Research report

Atypical cognitive profile in patients with depression after myocardial infarction

Jeanette B. Dijkstra\textsuperscript{a}, Jacqueline J.M.H. Strik\textsuperscript{a}, Richel Lousberg\textsuperscript{a}, Jos Prickaerts\textsuperscript{b,*}, Wim J. Riedel\textsuperscript{b}, Jelle Jolles\textsuperscript{b}, Herman M. van Praag\textsuperscript{a}, Adriaan Honig\textsuperscript{a}

\textsuperscript{a}Department of Psychiatry and Neuropsychology, Maastricht University Hospital, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands
\textsuperscript{b}Department of Psychiatry and Neuropsychology, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands

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Abstract

\textbf{Background:} We evaluated the cognitive profile of 48 patients with major depression following their first myocardial infarction (MI). \textbf{Methods:} The cognitive performance of the patients was compared with the performance of 48 non-depressed MI patients and 48 healthy controls. \textbf{Results:} Depressed MI patients performed slower on a simple cognitive speed related measure compared with non-depressed MI patients and healthy controls. Attention and speed-related aspects of cognitive functioning were not affected. Surprisingly, (depressed) MI patients showed even better performances with respect to memory function. \textbf{Limitation:} No patients with non-MI-related depression were included. \textbf{Conclusions:} The cognitive profile of major depression after MI differs from that of non-cardiac-related depressive disorder, as described in the literature. This may reflect a different etiology of post MI depression from non-cardiac-related depression.

Keywords: Myocardial infarction; Depression; Cognition

1. Introduction

Myocardial infarction (MI) is frequently complicated by a depressive disorder (Forrester et al., 1992; Frasure-Smith et al., 1993; Honig et al., 1997; Roose et al., 1998). Patients with depression after MI are probably doubly at risk for cognitive decline. First, depressive disorder is related to a decline in almost all cognitive domains such as impaired attention (Mialet et al., 1996), frontal lobe dysfunction (Veiel, 1997), executive deficits (Degl’Innocenti et al., 1998) and, especially, memory impairment (Cassens et al., 1990; Burt et al., 1995; Riedel et al., 1998a). Also a slowing of mental processes termed ‘psychomotor retardation’ is often found (Goodwin, 1997; Sabbe et al., 1997; Degl’Innocenti et al., 1998). Improvement in cognitive function is expected following remission of depressive symptoms.

Secondly, patients with chronic cardiac disease in general perform worse than healthy controls on...
cognitive tests (Townes et al., 1989; O’Brien et al., 1992). The cause of this cognitive impairment in cardiovascular disease is not known (Vingerhoets et al., 1997), but these patients are more likely than healthy controls to have significant stenoses in their cerebrovascular circulation. For this reason, it has been hypothesized that limited oxygenation of the brain may be a risk factor or vulnerability factor for cognitive dysfunction (Stanton, 1988; Benedict, 1994). Two studies investigating the effect of a history of MI on cognitive function among elderly subjects (≥64 years) found no association (Petrovitch et al., 1998; Ahto et al., 1999). However, Breteler et al. (1994) suggested that MI is associated with white matter lesions in subjects older than 65 years of age, and related these lesions to cognitive dysfunction. Grubb et al. (1996) compared the memory function of patients with acute MI with and without cardiac arrest and only found moderate to severe memory impairment in patients with acute MI and cardiac arrest. It is possible that the patients with acute MI and cardiac arrest suffered from cerebral hypoxia due to cardiac arrest. Hypoxia is known to cause damage to the hippocampus and other medio temporal lobe structures, as well as memory impairment (Hopkins et al., 1995; Rempel-Clower et al., 1996; Caine and Watson, 2000; Stefanacci et al., 2000).

The present study is the first to investigate cognitive performance in patients with a major depressive episode (according to DSM-IV) after their first MI, in non-depressed first MI patients, and in normal healthy controls. We hypothesized that cognitive performance would be worse in MI patients than in healthy controls and that MI patients with a depressive disorder would show an even worse cognitive performance. This study is part of a larger study investigating the efficacy and side-effects of a placebo controlled treatment with an SSRI (Strik et al., 2000).

2. Methods

2.1. Inclusion criteria of patients

Patients were recruited from the in-patient Department of Cardiology of the Maastricht University Hospital and an affiliated hospital. Inclusion criteria were: age between 18 and 75 years and a first acute MI, defined as a clinical picture typical for an acute MI without cardiac arrest, a plasma concentration of aspartate aminotransferase (ASAT) twice as high as the upper limit of the normal range (80 U/l), and ECG changes specific for MI (Pasternak et al., 1992). Patients were screened for depressive symptomatology using the Dutch version of the Symptom Check List, 90 items (SCL-90, validated Dutch version; Arrindell and Ettema, 1981). Patients with a score above the cut-off on the SCL-90 depression scale ($≥23$ for males and $≥28$ for females) were invited for a diagnostic interview by an experienced psychiatrist. Severity of depression was measured by means of the Hamilton Depression Rating Scale, 17-item version (HAMD; Hamilton, 1960). All patients diagnosed with a major depressive episode according to DSM-IV criteria with a HAMD score higher than 17 entered the depressed group. The non-depressed patients did not show any signs of a depression up to 12 months after MI. These non-depressed patients were matched individually with the depressed patients for age, level of education, sex, and plasma concentration of aspartate aminotransferase (ASAT). Background characteristics of the patients are presented in Table 1.

Exclusion criteria were psychotic symptomatology, the presence of a second psychiatric diagnosis, a previous history of manic symptoms, pregnancy or lactation, a life-threatening physical illness (other than the present MI), concurrent use of psychotropic drugs (except a benzodiazepine in an equivalent of oxazepam to a maximum dose of 50 mg/day), fluoxetine hypersensitivity, liver dysfunction, or severe kidney dysfunction (creatinine clearance, 10 ml/min). Patients with an aorta interval (AI) less than 20 and/or a right ventricular systolic pressure higher than 30 were excluded.

Medication for the MI patients was usually prescribed by the cardiologist. For an overview of the medication taken by the patients see Table 3. The median number of cardiovascular drugs, i.e. all nine drugs mentioned except benzodiazepines/tranquilizers, taken per non-depressed MI patient was four, ranging from one to six. The median number of cardiovascular drugs taken per depressed MI patient was three, ranging from zero to six. In both MI
groups no anti-depressive medication was used at the time of the cognitive assessment.

The study was approved by the local Ethics Committee at the two sites, and all participants gave their written informed consent after the study had been explained to them.

### 2.2. Selection criteria of normal volunteers

The normal volunteers (n = 48) were drawn from 1450 healthy subjects who were recruited from a patient register of general practices in the region of Maastricht, The Netherlands (Jolles et al., 1995). This register contains all relevant past and current medical morbidity as documented by the general practitioners. Subjects with previous or actual medical conditions with known impact on cognitive or motor functions were excluded from the selection. Other exclusion criteria were depression (scores higher than the cut-off on the SCL-90 depression scale (≥23 for males and ≥28 for females), overt cerebrovascular disease, chronic neural pathology (e.g. dementia, epilepsy, parkinsonism), mental retardation, and psychotropic drug use. The subjects who were eligible for the study filled out a postal questionnaire and participated in an extensive medical and neuropsychological investigation. The 48 control subjects were matched individually with the patients for age, level of education and sex (Table 1).

### 2.3. Procedure and cognitive test battery

MI patients entered the study not earlier than 4 weeks after the MI, because during the first weeks after an MI it is possible to attribute depressive symptoms to a major depressive episode or to intense distress due to the cardiac event. The MI patients were followed during 12 months to see whether they developed a depressive disorder. Depressive symptoms were assessed on four occasions (1, 3, 6 and 12 months) during the 1st year post MI. Patient who developed a depressive disorder in this period underwent a neurocognitive investigation. Cognitive data of the non-depressed MI patients, who did not develop a depression during the year following MI, were collected at 12 months post MI.

Neurocognitive tests were used which have been found to be sensitive to small differences between patient groups and which are in widespread use in large-scale studies into cognitive disorders and age-related cognitive decline (Moller et al., 1998; Van Boxtel et al., 1998; Dijkstra et al., 1999; De Groot et al., 2000; Krabbendam et al., 2000). The tests are part of a cognitive screening battery used in various studies with patients and healthy subjects (for further

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**Table 1**

Background characteristics of the study population

<table>
<thead>
<tr>
<th>Group (range, years)</th>
<th>n (%)</th>
<th>Age (mean±S.D.)</th>
<th>Education score (mean±S.D.)</th>
<th>Sex, n (male/female)</th>
<th>SCL depression score (mean±S.D.)</th>
<th>HAMD score (mean±S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total group (33–76)</strong></td>
<td>144 (100)</td>
<td>56.6±10.9</td>
<td>3.0±2.0</td>
<td>105/39</td>
<td>25.8±11.2</td>
<td>n.m.</td>
</tr>
<tr>
<td>Young (33–56)</td>
<td>73 (51)</td>
<td>47.3±5.7</td>
<td>3.6±1.7</td>
<td>67/6</td>
<td>24.6±9.4</td>
<td>n.m.</td>
</tr>
<tr>
<td>Old (57–76)</td>
<td>71 (49)</td>
<td>66.3±4.9</td>
<td>2.4±2.1</td>
<td>38/33</td>
<td>27.0±12.8</td>
<td>n.m.</td>
</tr>
<tr>
<td><strong>Healthy control group (37–76)</strong></td>
<td>48 (33)</td>
<td>56.7±11.1</td>
<td>2.9±2.0</td>
<td>35/13</td>
<td>18.0±1.8</td>
<td>n.m.</td>
</tr>
<tr>
<td>Young (37–56)</td>
<td>25 (17)</td>
<td>47.4±5.8</td>
<td>3.6±1.7</td>
<td>23/2</td>
<td>17.8±1.7</td>
<td>n.m.</td>
</tr>
<tr>
<td>Old (59–76)</td>
<td>23 (16)</td>
<td>66.8±4.6</td>
<td>2.2±2.0</td>
<td>12/11</td>
<td>18.3±1.9</td>
<td>n.m.</td>
</tr>
<tr>
<td><strong>MI non-depressed (33–76)</strong></td>
<td>48 (33)</td>
<td>56.5±10.8</td>
<td>3.1±1.9</td>
<td>35/13</td>
<td>22.4±5.8</td>
<td>8.0±4.1</td>
</tr>
<tr>
<td>Young (33–55)</td>
<td>23 (16)</td>
<td>46.9±5.7</td>
<td>3.5±5.7</td>
<td>21/2</td>
<td>21.5±5.4</td>
<td>8.4±4.2</td>
</tr>
<tr>
<td>Old (57–76)</td>
<td>25 (17)</td>
<td>65.4±5.5</td>
<td>2.8±2.2</td>
<td>14/11</td>
<td>23.1±6.2</td>
<td>7.6±4.1</td>
</tr>
<tr>
<td><strong>MI depressed (37–76)</strong></td>
<td>48 (33)</td>
<td>56.7±11.0</td>
<td>3.0±2.1</td>
<td>35/13</td>
<td>37.0±12.0</td>
<td>21.1±2.3</td>
</tr>
<tr>
<td>Young (37–56)</td>
<td>25 (17)</td>
<td>47.4±5.8</td>
<td>3.6±1.9</td>
<td>23/2</td>
<td>34.4±8.8</td>
<td>20.9±2.4</td>
</tr>
<tr>
<td>Old (58–76)</td>
<td>23 (16)</td>
<td>66.7±4.6</td>
<td>2.2±2.0</td>
<td>12/11</td>
<td>39.8±14.4</td>
<td>21.4±2.2</td>
</tr>
</tbody>
</table>

n.m., not measured.
description and psychometric properties see Jolles et al. (1995). The tests exist in parallel versions and can therefore be used in repeated measurements.

2.3.1. Visual Verbal Learning Test (VVLT)
A visual version (Brand and Jolles, 1985; Riedel et al., 1998a) of the Auditory Verbal Learning Test (Lezak, 1995) was used. The psychometric properties are described in Bouma et al. (1998). In procedure it is quite similar to the California Verbal Learning Test and the Auditory-Verbal Learning Test (AVLT) (Lezak, 1995) except that words are presented visually to control for hearing loss. In this version, a set of 15 frequently used monosyllabic meaningful words is visually presented in a fixed order at a rate of one every 2 s in three consecutive trials. After each trial or presentation the subject is requested to recall as many words as possible with no restriction concerning the order of recall. The dependent variable is the total number of words recalled over the three trials (VVLTTOT). Then 20 min after the last presentation, the subject is again requested to recall as many words as he or she can remember (delayed recall; VVLTDDEL). This test measures memory storage and retrieval of verbal information in episodic memory.

2.3.2. Concept Shifting Test (CST)
This test is derived from the Trail Making Test (Lezak, 1995), which is used to measure the ease of shifting between different sets of attention. Compared with the Trail Making Test, the effect of CST on motor function is limited and thereby controls for the influence of simple motor speed on test performance. It consists of four parts. On each test sheet, 16 small circles are grouped in a larger circle. In the first part empty circles have to be crossed out as fast as possible (CST0). In the other three parts the circles contain numbers (CSTA), letters (CSTB), or both (CSTC), appearing in a fixed random order. Subjects are requested to cross out the items in the right order. The dependent variable is the time needed for each part (Jolles et al., 1995).

2.3.3. Stroop Colour-Word Test (SCWT)
The SCWT is a test of selective attention and interference susceptibility. The test involves three cards displaying 40 stimuli each: colour names (SCWT I), coloured patches (SCWT II), and colour names printed in incongruously coloured ink (SCWT III). For the last card, the colour of the ink has to be named instead of the colour name. This task is particularly sensitive to interference. The variables of interest are the times (s) needed to complete each card (Lezak, 1995; Klein et al., 1997).

2.3.4. Letter-Digit Substitution Test (LDST)
This test is a modification of the procedurally identical Symbol-Digit-Modalities Test (Lezak, 1995). The subjects are supplied with a code at the top of a page where a digit corresponds to a letter. They then have a short time to fill in blanks which correspond to the correct codes. The test is used to measure the speed of processing of general information, i.e. the test is supposed to draw upon several (cognitive) processes such as visual perception, attention, and memory. The dependent variable is the total number of letters written correctly in 1 min (LDSTTOT) (Jolles et al., 1995).

The cognitive measurements assess the following theoretical underlying cognitive constructs: memory (VVLTTOT, VVLTDDEL) and attention-related aspects such as cognitive flexibility (ability to shift between two sequences; CSTC), interference susceptibility (ability to ward off distractions; SCWT III), sensorimotor speed (simple cognitive speed; CST0, CSTA, CSTB, SCWT I and II), and speed of general information processing (LDSTTOT) (Dijkstra et al., 1999).

2.4. Data analysis
The number of males and females in each experimental group, that is control non-depressed, MI patients non-depressed and MI patients depressed, were equal. The three groups were matched for age and education. Since all primary efficacy and safety variables were normally distributed and no outlying values more than 3 S.D. below or above the mean were found, parametric tests were applied. A P-value ≤ 0.05 was considered significant. Besides group effects the impact of age and sex was also studied. Age was studied as an independent variable to control for possible interactions with group because of the wide age range (33–76 years). Two age groups (middle-aged and elderly) were formed using
3. Results

Patients were enrolled in the study from May 1994 until December 1997. Each experimental group contained 48 subjects which consisted of 35 males and 13 females. The mean age of the three groups was 56.6 and the education level of all groups was 2.5 (median) on an 8-point scale (de Bie, 1987).

On all cognitive test variables age effects were found (all $F_s > 6.8$, $P < 0.01$). The older subjects showed a worse cognitive performance on all test variables (Fig. 1). Gender effects were found on the two memory variables (VVLTOT, VVLDEL); females showed a better performance compared to males ($F_s > 7.4$, $P < 0.01$). No interactions were found between group, age and sex. This indicates that the effect of MI and MI and depression were not different between the age groups and gender.

Group effects of the various tests of cognitive function are summarized in Table 2. With respect to memory performance (VVLT) it was found that for both measures the groups were different between each other (Group effect: both $F_s > 3.09$, $P < 0.05$). Post hoc analysis of the measure VVLTTOT showed that MI patients performed better than healthy controls. Furthermore, depressed MI patients had an even better performance on this measure than MI patients without a depression (Fig. 1A). The latter was also found for the measure VVLTDDEL, although separately both MI groups were not different from the control group.

With respect to the CST, it was found that there were differences between the groups for the simple cognitive speed-related measure CST0 only (Group effect: $F = 8.61$, $P < 0.01$). There were no differences found for the other three measures, that is CSTA, CSTB and CSTC (Group effect: all $F_s < 1.67$, n.s.). Post hoc analysis of the CST0 measure
Table 2
Differences in cognitive performance of MI patients and controls in various tests of cognitive function

<table>
<thead>
<tr>
<th></th>
<th>Control non-depressed (n = 48)</th>
<th>MI patients non-depressed (n = 48)</th>
<th>MI patients depressed (n = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visual Verbal Learning Test (VVLTTOT)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VVLTDEL</td>
<td>21.3 ± 5.4ⁿ</td>
<td>23.8 ± 5.0ⁿ</td>
<td>26.4 ± 6.8ⁿ</td>
</tr>
<tr>
<td>Visual Verbal Learning Test (VVLTTOT)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concept shifting Test (CST)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CST0</td>
<td>5.3 ± 1.1ⁿ</td>
<td>6.0 ± 1.6ⁿ</td>
<td>7.3 ± 3.1ⁿ</td>
</tr>
<tr>
<td>CSTA</td>
<td>21.4 ± 5.6ⁿ</td>
<td>24.2 ± 8.0ⁿ</td>
<td>25.5 ± 8.3ⁿ</td>
</tr>
<tr>
<td>CSTB</td>
<td>26.7 ± 6.9ⁿ</td>
<td>29.4 ± 12.3ⁿ</td>
<td>31.5 ± 13.3ⁿ</td>
</tr>
<tr>
<td>CSTC</td>
<td>35.6 ± 9.8ⁿ</td>
<td>38.8 ± 13.8ⁿ</td>
<td>42.4 ± 18.2ⁿ</td>
</tr>
<tr>
<td>Concept shifting Test (CST)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stroop Color Word Test (SCWT)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCWT I</td>
<td>17.9 ± 3.5ⁿ</td>
<td>17.3 ± 3.3ⁿ</td>
<td>19.0 ± 4.7ⁿ</td>
</tr>
<tr>
<td>SCWT II</td>
<td>23.6 ± 4.4ⁿ</td>
<td>23.3 ± 4.3ⁿ</td>
<td>23.7 ± 5.0ⁿ</td>
</tr>
<tr>
<td>SCWT III</td>
<td>37.8 ± 9.4ⁿ</td>
<td>47.0 ± 15.7ⁿ</td>
<td>43.7 ± 22.2ⁿ</td>
</tr>
<tr>
<td>Stroop Color Word Test (SCWT)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letter Digit Substitution Test (LDST)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDST</td>
<td>29.9 ± 6.9ⁿ</td>
<td>30.8 ± 6.4ⁿ</td>
<td>27.9 ± 8.6ⁿ</td>
</tr>
</tbody>
</table>

For the CST and SCWT, a higher score indicates a lower test performance. For VVLT and LDST a higher score indicates a higher test performance. Data represent means ± S.D. Group effects were evaluated in more detail with a Student–Newman–Keuls’ test (P, 0.05) and, subsequently, means which were different were marked with different superscripts.

showed that MI on its own had no clear effect on simple cognitive speed when compared to that of the controls. However, depressed MI patients were slower than controls (Table 2 and Fig. 1B).

On the SCWT and LDST there were no differences between the MI patients and the controls (Group effect: all Fs < 2.89, n.s.).

4. Discussion

In the present study it was found that depressed MI patients had a better memory performance (VVLT) than MI patients without a depression or controls. In addition, no differences were found between the groups with respect to attention-related aspects (CSTC, SCWT III), speed of general information processing (LDST) and sensorimotor speed (CSTA, CSTB, CSTC, SCWT I and II). However, there was one exception. Depressed MI patients were slower on the most simple cognitive speed related measure, the CST0. The overall performances on the VVLT and CST0 of MI patients without a depression appeared to be equal to the performances of the controls or intermediate between that of the controls and depressed MI patients.

Therefore, it can be concluded that the occurrence of a depression in MI patients may result in cognitive symptoms (e.g. VVLTDDEL, CST0) on its own which may even further increase cognitive symptoms (e.g. VVLTTOT) already due to an MI. However, MI or MI with a depression has no effect on the other cognitive variables (e.g. CSTA, CSTB, CSTC, SCWT II and III, and the LDST) which indicates the selectivity of the cognitive effects. The overall negative effect of age on cognitive performance is in agreement with findings of others (e.g. Birren and Schaie, 1990). There was no interaction with age on the VVLT and CST0 measures, although a closer inspection of the data revealed a tendency of an interaction effect on CST0 (F = 2.4, 0.05 < P < 0.1). This indicates that especially older depressed MI patients are vulnerable to a decline in simple cognitive speed. Finally, women showed in general better verbal memory performances than men as has been described by others (Herlitz et al., 1999).

Decreased memory performance is often reported in patients with a depressive disorder (Weingartner et al., 1981; Riedel et al., 1998a; Watts et al., 1990). Riedel et al. (1998a), using the same memory test, found that patients with non-cardiac-related depression performed worse on immediate and delayed
recall than normal healthy controls. Surprisingly, these findings are clearly in contrast to ours in which depressed MI patients performed better on both memory measures when compared with non-depressed MI patients. With respect to the immediate recall the performance of the depressed MI patients was even better than that of the controls. Unexpectedly, no group differences were found on attention-related aspects, sensorimotor speed and speed of general information processing. In general, (based on the literature) we hypothesized that depressed MI patients would show a worse cognitive performance than healthy controls and that non-depressed MI patients would show an intermediate cognitive performance. The slower performance of depressed MI patients on measures of simple cognitive speed (‘psychomotor retardation’) is consistent with the findings of others (Goodwin, 1997; Sabbe et al., 1997; Degl’Innocenti et al., 1998). The trend towards an interaction with age on simple cognitive speed can be explained by a general cognitive slowing with age (Birren and Schaie, 1990). Thus the cognitive profile of depressed MI patients following a first MI appears to differ from that of patients with a non-cardiac-related depressive disorder.

A possible explanation for this finding is that the underlying cause of depression post MI differs from that of non-cardiac-related depression. The symptomatology of MI depression, although it fulfils DSM-IV criteria, is atypical in that these patients are more hostile than patients with non-cardiac-related depression (Honig et al., 1997). This hostility is reflected by irritability, resentment about the illness, anger, and frequent disagreement. Increased hostility (and anxiety) might be a ‘pacemaker’ of a discrete type of depression called anxiety/aggression-driven depression, which has been hypothesized to have a pathogenesis different from that of other subtypes of depression (van Praag, 1994, 1996). Post-MI depression might belong to this subtype. It is possible that in this subtype no decline in memory function occurs or even a better performance compared to normal healthy controls. The hypothesis of a putative subtype is supported by the finding that the immediate recall was already improved in non-depressed MI patients when compared with controls, which suggests that the memory function in MI patients appears to be a different subtype. Concomitantly, the effects of a depression on memory (or cognitive) function in MI patients may be different from the effects of a depression in healthy controls. However, still other explanations remain possible which may coincide (see below).

A second possible explanation is the role of personality factors. Personality and coronary heart disease (CHD) are suggested to be related in MI patients (Dimsdale, 1988). In a recent study, type-D (the tendency to suppress emotional distress) personality was a significant predictor of long-term mortality in patients with established CHD (Denollet et al., 1996). The involvement of personality characteristics should be studied in relation to cognitive performance in these groups. Gold and Arbuckle (1990) reviewed the interactions between personality and cognition and found that while high neuroticism improves reaction time, other cognitive abilities are detrimentally affected. In line with these findings it may be hypothesized that type-D personality has a positive effect on cognitive performance.

A third explanation concerns the possible psychoactive properties of medication used. The MI patients differed considerably in this respect from the healthy control group in that the latter group was not taking psychoactive medication. Several of the drugs could have influenced cognitive performance. Many patients took several drugs simultaneously. There were no differences between the depressed and non-depressed patient groups in the number of drugs taken (Mann–Whitney U-test; overall median 3.5). It remains difficult, if not impossible, to evaluate the influence of each individual substance, let alone their interactions, on cognitive performance. On the basis of current available knowledge on the psychoactive mechanisms of these drugs, five of the nine drugs mentioned can be considered to possess psychoactive properties and hence may have had direct effects on cognitive performance (Table 3).

In general, antihypertensive drugs may have adverse cognitive effects which, however, tend to be more than offset by the beneficial effect of lowering blood pressure. Benzodiazepines/tranquilizers have a detrimental effect on cognitive performance and can contribute to psychomotor slowness and memory impairment, although the latter effects are in most cases transient (Riedel et al., 1998b). Lipophilic beta-blockers have been shown to slow psychomotor
Table 3
Medication for the depressed and non-depressed MI patients and psychoactive effects

<table>
<thead>
<tr>
<th>Medication</th>
<th>Non-depressed (%)</th>
<th>Depressed (%)</th>
<th>Psychoactive</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-coagulation agents</td>
<td>48 (100)</td>
<td>42 (80)</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Isosorbide nitrate</td>
<td>30 (63)</td>
<td>20 (42)</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Beta blockers (lipophilic)</td>
<td>36 (75)</td>
<td>30 (63)</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>7 (15)</td>
<td>15 (32)</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>Benzodiazepines/tranquilizers</td>
<td>10 (21)</td>
<td>23 (48)</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td>Cholesterol-lowering drugs</td>
<td>38 (79)</td>
<td>18 (38)</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>Diuretics</td>
<td>4 (8)</td>
<td>12 (25)</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>11 (23)</td>
<td>14 (29)</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>Beta blockers (hydrophilic)</td>
<td>3 (6)</td>
<td>5 (10)</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

+, Positive effect; –, negative effect.

performance in some studies (Kalra et al., 1994). In contrast, ACE inhibitors, calcium channel antagonists, and cholesterol lowering medication are considered to enhance cognitive performance (Riedel and Jolles, 1996). For example, ACE inhibitors are thought to have a direct effect on angiotensin receptors in the brain, and via inhibition of angiotensin II, stimulate acetylcholine turnover, enhancing cognition through this mechanism (Lines et al., 1991; O’Brien and Bulpitt, 1995). Calcium antagonists are thought to enhance cognition by causing dilatation of cerebral blood vessels and an increase in cerebral blood flow (Fletcher and Bulpitt, 1992). Cholesterol-lowering agents are thought to act by preventing cerebral blood flow abnormalities (Cutler et al., 1995). However, the clinical evidence for the cognition-enhancing potential of these drugs in humans is not convincing.

It remains therefore to be established what the effect of psychoactive medication on cognition actually is. There is no strong evidence that the drugs used can explain the difference in cognitive profile between the patients and control group. This also applies to the two MI patients groups. Of the psychoactive drugs mentioned only the medication of two was different between the depressed and non-depressed MI patients (Mantel–Haenszel chi-square), viz. benzodiazepines and cholesterol lowering drugs (Table 3). Benzodiazepines and cholesterol lowering drugs were given to, respectively, more and less depressed MI patients when compared to those given to the number of non-depressed MI patients. These two findings, however, would suggest an impaired cognitive performance in depressed MI patients, which was not the case. Moreover, even less is known about the possible interactions of these psychoactive substances and their putative effects on cognition. Future studies could address this problem by selecting more homogeneous patient groups, at least in terms of their prescribed psychoactive medications.

In the present study all patients experienced an MI without cardiac arrest. Therefore, it is unlikely that they suffered from cerebral hypoxia, hippocampus damage or damage to other medial temporal lobe structures. Even if these structures were damaged a worse memory performance was expected which is the opposite to the present findings.

This is the first study looking at cognitive function in depressed MI patients. An (expected) slower performance on a measure of simple cognitive speed (‘psychomotor retardation’) was found. However, attention, sensorimotor speed and speed of general information processing were not affected and memory function appeared to be even improved in (depressed) MI patients. In order to find an explanation for this finding, future research should study personality traits and coping mechanisms in relation to cognitive performance in this population.

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References


