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Neurocognitive Characteristics of Major Depressive Disorder Measured by Degraded Continuous Performance Test

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ABSTRACT

Background: Depression is a prevalent mental health problem, representing the third major cause of disability worldwide. Besides mood symptoms, depression is characterized by cognitive impairment, which is believed to be one variable that reduces recovery, influences recurrence rates, and increases the risk of chronicity. However, the characteristics of cognitive impairment among depressive patients have not been sufficiently investigated so far, and clinical practice lacks objective tools to detect and measure it.

Objectives: The study aims to investigate the neurocognitive patterns of major depressive disorder (MDD) and the association of those patterns with clinical symptoms, particularly with levels of daily functioning.

Methods: To objectively measure neurocognitive impairment and the nature of cognitive functioning, a 12-min duration computerized degraded continuous performance test (CPT-DS) with three blocks (720 digits, 10% targets, degradation 40%) was administered to two groups: a study group consisting of patients with recurrent moderate MDD episodes with similar motor retardation, and a control group of healthy participants. Nonparametric correlational techniques (Spearman), Student's t-tests, or nonparametric Mann-Whitney (M-W) U-tests were applied for statistical analysis.

Results: The following variables were analyzed: d' value (average reaction time and coefficient of variance for both correct reactions and commission errors), omission and commission errors, and the clinical parameter "Work and Activities" (item seven on HDRS). Depressed patients showed a significantly lower d' value and more omission errors than healthy controls. The number of omission errors was significantly positively correlated with the score on HDRS item seven. The d' value was negatively correlated with the identical item scores.

Conclusions: In conclusion, our study showed that the CPT, which runs longer and requires more effort to complete the task (degraded version), is relatively sensitive in detecting the specific characteristics of cognitive impairment in depression. Some specific symptoms of depression, indicating the daily functioning of patients, are linked to decreased sustainability of attention and vigilance. This demonstrates that cognitive impairment is a different essential factor of depression, affecting the functioning of patients and emphasizing the need to introduce novel treatment strategies specifically targeting cognitive impairment in patients with MDD.

Keywords: Continuous performance test, CPT; major depressive disorder, MDD; neurocognitive impairment.

INTRODUCTION

During the last decades, a large number of studies demonstrated that depressed patients showed impairment in a variety of neuropsychological tasks in comparison to healthy controls.[1,2,3] According to the DSM-V (APA 213), a diminished ability to think or concentrate is one of the common symptoms of a depressive state. Several mechanisms are proposed to underlie these cognitive deficits. Based on their review of studies on cognitive processing, Hartlage and Cohen suggested that depressed patients have a reduced capacity to process information, leading to difficulties with effortful cognitive tasks.[4,5] Several authors suggested that specific cognitive deficits (e.g., memory impairment, problem-solving, and learning) in depressed patients cannot be separated from general deficits of motivation and attention.[6,7] Several neuroimaging studies found an impairment of brain functions in depressed patients with particular involvement of the frontal lobes, which are generally thought to play an essential role in cognitive performance.[1,8] This indicates that cognitive dysfunction in depression may have a neurobiological basis. Attentional deficits are common in major depression and have been proposed to be a basic phenomenon to understanding the cognitive impairments in patients with mood disorders.[9-13] Attention can be represented as an information process with different stages (stimulus processing, cognitive processing, and motor adjustment), mediating the transformation of stimuli into (behavioral) responses. Furthermore, attention can be distinguished by different dimensions: selectivity (perceiving or ignoring information coming from the environment), intensity (mental effort devoted to an object), and vigilance (a sustaining process whereby the receptivity of incoming information is maintained over the long term).[14]

The Continuous Performance Test (CPT) is often applied as an attentional task in psychiatric research. Beck first developed the CPT to investigate brain-injured patients and

measures the ability to detect and respond to a predesignated target stimulus.[15] The subject monitors a continuous presentation of stimuli, rapidly presented over an extended period, and reacts as fast as possible to the occurrence of the critical signal. Storage of individual responses to the CPT allows for computation of mean reaction times, omission errors (misses) and commission errors (false alarms), d' value - average reaction time, and coefficient of variance for correct reactions and commission errors. Thus, even brief periods of inattention can be assessed. Significant shortcomings of previous CPT studies in depressed patients should be mentioned. In the first place, it is not easy to compare the outcomes of the different studies with each other because the applied CPT tasks varied concerning duration, types, and complexity of the presented (target) stimuli, speed of stimulus presentation, and conditions under which the task was completed. Most studies refer to the CPT as a sustained attention or vigilance measure. However, the duration of the applied CPT versions generally was too short (< 10 min) to measure a decline in performance over time.[16] Furthermore, CPT outcomes are multidimensional. They may reflect smoothly integrated perceptual, cognitive, and motor functions. Therefore, poor performance on a CPT can be due to deficits in any of these stages of the attentional process.[17] To clarify the mechanisms underlying the impaired CPT performance in depressed patients, some investigators studied the relationship between CPT performance and clinical state.[12,18] It was found that CPT performance was significantly associated with the severity of the depression, as measured by the Hamilton Rating Scale of Depression (HRSD) and motor proficiency, indicating that deficits in a CPT task may be partially attributable to motor retardation. Using a CPT, Horesh found higher omission and commission error rates in adolescent suicide attempters than hospitalized non-attempters with depression.[19] Overall, a limited number of studies have investigated attentional performance in depression. In this study, we used the degraded continuous performance test CPT-DS for twelve minutes to investigate the attentional performance in a group of patients with the major depressive disorder compared to healthy controls.[15] Also, the association of clinical symptoms related to patients' functioning and objective measures of CPT-DS was investigated. We hypothesized that patients who scored higher on the item "Work and Activities" on Hamilton Depression Rating Scale (HDRS) would perform worse on CPT-DS.

METHODS

Study population

All participants had a normal or corrected-to-normal vision, with a visual acuity superior or equal to 0.8 determined for both eyes with setup and pre-processing pipeline. Procedure details can be found in da Cruz et al.[20] All participants signed an informed consent after the study protocol was fully explained and were informed that they could quit the experiments at any time. All procedures complied with the Declaration of Helsinki and were approved by the Medical Ethical Committee of Tbilisi State Medical University. The study was conducted from January 2017 to May 2021 at Tbilisi Mental Health Center, Tbilisi, Georgia.

Patients were recruited from (i) the outpatient service of Tbilisi Mental Health Centre; (ii) Psychiatric private practices; and (iii) Through the screening surveys conducted among medical students. All participants recruited in the study group had a major depressive disorder in a recurrent moderate episode, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (APA, 2013), utilizing an interview based on the Structured Clinical Interview and the study of the medical records.

During selection, we used the following exclusion criteria: drug or alcohol abuse, neurological or other somatic illnesses influencing the subjects' mental state; severe or mild depressive episodes, treatment with benzodiazepines or second-generation sedative antipsychotics (olanzapine, quetiapine); a score above one on eighth item" Retardation" on HDRS.

All patients took antidepressants (fluoxetine, fluvoxamine, clomipramine, venlafaxine, escitalopram, duloxetine, and trazodone). Fourteen patients were receiving second-generation antipsychotics or mood stabilizers as an adjunctive treatment – eleven patients took aripiprazole, and three took lamotrigine. An experienced psychiatrist assessed psychopathology. The Brief Psychiatric Rating Scale was administered to exclude psychiatric comorbidity.[21] The severity of the depression was measured utilizing the 17-item version of the Hamilton Depression Rating Scale.[22] Overall, 73 participants with moderate recurrent depressive episodes were recruited in the study.

The control group consisted of healthy participants recruited by advertisement and personal contacts. All were screened for psychiatric symptoms utilizing an interview conducted by an experienced psychiatrist. Besides the general exclusion criteria, participants, who had psychiatric symptoms in the past or during the given period, were excluded. Overall, 68 healthy participants were recruited for the study.

We administered a degraded continuous performance test CPT-DS to both groups of patients and controls. Computerized CPT-DS with 3 blocks (720 digits, 10% targets, degradation 40%) with a total duration of twelve minutes was performed in a quiet environment. Observers had to detect the pair "1-9" and push the button when the target appeared on the screen. The digits were presented randomly with a rate of one per second with a presentation time of 50 ms. The following variables were measured: omission errors (number of times subjects fail to respond to target stimulation), commission errors (number of times

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subjects respond to nontarget stimulation), d' value - average reaction time, and coefficient of variance for both correct reactions and commission errors.[23]

To examine group differences in demographic data, The two-tailed independent samples t-tests were applied to evaluate differences between groups. Because the omission and commission errors were not normally distributed, nonparametric Mann– Whitney (M-W) U-tests were used to study differences in these parameters. The association between devalue, omission, and commission errors and the clinical parameter (item seven on HDRS) was calculated by nonparametric correlational techniques (Spearman's rho). A P-value of <0.05 was used for all statistical analyses to indicate a significant effect. SPSS performed the statistical analyses for Mac.

RESULTS

Data from 73 depressed patients and 68 healthy controls were analyzed. Group characteristics, HDRS, and BPRS scores (Mean±SD) are shown in Table 1. No significant differences between groups were found regarding education years, age, and gender ratio.

TABLE 1. Characteristics (Mean±SD) for the depressive patients and the depressive patients

Characteristics	*Depression (n=73)*	*Control (n=68)*
Gender, F/M	42/31	
Age, years	32.6±10.0	34.9±8.1
Education, years	14.8±2.6	15.0±2.8
Illness duration, years	6.8±5.5	
BPRS	30.4±5.0	
Hamilton (HDRS)	22.9±3.4	
CPZ Equivalent	115±82.3	
Handedness (L/R)	8/65	6/62
Visual Accuracy	1.4±0.4	1.6±0.4

Abbreviations: BPRS, brief psychiatric rating scale; CPZ, chlorpromazine; F, female; HDRS, Hamilton depression rating scale; L, left; M, male; R, right.

CPT-SD performance of groups

The value was significantly higher in healthy controls than depressed patients, indicating better performance in healthy individuals. At the same time, the number of omission errors was significantly higher in depressed patients than in controls (Tab.2).

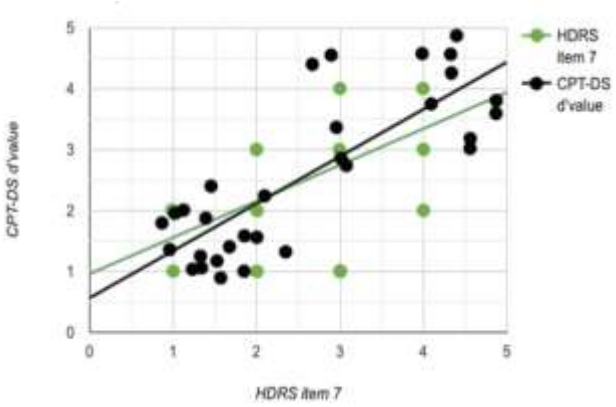
TABLE 2. Characteristics (Mean±SD) for the depressive patients and the depressive patients

Characteristics	*Depression (n=73) M±SD*	*Control (n=68) M±SD*	*t/U*
d' value, p<0.05,	3.72±0.8	4.56±0.3	-6.40
Omission errors (n), p<0.01,	7.26±9.98	0.19±0.54	-9.07
Commission errors (n), p<0.06	7.35±2.90	3.00±1.39	-2.35

CPT-SD performance in the clinical state

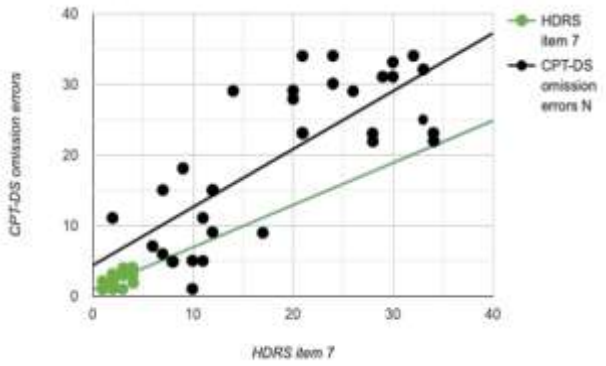
The CPT-SD parameters were significantly correlated with the scores of item 7, "Work and Activities," on HDRS. D' value was negatively correlated with the item 7 scores (rs=-0.8739, p=0.001) (Fig.1). The number of omission errors significantly correlated with the score on item 7 (rs=0.7778, p=0.01) (Fig.2). No statistically significant correlation was found between commission errors and item 7 (rs=0.287, p=0.074).

FIGURE 1. Correlation between HDRS item 7 and CPT-DS d' value



Abbreviations: CPT-DS, computerized degraded continuous performance test; HDRS, Hamilton depression rating scale.

FIGURE 2. Correlation between HDRS item 7 and CPT-DS d' value



Abbreviations: CPT-DS, computerized degraded continuous performance test; HDRS, Hamilton depression rating scale.

DISCUSSION

This study found that depressed patients with the same severity of the episode and the same levels of psychomotor retardation had worse CPT performance than control subjects. Depressed patients showed a significantly lower value and significantly more omission errors. Data are consistent with the findings of some previous CPT studies comparing unmedicated depressed patients with healthy controls,[24] suggesting that deficits in CPT tasks are most likely to be found in depression when tasks run longer than 10 minutes.[1,25] (Egeland, 2003; Wagner, 2006), like in our actual study with CPT continuing for 12 Minutes. Deficits in depressed patients, then, only tend to emerge in later blocks

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of trials or when stimuli are more difficult to notice (due to degraded stimuli in this study). Data coincides with theories linking cognitive impairments in depression to failures of right-sided cortical and subcortical arousal mechanisms.[26,27] The lower value in the patient group indicates that depressed patients respond slower to environmental stimuli and are less able to identify stimuli in effortful tasks (degraded stimuli). In general, the slower response may indicate two components: a central component, reflecting the efficiency of the decision-making process, and a peripheral component, reflecting the speed of the neuromuscular response.[28]

Consequently, the slower response could disturb the information processing mechanism and impair motor proficiency. As our patients had the same level of retardation (0 or 1 score on item 8 of HDRS), the slower response can be explained by the central component – decision-making efficiency, rather than with neuromuscular response. The high number of omission errors in the depressed patient group can be seen as a measure of the sustainability of inattention. During the test, patients missed target stimuli frequently, suggesting that depressed patients have a problem with the overall intensity of attention. A lower number of commission errors was shown in the patient group, in contrast to the omission errors. The score of commission errors is generally used as a measure of impulsivity and decontrol.[18,29] Depressed patients showed a low number of randomly made commission errors, which indicates that they were more able to control the reaction and inhibit their (motor) response when nontarget stimuli appeared on the screen. Results of this study suggest that more specific clinical symptom of disturbances in work and activities was also significantly correlated with the CPT outcomes; patients with more disturbances in work and daily activities on item 7 of HDRS performed significantly more commission errors in comparison to patients having fewer disturbances, indicating that effort-fulness and motivational aspects of depression are associated with attentional disturbance found in depressed patients, suggesting that decreased vigilance makes patients less ready and less motivated to respond.[3,16] The main shortcoming of the present study should be acknowledged, as the effects of antidepressant treatment were not controlled. Only patients taking medications less likely to worsen cognitive performance were involved in the study.

Our study showed that CPT, which runs longer (12 min) and requires more effort to complete the task (degraded version), is more sensitive to detecting the specific characteristics of cognitive impairment in depression. Some symptoms of depression, indicating the daily functioning of depressed patients, seem tightly linked to decreased sustainability of attention and vigilance. This shows that cognitive impairment is an important, separate factor affecting the functioning of depressed patients and emphasizes the need to introduce in clinical practice novel treatment strategies specifically targeting cognitive impairment in patients with MDD.

CONCLUSIONS

CPT, which runs longer and requires more effort to complete the task (degraded version), is relatively sensitive in detecting the specific characteristics of cognitive impairment in depression. Some specific symptoms of depression, indicating the daily functioning of patients, are linked to decreased sustainability of attention and vigilance. This demonstrates that cognitive impairment is a different essential factor of depression, affecting the functioning of patients and emphasizing the need to introduce novel treatment strategies specifically targeting cognitive impairment in patients with MDD.

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