

# A SYSTEMATIC REVIEW AND META-REGRESSION ANALYSIS OF THE RELATIONSHIP BETWEEN PHYSICAL AND PSYCHOLOGICAL SYMPTOMS IN INDIVIDUALS WITH PARKINSON'S DISEASE

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## Introduction

People with Parkinson's Disease (PwPD) can experience both physical and psychological symptoms such as tremor, muscle stiffness, anxiety, depression, and apathy.

At present, any potential relationship between common physical and psychological symptoms is poorly understood.

Considering any relationship between physical and psychological symptoms should improve our understanding of the condition and may translate to improved symptom management and outcomes for patients.

## Purpose

This systematic review and meta-regression analysis aimed to examine available literature reporting measures of physical function, anxiety and/or depression.

## Methods

The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Systematic searches of four databases (MEDLINE, CINAHL, AMED, and APA PsychInfo) were completed, identifying studies published before 22/10/2021 (PROSPERO CRD42021281392).

Studies were screened against pre-defined criteria, with included studies reporting objective findings from physical and psychological assessments commonly used in clinical and research settings.

Abstract and full-text screening was completed by two reviewers independently. Quality and risk of bias was assessed using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies.

Quantitative baseline measures for physical and psychological outcome measures were extracted and meta-regression analysis of the relationship between variables completed using R Studio.

## Results

Of 1,175 studies retrieved, 40 were selected for analysis with only one study assessing the relationship between physical and psychological outcomes within their cohort. 27 studies were also eligible for meta-regression analysis - a total sample of 1,211 participants.

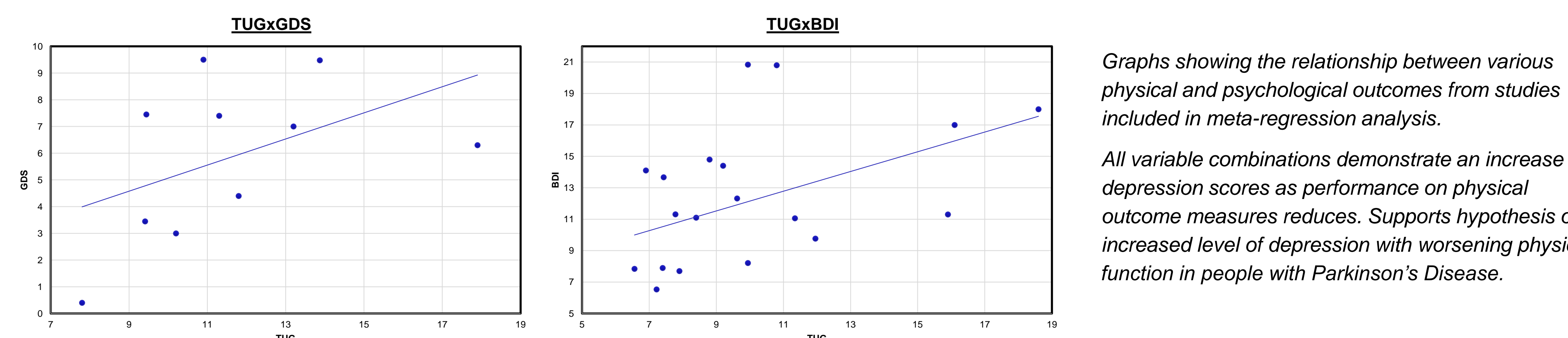
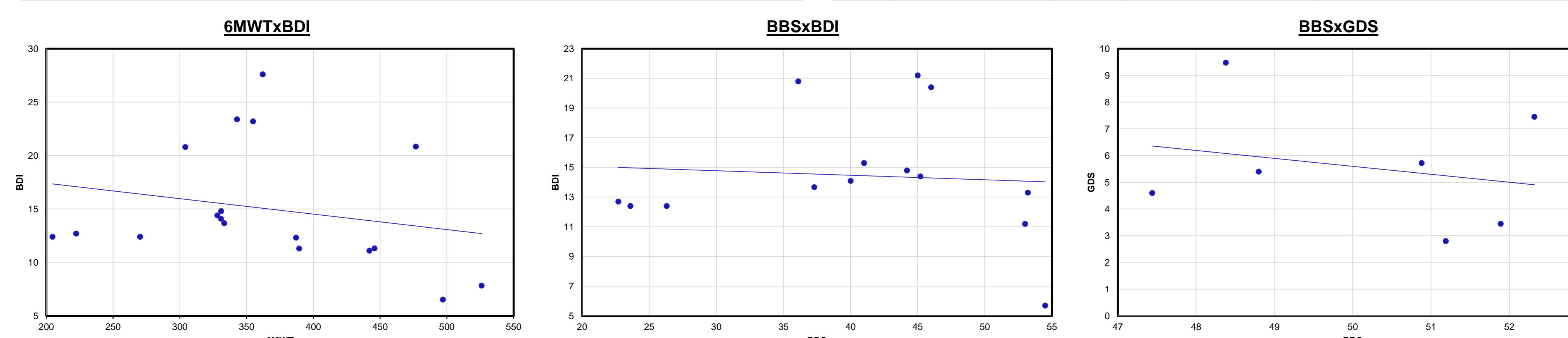
Meta-regression analysis of 5 combinations of paired physical and psychological outcomes showed a significant moderating effect of symptoms of depression (Beck Depression Index) on mobility (Timed-Up-and-Go Test) (Coefficient = 0.3675, 95% CI 0.0901 to 0.6450, P = 0.0123) and balance (Berg Balance Score) scores (Coefficient = -1.2518, 95% CI -1.7687 to -0.7349, P = 0.0002).

Table 1: Outcome measures eligible for selection:

Physical Outcome Measures:	
<b>Gait</b>	10MW (10m Walk Test), 6MWT (6 Minute Walk Distance), Rapid Turns, M-PAS (Modified Parkinson Activity Scale), TUG (Timed-Up-And-Go Test).
<b>Balance</b>	Push and Release, Berg Balance Scale, M-PAS Chair (Modified Parkinson Activity Scale - Chair), FTSTS (Five times Sit to Stand), M-PAS Gait (Modified Parkinson Activity Scale - Gait), TUG (Timed-Up-And-Go Test), Rapid Turns, DGI (Dynamic Gait Index), FGA (Functional Gait Assessment), Mini-BESTest (Mini Balance Evaluation Systems Test).
<b>Transfers</b>	M-PAS Bed (Modified Parkinson Activity Scale - Bed), M-PAS Chair (Modified Parkinson Activity Scale - Chair), FTSTS (Five times Sit to Stand), TUG (Timed Up-And-Go Test).
<b>Physical Capacity</b>	6MWT (6 Minute Walk Distance) with Borg 6-20.
Psychological Outcome Measures:	
<b>Anxiety</b>	PAS (Parkinson's Anxiety Scale), BAI (Beck Anxiety Inventory), STA (State Trait Anxiety Inventory), GAD-7 (Generalised Anxiety Disorder Assessment), HADS (Hospital Anxiety and Depression Scale)
<b>Depression</b>	Depression - BDI-II (Beck Depression Inventory-II), Ham-D (Hamilton Depression Rating Scale), PHQ-9 (Patient Health Questionnaire), GDS-15 (Geriatric Depression Scale), HADS (Hospital Anxiety and Depression Scale).

Table 2: Outcome measure combinations from included studies:

Physical Outcome Measures	Psychological Outcome Measures							
	PAS	BAI	STAI	GAD-7	HADS	BDI	HAM-D	GDS
Timed 10m Walk	0	1	0	0	2	2	1	2
6MWT	0	1	2	0	0	10	0	3
Rapid turns	0	0	0	0	0	0	0	0
M-PAS	0	0	0	0	0	0	0	0
TUG	0	1	1	0	3	11	2	6
Push and Release	0	0	0	0	0	0	0	0
BBS	0	0	0	0	0	8	2	6
FTSTS	0	0	0	0	0	3	0	1
DGI	0	0	0	0	1	1	0	1
FGA	0	0	0	0	0	0	0	0
Mini-Best	0	0	1	0	0	2	0	2



Graphs showing the relationship between various physical and psychological outcomes from studies included in meta-regression analysis.

All variable combinations demonstrate an increase in depression scores as performance on physical outcome measures reduces. Supports hypothesis of increased level of depression with worsening physical function in people with Parkinson's Disease.

**Sample Heterogeneity:** Cohen's Q-test confirmed the heterogeneity of the sample in all outcome combinations 6MWT and BDI:  $Q(df=19) = 17866.1999, p < 0.0001$ , BBS and BDI:  $Q(df=13) = 777.0983, p < 0.0001$ , TUG and BDI:  $Q(df=19) = 112.3925, p < 0.0001$ , TUG and GDS:  $Q(df=9) = 35.5070, p < 0.0001$ , BBS and GDS:  $Q(df=5) = 10.8870, p = 0.05$ .

**Coefficients:** Analysis showed that higher scores in TUG were associated with higher scores on BDI (Coefficient=0.3675, 95% CI 0.0901 to 0.6450) and GDS (Coefficient=0.4481, 95% CI -0.2111 to 1.1073). Shorter 6MWT distances were associated with higher BDI scores (Coefficient=-2.2732, 95% CI -9.8007 to 5.2543), whilst lower BBS scores were associated with higher BDI (Coefficient=-1.2518, 95% CI -1.7687 to -0.7349) and GDS scores (Coefficient=-0.2205, 95% CI -1.3136 to 0.8727).

**Moderating Effects:** Analysis showed a significant moderating effect of BDI on BBS ( $F(df1=1, df2=12) = 27.8439, p = 0.0002$ ) and TUG ( $F(df1=1, df2=18) = 7.7446, p = 0.0123$ ). There was no significant moderating effect of BDI on 6MWT. Similarly, there was no significant moderating effects of GDS on TUG or BBS.

## Discussion & Conclusions

This systematic review highlighted that despite both physical and psychological outcome measures being routinely collected, only one study included in this review directly examined their relationship.

Our exploratory meta-regression analysis showed a trend for the physical ability of PwPD to reduce as scores on depression outcomes increase, showing a significant moderating effect of depression on gait, balance, and transfer performance.

These findings support the existence of a complex relationship between common physical and psychological symptoms in PD, which warrants further investigation.

## Recommendations

Clinicians with physical-health focused roles should screen individuals at risk for depression, and refer to psychological services where needed.

Future research is required to uncover the true extent of any psycho-physical symptom interaction in PD. This should include considering the views of PwPD and how any relationship between symptoms develops over time.

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Further information

