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IMPLICATIONS OF COGNITIVE IMPAIRMENT ON SEVERAL ASPECTS OF FUNCTIONALITY AND QUALITY OF LIFE IN MAJOR DEPRESSED PATIENTS

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Abstract

Background: Depression is considered one of the main determinants of economic deficits by limiting the functionality of the patients. Our study aimed to longitudinally assess the implications of cognitive deficits on functionality and quality of life for patients with major depressive disorder, during an acute depressive episode and also during euthymia.

Materials and methods: Our study included 65 patients diagnosed with recurrent major depressive disorder. The quality of life domains were tested during an acute episode and after 6 months of euthymia. For both phases, the results were correlated with 35 healthy controls.

Results: Patients during an acute depressive episode who performed better at the evaluation of psychomotor speed reported higher levels of quality of life. For verbal memory and psychomotor speed, statistically significant correlations were identified with the level of functionality and the general living environment. During the euthymic phase, significant associations were identified between psychomotor speed and the global level of functionality. Also, memory and psychomotor coordination presented significant correlations with quality of life.

Conclusions: Results from our study confirmed the relationship between cognitive functions and functionality of patients with depressive disorder and the predictive value of psychomotor speed for the quality of life domains during both phases.

Keywords: cognitive impairment, functionality, quality of life, major depression, euthymia.

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Clinical research shows that major depressive disorder is one of the primary causes of dysfunction reflected by decreased productivity or absence from work, altered interpersonal and social relationships, and deteriorated health status, being responsible in the end for the low quality of life (Demyttenaere, 2006; Rock et al., 2014; Szmulewicz et al., 2018). Also, depression involves high economical costs for the individual and the community (Reischies & Neu, 2000). Comparative studies identified a higher degree of dysfunction in depressive disorder compared to the level of functionality's impairment of other chronic pathologies such as asthma, arthritis, or hypertension (Evans et al., 2014; Reed et al., 2018).

Over the last years, cognitive impairment has become recognized as an important characteristic of Major Depressive Disorder, explained by the presence of deficits in inhibitory processes, inability to make decisions and a decrease of communication skills to a suboptimal level. Patients tend towards isolation, thus affecting the quality of life (Fennig et al., 2002; Lam et al., 2009; Lam et al., 2012; Păunescu & Micluția, 2015). These deficits have been shown to persist even after the remission of affective symptoms, making it difficult to reintegrate the patient into the workplace after an absence caused by a depressive episode (Wang et al., 2014). Numerous studies have attempted to explain the increased level of disability in depression by the presence of cognitive deficits, which can also contribute to decreased quality of life and can influence occupational status, but other studies suggest the severity of symptoms as an important determinant of dysfunction in depression (Gallagher et al., 2007; Martinez-Aran et al., 2007).

Because the relationship between cognitive deficits and global functionality in recurrent depressive disorder is complicated due to the heterogeneity of depressive symptoms, multiple cognitive domains, and different areas of psychosocial functionality, we assumed in the present study that cognitive dysfunction could be a mediator of psychosocial limitations. The study aimed to longitudinally assess the implications of cognitive deficits on functionality and quality of life for patients with major depressive disorder, during an acute episode at the first assessment, which was subsequently followed by a second assessment, in euthymia, at 6 months from baseline. We expect some correlations between different variables on depressed patients and on healthy controls, as the functionality and the domains of life quality for patients diagnosed with recurrent depressive disorder to be influenced by the presence of cognitive deficits during the acute depressive episode and also this relationship to manifest during the euthymic phase.

Methods

Study Design

This study included 65 depressed patients that were admitted to the Psychiatric Hospital from Cluj-Napoca for a depressive episode, each patient was identified during his first day of hospitalization by his chart. The duration of admission differed from patient to patient in relationship with the severity of the illness and the response to treatment, but after discharge, each patient was clinically assessed for the depressive symptoms on a monthly basis. The second cognitive evaluation was performed at 6 months since a patient meet the euthymic inclusion criteria. Also, 35 healthy control subjects who requested medical certificates over 6 months at the same hospital, were included in the study.

Participants

Patients were of both genders, with ages between 18 and 60, with a minimum level of 8 years of education, who were currently experiencing a MDE (major depressive episode). Aiming to assess the longitudinal relationship between cognitive impairment and different life quality areas, all subjects were clinically and neurocognitively evaluated twice by the same evaluator, and the quality of life domains were tested during an acute depressive episode and after 6 months of euthymia. The inclusion criteria for depressive patients consisted of DSM-IV-TR and ICD-10 diagnosis of Major Depressive Disorder and Hamilton Depression Rating Scale (HAM-D) ≥ 8. For euthymic patients, the inclusion criterium was established by a HAM-D score ≤ 7. Subjects were excluded if they met the criteria for mental retardation, dementia, chronic alcoholism, or any other substance dependence, history of head trauma, or any current medical condition which could interfere with the level of cognitive performances. The patients' group was compared to 35 healthy control subjects who requested medical certificates over 6 months at the same Psychiatric hospital from Cluj-Napoca, who met the same exclusion criteria and matched by demographic characteristics. Before being admitted to the study all subjects had to give written informed consent. The study was approved by our university Ethics Committee.

Demographic and clinical data

Sociodemographic data (age, gender, education level) and other clinical information were collected through the combination of a clinical interview and data from medical records. First, patients were clinically assessed upon admission for a major depressive episode and the diagnosis was made according to DSM IV-TR and ICD-10 diagnosis criteria for recurrent depressive disorder and a major depressive episode. Additional inclusion criteria consisted of a HAM-D score ≥ 8. Absence of

any affective symptoms for six months and a HAM-D score ≤ 7 defined the remission state. In comparison with the outpatient population, all patients had more severe symptoms and episodes, because they were recruited while being hospitalized in an acute emergency ward.

Instruments

The cognitive domains were assessed with a battery of neuropsychological tests, called Brief Assessment of Cognition in Schizophrenia (BACS) (Clark et al., 2005) that was initially developed for schizophrenic patients in clinical trials. The scale has been shown to have a high degree of reliability, with a sensitivity in the evaluation of cognition similar to that of standard cognitive tests, in which the evaluation time is extended to 2 hours. As follows, the battery includes six different neurocognitive subtests for each specific cognitive domain:

Verbal memory – assessed with the List learning test (BACS), which analyzes the coding, organization, retention and then extraction of the newly presented information. The subject was read a list of 15 words at a rate of one word per second, and was asked to memorize as many of them as possible. The exam was repeated 5 times, and the final score corresponded to the number of words retained.

Working memory – evaluated by Digit sequencing test (BACS), from the short-term memory analyze, through a presentation to the subject series of numbers of increasing length and asked to repeat them starting with the shortest number and ending with the longest.

Attention and processing speed – was assessed with the Symbol coding test (BACS), at which subjects received a correspondence table between certain symbols with numbers from 1 to 9, they were asked to fill in the corresponding numbers next to a series of symbols as fast as they could within 90 seconds.

Verbal fluency- was evaluated by the Category instances test and controlled oral word association test (BACS), the subjects were asked to name in one minute as many words as possible, belonging to a given semantic category or words beginning with a certain letter.

Motor speed – was tested with the Token motor test (BACS), where patients were given 100 plastic chips and asked to place them in a stable container 8 cm high and 13 cm in diameter as fast as they could, within 60 seconds.

Executive functions – were assessed by the Tower of London (BACS), a test in which the patients specified the minimum number of moves by which the balls in one image could reach the same arrangement as in the other image.

Severity of depression was evaluated with the 17 items Hamilton scale (Hamilton, 1960) which is one of the most widely used clinician-administered depression assessment scale. It was designed to measure the effectiveness of antidepressant medication in clinical trials and became the gold standard measurement for depression (Alexpoulos et al., 2015). The internal consistency is 0.83, the accuracy of the results from one clinician to another is very high in terms

of the final score (0.80-0.98) and the accuracy of the retest is also very high (0.81) following the achievement by Janet Williams in 1988 of a Structured Interview Guide (Hamilton, 1960).

All four quality of life domains, such as physical health, mental health, social relationships, and general environment were evaluated with the WHOQOL – Bref and the functionality of each individual was assessed with GAF. The Global Functional Assessment Scale is a newer version of the Global Assessment Scale (GAS), published in DSM III-R in 1994. The scale provides an overall impression of the functionality based on a clinical judgment, being extremely useful when the clinical evolution of a patient must be evaluated in global terms, using a single measure. Psychological, social, and professional functioning is assessed, deterioration in functioning as a result of somatic complaints is not included. The maximum score is 100 and represents the healthy individual, and 1 represents the most affected individual. To calculate a GAF score, a single value will be chosen that best reflects the overall level of functioning of the individual. The application time of the scale is about 3 minutes. The WHOQOL – Bref is a shorter version that includes 26 items and 4 areas of evaluation. These are physical health, mental health, social relationships, and living environment, with a Cronbach's alpha coefficient ranging from 0.68 for social relationships to 0.82 for physical health. Therefore, this shorter version is a useful self-assessment scale with a high internal consistency, easily to be applied in a short time. This scale is validated on the population of Romania (Skevington et al., 2004; Taylor et al., 2004).

Statistical analysis

In the first part of the analysis, data were descriptively assessed, based on frequencies and ratios for the nominal variables and the most important descriptive statistics for the numerical ones. Means, medians, and standard deviations are provided for these variables through the article. To evaluate the relationship between cognitive performances and quality of life domains, correlation analysis was conducted (using Pearson's correlation coefficient), for both depressed and euthymic patients. Statistical significance was evaluated at the standard level of 5%. Statistical analysis was performed using IBM Statistical Package for Social Sciences 24 (SPPS) software, the Windows version.

Results

Clinical Characteristics

Table 1 presents data for both groups, depressed patients and healthy controls, who were matched for demographic characteristics: gender, age, and level of education.

Table 1. Demographic and clinical characteristics for the depressed group (n = 65) and the control group (n = 35)

Demographic and clinical aspects	Depressed patients (n = 65) mean/SD	Normal controls (n = 35) mean/SD
Age (in years)	48.48 (SD = 10.484)	41.20 (SD = 11.063)
		Sex
1. Male	n = 13 (20.00 %)	n = 8 (22.9 %)
2. Female	n = 52 (80.00 %)	n = 27 (77.1 %)
Level of education (years)	11.86 (SD = 3.115)	11.55 (SD = 2.708)
1. Gymnasium	n = 5 (7.7 %)	n = 2 (5.7 %)
2. Vocational school	n = 6 (9.2 %)	n = 2 (5.7 %)
3. High school	n = 34 (52.3 %)	n = 13 (37.1 %)
4. University education	n = 20 (30.8 %)	n = 18 (51.4 %)
HAM-D scores (depression)	23.20 (SD = 5.423)	–
HAM-D scores (euthymia)	3.73 (SD = 1.387)	0.74 (SD = 0.919)

HAM-D Hamilton Depression Rating Scale, SD standard deviation

Results obtained during the depression phase

During a depressive episode, correlations between cognitive performances and different quality of life domains, including global functionality, physical health, mental health, social relationships, and general environment, were obtained using the Pearson correlation test. The results are presented in Table 2.

Table 2. Correlations of mean scores between the cognitive functions and the domains of the WHOQOL scale - Brief and GAF scale, during a depressive episode

Cognitive function	Statistic Test	GAF	Physical health	Mental health	Social relationships	General environment
List learning test - try nr.1	Pears. Correl.	.099	.158	.103	.137	.013
	Sig.2-tailed	.432	.210	.416	.277	.921
List learning test - try nr.2	Pears. Correl.	.333**	.243	.167	.186	.233
	Sig.2-tailed	.007	.051	.184	.137	.061
List learning test - try nr.3	Pears. Correl.	.247*	.135	.097	.210	.252*
	Sig.2-tailed	.047	.283	.442	.093	.043
List learning test - try nr.4	Pears. Correl.	.178	.063	.001	.134	.195
	Sig.2-tailed	.155	.615	.996	.288	.119
List learning test - try nr.5	Pears. Correl.	.060	.110	-.004	.187	.236
	Sig.2-tailed	.635	.384	.972	.135	.058
Sequencing test	Pears. Correl.	.178	-.009	-.073	.056	.204
	Sig.2-tailed	.155	.946	.562	.660	.103
Symbol coding	Pears. Correl.	.051	.118	.063	.153	.110
	Sig.2-tailed	.689	.349	.616	.223	.383
Category instances test	Pears. Correl.	.160	.145	.038	.213	.170
	Sig.2-tailed	.204	.249	.766	.088	.177
Controlled oral word association test-first try	Pears. Correl.	.069	-.017	-.055	.014	-.009
	Sig.2-tailed	.582	.891	.664	.913	.945
	Pears. Correl.	.145	.096	.052	.093	.088

Cognitive function	Statistic Test	GAF	Physical health	Mental health	Social relationships	General environment
Controlled oral word association test -second try	Sig.2-tailed	.250	.449	.678	.462	.486
Token motor test -token left on the table	Pears. Correl.	-.264*	-.197	-.212	-.086	-.286*
	Sig.2-tailed	.033	.115	.089	.495	.021
Token motor test -total token in the recipient	Pears. Correl.	.287*	.181	.198	.069	.276*
	Sig.2-tailed	.020	.148	.114	.585	.026
Token motor test -token incorrectly put in recipient	Pears. Correl.	-.190	-.138	-.158	.088	-.193
	Sig.2-tailed	.130	.273	.208	.486	.123
Token motor test -token correctly put in recipient	Pears. Correl.	.242	.194	.202	.152	.249*
	Sig.2-tailed	.052	.122	.106	.226	.046
Tower of London	Pears. Correl.	.022	-.063	.010	-.083	-.093
	Sig.2-tailed	.860	.619	.934	.511	.463

Pears. Correl. – Pearson Correlation; Sig- significance, WHOQOL – Bref- World Health Organization Quality-of-Life Scale, GAF- Global Assessment of Functioning Scale, nr- number.

Statistically significant correlations ($p < .05$) were identified between the global level of functionality and the cognitive domains represented by verbal memory and psychomotor speed. In both cases, the Pearson correlation coefficients were positive.

For verbal memory, evaluated with the List learning test, statistically significant associations ($p < .05$) were identified with one of the quality of life domains. Pearson correlation coefficient = .252; $p < .05$, displayed a positive association between the third try of verbal memory testing and the general environment domain.

Psychomotor speed was statistically significantly correlated ($p < .05$) with the quality of life domain represented by the general living environment. For the Token motor test, the Pearson correlation coefficient was positive = .249 in the evaluation of tokens correctly placed in the recipient and negative = -.286 for the number of tokens left on the table.

The cognitive functions: working memory evaluated by the Sequencing test, attention and information processing speed assessed with symbol coding test, verbal fluency tested with category instances and controlled oral word association, and the executive functions assessed with Tower of London, were not correlated with any of the quality of life domains.

Results obtained during the euthymic phase

Within the euthymic phase, correlations between the cognitive scores and the domains of quality of life were obtained using the Pearson correlation test. The quality of life domains and the cognitive functions examined were identical to those

examined during the acute depressive episode, 6 months earlier. The results are presented in Table 3.

Table 3. Correlations of means scores between the cognitive functions and the domains of the WHOQOL scale - Brief and GAF scale, during an euthymic phase

		GAF	Physical health	Mental health	Social relationships	General environment
List learning test - try nr.1	Pears. Correl.	-.187	-.211	-.239	-.364**	-.145
	Sig. 2-tailed	.188	.138	.092	.009	.309
List learning test - try nr.2	Pears. Correl.	-.105	-.142	-.141	-.279*	-.020
	Sig. 2-tailed	.461	.321	.324	.048	.890
List learning test - try nr.3	Pears. Correl.	-.146	-.341*	-.293*	-.468**	-.168
	Sig. 2-tailed	.308	.014	.037	.001	.239
List learning test - try nr.4	Pears. Correl.	-.252	-.367**	-.379**	-.522**	-.241
	Sig. 2-tailed	.074	.008	.006	.000	.089
List learning test - try nr.5	Pears. Correl.	-.213	-.265	-.329*	-.428**	-.268
	Sig. 2-tailed	.134	.060	.019	.002	.058
Sequencing test	Pears. Correl.	-.090	.323*	.173	.082	.263
	Sig. 2-tailed	.531	.021	.226	.566	.062
Symbol coding	Pears. Correl.	.097	.074	-.033	.035	.037
	Sig. 2-tailed	.500	.607	.819	.808	.798
Category instances test	Pears. Correl.	-.029	-.115	-.095	-.197	-.065
	Sig. 2-tailed	.842	.421	.507	.165	.651
Controlled oral word association test-first try	Pears. Correl.	.114	.088	-.040	-.017	.036
	Sig. 2-tailed	.427	.538	.778	.904	.804
Controlled oral word association test-second try	Pears. Correl.	.141	.075	-.012	-.062	.055
	Sig. 2-tailed	.325	.603	.935	.667	.702
Token motor test -token left on the table	Pears. Correl.	-.403**	-.287*	-.367**	-.224	-.443**
	Sig. 2-tailed	.003	.041	.008	.114	.001
Token motor test -total token in the recipient	Pears. Correl.	.403**	.287*	.367**	.224	.443**
	Sig. 2-tailed	.003	.041	.008	.114	.001
Token motor test- token incorrectly put in recipient	Pears. Correl.	-.302*	-.322*	-.431**	-.339*	-.331*
	Sig. 2-tailed	.031	.021	.002	.015	.018
Token motor test- token correctly put in recipient	Pears. Correl.	.416**	.319*	.418**	.260	.471**
	Sig. 2-tailed	.002	.023	.002	.065	.000
Tower of London	Pears. Correl.	.111	-.006	.148	.219	.015
	Sig. 2-tailed	.437	.968	.301	.122	.917

Pears. Correl. – Pearson Correlation; Sig- significance, WHOQOL – Bref- World Health Organization Quality-of-Life Scale, GAF- Global Assessment of Functioning Scale, nr- number.

Statistically significant associations ($p < .05$) were identified between the cognitive domain of psychomotor speed and the global level of functionality in

euthymic patients. For this association the Pearson coefficient was positive (Pearson coefficient = .416), so euthymic patients who performed well at the token motor test associated increased levels of functionality.

Euthymic patients who performed well at the psychomotor speed evaluation associated increased levels of functionality, as well as satisfaction in the areas of physical health, mental health, social relationships, and general environment. A higher level of quality in the field of physical health was obtained by the euthymic subjects who had good working memory.

For the Sequence test, a single statistically significant correlation with the physical health domain was identified. Pearson correlation coefficient was positive = .323, indicating that euthymic patients who managed to correctly reproduce an increased number of strings for the working memory evaluation reported a higher level of quality life in the field of physical health.

Correlation analyses showed that psychomotor speed was statistically significantly associated with all quality of life domains tested. Specifically, for the subtest total tokens put in the recipient of Token motor test, which evaluates the psychomotor speed, for all the statistically significant associations ($p < .05$) were identified positive Pearson coefficients, which showed that euthymic patients who had less psychomotor speed impairment reported higher levels of satisfaction and quality of life.

No significant statistical correlations were found between verbal fluency, executive functions or attention and information processing speed with any of the quality life domains.

Discussions

Numerous reports have described the association between cognitive deficits and the influence they have on different areas of life satisfaction and quality of life (Druss et al., 2009; Maruff et al., 2009). The present study is based on a six months follow-up design; it is a naturalistic and longitudinal study, performed for a better understanding of the relationship dynamics between cognitive impairment and life quality in major depressed patients.

The results from the present study identified that depressed patients who perform better in areas of verbal memory and psychomotor speed associated higher levels of functionality ($p < 0.05$), showing that during an acute depressive episode the level of functionality is influenced by the presence of cognitive deficits. A similar result was obtained by another study, which concluded that the level of functional disability for patients having a depressive episode was strongly influenced by the presence of cognitive deficits, in domains such as psychomotor speed and verbal memory (Naismith et al., 2007).

Also, our data showed that, during the euthymic phase, functionality was influenced by the scores obtained on psychomotor speed evaluation, proving that this cognitive field has an important role for an optimal level of functionality. These findings are consistent with those reported by Jaeger et al., 2006, who identified strong correlations between attention, verbal memory, and psychomotor speed with the degree of functional disability during an acute depressive episode. Also, the scores obtained in testing psychomotor speed were predictive for the functional outcome on the subsequent examination at six months. A considerable enhancement was found in the level of functionality in those who showed improvement in cognitive deficits (Jaeger et al., 2006). On the other hand, Airaksinen et al., 2006, in a study that assessed the trajectory of episodic memory deficits and their correlation with the degree of functionality in depression, observed improvements in functionality although memory deficits were still present in the euthymic phase. It can be assumed that certain aspects of functionality appear to be dependent on the presence of affective symptoms and that functionality may improve while the depressive episode remits (Airaksinen et al., 2006).

Our results showed that patients during an acute depressive episode who perform better at the evaluation of psychomotor speed reported higher levels of quality of life for the general living environment domain. But no significant statistical correlations were found for the other cognitive functions tested, such as working memory, verbal fluency, executive functions, attention, or information processing speed, with any of the quality of life domains. These findings are not in line with those reported by McCall at al., which identified the field of social relationships as being significantly correlated with the scores obtained from the verbal memory test in a group of depressed subjects (Greer et al., 2013). Moreover, a study conducted by Greer et al., which also assessed the correlations between quality of life and cognition, using the CANTAB battery, obtained significant correlations between working memory and physical health, as well as between the field of social relations and executive functions (McCall & Dunn, 2003). Other research found, besides the correlation between psychomotor speed and general environment domain, other cognitive functions associated with quality of life areas (Naismith et al., 2007).

Among the cognitive functions that were evaluated in the current study during the euthymic phase, only memory and psychomotor coordination presented statistically significant correlations with the domains of quality of life at a level of statistical significance of 5%. Therefore, euthymic patients who performed better in the cognitive domain of working memory reported a better level of quality of life in the field of physical health. Comparing with other chronic somatic pathologies, such as migraine, obesity, diabetes, or pain, studies report even a higher level of impairment in the field of physical health for depression (Buist-Bouwman et al., 2008). Psychomotor speed was positively correlated with the quality of life, so a higher performance in this cognitive domain was associated with a higher level of quality of life. The results obtained in the study are similar to those described by

Shimizu et al., who concluded that although depressive symptoms remit, cognitive functioning can influence the quality of life, as he observed a significant association between verbal memory, psychomotor speed and the quality of life perceived by the subjects (Shimizu et al., 2013). Furthermore, the study conducted by Godard et al. identified significant correlations between the social domain of quality of life and cognitive functions represented by attention, psychomotor speed, and executive functions, in an euthymic patient group known with major depressive disorder (Godard et al., 2011).

Limitations

Despite the fact that some results obtained are congruent with the data published in the literature, it is necessary to mention the limits of the presented study. An important aspect would be the relatively small size of some of the examined subgroups, that has implication on decreasing the statistical power of the study. A second limitation could be the fact that some of the questionnaires applied are self-assessment, so there is the possibility that participants could lie, disguise the aspects and symptoms assessed or simply respond according to expectations and not the actual reality. In current clinical practice there are often different clinical parameters that from one point of view can individualize the patient, but also can make it difficult to analyze in part, the influence of each of them on cognition or functionality, because they cannot be calculated with accuracy.

Implication and future directions

One of the benefits of these results sustain the admission that cognitive impairment is present in depressed patients with different implications on functionality and quality of life and translate this knowledge in possible therapeutic interventions targeting the cognitive deficits. Recurrent depressive disorder is associated with an overall impairment of functionality and various areas of quality of life that the individual experiences, involving many areas such as general health, both physical and mental, decreased life satisfaction, interpersonal relationships, having the frequent consequence of losing a job, which determines a real disability. In connection with job related difficulties future studies should be designed to investigate the level of productivity, or absenteeism from work, regarding the associated cognitive deficits for major depressed patients.

Conclusions

Following the results obtained in the present study, the relationship between cognitive functions and quality of life is confirmed for patients diagnosed with

recurrent depressive disorder. During an acute depressive episode, those who obtained better scores at the evaluation of verbal memory and psychomotor speed presented higher levels of functionality and quality of life for the general living environment. Euthymic patients who performed well at the psychomotor speed evaluation associated increased levels of functionality, as well as satisfaction in the areas of physical health, mental health, social relationships, and general environment. Also, a higher level of quality in the field of physical health was obtained by the euthymic subjects who had good working memory.

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