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Research paper

Experience of negative emotions in Parkinson's disease: An fMRI investigation

Anne Schienle*, Rottraut Ille, Albert Wabnegger

Clinical Psychology, University of Graz, BioTechMed, Graz, Austria

HIGHLIGHTS

- First neuroimaging study on disgust and fear experiences in Parkinson's disease.
- Patients were nondemented, nondepressed and nonmedicated during the experiment.
- Despite long disease duration no indication of diminished brain activation and emotion experience.

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ABSTRACT

Objective: Amygdala abnormalities have been discussed as a possible mechanism underlying reduced reactivity to negative stimuli in Parkinson's disease (PD).
Methods: The present investigation used functional magnetic resonance imaging (fMRI) in order to test this hypothesis. We compared brain activation of 17 nondepressed and nondemented PD patients with 22 healthy controls during the elicitation of negative affective states. The patients suffered from moderate motor symptoms for an average of 75 months and had stopped their antiparkinson medication 10–12 h prior to the fMRI testing. All participants were shown images which depicted disgusting, fear-relevant and neutral contents and they answered self-report scales for the assessment of disgust proneness and trait anxiety.
Results: Both groups did not differ from each other in affective state and trait ratings. In line with the self-report, the fMRI data showed similar activation (including the amygdala) in both groups during disgust and fear elicitation.
Conclusion: This fMRI investigation found no indication of diminished disgust and fear experience in PD.
Significance: Previously reported affective processing deficits in PD might be due to insufficiently controlled confounding variables (medication, depression, cognitive impairment).

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease related to progressive degeneration of nigrostriatal dopaminergic pathways. While motor problems such as tremor, rigidity, and bradykinesia are key symptoms of this syndrome, impairments in emotional functioning additionally have been reported (for a review see Peron et al. [1]).

A variety of tests have been applied to analyze PD-related difficulties in affective processing. There are numerous studies on facial emotion recognition in PD. Surprisingly these studies produced very heterogeneous outcomes. Whereas some authors reported general or at least emotion-specific deficits, others observed no problems at all (for a review see Gray et al. [2]).

Other investigations focused on the experience of emotions, which were elicited by affective scenes. The findings of those studies which combined self-report with electro-cortical and startle measures were also mixed, but rather pointed to a diminished experience of aversive feelings in PD patients [3–6].

Dietz et al. [4] conducted an event-related potential (ERP) study and presented the participants with (un) pleasant and neutral images. The authors focused on the late positive potential (LPP), which is a reliable electrophysiological index of emotional perception that originates in visual cortex regions. The LPP amplitude increases with the experienced intensity of the affective stimulus. Therefore, the LPP is considered an indicator of motivated attention, in which survival-relevant stimuli draw automatic attention

* Corresponding author at: University of Graz, Universitätsplatz 3, A-8010 Graz, Austria.
E-mail address: Anne.schienle@uni-graz.at (A. Schienle).

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in order to facilitate perceptual processing [7]. The results showed that PD patients' LPP amplitude for unpleasant pictures did not differ from the neutral condition and was smaller than those of control participants. This effect was interpreted as reduced LPP modulation to aversive stimuli in the clinical group. However, patients and controls did not differ in their valence and arousal ratings for the pictures.

A discrepancy between ERP findings and explicit ratings for affective pictures had also been observed by Wieser et al. [6]. PD patients experienced arousing pictures as less intense than healthy controls, although they had displayed comparable ERP waveforms.

In experiments with the startle paradigm, the participants are presented with a sudden loud noise while looking at affective scenes (pleasant, unpleasant, and neutral). The elicited emotional state influences the strength of the startle reflex. Aversive emotional states have been shown to potentiate this reflex, whereas appetitive emotional states are inhibitors. Bowers et al. [3] reported that relative to healthy controls the startle reflex amplitude was selectively reduced in PD patients when presented with aversive pictures. As the startle reflex is mediated by the amygdala, the authors speculated that PD patients show reduced amygdala activation during the processing of threatening information.

Amygdala abnormalities are often discussed as a possible mechanism underlying PD-related emotional dysfunctions (e.g., Tessitore et al. [8]). Further, it has been proposed that frontal brain regions (e.g., orbitofrontal cortex (OFC)) show activation changes due to degeneration-based changes of striatal input. These hypotheses can be directly tested via functional magnetic resonance imaging (fMRI). To the best of our knowledge this is the first neuroimaging study to investigate neuronal and subjective responses to affective scenes in PD. We tested nondepressed, and nondemented patients, who had discontinued their Parkinson medication for 10–12 h prior to experiment. The patients were compared with healthy controls during emotion elicitation. All participants were shown images which depicted disgusting, fear-relevant and neutral contents. They were asked to rate the intensity of experienced emotions and to answer questionnaires for the assessment of affective traits (disgust proneness and trait anxiety). We expected that PD patients would show reduced activation of the amygdala, basal ganglia and prefrontal regions (e.g., OFC) during the viewing of aversive scenes and that they would rate the pictures as less intense than the control group.

2. Methods

2.1. Participants

Seventeen PD patients (8 women, 9 men) and 22 healthy controls (11 women, 11 men) participated in this study. All patients had been diagnosed with idiopathic PD by neurologists of the University Hospital in Graz (Austria).

The clinical and the control groups did not differ in mean age (M_{PD} = 55.2 years (9.4)), M_{CO} = 51.8 years (9.8), $t(37) = 1.12$ ($p = 0.272$), years of education (M_{PD} = 13.4 years (3.4)), M_{CO} = 13.9 (3.9), $t(37) = 0.42$ ($p = 0.679$), and did not show signs of cognitive impairment as assessed by the Test for Early Detection of Dementia (M_{PD} = 46.2 (1.9); M_{CO} = 44.6 (3.1), $t(38) = 1.88$, $p = 0.068$). The scores of this scale [9] range between 0 and 50; a score below 35 indicates a tentative dementia diagnosis. The scores on the rating scale by Hoehn and Yahr [10] were either 2.0 (14 patients) or 3.0 (3 patients). Eleven PD patients had right body side onset of motor symptoms and 6 had left-side onset. The patients had a sum score on the Unified Parkinson's Disease Rating Scale of $M = 36.1$ (SD = 13.0) ranging between 17 and 49 [11]. This implies mild to moderate motor impairment. The symptom duration was on average $M = 75.4$ months (SD = 43.7).

With one exception all patients were treated with L-Dopa and/or a dopamine agonist (pramipexole, ropinirole). Medication was discontinued overnight for 10–12 h prior to the fMRI experiment and later continued.

Written informed consent was obtained from each participant. The study was carried out in accordance with the Declaration of Helsinki and had been approved by the Ethics Committee of the Medical University of Graz.

2.2. Questionnaires

All participants answered the following trait scales: *The Questionnaire for the Assessment of Disgust Proneness* (QADP, [12]) measures disgust propensity and describes 37 situations, which have to be judged on 5-point scales with regard to the experienced disgust (0, 'not disgusting'; 4, 'very disgusting'). The QADP has five subscales (death, spoilage, poor hygiene, oral rejection, body secretions) for the assessment of domain-specific disgust proneness. The Cronbach's alpha for the subscales varies between 0.69 and 0.87 (total scale = 0.90). The trait scale of the *State-Trait Anxiety Inventory* (STAI; [13]) measures the frequency of anxious feelings. The questionnaire consists of 20 items which are answered on 4-point scales (1 = almost never, 4 = almost ever). The Cronbach's alpha of the scale is 0.88. *The Beck Depression Inventory* (BDI, [14] consists of 21 items rated on 4-point scales. A sum score of 18 or higher indicates clinical relevance. This questionnaire was applied since depressive tendencies influence affective processing.

2.3. Stimuli and design

In this experiment the participants were asked to view 10 disgusting (e.g. dirty toilets, maggots), 10 fear-eliciting (attacks by humans and animals) and 10 neutral pictures (e.g. nature scenes, geometric figures) from a validated set [12] with the instruction to simply experience the elicited emotions. There was no specific task. The pictures were presented in blocks of 10 pictures each taken from the same affective category. Each picture was shown for 3 s. Thus, the block duration was 30 s. In total, 9 blocks were shown as each block was repeated twice. The block sequence was pseudo-randomized. This fMRI methodology represents a mixed design. We had introduced the restriction that two categories of the same type were not allowed to follow each other. Between the blocks a fixation cross was shown for 5 s. Consequently, the total experiment lasted 310 s. The short duration was chosen in order to allow the patients to stay still during scanning. This was achieved; none of the patients had to be excluded from the sample due to movement artefacts.

Subsequent to the fMRI experiment, the participants gave affective ratings for the pictures. For each image they indicated the intensity of experienced disgust and fear (*Please indicate how intensely you experienced disgust/fear* 1 = very little, 9 = very intense).

2.4. fMRI: recording and analysis

Brain images were acquired using a 3 Tesla Siemens TrioTim (Siemens, Erlangen, Germany) with a 12-channel head coil. For the functional runs a total of 164 volumes were acquired by using an echo-planar imaging protocol (35 descending slices; slice thickness: 3 mm; TE = 30 ms; TR = 2300 ms; voxel size: 3.0 × 3.0 × 3.0 mm; FoV: 192; flip angle: 90°; slice orientation −25° tilted from the AC–PC line). To account for saturation effects 3 slices from the beginning of the time series were discarded.

All analyses were conducted using SPM12 (Wellcome Department of Cognitive Neurology, London). For compensating field