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Impaired probabilistic classification learning with feedback in patients with major depression

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ABSTRACT

Background: The function of basal ganglia (BG) in the pathophysiology of major depression (MD) is still unclear. Recent research found changes in BG regarding size, structure and cerebral perfusion in patients with MD. Neuroimaging shows recruitment of the striatum during feedback (FB) based incidental learning of probabilistic classification learning, while the medial temporal lobe (MTL) is associated with paired associate (PA) based incidental learning. The purpose of this study was to evaluate whether FB-based incidental learning is affected in MD.

Methods: The FB and PA versions of the weather prediction task (WPT), a task of incidental probabilistic classification learning, were completed by patients with MD ($n = 44$) and healthy controls ($n = 44$). In FB-learning the participants received either a "thumbs-up" or "thumbs-down" message according to their right or wrong classification of cards to a certain kind of weather (either rainy or fine), while in PA learning no classification was required. Severity of MD was rated on the Beck Depression Inventory and Hamilton Rating Scale for depression.

Results: Patients with MD were selectively impaired on the FB task relative to controls ($p < 0.05$), while no significant difference was found for PA learning between the two groups. Furthermore, there were no significant differences between FB and PA-learning within the patient and control groups.

Conclusion: Our results indicate a distinct impairment on the FB-based version of the weather prediction task. These findings implicate disturbed reinforcement learning in this group of patients.

1. Introduction

The relationship between explicit learning and mood is relatively well explored, while the effects of affective disorders on incidental learning received less attention so far.

The basal ganglia (BG) are a group of subcortical nuclei consisting of the striatum (caudate and putamen), the globus pallidus, substantia nigra and the subthalamic nucleus. They communicate with the cortex via corticostriatal circuits. In these circuits information is conveyed from the cortex to the striatum, from the striatum to the BG output nuclei, onward to the thalamus and back to the cortex (Alexander, DeLong, & Strick, 1986). Two circuits are responsible for motor-function and oculomotor function, while the three non-motoric loops are associated with associative–cognitive and emotional–motivational control. The functioning of the associative and limbic fronto-striatal circuits is highly disturbed in patients with MD; the cognitive dysfunction results not only from cortical impairment, but also from a disturbance of BG function (Middleton & Strick, 2000).

Historically, the two memory systems, the declarative and the procedural, were considered to function independently and to rely on different neural substrates with the declarative memory associated with the medial temporal lobes (MTL) including the hippocampus, and the BG being linked with procedural memory (Squire & Zola, 1996). However, more recent evidence suggests interaction between the declarative and procedural memory systems which are now known to interact cooperatively or competitively during different stages and conditions of learning (Foerde, Knowlton, & Poldrack, 2006; Moody, Bookheimer, Vanek, & Knowlton, 2004; Seger & Cincotta, 2005).

Studies regarding striatal-based incidental learning have obtained inconclusive results. There are some studies which found impaired implicit learning in depression (Exner, Lange, & Irle, 2009; Naismith, Hickie, Ward, Scott, & Little, 2006; Polgar et al., 2007), while others did not (Aizenstein et al., 2005; Elderkin-Thompson, Moody, Knowlton, Hellemann, & Kumar, 2011; Joel et al., 2005).

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Furthermore, implicit learning performance in MD might be linked to the kind of feedback received (Elliott et al., 1996). Some studies pointed out that MD patients show an increased sensitivity to negative feedback (Sloan, Strauss, & Wisner, 2001; Tremblay, Naranjo, Cardenas, Herrmann, & Busto, 2002) and reduced sensitivity to positive feedback (Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008), others claimed that there is a global sensitivity reduction to feedback called blunting (Chase et al., 2010).

An important task to study procedural probabilistic learning is the Weather Prediction Task (WPT) developed by Knowlton, Squire, and Gluck (1994). The WPT is a non-motor probabilistic classification task; iterative learning is performed over several trials, which is considered to occur without explicit knowledge. On each trial, a pattern of 1–3 out of 4 tarot cards with different geometric shapes is presented. Participants need to use the specific cards to make a prediction about the "weather", whether rainy or fine. Each card predicts each of the two possible outcomes with a fixed probability. There are two versions of the WPT-task, the feedback (FB) version and the paired associate (PA) version. Each task, FB and PA consists of 150 trials. Implicit learning, which was investigated with the feedback (FB) version of the weather prediction task provides positive and negative feedback with either a "thumbs up" or "thumbs down" message according to the right or wrong prediction of the "weather", while in PA learning no feedback is given. After 150 trials there were further 42 test trials during which participants were required to predict the weather without receiving feedback. Neuroimaging during learning with corrective FB in controls showed activation of the body and tail of the caudate and putamen during the learning phase (Seger & Cincotta, 2005). In PA learning, study results suggest a more distinct MTL involvement (Sperling et al., 2001; Zeineh, Engel, Thompson, & Bookheimer, 2003).

Based on and in the light of neurobiological evidence which implicates BG-dysfunction in MD and the FB version of the WPT is additionally to midbrain, thalamus and associative cortical areas, associated with BG-function, we hypothesized that patients with MD would be selectively impaired on WPT learning with FB but not on the PA learning version of the task. In order to test this hypothesis the FB and the PA versions of the WPT were administered to patients with MD and their performance was compared to controls. The goal of the present study was to test this hypothesis in a medicated in-patient sample meeting the DSM-IV criteria for MD with melancholic features, as anhedonia, a key feature of the DSM IV diagnosis of melancholic depression, is associated with dysfunctions in reward learning (Keedwell, Andrew, Williams, Brammer, & Phillips, 2005; Tremblay et al., 2002).

2. Methods

2.1. Participants

44 individuals (13 male) with the diagnosis of MD aged between 18 and 60 years (M = 39.27, SD = 11.59) took part. All MD patients were recruited from the in-patients-wards of the department of psychiatry of Graz Medical University.

Depressed inpatients were enrolled if the following inclusion criteria were met: (1) diagnosis of melancholic depression according to DSM-IV, (2) absence of any other Axis I diagnosis, (3) absence of electroconvulsive-therapy treatment in the previous 6 months, (4) absence of any other neurological disorder, head injury, alcohol- or drug-abuse.

29 patients suffered from recurrent episodes of MD, while 15 patients had the first depressive episode. 28 patients suffered from severe depression, while 16 patients suffered from moderately severe depression. The duration of the current depressive episode ranged from three weeks to 36 months (M = 6.24 months, SD = 7.71 months).

The diagnosis was made by our experienced consultant psychiatrist (AH) according to clinical features at admission to our hospital and was controlled and approved by consultants on the wards. The diagnosis was not based on a structured clinical interview but depression was evaluated with the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) and the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960). All patients were non-demented, as demonstrated by scores above 24 on the Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). At the time of testing all patients received antidepressant medication, 21 patients received antipsychotics (mainly quetiapine as a low dose-add on therapy for recurrent severe depression (Daly & Trivedi, 2007)) and 3 patients received benzodiazepines.

44 healthy volunteers (15 male) aged between 21 and 74 (M = 40.5, SD = 14.9) took part in the study. Controls were recruited at the Campus of the Karl-Franzens-University and at the Medical University of Graz and via a participant recruitment website. Prior to participation, controls were interviewed to exclude a history of neurological disorders, psychiatric illnesses, head injury and alcohol- or drug-abuse. No control suffered from depression; additionally controls completed the BDI and HAMD, on which all controls had scores in the normal range. Furthermore, all controls had normal scores on the MMSE. For all participants an estimate of premorbid IQ was obtained with the Mehrfachwahl-Wortschatz-Intelligenztest (MWT-B) (Lehrl, Triebig, & Fischer, 1995), whereas all showed IQ-scores within the normal range. Information about controls and MD patients is presented in Table 1.

The study was approved by the Ethics Committee of Graz Medical University. Informed consent was obtained prior to participation in the study from all controls and MD patients. Neither controls nor patients received remuneration for taking part in the study.

2.2. Apparatus and materials

The WPT was presented on a PC with 15″ colour monitor. All participants were tested in a quiet room. The cards presented, each with a different pattern, were set horizontally across the middle

Table 1
Demographic characteristics for patients with major depression and controls and clinical characteristics of the patients. A single asterisk indicates $p < 0.05$.

Group	Patients (n = 44) Mean (SD)	Controls (n = 44) Mean (SD)	P t-Test
Age (years)	39.27 (11.59)	40.50 (14.90)	0.66
Education (years)	14.61 (3.67)	15.74 (2.71)	0.23
Mini mental state examination (0–30)	29.09 (1.07)	29.77 (0.47)	0.001*
Beck depression inventory (0–63)	25.02 (9.22)	0.20 (0.67)	0.001*
Hamilton rating scale for depression (0–66)	22.70 (4.90)	0 (0)	0.001*
Premorbid intelligence	104.3 (8.43)	107.63 (8.34)	0.14
Age at onset	27.15 (12.50)		
Duration of current episode (in months)	4.65 (4.84)		