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# Effortful information processing in patients with major depression — A 10-year follow-up study

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ABSTRACT

The aim of the present study was to longitudinally investigate effortful cognitive functioning in a group of patients diagnosed with major depressive disorder (MDD) in a 10-year follow-up period. Results at inclusion in the acute phase of MDD showed impaired effortful processing and that this impairment prevailed at a 6-month follow-up, despite significant symptom reduction. Non-effortful processing was normal as compared to healthy controls. Sixteen patients along with 16 healthy controls were included in the 10-year follow-up. They all participated in the original study and were matched for age and educational length. The mean symptom load at the time of testing at the 10-year follow-up indicated that the patients as a group were in remission. All participants were examined with a visual search paradigm, with demands for effortful and non-effortful processing. Results showed that the patient group had normalized their performance for effortful information processing and no longer differed significantly from the healthy controls at the 10-year follow-up, and the lack of difference between the groups for non-effortful processing remained the same. These results indicate that short-term effortful cognitive impairments normalize over the course of long-term recovery that goes together with clinical improvement and remission.



## 1. Introduction

Few studies have followed cognitive functioning in major depressive disorder (MDD) from the acute phase of illness to episodes of symptom reduction and remission, or examined cognitive functioning in a population of patients in remission (for overview see Douglas and Porter, 2009; Hammar and Årdal, 2009). Some studies imply that the cognitive impairment observed during episodes of illness also endures during episodes of symptom reduction (Neu et al., 2001; Hammar et al., 2003a; Airakinsen et al., 2006; Hammar et al., 2010), and continues to endure even in remission (Reischies and Neu, 2000; Majer et al., 2004; Weiland-Fiedler et al., 2004; Neu et al., 2005; Paelecke-Habermann et al., 2005; Smith et al., 2006; Gruber et al., 2007; Nakano et al., 2008; Årdal and Hammar, 2011). Other studies report no such findings and state normalized functioning over time (Beats et al., 1996; Koetsier et al., 2002; Biringer et al., 2005; Jaeger et al., 2006; Biringer et al., 2007; Lahr et al., 2007). Recently, in a review of longitudinal studies of cognition and MDD, Douglas and Porter (2009) summarized that it seems that whiles measures of verbal learning and memory and fluency improve by clinical recovery, measures of attention and executive functioning remain impaired despite treatment response. Based on the diverse findings in the literature, it is possible to expect that prolonged cognitive impairment holds true for selected aspects of cognitive functions, e.g. attention and executive functioning. On the contrary, the literature also supports that not all cognitive functions are characterized by prevailing or irreversible impairment, but instead, normalize over time independent of symptom recovery.

However, a shortcoming of these studies is that the periods studied are relatively brief, preventing firm conclusions of recovery of symptoms over extended periods. We have retested a group of MDD patients after an extended period of 10 years, and we have included a matched healthy control group that had been retested after the same period of time. This is to our knowledge the longest follow-up study within MDD concerning cognitive functioning in which the same patients and controls were retested. In addition, the patients and controls have been examined with the Stroop test (see Årdal and Hammar, 2011). These findings indicated an irreversible impairment of the response inhibition in a component of executive functioning within the patient group despite the fact that the group was in remission. The Stroop test is, however, limited to measures of response inhibition, in order to move attention to the color information in the incongruent stimulus. It does not provide an answer to the question of whether patients with MDD show impairment over time whenever there is a demand for more general effortful processing. It would be an advantage to have an experimental approach to this question as well, with as little procedural difference as possible between task conditions. Thus,

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effortful and non-effortful processing was examined in a 10-year follow-up, with an experimental paradigm based on visual search theory (Treisman and Gelade, 1980; see also Hammar et al., 2003a,b). When we investigated them for the first time 10 years ago (Hammar et al., 2003a), the patients showed impaired effortful information processing and intact non-effortful information processing in the acute phase compared to the healthy control group. Moreover, this pattern prevailed at a 6-month follow-up, despite significant improvement in depressive symptoms (Hammar et al., 2003b). We now asked the question whether the prevailed cognitive impairment in effortful processing seen at the 6-month follow-up still remained after 10 years, or whether the initial impairment was recovered, thus representing a potential cognitive capacity to be captured early on in the disorder as a potential training or treatment target.

## 2. Method

### 2.1. Design of the study

The study was a longitudinal study, investigating the same patient and control groups over 10 years. Both the patient and control groups were examined on three different occasions: the acute phase, short-term follow-up, and long-term follow-up after 10 years (mean 9.5 years). The results from the acute phase and the short term follow-up have been published earlier (Hammar et al., 2003a; Hammar et al., 2003b). All patients went through a diagnostic assessment by a senior psychiatrist, or psychologist, on all test occasions of the project.

### 2.2. Subjects

At inclusion (T1), 21 patients (10 males and 11 females: 18 in-patients and 3 out-patients) diagnosed with unipolar major depression (MDD) were recruited from psychiatric institutions and clinics in Bergen, Norway and included in the study. All patients met the DSM-IV (APA, 2000) criteria for recurrent unipolar depression and had a minimum score of 18 ($M=21.6$, S.D. = 3.6) on the Hamilton Depression Rating Scale (HDRS), (Hamilton, 1960). The age range was 20–56 years ($M=42.5$ years, S.D. = 10). Mean educational time period was 14 years (S.D. = 4.0). Inclusion criteria were at least one previous episode of MDD. Exclusion criteria were previous or present psychotic symptoms, a history of manic episodes, central nervous system (CNS) damage or disease, or any somatic condition that could interfere with cognitive functioning. A healthy control group was recruited and individually matched for age, gender, level of education, IQ level and each subject had no history of psychiatric illness or CNS damage/disease. All participants in the study were native Norwegian speakers. All participants using glasses were instructed to use them during testing.

At the 10-year follow-up (T2), the same patient and control group were invited to participate. All participants were retested using the same method as at initial inclusion. Sixteen of the original 21 patients were available for testing for the 10-year follow-up assessment. Of the five missing patients, one had a stroke and was not able to go through testing, one patient died during the follow-up period, one patient was not able to participate due to severe mental and physical illness and two patients were otherwise lost for the follow-up. There were 16 matched healthy controls that had also participated in the initial testing 10 years ago. The mean HDRS score of the 16 remaining patients was 5.5 (S.D. = 5.26) at the 10-year follow-up, indicating that the patients as a group were in remission. Ten patients were in full remission, five patients reported mild symptoms and one patient scored moderate symptoms on the HDRS scale. See Table 1 for demographical and clinical data in the two groups. For each patient, information on depression duration and number of depressive episodes was obtained.

Eight patients were using antidepressant medication, primary SSRIs, at the 10-year follow-up.

**Table 1**
Demographic, clinical variables and RTs at 10 year follow-up (mean, standard deviation).

| Variable | Patient group ($N=16$) | Control group ($N=16$) |
|---|---|---|
| Age | 50.06 (9.8) | 50.38 (9.2) |
| IQ (WASI) | 115 (16) | 118 (11) |
| Total number of episodes | 10.46 (13.3) | NA |
| Number of episodes since T1 | 8.33 (13.4) | NA |
| Months since last episode | 43 (42) | NA |
| Non-efforful (RT ms) | 1346 (958) | 1102 (337) |
| Effortful (RT ms) | 2705 (1658) | 2127 (731) |

The study was performed in accordance with the Helsinki Declaration of the World Medical Association Assembly. The Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate approved the study.

### 2.3. Apparatus, stimuli and procedure

All participants were given information about the study and were informed that participation was voluntary. In addition to the experimental paradigms, all subjects underwent a minor standardized neuropsychological test battery with measures of memory, executive functioning and attention. The complete assessment was conducted within approximately 2 h and was carried out in order to give a neuropsychological report to the participants. After informed consent was obtained, the patients were tested on the visual search task. The experimental paradigm has previously been described in Hammar et al. (2003a) and Hammar et al. (2003b). All stimuli were presented on a PC screen in front of the subject. The target stimulus was a black rectangle in a vertical position. One type of distractor stimuli consisted of horizontal black rectangles (see Fig. 1a–b). The other type of distractor stimuli consisted of black horizontal rectangles and gray vertical rectangles (see Fig. 1c–d). For half of the trials, a target stimulus was presented together with the distractors. For the other half of the trials, only distractors were presented. In half of the trials there was one type of distractor. In the other half of the trials, both types of the distractors were presented. The logic was that trials with both types of distractors presented would be a cognitively more demanding condition, requiring effortful information processing, while trials with distractors only would require non-effortful processing. See below and Fig. 1 for further explanations.

The experiment consisted of two blocks of 20 trials each, with 10 trials with target and one distractor type; 10 trials without target and one distractor type; 10 trials with target and two distractor types; 10 trials without target and two distractor types. There was a break of 30 s between the blocks. Before each trial, a fixation cross was presented which lasted for 1.5 s. The visual search display stayed on, on each trial, until a response was made. The different displays were presented in randomized order across the trials. The subject was instructed to press the "A" key on the PC keyboard with the left hand if the screen only consisted of distractors, and to press the "L" key with the right hand, if a target was present. The "A" and the "L" keys are the most left- and rightward placed keys on the mid-row of the PC keyboard. The stimulus presentation and recording of responses were programmed in the E-prime programming platform (www.pstnet.com). The experiment was presented on a Dell laptop PC screen.

The data were automatically collected by the E-prime program and scored as mean response latency (RT) for each condition, and statistically analyzed in a repeated-measures analysis of variance (ANOVA). The basic design was a 2×2×2 factorial design with Group (depressed patients and control subjects)×Condition (Effortful and Non-effortful information processing)×Test occasion (T1 and T2). The first factor was treated as a between-group factor and the second and third factors were treated as within-group factors. In addition to analysis of main effects, a two-way ANOVA was carried out with Group (Depressed patients and Control group)×Condition (Effortful and Non-effortful) for each Test occasion separately. In order to further probe differences between groups and to rule out the possibility that results could be explained by a general slowing effect, an interference RT score was calculated by subtracting the scores of the non-effortful condition (one-distractor condition, with and without target) from the scores in the effortful condition (two-distractor condition, with and without target). Only trials with a correct response were included in the statistical analyses.

## 3. Results

There was a significant main effect of Condition, $F(1,30)=183.78$, $p$ 0.001, partial eta squared = 0.86. Tukey's HSD post-hoc test showed longer RTs in the effortful condition compared to the non-effortful condition $p<0.001$. There were no significant main effects for Group or Test occasion.

The two-way interaction between Group and Condition was significant $F(1,30)=4.45$, $p<0.05$, partial eta squared = 0.129. The other two-way interactions were not significant, and neither was the three-way interaction. The follow-up test with Group (Depressed patients and Control group)×Condition (Effortful and Non-effortful) for each Test occasion separately showed that the patient group ($M=2876$ ms, S.D. = 1103) had significantly longer RTs for effortful information processing compared to the control group at T1 ($M=2215$ ms, S.D. = 643), $t$ (30) = 2.068, $p<0.01$, that had disappeared at T2 with no significant differences between groups for effortful information processing. There were no differences between the two groups in the non-effortful condition, either on T1 or T2. See Fig. 2.