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Meta-analysis

The relationship between Impulse Control Disorders and cognitive dysfunctions in Parkinson's Disease: A meta-analysis☆

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ABSTRACT

Impulse Control Disorders (ICD) are associated with impairment in cognitive flexibility and cortical inhibition. In Parkinson's Disease (PD) the relationship between ICD and cognitive dysfunctions is still unclear: some studies found different cognitive profiles between Parkinsonians with and without ICD, whereas others did not. Moreover, findings from studies on ICD in PD are conflicting on which cognitive function is altered. A meta-analysis of 34 studies was performed to shed light on relationship between ICD and cognitive dysfunctions and to reveal the cognitive function compromised in Parkinsonians with ICD. Data were analysed in global cognitive functioning, memory, executive functions, attention/working memory, language, and visuospatial functions. Significant relationship between ICD and dysfunction of abstraction ability/concept formation, set-shifting, visuospatial/constructional abilities and decision-making was found. These findings suggested that people affected by PD with specific frontal dysfunctions are more vulnerable to develop ICD when they take antiparkinsonian drug. Evaluation of specific cognitive functions in routine clinical practice might help to detect those people with PD susceptible to ICD before treating them with antiparkinsonian drugs.

Contents

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1. Introduction

In Parkinson's Disease (PD) Impulse Control Disorders (ICD) include pathological gambling (PG), hypersexuality (HS), compulsive shopping or buying (CS), compulsive or binge eating (CE).

These disturbances can have devastating psychosocial consequences for the person involved and her/his family. The ICD are characterized by impulsive aspects because of their strong relationship between high novelty-seeking and impulsivity traits and also by compulsive aspects because of their similarities to substance abuse (i.e. experience of withdrawal symptoms and/or the development of tolerance) (Leeman and Potenza, 2012).

The ICD in PD are considered as effect side of dopaminergic treatment (Voon et al., 2011a); in particular, a stimulation of DA in a relatively intact reward system may lead a hyper-dopaminergic state, a condition predisposing to development of ICD.

As regard factors associated with ICD in PD, decision-making and cognitive control processes were found dysfunctional in people with PD and with ICD. While findings of impaired decision-making in PD are consistent across studies (Voon et al., 2011a; Voon et al., 2010; Djamshidian et al., 2010, 2012; Housden et al., 2010; Leroi et al., 2013; Rossi et al., 2010), reports of cognitive dysfunctions associated with ICD in PD are conflicting (Santangelo et al., 2013a, 2013b). Some studies revealed that patients with ICD performed significantly worse than patients without ICD on several frontal tasks (Santangelo et al., 2009; Vitale et al., 2011; Voon et al., 2010; Djamshidian et al., 2010; Biundo et al., 2011, 2015; Tessitore et al., 2016; Yoo et al., 2015a), whereas some studies failed to reveal a significant association between ICD and cognitive dysfunctions or revealed that patients with ICD functioned cognitively better than those without ICDs (Siri et al., 2010, 2015; Pineau et al., 2016). Therefore, until now the role of cognitive dysfunction as contributor to ICD is unclear and should be better elucidated.

Another issue, which remains unclear and deserves further studies, is the type of cognitive functions altered in Parkinsonians with ICD. About this, studies reporting an association between ICD and cognitive dysfunctions revealed dysfunction of inhibition (Vitale et al., 2011; Yoo et al., 2015a), generativity (Santangelo et al., 2009; Tessitore et al., 2016), set-shifting (Vitale et al., 2011; Biundo et al., 2011, 2015; Santangelo et al., 2009; Tessitore et al., 2016; Voon et al., 2010), spatial planning (Vitale et al., 2011), abstraction ability/concept formation (Vitale et al., 2011; Santangelo et al., 2009; Tessitore et al., 2016), reasoning (Santangelo et al., 2009; Tessitore et al., 2016) and memory (Djamshidian et al., 2010; Tessitore et al., 2016; Vitale et al., 2011; Santangelo et al., 2009; Voon et al., 2010). This inconsistency among the studies may depend on a host of factors associated with cognitive impairment including, for example, selection criteria and characteristics of patients, comorbid disorders, and sample size.

A meta-analytic review aims to shed light on the relationship between ICDs and cognitive impairment in people with PD and on which cognitive domain is damaged in this type of Parkinsonians. Moreover, a meta-analysis of these relationships may help clarify findings where statistical power has been inadequate in individual studies, where findings are not consistent across. We examined the influence of demographic and clinical confounders (i.e. clinical stage, treatment, age at onset of PD and disease duration) on cognitive performances in people with PD.

1.1. Objectives

Aims of meta-analysis were: 1. to systematically investigate the relationship between ICD and cognition in PD; 2. to identify alterations of specific cognitive functions associated with ICDs (CE, HS, PG, punding, compulsive shopping or buying) in PD.

2. Method

2.1. Search strategy

A systematic literature search was performed in 19 June 2016 using PsychoInfo (PROQUEST), PubMed, Scopus restricted to papers in English from peer-reviewed journals, supplemented by hand searches of reference lists from included and seminal papers. We excluded conference proceedings, theses, and case studies. Where the same data was presented in more than one publication, we used the primary (first) publication.

Search terms are shown in supplemental material 1 and produced a total of 1112 articles. After exclusion of duplicates and reports judged to be irrelevant based on title and abstract screening, 42 articles were retrieved for detailed inspection (Fig. 1). Two reviewers independently evaluated all papers in according to inclusion and exclusion criteria summarized below. All aspects of study selection, extraction, and assessment were performed by two reviewers working independently (GS, SR). Disagreements between reviewers were resolved through discussion or with recourse to a third arbitrator if required (PB).

2.2. Study eligibility criteria

Studies were included if: 1. Participants were adults diagnosed with idiopathic PD; 2. The study was based on a neuropsychological perspective or included a cognitive evaluation; 3. Cognition were measured by validated neuropsychological tests (i.e. Mini Mental State Examination, MMSE); 4. Samples were independent (for prospective study we used baseline data); 5. Cognitive comparisons between Parkinsonians with and without ICDs were reported statistically. The studies were also excluded if: 1. The study included atypical PD or parkinsonian syndromes; 2. The study investigated only the neuronal or neurochemical basis of ICD in PD; 3. The study concentrated on cognitive functions without linking them directly to ICD in PD; 4. The study investigated cognition by self-report assessment tools.

2.3. Outcomes

For each study, the primary outcome was neuropsychological test scores. Over thirty individual neuropsychological variables were found to be employed in all studies included in the present meta-analysis. We grouped individual cognitive task under six cognitive domains and their subdomains (Table 1) based on approach reported in Litvan et al. (2012) or on indication provided in primary study, or when no literature was available, on agreement between two authors (GS, PB) with specific expertise in neuropsychological assessment in PD. Subsequently, we analysed 1. Global Cognitive Function; 2. General Executive Functioning; 3. the sub-domains of memory (i.e. verbal and spatial short term and long-term recall) 4. the sub-domains of executive functions (i.e. abstraction ability/concept formation, shifting, updating, inhibition, generativity and fluid reasoning), 5. Language, 6. Processing Speed/Complex Attention/Working Memory; 7. Visuospatial/constructional abilities; 8. Decision Making.

When in a primary study the same outcome was evaluated using more than one instrument, extracted data were reported from the most relevant instrument, which was determined by consensus of two authors (GS, PB).

2.4. Data extraction and coding

Data extracted and coded from the final articles included: 1. characteristics of the publication: (i.e. authors, publication status, year of publication, journal); 2. characteristics of the sample (i.e.