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Research report

Memory impairment in patients with late-onset major depression: The effect of antidepressant therapy

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Abstract

Background: Cognitive deficits have been described in patients with major depression (MD), although many aspects remain unsettled.
Method: During an episode of MD and after remission we used tasks exploring attention, implicit, anterograde and retrograde memory to investigate 48 drug-free patients aged over 50 years without dementia, comparing them with 15 normal volunteer controls (NC). We also evaluated the effect of antidepressant therapy (ADT) with fluoxetine (F) or reboxetine (R) at baseline (T0) and six months later (T6).
Results: 42 patients completed the study and 6 dropped out; 33 patients were considered "Remitters" (RP) (17 F pts and 16 R pts). At T0, the entire group of MD patients (MDP) had worse performances than NC in Mini Mental Status Examination (MMSE), Wechsler Memory Scale (WMS) total score (TS), in a few subtests of WMS and in autobiographical memory. RP at T0 had the same impaired tasks and at T6 had significantly improved in MMSE, WMS. TS and many memory tests but they still differed from NC in a few complex tasks requiring more cognitive effort.
Limitations: The effects and differences between F and R must be viewed with caution considering the relatively small sample; only attention and memory were investigated.
Conclusions: Our findings confirm a negative effect of depression on memory with a significant but incomplete improvement after remission and without differences between F and R. We speculate that both a "state" and a "trait" depressive component underlie this memory impairment.

Keywords: Depression; Cognitive functions; Memory; Antidepressant therapy; Fluoxetine; Reboxetine

1. Introduction

The relation between depression and cognitive functions has been described, namely the effect on psychomotor performance, attention, memory and executive functions (Caligiuri and Ellwanger, 2000; Gallassi et al., 2001; Austin et al., 2001; Lockwood et al., 2002; Fossati et al., 2002; Porter et al., 2003; Weilland-Fiedler et al., 2004), although not all depressed patients show cognitive deficits and many aspects remain controversial (Austin et al., 1999). The influence of age, other cognitive dysfunctions (especially executives ones), severity and type of depression

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(i.e. with or without melancholia), single or multiples episodes, comorbidity and the effect of antidepressant therapy (ADT) on memory performance has not been fully clarified (Gallassi et al., 2001; Porter et al., 2003). There are many theories on how depression affects various memory components (implicit and explicit, anterograde and retrograde), with a possible dissociation among them (Isley et al., 1995). The congruence between affective tonality of memorandum and mood was postulated (Teasdale and Taylor, 1981) or denied (Bazin et al., 1994) and it was debated whether cognitive disturbances induced by depression are due to a "state" (Fromholt et al., 1995) or rather a "trait" depressive condition (Moffot et al., 1994).

Patients with depression arising in adult-senile age or so called "late-onset depression" have been considered a heterogeneous biological group (Krishnan et al., 1995), frequently associated with neurological illness (Cummings, 1992), especially cerebrovascular disease (Krishnan et al., 1995; Alexopulos, 1989), neuroradiological changes (Lasser et al., 1996) and a more prevalent cognitive impairment (Salloway et al., 1996; Lockwood et al., 2002). Nevertheless, others found no clinical and cognitive differences between early and late onset depressed patients (Brodaty et al., 2001).

The aim of the present study was to investigate memory in major depressed patients (MDP) in adult-senile age before and after remission of depression. In addition, we compared the antidepressant (AD) efficacy of fluoxetine (F) and reboxetine (R) to determine if agents with selective serotonin (5-HT) (F) or norepinephrine (NE) (R) reuptake inhibition have different effects on cognitive functions in depressed patients.

2. Patients and methods

We selected outpatients among those consecutively examined over an 18 month period at the "Center for Mood and Anxiety Disorders" of the Institute of Psychiatry, University of Bologna. Patients had to be over 50 years and have MD (single episode or recurrent) diagnosed according to the criteria of DSM IV-TR (American Psychiatric Association, 1994). Exclusion criteria were: global mental deterioration or neurological and internal diseases (i.e. patients responding to DSM-IV criteria for dementia and with a comorbid medical diagnosis), a lifetime diagnosis of schizophrenia or recent history of alcohol/substance abuse. All patients had been psychotropic medication-free for at least 6 weeks before recruitment (patients taking other medication active in the central nervous system were excluded; only a low dosage of benzodiazepines assumed continuously for a long time were admitted i.e. lorazepam 1 mg/daily). Out of a total number of 217 patients taken into account over the 18 month period, 48 met the selection criteria and were enrolled.

Neuropsychological examination was performed at the "Centre for the Neurological Study of Cerebral Ageing" at the Neurological Sciences Department of the same University where a control group of 15 healthy volunteer controls (NC) matched for age and education level was also examined. Sex, age and educational level of the patients and controls are reported in Table 1; no

Table 1
Demographic parameters of the various groups of patients and controls at T0

Groups	*N*	Sex (M/F)	Age		Schooling		MMSE	
			Mean	SD	Mean	SD	Mean	SD
Controls	15	6/9	69.33	5.49	7.07	3.77	28.33	1.30
Patients	48	12/36	67.54	8.08	7.15	3.39	25.75**	9.3
Remitters	33	8/25	66.73	8.10	7.06	3.33	25.76**	.86
Non responders	9	1/8	69.44	7.63	7.44	3.90	25.89**	.78
Drop-outs	6	3/3	69.17	9.32	7.17	3.48	25.50	1.51
Patients F	24	4/20	67.33	7.65	6.79	3.03	25.67**	0.96
Patients R	24	8/16	67.75	8.65	7.50	3.74	25.83**	0.91
Remitters F	17	3/14	66.35	7.43	6.88	3.21	25.76**	.97
Remitters R	16	5/11	67.12	8.98	7.25	3.55	25.75**	.77
Non responders F	4	1/3	67.75	.95	6.50	3.10	25.50*	1.00
Non responders R	5	0/5	70.80	10.52	8.20	4.65	26.20*	.44
Drop-outs F	3	0/3	72.33	13.57	6.67	2.88	25.33*	1.15
Drop-outs R	3	3/0	66.00	1.73	7.67	4.61	25.67	2.08
Total	63	18/45	67.97	7.54	7.13	3.44	26.27	1.44

∗Differences in comparison to controls; $^{**}p<0.001$; $^{*}p<0.01$.
Legend: F: Fluoxetine; R: Reboxetine.