Türk Psikiyatri Dergisi 2010;
Turkish Journal of Psychiatry

Executive Function Differences Between First Episode and Recurrent Major Depression Patients

Aytül KARABEKİROĞLU[1], Volkan TOPÇUOĞLU[2], Aylan GIMZAL GÖNENTÜR[3], Koray KARABEKİROĞLU[4]

Abstract

Objectives: *The differences between recurrent episodes and first episode depression among depressive patients in terms of executive functions had not previously been investigated. In this study, we aimed to explore executive function differences between patient groups with depression and healthy control subjects.*

Method: *19 first episode sufferers of depression, 14 sufferers of recurrent major depression and 33 healthy subjects, selected as suitable with regard to gender and educational level, were enrolled in this study. In the first session, we applied the SCID-I, State-Trait Anxiety Inventory (STAI), Mini Mental Test (MMT) and the Beck Depression Inventory (BDI). In the second session we applied neuropsychological tests including the Wisconsin Card Sorting Test (WCST), Verbal Fluency Test (VFT) and Stroop Tests to all participants.*

Results: *Patients with depression exhibited worse performance in all tests compared to control subjects. While there were no differences between first episode and recurrent depression patients in terms of depression severity and anxiety levels, recurrent depression patients had significantly more perseveration tendency in WCST and significantly worse performance in word production. Among patients in the recurrent depression group, 63,5% had second, 22,2% third, 14,2% had had a fourth episode. There is a significant correlation between the number of depressive episode and the perseveration tendency in WCST.*

Discussion: *The results indicate that, compared to first episode depression, the patients with recurrent depression have worse executive function performance and perseveration tendencies. Episode quantity and perseveration tendency were associated.*

Key Words: *Recurrent major depression, perseveration, WCST, Verbal Fluency Test.*

INTRODUCTION

Lifetime prevalance of major depressive disorder (MDD) is 10-25% among females and 5-12% among males. According to World Health Organization (WHO) reports unipolar MDD consitutes 36% of all mental disorders (WHO, 2001). It is estimated that in 2020 MDD will be the second most common cause of loss of workforce after ischemic heart disease (Milchaud et al. 2001). This data suggests that MDD is a major public health problem and needs a better understanding (Aydemir et al.. 2009). It is already known that, in addition to emotional and physical symptoms, cognitive disturbances also coexist in MDD (Ottowitz et al. 2002). Neuropsychological assessments of depressive patients, compared with healthy control subjects, revealed deterioration in psychomotor speed, attention, memory and executive functions (Zakzanis et al. 1998). Executive functions are the brain functions necessary to solve problems experienced in daily life. Under changing circumstances and depending on feedback received, cognitive and behavioral responses can be changed only if executive functions are intact. Impairment of executive functions may prevent the individual's ability to live independently and sustain social relationships (Atre-Vaidya et al. 1998). On the other hand, the brain imaging studies determined that the brain regions associated with major depression

Received: 23.11.2009 - **Accepted:** 23.03.2010
[1]Psychiatrist MD. Samsun Mental Health Hospital, Samsun Turkey, [2]Assoc. Prof. Marmara University School of Medicine, Department of Psychiatry, Istanbul, Turkey, [3]Psychiatrist MD. Marmara University School of Medicine, Department of Psychiatry, Istanbul, Turkey, [4]Assoc. Prof. Child and Adolescent Psychiatry, Department of Child and Adolescent Psychiatry, Ondokuz Mayis University, Samsun, Turkey.
Aytül Karabekiroğlu MD., e-mail: *draytulk@yahoo.com*

TABLE 1. Demographic and clinical characteristics: comparison of all patients with major depression and control groups

	Major depression subjects (n=33)	Control group (n=33)	χ2	t	z	p
Gender	31 (93,6%)	31 (93,6%)	1			NS
Female	2 (71,1%)	2(71,1%)				
Male						
Years of education Mean±SD	9,45± 4,1	9,81±4		0,384		NS
Age Mean± SD	34,79± 8,6	36,63± 7,9		0,718		NS
Instrument scores	28 (26-32,5)	5 (2,5-9)			-6,99	<0,01*
BDI [Median (25-75%)]	54,4 ± 8,1	37,2± 8,6		10,5		< 0,01*
STAI-State (Mean± SD)	58,1 ± 7,1	37,9 ± 8,3		10,5		<0,01*
STAI- Trait (Mean± SD)	29 (28,5-30)	30 (29,5-30)		-2,67		<0,05*
MMT[Median (25-75%)]						

*: Statistically significant; BDI: Beck Depression Inventory; MMT: Mini Mental Test. NS: Not statistically significant STAI: State and Trait Anxiety Inventory;

are located in the frontal cortex, limbic system, thalamus and striatum (Drevets et al. 1992). Brain functions that are collected under the title of executive functions are considered to be adversely affected by prefrontal cortex dysfunction (Rogers et al. 2004). Therefore, among patients with major depression, executive function tests can be expected to show deterioration.

Studies assessing executive function in major depression have identified disruptions in working memory, changing cognitive categories, planning and understanding emotional content. Deterioration in working memory performance was identified especially in patients with severe, untreated MDD (Morizt et al. 2002) and were eliminated through treatment (Trichard et al. 1995). Changing the cognitive category skills, has been shown to be associated particularly with depressed mood, and also in patients with dysphoric mood and without any major depressive episode, they reported similar cognitive category changing problems similar to MDD patients (Ravnkilde et al. 2002). Austin and colleagues (1999), stated that, particularly in the melancholic subtype perseveration was more frequent. On the other hand, there are several research findings revealing no differences in these executive functions in major depression (Grant et al. 2001; Sweney et al. 2000). Differences in results reported in several studies have been assumed to be linked to the heterogenity of the study groups, comorbid disorders associated with MDD, and disruptive effects of drugs in terms of performance tests. Studies that might be able to provide insight into the relationship between executive functions and the clinical variables in major depression are very limited. Lampe and colleagues (2003) identified that patients with recurrent major depression have more defective executive functions than healthy control subjects. It is not known whether the executive function of patients with recurrent depression differs from that of patients having experienced their first episode of depression. Clarification of the effects of repetition in major depression episodes on executive functions may contribute to knowledge about cognitive impairment in MDD. In this study, the executive functions of these two subtypes of major depression sufferers and healthy control groups were compared.

METHODS

The sample and control group

Over the period of June 2007 - August 2008, in the Marmara University Psychiatry out-patient clinic, 19 patients having undergone their first episode of major depression and 14 patients with recurrent major depression, who were statistically similar in terms of age, sex and educational status, were engaged as study participants. As it may have possibly affected accurate assessment of the study hypothesis, patients with another psychiatric comorbidity, chronic neurological disease or dementia, patients using psychotropic drugs during the evaluation, and patients with major depression including psychotic features were excluded from this study. As patients who had attempted suicide were, at the time, subject to immediate intervention in the emergency room, these patients were not included in the study.

In the first session, to confirm the diagnosis of major depression and to exclude comorbid diagnoses, SCID-I was applied. In the same session State and Trait Anxi-

TABLE 2. Neuropsychological test scores: comparison of all patients with major depression and control groups

	Major depression subjects Median (25-75%)	Control subjects Median (25-75%)	Z	P
Total number of correct	72 (47,5-89,5)	96 (89-101)	-4,68	<0,001
Total number of errors	56 (56-80,5)	32 (27-39)	-4,68	< 0,001
Total number of perseverative reactions	23 (16,5-35)	18 (12- 26)	-2,39	<0,05
Total number of non-perseverative errors	25 (18-40)	15(12-20)	-4,18	<0,001
Total number of perseverative errors	22 (17-35)	17 (12-20,5)	-3,08	<0,001
Total number of completed categories	3 (0-4,5)	7 (5-8)	-4,88	< 0,001
Percent of perseverative errors	17,19 (13-24,61)	13,28 (9,3-16)	-3,08	<0,001
Percent of conceptual level reactions	44,5 (19,5-59,7)	67,9 (57,4-75,3)	-4,37	< 0,001
Stroop 1 completion time	11,96 (10,3-14,5)	10 (8,7- 10,9)	-3,91	<0,01
Stroop 5 completion time	33,6 (27,5-41)	25,43 (19,7- 30,9)	-2,99	<0,01
Stroop 5 number of errors	3 (1-5)	1 (0-2)	-2,80	<0,01
Verbal Fluency Test number of words	27 (21,5-35)	42 (29-53)	-4,53	<0,01

ety Inventory, Minimental Test, and Beck Depression Inventory were also administered. In the second session, as a means of neuropsychological evaluation, the Wisconsin Card Sorting Test, Verbal Fluency Test and the Stroop test were performed.

In order to determine differential findings in the healthy subjects, age, gender and educational status were matched, and after SCID-I evaluation, 33 volunteer subjects without any psychopathology constituted the control group. Finally all tests were applied to all subjects. After all the volunteers within the patient and control groups were informed about the study and methods, their oral and written consent was received. The study received approval from the Ethics Committee of the Marmara University, Faculty of Medicine. The first author AK had already implemented the training on the use of neuropsychological tests at Ondokuz Mayis University Hospital, Department of Neurology, Clinical Dementia Clinic, within six months of work in 2006.

Instruments

Semi-structured Questionnaire: With this form, sex, age, marital status, education, employment status and family history of psychiatric illness were investigated.

Structured Clinical Interview of Disorders of Axis I- Clinical Version (SCID-I-CV): This is a clinical interview developed to diagnose axis I psychiatric disorders. An adaptation and reliability study was conducted in Turkey (First et al. 1997, Çorapçıoğlu et al. 1999).

Beck Depression Inventory (BDI): This is a self-report that consists of 21 items which are scored between "0" and "3". In our country, the reliability and validity study was conducted among university students (Hisli 1989).

State and Trait Anxiety Inventory (STAI): This was developed to assess state and trait anxiety levels and the reliability and validity study of STAI was conducted by Öner and Le Compte (1985).

Mini Mental Test (MMT): This is an instrument developed to assess cognitive competence in patients in a valid way and in a very short duration. The instrument was developed by Folstein et al (1975) and Güngen and colleagues (2002) conducted the Turkish adaptation, and reliability and validity study.

Wisconsin Card Sorting Test (WCST): The test is applied with two decks of cards that include 4 stimulus cards and 64 response cards. The cards have different colors and a number of shapes. The shapes are "plus", "circle", "star" or "triangle" figures, the number of shapes are "one", "two", "three" or "four", and the colors are "red", "green", "blue" or "yellow". The instruction for the test that the respondent has to do is to match each response card with one of the stimulus cards. Correct matching categories are in sequence of color, shape, and number. After the respondent makes a consequent 10 correct matches, the next category is applied. Soon after each match, the respondent is informed whether his or her response is correct or not. However, no information is given concerning which is the correct matching category. When the respondent completes all six categories or uses all the cards in the two decks the test is terminated (Heaton et al. 1993). The Turkish adaptation studies on WCST were carried out by Karakaş and colleagues (1998).

TABLE 3. Sociodemographic and clinical characteristics: comparison of RMD and FEMD patients.

	RMD (1) n= 14	FEMD (2) n= 19	Control (3) n=33	F	χ2	p	Source of statistical significance
Gender							
Female	92,9 (13)	94,5 (18)	93,9 (31)	0,5		>0,01	NS
Male	7,1 (1)	5,5 (1)	7,1 (2)				
Years of education							
Mean±SD	10,21± 4	8,89± 4,21	9,81±4	0,48		>0,01	NS
Age							
Mean± SD	33,7± 9,5	35,75± 7,9	36,63± 7,9	0,62		>0,01	NS
Instrument scores							
BDI [Median (25-75%)]	27 (23-31)	30,5 (27-38)	5 (2,5-9)		50,16	<0,01*	1-3; 2-3**
STAI- Trait (Mean± SD)	54.7 ± 9,9	54 ± 6,9	37,2± 8,6	34		<0,01*	1-3; 2-3**
STAI-State (Mean± SD)	57,3 ± 7	59,7 ±7,4	37,6 ±7,4	55,7		<0,01*	1-3; 2-3**
MMT[Median (25-75%)]	26,8 (28-30)	29,1(28-30)	30 (29,5-30)		7,5	>0,01	NS

*: Statistically significant (p<0.017); **: RMD is statistically significantly different from control and FEMD groups. BDI: Beck Depression Inventory; FEMD: First Episode Major Depression; MMT: Mini Mental Test. NS: Not statistically significant: RMD: Recurrent Major Depression; STAI: State and Trait Anxiety Inventory

Verbal fluenct Test: In this test, the respondent is instructed to reproduce words, the first letter of which are K, A and S wherever possible. The original version of the test is applied with the letters F, A, and S, however in the standardization studies in our country the K, A, and S letters were used (Umaç, 1997). In our study, the total number of words are counted in the results.

Stroop Test: The test has several different forms. In our study we used the TBAG (Temel Bilimler Araştırma Grubu) form. The TBAG version of the Stroop Test consists of 4 cards of 14x21.5 cm dimensions. Every card includes six rows of 4 randomly assigned items. These cards are the "stimulating" items of the test. After the respondent completes the task in each section, the duration, number of incorrect responses and corrections are recorded. It was reported that the most valid assessment of the TBAG version of Stroop Test is the disruptive effect (fifth step where the colors are announced on the second card). In addition, it has been suggested that the test also evaluates the reading velocity which indicates attention (time required for the completion of the first card) and announcement of the color (time required for the completion of the third and fourth cards). The standardization studies of the TBAG version of the Stroop Test have been conducted (Karakaş, 2002).

Statistical analysis

Analysis of the data is conducted using the SPSS (Statistical Program for Social Sciences) 13.0 version. The distribution of continuous variables of the scales and neuropsychological tests were evaluated with single-sample Kolmogorov-Smirnov tests. The variables with normal distribution with parametric statistics and non-normal distribution variables were assessed using non-parametric statistics. For quantitative variables, when the distribution of the group scores is normal, the mean and standard deviation values are presented in tables. For quantitative variables, when the distribution of the group scores is not normal, the median and 25-75 percentile scores are presented. In comparisons between the three groups, the Kruskal Wallis test was applied where the distribution was not normal, and where there was a significant difference between groups, Mann Whitney U Tests were applied in the post-hoc analysis. Where the distributions were normal, the ANOVA test and in the post-hoc, t-tests were conducted. While three groups were compared in the post-hoc analysis and three Mann Whitney U and/or t-tests were applied, Bonferroni correction was used, and statistical significance was approved as 0.05/3 (0.017).

RESULTS

The first episode major depression group (FEMD), recurrent major depression group (RMD), and control group included subjects ranging between 18-55 years of age and who were at least primary school graduates. There were no statistically significant differences between the groups in terms of gender, education level or mean age.

All patients with major depression were compared with the control group and the results showed a statistically significant difference in all tests that evaluated executive functions. Sociodemographic and clinical features of the MDD and control groups are presented in Table 1, and the executive functions in Table 2.

TABLE 4. Neuropychological test scores: comparison of RMD, FEMD, and control groups

	RMD (1) Median (25-75%)	FEMD (2) Median (25-75%)	Control (3) Median (25-75%)	χ2	p	Source of statistical significance
Total number of correct	63 (44-82)	82,5 (69-96,7)	96 (89-101)	27	<0,001*	1:3
Total number of incorrect	65 (46-84)	45,5 (31,2-59)	32 (27-39)	27	<0,001*	1:3
Total number of perseverative reactions	30 (21-45)	17 (14,5-21,7)	18 (12-26)	13,3	0,001*	1:3, 1:2
Total number of non-perseverative errors	34 (21-48)	24 (16-33,2)	15 (12-20)	18,8	<0,001*	1:3, 2:3
Total number of perseverative errors	29 (21-41)	17 (14-20,2)	17 (12-20,5)	19,3	<0,001*	1:3,1:2
Total number of completed categories	2 (0-3)	4,5 (1,7-7,2)	7 (5-8)	30,9	<0,001*	1:3, 1:2
Percent of perseverative false	22,6 (16,4-31)	13,2 (10-15,8)	13,28 (9,3-16)	19,3	<0,001*	1:3, 1:2
Percent of conceptual level reactions	32 (13,2-47,6)	53,1 (42,1-71)	67,9 (57,4-75)	13,8	<0,001*	1:3, 1:2
Stroop 1 completion time	13,5 (10,3-14,8)	11,3(10,3-14,2)	10 (8,7-10,9)	15,59	<0,001*	1:3,2:3
Stroop 5 completion time	31,3 (23-41,6)	34,9 (30,1-38,6)	25,3 (19-30,9)	9,3	<0,017*	2:3
Stroop 5 number of errors	2 (1-4)	4 (1-6)	0 (0-2)	8,8	<0,017*	2:3
Verbal Fluency Test number of words	23 (19-28)	32 (27-38)	42 (29-53)	0,261	<0,001*	1:3; 1:2

*: Statistically significant (p<0.017); FEMD: First Episode Major Depression; RMD: Recurrent Major Depression

There was no any significant difference between FEMD and RMD in terms of severity of depression, anxiety or MMT scores. Sociodemographic and clinical features of the FEMD, RMD, and control groups are presented in Table 3.

In WCST, FEMD showed significant differences from the control group only in terms of the nonperseverative number of false responses (z=-2,505; p< 0,017). On the other hand, RMD sufferers had significant differences from the control group in all tests. In subtests of WCST that reflect the pereseveration tendency, the scores of RMD sufferers were found to be higher than those of FEMD. Between these two groups, there were statistically significant differences in the number of perseverative responses (z=-2,82; p<0,017), total number of perseverative false responses (z=-3,176; p<0,017), and percentage of perseverative false responses (z=-3,176; p<0,017) (Table 5). In our study, we found that RMD compared to FEMD has differences in the percentage of the conceptual level response associated with the identification of the classification rule (z=-2,405; p< 0,017).

When the patients in the RMD group were recruited into the study, 63.5% (n=9) of them were in the second episode, 22.2% (n=3) were in third, and 14.2% (n=2) were in the fourth episode of depression. We found a significant correlation between the number of episodes and total number of perseverative responses in WCST (r=0,422; p< 0,01).

In the Stroop Test, between the FEMD and control group, we found significant differences in the time taken until completion on the first and fifth step (z=-2,838; p<0,017; z= -2,72; p<0,017) and total number of false responses on the fifth step (z= -2,680; p<0,017). Compared to the control subjects, the patients completed the subtests over a longer time period and made more mistakes. RMD, in comparison to the conrtol group, revealed differences in the time taken until the completion of the first part of the test (z=-3,478; p<0,017); they were worse in terms of length of time required for completion and number of mistakes at the fifth step, but this difference was not significant (z=-1,99; p=0,46). RMD and FEMD did not reveal differences in the scores of the Stroop Test.

In the Verbal Fluencey Test, there was no difference between the FEMD and control group, in terms of word reproduction performance (z= -2,259; p=0,024). RMD patients produced fewer words compared to healthy control subjects (z= -4,604; p<0,017) and FEMD patients (z=-2,755; p<0,017).

DISCUSSION

In our study, the FEMD, RMD and healthy control group, that did not differ in terms of age, gender, or level

TABLE 5. Neuropychological test scores: comparison of RMD and FEMD groups

	RMD Median (25-75%)	FEMD Median (25-75%)	Z	P
Total number of correct	63 (44-82)	82,5 (69-96,7)	-2,278	NS
Total number of incorrect	65 (46-84)	45,5 (31,2-59)	-2,278	NS
Total number of perseverative reactions	30 (21-45)	17 (14,5-21,7)	-2,826	< 0,017
Total number of non-perseverative errors	34 (21-48)	24 (16-33,2)	-1,258	0,208
Total number of perseverative false	29 (21-41)	17 (14-20,2)	-3,176	< 0,017
Total number of completed categories	2 (0-3)	4,5 (1,7-7,2)	-2,606	< 0,017
Percent of perseverative errors	22,6 (16,4-31)	13,2 (10-15,8)	-3,176	< 0,017
Percent of conceptual level reactions	32 (13,2-47,6)	53,1 (42,1-71)	-2,405	< 0,017
Stroop 1 completion time	13,5 (10,3-14,8)	11,3 (10,3-14,2)	-0,801	NS
Stroop 5 completion time	31,3 (23-41,6)	34,9 (30,1-38,6)	-0,583	NS
Stroop 5 number of errors	2 (1-4)	4 (1-6)	-1,122	NS
Verbal Fluency Test number of words	23 (19-28)	32 (27-38)	-2,755	< 0,017

FEMD: First Episode Major Depression; NS: Not statistically significant; RMD: Recurrent Major Depression

of education, were compared in terms of executive function performance. In the executive function test, particularly in tests that indicate pereseveration tendency, the patients in the RMD group were found to be less successful compared to the FEMD and control group. This lack of success was found to increase in correlation with the number of episodes.

The results showed significant differences between the FEMD and RMD group in all subtests of WCST that indicate the perseveration tendency. However, FEMD showed a difference from the control group only in the nonperseverative false responses. This results suggest that the perseverative tendency becomes more significant as the depression episodes recur. Similar to our results, Lampe and colleagues (2004) had previously reported that, among RMD patients, persevaration scores are higher on the WCST, and this result was not found to be related to the severity or duration of depression. However, in that study, as patients who had been taking drugs for a long period of time were also included, it was not clear whether the perseveration tendency was related to the medication or to the depression itself. In addition, Grant and colleagues (2001) reported WCST scores that indicate perseveration tendencies were higher in the young MDD patients compared to the control group. As RMD patients show greater disturbance in several subtests of WCST, this finding suggests that executive function problems are more significant in RMD patients compared to those in the FEMD and control group. In addition, the correlation found between the number of episodes and perseverative response subscores of WCST indicate that the perseveration tendency becomes more significant as the depressive episodes increase in number.

In the Verbal Fluency Test, in terms of the number of reproduced words, RMD patients, compared to FEMD and control group, show significant difference. There was no such difference between the FEMD and control groups. This may suggest that recurrence of the depressive episodes may negatively influence the word production of the patients. This finding is another indicator of the disturbance of executive functions in the RMD group.

In our study, there was no difference between the RMD and FEMD group in terms of the Stroop performance. This result may suggest that the Stroop Test may be a less sensitive test in comparison to the WCST and Verbal Fluency Test for expressing the differences in executive function performance between the major depression groups. On the other hand, we noticed that the Emotional Stroop Test is preferable to the classical version of the Stroop Test for the patients with psychiatric disorders (Mitterschiffthaler et al. 2008). In the Emotional Stroop Test, "stimulus" words in the Stroop Test are set among the words associated with depression. In our study, not having used the Emotional Stroop Test may be considered as a limitation.

It has been previously suggested that the WCST and Verbal Fluency Test are the best predictor executive function tests detecting prefrontal cortical dysfunction (Henry and Crowford 2004a). Our findings may reveal that the prefrontal functions of RMD patients are more disrupted than those of FEMD patients. In recent years, in the etiopathogenesis of depression, the role of dysfunction in the limbic-cortical circuits is more emphasized (Eliot et al. 2000). Taking the results of our study into consideration, we suggest that depression increases the frontal-striatal dysfunction whereas recurrence of the epi-

sodes cystallizes the dysfunction and this becomes obvious in the neuropsychological tests as disturbances of the executive functions and increase in perseveration tendency. As a characteristic of RMD, perseveration tendency may make the patients unable to understand certain feedback or inappropriately deal with the new expreriences. In addition, the perseveration tendency makes it more difficult to change mental and behavioral responses (Alexopoulos et al. 2008). Alexopoulos et al (2000) reported an association between recurrence of depression and the perseveration subscore of the Dementia Rating Scale. As we already know, the cognitive theory of depression suggests that the appearance and persistence of depression is due to the negative beliefs of patients concerning themselves, their environment and their future that they believe they can not change (Sungur 1994). Our findings indicate that because of perseveration in the mental processes of recurrent major depression patients, they have difficulties in evaluating and changing their negative beliefs using positive feedback from the environment.

Ninety-three percent of our study group was female. Therefore, the results may be valid for adult female patients but may not be generalized to both genders. In addition, the limited sample size may be considered as a limitation and makes it difficult to discuss the results. On the other hand, the sample included one depressive patient with moderate to severe pathology and it was not possible to come to a conclusion for the MDD patients with mild severity. The mental capacity of the patients was not evaluated and this may be another limitation of the study. The cross-sectional design of the study should be taken into consideration as well. The results may not clarify whether executive dysfunction is a risk factor for the recurrence of depression or a result of the recurrence of depression. Although the study has several limitations, as comorbid disorders and concurrent medication may effect the results, the exclusion of these factors may be assumed to be a strength of the study.

In this study, we found executive function differences between the first episode depression and recurrent depression patients, where the groups did not differ in terms of anxiety and depression levels, age, educational level and certain cognitive functions such as attention and memory. As major depression recurs the patients suffering from this condition have more executive dysfunction and show a perseveration tendency, and this perseveration tendency increases as the number of major depression episodes increases.

REFERENCES

Alexopoulos GS, Raue PJ, Kanellopoulos D et al. (2008) Problem solving therapy for the depression-executive dysfunction syndrome of late life. Int J Geriatr Psychiatry 23:782-8.

Atre-Vaidya N, Taylor MA, Spidenberg M et al. (1998) Cognitive deficits, psychopathology and psychosocial functioning in bipolar and mood disorder. Am J Psychiatry 161: 262-70.

Austin MP, Mitchell P, Wilhelm K et al. (1999) Melancholic depression: a distinct pattern of frontal impairment in melancholia. Psychol. Med 24: 73–85.

Aydemir Ö, Ergün H, Soygür H et al. (2009) Majör Depresif Bozuklukta Yaşam Kalitesi: Kesitsel Bir Çalışma. Türk Psikiyatri Dergisi 20:205-212.

Çorapçıoğlu A, Aydemir A, Yıldız M et al. (1999). DSM-IV Eksen I Bozuklukları İçin Yapılandırılmış Klinik Görüşme. Hekimler Yayın Birliği.

Drevets WC, Videen TO, Price JL et al. (1992) A functional anatomical study of unipolar depression. J Neurosci 12:3628-41.

Elliott R, Friston KJ, Dolan RJ. (2000) Dissociable neural responses in human reward systems.

First MB, Spitzer RL, Gibbon M et al. (1997) Structured Clinical Interview for DSM-IV Clinical Version (SCID-I/ CV). American Psychiatric Press, Washington DC.

Folstein MF, Folstein S, McHugh PR. (1975) "Mini-mental state" A practical method for grading the cognitive state of patients for the clinician. J Psychiatry Res 12:189-98.

Grant MM, Thase ME, Sweeney JA. (2001) Cognitive disturbance in outpatient depressed younger adults: evidence of modest impairment. Biol. Psychiatry 50:35–43.

Güngen C, Ertan T, Eker E et al. (2002) Standardize Mini-Mental Test'in Türk toplumunda hafif demans tanısında geçerlik ve güvenirliliği. Türk Psikiyatri Dergisi 13:273-81.

Heaton RK, Chelune GJ, Talley JL et al. (1993) Wisconsin card sorting test manual: Revised and expanded. Florida: Psycological Assesment Resources.

Hisli N. (1989) Beck Depresyon Envanterinin üniversite öğrencileri için geçerliği, güvenirliği. Psikoloji Dergisi 7:3-13.

Karakaş S, Irak M, Ersezgin ÖU. (1998) Wisconsin Kart Eşleme Testi (WCST) ve Stroop Testi TBAG formu puanlarının test içi ve testler-arası ilişkileri. X. Ulusal Psikoloji Kongresi özet kitabı, s: 44.

Karakaş S. (2002) Bilişsel fonksiyonların değerlendirilmesinde nöropsikolojik testler. Türk Nöroloji Dergisi 8:61-69.

Lampe JK, Hulshoff Pol HE, Janssen J et al. (2003) Association of depression duration with reduction of global cerebral gray matter volume with recurrent major depressive disorder. Am J Psychiatry 160: 2052-2054.

Lampe IK, Sitskoorn MM, Heereb TJ. (2004) Effects of recurrent major depressive disorder on behavior and cognitive function in female depressed patients. Psychiatry Res 15:73-79.

Milchaud CM, Murray CJ, Bloom BR. (2001) Burden of disease-implications for future research. JAMA 285:535-39.

Mitterschiffthaler MT, Williams SC, Walsh ND et al. (2008) Neural basis of the emotional Stroop interference effect in major depression. Psychol Med 38:247-56.

Moritz S, Birkner C, Kloss M et al. (2002) Executive functioning in obsessive–compulsive disorder, unipolar depression and schizophrenia. Arch Clin Neuropsychol 17:477–83.

Ottowitz WE, Dougherty DD, Savage CR. (2002) The neural

network of attention and executive function in major depressive disorder: implications for application of medical disease model of psychiatric disoder. Havard Rev Psychiatry 10:86-99.

Öner N, Le Compte A. (1985) Durumluk-sürekli kaygı envanteri elkitabı. Boğaziçi Yayınları, İstanbul.

Ravnkilde B, Videbech P, Clemmensen K et al. (2002) Cognitive deficits in major depression. Scand J Psychol 43:239–251.

Rogers MA, Kasai K, Koji M et al. (2004) Executive and prefrontal dysfunction in unipolar depression: a review of neurpsychological and imaging evidence. Neuroscience Research 50:1-11.

Sungur MZ (1994) Depresyonda bilişsel terapiler. Depresyon Monografları Serisi 10. Ankara, Hekimler Yayın Birliği, 447-458.

Sweeney JA, Kmiec JA, Kupfer DJ. (2000) Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. Biol Psychiatry 48:674–85.

Trichard C, Martinot JL, Alagille M et al. (1995) Time course of prefrontal lobe dysfunction in severely depressed in-patients: a longitudinal neuropsychological study. Psychol. Med 25:79–85.

Umaç A. (1997) Normal deneklerde frontal hasarlara duyarlı bazı testlerde performansa yaş ve eğitimin etkisi. İstanbul Üniversitesi Sosyal Bilimler Enstitüsü Psikoloji Bölümü, Yüksek Lisans Tezi; İstanbul.

WHO (2001) Chapter 2: Burden of Mental and Behavioral Disorders. WHO Report 2001: Mental Health, New Understanding, New Hope. web adresi (19.11.2009 tarihinde indilidi): http://www.who.int/whr/2001/chapter 2/en/index4.html

Zakzanis KK, Leach L, Kaplan E. (1998) On the nature and pattern of neurocognitive function in major depressive disorders. Neuropsychiatry Neuropsychol Behav Neurol 11:111-19.