



## Review

## Re-examining the Parkinsonian Personality hypothesis: A systematic review

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## ARTICLE INFO

## Keywords:

Parkinson's disease  
 Premorbid personality  
 Introversion  
 Neuroticism  
 Novelty seeking  
 Harm-avoidance

## ABSTRACT

The main objective of neurological examination for Parkinson's disease (PD) is to discover premorbid signs of the neurodegenerative disease. This is based on the definition of subclinical motor and non-motor symptoms, while psychological features are frequently neglected. However, the idea of premorbid “parkinsonian” personality (PP) has been discussed for over a century in clinical writings. Here, thirty-one articles have been included in this qualitative synthesis of literature aimed at re-examining this question.

Early retrospective studies described personality profile using framed psychoanalytic terms such as negative emotionality, emotive rigidity and depression. Nowadays, the employment of standardized taxonomies of personality allows defining PP in a more unified framework. However, this large amount of evidence could not unravel the premorbid nature of PP. Four recent long-term prospective works have provided new impetus to this field of study demonstrating that low novelty seeking, high introversion, neuroticism and harm avoidance precede PD onset and might be a risk factor. Moreover, some PP dimensions (novelty seeking) change dynamically over time as a function of dopaminergic treatment or dysfunctions.

The reviewed literature demonstrates that personality profile is an important hallmark of clinical course of PD, which should be used to assess subjects' vulnerability into daily clinical practice.

## 1. Introduction

Neurologists engaged in clinical management of Parkinson's disease (PD) recognize that non-motor symptoms are fundamental to better understand the disease phases (Chaudhuri, Healy, & Schapira, 2006). These are often considered “invisibles” when compared to the classical motor signs of PD. Generally, the course of PD follows three main phases: (1) *preclinical*, which is asymptomatic but can be detected through molecular or imaging markers; (2) *premotor*, characterized by the appearance of non-motor symptoms (i.e., loss of sense of smell, sleep disorders or orthostatic hypotension), which however are insufficient to diagnose the disease; and (3) *motor*, which presents the classical motor symptoms that allow the clinical diagnosis of PD (such as slowness of movement, tremor and stiffness) (Braak et al., 2003; Stern, Lang, & Poewe, 2012). Nowadays, diagnosis of PD is still based on clinical evaluation of motor symptoms, while preclinical behavioral signs remain invisibles.

## 1.1. The premorbid Parkinsonian Personality: the beginning of story

The individuation of behavioral features underpinning the occurrence of PD has always exercised a fascination in neurologists. Since

1817, clinicians retrospectively observed that one specific type of individuals who “...industriously followed business of a gardener...” [Parkinson, 1817] or “...are devoted to hard work...” [Camp, 1913] was the kind more frequently affected by PD. From 1817 to the first half of 20th century, the clinical psychoanalytic-related description of premorbid personality in PD patients was enriched by other traits such as: the repression of emotional reactions (affectively inconstant and passive (Machover, 1957)), along with a persistent anxiety (worried sick about body image) and depression (Booth, 1948). All these behavioral features would seem to characterize individuals who had developed PD.

## 1.2. The premorbid Parkinsonian Personality: from psychoanalytic description to modern personality framework

For a long time, from the initial Parkinson's subjective clinical impression (Parkinson, 1817) to the first retrospective studies, the existence of PP remained vague (Ishihara & Brayne, 2006). This was dependent upon two factors: the lack of a definite model of personality for explaining PD-related neurodegenerative changes and the lack of consistent study designs. At the beginning of the new century, the employment of standardized personality inventories as well as the

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employment of case-control methodology has reopened the interest on this field of study.

Several models of personality and its organization in dimensions have been proposed in the last few years. The most famous personality taxonomies are the Five-Factor Model (FFM) of Costa and McCrae (1992) and the Cloninger's Psychobiological Model (CPM) (1987). The FFM of personality is a conceptualization of personality comprising behavioral, emotional and cognitive patterns. The five traits (Neuroticism, Introversion, Openness, Agreeableness and Conscientiousness) are considered as enduring dispositions that underlie individuals' cognitive and emotional tendencies together with brain functioning (McCrae & Costa, 2003). On the contrary, a more biologically grounded personality has been put forward by Cloninger (1987), where personality dimensions (Harm Avoidance (HA), Novelty Seeking (NS), Reward Dependence, and Persistence) are called temperaments and manifest in unique emotional/behavioral patterns expressed in response to environmental stimuli.

This progress has provided new impetus for the subsequent researches aimed at assessing the existence of premorbid *PP*. The conceptual links between PD and the presence of a specific personality profile before disease onset relied on the hypothesis that: a) some personality traits are linked to behaviors known to be associated with increased health risk (indirect hypothesis) or b) some personality traits are linked to the biological functioning of specific neurotransmitter system associated with increased neurodegenerative risk (direct hypothesis).

### 1.3. The premorbid Parkinsonian Personality: the adoption of healthy lifestyles

A large amount of empirical researches supports the “indirect” effect of personality on the development of neurodegenerative diseases. Indeed, it has been demonstrated that some personality traits are linked to habits and attitudes, which in turn may be associated with the health risk (Goodwin & Friedman, 2006; Sutin et al., 2010; Sutin, Ferrucci, Zonderman, & Terracciano, 2011; Terracciano et al., 2014; Terracciano, Stephan, Luchetti, Albanese, & Sutin, 2017). Individuals high on neuroticism/extraversion and low on conscientiousness are characterized by sedentary, cigarette smoking, and other behavioral, cardiovascular, and metabolic risk factors for chronic diseases (Friedman, 2000; Terracciano & Costa, 2004). (Costa, Terracciano, & McCrae, 2001). These traits are generally stable in adulthood (Terracciano, Costa, & McCrae, 2006), but sudden changes could underlie the development of a variety of mental and physical disorders (Goodwin & Friedman, 2006; Sutin et al., 2010; Terracciano et al., 2017). For instance, low values on agreeableness have likewise been associated with obesity in older adulthood (Sutin et al., 2011), whereas high-level of conscientiousness is associated with significantly reduced likelihood of a wide range of heart diseases and stroke (Goodwin & Friedman, 2006). However, neuroticism would seem the most important risk factor for a large series of disorders. Indeed, it has recently been demonstrated that individuals who tend to be more angry, anxious, depressed, hostile and nervous are more vulnerable to develop health-risk behaviors (Sutin et al., 2011) or dementia (Terracciano et al., 2014; Wilson, Schneider, Arnold, Bienias, & Bennett, 2007).

Interestingly, some studies have reported a reduced propensity to smoking, alcohol consumption, and caffeine intake in the presence of PD, probably related to the restrained and rigid *PP* characteristics, such as introversion and depression (Benedetti et al., 2000). However, how the interplay between personality profile and health behaviors may be associated with the risk to develop PD remains to be ascertained.

### 1.4. The premorbid Parkinsonian Personality: the psychobiological hypothesis

More intuitively, the relationship between premorbid personality

and PD-related neurodegenerative mechanisms might “directly” rely on the common dopaminergic (dys-) functioning. Indeed, it has been widely demonstrated that some personality dimensions are regulated by dopaminergic system (DeYoung et al., 2010; Laricchiuta, Markett, Reuter, & Montag, 2017; Menza, Mark, Burn, & Brooks, 1995). On the other hand, PD patients are characterized by dopaminergic loss in the striato-frontal, mesocortical and mesolimbic networks, which in turn affect motor, cognitive and emotional regulation (Jenner, 2008). For the CPM (Cloninger, 1987) one specific personality dimension would seem to be strongly dependent upon functioning of dopaminergic system: NS. This is a heritable bias in the activation of behaviors, such as exploratory activity in response to novel stimulation, which causes a normal pleasurable rewarding mediated by dopamine system. Neurodegeneration of dopaminergic system causes, on the one hand, the emergence of PD-related symptoms in the motor domain and, on the other, the general worsening of NS-related attitudes (Menza, Forman, Goldstein, & Golbe, 1990; Menza, Golbe, Cody, & Forman, 1993). However, the relationship between this CPM-related personality temperament and dopamine has strongly been rejected by Kaasinen et al. (2001) who investigated, in a large sample, the dopaminergic function in the PD's brain using  $^{18}\text{F}$ -dopa uptake PET-imaging. They found that drug-naïve PD patients with low score of NS did not present pathological dopaminergic changes in the brain, whereas HA level was clearly increased in PD as also demonstrated by increased dopaminergic metabolism inside the basal ganglia. This temperament is defined as a heritable bias in the inhibition or cessation of behaviors, such as pessimistic worry in anticipation of future problems, passive avoidant behaviors and shyness of strangers. However, high HA has also been reported in several other chronic diseases, such as major depression (Kimura et al., 2000), obsessive-compulsive disorder (Alonso et al., 2008) and multiple sclerosis (Christodoulou et al., 1999).

### 1.5. The premorbid Parkinsonian Personality: is this the end of story?

Despite this large amount of evidence, until the 2010s, the existence of premorbid *PP* remained obscure since either healthy lifestyles or psychobiological hypotheses still required empirical confirmations. Moreover, although the vast majority of these studies reported similarity in identifying the same *PP* (Ishihara & Brayne, 2006; Poletti & Bonuccelli, 2012), this kind of evidence did not help to solve the primary question: “is the emerging of PD predicted by personality traits”? Indeed, the cross-sectional or retrospective nature of studies cannot confirm the premorbid phase of PD symptoms, while prospective researches play a crucial role.

Fortunately, in the last few years four independent long-term prospective works have finally made a worthy contribution to this field of study. For this reason, we sought to perform a new qualitative synthesis of literature aimed at re-examining the question whether there is sufficient evidence to conclude that *PP* may or not be considered a risk factor for the development of clinical symptoms. Moreover, we proposed a tentative to overcome the classical dopaminergic interpretation of premorbid *PP* with a more modern anatomo-functional hypothesis.

## 2. Methods

### 2.1. Information sources, search strategy and eligibility criteria

For the present systematic review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009). The statement consists of a checklist of recommended items to be reported and a four-step flow diagram (Fig. 1). Published titles and abstracts in the English language from the first of January 1990 to the first of January 2017 were searched systematically across the following databases: PubMed, Scopus, Google Scholar and Web of Science. The search terms were concatenated in an advanced query using boolean operators as follows (“Parkinson's

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