



Review

Cognitive impairment in major depression

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ABSTRACT

In the past decade, a growing bulk of evidence has accumulated to suggest that patients suffering from major depression (MD) present some cognitive disturbances, such as impairment in attention, working memory, and executive function, including cognitive inhibition, problem- and task-planning. If the results of short-term memory assessment in depressed patients are equivocal, a general consensus exists that memory problems are secondary to attentional dysfunctions, and reflect the inability to concentrate. Moreover, both unipolar and bipolar patients show evidence of impaired verbal learning that has been commonly interpreted as reflecting an inability to transfer information from short-term to long-term storage. According to some authors, there would be a gender-related as well age-related specificity of some disturbances. Depressed patients also show impairments of executive functions and their recent exploration through brain imaging techniques has recently permitted to formulate some general hypotheses on the possible involvement of different brain areas in MD.

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1. Introduction

Major depression (MD) unquestionably may affect the ability to think, concentrate, make decision, formulate ideas, reason, and remember. Other cognitive symptoms typical of MD are represented by negative self-evaluation, worthlessness, thoughts of death, suicidal ideation, ruminative thinking over minor past failings, delusions (50% of patients tend to focus on fixed ideas of guilt and sinfulness, poverty, somatic concerns, and feelings of persecution), and hallucinations (auditory are more common than the visual one, in 20% of the patients).

Less clear are the nature and extent of such disturbances, as well as their specificity to affective illness, their etiology, or their existence before the onset of the symptoms. The degree of progression, chronicity, and reversibility of cognitive impairment in treated or untreated MD patients is, likewise, inadequately understood. Problems of particular significance arise when attempting to distinguish between general factors that might account for intellectual impairment across psychiatric, psychological or medical conditions – e.g., distractibility, attention, fatigue, or motivation – and those specific to MD, like lateralization differences.

Cognitive dysfunctions are generally assessed by a neuropsychological examination including an interview of the patient's background and present situation, a behavioral observation, and the administration of a battery of neuropsychological tests. Data obtained are useful to treatment planning, to assess the efficacy of the treatment, as well as

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to differentiate deficits which are state-dependent from those that may be trait-related or vulnerability markers of the disorder.

The aim of this paper is to review the main data on cognitive disturbances in MD, with a focus on findings derived from neuropsychological tests exploring general intelligence, verbal memory, non-verbal memory, psychomotor skills, attention and executive functions.

2. General intelligence

The most used test batteries to estimate general intelligence are the Intelligence Quotient (IQ), the Wechsler Adult Intelligence Scale (WAIS), the Wide Range Achievement Test (WRAT), and the National Adult Reading Test (NART). General intelligence seems to be impaired in depression, however, it is not considered a primary disturbance, but rather the result of impairment of memory, psychomotor skills or attention. Data on premorbid intellectual level in patients affected by mood disorders and family members are scarce and, therefore the interpretation of pre- and post-illness functioning data is difficult. Early studies of intelligence in drug-free patients showed general intellectual impairment in bipolar patients only, but the cognitive deterioration was reversible (Wittman, 1933; Rapaport, 1946; Shapiro and Nelson, 1955), as patients in remission performed better than during the episode (Miller, 1975; Sackeim and Steif, 1988). However, at the WAIS, manic and depressed patients presented the same score (Abrams and Taylor, 1981; Donnelly et al., 1982).

3. Memory

Verbal memory is usually assessed by the California Verbal Learning Test (CVLT), the Wechsler Memory Scale (WMS) and the Rey Auditory Verbal Learning Test (RAVLT). Non-verbal (visuo-spatial) memory can be evaluated by two neuropsychological tests, the Rey–Osterrieth Complex Figure Test (ROCF) and the Benton Visual Retention Test (BVRT). These instruments assess visual perception, visual memory, and visuo-constructive abilities, as well as perception of spatial relations and memory for newly learned material. Depressed patients show particular difficulties with memory tasks requiring sustained effort, such as list learning and free recall, which are qualitatively different from tasks carried out automatically (e.g., memory for spatial events). Memory deficits seem to be independent from the patients' current mood state, but they are trait-related or linked to the course (Bartfai et al., 1991; MacQueen et al., 2002). Data of short-term memory assessment in depression are equivocal. Some studies reported minimal impairment, while others described short-term memory problems (Breslow et al., 1980; Steif et al., 1986a). However, a wide agreement exists that it is secondary to other dysfunctions, such as attentional deficit, cognitive interference, negative schemata, lack of motivation and impaired cognitive initiative, rather than the ability of short-term memory storage (Sackeim and Steif, 1988; Ellis, 1990). Several studies reported a decreased ability to acquire new information, without a reduction in the ability to retain it in MD patients, because depressed states are frequently accompanied by intrusive, irrelevant and/or pessimistic thoughts that decrease memory (Cronholm and Ottosson, 1961; Sternberg and Jarvik, 1976; Strömberg, 1977; Steif et al., 1986b). Impaired verbal learning was described in both unipolar and bipolar patients: this has been interpreted as reflecting an inability to transfer information from short-term to long-term storage (Henry et al., 1971, 1973; Sackeim and Steif, 1988), but it remains unclear if these deficits represent a state-dependent changes or reflect underlying trait characteristics.

4. Psychomotor skills

Psychomotor retardation is not necessarily typical of depression, however, when present, it is one of its most dramatic symptoms. It can be demonstrated in depressed patients in different ways, including

reaction time measures, information processing speed, writing and drawing tasks, and other measures.

Cognitive and psychomotor speed are commonly slowed in depression and seem more typical of older than younger patients (Sabbe et al., 1999; Caligiuri and Ellwanger, 2000; Tsourtos et al., 2002; Porter et al., 2003). The majority of depressed patients report decreased speed of thought and a high incidence of psychomotor retardation. There is some evidence that depressed patients tend to underestimate their performance on motor speed tests and overestimate their degree of retardation, however slowed thinking and movement are central to the depressive state (Morgan, 1967; Colbert and Harrow, 1967; Miller, 1975). Cognitive and psychomotor activity include three components: reaction time, speech and psychomotor activity.

4.1. Reaction time

Different studies highlighted that depressed patients show slower reaction times than do normal subjects, although bipolar and “endogenously depressed” unipolar patients exhibit faster reaction times than chronic schizophrenic patients (Huston and Senf, 1952; Hall and Stride, 1954). Slowed reaction time is not specific to depression and is probably more likely to reflect the severity of illness. It seems that reaction time performance deteriorates more quickly in depressed than in normal subjects and that the last reaction time in a series is slower than the first. Several explanations have been offered for these data: patients affected by depression may have an increased susceptibility to fatigue, may be lacking in sustained motivation, may be unable to maintain concentration, and may be lacking in physiological preparedness to react (Miller, 1975).

4.2. Speech

Depressed patients may show slowed speech, with a low rate of total speech rate and a high rate of silence (Pope et al., 1970) and long pause times (Szabadi et al., 1976; Greden et al., 1979, 1981; Greden and Carroll, 1980). One study reported even a diurnal variation in the speech rate, with a greater slowing in the morning (Greden et al., 1979).

4.3. Psychomotor activity

Several studies showed a decrease of psychomotor activity in depressed patients. Bipolar depressed patients tend to present more retardation, and unipolar patients appear relatively more active (Kotin and Goodwin, 1972; Kupfer et al., 1974; Weiss et al., 1974; Blackburn, 1975; Dunner et al., 1967). An increase in nighttime psychomotor activity Wolfe et al., 1987; related to the development of psychotic symptoms (Weiss et al., 1974).

5. Executive functions

The executive system is thought to be involved in handling novel situations outside the domain of some of automatic psychological processes that could be explained by reproduction of learned schemas or set behaviors. The novel situations are those that involve planning or decision making; those that involve error correction or troubleshooting; situations where responses are not well-learned or contain novel sequences of action; dangerous or technically difficult situations; and situations which require the overcoming of a strong habitual response or resisting temptation. The executive functions are often invoked when it is necessary to override responses that may otherwise be automatically elicited by stimuli in the external environment. For example, on being presented with a potentially rewarding stimulus, such as a tasty piece of chocolate cake, the automatic response might be to take a bite. However, where this

behavior is in contrast with internal plans (such as having decided not to eat chocolate cake while on a diet), the executive functions might be engaged to inhibit this response. The neural mechanisms by which the executive functions are implemented are a topic of ongoing debate in the field of cognitive neuroscience. In addition, they are involved in the learning of social skills, in particular when it is necessary to be sensitive towards the others.

Attention and executive functions are usually rated by the Wisconsin Card Sorting Task (WCST, Bergh, 1948) that explores abstract ability, namely the ability to shift cognitive strategies in response to changing environmental conditions, by assessing the kind of executive functioning which involves strategic planning, organized searching and the ability to use environmental feedback to modify cognitive sets. Another test widely used is the Verbal Associative Fluency Test (FAS, Benton and Hamsher, 1989) that evaluates the verbal fluency for phonological stimuli that is the ability to produce fluent and spontaneous language without unnecessary pauses or being unable to find more appropriate words (Silberman et al., 1983).

Performance on measures of executive functioning tend to be impaired in depressed patients of different ages, although not to the degree found in schizophrenic patients (Fossati et al., 1999; Stordal et al., 2004). At the WCST, depressed patients show a certain difficulty with hypothesis testing and cognitive flexibility. This state of cognitive rigidity can prevent patients from coping with life events, thus perpetuating depressed mood by prolonging stress exposure. Such studies, moreover, highlight the fragility of their subjective responses, the interaction between cognition and emotional response and an overreaction to the mistakes they make, e.g., they respond “catastrophically” to errors: a mistake, even on a simple task of sustained attention, seems to heighten their subjective sense of failure (Farrin et al., 2003).

Some recent brain imaging findings, while showing reduced blood flow, particularly in the medial prefrontal cortex and dorsal anterior cingulate cortex, suggest that these brain areas may underlie executive function impairments in MD and highlight the need of further studies on this intriguing topic (Mayberg, 2003).

6. Cognitive impairment and age or gender

Several studies reported that young depressed patients show deficits in some components of executive functioning, such as attention, short-term and working memory, and in psychomotor skills, while data on verbal memory and learning functions are controversial (Savard et al., 1980; Mormont, 1984; Rubinow et al., 1984; Castaneda et al., 2008). On the contrary, in elderly patients suffering from MD, memory difficulties may be the chief complaint and may be mistaken for early signs of a dementia (“pseudodementia”). In addition, other disturbances of executive functions have been described in late-onset depression, in particular impairment in planning, sequencing, organizing and abstracting, sometimes associated with relapse and recurrence with residual symptoms (Pislarj et al., 2008).

The cognitive impairment of older depressed patients with late-onset as opposed to early-onset illness may show important differences, in that patients with early onset may suffer predominantly from impaired episodic memory, and those with late onset mainly from reductions of executive function and processing speed (Herrmann et al., 2007).

According to some authors, there would be a gender-related specificity, since depressed women appear to perform significantly worse on the tests of cognitive threshold and in the one of visual recall, as compared with depressed men (Sárosi et al., 2008).

7. Conclusions

There is now a consistent, albeit not exhaustive, literature on cognitive impairments in MD. The most consistent findings are those related to memory disturbances as a result of attention deficit, and of

executive functions that highlight a certain rigidity in shifting the focus. A wide agreement exists also on the notion that there exists an age-related specificity in some cognitive symptoms, as older patients may show a marked psychomotor retardation and memory difficulties.

Interestingly, a correlation between depression severity and the magnitude of cognitive deficits has been reported in young adulthood patients with major depression since a decade, and how these deficits disappear after the clinical remission (Basso and Bornstein, 1999; Merriam et al., 1999; Egeland et al., 2003). However, this notion is challenged by a recent study describing that some cognitive dysfunctions, particularly in executive functioning, verbal learning and memory, persist amongst remitted young adult depressed patients (Smith et al., 2006), and may represent a trait marker of the disorder. In any case, further studies are needed to better explore the cognitive impairments in MD, as well as their relationships to clinical and course features.

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