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Brief report

Persistent non-verbal memory impairment in remitted major depression — Caused by encoding deficits?

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ABSTRACT

Background: While neuropsychological impairments are well described in acute phases of major depressive disorders (MDD), little is known about the neuropsychological profile in remission. There is evidence for episodic memory impairments in both acute depressed and remitted patients with MDD. Learning and memory depend on individuals' ability to organize information during learning. This study investigates non-verbal memory functions in remitted MDD and whether nonverbal memory performance is mediated by organizational strategies whilst learning.

Methods: 30 well-characterized fully remitted individuals with unipolar MDD and 30 healthy controls matching in age, sex and education were investigated. Non-verbal learning and memory were measured by the Rey-Osterrieth-Complex-Figure-Test (RCFT). The RCFT provides measures of planning, organizational skills, perceptual and non-verbal memory functions. For assessing the mediating effects of organizational strategies, we used the Savage Organizational Score.

Results: Compared to healthy controls, participants with remitted MDD showed more deficits in their non-verbal memory function. Moreover, participants with remitted MDD demonstrated difficulties in organizing non-verbal information appropriately during learning. In contrast, no impairments regarding visual–spatial functions in remitted MDD were observed.

Limitations: Except for one patient, all the others were taking psychopharmacological medication. The neuropsychological function was solely investigated in the remitted phase of MDD.

Conclusions: Individuals with MDD in remission showed persistent non-verbal memory impairments, modulated by a deficient use of organizational strategies during encoding. Therefore, our results strongly argue for additional therapeutic interventions in order to improve these remaining deficits in cognitive function.

1. Introduction

There has been an increasing interest in cognitive impairments of major depressive disorder (MDD) during the past few years. In clinical samples of depressed patients, neuropsychological deficits have mainly been researched in acute phases of depression (for reviews see Burt et al., 1995; Veiel, 1997; Zakzanis et al., 1998; Austin et al., 2001). So far, it remains unclear whether cognitive impairment in depressed patients improves along with recovery from depression or persists independently of improvement of affective symptoms.

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This is of major relevance as persistent cognitive deficits may hamper full rehabilitation in social functioning (Martínez-Arán et al., 2004) and/or largely influence therapeutic outcome and risk to relapse (Majer et al., 2004).

Many studies reported lasting memory impairments in unipolar MDD patients even after the recovery from affective symptoms in post-depressive euthymic intervals (cf. Abas et al., 1990; Marcos et al., 1994; Trichard et al., 1995; Kuny and Stassen, 1995; Beats et al., 1996; Paradiso et al., 1997; Tham et al., 1997; Kessing, 1998; Frasch et al., 2000; Neu et al., 2001; Weiland-Fiedler et al., 2004; Majer et al., 2004; Smith et al., 2006; Reppermund et al., 2007; Biringer et al., 2007). However, studies often did not attempt to differentiate between specific memory domains, such as working memory, episodic memory, and semantic memory, verbal and spatial memory, and disregarded that memory function depends on the individuals' ability to organize information during learning. Moreover, in most studies only the overall scores of neuropsychological testing were utilized instead of a more differentiated view on single items. Further limitations of the previous studies are conceptual and methodological problems, since bipolar and unipolar patients as well as patients with psychotic features were studied together as one group. Furthermore, unclear definitions of remission were used, or no age of onset was reported. Finally, the number of previous depressive episodes or hospitalizations was often not documented.

The underlying pathomechanism of memory functions is poorly understood. It has been hypothesized that organizational strategies are important basic skills for many cognitive performances, especially learning and memory (Savage et al., 2000). Perusing this hypothesis, it is important to investigate whether memory deficits are caused by encoding or retrieval problems. Disrupted encoding processes may have a strong impact on daily life activities, such as occupational affairs (Deckersbach et al., 2004).

Despite the link between persistent neuropsychological impairments and depression, the association between depression and memory for non-verbal material and the role of organizing visual–spatial information to enhance retrieval has rarely been investigated. The present study therefore investigated the specific influence of organizational encoding strategies on non-verbal memory processes. In order to address the limitations of the previous studies, patients and control subjects were carefully matched according to gender, age, and education. We hypothesized that patients with remitted MDD show impaired non-verbal memory performance, which might be due to a lack of organizational strategies.

2. Methods

Thirty remitted MDD patients from the Department of Psychiatry of the University of Muenster or from the LWL-Clinic Muenster who met DSM-IV-TR criteria for MDD (APA, 2000) and 30 healthy controls were investigated. Diagnoses were determined by the *Structured Clinical Interview for DSM-IV* (SCID; Wittchen et al., 1997) and confirmed by two independent psychiatrists. Patients had either suffered a single episode ($n=10$) or recurrent depressive episodes ($n=20$). Five patients had co-morbid lifetime diagnoses including dysthymia ($n=3$), panic disorder ($n=1$), and social phobia ($n=1$). Patients treated with electroconvulsive therapy in the last six months or benzodiazepine within three days prior to testing were not included. A *Hamilton Depression Rating Scale* (HAMD; Hamilton, 1960) score ≤ 8 was chosen to define remission (Smith et al., 2006). Patients with a history of psychotic depression, neurological disorders, substance abuse, bipolar disorders, any axis-II-disorder or suicidal tendencies were excluded. Twenty-nine patients had been taking psychopharmacological medication in a stable dosage during the last week before testing. The following antidepressive agents were prescribed alone or in combination: citalopram ($n=2$), escitalopram ($n=8$), mirtazapine ($n=12$), venlafaxine ($n=11$), reboxetine ($n=1$), duloxetine ($n=1$), and tranylcypromine ($n=1$). Ten patients were medicated with quetiapine (chlorpromazine equivalent daily dosage (CPZ) 215.0 mg $\pm$ 176.1), two patients received risperidone (CPZ 87.5 mg $\pm$ 53.0), two patients were given pipamperone (CPZ 32.0 mg $\pm$ 22.6), and one patient flupentixol (CPZ 150 mg; CPZ converted according to Sackeim, 2001). Two patients took lithium and three patients lamotrigine.

Thirty healthy controls, matched for gender and age, were recruited via advertisement. Education and IQ were balanced between patients and controls. All control subjects underwent an initial telephone screening to assure matching criteria and to exclude medical and neurological diseases. The SCID-Interview was performed to exclude any history of psychiatric disease. There were no records of any mental disorders in the first-degree relatives of healthy controls. In addition, a *Beck Depression Inventory* (BDI; Beck et al., 1961) score ≤ 12 with reference to Viinamäki et al. (2002) was applied to exclude the existence of self-reported depressive symptoms. Both patients and controls were right-handed as measured by the *Edinburgh Handedness Inventory* (Oldfield, 1971). The local Institutional Ethical Review Board approved all procedures. The ethical standards of the Declaration of Helsinki were met and all participants provided written informed consent after the study had been fully explained.

Intellectual performance was examined by means of a multiple choice vocabulary intelligence test (*Mehrfachwahl-Wortschatz-Test, Version B* (MWT-B); Lehrl, 1991). Non-verbal learning and memory were measured by the *Rey-Osterrieth-Complex-Figure-Test* (RCFT; Rey, 1941; Osterrieth, 1944). The RCFT-copy score composed of the accuracy of the original copy is a parameter of the visual-constructional ability; and the RCFT-recall score is a measure of the amount of information retained over time, and was scored with reference to Spreen and Strauss (1991). Organizational strategies, which mean the ability to organizing the RCFT-Figure into meaningful perceptual units whilst encoding, were assessed following the *Savage Organizational Scoring* (SOS) system (Savage et al., 1999), resulting in a range of scores from 0 to 6. Two independent psychologists evaluated the RCFT-copy scores, -recall scores and the SOS scores of all participants, to ensure sufficient reliability. Subsequently calculations were based on the scores of one examiner.

The primary objective of the present study was to compare the group of patients and healthy controls with respect to RCFT-copy scores, RCFT-recall scores, and SOS scores. Interrater reliability was evaluated by intra-class correlations.