Depressive symptoms in Parkinson’s disease and in non-neurological medical illnesses

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Background: Patients with neurological and non-neurological medical illnesses very often complain of depressive symptoms that are associated with cognitive and functional impairments. We compared the profile of depressive symptoms in Parkinson’s disease (PD) patients with that of control subjects (CS) suffering from non-neurological medical illnesses.

Methods: One-hundred PD patients and 100 CS were submitted to a structured clinical interview for identification of major depressive disorder (MDD) and minor depressive disorder (MIND), according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR), criteria. The Hamilton Depression Rating Scale (HDRS) and the Beck Depression Inventory (BDI) were also administered to measure depression severity.

Results: When considering the whole groups, there were no differences in depressive symptom frequency between PD and CS apart from worthlessness/guilt, and changes in appetite reduced rates in PD. Further, total scores and psychic and somatic subscores of HDRS and BDI did not differ between PD and CS. After we separated PD and CS in those with MDD, MIND, and no depression (NODEP), comparing total scores and psychic/somatic subscores of HDRS and BDI, we found increased total depression severity in NODEP PD and reduced severity of the psychic symptoms of depression in MDD PD, with no differences in MIND. However, the severity of individual symptom frequency of depression was not different between PD and CS in MDD, MIND, and NODEP groups.

Conclusion: Although MDD and MIND phenomenology in PD may be very similar to that of CS with non-neurological medical illnesses, neurological symptoms of PD may worsen (or confound) depression severity in patients with no formal/structured DSM-IV-TR, diagnosis of depressive mood disorders. Thus, a thorough assessment of depression in PD should take into consideration the different impacts of neurological manifestations on MDD, MIND, and NODEP groups.

Keywords: Parkinson’s disease, neuropsychiatry, depression, nonmotor symptoms

Introduction
Depression is one of the most common complications in Parkinson’s disease (PD) and is well known for having a major impact on the prognosis\textsuperscript{1–5} and upon patient and carer quality of life.\textsuperscript{6–8} However, whether the phenomenology of depression in PD is similar to the phenomenology of depression among individuals with other non-neurological diseases is still unclear, especially concerning the hypothesis that depressive symptoms might reflect a reaction to a chronic disabling condition or may be worsened by neurological symptoms.

Many authors have previously addressed the question about whether depression in PD is characterized by specific symptoms that distinguish it from depression in non-PD patients. For instance, by comparing the depressive symptoms of PD patients with those...
of matched patients with other chronic disabling illnesses, Ehmann et al found that the symptoms of PD patients were more severe than those of disabled control subjects (CS). On the other hand, several studies showed that the depressive profile of PD patients does not significantly differ from that of non-PD subjects. In addition, Lieberman showed that depression in PD seems to be characterized by the relative absence of symptoms such as guilt, sorrow, and suicidal ideation, which are traditionally symptoms of depression in non-PD subjects.

All these studies employed different control groups and measures of depression; thus, a rather contradictory picture emerges. Moreover, the vast majority of these studies lack a homogeneous set of criteria for diagnosing depression in PD.

There is much debate about the most valid strategy to diagnose depression in PD. One of the major problems concerns the core cognitive-somatic feature of depression (ie, symptoms of difficulty in concentrating, loss of energy, psychomotor retardation, hypomimia, fatigue, apathy), which may be present in PD patients with no depressive mood disorder diagnosis. Nowadays, in the absence of specific screening tools, the conventional approach for establishing the diagnosis of depressive disorder in PD patients is based on the Diagnostic and Statistical Manual of Mental Disorders. In particular, the National Institute of Neurological Disorders and Stroke (NINDS)/National Institute of Mental Health (NIMH) Work Group proposed provisional diagnostic criteria for depression in PD using an inclusive approach: ie, by considering all symptoms as related to depression, regardless of their overlap with PD or other medical conditions, and conducting depression assessments at a consistent time and during an “on” state, in order to avoid a negative reporting or assessment bias.

Given these considerations, the primary aim of this study was to extend findings of previous research about whether the phenomenology of depression in PD is qualitatively different from that of subjects with other disabling non-neurological medical illnesses. In particular, we addressed previous methodological flaws by comparing a sample of PD outpatients under stable dopaminergic therapy during an “on” state with a group of CS referred to an outpatient clinic for medical illnesses. Here, we adopted the diagnostic criteria developed by the NINDS/NIMH Work Group to diagnose depression in PD. Moreover, we analyzed the extent of overlap between symptoms of PD and symptoms of depression by comparing the depressive phenomenology of PD with CS separately in groups with a diagnosis of major depressive disorder (MDD), minor depressive disorder (MIND), or no depression (NODEP).

Methods

Participants

The study was carried out on 100 subjects diagnosed as having idiopathic PD according to international guidelines. PD patients were recruited at the outpatient services for movement disorders of three institutions (Department of Neuroscience, Mental Health and Sensory Systems, University “Sapienza”, Sant’Andrea Hospital, Rome, Italy; Department of Neurology and Psychiatry, Umberto I General Hospital, Rome Italy; and Department of Neuroscience, University “Tor Vergata”, Rome, Italy) and compared with 100 CS matched for age, gender, educational attainment, and global cognitive level. CS suffered from medical illnesses, but not neurological diseases, were enrolled at the outpatient clinic of the IRCCS Santa Lucia Foundation, Rome, Italy, and were under stable pharmacological therapy. Medical illnesses of CS enrolled in the study were hypertension (62%), arthritis (26%), chronic obstructive pulmonary disease (24%), coronary artery disease (22%), diabetes mellitus (18%), cataract (14%), gastrointestinal disease (9%), osteoporosis (7%), hypothyroidism (6%), gout (6%), and urinary disease (4%). Common inclusion criteria for PD patients and CS were the following: (1) vision and hearing sufficient for compliance with testing procedure, (2) Mini-Mental State Examination score ≥ 25, and (3) no dementia according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR), criteria.

Common exclusion criteria were: (1) the presence of major nonstabilized medical illnesses (nonstabilized diabetes; nonstabilized obstructive pulmonary disease or asthma; hematologic/oncologic disorders; vitamin B12 or folate deficiency; pernicious anemia; clinically significant and unstable active gastrointestinal, renal, hepatic, endocrine, or cardiovascular disorders; and recently treated hypothyroidism); (2) known or suspected history of alcoholism, drug dependence and abuse, head trauma, and mental disorders (apart from mood or anxiety disorders), according to the DSM-IV-TR criteria; and (3) presence of vascular brain lesions, brain tumor, and/or marked cortical and subcortical atrophy on computed tomography and/or magnetic resonance imagery scan. A specific exclusion criterion for PD patients was an unclear history of chronic dopaminergic treatment responsiveness. The PD patients enrolled in the study have been under stable dopaminergic therapy for at least 2 months and did not require booster doses of L-dopa or dopamine agonists.
Clinical evaluation of motor symptoms was made using the Unified Parkinson’s Disease Rating Scale – Part III (UPDRS-III).25,26 All testing and clinical evaluations were carried out 2 hours after the PD patients had received their first daily dose of medication, during the “on” states, from trained specialists who were blind to the aims of the study. Evaluation of inter-rater reliability in this study was in the excellent to good range for clinical and psychopathological scales used, with intraclass correlations ranging from 0.80 to 0.93.

The study was approved by the Santa Lucia Foundation Ethical Committee, and, in accordance with the Helsinki Declaration, each subject signed an informed consent form prior to enrolment.

Clinical and psychopathological evaluation
Sociodemographic data were collected by the neurologist during the clinical examination. Clinical characteristics, such as age of onset of first symptoms and duration of illness in years, were also assessed. Global cognitive performance was evaluated with the Mini-Mental State Examination.24

Quantification of depressive symptom severity was evaluated with the Beck Depression Inventory (BDI)27 and the Hamilton Depression Rating Scale-17 items (HDRS).28 According to Leentjens et al,21 in this study the HDRS and the BDI were used to measure symptom severity and not as diagnostic scales; for the statistical analyses, we considered both the psychic (PSY) and somatic (SOM) subscores of these scales in order to distinguish the possible differences between the two dimensions of depression.29–31

All PD and CS underwent the structured clinical interview for DSM-IV-TR, patient edition,32 for the identification of MDD and MIND according to the DSM-IV-TR criteria.33 Only symptoms that contributed to cause clinically significant impairment in important areas of functioning, such as social, occupational, or other, in accordance with Criterion C of Major Depressive Episode of the DSM-IV-TR, were scored as present. We adopted an inclusive approach (in accordance with the NINDS/NIMH Work Group for depression in PD) that considers all symptoms as related to depression, regardless of their overlap with PD or other medical conditions.19 In each PD patient or CS, the presence of individual depressive symptoms was rated using the structured clinical interview for DSM-IV-TR, patient edition.

Statistical analysis
Comparisons between PD and CS groups for age and educational attainment were performed using the t-test. Difference in frequency of the individual depressive symptoms between males and females was tested using the χ² test. To determine the significance of correlations between continuous variables, correlation analyses and Fisher’s r to z transformation were performed.

Independent t-tests were used to compare differences between PD and CS groups on the HDRS and BDI total score and PSY and SOM subscores. We used a statistical model corrected for multiple comparisons according to the Bonferroni procedure (P < 0.05/number of comparisons) to minimize the likelihood of type I (false positive) errors. In particular, the level of statistical significance was defined as P < 0.0028 (P < 0.05/18 comparisons – see Tables 1 and 3) for individual depressive symptom frequency comparisons between PD and CS considered either as whole groups or as a function of the depression category, and P < 0.0028 (P < 0.05/18 comparisons – see Table 2) for measuring significant differences in HDRS and BDI scores between PD and CS.

Results
Comparisons of PD and CS considered as whole groups
Table 1 shows the sociodemographic and clinical characteristics of the study populations. As expected from the matching procedure, the PD and CS groups did not differ significantly for age, gender, educational attainment, and global cognitive level.

After the correction for multiple comparisons, the two groups did not significantly differ in any total scores and PSY and SOM subscores of HDRS or BDI.

Further, we found that PD patients reported significantly lower frequency of the individual depressive symptoms “changes in appetite” and “worthlessness/guilt” than CS (Table 1).

An exploratory analysis investigating the possible differences between PD and CS groups in the total number of DSM-IV-TR depressive symptoms showed no difference between the PD group (mean ± standard deviation [SD] = 2.6 ± 1.6) and the CS group (mean ± SD = 3.1 ± 2.2) (t = 1.808; df = 198; P = 0.0722).

Comparisons of PD and CS in function of category of MDD, MIND, and NODEP
When considering differences between the two PD and CS groups on the scores of HDRS and BDI as a function of the category of depression (ie, separately for MDD, MIND, and NODEP groups), after the correction for multiple comparisons, as shown in Table 2, the two depression rating scales
described a quite coherent picture. Both HDRS and BDI highlighted an increased level of total and SOM scores of depression in NODEP PD patients in comparison with NODEP CS. Further, severity scores of the two scales did not differ in MIND patients. The only inhomogeneous result between the two depression rating scales was found in the PSY subscore. Indeed, the HDRS described reduced severity of PSY subscore in MDD PD patients, whereas the BDI described increased severity of PSY subscore in NODEP PD patients (Table 2).

An exploratory analysis of the total number of DSM-IV-TR depressive symptoms in PD and CS groups, considered separately in the different depression categories, showed significant differences between MDD PD patients (mean ± SD = 5.1 ± 0.9) and MDD CS (mean ± SD = 5.9 ± 0.8) (t = 2.614; df = 40; P = 0.0126) and between NODEP PD patients (mean ± SD = 1.2 ± 0.9) and NODEP CS (mean ± SD = 0.7 ± 0.7) (t = -2.783; df = 81; P = 0.0067). On the contrary, no significant difference was found between MIND PD (mean ± SD = 3.4 ± 0.6) and MIND CS (mean ± SD = 3.4 ± 0.6) (t = 1.402; df = 73; P = 0.1651).

Furthermore, when we considered the frequency of individual depressive symptoms separately in MDD, MIND, and NODEP patients, no difference was found between PD and CS (Table 3).
Table 2 Total, psychic, and somatic scores of HDRS and BDI in MDD, MIND, and NODEP PD patients and CS

| Variables | Mean (SD) | t | P  |
|-----------|-----------|---|----|
| HDRS      |           |   |    |
| MDD       | 6.0 (1.8) | 3.459 | 0.0013*  |
| MIND      | 4.7 (1.5) | 1.353 | 0.1801  |
| NODEP     | 1.3 (1.0) | -2.608 | 0.0108  |
| Somatic score |     |    | |
| MDD       | 9.3 (2.4) | 1.345 | 0.1862  |
| MIND      | 7.0 (2.1) | -0.825 | 0.4119  |
| NODEP     | 4.4 (2.0) | -4.861 <0.0001* |
| Total score |     |    | |
| MDD       | 15.3 (2.9) | 2.385 | 0.0219  |
| MIND      | 11.9 (3.0) | 0.030 | 0.9763  |
| NODEP     | 5.7 (2.7) | -4.816 <0.0001* |
| BDI       |           |   |    |
| MDD       | 11.9 (5.1) | 2.451 | 0.0187  |
| MIND      | 7.8 (3.7) | 0.574 | 0.5677  |
| NODEP     | 2.8 (2.1) | -3.577 <0.0001* |
| Somatic score |     |    | |
| MDD       | 8.9 (2.5) | 1.898 | 0.0649  |
| MIND      | 7.3 (2.8) | -1.697 | 0.0939  |
| NODEP     | 4.0 (2.3) | -4.991 <0.0001* |
| Total score |     |    | |
| MDD       | 20.9 (6.1) | 2.684 | 0.0105  |
| MIND      | 15.1 (5.0) | -0.573 | 0.5685  |
| NODEP     | 6.8 (3.8) | -5.050 <0.0001* |

Note: *Statistically significant differences after Bonferroni correction for multiple comparisons (P < 0.05/18 comparisons).

Abbreviations: BDI, Beck Depression Inventory; CS, control subjects; HDRS, Hamilton Depression Rating Scale; MDD, major depressive disorder; MIND, minor depressive disorder; NODEP, no depression; PD, Parkinson’s disease; SD, standard deviation.

Correlation analysis

In the PD group, a significant positive correlation was found only between UPDRS-III and BDI-SOM subscore (r = 0.223, P = 0.0345).

Discussion

In this study we examined the phenomenology of depression in PD patients. In particular, we analyzed the depressive profile of PD patients compared with that of patients affected by non-neurological medical illnesses, in order to control for the confounding effect of having a disabling illness.

Our results, after correction for multiple comparisons, showed that PD patients and CS as whole groups did not differ for severity of depressive symptomatology as measured by both the HDRS and BDI total score and PSY and SOM subscores. When we considered the frequency of specific symptoms of depression using the inclusive approach recommended by the NINDS/NIMH Work Group, we found that PD patients experienced lower rates of worthlessness/guilt and changes in appetite than CS. Our results are in line with previous papers describing reduced negative affective feelings of guilt and worthlessness, but are discordant with regard to changes in appetite. In fact, in PD patients, changes in appetite associated with weight loss had been previously described even before the onset of the illness or at the very early stage. Moreover, depression had been proposed as a contributor to appetite loss. In our PD sample we found reduced rates of loss of appetite, and one of the explanations we propose could be the effect of L-dopa treatment on the hypothalamus, a region associated with appetite regulation. In fact, it is reported that dopamine in the ventromedial hypothalamus is associated with stimulation of food intake. The L-dopa administration could increase the extracellular dopamine in the ventromedial hypothalamus with a restoration of food intake, thus contributing to maintain this aspect in equilibrium.

Results found in PD patients with MDD are sometimes different because they showed reduced severity of psychic depressive symptomatology using the HDRS (with a trend using the BDI), indicating that in well-structured and more severe clinical depression, such as MDD, the psychic dimension of depression may be less severe in PD patients than compared with CS. This finding is also reinforced by the fewer depressive symptoms of DSM-IV-TR found in PD patients with MDD in comparison with CS with MDD. On the other hand, in MIND patients we did not find any significant difference between PD and CS, probably because this diagnostic category of depression is less homogeneous and stable than MDD, thus impeding the capture of specific differences between these two groups of patients. Finally, only NODEP PD patients consistently reported increased severity of psychic, somatic, and total depressive symptoms in comparison with NODEP CS. In line with this, NODEP PD patients suffered from a greater number of DSM-IV-TR depressive symptoms compared with NODEP CS. These results support the idea that in PD patients with subtle depressive symptoms but without formal diagnosis of mood disorder, the neurological symptoms could overlap the depressive phenomenology, leading to a more severe symptom expression. Accordingly, severity of motor symptoms measured by UPDRS-III was found to be associated with the somatic symptoms of depression, highlighting a relationship between the somatic symptoms of the neurological illness and the somatic symptoms of depression.

When we focused on groups with MDD, MIND, and NODEP separately, the frequency of the nine depressive...
Table 3 Differences in depressive symptoms as to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision, between MDD, MIND, and NODEP PD and CS

| Depressive symptoms | PD n (%) | MIND n (%) | NODEP n (%) | χ² | df | P uncorrected |
|---------------------|---------|------------|-------------|----|----|---------------|
| Sad mood (yes)      | MDD 14 (93.3) | 26 (96.3) | 0.187 | 1 | 0.6657 |
|                     | MIND 33 (84.6) | 32 (88.9) | 0.296 | 1 | 0.5865 |
|                     | NODEP 1 (2.2) | 0 | 0.814 | 1 | 0.3669 |
| Loss of interest/pleasure (yes) | MDD 10 (66.7) | 25 (92.6) | 4.667 | 1 | 0.0308 |
|                     | MIND 12 (30.8) | 15 (41.7) | 0.965 | 1 | 0.3260 |
|                     | NODEP 0 | 0 | 0 | 1 | 1.0 |
| Changes in appetite/weight (yes) | MDD 4 (26.7) | 13 (48.1) | 1.847 | 1 | 0.1741 |
|                     | MIND 4 (10.3) | 5 (13.9) | 0.234 | 1 | 0.6286 |
|                     | NODEP 1 (2.2) | 0 | 0.814 | 1 | 0.3669 |
| Changes in weight (yes) | MDD 2 (13.3) | 12 (44.4) | 4.200 | 1 | 0.0404 |
|                     | MIND 4 (10.3) | 3 (8.3) | 0.082 | 1 | 0.7749 |
|                     | NODEP 1 (2.2) | 0 | 0.814 | 1 | 0.3669 |
| Changes in appetite (yes) | MDD 2 (13.3) | 11 (40.7) | 3.389 | 1 | 0.0656 |
|                     | MIND 0 | 3 (8.3) | 3.385 | 1 | 0.0658 |
|                     | NODEP 0 | 0 | 0 | 1 | 1.0 |
| Sleep changes (yes) | MDD 12 (80) | 24 (88.9) | 0.622 | 1 | 0.4302 |
|                     | MIND 20 (51.3) | 27 (75) | 4.501 | 1 | 0.0339 |
|                     | NODEP 13 (28.3) | 9 (24.3) | 0.163 | 1 | 0.6863 |
| Early insomnia (yes) | MDD 6 (40) | 20 (74.1) | 4.747 | 1 | 0.0293 |
|                     | MIND 9 (23.1) | 18 (50) | 5.889 | 1 | 0.0152 |
|                     | NODEP 11 (23.9) | 4 (10.8) | 2.378 | 1 | 0.1231 |
| Middle insomnia (yes) | MDD 9 (60) | 21 (77.8) | 1.493 | 1 | 0.2217 |
|                     | MIND 21 (53.8) | 22 (61.1) | 0.404 | 1 | 0.5251 |
|                     | NODEP 11 (23.9) | 15 (40.5) | 2.635 | 1 | 0.1045 |
| Late insomnia (yes) | MDD 8 (53.3) | 21 (77.8) | 2.696 | 1 | 0.1006 |
|                     | MIND 14 (35.9) | 20 (55.6) | 2.919 | 1 | 0.0875 |
|                     | NODEP 12 (26.1) | 10 (27) | 0.009 | 1 | 0.9232 |
| Psychomotor changes (yes) | MDD 2 (13.3) | 3 (11.1) | 0.045 | 1 | 0.8313 |
|                     | MIND 2 (5.1) | 0 | 1.897 | 1 | 0.1684 |
|                     | NODEP 3 (6.5) | 0 | 2.504 | 1 | 0.1136 |
| Agitation (yes) | MDD 0 | 2 (7.4) | 1.167 | 1 | 0.2801 |
|                     | MIND 0 | 0 | 0 | 1 | 1.0 |
|                     | NODEP 0 | 0 | 0 | 1 | 1.0 |
| Slowness (yes) | MDD 2 (13.3) | 1 (3.7) | 1.348 | 1 | 0.2456 |
|                     | MIND 2 (5.1) | 0 | 1.897 | 1 | 0.1684 |
|                     | NODEP 3 (6.5) | 0 | 2.504 | 1 | 0.1136 |
| Loss of energy (yes) | MDD 15 (100) | 26 (96.3) | 0.569 | 1 | 0.4506 |
|                     | MIND 35 (89.7) | 28 (77.8) | 1.994 | 1 | 0.1579 |
|                     | NODEP 29 (63) | 17 (45.9) | 2.426 | 1 | 0.1193 |

Table 3 (Continued)

| Depressive symptoms | PD n (%) | CS n (%) | χ² | df | P uncorrected |
|---------------------|---------|---------|----|----|---------------|
| Worthlessness/guilt (yes) | MDD 5 (33.3) | 18 (66.7) | 4.325 | 1 | 0.0376 |
|                     | MIND 3 (7.7) | 6 (16.7) | 1.428 | 1 | 0.2321 |
|                     | NODEP 0 | 0 | 0 | 1 | 1.0 |
| Changes in concentration (yes) | MDD 13 (86.7) | 23 (85.2) | 0.017 | 1 | 0.8954 |
|                     | MIND 16 (41) | 10 (27.8) | 1.451 | 1 | 0.2284 |
|                     | NODEP 10 (21.7) | 1 (2.7) | 6.464 | 1 | 0.0110 |
| Concentration deficits (yes) | MDD 7 (46.7) | 5 (18.5) | 3.744 | 1 | 0.0530 |
|                     | MIND 5 (12.8) | 7 (19.4) | 0.611 | 1 | 0.4344 |
|                     | NODEP 3 (6.5) | 1 (2.7) | 0.652 | 1 | 0.4194 |
| Decisional incapability (yes) | MDD 10 (66.7) | 20 (74.1) | 0.259 | 1 | 0.6106 |
|                     | MIND 11 (28.2) | 6 (16.7) | 1.422 | 1 | 0.2331 |
|                     | NODEP 7 (15.2) | 0 | 6.149 | 1 | 0.0131 |
| Suicide ideation (yes) | MDD 2 (13.3) | 0 | 3.780 | 1 | 0.0519 |
|                     | MIND 0 | 0 | 0 | 1 | 1.0 |
|                     | NODEP 0 | 0 | 0 | 1 | 1.0 |

Note: *Statistically significant differences after Bonferroni correction for multiple comparisons (P < 0.05/18 comparisons).

Abbreviations: CS, control subjects; df, degrees of freedom; MDD, major depressive disorder; MIND, minor depressive disorder; NODEP, no depression; PD, Parkinson’s disease.

Strengths of our study are the s...
using specific and validated scales, as well as a structured interview for diagnostic criteria.

One may criticize our study because we compared an unbalanced number of subjects in each category of depression: i.e., MDD, MIND, and NODEP. This methodological confound could have resulted in weak statistical control. However, using this procedure we recruited a consecutive sample of individuals with depression, leaving preserved the clinical impact of depression in this population of individuals. Moreover, we employed a control group with different non-neurological medical illnesses in which the comorbidity could play an important role in depression prevalence, but, at the same time, this sample provides a clear picture of depression characteristics in elderly patients without neurological diseases. Nevertheless, future research should be dedicated to definitively confirm the hypotheses derived by our results.

Conclusion
Our findings support previous evidence that the profile of depressive symptoms in PD patients with mood disorders is quite comparable with that of patients suffering from other disabling non-neurological medical illnesses, although PD patients with MDD exhibited fewer psychic symptoms. Conversely, the evidence that nondepressed PD patients showed more severe depressive symptoms than nondepressed CS suggests that increased severity of depressive symptoms in PD with no comorbid depressive disorders could be secondary to, or influenced by, neurological symptoms, and could result from loss of endogenous neurotransmitters such as dopamine, serotonin, and norepinephrine, which are described in PD.50–42 Therefore, future research should clarify the question about the nature of depression in PD, which still remains uncertain and inhomogeneous among the three groups of MDD, MIND, and NODEP, in order to help clinicians to form diagnostic or therapeutic decisions. Moreover, the diagnostic process of depression in PD should take into consideration the possible overlap between neurological and depressive symptoms. Thus, an integrated neuropsychiatric approach, in which biological and psychological processes are considered to be thoroughly intertwined, should be encouraged in PD.

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Disclosure
The authors report no conflicts of interest in this work.

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