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Review article

Neurobiological correlates of emotional processing in Parkinson's disease: A systematic review of experimental studies

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ABSTRACT

Deficits in emotional processing in patients with Parkinson's disease (PD) have received increasing interest over the past decades. In this systematic review, we present the results of 18 behavioral studies that have examined the neurobiological base of emotional processing in PD. Multiple aspects of emotional processing have been studied, using a variety of research methods. Deficits in PD are mainly related to autonomic and perceptive processing of intense emotional stimuli, which is accompanied by structural and functional neurobiological abnormalities in predominantly ventral regions of affective neurocircuitry. These structures are more strongly dependent on dopaminergic neurotransmission than the dorsal structures of affective neurocircuitry, which are more related to the cognitive and regulatory aspects of emotion and appear to remain largely intact in PD patients. Considering the importance of active dopaminergic neurotransmission, PD can serve as a prolific model for studying the neurobiological correlates of normal human emotional behavior as well as psychiatric disorders such as anxiety, depression, and apathy. Moreover, the fact that PD patients are able to cognitively regulate or modulate their emotional responses despite reduced dopamine supplies, can have important implications for the treatment of affective disorders not only in PD patients but in the general population likewise.

1. Introduction

Non-motor manifestations in Parkinson's disease (PD) have been the focus of a growing number of scientific studies over the past decades. Apart from the characteristic motor symptoms such as tremor, hypokinesia, rigidity, and postural instability, PD patients frequently suffer from psychopathological syndromes, including affective disorders, cognitive deterioration, sleep disturbances and hallucinations [1]. Moreover, several studies have shown that these non-motor symptoms affect the quality of life of PD patients to a greater extent than the motor symptoms and have a negative impact on the prognosis of the disease [2–5].

Even in the absence of clinical disturbances in mood and motivation, patients with PD encounter difficulties in generating and experiencing emotions. For instance, they often have difficulties in interpreting emotions in facial expressions [6–9], which may affect interaction with other people. Considering the disease-related neurological damage to the dopaminergic systems, which are thought to be critical in the processing of emotions [10], the possibility of a more extended emotional deficit in PD patients was raised. Experimental studies on this topic find rather mixed results. Several studies reported altered emotional functioning in PD patients ([11]; [12,13].), whereas other studies do not [14,15]. Moreover, some studies report modality-specific deficits instead of a general dysfunction of emotional processing in PD patients [11,13,16], which suggests the possible involvement of multiple neural substrates.

The present review aims to expand our understanding of the neurobiological base of emotional processing in PD by providing a systematic overview of experimental studies that have incorporated both behavioral and neurobiological correlates (e.g., brain activity, structural volume, sympathetic arousal).

2. Methods

2.1. Search strategy

A systematic literature search was conducted in PubMed and PsycINFO, which was extended with searches of references listed in the reviewed papers. The entire timescale was used, which comprised all literature between 1965 and March 2017 (included). There were no

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Box 1
Search strategy.

Search terms	
PubMed	Parkinson*(title/abstract) OR Parkinson's disease (MeSH) AND (emotion* OR facial* OR arousal OR prosody OR subjective*) AND Humans (MeSH) NOT "review"(filter)
PsycINFO	Parkinson*[title/abstract] AND (emotion* OR facial* OR arousal OR prosody OR subjective*)

language restrictions. Animal studies were excluded. Our search resulted in a total of 4022 articles (without duplicates). For an overview of the Medical Subject Headings and free text words that were used in the search strategy, see Box 1.

2.2. Selection of studies

Papers were selected according to the following inclusion criteria: i) patients were diagnosed with idiopathic Parkinson's disease ii) emotional processing, measured in a behavioral task was the main outcome iii) the study included a neurobiological measure of emotional processing, iv) data analyses incorporated both the behavioral and neurobiological measurements of emotional processing. Papers dealing with the emotional effects of deep brain stimulation (DBS) or ablative brain surgery (e.g., pallidotomy, thalamotomy) were excluded from the present review. We only included papers from completed studies, hence papers reporting on interim analyses were excluded.

The abstracts from all 4022 articles were screened by two authors (AM and AW) based on the above-mentioned criteria. Full copies were screened from articles that could not be classified by abstract or title alone. All potential relevant articles were read in full and screened by two authors (AM and AW). In case of discrepancies between the two authors, consensus was reached after discussion, or by consulting a third author (AL) who made the final decision.

For the selection process the authors followed the guidelines from the PRISMA statement (Preferred Reporting of Systematic reviews and Meta-analyses; [17]). Fig. 1 illustrates the PRISMA Flow Diagram, which summarizes each step in the selection process (see Appendix A for the PRISMA checklist). From the 4022 papers, 3974 could be excluded after reading the title and abstract alone. Further screening for eligibility resulted in 17 studies that were included for extensive review. One additional study was included after checking the reference lists of the included papers.

2.3. Quality assessment

At present, there is no 'gold standard' available for assessing the quality of non-randomized quasi-experimental research. We therefore combined items from two checklists [18,19] that have been systematically reviewed [20]. We selected the items that specifically rated descriptive, statistical and internal validity, leaving out those items that were not relevant for our study (e.g., items on specific pharmaceutical issues). We then expanded our selection with four additional items from the STROBE statement, concerning study design, statistical interpretation of data, and power calculation [21]. Items were scored as either good (2), moderate (1), or inadequate/undefined (0), which enabled us to compare the quality of included studies mutually, despite the fact that we combined items from different checklists. The full checklist is included as supplementary material (Appendix B).

Two authors (AM and AW) reviewed the methodological quality of the included studies according to the selected items. In case of disagreement, consensus was reached after discussion, or by consulting a third author (AL) who made the final decision.

3. Results

3.1. Study characteristics

The literature search resulted in 18 articles that were included for further review. All studies investigated emotional processing in patients with Parkinson's disease (PD) at a neurobiological level. Table 1 illustrates the characteristics and outcomes of the included studies. All studies were cross-sectional. They varied widely in experimental paradigms with multiple aspects of emotional processing being researched. A total of 11 studies investigated facial emotion recognition, 3 studies measured physiological arousal, 2 studies looked at emotional prosody recognition, and 2 studies used a multimodal audio-visual approach. Seven studies measured neurobiological correlates of emotional processing by using electro-encephalogram (EEG) and measuring the event-related potentials (ERP) or spectral modifications (1 study), 6 used blood-oxygen-level dependent functional magnetic resonance imaging (BOLD-fMRI), 2 used structural magnetic resonance imaging (MRI), 2 used positron emission tomography (PET), and 1 used single photon emission CT (SPECT).

3.2. Methodological quality

Table 2 shows that the methodological quality varied among the included studies and remained fairly stable over time. The mean quality score was 26,1 (range 11–32) out of 36, with the majority of scores lying above 20. Studies with a lower quality score poorly described their sample, design and outcomes and their subject groups were not adequately matched in terms of age, sex and education. Sample sizes ranged from 9 to 39 and none of the studies included a formal sample size calculation. Moreover, 8 studies did not report any indicators for strength of evidence and 14 studies lacked adequate adjustment for important confounding factors such as dopaminergic or psychiatric medication, disease severity, or presence of psychiatric disorders. However, the majority of the studies clearly specified their aim, sample characteristics, experimental design and outcomes, and provided extensive and clear interpretations of the reported findings. Given the limited number of included studies we decided not to exclude studies on the basis of an arbitrary cut-off on the quality score.

In the next section, the main results for each modality of emotional processing will be discussed. Per modality results are further subdivided by research method and are presented chronologically.