npj | parkinson's disease

Article

Published in partnership with the Parkinson's Foundation

https://doi.org/10.1038/s41531-025-01168-9

Apathy self-awareness and its neural correlates in Parkinson's Disease

Hannah Conn[1], Hideo Suzuki[1], Zekai Jin[2], Ana Marin[1], Xi Zhu[3], Seonjoo Lee[2,3,4], Edward Huey[5], Ratko Radakovic[6,7,8,9], Sarah R. Heilbronner[10] & Nora Vanegas-Arroyave[1]

Apathy is a prevalent non-motor symptom in Parkinson's disease (PD) that negatively impacts quality of life. Impaired self-awareness of apathy (ISA-a) further impacts patient care by limiting engagement. While apathy has been associated with reduced fronto-striatal functional connectivity (FC), the neural basis of ISA-a remains unclear. We examined ISA-a in 52 individuals and the neural basis of ISA-a in 35 individuals with PD using a dimensional approach (i.e., initiation, executive, and emotional apathy) and resting-state fMRI (3T scanner). Apathetic PD patients (42%) showed poorer self-awareness than non-apathetic peers. Apathetic PD patients showed a trend towards reduced FC between the left anterior cingulate cortex (ACC) and the left nucleus accumbens (NAcc). A trend for ISA-a in the emotional domain showed altered FC between the left NAcc and orbitofrontal cortices, and the right ACC and right anterior insular cortex. These findings suggest potential neural mechanisms underlying apathy and ISA-a to be studied in larger populations.

Apathy, or loss of motivation, is one of the most common neuropsychiatric symptoms across neurodegenerative diseases of aging[1,2]. Apathy is characterized by difficulties with initiation and self-motivation toward goals (i.e., self-care, physical activity, social participation)[3]. In Parkinson's disease (PD), although the motor syndrome remains the core symptomatology of the disease, PD patients also share an increased risk for this highly prevalent non-motor neuropsychiatric symptom. Apathy is now recognized as one of the most debilitating non-motor symptoms in PD patients, reducing participation in everyday activities, lowering functional capabilities, and increasing risk of death and caregiver burden[1,2,4–6].

According to the original description by Levy and Dubois[3] and to the proposed diagnostic criteria for apathy in neuropsychiatric disorders[7], apathy is thought to be composed of three dimensions—*auto-activation/initiation, cognitive/executive and emotional/affective*. Several assessment scales have been used to examine apathy, with substantial variability in their ability to encompass these dimensions. More recently, a unified Dimensional Apathy Scale (DAS) Framework[8] has served to distinguish three separate apathy subtypes within neurodegenerative diseases, controlling for common measurement confounds of physical disability and depression. The DAS framework[8] recognizes a triadic structure of initiation, executive, and emotional apathy. An additional factor that overlaps with all apathy subtypes is apathy self-awareness or concern, which can be assessed by comparing caregiver (informant) and patient reports.

Lack of awareness about one's own deficits, or anosognosia, has also been commonly described in patients with PD[9–11]. Operationally, this means that caregivers and doctors perceive higher levels of impairment than patients themselves do. Impaired self-awareness (ISA) has a negative impact on both patients and their caregivers, preventing patients from seeking timely medical attention, delaying diagnoses, decreasing treatment compliance, and increasing caregiver's burden. ISA for motor symptoms (ISA-m) has been described in up to 66% of PD patients, including ISA of levodopa-induced dyskinesias[11–15] and ISA of hypokinetic symptoms[16].

Deficits of self-awareness for non-motor symptoms in PD patients are also prevalent and may be clinically relevant[9,17,18]. Similar to patients with Alzheimer's Disease, PD patients with mild cognitive impairment (MCI) have greater ISA for cognitive deficits than those without MCI[19]. Importantly, the ISA for cognitive deficits appears to be highly influenced by levels of depression[19]. Although still poorly understood, ISA for apathy (ISA-a) has been described to have a profound impact on a patient's quality of life perception and self-advocacy[20].

[1]Department of Neurology, Baylor College of Medicine, Houston, TX, USA. [2]Mental Health Data Science, New York State Psychiatric Institute, New York, NY, USA. [3]Department of Bioengineering, The University of Texas at Arlington, Arlington, TX, USA. [4]Department of Biostatistics, Columbia University Irving Medical Center, New York, NY, USA. [5]Department of Psychiatry and Human Behavior, Brown University Warren Alpert Medical School, Providence, RI, USA. [6]Department of Medicine and Health Sciences, University of East Anglia, Norwich, UK. [7]Euan MacDonald Centre for Motor Neuron Disease Research, University of Edinburgh, Edinburgh, UK. [8]Alzheimer Scotland Dementia Research Centre, University of Edinburgh, Edinburgh, UK. [9]Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, UK. [10]Department of Neurosurgery, Baylor College of Medicine, Houston, TX, USA.
e-mail: Nora.VanegasArroyave@bcm.edu

Phenotypes like apathy and self-awareness usually involve many brain regions. For apathy, most heavily implicated are regions involved in reward and effort-guided decision making, such as the anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), and their connections to the striatum[21–23]. Self-awareness implicates many (but not all) of the same circuits. For example, ISA-m deficits in patients with PD is related to ACC dysfunction[18,24]. However, equally important is another cortical region, the anterior insula, which helps to link consciousness of one's own body with the external world[25]. In fact, insular lesions have been associated with a broad range of deficits of self-awareness in neurodegenerative diseases including PD[26,27].

Here, we set out to characterize ISA-a in a cohort of PD patients without dementia. We used a dimensional approach to examine clinical and neural contributions to initiation, executive, and emotional ISA-a. We hypothesized that ISA-a would be related to degree of apathy and fronto-striatal functional connectivity patterns, implicated in apathy and in self-awareness more generally.

Results

Participant selection

We screened a total of 96 patients between 2022 and 2024 (Fig. 1). Forty-two patients were excluded due to a variety of reasons: established diagnosis of mood disorder and/or other neurological condition, unable to complete an MRI due to safety checks or claustrophobia. The remaining 54 patients were enrolled and participated in the 2 days of testing, described above. One patient was excluded due to the presence of a brain tumor, and another 1 patient was excluded due to inability to complete the fMRI portion of the study. The remaining 52 patients were included in the behavioral analysis. Following quality control measures, 17 patients' fMRI data could not be included in FC analysis. The remaining 35 patients' data were then included in the FC analysis (Fig. 1).

The sample was derived from an on-going study. Current sample size ($n = 52$) is powered to detect a medium-to-large effect size correlation ($r = 0.38$) for the behavior measures to have 80% power at 5% significance level. For resting state fMRI, 32.7% of participants were excluded due to imaging quality (mostly head motion), resulting $n = 35$, with minimum detectable effect size of $r = 0.45$ (a moderate-to-large effect size).

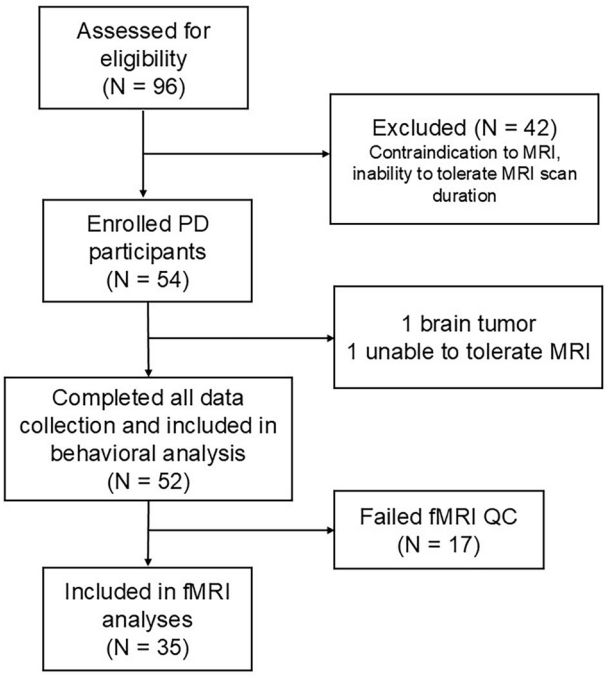

Fig. 1 | Flow graph depicting the final patient cohort after inclusion and exclusion criteria were considered. fMRI = functional magnetic resonance imaging, PD = Parkinson's disease, QC = quality control.

Demographic and clinical characteristics

Demographic and clinical characteristics are provided in Table 1. The prevalence of apathy was 40.38% (21 patients) while the prevalence of depression, as determined by a score of 6 or greater on the GDS, was 19% (10 patients). There were no statistically significant differences in demographic and clinical characteristics (including age, MoCA, GDS, and MDS-UPDRS part III scores), between apathetic and non-apathetic patient groups. There were also no significant differences in Levodopa equivalent daily dose (LEDD) requirements between the two groups.

ISA-a increased as a function of apathy levels

There was a significant correlation between apathy levels and the severity of ISA-a, with more apathetic PD patients exhibiting also more pronounced ISA-a ($r = 0.593$, $p < 0.00001$). This correlation was further strengthened after adjusting for age, MoCA, GDS, and MDS-UPDRS part III scores as covariates (partial $r = 0.596$, $p < 0.00001$, Fig. 2A). In our patient cohort, the total ISA-a was correlated with the executive and initiative apathy subscales ($r = 0.473$, $p < 0.001$, Fig. 2C and $r = 0.609$, $p < 0.001$, Fig. 2D, respectively). We did not find a significant association with the emotional apathy subscale ($r = 0.233$, $p = 0.096$), although the direction of the effect was the same as for the other two subscales.

Contrasting patterns of apathy self-awareness between apathetic and non-apathetic PD patients

When considering the full cohort, there were no significant differences between DAS scores reported by PD patients and their informants. When analyzed separately, PD patients with apathy ($n = 21$) under-reported apathy levels as compared to their informants (Table 2). This difference was statistically significant for the total DAS score when adjusting for age, MoCA, GDS, and MDS-UPDRS part III (Table 2, Fig. 3A, $p < 0.001$). A similar trend was observed for each DAS subscale but only statistically significant for the DAS initiation subscale ($p < 0.05$) (Table 2, Fig. 3B).

Conversely, among non-apathetic PD patients ($n = 31$) there was a tendency to report higher DAS scores as compared to their informants (Table 2). After adjusting for age, MoCA, GDS, and MDS-UPDRS part III, the difference in self-reported total DAS score and subscales was not statistically significant (Table 2). The interaction model was used to compare ISA-a between apathetic and non-apathetic patients. There were significant differences in total and all apathy sub-scores (Table 3). All significant findings survived multiple comparison correction.

FC correlates with apathy and ISA-a

As a result of the image quality check, 17 patients with PD (32%) were excluded from subsequent analyses. Importantly, there were no statistically significant differences in demographic characteristics (i.e., age, gender, ethnicity, education, disease during, motor disease severity) between those who failed quality control and those included in the fMRI analyses (Supplementary Table 1). Also, within the final sample size following the quality check ($N = 35$), there were no differences in demographics or neuropsychiatric features between apathetic and nonapathetic PD patients (Supplementary Table 2).

After controlling for covariates, higher (worse) emotional apathy scores showed a negative trend, or decreased FC, between the left ACC and the left NAcc (Table 4). This association did not survive FDR-adjusted correction. Nonetheless, the effect size exceeded the medium threshold $|r| > 0.3$, indicating a trend worth highlighting.

The association between FC and ISA-a was also studied (Table 5). The ISA for emotional apathy also showed a trend FC[1] between the left NAcc and left OFC ($b = 7.24$, $t^{27} = 2.19$, $p < 0.05$) and[2] between the left NAcc and right OFC($b = 8.58$, $t^{27} = 2.36$, $p < 0.05$). In addition, increased emotional ISA-a was marginally associated with FC between the right AIC and the right ACC ($b = 7.87$, $t^{27} = 2.03$, $p = 0.05$) before FDR-adjusted correction.

Table 1 | Demographic and clinical characteristics of PD patients

Characteristic	Total, $N = 52$[a]	Apathetic, $N = 21$[a]	Non-apathetic, $N = 31$[a]	p-value[b]
Age	63.19 (9.44)	62.95 (11.32)	63.35 (8.13)	0.89
Gender				0.25
female	13 (25%)	3 (14%)	10 (32%)	
male	39 (75%)	18 (86%)	21 (68%)	
Ethnicity				0.46
Hispanic	14 (27%)	4 (19%)	10 (32%)	
non-Hispanic	38 (73%)	17 (81%)	21 (68%)	
Race				0.70
non-white	10 (19%)	3 (14%)	7 (23%)	
white	42 (81%)	18 (86%)	24 (77%)	
Handedness				0.93
ambidextrous	5 (9.6%)	2 (9.5%)	3 (9.7%)	
left	11 (21%)	5 (24%)	6 (19%)	
right	36 (69%)	14 (67%)	22 (71%)	
Education	17.08 (2.67)	17.29 (2.49)	16.94 (2.82)	0.64
MDS-UPDRS-III	38.98 (9.93)	40.67 (7.98)	37.84 (11.04)	0.29
Disease Duration	9.67 (5.04)	9.38 (5.23)	9.87 (4.98)	0.74
LEDD	1,345.21 (716.64)	1,314.38 (686.59)	1,366.10 (746.79)	0.80
MoCA	25.56 (3.21)	26.48 (2.04)	24.94 (3.71)	0.061
GDS	3.60 (3.01)	4.10 (3.16)	3.26 (2.91)	0.34
depressed, GDS > 6	10 (19%)			
GAD-7	5.11 (5.56)	6.25 (5.79)	4.27 (5.36)	0.29

GAD-7 generalized anxiety disorder 7 scale, *GDS* Geriatric Depression Scale, *LEDD* levodopa equivalent daily dose, *MDS-UPDRS-III* Movement Disorders Society-Unified Parkinson's Disease Rating Scale part III, *MMSE* Mini-Mental State Examination, *MoCA* Montreal Cognitive Assessment Scale, *SD* standard deviation.

[a]*n* (%); Mean (SD).

[b]Pearson's Chi-squared test; Welch Two Sample *t*-test.

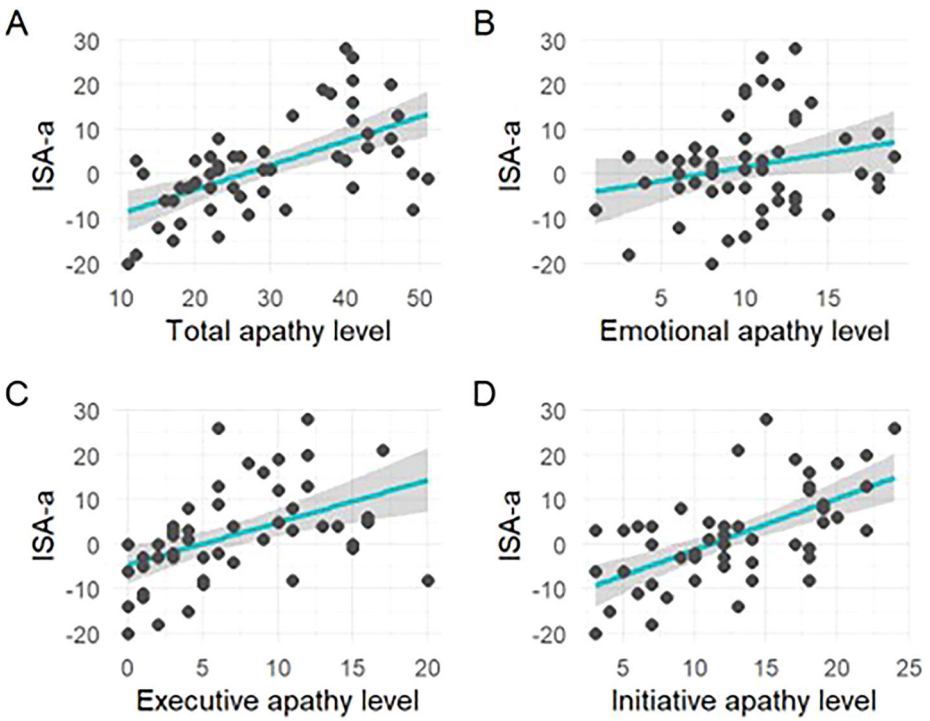

Fig. 2 | Scatter plot between ISA-a and apathy severity. A More apathetic patients exhibited higher levels of ISA-a (partial $r = 0.596$, $p < 0.00001$). **B** Emotional apathy level did not significantly correlate with ISA-a ($r = 0.233$, $p = 0.096$). **C** Executive apathy level significantly correlates with ISA-a ($r = 0.473$, $p < 0.001$). **D** Initiative apathy level also significantly correlates with ISA-a ($r = 0.609$, $p < 0.001$). ISA-a impaired self-awareness of apathy.

Table 2 | Statistical analysis of apathy measurements

Group	DAS Sub-scales	Summary Statistics[a]				LMM Result		
		Patients	Informants	Informants-Patients	Cohen's *d*	Estimate	t-value[b]	*p*-value[c]
All, *N* = 52	Executive	6.54 (4.33)	6.73 (5.31)	0.19 (4.55)	−0.039	0.19	0.35	0.73
	Emotional	9.87 (3.82)	10.25 (4.03)	0.38 (4.12)	−0.096	0.38	0.71	0.58
	Initiation	11.40 (4.98)	12.62 (5.65)	1.21 (5.81)	−0.224	1.21	1.60	0.18
	Total	27.81 (10.10)	29.60 (11.64)	1.79 (10.66)	−0.161	1.79	1.33	0.25
Apathetic, *N* = 21	Executive	8.43 (5.10)	11.00 (4.40)	2.57 (3.78)	−0.513	1.64	2.04	0.18
	Emotional	10.62 (5.08)	12.67 (4.02)	2.05 (4.27)	−0.422	2.12	2.04	0.18
	Initiation	13.81 (4.70)	17.57 (4.39)	3.76 (6.00)	−0.796	3.56	2.71	0.09 +
	Total	32.86 (11.77)	41.24 (6.60)	8.38 (9.66)	−0.772	7.31	3.96	0.01 +
Non-apathetic, *N* = 31	Executive	5.26 (3.21)	3.84 (3.70)	−1.42 (4.37)	0.399	−1.13	−1.61	0.18
	Emotional	9.35 (2.63)	8.61 (3.17)	−0.74 (3.67)	0.248	−1.03	−1.73	0.18
	Initiation	9.77 (4.54)	9.26 (3.55)	−0.52 (5.07)	0.123	−0.40	−0.40	0.73
	Total	24.39 (7.15)	21.71 (6.48)	−2.68 (8.95)	0.382	−2.55	−1.61	0.18

DAS dimensional apathy scale, *FDR* false discovery rate, *LMM* linear mixed model, *SD* standard deviation.
[a]Mean (SD).
[b]Degree of freedom is 51 for "All", 24 for "Apathetic" and 26 for "Non-apathetic" groups.
[c]Raw *p*-value. +: *p* value < 0.05 after FDR correction.

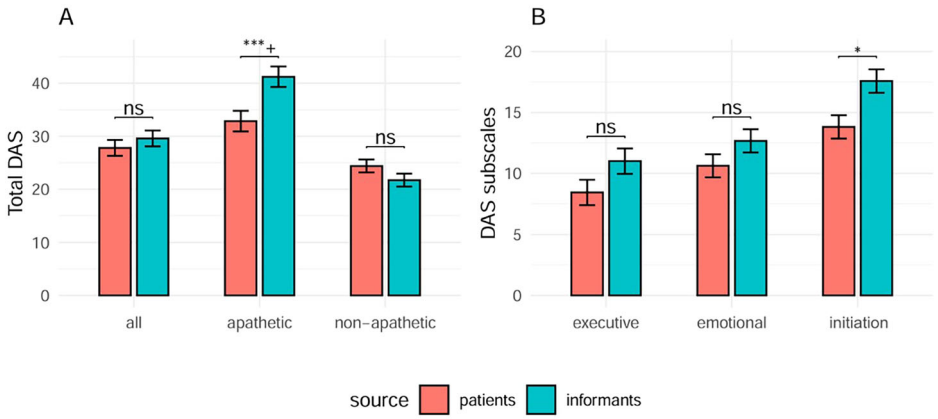

Fig. 3 | Bar plots of DAS scores as reported by patients and informants. Y axes represent DAS score where higher values indicate greater apathy. **A** Total DAS stratified by source (i.e., patients or informants) for all study participants as well as for apathetic and non-apathetic sub-groups. For the full cohort, there were no significant differences between DAS scores reported by patients and their informants. When considered separately, apathetic patients reported lower levels of apathy as compared with informant reports. Non-apathetic patients reported higher levels of apathy as compared with informant reports. **B** DAS sub-scales for apathetic subjects only, stratified by source (i.e., patients or informants). Error bars indicate LS mean ± SE. ns = not significant, *: p < 0.05, **: p < 0.01, ***: p < 0.001, +: FDR corrected p < 0.05. DAS Dimensional Apathy Scale, FDR false discovery rate.

Table 3 | Differences in ISA-a

DAS Scales	Apathetic vs. Non-apathetic PD patients		
	Estimates[a]	t-value (df = 46)	*p*-value[b]
Executive	2.88	2.57	0.02 +
Emotional	3.20	2.97	0.01 +
Initiation	3.85	2.48	0.02 +
Total	9.93	3.92	0.001 ++

DAS dimensional apathy scale, *df* degrees of freedom, *FDR* false discovery rate, *PD* Parkinson's disease.
[a]Parameter is the interaction between source and apathy group.
[b]Raw *p*-value. +: *p* value < 0.05 after FDR correction. ++: *p* value < 0.001.

Discussion

Deficits of self-awareness for neuropsychiatric symptoms are common among patients with PD and have compounded effects on a patient's perceived quality of life and self-advocacy. A deeper understanding of the clinical and neural mechanisms underlying ISA-a is crucial for addressing this poorly characterized phenomenon. Here, we examined ISA-a in a cohort of non-demented PD patients using a dimensional approach. The results of this first-of-its-kind study represent a novel contribution on the presentation and neurobiology of ISA-a in PD patients.

The prevalence of apathy varies across PD cohorts, ranging from 40–63%[1,5,6,28], becoming more common over the time course of disease[6]. Although our recruitment strategy (PD patients with motor fluctuations referred for DBS) may have introduced selection bias, the apathy prevalence in this subgroup resembles that of the larger PD population, supporting generalizability of our results. While not statistically significant, anxiety scores were higher amongst apathetic PD patients. Importantly, although apathy and depression are often comorbid[1,5,29], the prevalence of depression in our cohort was similar between apathetic and non apathetic individuals.

Executive and initiation apathy were previously found to be higher in PD compared to controls[30]. Similarly, initiation apathy was the most prominent profile in our cohort. We found a strong association between apathy and the degree of ISA-a, such that more apathetic patients were found to significantly under-report apathy as compared to those without apathy. Interestingly, non-apathetic individuals exhibited opposite reporting patterns, with a tendency to over-report their levels of apathy. In a recent study by Maggi et al.[21], ISA-a was associated with lower executive functioning and motor disease severity, but the effects of apathy levels on ISA-a were not

Table 4 | FC between ROI pairs correlated with DAS subscales

DAS subscale	FC	Estimate	*t*-value (df = 28)	*p*-value[a]	Effect size[b]
Emotional	left ACC - left NAcc	−7.81	−2.15	0.04	−0.33
Executive	left NAcc - right OFC	−9.02	−1.75	0.09	−0.29
Executive	left NAcc - left OFC	−8.02	−1.72	0.1	−0.28
Emotional	right ACC - left NAcc	−8.28	−1.72	0.1	−0.29
Initiation	right ACC - left DS	10.79	1.60	0.12	0.28

The analysis did not survive FDR correction, so we present the raw *p*-values.
This significant result ($p < 0.05$) did have an effect size that is greater than medium effect size, $|r| > 0.3$.
ACC anterior cingulate cortex, *DAS* dimensional apathy scale, *df* degrees of freedom, *DS* dorsal striatum, *FC* functional connectivity, *NAcc* nucleus accumbens, *OFC* orbitofrontal cortex.
[a]Raw *p* value (unadjusted).
[b]Standarized regression coefficient.

Table 5 | FC between ROI pairs correlated with ISA-a. The analysis did not survive FDR correction, so we present the raw *p*-values

ISA-a subscale	FC	Estimate	*t*-value (df = 27)	*p*-value[a]	effect size[b]
ISA-a, Emotional	left NAcc - left OFC	7.24	2.19	0.04	0.33
ISA-a, Emotional	left NAcc - right OFC	8.58	2.36	0.03	0.36
ISA-a, Emotional	right ACC - R AIC	7.87	2.03	0.05	0.32
ISA-a, Initiation	left DS - right OFC	8.65	1.93	0.06	0.27
ISA-a, Emotional	right NAcc - right OFC	5.43	1.76	0.09	0.27

These significant results ($p < 0.05$) did have an effect size that is greater than medium effect size, $|r| > 0.3$.
ACC anterior cingulate cortex, *AIC* anterior insular cortex, *DAS* dimensional apathy scale, *df* degrees of freedom, *DS* dorsal striatum, *FC* functional connectivity, *ISA-a* impaired self-awareness of apathy, *NAcc* nucleus accumbens, *OFC* orbitofrontal cortex.
[a] Raw *p* value (unadjusted).
[b] Standarized regression coefficient.

examined. Notably, ISA-a in that cohort was only observed for the executive and initiation dimensions, while awareness for emotional apathy was preserved.

Our correlation analyses suggest that ISA-a is driven by executive and initiative apathy, whereas the emotional apathy subscore did not have a significant effect on the ISA-a (Fig. 2). In line with these results, an early study[31] found that apathy measured in PD were significantly different from healthy controls in the executive and initiative domains. These two dimensions of apathy are "observable" measures, such that the caregiver's/informant's report are based on observations in motivation and beginning a task. The emotional subscale is the dimension of apathy related to an individual's diminished concern or blunting of responses and perhaps incompletely described by an informant (i.e., observer) making it better explained by the underlying circuitry involved in ISA-a (see further discussion below).

Although none of the observed neuroimaging associations survived correction for multiple comparisons, several trends emerged with effect sizes exceeding a medium magnitude. While these findings should be interpreted with caution, they align with prior evidence implicating fronto-striatal and salience network pathways in motivational processes[18,22–27]. As such, our neural results suggest potential mechanisms of apathy and ISA-a that can be tested in larger cohorts. Before adjustment, the emotional DAS subscale was inversely correlated with FC between the left ACC and left NAcc. In other words, ACC-NAcc FC was lower in patients with higher emotional apathy. The ACC and NAcc are part of a broader network, that also includes the OFC, responsible for motivated behavior. In particular, the ACC-NAcc circuit is implicated in the effort exerted to obtain a reward, which suggests an integrative experiential function associated with this circuit. Nonhuman animal studies demonstrate that ACC-NAcc activation is associated with effort application, and disrupting this circuit results in subjects being unwilling to complete reward-driven tasks[32,33]. These studies match the human neuroimaging literature, in which the ACC is engaged when determining the amount of effort to exert in relation to the magnitude of the reward[22,34,35]. Other studies have also described decreased gray matter volumes in fronto-striatal circuits amongst apathetic PD patients as compared with nonapathetic ones[23,36–38]. Taken with our results, there is a substantial body of evidence supporting the role of the ACC-NAcc connection and apathy in PD, possibly in terms of the rewards-effort based integrative nature of this relationship.

Given the degeneration of dopamine neurons at the heart of PD pathophysiology, apathy has been hypothesized to result from dopamine depletion along the mesocorticolimbic pathway which communicates with the ACC and OFC, which themselves project to the NAcc[33]. These projections originate in the ventral tegmental area, which traditionally is thought to be spared in early to middle stages of PD[39]. However, apathy does not appear to develop particularly late in the clinical progression of PD. Instead, apathy can actually serve as an early sign of PD, even preceding the onset of noticeable motor symptoms[40]. One possibility is that the postmortem studies suggesting the relative health of the ventral tegmental area dopaminergic projections are not well-suited to capturing downstream mesolimbic network dysfunction rather than Lewy body pathology within the midbrain.

A unique aspect of our study is the dimensional approach to investigate neural correlates of apathy in PD, focusing on reward and self-awareness networks. Based on the known functions of this circuit (ACC-NAcc), it is not surprising that we find only a relationship with the emotional subscale of the DAS. The emotional subscale measures emotional motivation, such as indifference, affective neutrality, flatness, and/or blunting of emotion (for example, being indifferent and thus unmotivated to engage with their environment). These signs contrast with those measured by the executive subscale (lack of motivation for planning, attention or organization, for example being unmotivated to complete steps involved in a tasks) and the initiation subscale (lack of motivation for self-generation of thoughts and/or actions, being unmotivated to get things started). Future research may explore wider brain networks associated with cognitive/executive and auto-activation/initiation apathy in PD but also across different neurodegenerative conditions. For example, we might expect functional connectivity between the lateral frontal and lateral parietal lobes, known to be involved in attention and executive control, to correlate with the executive subscale.

Furthermore, it has been proposed that emotional apathy is composed of subconstructs relating to individually focused emotional motivation (Individual Emotional apathy) but also externally based interactive aspects (Social Emotional apathy)[41]. Future research may look to explore these elements in the context of ISA-a to further explore FC relationships relating to internal and external emotional motivation.

Separately, we examined the relationship between fronto-striatal FC and ISA-a. Specifically, we found a trend between the emotional subscale of the DAS and the FC between the left NAcc and the left OFC and between the left NAcc and the right OFC. In this case, we saw a trend for impaired self-awareness to be associated with higher NAcc-OFC FC. Because ISA-a scales with apathy, and apathy itself, was associated with reduced ACC-NAcc FC[19,22,23], we were surprised by this result. We would have expected the opposite association (reduced NAcc-OFC FC with ISA-a). However, although OFC and ACC are both part of the brain's reward network and are often co-activated[42,43], they may play different roles in apathy in PD. Interestingly, Buchwitz et al.[16] found that FC with the right OFC was increased in proportion to ISA for motor disease severity in PD. Thus, although reduced ACC-NAcc connectivity may be generating the motivational loss that leads to apathy itself, NAcc-OFC connectivity may be involved in resistance to accurately evaluating one's own state. However, given that these associations did not survive FDR correction, any interpretation should be considered speculative. Our small sample size further limits our ability to draw firm conclusions, and additional data will be needed to disentangle the neural circuitry underlying ISA-a. Moreover, other neuropsychiatric features common in PD, such as impulsivity and anxiety, may also influence ISA-a. Larger studies will be required to clarify these relationships and address the potential contributions of comorbid neuropsychiatric symptoms.

Similarly, we observed a trend towards significance of ISA-a in relation to connectivity between the right ACC and AIC, even though we might have expected this circuit to be engaged in enhancing self-awareness[16,24,33]. The ACC-AIC pathway has been observed to be key to detecting behaviorally relevant events in the environment as part of the salience network[44], but it does so in the context of a representation of the self. This has led to speculation that the ACC-AIC pathway may be a major factor in mediating self-awareness[45]. Indeed, metabolic analyses with FDG-PET have revealed a correlation of reduced metabolism in the ACC with impaired cognitive awareness[18]. With just a trend toward a positive (unexpected) relationship with ISA-a, further study is certainly warranted but may be related to inaccurate interoception.

We suggest that domain-specific ISA may share some underlying circuitry—perhaps of the insular cortex and OFC[16,24]—but that the substrate for other types of self-awareness will be different. For example, ISA-m may more heavily involve lateral portions of the PFC, such as the inferior frontal gyrus[46] and dorsolateral prefrontal cortex[24]. Indeed, the presence of the ACC in studies of neural underpinnings of ISA-m and ISA-a fit with this structure's known motor and cognitive/emotional components, respectively[47].

Our study encountered a few limitations. First, while MRI sessions were scheduled with participants in the ON dopaminergic medication state to enhance comfort and reduce motion artifacts, some variability in their motor state at the time of scanning was unavoidable. Such variability could introduce noise into the data, particularly for analyses sensitive to motor state. However, because our neuroimaging analyses targeted apathy (as perceived by patients and caregivers over the preceding month), the potential influence of transient motor fluctuations is less of a concern. Second, approximately 30% of participants' FC data did not meet quality control criteria due to motion artifacts. While this reduced the final sample size, applying rigorous motion thresholds strengthens confidence that the observed trends reflect neural signals worthy of further investigation, rather than motion artifacts. The OFC is particularly vulnerable to susceptibility artifacts, including distortions and signal dropout, which can lead to misinterpretation of fMRI findings. Thus, special caution is warranted when drawing OFC-related conclusions.

In conclusion, PD patients with apathy exhibited higher levels of ISA-a compared to their non-apathetic counterparts. Apathy was associated with reduced FC between the left ACC and NAcc, but ISA-a was associated with enhanced FC between the OFC and NAcc. Future comprehensive studies combining different dimensions of apathy and other types of symptoms should fully elucidate the shared vs distinct neural circuits for each symptom category and its ISA in PD.

Methods

Participants

Participants with a diagnosis of idiopathic PD were recruited at the Baylor College of Medicine (BCM) Parkinson's Disease Center and Movement Disorders Clinic (PDCMDC) between 2021 and 2024 under H-48651 protocol approved by the BCM Institutional Review Board. PD patients were included in the study and signed informed consent if they had a diagnosis of idiopathic PD, complicated by motor fluctuations, had the capacity to consent and an informant who had consistent contact with them and could provide information about their behavior. The study cohort is part of a larger study that recruits participants who have been referred for deep-brain stimulation (DBS) surgery, a precondition of which is motor fluctuations.

Patients with severe dementia (Mini-Mental State Examination, MMSE, <20), additional medical and neurological conditions and imaging artifacts that could affect neuroimaging measures (i.e., stroke, traumatic brain injury, or previous brain surgery or pre-existing chronic Axis I psychiatric illness) were excluded from participation in the study.

The following data were collected during two separate study visits separated by 2–4 weeks, one during which the motor assessments were performed (OFF dopaminergic medication), and one during which the MRI and the neuropsychiatric/cognitive assessments were obtained (ON dopaminergic medication).

Motor assessment

Motor disease severity was assessed in the OFF dopaminergic medication state (defined as overnight medication withdrawal) using the Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III. During this portion of the MDS-UPDRS, an examiner (rater) instructs the patient to complete motor tasks and rates the severity of motor aspects of PD (i.e., tremor, rigidity, bradykinesia, gait and posture).

Cognitive assessments

The Montreal Cognitive Assessment Scale (MoCA) was used as routine cognitive screening to assess multiple cognitive domains (i.e., visuospatial, language, memory, attention, executive function, and orientation). The MoCA is rated on a 30-point scale with lower scores indicating decreased cognitive abilities. The MoCA[48] is more sensitive to subtle cognitive deficits in patients with PD and is considered superior to other screening instruments in discriminating between individuals with PD and MCI, and those without cognitive impairment[49].

Neuropsychiatric assessments

The DAS[50] was completed by both the participants and informants. The DAS has been previously validated in populations with PD for assessing the apathetic syndrome using a dimensional framework, minimizing the impact of motor symptoms in both participant and informant versions[51]. The DAS encompasses the previously proposed domains of auto-activation, cognitive and emotional-affective[8]. The initiation subscale of the DAS is similar to the originally proposed auto-activation domain, but it is less dependent on motor functions[30,52]. The executive subscale is most comparable to the cognitive domain. The emotional subscale of the DAS is largely similar to the previously described emotional-affective domain, but it differs by its focus on the integration of emotional behaviors rather than on the facets of expression, processing and recognition. The scale is composed of 24 items scored on a 4-point Likert response scale and can range from 0 (least apathy)

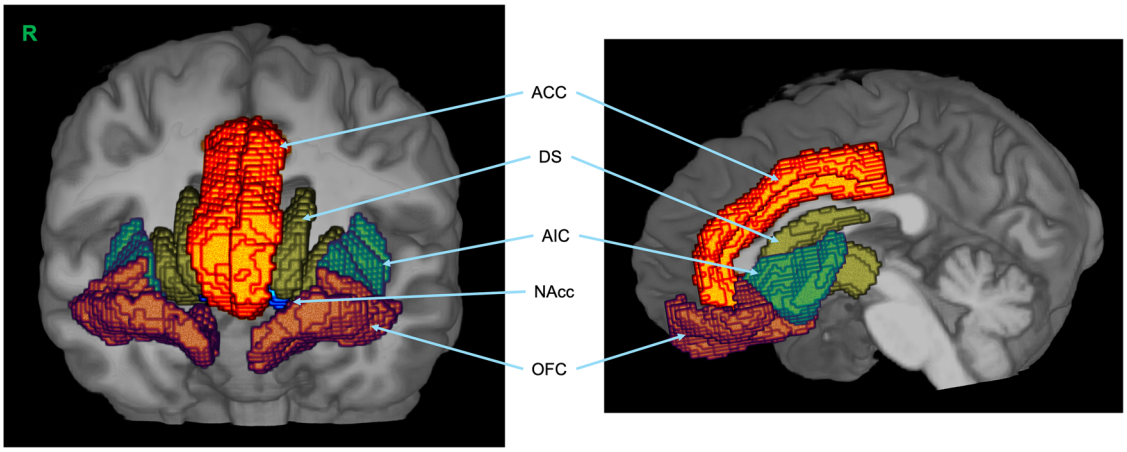

Fig. 4 | Cortical and subcortical regions of interest (ROIs) were selected in the current study. ACC anterior cingulate cortex; DS dorsal striatum; AIC anterior insular cortex; NAcc nucleus accumbens; OFC orbitofrontal cortex.

to 72 (most apathy). The total scale can be categorized into three 8-item subscales: executive, emotional, and initiation. Higher scores represent more apathy. Previously established cutoffs were available for each DAS subscale; executive subscore ≥14, emotional subscore ≥15 and initiation subscore ≥16[51].

Depression was assessed using the Geriatric Depression Scale (GDS)-15. The GDS-15 was completed by participants only, with the assistance of a research coordinator. The GDS[53,54] is a reliable self-report instrument for assessing depression in PD, incorporating items with ecological validity specifically for older individuals and steering away from the predominant focus on somatic symptoms commonly included in other depression instruments. A score of 6 or greater was considered consistent with the diagnosis of depression.

PD patient anxiety was assessed with the generalized anxiety disorder (GAD)-7 scale[55]. The scale consists of 7 items scored on a 4-point Likert response scale (0-not at all, 1-several days, 2-more than half the days, 3-nearly every day). Higher scores are consistent with more anxiety.

Magnetic resonance imaging (MRI) protocol

All participants received a comprehensive set of magnetic resonance imaging (MRI) sequences to assess structural and functional characteristics, in the ON dopaminergic medication state. All participants were imaged in a Siemens MAGNETOM Prisma Fit 3T scanner (Siemens Healthineers, Erlangen, Germany) with a 32-channel head coil. Scan sequences used for analyses included T1-weighted magnetization-prepared rapid acquisition gradient-echo (MP-RAGE) with 208 sagittal volumes, TR = 2.4 s, TE = 2.24 ms, flip angle = 8°, voxel size = 0.8 mm isotropic, and FOV = 256 mm; and multi-band T2*-weighted blood-oxygen-level-dependent (BOLD) sequences with 66 axial slices × 650 volumes, TR = 0.925 s, TE = 37 ms, flip angle = 61°, voxel size = 2.2 mm isotropic, FOV = 228 mm, pixel bandwidth = 2404 Hz, and imaging frequency = 123.25 MHz in the anterior-posterior phase encoding direction during resting state. Participants were instructed to remain still with their eyes open and not to think of anything particular. Notably, during the resting-state functional scans, PD patients were in the ON medication state.

Anatomical image preprocessing and ROI masks

T1-weighted structural scans were performed to obtain a high-resolution anatomical image of brain structures. Using version 7.3.2 of FreeSurfer (https://surfer.nmr.mgh.harvard.edu)[56], cerebrospinal fluid (CSF), gray matter (GM) and white matter (WM) were segmented in each participant's native space. Manual corrections of the automatic segmentations from FreeSurfer were made as needed upon inspection.

In addition, a priori regions-of-interest (ROI) masks were created to conduct the subsequent resting-state functional connectivity analysis. Based on the literature review and wanting to limit the number of analyses performed with our small sample, our ROIs included the ACC, OFC, dorsal striatum (DS), nucleus accumbens (NAcc), and anterior insular cortex (AIC) (Fig. 4). ROI masks were identified on an atlas from the Medical Image Computing and Computer-Assisted Intervention Society (MICCAI) 2012 Multi-Atlas Labeling Workshop and Challenge data (https://www.neuromorphometrics.com/) in the Montreal Neurological Institute (MNI) space. The MICCAI 2012 atlas parcellates some cortical regions by their functional structure, which enables more direct hypothesis testing than the gyral and/or sulcal-based atlases available in the FreeSurfer package. We separately examined left and right ACC and OFC functional connectivity with the DS, NAcc, and AIC, for a total of 24 comparisons.

Functional image preprocessing

The resting-state fMRI data were preprocessed with fMRIPrep version 23.0.0 (https://fmriprep.org)[57]. With a vast array of analytical approaches for examining fMRI, fMRIPrep takes advantage of the leading image processing suites and incorporates the most validated steps from each software into a single standardized pipeline, maximizing replicability across studies[57]. Preprocessing steps included head motion estimation using FSL's MCFLIRT (https://www.fmrib.ox.ac.uk/fsl/fslwiki)[58], followed by slice-timing correction using AFNI's 3dTShift (https://afni.nimh.nih.gov) with timing for the middle of each TR as reference. Denoising and time series extraction were performed using the established SPM CONN implementation, as in our prior published work[59]. The order of head motion estimation before slice timing is recommended by Power et al.[60] for greater accuracy in head-motion estimation. Alignment between the fMRI time series and T1-weighted image was then performed using FreeSurfer bbregister routine[61]. To minimize loss of information, the fMRI time series were corrected for head-motion and registered to T1-weighted image all in one step by concatenating and applying one interpolation step using the Lanczos resampling. Co-registration was configured with six degrees of freedom. The BOLD time series were resampled into standard MNI152NLin2009cAsym space. Frame-wise displacement (FWD) was calculated from the six motion parameters and the root-mean-square difference (RMSD) of the BOLD percentage signal in the consecutive volumes. Contaminated volumes were then detected and classified as outliers by the criteria FWD > 0.5 mm or RMSD > 0.3% and replaced with new volumes generated by linear interpolation of adjacent volumes. Any BOLD images with greater than 30% of outliers were excluded from the analysis. The three global signals are extracted within the CSF and the WM masks defined by FreeSurfer. A bandpass filter with cut-off frequencies of 0.01 and 0.09 Hz was used. Finally, the covariates corresponding to head motion (6 realignment parameters), outliers, and the BOLD time series from the subject-specific white matter and CSF masks were used in the connectivity analysis as predictors of no interest and were removed from the BOLD functional time

series using linear regression. Our ROI masks, identified by the MICCAI 2012 Multi-Atlas, were warped to the MNI 152 space, and the average BOLD signal within each ROI was computed at each time point across subjects. The time series BOLD signals in each ROI were then averaged. Finally, we assessed functional connectivity (FC) coefficients in each of our 24 hypothetical ROI pairs. The resultant coefficients were transformed into z-scores using Fisher's transformation to satisfy normality assumptions.

Statistical analysis

All statistical analyses were performed using R (version 4.2.2). Partial correlation coefficients with *p*-values were computed using ppcor package (version 1.0) and LMMs were performed using lmerTest package (version 3.1.3). Multiple comparison correction was performed controlling for False Discovery Rate (FDR) correction for each hypothesis[62].

PD patients were first categorized into apathetic and non-apathetic groups based on previously established DAS cutoffs. We compared demographic and clinical characteristics between apathetic and non-apathetic individuals using Pearson's Chi-squared tests for categorical variables and two sample *t*-tests for continuous variables.

Following established methodology in apathy research[8,30], ISA-a was next calculated as the discrepancy between self- and informant-rated DAS total scores (ISA-a = $DAS_{informant} - DAS_{patient}$). The resulting continuous score ranges from −72 to 72 for the total scale and −24 to 24 for each DAS subscale (executive, initiation, emotional apathy). Positive values indicate that the informant rated the patient as more apathetic than the patient rated themselves, reflecting greater impairment of self-awareness for apathy. The use of a continuous variable preserves the full variability of the data and increases statistical sensitivity in subsequent correlation and regression analyses.

We then examined whether total ISA-a was associated with DAS total score and subscale scores using Pearson correlation coefficients since data points were evenly distributed. For covariate-adjusted correlation, we performed partial correlation adjusting for additional covariates (age, MoCA, GDS, and MDS-UPDRS part III).

To examine whether ISA-a exists (differs from zero) in PD patients across total DAS and each subscale, we next performed linear mixed-effects modeling (LMM) with each DAS score as a dependent variable, source (informant vs. patient), age, MoCA, GDS, and MDS-UPDRS part III scores as fixed effects and random intercepts of patients. The significant effect of the source indicates differences between patients and informants, i.e., ISA-a differs from zero, and the parameter estimates of the source (with patient as the reference) were interpreted as average ISA-a adjusted by covariates. We then compared ISA-a between apathy groups by adding the source x apathy group (apathetic vs. non-apathetic) interaction and apathy group as fixed effects to the LMMs. Significant source × apathy group interaction indicates differences in ISA-a by the apathy group.

To account for potential selection bias from failures on fMRI QC, we compared the demographic and clinical characteristics of participants for whose FC measures failed or failed quality control thresholds. To examine the association between FC and apathy, we performed separate linear regressions for each FC pair (ACC-DS, ACC-NAcc, ACC-AIC, OFC-DS, OFC-NAcc and OFC-AIC) and DAS total score as well as dimensional subscales. For this analysis, only informant scores for the DAS and its subscales were used. Each regression included a DAS score evaluated by an informant as the dependent variable, FC as the independent variables adjusting for age, MoCA, GDS, MDS-UPDRS part III scores and mean FWD.

Additionally, we tested the association between ISA-a and FC. For this analysis, we included the DAS score evaluated by the informant as a covariate, in addition to all of the above covariates, to control for the level of the patients' apathy.

Data availability

Behavioral and neuroimaging data are available on the National Institute of Mental Health (NIMH) Data Archive (https://nda.nih.gov/), Collection ID: C3993. For access, a Data Access Request (DAR) should be submitted to the NIMH Data Archive Permissions Group (https://nda.nih.gov/nda/tutorials/electronic-data-access-request).

Received: 10 June 2025; Accepted: 29 September 2025;
Published online: 18 November 2025

References

1. Aarsland, D. et al. Neuropsychiatric symptoms in patients with Parkinson's disease and dementia: frequency, profile and associated care giver stress. *J. Neurol. Neurosurg. Psychiatry* **78**, 36–42 (2007).
2. Massimo, L. & Evans, L. K. Differentiating subtypes of apathy to improve person-centered care in frontotemporal degeneration. *J. Gerontol. Nurs.* **40**, 58–65 (2014).
3. Levy, R. & Dubois, B. Apathy and the functional anatomy of the prefrontal cortex–basal ganglia circuits. *Cereb. Cortex* **16**, 916–928 (2006).
4. Williams-Gray, C. H., Foltynie, T., Brayne, C. E. G., Robbins, T. W. & Barker, R. A. Evolution of cognitive dysfunction in an incident Parkinson's disease cohort. *Brain J. Neurol.* **130**, 1787–1798 (2007).
5. Weintraub, D. & Mamikonyan, E. The neuropsychiatry of Parkinson Disease: a perfect storm. *J. Am. Assoc. Geriatr. Psychiatry* **27**, 998–1018 (2019).
6. Pedersen, K. F., Larsen, J. P., Alves, G. & Aarsland, D. Prevalence and clinical correlates of apathy in Parkinson's disease: a community-based study. *Park. Relat. Disord.* **15**, 295–299 (2009).
7. Robert, P. et al. Proposed diagnostic criteria for apathy in Alzheimer's disease and other neuropsychiatric disorders. *Eur. Psychiatry J.* **24**, 98–104 (2009).
8. Radakovic, R. & Abrahams, S. Multidimensional apathy: evidence from neurodegenerative disease. *Curr. Opin. Behav. Sci.* **22**, 42–49 (2018).
9. Pennington, C., Duncan, G. & Ritchie, C. Altered awareness of cognitive and neuropsychiatric symptoms in Parkinson's disease and Dementia with Lewy Bodies: a systematic review. *Int. J. Geriatr. Psychiatry* **36**, 15–30 (2021).
10. Sitek, E. J. et al. Assessing self-awareness of dyskinesias in Parkinson's disease through movie materials. *Funct. Neurol.* **26**, 121–126 (2011).
11. Pietracupa, S., Latorre, A., Berardelli, A. & Fabbrini, G. Parkinsonian patients and poor awareness of dyskinesias. *Front. Neurol.* **5**, 32 (2014).
12. Maier, F. et al. Development and psychometric evaluation of a scale to measure impaired self-awareness of hyper- and hypokinetic movements in Parkinson's disease. *J. Int. Neuropsychol. Soc. Jins.* **21**, 221–230 (2015).
13. Maier, F. & Prigatano, G. P. Impaired self-awareness of motor disturbances in Parkinson's Disease. *Arch. Clin. Neuropsychol.* **32**, 802–809 (2017).
14. Amanzio, M. et al. Self-unawareness of levodopa-induced dyskinesias in patients with Parkinson's disease. *Brain Cogn.* **90**, 135–141 (2014).
15. Maier, F. et al. Impaired self-awareness of motor deficits in Parkinson's disease: association with motor asymmetry and motor phenotypes. *Mov. Disord. J. Mov. Disord. Soc.* **27**, 1443–1447 (2012).
16. Buchwitz, T. M. et al. Exploring impaired self-awareness of motor symptoms in Parkinson's disease: Resting-state fMRI correlates and the connection to mindfulness. *PloS One* **18**, e0279722 (2023).
17. Yoo, H. S. et al. Neural correlates of self-awareness of cognitive deficits in non-demented patients with Parkinson's disease. *Eur. J. Neurol.* **28**, 4022–4030 (2021).
18. Maier, F. et al. Impaired self-awareness of cognitive deficits in Parkinson's disease relates to cingulate cortex dysfunction. *Psychol. Med.* **53**, 1244–1253 (2023).
19. Sitek, E. J., Soltan, W., Wieczorek, D., Robowski, P. & Slawek, J. Self-awareness of memory function in Parkinson's disease in

relation to mood and symptom severity. *Aging Ment. Health* **15**, 150–156 (2011).
20. Maggi, G., Vitale, C., Delle Curti, A., Amboni, M. & Santangelo, G. Unawareness of apathy in Parkinson's disease: the role of executive dysfunction on symptom recognition. *Brain Sci.* **13**, 964 (2023).
21. Le Heron, C., Holroyd, C. B., Salamone, J. & Husain, M. Brain mechanisms underlying apathy. *J. Neurol. Neurosurg. Psychiatry* **90**, 302–312 (2019).
22. Morris, L. A. et al. Altered nucleus accumbens functional connectivity precedes apathy in Parkinson's disease. *Brain J. Neurol.* **146**, 2739–2752 (2023).
23. Baggio, H. C. et al. Resting-state frontostriatal functional connectivity in Parkinson's disease-related apathy. *Mov. Disord. J. Mov. Disord. Soc.* **30**, 671–679 (2015).
24. Palermo, S. et al. Role of the cingulate cortex in dyskinesias-reduced-self-awareness: an fMRI Study on Parkinson's Disease patients. *Front Psychol.* **9**, 1765 (2018).
25. Tisserand, A., Philippi, N., Botzung, A. & Blanc, F. Me, myself and my insula: an oasis in the forefront of self-consciousness. *Biology* **12**, 599 (2023).
26. Criaud, M. et al. Contribution of insula in Parkinson's disease: a quantitative meta-analysis study. *Hum. Brain Mapp.* **37**, 1375–1392 (2016).
27. Hallam, B., Chan, J., Gonzalez Costafreda, S., Bhome, R. & Huntley, J. What are the neural correlates of meta-cognition and anosognosia in Alzheimer's disease? A systematic review. *Neurobiol. Aging* **94**, 250–264 (2020).
28. Starkstein, S. E., Mayberg, H. S., Preziosi, T. J., Andrezejewski, P., Leiguarda, R. & Robinson, R. G. Reliability, validity, and clinical correlates of apathy in Parkinson's disease. *J. Neuropsychiatry Clin. Neurosci.* **4**, 134–139 (1992).
29. Sockeel, P. et al. The Lille Apathy Rating Scale (LARS), a new instrument for detecting and quantifying apathy: validation in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* **77**, 579–584 (2006).
30. Radakovic, R. et al. Multidimensional apathy in behavioral variant frontotemporal dementia, primary progressive aphasia, and Alzheimer's Disease. *J. Geriatr. Psychiatry Neurol.* **34**, 349–356 (2021).
31. Radakovic, R., Davenport, R., Starr, J. M. & Abrahams, S. Apathy dimensions in Parkinson's disease. *Int. J. Geriatr. Psychiatry* **33**, 151–158 (2018).
32. Walton, M. E. et al. Comparing the role of the anterior cingulate cortex and 6-hydroxydopamine nucleus accumbens lesions on operant effort-based decision making. *Eur. J. Neurosci.* **29**, 1678–1691 (2009).
33. Pessiglione, M., Vinckier, F., Bouret, S., Daunizeau, J. & Le Bouc, R. Why not try harder? Computational approach to motivation deficits in neuro-psychiatric diseases. *Brain* **141**, 629–650 (2018).
34. Prévost, C., Pessiglione, M., Météreau, E., Cléry-Melin, M. L. & Dreher, J. C. Separate valuation subsystems for delay and effort decision costs. *J. Neurosci.* **30**, 14080–14090 (2010).
35. Naccache, L. et al. Effortless control: executive attention and conscious feeling of mental effort are dissociable. *Neuropsychologia* **43**, 1318–1328 (2005).
36. Lucas-Jiménez, O. et al. Apathy and brain alterations in Parkinson's disease: a multimodal imaging study. *Ann. Clin. Transl. Neurol.* **5**, 803–814 (2018).
37. Skidmore, F. M. et al. Apathy, depression, and motor symptoms have distinct and separable resting activity patterns in idiopathic Parkinson disease. *NeuroImage* **81**, 484–495 (2013).
38. Sun, H. H. et al. Alterations of regional homogeneity in Parkinson's disease with "pure" apathy: a resting-state fMRI study. *J. Affect Disord.* **274**, 792–798 (2020).
39. Alberico, S. L., Cassell, M. D. & Narayanan, N. S. The vulnerable ventral tegmental area in Parkinson's disease. *Basal Ganglia.* **5**, 51–55 (2015).
40. Cohen, E., Bay, A. A., Ni, L. & Hackney, M. E. Apathy-related symptoms appear early in Parkinson's Disease. *Health* **10**, 91 (2022).
41. M'Barek, L., Radakovic, R., Noquet, M., Laurent, A. & Allain, P. Different aspects of emotional processes in apathy: Application of the French translated dimensional apathy scale. *Curr. Psychol.* **39**, 564–570 (2020).
42. Heather Hsu, C. C. et al. Connections of the human orbitofrontal cortex and inferior frontal gyrus. *Cereb. Cortex.* **30**, 5830–5843 (2020).
43. Phan, K. L. et al. Neural correlates of individual ratings of emotional salience: a trial-related fMRI study. *NeuroImage* **21**, 768–780 (2004).
44. Menon, V. & Uddin, L. Q. Saliency, switching, attention and control: a network model of insula function. *Brain Struct. Funct.* **214**, 655–667 (2010).
45. Critchley, H. & Seth, A. Will studies of macaque insula reveal the neural mechanisms of self-awareness? *Neuron* **74**, 423–426 (2012).
46. Maier, F. et al. Behavioural and neuroimaging correlates of impaired self-awareness of hypo- and hyperkinesia in Parkinson's disease. *Cortex J. Devoted Study Nerv. Syst. Behav.* **82**, 35–47 (2016).
47. Heilbronner, S. R. & Hayden, B. Y. Dorsal anterior cingulate cortex: a bottom-up view. *Annu Rev. Neurosci.* **39**, 149–170 (2016).
48. Nasreddine, Z. S. et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J. Am. Geriatr. Soc.* **53**, 695–699 (2005).
49. Pinto, T. C. C. et al. Is the Montreal Cognitive Assessment (MoCA) screening superior to the Mini-Mental State Examination (MMSE) in the detection of mild cognitive impairment (MCI) and Alzheimer's Disease (AD) in the elderly? *Int. Psychogeriatr.* **31**, 491–504 (2019).
50. Radakovic, R. & Abrahams, S. Developing a new apathy measurement scale: Dimensional Apathy Scale. *Psychiatry Res.* **219**, 658–663 (2014).
51. Radakovic, R. et al. Multidimensional apathy in ALS: validation of the Dimensional Apathy Scale. *J. Neurol. Neurosurg. Psychiatry* **87**, 663–669 (2016).
52. Santangelo, G. et al. Assessment of apathy minimising the effect of motor dysfunctions in Parkinson's disease: a validation study of the dimensional apathy scale. *Qual. Life Res Int J. Qual. Life Asp. Treat. Care Rehabil.* **26**, 2533–2540 (2017).
53. Yesavage, J. A. et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J. Psychiatr. Res.* **17**, 37–49 (1983). 1982.
54. Kørner, A. et al. The Geriatric Depression Scale and the Cornell Scale for depression in dementia. a validity study. *Nord J. Psychiatry* **60**, 360–364 (2006).
55. Spitzer, R. L., Kroenke, K., Williams, J. B. W. & Löwe, B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch. Intern. Med.* **166**, 1092–1097 (2006).
56. Fischl, B. et al. Automatically parcellating the human cerebral cortex. *Cereb. Cortex* **14**, 11–22 (2004).
57. Esteban, O. et al. fMRIPrep: a robust preprocessing pipeline for functional MRI. *Nat. Methods* **16**, 111–116 (2019).
58. Jenkinson, M., Bannister, P., Brady, M. & Smith, S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage* **17**, 825–841 (2002).
59. Kim, H. et al. Resting-state functional connectivity changes in older adults with sleep disturbance and the role of amyloid burden. *Mol. Psychiatry* **28**, 4399–4406 (2023).
60. Power, J. D., Plitt, M., Kundu, P., Bandettini, P. A. & Martin, A. Temporal interpolation alters motion in fMRI scans: magnitudes and consequences for artifact detection. *PLOS One.* **12**, e0182939 (2017).
61. Greve, D. N. & Fischl, B. Accurate and robust brain image alignment using boundary-based registration. *NeuroImage* **48**, 63–72 (2009).
62. Benjamini, Y. & Hochberg, Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J. R. Stat. Soc. Ser. B Methodol.* **57**, 289–300 (1995).

Acknowledgements

We would like to thank all participants who took part in this study. We also would like to thank the research coordinators who supported data collection

for this study: Jaqueline Soto, Nora Abu-Hamdan, Morgan Carpenter. This study was funded by the National Institutes of Mental Health [R01 MH127200].

Author contributions

Name – Contribution according to definition below: H.C. – 2A, 2C, 3A, 3B. H.S. – 1B, 1C, 2A, 2C, 3B. Z.J. – 2A, 2B, 2C, 3B. A.M. – 1B, 1C. X. Z. – 2A, 2C. S. L. - 2A, 2B, 2C, 3B. E.H. – 1A, 3B. R.R. – 2A, 2C, 3B. S.R.H. – 1A, 2A, 2C, 3B. N.V.A. – 1A, 1B, 1C, 2A, 2C, 3A, 3B. (1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical analysis: A. Design, B. Execution, C. Review and critique; (3) Manuscript: A. Writing of the first draft, B. Review and critique. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41531-025-01168-9.

Correspondence and requests for materials should be addressed to Nora Vanegas-Arroyave.