

SHORT REPORT

Physical anhedonia in Parkinson's disease

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Anhedonia is the inability to experience physical or social pleasure. Its physical component is hypothesised to be due to dysfunction of a dopaminergic frontotemporal-subcortical circuit and has never been investigated as a possible affective complication of Parkinson's disease (PD). The aim of this study was to formally assess prevalence and correlates of physical anhedonia in PD patients compared with normal controls. Twenty five people with PD and 25 matched controls were administered a psychometric battery exploring mainly executive functions and mood. Hedonic tone was assessed using Chapman's Physical Anhedonia Scale. PD patients also underwent MRI linear measurement of frontal structures. Anhedonia levels were significantly higher in PD patients with respect to controls, although not extremely elevated; prevalence rate was 40% for parkinsonians, while no anhedonics were found among controls. Clinical, neuropsychological, and quantitative neuroradiological features did not show any significant correlation with physical anhedonia. Physical anhedonia appears to be a relatively frequent, although mild, affective disturbance of PD, independent from neurological, frontal, and depressive aspects.

Besides motor and cognitive symptoms, affective and behavioural disturbances are often observed during the course of Parkinson's disease (PD).¹ Attention of clinicians and researchers has classically focused on depression, although other aspects, such as anxiety and apathy, have more recently started to be examined.^{2–3}

Anhedonia, defined as a lowered ability to experience physical or social pleasure, may either represent a personality trait predisposing to depression and psychosis, or a neuropsychiatric symptom of endogenomorphic depression and schizophrenia.⁴ Its putative neural substrate is represented by the dysfunction of a dopaminergic mesolimbic reward circuit involving the ventral striatum and the prefrontal cortex.⁵ Neuropathological,⁶ pharmacological,^{7–8} and functional imaging⁹ data suggest that degeneration of the dopaminergic system in PD might extend to the hedonic network as well. From a clinical point of view, both physical and social aspects of anhedonia represent relevant elements of affection and quality of life in PD. However, sensitivity to sensory experiences (eg food) appear more suitable for the investigation of the putative neural substrates of pleasure. In fact, interpersonal relationships and participation in social events are heavily influenced by psychological and cultural factors; the disability associated with PD may limit social life, despite intact ability of enjoyment. For the present anatomo-clinical correlational study we thus concentrated on physical anhedonia only.

The aim of the present research was to systematically investigate presence and severity of physical anhedonia in PD patients compared with healthy individuals, and evaluate its

neurological, cognitive (mainly executive), affective, and morphometric (frontal) correlates.

SUBJECTS

We examined a consecutive series of 25 subjects affected by idiopathic PD and 25 normal controls enrolled among patients' healthy relatives. History of neuropsychiatric disease or drugs or alcohol misuse represented exclusion criteria for both groups. Subjects with an abnormal performance on the Mattis Dementia Rating Scale (MDRS; <121) were also excluded, in order to avoid unreliable completions of the anhedonia questionnaire. All subjects gave their informed consent.

METHODS

Patients underwent neurological assessment with the Unified Parkinson's Disease Rating Scale (UPDRS), part III. Global cognitive status was evaluated with the MDRS and spatial span. Frontal functions were further assessed with the Letter and Category Verbal Fluency Tests and with the Executive Interview (EXIT).¹⁰ The EXIT is a 25 item battery for the assessment of set-shifting, sensitivity to interference, and ability to inhibit automatic behaviour. Each item is scored 0–2 (maximum score = 50) and the cut off value for normality is >15 (the lower the score, the more severe is executive impairment).

Brink's Geriatric Depression Scale (GDS)¹¹ and Marin's Apathy Scale¹² were used for mood assessment. LJ and JP Chapman¹³ developed an instrument for the evaluation of the ability to experience sensory pleasure: the Physical Anhedonia Scale (PAS). The PAS is a self-rated questionnaire with "true or false" answers whose items describe various common pleasant situations involving directly sensory experiences, for example "The beauty of sunsets is greatly overrated" and "I have always had a number of favourite foods". The accuracy of the scale has been assessed in a sample of patients with depression for the French translation: reliability was 0.83, while concurrent validity, with respect to the Fawcett-Clark Pleasure Capacity Scale, was 0.53.¹⁴ Score range is 0–61 (the lower the score, the more severe is anhedonia); according to our Italian normative study¹⁵ no adjustment is needed for age, sex, or education and the cut-off value for anhedonia (two standard deviations below normals' mean score) is <31. An examiner was always present and ready to provide any explanation the patient might need while answering the questionnaire. Twenty two PD subjects (three did not give their consent) underwent linear measurement of frontal atrophy with MRI (the methodology is described in detail elsewhere).¹⁶ For the present study

Abbreviations: PD, Parkinson's disease; MDRS, Mattis Dementia Rating Scale; EXIT, Executive Interview; UPDRS, Unified Parkinson's Disease Rating Scale; PAS, Physical Anhedonia Scale; GDS, Geriatric Depression Scale

Table 1 Demographic, clinical, neuropsychological, and neuroradiological variables of the two study groups.

Variable	Parkinsonians n=25 (mean SD)	Controls n=25 (mean SD)	t/ χ^2	p
Physical Anhedonia Scale	32.4 (10)*	43.1 (5.5)	1.84	0.000
Age (years)	67.4 (5.9)	66.2 (6.1)	0.19	0.536
Sex (M)	15	12	0.67	0.31
Education (years)	7.6 (3.9)	8.1 (3.4)	0.90	0.672
UPDRS part III	30.3 (15.4)	–	–	–
Disease duration (months)	58.8 (48.2)	–	–	–
Levodopa daily dosage (mg)	370.6 (329.6)	–	–	–
MDRS	129.5 (6.2)*	137.3 (4.2)	6.22	0.000
Letter verbal fluency	10.1 (2.7)*	12.0 (2.2)	2.07	0.019
Category verbal fluency	12.4 (3.1)*	14.8 (2.4)	1.89	0.009
Executive Interview	10.7 (5.3)*	5.3 (3.7)	3.57	0.001
Spatial span	5.1 (1.1)	5.5 (0.8)	1.31	0.200
Geriatric Depression Scale	12.8 (6.1)*	6.7 (3.1)	6.90	0.001
Apathy Scale	16.9 (5.6)*	11.8 (3.2)	3.77	0.003
Bifrontal Index Cortex/Head	91.5 (2.5)	–	–	–
Bifrontal Index Ventricles /Head	26.5 (2.3)	–	–	–

UPDRS, Unified Parkinson's Disease Rating Scale; MDRS, Mattis Dementia Rating Scale.

Table 2 Correlations between anhedonia and demographic, clinical, neuropsychological, and neuroradiological variables.

	Physical Anhedonia Scale
Age	-0.26
Education	0.23
UPDRS part III	0.01
Disease duration (months)	-0.37
Dementia Rating Scale	-0.17
Letter verbal fluency	0.19
Category verbal fluency	-0.03
Executive Interview	-0.39
Spatial Span	0.17
Geriatric Depression Scale	-0.23
Apathy Scale	-0.17
Bifrontal Index Cortex/Head	0.18
Bifrontal Index Ventricles /Head	0.18

UPDRS, Unified Parkinson's Disease Rating Scale.

we considered the Bifrontal Index Cortex/Head (corresponding to the ratio of brain width measured between frontal dorsolateral cortex surfaces to head width $\times 100$) and the Bifrontal Index Ventricles/Head (corresponding to the ratio of the maximum distance between the frontal horns of the lateral ventricles to head width $\times 100$). This latter measure can be viewed as a more specific orbito-frontal index.

RESULTS

The sociodemographic, neurological, neuropsychological, and neuroradiological features of both study groups are shown in table 1.

No significant between group differences were found on any of the demographic variables examined. Patients with PD had an overall worse performance at the neuropsychological tests (except for spatial span) and also presented more severe depression on the GDS and more apathy on the Marin's Scale compared with controls.

With regard to physical anhedonia, 10/25 people with PD (40%), but no control subject, were found to be anhedonic. Overall, mean anhedonia scores were significantly worse for the PD group compared with normal controls; score range for the 10 anhedonic PD subjects was 8–30; however, eight subjects (80%) scored above 20, which is indicative of mild impairment.

Correlation analysis (table 2) showed no relevant relationship between physical anhedonia and any of the neurological, neuropsychological, and neuroradiological variables; only the

EXIT scores showed a trend towards a statistically significant correlation ($p=0.055$).

DISCUSSION

We evaluated incidence and nature of physical anhedonia using a correlational approach and we found data of both clinical and heuristic value. A high percentage of our PD patients (40%) showed some degree of subsensitivity to physical pleasure, although most of them presented only mild levels of anhedonia. Anhedonia thus appears to be a frequent complication of PD and deserves to be systematically investigated. To this aim, a reliable and easy to use instrument should be available. From this point of view, Chapman's PAS showed some limitations: some of the items had a very complex syntactic structure and the scale as a whole was excessively long, especially for patients as bradyphrenic and exhaustible as those with PD. Aid from investigators was often needed. Staff administered questionnaires or shorter and simpler self-rating instruments would thus be recommendable for future use in the clinical setting. In our study sample anhedonia levels did not parallel the clinical course of PD. The correlation with disease duration approached significance ($r = -0.37$) and should be verified in a larger sample of patients; the correlation with motor impairment was far from significant. This observation replicates previous findings about depression in PD, which appears to be unrelated to disability,¹ supporting different patterns of degeneration for the nigro-striatal circuit responsible for the extrapyramidal syndrome and the mesolimbic projections that control affection (including hedonic attitudes). The present neuropsychological and neuroradiological protocol also aimed at exploring possible relationships between physical anhedonia and the prefrontal component of the reward system. We considered executive tests and frontal atrophy measures; both types of indexes failed to show a consistent relationship with anhedonia. The correlation between frontal psychometric variables and anhedonia scores ($r = -0.39$) would have probably reached statistical significance with a larger sample size. The relevance of such a correlation would still appear lower than expected on the basis of the putative locus of the hedonic system. This dissociation might tentatively be explained by hypothesising that control processes for cognitive and affective aspects are relatively segregated within the frontal lobe and tend to degenerate in a differential manner in PD. With regard to morphometry, negative results might first of all be due to insufficient sensitivity of the linear technique, although previous studies had found it accurate enough for the detection of even mild cognitive and affective disorders.^{16,17} The disregard of subcortical components of the hedonic circuit, most likely affected by

degeneration in PD (particularly the striatum), might also have contributed to the lack of evidence for a specific pattern of brain atrophy associated with anhedonia. An alternative explanation might be that derangements of the reward system may be underlain by very subtle structural alterations; undetectable by gross measures of neuroanatomical changes, they could be explored with functional imaging techniques only.

Anhedonia might, in principle, have either an endogenous or a reactive origin, as chronic, progressive disablement might by itself interfere with access to and enjoyment of physical pleasurable experiences; the use of a non-neurological physical disease control group would have allowed us to more adequately explore the hypothetical neurobiological basis of anhedonia in PD, making our conclusions less speculative. However, in our sample the lack of correlation between PAS and both depression and severity of motor impairment is supportive of a non-reactive nature of this disturbance. In any case, the putative neural substrate of hedonic tone is represented by a complex dopaminergic circuit rising from the ventral tegmental area to the ventral striatum (nucleus accumbens), the prefrontal cortex, and the entorhinal and amygdaloid complex.⁵ These structures, and particularly the dopaminergic receptors in the nucleus accumbens, are considered to mediate the euphorising effects of psychostimulants¹⁸ and antiparkinsonian drugs.^{19–21} Ventrostriatal dopaminergic receptors are even thought to be involved in various forms of addiction, including the hedonistic homeostatic dysregulation seldom reported in PD. Evidence from anatomo-pathological, biochemical, and functional imaging studies suggest dysfunction of the reward circuit in parkinsonians.^{6–18} The present prevalence rate and severity level of anhedonia are consistent with such observations.

The relationship between anhedonia and apathy appears particularly intriguing, given the close link usually hypothesised between reward and motivation. Neurobiological studies in animals suggest that generation and implementation of goal directed responses are in fact thought to depend on positive reinforcement via the nucleus accumbens, which acts as an emotion behavioural interface.¹⁹ A recent study by Pluck and Brown detected higher anhedonia levels in apathetic, compared with non-apatetic, people with PD examined with the Snaith-Hamilton Pleasure Scale.³ Contrarily, our findings show that lack of reward is not necessarily associated with lack of motivation and vice versa, also suggesting distinct neural substrates for the emotional experience of physical pleasure and volitional outputs.²² Given its potential theoretical interest, such interconnection should be more extensively investigated in other clinical samples. In agreement with previous literature data from subjects with depression, schizophrenia, and healthy subjects,^{23–25} we also found no correlation between physical anhedonia and mood. PD associated depression often represents a reaction to disability, but may as well be of endogenous origin. Our study design did not permit discrimination between these two conditions. As reactive depression is traditionally considered to be less strongly related to anhedonia than endogenous melancholia, a high prevalence of reactive depression in the present series of people with PD might perhaps explain the observed dissociation between lowered hedonic capacity and affective status. In possible endogenous cases, such a dissociation seems to argue against the dopaminergic hypothesis of PD associated depression (whose neural substrate would substantially coincide with the hedonic circuit), in favour of a major role for the serotonergic and noradrenergic systems.²⁶ Finally, a low sensitivity to anhedonic components of depression of the mood level scale we used might have contributed to the limited overlap between depression and anhedonia. No item included in the GDS appears to deal with experience of physical pleasure.

Higher correlations might possibly exist between depression and social aspects of anhedonia (not considered in the present paper).

In summary, the present study represents a first demonstration of the clinical relevance of anhedonia as a neuropsychiatric complication in PD. In agreement with previous findings in pathological and normal samples, PD associated anhedonia appears as a mainly independent construct. Indirect suggestions were derived about its putative substrate; further investigation of this aspect of emotionality in extrapyramidal disorders could contribute to its better definition.

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