medication status when drawing inferences in comparing cognition between freezers and non-freezers.

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Declaration of Competing Interest

The authors report no financial interests or potential conflicts of interest.

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Figure Captions

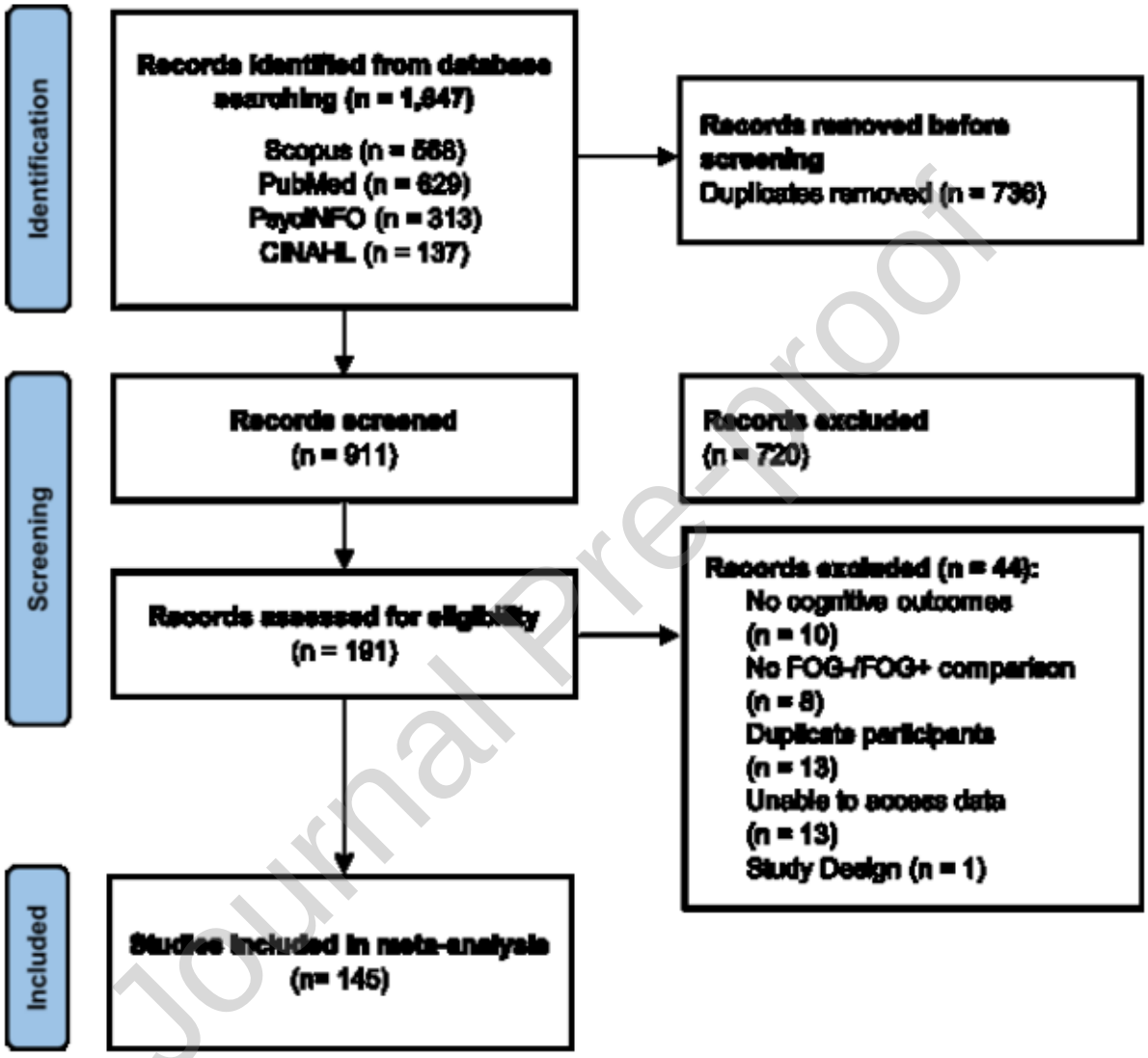

Figure 1: The PRISMA Flowchart of the Study Selection Process

Global_Cog_Forest plot.svg

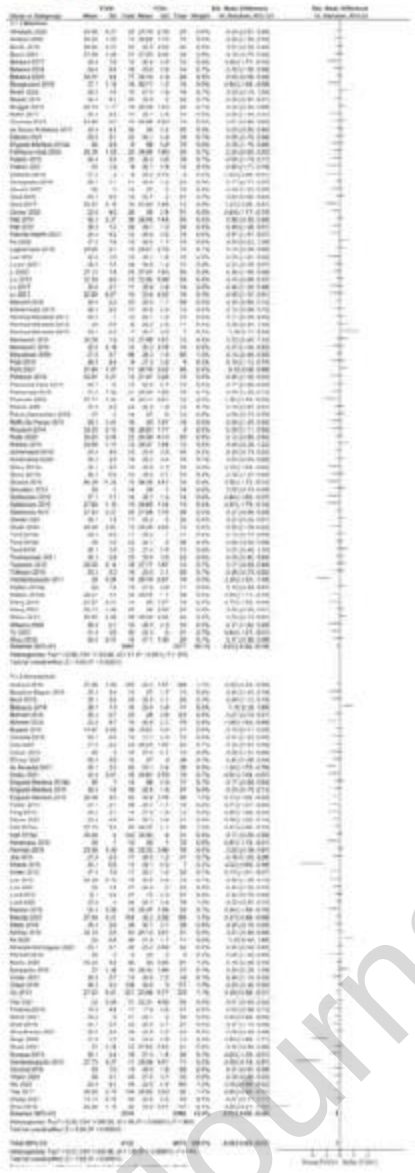

Figure 2: Primary analysis (test for overall effect) comparing global cognition between FOG+ and FOG- and secondary analysis comparing the effect of disease severity. Hall 2015 compared cognition between a) early FOG+ and FOG- b) advanced FOG+ and FOG-.

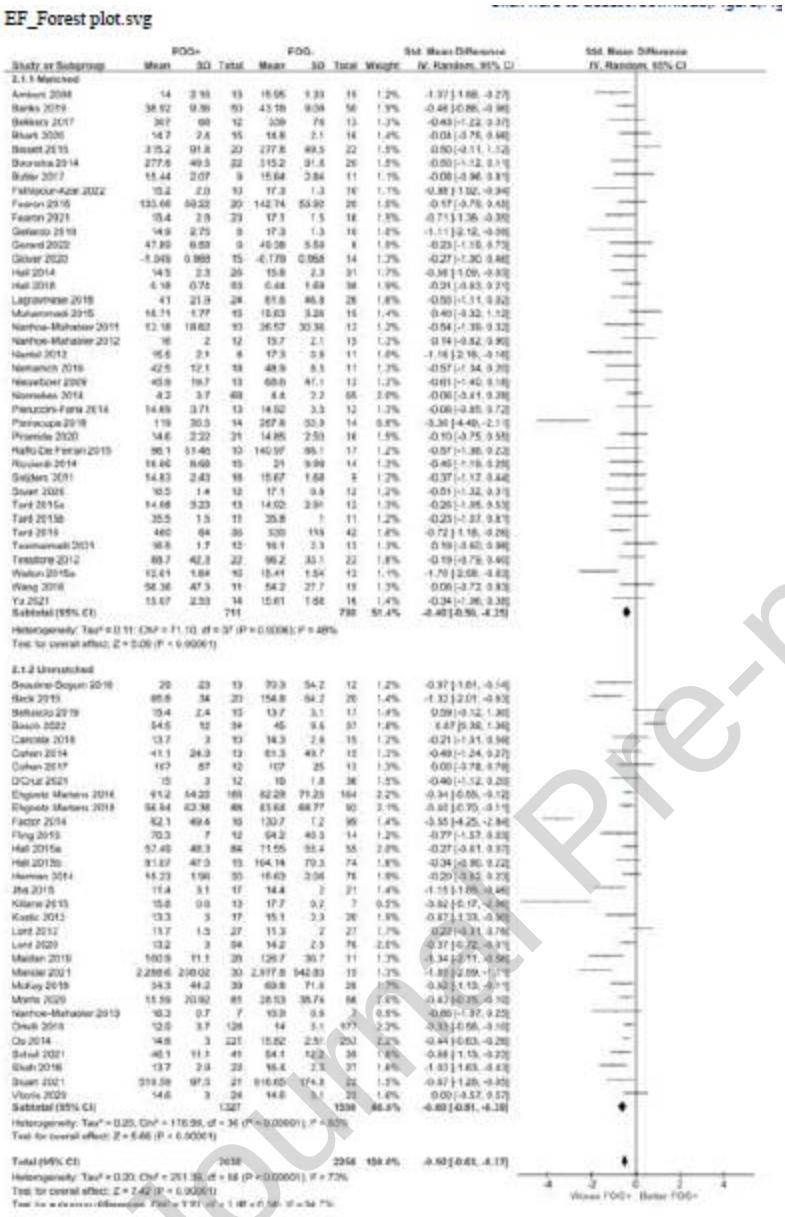

Figure 3: Primary analysis (test for overall effect) comparing executive function/attention between FOG+ and FOG- and secondary analysis comparing the effect of disease severity. Hall 2015 compared cognition between a) early FOG+ and FOG- b) advanced FOG+ and FOG-.

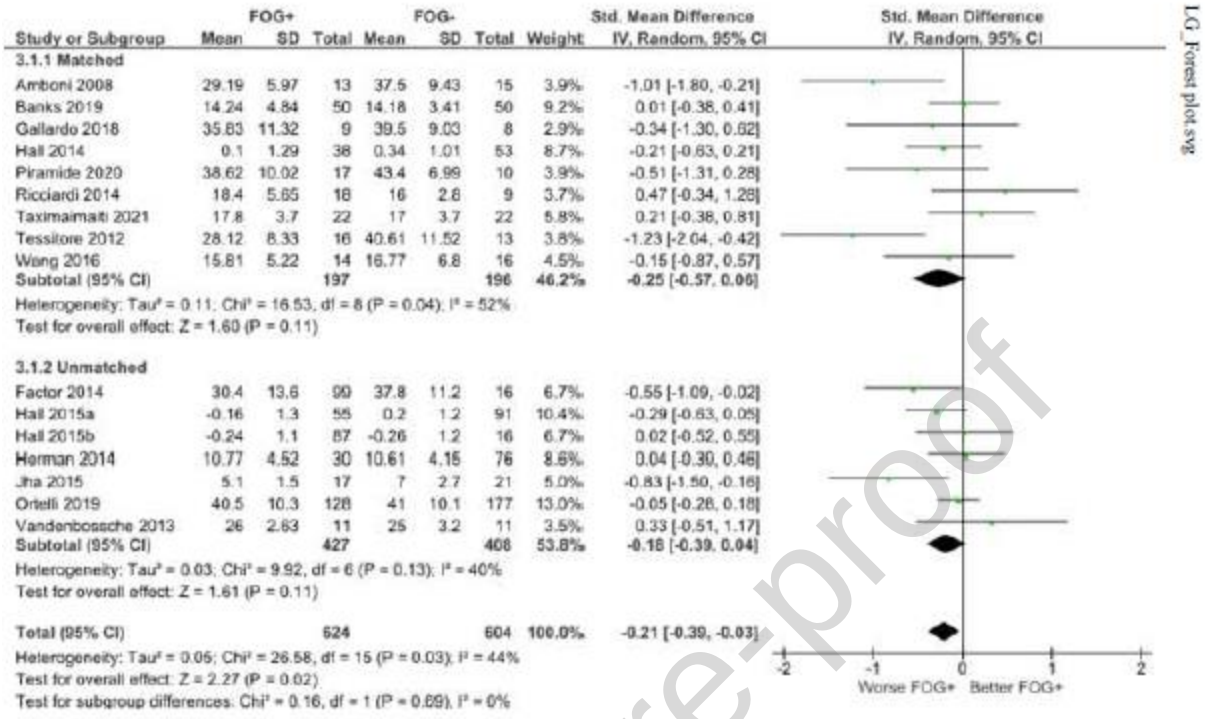

Figure 4: Primary analysis (test for overall effect) comparing language between FOG+ and FOG- and secondary analysis comparing the effect of disease severity. Hall 2015 compared cognition between a) early FOG+ and FOG- b) advanced FOG+ and FOG-.

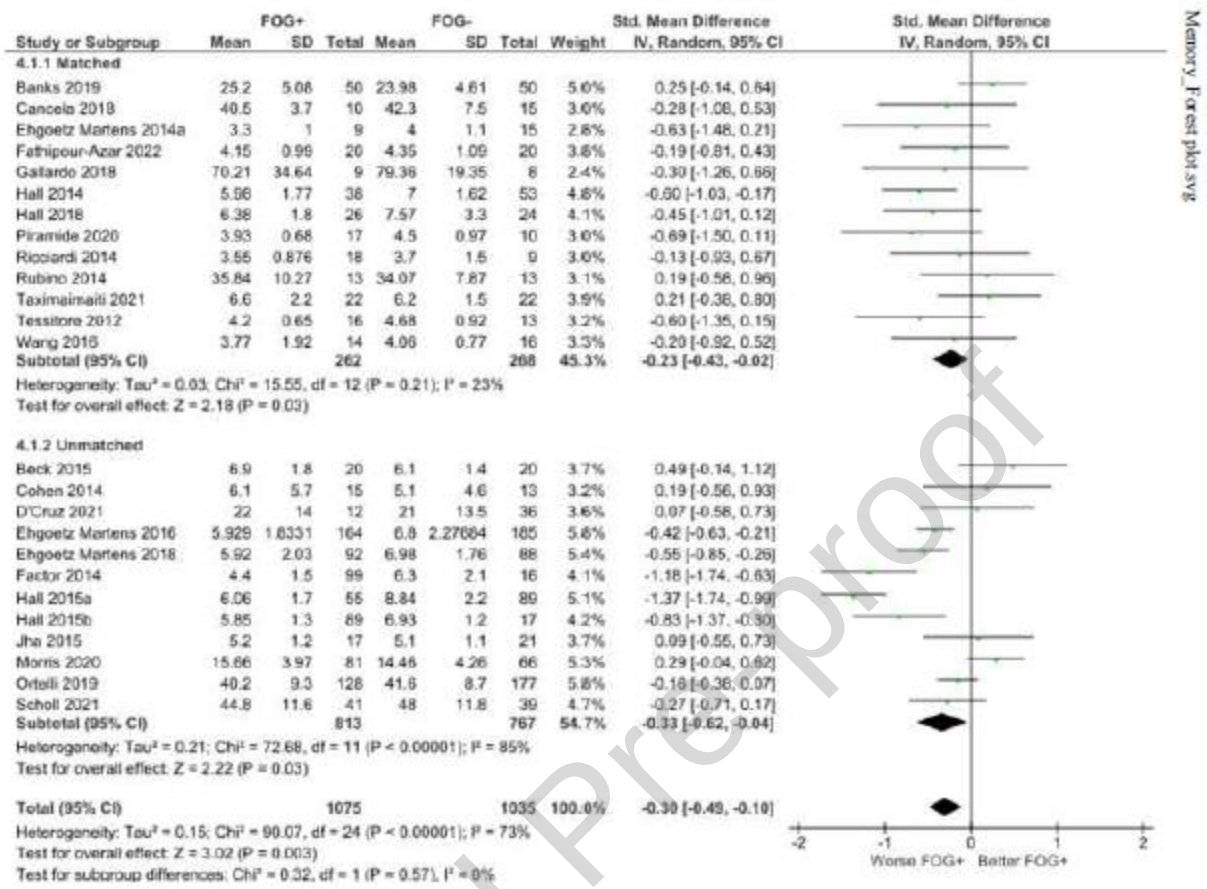

Figure 5: Primary analysis (test for overall effect) comparing memory between FOG+ and FOG- and secondary analysis comparing the effect of disease severity. Hall 2015 compared cognition between a) early FOG+ and FOG- b) advanced FOG+ and FOG-.

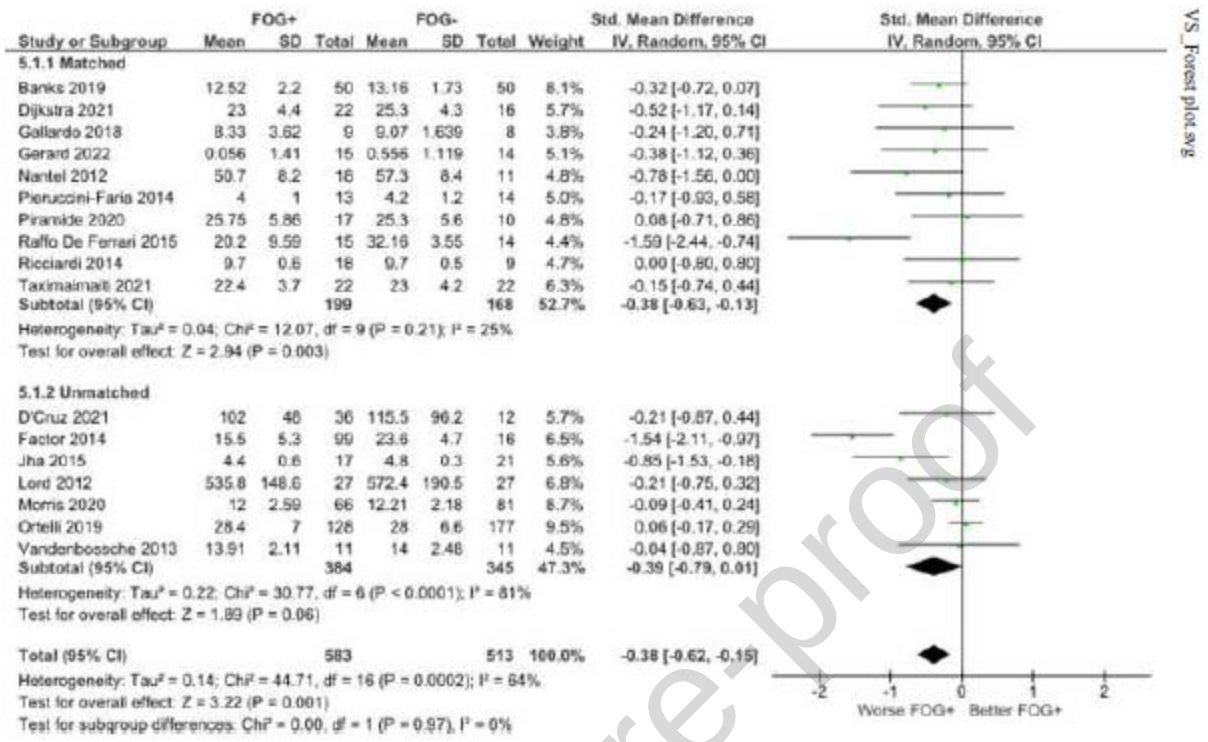

Figure 6: Primary analysis (test for overall effect) comparing visuospatial function between FOG+ and FOG- and secondary analysis comparing the effect of disease severity.

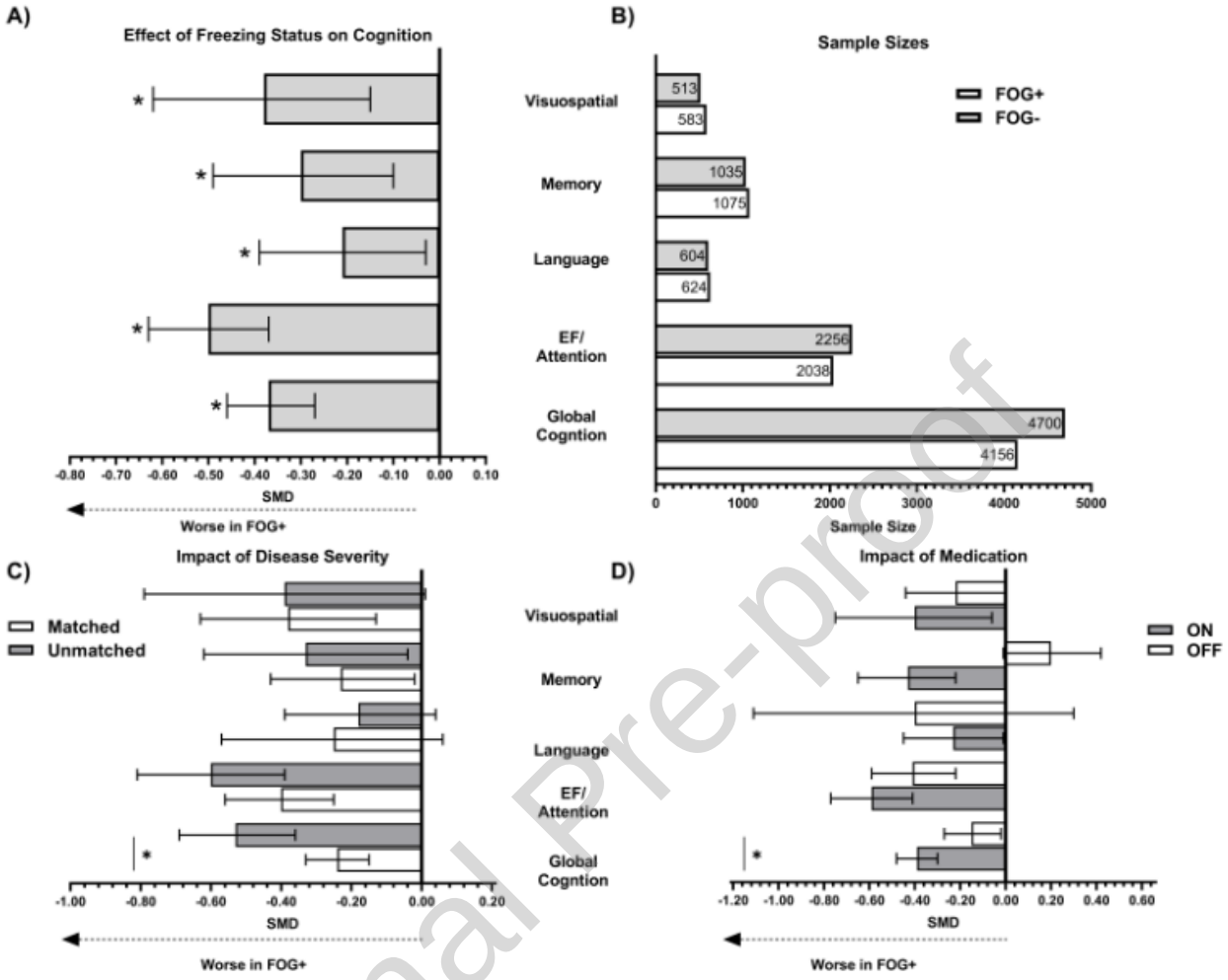

Figure 7: Summary of observed effects. **A)** The standardized mean difference (SMD) in cognitive domains between freezers (FOG+) and non-freezers (FOG-). **B)** The measured sample sizes within each cognitive domain. **C)** The impact of disease severity on cognition between freezers and non-freezers. **D)** The impact of medication state on cognition between freezers and non-freezers.

Table 1. Summary of Included Studies

						FOG+					FOG-				
Study	**FOG Assessment**	**Cognitive Domain**	**Cognitive Test**	**Disease Severity**	**Medication Status**	**N**	**Age**	**Disease Duration**	**H & Y**	**(MDS) UPDRS***	**N**	**Age**	**Disease Duration**	**H & Y**	**(MDS) UPDRS***
Alhassan, 2020	Q	GC	MoCA	M	ON	22	72.31	10.52	- -	22.41	25	67.52	8.08	- -	19.96
Amboni 2008	Q	GC EF LG	MMSE TMT B-A WF	M	ON	13	66.46	5.23	2.00	12.08	15	62.60	5.69	1.93	9.87
Amboni, 2015	Q	GC	MMSE	UM	ON	32	67.50	9.80	- -	28.30	26	66.10	6.10	- -	18.90

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Banks, 2019	MDS-UPDRS	GC EF LG M VS	MoCA SDMT WF HVLT JLO	M	OFF	50	60.46	- -	- -	34.23	50	60.74	- -	- -	29.73
Bayot, 2021	Q, O	GC	MMSE	M	ON	27	64.00	16.19		24.22	30	64.63	3.08		19.89
Beaulne-Seguin, 2016[#]	Q	GC EF	MoCA TMT B-A	UM[#]	ON	12	69.50	7.90	- -	- -	13	62.90	5.40	- -	- -
Beck, 2015	O	GC EF M	MoCA TMT B DMT	UM	ON	20	72.00	- -	- -	38.80	20	70.50	- -	- -	24.70
Bekkers, 2017	Q	GC EF	MoCA Simple RxT	M	ON	13	67.00	13.70	2.60	38.10	12	63.00	5.70	2.20	29.50
Bekkers, 2018	Q	GC	MMSE	M	ON	19	67.90	10.80	2.00	35.50	14	65.80	7.50	2.00	33.90
Bekkers, 2020	Q	GC	MMSE	M	ON	77	70.57	10.43	2.58	31.83	44	71.66	7.25	2.33	26.11
Belluscio, 2019	Q	GC EF	MoCA FAB	UM	OFF	15	66.50	13.50	- -	46.90	17	69.90	9.35	- -	33.50
Bengevoord, 2016	Q	GC	MMSE	M	OFF	16	68.71	9.35	2.53	37.85	14	66.57	7.79	2.31	34.50
Bharti, 2020	O	GC EF	MMSE FAB	M	ON	15	71.00	11.00	2.30	36.20	16	66.30	8.60	2.00	29.00
Bissett, 2015	Q, UPDRS	GC EF	MoCA SST	M	ON	20	63.60	8.60	- -	25.40	22	63.20	5.50	- -	22.00
Bohnen, 2019	MDS-UPDRS, O	GC	MoCA	UM	OFF	15	73.10	9.10	3.20	48.50	79	66.90	5.40	2.30	31.20
Bohnen, 2014	MDS-UPDRS, O	GC	MoCA	UM	OFF	20	66.40	8.30	3.00	46.70	123	65.40	5.60	2.40	30.30
Boonstra, 2014	Q, O	EF	FAB	M	OFF	9	61.27	6.81	- -	31.33	11	64.97	4.05	- -	24.46
Bosch, 2022	Q, MDS-UPDRS	EF	DCCS	UM	ON	24	70.00	5.80	- -	17.00	37	68.40	4.40	- -	9.00
Brugger, 2015	Q	GC	MMSE	M	- -	18	31.07	11.62	2.28	29.33	20	61.54	6.93	2.08	22.75
Buated, 2016	Q	GC	MoCA	M	ON	39	35.13	6.14	2.36	24.72	21	69.00	3.79	1.86	19.43
Butler, 2017	Q, O	GC EF	MoCA FAB	M	ON	10	65.30	13.50	2.60	28.30	10	62.50	7.00	2.30	29.10

Cancela, 2018	UPDRS, O	GC EF M	MMSE FAB FOM E	UM	ON	10	69.70	9.00	2.30	15.00	15	69.50	9.20	2.60	12.20
Cao, 2020	Q, O	GC	MMSE	UM	ON	20	71.47	8.07	2.53	38.27	20	67.55	5.50	1.58	26.60
Chomiak, 2015	Q	GC	MoCA	M	ON	10	64.70	9.70	2.50	18.00	14	66.80	6.60	2.00	15.71
Cohen, 2017	SR	EF	Stroop	UM	OFF	12	67.70	10.00	3.00	43.00	13	66.60	6.20	2.20	32.20
Cohen, 2014	Q	GC EF M	MoCA TMT B-A Ltr Memory	UM	OFF	15	67.10	10.60	2.70	36.50	13	65.30	6.50	2.10	29.90
D'Cruz, 2021	Q	GC EF M VS	MoCA FAB RCFT RCFT	UM	OFF	12	69.00	7.50	- -	39.00	36	59.00	5.00	- -	23.50
de Almeida, 2021	Q, O	GC	MoCA	UM	ON	40	62.30	8.70	2.50	51.70	39	62.70	8.80	3.20	42.40
de Souza Fortaleza, 2017	Q	GC	MoCA	M	OFF	26	69.20	8.30	- -	43.10	30	68.60	6.30	- -	38.70
Dijkstra, 2021	Q,O	GC VS	MoCA JLO	M	OFF	22	68.10	10.77	- -	36.23	16	65.40	7.53	- -	31.19
Droby, 2021	Q	GC	MoCA	UM	ON	16	72.00	- -	2.30	27.91	15	68.20	- -	1.75	18.87
Ehgoetz Martens, 2014	O	GC M	MMSE Corsi BTT	M	ON	9	73.00	- -	- -	30.90	15	71.00	- -	- -	24.60
Ehgoetz Martens, 2014	O	GC	MMSE	UM	ON	14	71.00	- -	- -	34.00	17	66.00	- -	- -	20.00
Ehgoetz Martens, 2016	Q	GC EF M	MMSE TMT B-A Digit Span	UM	ON	164	69.22	8.17	- -	39.78	185	67.80	3.80	- -	28.30
Ehgoetz Martens, 2018	Q	GC EF M	MMSE TMT B-A Digit Span	UM	ON	92	70.24	9.66	- -	48.64	88	65.37	3.16	- -	24.51
Factor, 2014	Q	GC EF LG M VS	MMSE TMT B-A WF Digit	UM	ON	99	64.40	7.00	- -	16.30	16	70.30	8.20	- -	22.30

			Span JLO												
Fathipour-Azar, 2022	Q	GC EF M	MoCA TMT B Digit Span	M	ON	20	63.55	8.55	2.40	31.70	20	64.15	7.20	2.10	27.80
Fearon, 2015	Q	GC EF	MoCA FAB	M	ON	23	68.70	14.00	3.00	38.00	16	66.70	5.20	2.50	30.00
Fearon, 2021	Q	GC EF	MoCA FAB	M	ON	8	65.00	12.30	2.50	28.63	10	62.50	7.00	2.25	29.10
Fling, 2013	Q	GC EF	MoCA Stroop	UM	OFF	14	67.10	10.40	2.70	37.10	12	65.50	6.40	2.00	29.30
Gerard, 2022	Q, O	GC EF VS	MoCA SDMT JLO	M	ON	15	63.00	9.00	2.50	22.00	14	61.00	9.00	2.00	18.00
Gallardo, 2018	O	GC EF LG M VS	MMSE Stroop WF Digit Span Block Design	M	ON	9	64.67	- -	- -	34.91	8	69.21	- -	- -	30.07
Georgiades, 2016	Q, MDS-UPDRS	GC	MMSE	M	OFF	31	66.20	7.00	2.20	25.80	23	64.70	6.60	2.00	22.80
Gilat, 2018	Q	GC	MoCA	M	OFF	19	68.40	9.31	2.00	42.70	21	66.90	6.01	2.00	36.10
Ginis, 2017	Q	GC	MoCA	M	ON	15	62.80	13.20	- -	37.93	13	61.15	7.54	- -	30.69
Glover, 2021	UPDRS, O	GC	MMSE	UM	ON	60	68.00	11.00	- -	22.20	31	70.70	6.20	- -	12.40
Glover, 2020	UPDRS, O	GC EF	MoCA FAB	M	ON	26	68.10	9.20	2.40	18.50	31	65.80	6.80	1.80	12.70
Hall, 2014	Q	GC EF LG M	MMSE TMT B WF Digit Span	M	ON	38	65.20	1.91	2.00	25.66	53	64.58	1.69	1.85	20.85
Hall, 2018	Q	GC EF M	MMSE TMT B-A Digit Span	M	- -	26	64.20	5.20	2.00	25.50	24	66.90	5.20	1.80	23.30

Hall, 2015	Q	GC EF LG M	MMSE TMT B-A WF Digit Span	UM	ON	62	65.03	- -	2.00	29.15	99	66.47	- -	2.00	21.50
Hall, 2015	Q	GC LG M	MMSE WF Digit Span	UM	ON	142	75.15	- -	3.00	51.00	31	78.50	- -	3.00	42.30
Hatcher-Martin, 2021	Q, O	GC	MoCA	M	ON	12	70.70	11.50		19.10	19	70.40	9.60		23.80
Hereman s, 2016	Q	GC	MMSE	UM	ON	15	65.00	9.00	2.00	40.00	15	65.00	8.00	2.00	29.00
Herman, 2014	Q	GC EF LG	MoCA FAB WF	UM	OFF	30	65.09	7.60	3.18	45.90	76	64.91	4.84	2.33	38.36
Hu, 2020	Q	GC	MMSE	M	OFF	13	60.80	5.80	2.90	36.50	15	60.90	4.30	2.10	34.60
Jha, 2015	Q	GC EF LG M VS	MMSE FAB WF Digit Span Design Const.	UM	- -	17	56.90	6.00	1.96	33.10	21	47.40	5.20	1.78	23.90
Killane, 2015	Q	GC EF	MoCA FAB	UM	ON	13	64.20	- -	2.60	31.80	7	64.00	- -	2.30	22.30
Kostic, 2012	Q, O	GC EF	MMSE FAB	UM	OFF	17	64.00	12.00	2.70	39.00	20	63.00	11.00	2.40	29.00
Lagravinese, 2018	Q	GC EF	MMSE FAB	M	ON	15	71.87	11.20	2.43	27.18	15	73.00	10.42	2.05	20.37
Lee, 2012	Q, UPDRS	GC	MMSE	M	OFF	15	69.10	7.60	- -	19.10	10	63.20	5.00	- -	17.70
Lee, 2019	Q	GC	MoCA	UM	ON	16	68.13	7.72	- -	21.44	15	64.67	3.37	- -	13.33
Lench, 2021	Q	GC	MMSE	M	ON	38	67.10	7.80	2.10	18.20	17	68.60	5.20	2.00	18.60
Li, 2020	Q, O	GC	MMSE	M	ON	25	66.52	6.86	2.60	29.16	30	60.00	2.72	2.03	25.10
Lira, 2020	Q, O	GC	MMSE	UM	ON	27	66.70	8.70	3.10	49.70	22	65.60	8.10	2.70	35.10
Liu, 2019	Q	GC	MMSE	M	ON	33	68.91	5.81	2.70	31.80	35	62.60	3.30	2.03	27.48
Lord, 2020	O	GC EF	MoCA FAB	UM	ON	54	69.20	12.30	- -	45.10	76	70.30	7.80	- -	36.40
Lord, 2012	Q	GC EF VS	MDRS MDRS	UM	ON	27	67.50	10.10	- -	27.80	27	70.40	6.30	- -	19.80

			JLO												
Lu, 2017	Q, O	GC	MoCA	M	OFF	11	66.30	7.80	- -	30.70	14	64.30	4.70	- -	29.00
Lv, 2021	Q, O	GC	MMSE	M	ON	10	65.75	10.45	- -	40.13	10	66.27	8.20	- -	36.67
Maidan, 2019	Q	GC EF	MoCA TMTB	UM	ON	26	73.90	11.70	- -	33.58	11	74.30	4.10	- -	21.00
Mancini, 2018	Q	GC	MMSE	M	ON	25	6.20	7.60	3.20	36.40	69	65.40	4.90	2.40	33.40
Mandal, 2021	Q, O	GC EF	MoCA Shifting	UM	ON	15	64.27	4.73	2.06	35.93	30	62.07	4.93	2.01	26.86
Matar, 2013	Q	GC	MMSE	UM	ON	36	66.20	- -	2.30	29.40	37	63.20	- -	1.60	21.03
McKay, 2018	Q	GC EF	MoCA TMTB-A	UM	- -	26	67.00	8.50		35.90	39	69.00	6.40		29.40
Mi, 2020	Q, O	GC	MoCA	UM	ON	40	62.03	8.18	2.58	42.23	31	58.03	5.23	1.90	30.81
Miranda-Domínguez, 2020	Q	GC	MMSE	UM	OFF	29	68.90	9.40	- -	45.90	42	69.20	5.90	- -	36.50
Mitchell, 2019	Q	GC	MoCA	UM	ON	9	69.00	6.00	- -	51.00	9	64.00	9.00	- -	42.00
Mohammadi, 2015	Q	GC EF	MoCA Stroop	M	OFF	10	60.40	14.60	- -	38.10	12	62.50	11.90	- -	34.60
Morris, 2020	Q, O	GC EF MVS	MoCA Trails B-A Dot Counting	UM	OFF	66	68.08	7.83	2.47	45.92	81	68.80	4.93	2.12	36.20
Myers, 2017	Q	EF LG	JLO Trails B-A WF	- -	OFF	- -	- -	7.50	- -	- -	- -	- -	4.30	- -	- -
Nackaerts, 2018	Q	GC	MoCA	UM	OFF	10	66.53	- -	- -	37.77	27	62.83	- -	- -	22.17
Nanhoe-Mahabier, 2012	Q	GC EF	MMSE FAB	M	OFF	8	53.80	7.90	2.20	19.60	11	59.30	5.30	2.10	15.70
Nanhoe-Mahabier, 2011	Q, O	GC EF	MMSE FAB	M	OFF	12	60.50	9.60	2.40	35.40	15	60.20	7.70	2.10	30.60
Nanhoe-Mahabier, 2013	Q	GC EF	MMSE FAB	UM	OFF	7	64.10	8.40	- -	29.00	7	62.10	6.30	- -	26.00
Nantel, 2012	O	EF VS	TMTB Block Design	M	ON	18	62.20	13.40	- -	39.80	11	63.60	6.70	- -	35.90

Nemanich, 2015	Q	GC	MMSE	M	OFF	13	68.15	9.27	- -	49.23	13	67.38	6.43	- -	40.77
Nemanich, 2016	Q	GC EF	MoCA TMT B-A	M	OFF	13	68.70	8.73	- -	40.40	13	68.10	4.73	- -	36.30
Nieuwboer, 2009	Q, O	GC EF	MMSE Brixton EFT	M	ON	68	67.30	8.70	- -	35.20	65	66.00	7.80	- -	32.00
Nonnekes, 2014	Q, O	EF	FAB	M	OFF	12	65.77	- -	2.65	- -	14	67.58	- -	2.42	- -
Onder, 2021	UPDRS	GC	MMSE	UM	ON	12	- -	- -	- -	18.20	18	- -	- -	- -	10.90
Ortelli, 2019	Q	GC EF LGM VS	MMSE FAB SF RAVLT RCFT	UM	ON	128	67.30	12.80		21.00	177	66.50	8.80		19.40
Ou, 2014	Q, O	GC EF	MoCA FAB	UM	ON	221	64.36	- -	- -	35.90	253	60.11	- -	- -	24.10
Park, 2014	Q, UPDRS	GC	MoCA	M	OFF	9	66.70	8.30	2.20	17.20	9	61.40	4.30	1.70	19.60
Park, 2021	Q	GC	MMSE	M	OFF	31	69.10	8.39	2.61	35.00	46	70.40	4.36	2.37	33.90
Paz, 2021	Q	GC	MoCA	UM	ON	51	65.94	8.26	2.79	22.74	52	64.52	5.52	2.00	17.40
Peterson, 2016	Q	GC	MoCA	M	ON	12	65.40	11.32	- -	28.88	15	66.35	6.83	- -	24.14
Pieruccini-Faria, 2014	Q, O	GC EF VS	MMSE TMT B-A Block Design	M	ON	13	73.60	8.30	- -	37.30	14	69.60	7.60	- -	33.10
Pietracupa, 2018	Q	GC EF	MMSE FAB	M	ON	21	66.30	11.00	2.00	35.10	16	69.70	9.50	2.50	29.80
Pimenta, 2019	Q	GC	MoCA	UM	ON	27	71.50	- -	3.00	39.80	51	69.13	- -	2.46	28.40
Piramide, 2020	O, UPDRS	GC EF LGM VS	MMSE TMT B-A SF Digit Span RCFT	M	ON	17	69.55	- -	- -	32.53	10	65.13	- -	- -	26.60
Plotnik, 2005	Q	GC	MMSE	M	ON	24	61.30	10.40	2.70	10.00	12	64.80	10.00	2.70	13.90
Potvin-Desrochers, 2019	Q	GC	MoCA	M	ON	14	67.70	7.90	2.50	39.00	13	65.80	6.00	2.10	33.00

Raffo De Ferrari, 2015	Q	GC EF VS	MMSE ToL RCFT	M	ON	15	72.00	10.20	2.60	31.00	14	71.00	7.90	2.40	30.80
Ricciardi, 2014	Q	GC EF LG M VS	MMSE FAB SF Digit Span VOSP	M	ON	18	72.52	- -	- -	25.25	9	69.50	- -	- -	25.67
Ruan, 2020	Q, O	GC	MMSE	M	OFF	23	65.00	6.02	2.45	28.78	33	63.79	3.27	2.09	27.86
Rubino, 2014	Q, O	GC M	MMSE Digit Span	M	ON	13	68.08	8.15	2.43	17.85	13	68.69	7.08	2.31	17.23
Schlenstedt, 2018	Q	GC	MoCA	M	OFF	33	69.20	7.80	2.50	44.20	30	69.60	6.70	2.20	41.10
Schlenstedt, 2020	Q	GC	MoCA	M	OFF	18	67.80	9.10	2.40	45.30	18	70.30	8.20	2.10	43.60
Scholl, 2021	Q, O	GC EF M	MoCA DCCS PSM	UM	ON	41	68.90	5.90	2.50	17.20	39	68.40	4.30	1.50	9.40
Shah, 2018	Q	GC EF	MoCA FAB	UM	ON	22	65.70	8.70	2.30	18.80	27	66.50	7.30	1.70	12.00
Shine, 2013	Q, MDS-UPDRS	GC	MMSE	M	OFF	14	63.20	5.90	2.20	31.90	15	63.40	4.90	1.90	29.10
Shine, 2013	Q, MDS-UPDRS	GC	MMSE	M	- -	10	67.10	7.30	2.30	26.20	10	66.30	4.80	2.70	19.70
Silva-Batista, 2021	Q	GC	MoCA	UM	OFF	39	68.10	8.60	2.30	46.00	43	69.20	4.40	2.10	38.30
Silveira, 2015	O	GC	MMSE	M	ON	13	74.00	10.15	- -	31.76	14	68.78	5.00	- -	28.14
Singh, 2020	Q	GC	MoCA	UM	ON	13	69.50	7.50	2.40	19.20	13	65.20	4.80	1.60	10.50
Smulders, 2015	Q	GC	MMSE	M	OFF	14	58.00	- -	- -	38.00	14	60.00	- -	- -	36.00
Snijders, 2011	Q, O, SR	EF	FAB	M	OFF	12	58.70	9.80	- -	34.60	12	62.60	7.10	- -	28.60
Spildooren, 2010	Q	GC	MMSE	M	OFF	14	68.60	9.00	2.50	37.90	14	66.70	7.80	2.40	34.40
Spildooren, 2012	Q	GC	MMSE	M	OFF	13	68.10	9.60	2.00	42.80	13	66.40	7.70	2.50	37.50
Stefanova, 2014	Q, O, SR	GC	MMSE	M	ON	30	64.90	11.61	2.77	37.50	36	64.67	10.09	2.29	32.33
Steidel, 2021	Q	GC	MMSE	M	OFF	27	66.50	5.40	2.40	27.20	32	64.40	4.60	2.20	22.40
Stuart, 2020	Q	GC EF	MoCA FAB	M	OFF	13	69.69	12.08	- -	40.00	12	68.67	7.75	- -	32.50

Stuart, 2021	Q	GCEF	MoCA Choice RxT	UM	ON	22	68.09	9.48	- -	38.86	21	69.33	5.50	- -	25.38
Sunwoo, 2013	Q, O, UPDRS	GC	MMSE	UM	- -	16	66.70	4.20	- -	30.70	30	68.80	3.30	- -	18.70
Tard, 2015	O	GCEF	MMSE MDRS	M	OFF	11	61.36	11.00	- -	34.60	11	62.18	8.10	- -	25.40
Tard, 2016	Q	GCEF	MMSE FAB	M	OFF	12	62.50	11.30	2.80	19.80	13	60.20	3.30	1.80	16.30
Tard, 2015	Q	GCEF	MMSE Go-No-Go	M	ON	42	61.90	14.30	- -	25.50	36	59.30	4.20	- -	22.80
Taximaimaiti, 2021	Q	GCEF LGM VS	MoCA TMT B-A WF Digit Span JLO	M	ON	22	67.70	7.90	- -	17.00	22	70.70	5.60	- -	14.00
Tessitore, 2012	Q, SR	GCEF LGM	MMSE FAB PF Corsi BTT	M	ON	16	66.94	5.44	1.81	17.50	13	66.31	6.17	1.75	13.00
Tolleson, 2015	Q	GC	MoCA	M	ON	14	65.30	9.10	- -	25.30	20	62.50	7.30	- -	21.90
Vandenbossche, 2013	Q	GC LG VS	MMSE COWAT Brixton SAT	UM	ON	11	67.32	10.45	2.5	38.91	11	68.20	8.55	2.23	34.18
Vandenbossche, 2011	Q	GC	MMSE	M	ON	14	65.72	10.79	- -	36.36	14	68.03	8.21	- -	33.21
Vervoort, 2016	Q	GC	MMSE	UM	OFF	13	65.80	7.90	2.20	38.30	60	58.20	5.80	2.00	25.90
Vitorio, 2020	Q	GCEF	MoCA FAB	UM	OFF	24	70.30	10.10	2.33	42.40	23	70.80	7.20	2.09	35.00
Walton, 2015	Q	GCEF	MMSE TMT B-A	M	ON	15	68.00	8.13	2.6	33.27	11	65.73	5.27	2	22.45
Walton, 2015	Q	GC	MoCA	M	ON	34	66.44	6.54	2.18	28.06	38	66.76	5.70	2.08	26.47
Wang, 2016	Q, SR	GCEF LGM	MMSE FAB PF Digit	M	OFF	14	72.36	3.29	- -	24.57	16	68.88	3.70	- -	20.94

			Span												
Wang, 2021	O	GC	MMSE	M	OFF	25	65.24	6.70	2.46	32.96	25	65.32	7.44	2.60	33.32
Weiss, 2015	Q	GC	MoCA	M	OFF	28	64.35	7.52	3.18	35.59	44	66.51	6.67	2.35	36.25
Willems, 2006	Q	GC	MMSE	M	ON	10	68.40	11.80	2.80	27.20	10	60.60	6.20	2.70	24.70
Wu, 2020	Q	GC	MoCA	UM	ON	45	66.50	4.00	- -	27.50	165	66.20	2.00	- -	15.50
Yao, 2017	Q	GC	MMSE	UM	ON	104	65.72	9.52	2.01	13.71	82	66.35	9.16	1.92	9.27
Yu, 2021	Q, O	GC EF	MoCA FAB	M	OFF	20	64.50	6.30	2.40	21.00	21	60.20	5.50	2.00	18.90
Zhang, 2021	Q	GC	MoCA	UM	ON	40	63.92	7.00	3.18	41.57	40	60.83	4.50	2.30	30.08
Zhou, 2018	Q, O	GC	MMSE	M	OFF	14	62.14	7.93	3.20	35.50	20	62.70	3.55	2.25	35.52
Zhou, 2019	Q, O	GC	MoCA	UM	- -	20	56.33	3.86	2.25	43.36	147	66.90	10.65	1.99	37.30

FOG Assessment Key: Q=questionnaire (e.g., FOG Questionnaire), O=observation; SR=self-report. Disease Severity Key: M=matched; UM=unmatched. # indicates group differences in disease severity were stated, but data were not provided. * Disease severity measures include scores from the UPDRS, and MDS-UPDRS, with studies reporting either Part II, III, or total scores. 'FOG- = non-freezers; FOG+ = freezers; H&Y= Hoehn & Yahr Scale; UPDRS III= Movement Disorder Society's Unified Parkinson's Disease Rating Scale Motor Component; FOG-Q= Freezing of Gait Questionnaire; N-FOG-Q= New Freezing of Gait Questionnaire. '- - indicates data was not stated in the study. Hall 2015 compared cognition between a) early FOG+ and FOG- b) advanced FOG+ and FOG-. Cognitive Domains: GC= Global Cognition; EF= Executive Function/Attention; LG= Language; M= Memory; VS= Visuospatial. Cognitive Tests- MoCA= Montreal Cognitive Assessment; MMSE= Mini-Mental State Examination; TMT= Trail Making Test; WF= Word Fluency Task; SDMT= Symbol Digit Modalities Test; HVLT= Hopkins Verbal Learning Test; JLO= Judgement of Line Orientation Test; DMT= Digit Memory Test; FAB= Frontal Assessment Battery; DCCS= Dimensional Change Card Sort; Fuld Object-Memory Evaluation; RCFT= Rey Complex Figure Test; MDRS= Mattis Dementia Rating Scale; SF= Semantic Fluency Test; RAVLT= Rey Auditory Verbal Learning Test; ToL= Tower of London Test; VOSP= The Visual Object and Space Perception Battery; PSM= Picture Sequence Memory Test; PF= Phonemic fluency Task; COWAT= Controlled Oral Word Association Test; Ltr Memory = Letter Memory; Simple RxT = Simple Reaction Time; SST= Stop Signal Task; Corsi BTT= Corsi Block Tapping Task.

Table 2. Future Recommendations

1. Consider using comprehensive, standardized assessment batteries across studies (e.g., NIH Toolkit).

2. Ensure FOG cohorts are well characterized for disease severity and current medications (dopaminergic and non-dopaminergic).

3. Consistently report medication status and clearly define criteria determining ON and OFF medication status.

4. Where possible, match or statistically account for varying disease severity across FOG+ or FOG- cohorts.

5. Further investigation into the effect of cognitive interventions (across cognitive domains) on FOG severity.

6. Recognition in clinical practice for likely cognitive deficits in FOG, routine assessment of cognition, and assessment of cognitive-related tasks (i.e., dual-tasking abilities).

FOG = freezing of gait; FOG+ = freezers; FOG- = non-freezers

Highlights

- In this meta-analysis we compared cognitive function between freezers and non-freezers
- A meta-analysis compared the cognition between freezers and non-freezers.
- Freezers exhibited worse cognition in all domains compared to non-freezers
- Worse disease severity and "ON" medication status may amplify the effect of FOG status on cognition
- Unequal sample size and study heterogeneity partially limit interpretability.