Chapter 13
Anhedonia in Parkinson's Disease and Other Movement Disorders

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Abstract Anhedonia, defined as lowered ability to experience physical or social pleasure, is a frequent symptom in patients with Parkinson's disease (PD). In this population, most studies report an association of anhedonia with neuropsychiatric disorders and syndromes such as depression, apathy and cognitive decline. Reports on the relationship between anhedonia and severity of motor symptoms in PD are inconclusive. The presence of anhedonia is diagnosed on the basis of history and mental status examination; its severity can be assessed by available rating scales. Several studies described anhedonia as strictly associated to depression in PD and probably related to degeneration of mesolimbic and mesocortical dopamine projections, thus contributing directly to the high incidence of depression and consequently of anhedonia in PD patients. This is supported by the observation that inhibition of dopamine system via D_2 receptor antagonists can be accompanied by reduced motivation, drive and spontaneity, and dysphoria.

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In contrast to PD, data on anhedonia in other movement disorders are still scarce.

Future research should be directed to a better understanding of the etiology and pathophysiology of anhedonia in order to be able to identify and provide new strategies for treatment of this neuropsychiatric phenomenon.

Keywords Parkinson's disease • Movement disorders • Anhedonia • Motor symptoms • Non-motor symptoms • Cognitive deficits • Apathy • Depression

Abbreviations

DBS-STN	Deep brain stimulation of the subthalamic nucleus
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-IV-TR	The fourth revised edition of the DSM
ICD-10	International Classification of Diseases
PD	Parkinson's disease

13.1 Introduction

Parkinson's disease (PD) is generally considered a multidimensional neuropsychiatric disease with a broad spectrum of symptoms. Following the Queens Square Brain Bank diagnostic criteria, motor symptoms such as tremor, rigidity, hypokinesia, and postural instability are essential for a diagnosis of PD [1]. In addition to motor symptoms, psychopathological symptoms often accompany, and sometimes precede, the disease [2–4]. Depression, anxiety, apathy, psychosis, and cognitive dysfunction all occur frequently in PD [2], while it is known that both depression and anxiety may precede the onset of motor symptoms [5–7].

The pathophysiology of PD is widespread and multisystemic, involving several brain structures. Braak et al. [8] proposed a staging system for this pathophysiology based on the presence of intraneuronal α synucleine deposits, known as Lewy bodies. Different cerebral regions that are part of different functional neuro-anatomic circuits and different neurotransmitter systems, are affected sequentially. In the first stages, the olfactory tract and lower brainstem regions are affected; then, the pathology proceeds upwards to the midbrain, and next to the basal forebrain and cerebral cortex. In this sequence, the substantia nigra, which is thought to be associated with the motor symptoms of PD, is affected in mid-stage disease. The diversity of systems affected, and the fact that some of these systems are affected before involvement of the substantia nigra, may explain the diversity of symptoms as well as the fact that some of the non-motor symptoms may precede motor symptoms.

Anhedonia is a non-motor phenomenon defined as lowered ability to experience physical or social pleasure. It is generally considered a symptom rather than a disorder. In fact, anhedonia is a key symptom of various psychiatric illnesses,

including depression, which is the most frequent neuropsychiatric disorder observed in PD [2], apathy [9], abstinence or intoxication with several substances of abuse [10–12] and a negative symptom of schizophrenia [13–15]. Altered hedonic capacity is probably due to a basic neuropsychophysiological dysfunction. It is a marker of vulnerability that potentially precedes and contributes to the likelihood of developing psychiatric disorders [16]. Moreover, mood related symptoms, including anhedonia and apathy, also occur frequently in a variety of movement disorders other than PD, such as Lewy bodies dementia, Huntington's disease, progressive supranuclear palsy, multisystem atrophy, corticobasal degeneration, essential tremor, tics and dystonia [17–22]. Unfortunately, there is still a lack of data on anhedonia in these movement disorders.

Although anhedonia is often confused with depression or apathy, it differs from these different non-motor symptoms in term of mechanisms, therapeutic approaches, and prognosis. In this chapter we will try to clarify the concept of anhedonia in the context of movement disorders in order to determine whether it is a symptom of depression and apathy or, rather, a specific phenomenon, independent from other behavioral characteristics. Furthermore, we will illustrate the clinical assessment of anhedonia and rating scales used to measure hedonic tone. Finally, we will explain the link among anhedonia, motor symptoms and cognitive deficits in movement disorders and discuss the pathophysiology and potential pro-dopaminergic treatment of anhedonia. Correct recognition of anhedonia in patients with these disorders could lead to better treatment of the diseases and their clinical features leading to improved quality of life.

13.2 Conceptual Issues and Phenomenology

The term "anhedonia" comes from the Greek ἀν (an = "without") and ἡδονή (hēdonē = "pleasure"), and refers to a group of clinical phenomena whose common denominator is the complaint of incapacity to experience pleasure. At the end of the nineteenth century, anhedonia was first defined by Ribot [23] as loss of the capacity to feel pleasure. Anhedonia has been included in the Diagnostic and Statistical Manual of Mental Disorders (DSM) series since 1980 [24] and in the International Classification of Diseases (ICD) since 1992 [25]. In both textbooks, it is considered a symptom of depression and schizophrenia, although it is unclear whether the mental states involved are the same in both cases. Finally, the fourth revised edition of the DSM (DSM-IV-TR) [26] defines anhedonia as diminished interest or pleasure in response to stimuli previously perceived as rewarding in a pre-morbid state.

More commonly, anhedonia is defined as the inability to experience pleasure or to get the accustomed satisfaction from everyday events or objects [27]. Sometimes a distinction into social and physical anhedonia is made, whereby physical anhedonia refers to the inability to experience pleasure from physical activities (including such activities as sporting or eating), while social anhedonia refers to the inability to experience pleasure from social encounters or relationships. Although this

distinction may be useful from a phenomenological point of view, there is as yet no pathophysiological evidence to support such division.

Several authors have recently proposed a more circumscribed definition of anhedonia centered on the distinction between anticipatory and consummatory pleasures [14]. Anticipatory pleasure is the pleasure that a subject experiences at the thought of a future event while consummatory pleasure reflects the pleasure that a subject experiences while he is engaged in an enjoyable activity. Anticipatory and consummatory pleasures correspond respectively to the neuroscientist concepts of liking and wanting in relation to reward. Moreover, some studies have strongly suggested that dopamine could be involved in the anticipatory experience of pleasure, whereas other neurotransmitters, such as opioids, could be involved in the consummatory experience of pleasure [28].

As previously mentioned, anhedonia is considered a symptom that can be present in various disorders, such as major depressive disorder, schizophrenia or schizophrenia spectrum disorders, dementia, or apathy [29]. In patients with movement disorders, symptoms of depression, such as apathy and anhedonia, may overlap with primary symptoms, thus making it more difficult to recognize secondary psychiatric symptoms. Flattening of the positive component of affect in anhedonia may lead to diminished facial expression of positive emotions and be confused with the hypomimia of PD or progressive supranuclear palsy. Moreover, anhedonia in PD may occur as a stand-alone symptom, but it mostly occurs as part of other syndromes, especially apathy and depressive disorder. In a recent review, all but one included studies reported that anhedonia was related to the presence of other psychiatric symptoms [30]. This issue was specifically addressed by Weintraub et al. [31]. In their study it was shown that PD patients showed no anhedonia in response to positive life events when compared with healthy controls. This was interpreted as evidence that anhedonia was not associated with PD as such, but instead must be due to other comorbidities, such as apathy or depression [31]. These findings are not surprising, since anhedonia is part of the proposed diagnostic criteria for apathy, as well as part of the criteria for major and minor depressive disorders of the DSM-IV-TR.

13.3 Clinical Assessment of Anhedonia

The fact that anhedonia is considered a *symptom* implies that it is improbable, or even impossible, to make a categorical (syndromal) diagnosis of anhedonia. The presence of anhedonia is defined on the basis of history and mental status examination. Unfortunately, there is no diagnostic test that can confirm the presence of this symptom on the basis of biological evidence. Patients themselves, or their spouse or caregiver, may reveal that they have difficulty in experiencing pleasure from activities that the person found pleasurable in the past. Sometimes this lack of pleasure is evident from observation as well. When anhedonia is present, it is fundamental to check for additional psychiatric comorbidity, especially the presence of apathy and

depression, for differential diagnosis. These two syndromal diagnoses based too on history and mental state examination.

In the case of apathy, it is usually not the patient that complains of apathy, but the spouse or caretaker. They observe that the patient is passive, disinterested, with a flattened affect. The patient may be inactive and spend a big part of the day sitting on the couch doing nothing, but typically he denies being bored. Usually, the patient's partner will suffer more from his inactivity than the patient himself. Moreover, the partner will report that the patient may need stimulation to perform everyday activities, involving grooming among other things. Often apathy is being mistaken for depression, which is understandable given the similarity of many of its symptoms. However, when the patient is questioned, he denies feeling sad and denies not being able to enjoy things. This enables the clinician to differentiate apathy from depression. In case of apathy, mental status examination will reveal reduced motivation, reduced activity, mental and physical slowing, poverty of thoughts, affective flattening and disinterest. A syndromal diagnosis of apathy can be made on the basis of proposed diagnostic criteria in case of apathy, and the DSM-IV criteria are used in case of depression [32]. The severity of anhedonia as a symptom, or of the syndromes of apathy and depression can be rated by specific rating scales mentioned (see below).

The syndromal diagnosis of depression is also made on the basis of history taking and mental state examination, and should meet the diagnostic criteria laid down in the DSM-IV [33]. A good starting point for history taking is to probe the two core symptoms of depression: depressed mood, and diminished interest or pleasure. If the patient admits to at least one of these two symptoms, a more detailed history should be carried out to reveal other symptoms of depression. One should not avoid asking for symptoms that may potentially be embarrassing for the patient or his spouse or caregiver, such as suicidal thoughts or plans. Such questions are essential for a proper appraisal of the potential risk involved in depression. Mental state examination may reveal mood symptoms, such as sadness, loss of interest, affective flattening and feelings of guilt, cognitive symptoms, including loss of concentration and mental slowing (relative to a previous level of functioning), and physical symptoms, such as loss of facial expression, slowing of movements, weight loss, insomnia and others.

13.4 Anhedonia Rating Scales

Two scales are available for the measurement of anhedonia, the Snaith-Hamilton Pleasure Scale [34] and the Chapman Scales for Physical and Social Anhedonia [35]. In patients with movement disorders, the Snaith-Hamilton Pleasure Scale is probably most widely used in spite of the fact that there are no validation studies in this group specifically. It is a self-rated instrument that consists of 14 statements that patients can agree or disagree to on a four-point Likert scale. Thus, the scale assesses the presence and severity of one single symptom using a number of items. It was

developed with the aim of producing a shorter and simpler scale for the measurement of anhedonia that is unlikely to be affected by social class, sex, age, dietary habits and nationality. In patients not suffering from PD, it has good face validity, internal consistency, item-total correlation, and test–retest correlation. There is some overlap between the items and symptoms of parkinsonism. This may lead to the inflation of scores in movement disorders patients if the cut-off score is not adjusted for these confounders.

The scale has been used by several authors to assess the level of anhedonia in PD patients and to evaluate the effect of (pharmacological) treatment of motor symptoms of PD on hedonic symptoms. It has proven to be sensitive to changes in hedonic tone.

The Chapman Scales for Physical and Social Anhedonia are probably the most widely used instruments to measure anhedonia in patients with psychiatric disorders, such as schizophrenia and depressive disorder. The original scale consists of 88 true/false questions, divided over two subscales: a subscale for physical anhedonia consisting of 40 items and one for social anhedonia consisting of 48 items. Higher scores indicate more severe anhedonia, except in the Italian translation, which is reversely scored with higher scores indicating less severe anhedonia. The scale for physical anhedonia was later revised to include 61 items and is often used independently from the social anhedonia scale. The time frame is not well defined. This scale was thought to lack face validity as it includes aspects of social withdrawal, loss of interest, lack of motivation, and other features that are currently considered part of the larger concept of "apathy" and not of pure anhedonia. In addition, many items are sensitive to personal opinions, preferences, and habits. Nevertheless, it has good internal consistency and item-total correlation. The scale was used in one study with PD patients. In this study, the researchers highlighted the shortcomings and impracticability of the scale.

Anhedonia is also assessed as a subdimension of various apathy and depression rating scales. A discussion of the many apathy and depression rating scales goes beyond the scope of the chapter and the reader is referred to the respective reviews of Movement Disorder Society task forces, that specifically review and critique these scales for use in PD patients [29, 36].

13.5 Epidemiology

Few studies assessed the prevalence of anhedonia as a symptom in movement disorders. In these studies, the presence of anhedonia is commonly defined using a cut-off score on an anhedonia rating scale. Based on this definition, 10–46 % of all PD patients suffer from anhedonia [2, 37–39].

Anhedonia is mostly studied in the context of apathy and depression. Until recently, apathy was ill defined, and usually diagnosed on the basis of an above threshold score on an apathy rating scale. Not surprisingly, these studies reported a wide range of frequencies of apathy in PD patients, varying from 17 % to 70 %,

depending on the population characteristics and the assessment procedure used [40–42]. Recently, consensus diagnostic criteria have been formulated that define apathy as a syndrome of deficient motivation, characterized by lack of motivation associated with deficits in three different domains: reduced spontaneous motor behavior, reduced spontaneous thoughts and cognition, and reduced emotional responsiveness [32]. This latter criterion includes both affective flattening and anhedonia. Following the diagnostic criteria, 17 % of PD patients suffered from apathy, with 52 % of patients showing reduced emotional responsiveness [43].

As mentioned above, the gold standard for the diagnosis of depressive syndromes are the criteria of the DSM-IV-TR [33]. For a major depressive episode, the presence of at least five out of nine specified symptoms are required, of which either reduced mood, or markedly diminished pleasure or interest is obligatory. This second criterion is ambiguous because it includes aspects of both anhedonia (diminished pleasure) as well as apathy (loss of interest), thus making it impossible to make a distinction between the two when making a depression diagnosis. A systematic review of prevalence studies of depressive syndromes in PD patients reported an average prevalence of 17 % for major depressive disorder, 22 % for minor depression and 13 % for dysthymia [44]. Clinically relevant depressive symptoms without a formal diagnosis of depressive disorder were reported in 35 % of patients [44]. Lemke et al. [38] reported that anhedonia occurs in 80 % of depressed PD patients.

13.6 Anhedonia and Psychiatric Symptoms

Prospective studies identifying risk factors for the development of anhedonia in PD patients are lacking, and all evidence on the etiology and associations of anhedonia with affective, motor and cognitive symptoms are based on cross-sectional studies.

Most, but not all, clinical studies found that anhedonia was closely related to depression or apathy and that in PD it could be considered a symptom of psychiatric disorders [31] (see Table 13.1). In particular, anhedonia has been identified as a frequent symptom of depression in PD [38, 39, 45, 49, 53, 56, 62, 63], and seems to be more severe in patients with more depressive symptoms.

Spalletta et al. [61] showed that patients with diagnosis of major depressive disorder were more anhedonic than those with minor depressive disorder, who were in turn more anhedonic than PD patients without depression. Similarly, most, but not all studies, report that anhedonia is associated with apathy in patients with PD [41, 43].

Zahodne et al. [59] tried to characterize depression in PD patients in terms of components, including negative affect, apathy and anhedonia. In a factor analysis these factors were highly correlated and overlapped. Moreover, these three components were significantly associated with depressive status but the strongest unique association with depressive episode status was exhibited by negative affect, followed by apathy and anhedonia. Apathy was most associated with global psychological disturbance in PD, while anhedonia was least discriminating of a depressive episode.

Table 13.1 Anhedonia and psychiatric symptoms in movement disorders

Author (year)	Sample (n)	Anhedonia assessment	Anhedonia vs. psychiatric symptoms
Fibiger (1984) [45]	Not available	Not available	Anhedonia: cardinal feature of clinical depression
Cantello et al. (1989) [46]	dPD = 13; NODEP PD = 11; dCS = 14; CS = 12	Fawcett and Clark Pleasure Scale	Anhedonia: main features of PD patients with major depression
Fleminger (1991) [47]	PD = 30 (LHP = 13; RHP = 17)	Three items added to the 21 items of the BDI (MBDI)	LHP: higher scores on all measures of depression and greatest increase in MBDI compared with RHP The total group: MBDI items selectively raised in only one patient. Thus, depression experienced by PD patients is atypical, with relatively little anhedonia
Rockwell et al. (2000) [48]	LBD = 26; AD = 26	Structured interviews	Higher level of anhedonia in LBD than AD patients
Pluk and Brown (2002) [41]	PD = 45 (PD-HA = 17; PD-LA = 28); Osteoarthritis patients = 17	SHAPS	PD vs. Osteoarthritis: significant differences on the SHAPS only when measured on a binary scale and with a cut-off ≥3 Osteoarthritis group: no one anhedonic PD group: 3 anhedonic PD-HA more anhedonic than PD-LA
Reichman et al. (2003) [39]	PD = 626	SHAPS-D	Prevalence of anhedonia: 45.7 % Significant correlation between the SHAPS-D scores and the SPES depression items
Isella et al. (2003) [37]	PD = 25; HC = 25	Physical Anhedonia Scale	Prevalence of anhedonia: 40 % in PD No significant correlations among anhedonia, depression and apathy
Lemke et al. (2005, 2006) [38, 49]	PD = 626 (dPD = 138; NODEP = 488); HC = 50	SHAPS-D	Prevalence of anhedonia: 45.7 % in PD and 79.7 % in dPD Significant correlation between anhedonia and depression
Weintraub et al. (2006) [31]	PD = 24; HC = 23	Lawton Positive and Negative rating scale	When present in PD, anhedonia is a symptom of neuropsychiatric disorders
Lieberman (2006) [50]	PD = 206	NPI	Anhedonia is more frequent in depressed PD and in demented PD patients

(continued)

Table 13.1 (continued)

Author (year)	Sample (n)	Anhedonia assessment	Anhedonia vs. psychiatric symptoms
Ehrt et al. (2006) [51]	PD = 145; dCS = 100	MADRS item on anhedonia	PD patients experienced a specific profile of depressive symptoms characterize by less anhedonia than dCS
Miller et al. (2007) [19]	PD = 354; ET = 53; Dystonia = 83	Item 4 of BDI	No significant between-groups differences in anhedonia
Zheng et al. (2009) [52]	PD = 131 (dPD = 27; sdPD = 71; NODEP = 33)	HDRS	Anhedonia is one of the most common symptoms in dPD (85.2 %), sdPD (88.7 %) and NODEP (60.6 %). It is concomitant with PD, it is not caused by mood disorders and it is not specific to the diagnosis of depression in PD
Santangelo et al. (2009a) [53]	PD = 125 (dPD = 65; NODEP = 60)	SHAPS	Anhedonia significantly associated with depression; dPD scored significantly higher on the HDRS and the SHAPS compared with NODEP
Santangelo et al. (2009b) [54]	PD = 939; VP = 68; MSA = 28; PSP = 27; LBD = 14	SHAPS	Anhedonia significantly correlated with depression (HDRS) in PD patients; LBD patients had a much higher anhedonic score that patients with other diagnosis Significant impact of apathy and depression on anhedonia in the total group
Pouladi et al. (2009) [55]	Animal model of HD	The sucrose intake test	HD animals displayed anhedonic behavior
Schrag et al. (2010) [21]	PSP = 188; MSA = 286	HADS	PSP patients were more anhedonic than those with MSA
Kaji and Hirata (2011) [56]	PD = 50	SHAPS-J	Anhedonia is present in 74 % of PD patients: anhedonia alone was present in 29 % of PD, anhedonia and depression in 4 % of PD, anhedonia, apathy and depression in 13 % of PD, and anhedonia and apathy in 29 % of PD A strong correlation was found between apathy and anhedonia
Fujiwara et al. (2011) [57]	PD = 100 (dPD = 46; NODEP = 54); HC = 111	SHAPS-J	Prevalence of anhedonia: 10 % in PD; anehdonic PD scored significantly higher on the SRQ-D than non-anhedonic PD; dPD scored significantly higher on the SHAPS-J

(continued)

Table 13.1 (continued)

Author (year)	Sample (n)	Anhedonia assessment	Anhedonia vs. psychiatric symptoms
Miura et al. (2012) [58]	PD = 86	SHAPS-J	Prevalence of anhedonia: 16.3 % in PD
Zahodne et al. (2012) [59]	PD = 95	SHAPS TEPS (TEPS-ANT/TEPS-CONS)	Possibility of statistically separating the 3 depression components in PD: negative affect, apathy and anhedonia. All 3 components were significantly associated with depression status. Anhedonia was least discriminating of a depressive episode, support ing the idea that anhedonia is not very prominent in PD depression
Di Giuda et al. (2012) [17]	PD = 21; Dystonia = 14; ET = 15; HC = 17	SHAPS	No significant differences in anhedonia between patients and HC
Zahodne et al. (2013) [60]	PD = 95	SHAPS TEPS (TEPS-ANT/TEPS-CONS)	Cognitive dimension of apathy, dysphoria, negative affect, and anxiety may better identify PD patients at risk for more global psychological dysfunction in comparison to anhedonia or affective flattening
Spalletta et al. (2013) [61]	PD = 254	SHAPS	MDD PD were more anhedonic than those with MIND and NODEP. Anhedonia prevalence was significantly higher in MDD patients (12.5 %) than MIND patients (7.2 %) or NODEP (1.5 %) Reduced hedonic tone was predicted from increased depression severity only in patients with MDD and NODEP, but not in MIND subgroup

AD Alzheimer disease, *BDI* Beck Depression Inventory, *CS* control subjects, *dCS* depressed control subjects, *dPD* PD patients with depression, *ET* essential tremor, *HADS* Hospital Anxiety and Depression Scale, *HC* healthy controls, *HD* Huntington's disease, *HDRS* Hamilton Depression Rating Scale, *LBD* Lewy bodies dementia, *LHP* PD patients with worse signs of PD on the left side, *MADRS* Montgomery-Asberg Depression Rating Scale, *MDD* major depressive disorder, *MIND* minor depressive disorder, *MSA* multisystem atrophy, *NODEP* PD without depression, *NPI* Modification of Cumming's Neuropsychiatric Inventory, *PD* Parkinson's disease, *PD-HA* PD patients with high apathy, *PD-LA* PD patients with low apathy, *PSP* progressive supranuclear palsy, *RHP* PD patients with worse signs of PD on the right side, *sdPD* PD with sub-threshold depression, *SHAPS-D* Snaith-Hamilton Pleasure Scale-German version, *SHAPS-J* Snaith-Hamilton Pleasure Scale-Japanese version, *SPES* Short Parkinson's Evaluation Scale, *SRQ-D* Self-Rating Questionnaire of Depression, *VP* vascular parkinsonism

Yet a minority of authors are of the opinion that anhedonia is not specifically associated with depression. Isella et al. [37] found no relationship among anhedonia, depression, and apathy. Others stress the fact that in PD patients anhedonia may be experienced in absence of depression [64]. Another study [52] reported a high presence of anhedonia in non-depressed PD patients.

To test Fibiger's hypothesis that anhedonia is a fundamental symptom of depression resulting from dopamine depletion, Fleminger [47] measured depression and anhedonia in PD patients with worse signs of disease on the left side of the body and those with worse signs on the right side of the body. In general, they found that depression experienced by PD patients was atypical, characterized by relatively little anhedonia, evident negative view of self, and prominent symptoms of anxiety. In line with this, Ehrt et al. [51] reported that PD patients experienced a specific profile of depressive symptoms characterized by less anhedonia than elderly depressed patients without PD.

Data on anhedonia in others movement disorders than PD are scarce. One study investigated anhedonia in patients with Lewy bodies dementia, and reported a higher level of anhedonia (56 %) in these patients compared to patients with Alzheimer disease (25 %) [48]. In another study [19], the prevalence of anhedonia was 60 % in patients with PD, essential tremor and dystonia, without between group differences in occurrence. In line with this, Di Giuda et al. [17] showed that patients with PD, essential tremor and dystonia did not differ in levels of anhedonia in comparison to healthy controls.

Santangelo et al. [54] explored anhedonia in patients with PD and in patients with different types of parkinsonism. They reported more severe anhedonia in patients with Lewy bodies dementia than in those with PD or other forms of parkinsonism, including vascular parkinsonism, multisystem atrophy, and progressive supranuclear palsy [34, 53].

In conclusion, in patients with PD, anhedonia seems to be related to neuropsychiatric symptoms, particularly depression. In other movement disorders, only few studies have assessed anhedonia.

13.7 Anhedonia and Motor Symptoms

The relationship between anhedonia and motor symptoms, which are the characteristic diagnostic feature of movement disorders, is still not very clear. Some studies found a relationship between these two symptoms whereas others did not (see Table 13.2). In particular, Bermanzohn and Siris [66] suggested a link between akinesia and anhedonia in people with parkinsonism and suggested that the common denominator is probably the reduced dopamine turnover in the brain. In line with this, Reichmann et al. [39] observed a significant association between anhedonia and psychomotor retardation. Similarly, Lemke et al. [38] reported that patients in the early stages of PD (Hoehn & Yahr stage ≤ 2) suffered from anhedonia less often than patients in more advanced stages (Hoehn & Yahr stage >2). They also reported that

Table 13.2 Anhedonia and motor symptoms in movement disorders

Author (year)	Sample (n)	Anhedonia assessment	Anhedonia vs. motor symptoms
Reichman et al. (2003) [39]	PD = 626	SHAPS-D	Significant relationship between anhedonia and psychomotor retardation as measured by the SPES
Isella et al. (2003) [37]	PD = 25; HC = 25	Physical Anhedonia Scale	No significant correlations between anhedonia and motor symptoms (UPDRS-III score)
Lemke et al. (2005) [38]	PD = 626 (dPD = 138; NODEP = 488); HC = 50	SHAPS-D	Significant correlation between anhedonia and motor disability; PD patients in earlier stages of the disease (Hoehn and Yahr $\leq$ 2) had anhedonia less often than PD patients in more advanced stages (Hoehn and Yahr > 2), and with more motor deficits (SPES motor status)
Witt et al. (2006) [65]	PD-DBS STN = 15	SHAPS-D	Significant correlation only between motor changes due to medication and changes in the BDI score. No correlation between the SHAPS-D scores and motor changes
Santangelo et al. (2009b) [54]	PD = 939; VP = 68; MSA = 28; PSP = 27; LBD = 14	SHAPS	No significant correlations between anhedonia, disease duration, disease severity, and motor disability (UPDRS-III score)
Fujiwara et al. (2011) [57]	PD = 100; HC = 111	SHAPS-J	No significant differences were identified between PD with anhedonia and PD with normal hedonic tone in duration of disease and Hoehn-Yahr stage
Miura et al. (2012) [58]	PD = 86	SHAPS-J	Significant positive effect of disease severity on anhedonia

dPD PD patients with depression, *HC* healthy controls, *LBD* Lewy bodies dementia, *MSA* multi-system atrophy, *NODEP* PD without depression, *PD* Parkinson's disease, *PSP* progressive supra-nuclear palsy, *SHAPS-D* Snaith-Hamilton Pleasure Scale-German version, *SHAPS-J* Snaith-Hamilton Pleasure Scale-Japanese version, *SPES* Short Parkinson's Evaluation Scale, *UPDRS-III* Unified Parkinson's Disease Rating Scale-part III, *VP* vascular parkinsonism

patients suffering from anhedonia showed more motor deficits, restrictions in daily living activities, and depression than patients without anhedonia. Miura et al. [58] also found that disease severity is one of the predictors of anhedonia, influencing positively the Snaith-Hamilton Rating Scale score.

By contrast, Fujiwara et al. [57] reported that, although PD patients with anhedonia tended to have a longer duration of disease and a higher Hoehn & Yahr stage [67], no significant differences were identified between PD patients with anhedonia and PD patients with normal hedonic tone. Isella et al. [37] reported no significant correlation among motor symptoms, disease duration, and physical anhedonia in PD patients.

In a sample of PD patients who had undergone deep brain stimulation of the subthalamic nucleus (DBS-STN), Witt et al. [65] reported a significant correlation between motor changes due to medication and changes in depression severity induced by medication but they did not find any correlation between anhedonia and motor symptoms.

There is only one study that addressed the relationship between anhedonia and motor symptoms in movement disorders other than PD. Santangelo et al. [53] reported that anhedonia was not affected by disease duration, disease severity, and motor disability in a mixed sample of patients including patients with PD, progressive supranuclear palsy, vascular parkinsonism, multisystem atrophy and Lewy bodies dementia.

Taken together these findings may support the hypothesis that reduced hedonic tone is not a simple reaction to motor disability due to the illness but rather a non-motor symptom of movement disorders.

13.8 Anhedonia and Cognitive Deficits

Anhedonia is mostly part of apathy and depression; thus it is unlikely that there would be no association between anhedonia and cognitive performance, since the association of cognitive dysfunction with these syndromes is well established [40, 41, 53, 68–70]. Apathy is also considered a predictor of cognitive decline and dementia in PD patients [40], whereas dementia and cognitive decline are predictors of incident apathy [71]. Moreover, apathy is associated with deficits in executive functions, more severe depressive symptoms, and a decreased quality of life [40, 41, 72, 73]. Depression is associated with worse motor function, more severe limitations in activities of daily living [74–77] and a lower quality of life [74, 75]. Furthermore, memory, concentration, and attention impairment are some of the depressive symptoms.

Santangelo et al. [53] analyzed anhedonia as symptom of major depressive disorder and reported significant correlations between anhedonia and cognitive functions (see Table 13.3). Depressed patients without apathy or anhedonia scored significantly worse than depressed patients with apathy or anhedonia on frontal and visuoconstructional tasks. The authors also stratified depressed PD patients

Table 13.3 Anhedonia and cognitive deficits in movement disorders

Author (year)	Sample (n)	Anhedonia assessment	Anhedonia vs. cognitive deficits
Isella et al. (2003) [37]	PD = 25; HC = 25	Physical Anhedonia Scale	No significant correlations between physical anhedonia, global cognitive status (MDRS and spatial span), and frontal functions (Letter and Category Verbal Fluency Tests and EXIT)
Santangelo et al. (2009a) [53]	PD = 125 (dPD = 65; NODEP = 60)	SHAPS	dPD with anhedonia and apathy (n = 11) scored worse on the FAB and the CT than NODEP (n = 50) dPD with anhedonia (n = 8) scored worse on the CT than NODEP
Santangelo et al. (2009b) [54]	PD = 939; VP = 68; MSA = 28; PSP = 27; LBD = 14	SHAPS	Significant correlations among anhedonia and FAB in PD, VP and PSP patients Significant correlations between anhedonia and MMSE only in PD patients
Spalletta et al. (2013) [61]	PD = 254	SHAPS	SHAPS score was significantly correlated with RDR, CRO, and SWCT interference time in MDD patients. In NODEP patients, SHAPS score was significantly correlated with SWCT word reading time and SWCT color naming time. No significant correlations between SHAPS and neuropsychological scores were found in MIND subgroup Predictors of hedonic tone differed in patients with different mood disorders: RDR scores in MDD patients and SWCT word reading time in NODEP patients

CRO Copy of the Rey-Osterrieth picture, *CT* Copying Task, *dPD* PD patients with depression, *EXIT* Executive Interview, *FAB* Frontal Assessment Battery, *HC* healthy controls, *LBD* Lewy bodies dementia, *MDD* major depressive disorder, *MDRS* Mattis Dementia Rating Scale, *MIND* minor depressive disorder, *MMSE* Mini Mental State Examination, *MSA* multisystem atrophy, *NODEP* PD without depression, *PD* Parkinson's disease, *PSP* progressive supranuclear palsy, *RDR* Rey's 15-word test – Delayed Recall, *SHAPS* Snaith-Hamilton Pleasure Scale, *SWCT* Stroop Word-Color Test, *VP* vascular parkinsonism

according to the occurrence of clinically relevant anhedonia and apathy. They found that PD patients with anhedonia performed worse than non-depressed PD patients without anhedonia or apathy on the copying task, whereas PD patients with apathy and anhedonia performed worse than the non-depressed group on the frontal and the copying tasks. Therefore, anhedonia/apathy symptoms were associated with more severe impairment of visuoconstructional and frontal functions.

Spalletta et al. [61] reported significant correlations between anhedonia and neuropsychological test scores in PD patients with major depressive disorder and PD patients without depression, but not in those with minor depressive disorder. In particular, anhedonia was significantly correlated with long-term verbal memory, complex constructional praxis, and attention shifting and control in patients with major depressive disorder. In non-depressed patients, anhedonia was correlated with simple attention. Thus, cognitive findings appear to be able to discriminate between PD patients with comorbid major depressive disorder and those without depression, indicating that cognition may be a useful marker of anhedonia in more homogeneous PD subpopulations.

By contrast, Isella et al. [37] found no significant correlations between physical anhedonia and the neuropsychological variables investigated; only one frontal task, the Executive Interview [78], showed a trend towards a statistically significant correlation with anhedonia.

In the only study [53] investigating the relationship between anhedonia and cognitive functions in a variety of movement disorders, a large group of patients were evaluated for global cognitive level and for frontal functions. Significant correlations emerged between anhedonia and frontal functions in patients with PD, vascular PD, and progressive supranuclear palsy [34, 53]. However, anhedonia and global cognitive level were significantly correlated only in PD patients. Moreover, a higher severity of anhedonia was found in demented compared to non-demented patients.

In conclusion, studies on both PD and other movement disorders support the hypothesis of the involvement of frontal and prefrontal circuits in anhedonia. However, results are sometime conflicting also because the multifaceted phenomenology (different mood disorders, apathy, illness stage, etc.) associated with anhedonia. Thus, a comprehensive assessment of all dimensions of PD must be performed for accurate conclusions.

13.9 Pathophysiology and Pro-dopaminergic Treatment of Anhedonia

Harvey et al. [16] investigated the brain correlates of anhedonia in nonclinical subjects using structural and functional magnetic resonance imaging techniques and showed that its severity was inversely correlated with anterior caudate volume but was positively related to ventromedial prefrontal cortex activity during the processing of pictures with positive emotional content. These findings suggest that anhedonia may be related to reduced volume of the basal ganglia and to abnormal prefrontal functioning during hedonic processing. It has also been postulated that experiencing joy and pleasure, in patients with a mixture of psychiatric diagnosis, depends on dopaminergic reward mechanisms in the limbic system that are thought to be the basis of motivation, drive, and activation [79].

In PD patients, neuropathological [80], pharmacological [46, 81], and functional imaging [82] data suggest that degeneration of the dopaminergic system not only involves brain motor structures (including the basal ganglia) but also brain emotional structures of the limbic system [83]. Therefore, the degenerative processes of PD may affect dopaminergic reward mechanisms and lead to anhedonia, loss of motivation, avolition, and apathy [45, 84–90]. This hypothesis has also been confirmed in research on animal models [91], which suggests that anhedonia may be a complication of PD [30]. Cantello et al. [46] conducted an experimental study into the role of dopamine in anhedonia and depression in PD patients. In particular, they studied the euphoric response to intravenous methylphenidate comparing PD patients with major depressive disorder with non-depressed PD patients, as well as with non-parkinsonian subjects suffering from major depressive disorder, and a group of controls with no central nervous system or psychiatric disease. They reported that PD patients with major depressive disorder had a significant lack of sensitivity to the euphorizing effects of methylphenidate, compared to the other groups. This result was interpreted as dysfunction of reward-related dopamine systems in PD patients with major depressive disorder.

Studies showing that performance-sparing doses of neuroleptic drugs attenuate lever-pressing and running for food reward in hungry rats suggest that dopamine D_2 receptor antagonists selectively blunt the rewarding impact of food and other hedonic stimuli and induce anhedonia [92]. In humans, inhibition of the dopamine system via D_2 receptor antagonists can be accompanied by a reduction in motivation, drive, spontaneity, and dysphoria [93]. Dopamine has come to be identified as a central neurotransmitter in the reward system and it is associated with several symptoms (i.e. anhedonia, apathy, and dysphoria) commonly found in neuropsychiatric disorders, such as depression in PD [85, 93, 94]. These symptoms may be caused by a functional deficit of dopaminergic transmission in the dopaminergic reward system, which ascends from the mesencephalon to the ventral striatum (nucleus accumbens). The high incidence of dysphoria and depression in PD patients suggests that damage of mesocorticolimbic dopamine projections may cause these symptoms [45]. However, recent evidence shows that anhedonia emerges not only from a depletion of dopamine but from combined lesions of dopaminergic, noradrenergic and serotonergic systems [95, 96]. Moreover, μ opioid and endocannabinoid receptors in nucleus accumbens and ventral pallidum mediate hedonic perception of rewards, and activation of these receptors enhances the affective response for highly palatable rewards, such as sucrose [97]. Activation of GABA-A receptors in the nucleus accumbens is also known to regulate the affective response to sucrose [98]. Human neuroimaging studies suggest that subjective evaluations of pleasure are also mediated by the orbitofrontal cortex [99], although it is unclear whether the orbitofrontal cortex mediates the perception of pleasure or rather codes for pleasure (e.g. by assessing relative reward value). Activity of the ventral striatum and orbitofrontal cortex is decreased in anhedonic individuals with major depressive disorder [100].

Returning to the crucial role of dopamine neurotransmitter in determining anhedonia, research conducted on animals indicates that dopamine is associated with

prediction or anticipation and motivation to obtain rewards [101]. Although in humans administration of addictive drugs that increase synaptic dopamine levels leads to feelings of euphoria [102], it is unclear whether this dopamine release mediates hedonic arousal. It is well established that dopamine projections from the ventral tegmental area to ventral striatum fire in response to unpredicted rewards [103]. Successively, dopaminergic neurons fire in response to cues that predict rewards. Thus, it has been hypothesized that one role of dopamine is to transfer positive incentive value from the reward to the cue that predicts the reward [104]. On the other hand, when predicted rewards are not presented, dopamine firing is blunted [103]. Therefore, ventral striatal dopamine regulates the prediction and anticipation of rewards, and two mechanisms may be responsible for basic reinforcement learning [105].

Summarizing, various regions of the limbic system, especially ventral striatal dopaminergic systems, are implemented in the anticipatory (appetitive) positive affective state. Dopaminergic independent mechanisms, utilizing opiate and GABA receptors in the ventral striatum, amygdala and orbitofrontal cortex, are important in elaborating consummatory (sensory pleasure) positive states. Therefore, the distinction between anticipatory and consummatory anhedonia could have a strong value in PD. In fact, it could be suggested that anticipatory anhedonia could characterize PD patients while consummatory anhedonia could characterize PD patients with melancholic depression.

There is evidence that supports a positive effect of dopaminergic antiparkinsonian treatment on tracts of anhedonia (see Table 13.4). Several studies [38, 39, 49, 65, 106, 107] showed that the prevalence of anhedonia and depression is significantly reduced during treatment with pramipexole, which seems to have a preferential action for D_3 versus D_2 receptors in the mesolimbic system and the prefrontal cortex. In fact, Reichmann et al. [39] found that pramipexole had beneficial effects on anhedonia, depression, and motor dysfunctions. Similarly, Lemke et al. [38, 49] reported that pramipexole, as add-on treatment to levodopa, reduced the frequency of anhedonia in two observational open studies that included large samples of levodopa responsive PD patients. Anhedonia was present in 286 (45.7 %) PD patients at the start of the study and in 160 (25.5 %) after 9 weeks of treatment. During the study period, the prevalence of anhedonia significantly decreased from 74.3 to 45.3 % in moderate to severely depressed PD patients, and from 34.6 to 18.3 % in non-depressed PD patients. These data were also confirmed by results found in animal models, that showed the efficacy of pramipexole on anhedonia and depression [110, 111]. In a large sample of PD patients with insufficient effect of treatment with non-pramipexole dopamine agonists [106] was described the effect of both direct or abrupt and overlapping switching to pramipexole. The authors reported that after 4–8 weeks of pramipexole treatment scores on depression and anhedonia scales improved equally in both groups. Thus, the authors confirmed their previous findings [39] of an antianhedonic and antidepressant effect of pramipexole. In accordance, another study [107] conducted to assess the effect of pramipexole on depressive symptoms, especially on the subjective experience of anhedonia and feelings of emptiness, revealed that the effects of pramipexole and ropinirole on

Table 13.4 Anhedonia and pro-dopaminergic therapy

Author (year)	Sample (n)	Anhedonia assessment	Impact of dopaminergic therapy on anhedonia
Reichman et al. (2003) [39]	PD = 626	SHAPS-D	Positive effects of pramipexole on anhedonia, depression, and motor symptoms
Lemke et al. (2005, 2006) [38, 49]	PD = 626 (dPD = 138; NODEP = 488); HC = 50	SHAPS-D	Positive effects of pramipexole on anhedonia, depression, and motor symptoms
Witt et al. (2006) [65]	PD-DBS STN = 15	SHAPS-D	Significant effect of medication (levodopa) on hedonic tone
Reichmann et al. (2006) [106]	PD = 485	Visual Analogue Scales	Positive effects of pramipexole after 4–8 weeks on anhedonia, depression, and motor symptoms
Lemke (2008) [107]	Unavailable	Unavailable	Pramipexole had antidepressant, anxiolytic, and antianhedonic properties
Fujiwara et al. (2011) [57]	PD = 100; CS = 111	SHAPS-J	Pramipexole had an antianhedonic effect. The frequency of anhedonia was 0 % in patients treated and 13 % in those not treated with pramipexole
Miura et al. (2012) [58]	PD = 86	SHAPS-J	Pramipexole improved anhedonia while entacapone increased anhedonia
Drijgers et al. (2012) [108]	PD = 23; HC = 23	SHAPS	Significant improvement on anhedonia, respect to baseline, was found after the challenge with MTP, but not after the challenge with pramipexole or placebo
Chaudhuri et al. (2013) [109]	PD = 267 (178 rotigotine, 89 placebo)	NMSS	Significant improvement on anhedonia after treatment with rotigotine

CS control subjects, *dPD* PD patients with depression, *HC* healthy controls, *MTP* methylphenidate, *NMSS* Non-Motor Symptoms Scale, *NODEP* PD without depression, *PD* Parkinson's disease, *PD-DBS STN* PD with Deep Brain Stimulation of subthalamic nucleus, *SHAPS-D* Snaith-Hamilton Pleasure Scale-German version, *SHAPS-J* Snaith-Hamilton Pleasure Scale-Japanese version

cortico-frontal D_2 and particularly D_3 receptors seem to have antidepressant, anxiolitic, and antianhedonic properties.

There is also evidence that depressive symptoms improve equally with dopaminergic therapy and DBS-STN; conversely, hedonic tone improves only with

administration of levodopa. Most emotional changes do not correlate with changes in motor performance, indicating they are not reactive responses but are specific to the treatment [65]. The authors explains the different effects of levodopa and DBS-STN on depressive symptoms and anhedonia in terms of the different physiological mechanisms of the two methods: levodopa restores the phasic activity of the midbrain dopamine neurons, which is necessary for the identification of primary rewards, whereas DBS-STN is supposed to suppress the pathological neuronal activity of the parkinsonian subthalamic nucleus. The limbic territory of the subthalamic nucleus is indirectly connected with the anterior cingulate cortex, which shows hypometabolism in depressed patients suffering from PD. Although both levodopa and DBS-STN bring about significant activation of the anterior cingulated cortex, the effect of levodopa is more diffuse and involves additional mesolimbic-cortical pathways projecting from the ventral tegmental area to the limbic parts of the basal forebrain. Therefore, dopaminergic medication is likely more effective, which may explain the dissociation of the effects of DBS-STN and levodopa on mood and hedonic tone. DBS-STN seems to partly mimic the psychotropic effects of levodopa but does not fully replicate the motivational effects of dopaminergic stimulation. Also, Kondo [112] proposed to reduce anhedonic symptoms stimulating the reward system through the administration of dopaminergic drugs, such as levodopa and dopamine agonists (in particular D_3 agonists). The underlying assumption is that patients return to be more active and therefore are able to perform their activities of daily living. However, this therapy can have adverse effects or can lead to a dopamine dysregulation syndrome characterized by a state of excitation which in turn could lead to the development of an impulse compulsive disorder (pathological gambling, compulsive shopping, hypersexuality, etc.) [113]. Thus, dopaminergic therapy would ensure the release of a large amount of dopamine and, in many cases, could determine a state of stimulation of dopamine receptors. One of the main drugs leading to this effect is pramipexole, as mentioned above, that is able to improve the motivational state in PD patients with anhedonic tone [49]. Supporting these data, Fujiwara et al. [57] compared the frequency of anhedonia between groups treated with different antiparkinsonian agents. A significant difference was observed only for pramipexole and specifically the frequency of anhedonia was 0 % in patients treated and 13 % in those not treated with pramipexole. Also Miura et al. [58] showed that pramipexole significantly reduced anhedonia, while entacapone and disease severity increased anhedonia.

Finally, in a recent randomized controlled trial [109] has been shown that rotigotine-treated patients improved in mood/apathy domain of the Non-Motor Symptoms Scale [114]. In particular, a positive effect was found on items of "lost interest in doing things", "lost interest in surroundings", "seems sad or depressed" and "difficulty experiencing pleasure". On the other hand, in a double-blind randomized placebo controlled study the authors analyzed the effects of: (i) a direct dopaminergic challenge with the D_2 receptor agonist pramipexole, (ii) an indirect challenge with the dopamine reuptake inhibitor methylphenidate, and (iii) placebo, on mood, motivation and cognition in PD patients and healthy controls. They found that at baseline, when the assessment was done prior to administration of the drug,

no significant differences between PD patients and healthy controls existed in hedonic tone. However, anhedonia improvement was found after the challenge with methylphenidate, but not after the challenge with pramipexole or placebo. In healthy controls there were no effects [108].

In conclusion, dopaminergic stimulation might be considered as a strategy for the treatment of both motor and non-motor symptoms in PD, particularly on depression and anhedonia [115]. However, additional dopaminergic therapy in patients who show sufficient control over motor symptoms may increase the risk of inducing adverse effects, such as lower limb edema, daytime drowsiness, valvular disease of the heart, psychiatric symptoms, and dyskinesia. Unfortunately, there are no data on the impact of pro-dopaminergic treatment on anhedonia in other movement disorders.

13.10 Conclusions and Future Directions

Anhedonia is a frequent symptom in patients with PD, while only limited data are available for other movement disorders. In particular, the majority of authors identified anhedonia as a symptom of depression in PD and other movement disorders. On the other hand, a minority of studies found no relationship between anhedonia and depression [37] or described anhedonia as independent from mood disorder [52, 56, 64] or least discriminant for a depressive episode [51, 59, 60]. In patients with major depressive disorder, anhedonia is correlated with increased activity in the ventromedial prefrontal cortex and reduced activity in the amygdala [100] and reduced volume of anterior caudate [116]. Similarly, fatigue and psychomotor symptoms are associated with frontal and caudate abnormalities in depression [117, 118]. Major depressive disorder, in particular the melancholic subtype, which is characterized by anhedonia and psychomotor retardation, seems to be related not only to serotonergic but also to dopaminergic dysfunctions [119]. Moreover, mesolimbic and mesocortical dopamine projections appear to be involved in the reward system and also in depression phenomenology [45]. Therefore, as these projections have been shown to degenerate in movement disorders, particularly PD, they might contribute directly to the high incidence of depression, and thus of anhedonia [85].

Dopamine agonists may have a positive effect on anhedonia [38, 39, 49, 106, 107], which supports the hypothesis that inhibition of dopamine system via D_2 receptor antagonists can be accompanied by reduced motivation, drive, spontaneity, and dysphoria.

As to the role of cognitive status in anhedonia, some studies [53, 61] support the hypothesis of involvement in patterns of frontal and prefrontal dopamine circuits, suggesting that frontal lobe dysfunctions may contribute to increase the severity of anhedonia.

Another issue of debate concerns the possible relationships among anhedonia, motor deficits, duration of illness and activities of daily living in PD patients and other movement disorders, but data are still inconsistent and do not allow any

conclusions [37–39, 54, 65]. This inconsistency can be attributed to several various factors: (a) the different scales used to measure anhedonia severity (Snaith-Hamilton Pleasure Scale, Chapman Scales for Physical and Social Anhedonia, items of depression scales); (b) the use of small samples which may have affected results, increasing negative findings; (c) the inadequate diagnosis of depressive disorders using depression rating scales instead of diagnostic interviews; and (d) the concomitant use of antiparkinsonian therapy.

In conclusion, from a clinical point of view the characterization of anhedonia (either physical or social) is important because it has negative effects on the activities of daily living, motor performance, and quality of life [29, 39]. Therefore, future studies aimed at investigating the relationship between anhedonia and other clinical features are required, particularly in the context of movement disorders other than PD.

Several questions remain unresolved and could be addressed by using better definition of anhedonia that distinguishes consummatory and anticipatory anhedonia. While anticipatory anhedonia may be present in both depressed and non-depressed PD patients, consummatory anhedonia may be characteristic of depressed PD patients only. The relationship between apathy and anhedonia could be explained by the anticipatory component of anhedonia that could be treated by dopamine therapy. Anticipatory *hyper*hedonia may be associated to impulse control disorders, which may also occur in PD. In view of the strong relationship between anticipatory anhedonia and dopamine deficits, anticipatory anhedonia may characterize non-PD subjects prone to develop an impulse control disorder. One hypothesis could be that patients with essential tremor and anhedonia, particularly anticipatory anhedonia, could be at a higher risk of developing PD that patients with essential tremor without anhedonia. Thus, the exploration of hedonic deficits in movement disorders may also have heuristic value for predicting disease progression, prevention of side effects of treatment with levodopa or a dopamine agonist, and the identification of vulnerability factors for movement disorders.

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