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Hatice Dogan, Didem Oztop, Ozlem Olguner Eker, Saliha Demirel Ozsoy, Ceren Şahin Özkartal, Feyza Arıcıoğlu, Erdem Tüzün, Rümeysa Keleş, Cansu Kandemir, Serap Şirvancı, Cem İsmail Küçükali, Tijen Utkan, Tuğçe Demirtaş Şahin, Yusufhan Yazir, Zehra Seda Halbutoğulları, Semil Selcen Gocmez, Feyza Arıcıoğlu, Övgü Sinem Buğan Gülbahar, Abda Mahmood, Enikő Zsoldos, Charlotte L. Allan, Anya Topiwala, Klaus P. Ebmeier, Vedat Ceylan, Samet Kose MD, PhD, Ercan Akin, Mehmet Hakan Turkcapar, Ercan Akin, Samet Kose MD, PhD, Vedat Ceylan, Gulizer Temel, Mehmet Hakan Turkcapar MD, Samet Kose MD, PhD, Mehmet Yalcin, Ercan Akin, Vedat Ceylan, Hakan Turkcapar MD, PhD, Isa Badur PhD, MPharm, Naciye Bilgin Badur, Yüksel Kıvrak, Yasin Taşdelen, İbrahim Yağcı, Fatih Aydın, Ayca Idil Aytekin, Melek Saka, Sule Aydin, Beyazit Garip, Hakan Kayir, Pelin Öztürk, Serkan Zincir, Cihad Yükselir, Feyza Ersan Unal, Şakir Gıca & Aytül Gürsu Hariri

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Effects of Presence of Maternal Psychiatric Disorders on Attachment to Parents and Peers in Children with Attention-Deficit/Hyperactivity Disorder

Hatice Dogan[a], Didem Oztop[b], Ozlem Olguner Eker[c] and Saliha Demirel Ozsoy[d]

[a]MD, Psychiatrist, Department of Child and Adolescencent Psychiatry, Giresun University Obstetric Gynecology and Child Research Hospital, Giresun, Turkey; [b]MD, Associate Professor, Department of Child and Adolescencent Psychiatry, Boylam Institute, Istanbul, Turkey; [c]MD, Psychiatrist, Department of Psychiatry, Kayseri Research Hospital, Kayseri, Turkey; [d]MD, Professor, Department of Psychiatry, Erciyes University Medical Faculty, Kayseri, Turkey

E-mail address: haticebozdogan2007@gmail.com

ABSTRACT

Objective: Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by inattention, hyperactivity, and impulsivity, which is observed in 3–7% of the children at school age. It is associated with significant disruption in developmental, cognitive, and academic domains. In recent years, intensive research has been conducted on the topic of Woman's Mental Health. Psychiatric disorders significantly affect individual and interpersonal relationships at all stages of individual's life.

Methods: 50 patients aged 11–17 years who were diagnosed as ADHD were enrolled to the study. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) interview and Wechsler Intelligence Scale for Children-Revised (WISC-R), Relationship Scale Questionnaire (RSQ), and Inventory of Parent and Peer Attachment (IPPA) were administered to all cases included.

Results: Mean age was 12.78±1.67 in patient group. Frequency of psychiatric disorder was 14% among mothers of the patients with ADHD. It was found that mean score for attachment to mother was 69, whereas mean score for attachment to father was 66. In peer attachment, highest mean score was found for disinterested attachment by 4.41±1.19. When attachment was assessed by maternal psychiatric disorder status, no significant differences were found in parent attachment, while a significant difference was found in favor of obsessive attachment to peer (p<0.05).

Conclusions: In our study, mean scores for obsessive attachment was found to be significantly higher in children in whom maternal psychiatric disorder was present. It was found that mothers of children with ADHD promoted less interaction with their children; that they were less responsive to positive and neutral interactions promoted by children; and that they used more negative, more reactive, more authoritative and more controlling but less positive parenting strategies. Previous studies reported that mothers of children with ADHD experienced more burn-out and have higher exhaustion levels when compared controls.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity, and impulsivity, which is observed in 3–7% of the children at school age [1]. It is associated with significant disruption in developmental, cognitive, and academic domains. Attachment is a condition that affects both individual's inner self and affiliations.

Attachment is a condition with outweighing emotional aspect that begins in the first days of life and evolves by interaction with surrounding. It is also defined as a deep and enduring emotional bond that develops between child and caregiver and manifests with child's behavior of seeking proximity with a caregiver, especially under stressful conditions [2]. Attachment theory examines role of this relationship between mother and infant and consequences of its disruption on child's development. According to Bowlby, attachment is not completed after infantile period and secure attachment continues throughout early childhood. Different trust-based attachment behaviors are seen during infancy, childhood, adolescent period and adulthood [3].

Ainsworth was the first who describe attachment patterns. Ainsworth observed responses of children during separation and reunion with his/her mother

in a laboratory setting and classified these responses into 3 groups as secure, anxious-avoidant insecure, and anxious-resistance insecure attachments. In recent years, disorganized-disoriented attachment was added to the classification [4]. Recently, Bartholomew and Harowitz proposed the 4-group model of attachment based on the idea that Bowlby's attachment system involves internal models about ego and others, which examined the role of attachment in the close relations of adolescents and adults. Accordingly, models of ego and others are assessed in 4 categories based on the self-image (positive or negative) and image of others (positive or negative) [5–9]. These categories are termed as secure, pre-occupied, dismissing, and fearful attachment [9,10].

It has been reported that secure attachment modulates regulation of attention and focusing capacity. In addition, it was shown that insecure attachment styles are risk factors for expressive communication disorders and ADHD [11]. Furthermore, it is also known that abnormalities of family functionality and child-family relationship as well as maternal-paternal attitudes play role in the development of ADHD. It has been reported that there is more negative-impulsive behavior control and less positive maternal-paternal attitudes in the parents of individuals with ADHD [12]. Many studies have been performed, indicating that this condition has influence on attachment [13–15]. In a study examining the association between ADHD and insecure attachment, Clarke et al. reported that children with ADHD showed insecure attachment more commonly [13]. Similarly, in a prospective study, Pinto et al. observed newborns until 7 years of age with assessments by using several scales and reported that both inattention and hyperactivity were associated with disorganized attachment [14]. Green et al. also reported that there was a marked association between disorganized attachment and attention problems, suggesting that dismissing attachment is more common among children with ADHD [15].

In recent years, intensive research has been conducted on the topic of Woman's Mental Health. Psychiatric disorders significantly affect individual and interpersonal relationships at all stages of individual's life. These women experience difficulties in important areas such as marriage and child care, as in all other areas of life [16].

Methods

Out of the patients presented to the Department of Child and Adolescent Psychiatry at the Erciyes University School of Medicine, 50 patients aged 11–17 years who were with ADHD were included to the study. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) interview and Wechsler Intelligence Scale for Children-Revised (WISC-R), Relationship Scale Questionnaire (RSQ), and Inventory of Parent and Peer Attachment (IPPA) were administered to all participants. Parents were asked to complete sociodemographic data sheet about their children and Turgay DSM-IV-based child and adolescent behavior disorders screening and rating scale.

Statistical analysis

Data analysis was performed by using the SPSS for IBM version 22.0 (IBM Corp., Armonk, New York, USA). Normal distribution was assessed by using Shapiro Wilk test and Q-Q graphics. Levene's test was used to assess homogeneity of variances. Descriptive statistics are presented as mean ± standard deviation ($\bar{x} \pm SD$) or median (25th–75th percentile). Independent samples t test and Mann-Whitney U test were used to compare groups. One-way variance analysis (ANOVA) was used for comparisons among more than 2 groups while Tukey test was used for multiple comparisons. Pearson's correlation analysis was used to assess associations among numerical variables. Chi-square exact test was used to assess associations among categorical variables. A p value <0.05 was considered to be statistically significant.

Results

Mean age was 12.78±1.67 in patient group included. There were 15 girls and 35 boys. Frequency of psychiatric disorder was 14% among mothers of the cases with ADHD. The diagnosis for all of the psychiatric disorder was major depressive disorder. It was found that mean score for attachment to healthy mother was 69, whereas mean score for attachment to mother with psychiatric disorders was 65. And also the score of attachment father whose wives were healthy was 67, whereas mean score for attachment to father whose wives had psychiatric disorders was 56. In peer attachment, highest mean score was found for dismissive attachment by 4.60, than secure attachment by 4.00. The score of obsessive and fearful attachment were nearly closed in the group of healthy mother. The attachment scores for children who had mother with psychiatric disorder were 4.00 for obsessive attachment, 3.80 for dismissive attachment, 3.60 for secure attachment and 3.25 for fearful attachment. When attachment was assessed by maternal psychiatric disorder status, no significant difference was detected in parent attachment, while a significant difference in favor of obsessive attachment to peer (p<0.05).

Discussion

In this present study, mean scores for obsessive attachment was reported to be significantly higher in children in whom maternal psychiatric disorder was present. Previous studies have shown that attitudes of parent

Table 1. Attachment style for Maternal Psychiatric Disorders.

	Maternal Psychiatric Disorders Median (25–75%)		
	Yes (n=7)	No (n=43)	Comparison
Secure Attachment	3.60 (2.80–4.40)	4.00 (2.75–5.00)	Z=1.097 p=0.282
Dismissive Attachment	3.80 (3.40–5.20)	4.60 (4.00–5.20)	Z=0.813 p=0.426
Obsessive Attachment	4.00 (3.25–4.75)	3.52 (3.00–4.00)	Z=2.180 p=0.029
Fearful Attachment	3.25 (3.00–4.75)	3.50 (2.75–5.00)	Z=0.182 p=0.870
Attachment to Mother	65 (63–71)	69 (63–75)	Z=0.672 p=0.510
Attachment to Father	56 (43–71)	67 (54–75)	Z=1.372 p=0.174

towards their children are strongly associated to attachment style of children. It has been reported that abnormalities of family functionality and child-family relationship as well as maternal-paternal attitudes play role in the development of ADHD. In a study, it was reported there is more negative-impulsive behavior control and less positive maternal-paternal attitudes in the parents of patients with ADHD [12]. Accordingly, these negative and judging behaviors will affect parent attachment and its quality in the child. It was shown that parental failure could enhance problems regarding self-regulation and could cause insecure attachment patterns [17]. It was suggested that authoritative or permissive parenting style could lead adopting insecure attachment patterns [17]. It was also proposed that disrupted self-regulation in children with ADHD could originate from stressful early interactions between child and caregiver and impaired primary attachment [18] and that insecure attachment could be premise of ADHD in adolescents [19]. In this present study, it was seen that maternal and paternal attachment scores were lower in ADHD group although there was no significant difference in IPPA scores between groups. However, pre-occupied attachment was reported to be significantly higher in cases with maternal history of psychiatric disease when compared to those without in ADHD group. In addition, a positive correlation was detected between maternal and paternal attachment. By the finding that there was positive correlation between maternal and paternal attachment in both ADHD and control group, out study shows that relationship with mother and father directly influences each other and that parenthood is perceived as a unitary. An individual who develops a secure attachment to mother will reflect this to his/her relationship with father.

It was reported that mothers of children with ADHD promoted less interaction with their children; that they were less responsive to positive and neutral interactions promoted by children; and that they used more negative, more reactive, more authoritative and more controlling but less positive parenting strategies. This cannot only cause family conflict but it also affects attachment patterns, particularly attachment to mother. In the literature, frequency of depressive

disorder is reported to be higher in mothers of children with ADHD, supporting this present study. Previous studies reported that mothers of children with ADHD experience more burn-out and have higher exhaustion levels when compared controls [20].

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Agmatine Produces Antidepressant Effect via Modulation of Neuroinflammation in Chronic Unpredictable Mild Stress Model of Rats: Implication in Inflammatory Perspective of Depression

Ceren Şahin Özkartal[a], Feyza Arıcıoğlu[a], Erdem Tüzün[b], Rümeysa Keleş[c], Cansu Kandemir[d], Serap Şirvancı[d] and Cem İsmail Küçükali[b]

[a]Department of Pharmacology and Psychopharmacology Research Unit, Marmara University School of Pharmacy, Istanbul, Turkey; [b]Istanbul University, Institute of Experimental Medical Research, Neurosciences Department, Istanbul, Turkey; [c]Sakarya University, Faculty of Medicine, Department of Pharmacology, Sakarya, Turkey; [d]Department of Histology-Embriology, Marmara University School of Medicine, Istanbul, Turkey

E-mail address: cerenshn@gmail.com

ABSTRACT

Objective: There is evidence that depression is linked to elevated inflammation which predicts antidepressant-resistance. Based on our previous work, agmatine, a novel neurotransmitter with antidepressant activity might also have therapeutic potential for inflammation aspect of depression. Therefore, we addressed the effect of chronically administered agmatine on certain indicators of brain inflammation induced by chronic unpredictable mild stress (CUMS), a well-validated animal model of depression, with regard to behavioral investigations.

Methods: Male Sprague Dawley rats (290–320 g) were divided into groups; Control (saline), CUMS (saline), CUMS+Imipramine (10 mg/kg; i.p.), CUMS+Agmatine (40 mg/kg; i.p.), (n=10–12 in each). In CUMS model, various stressors were applied for 6 week. At 3rd week, the treatments were started for 21 days. Sucrose preference test (SPT) was applied in every two weeks. Finally, forced swim (FS) test was performed and rats were sacrificed. Prefrontal cortex tissues were used for Real-time PCR analysis of IL-1β, IL-6, Nod-like receptor protein 3 (NLRP3), NLRP1 and caspase-1. Microglial activation was assessed by immunohistochemical analysis. One-way ANOVA was used for statistical analysis with a $p < 0.05$ value to indicate statistical significance.

Results: Sucrose preference was significantly reduced in CUMS exposed rats compared to control group while imipramine and agmatine treatments significantly ameliorated anhedonia behavior. In FS test, imipramine and agmatine treatments caused significant reductions of immobility time induced by CUMS. Agmatine reversed CUMS-induced microglial activation and significant elevations in IL-1β, IL-6, NLRP1, and caspase-1 but not NLRP3 levels. Unlike imipramine, agmatine significantly reduced CUMS-induced IL-1β, IL-6, NLRP1, and caspase-1 levels.

Conclusions: Our initial results demonstrated that agmatine exerted antidepressant-like effect in CUMS model of depression. In addition, unlike imipramine agmatine reduced neuroinflammatory response. Therefore, these findings provided translational aspects for clinical studies addressing agmatine as potential antidepressant for treatment-resistant depression especially when occured with elevated inflammation.

KEYWORDS
Agmatine; antidepressant; CUMS; depression; inflammasome; neuroinflammation

Introduction

Major depressive disorder (MDD) is one of the most debilitating and highly prevalent complex psychiatric disorders around the world. Today, the adequate treatment of MDD with current antidepressants, mainly targeted on enhancing monoaminergic neurotransmission, unfortunately remains to be poorly achieved. In fact, satisfactory treatment response

cannot be obtained in almost 1/3 patients. Additionally, by 2030 depression is estimated to be the first-line disease in terms of bringing social and economic burden to society worldwide. Therefore, there is certain need for novel pharmacological approaches under the guidance of improved understanding the neurobiology of depression [1].

During the last period, preclinical/clinical studies suggest the strong link between depression and inflammation. In this context, amongst other inflammatory cytokines, especially changes in levels of interleukin-1beta (IL-1β), is considered to possibly be one of the important markers for depression. Especially, during the last period, innate immune mechanisms that initiate cytokine responses namely as inflammasome has been growingly addressed with regard to inflammation aspect of depression. Within this framework, inflammasome activation and subsequent increase in cytokines levels have been shown in animal depression models and also in MDD patients [2,3].

Agmatine, decarboxylated metabolic product of L-arginine, is now considered as a novel neurotransmitter/neuromodulator in the mammalian brain. Agmatine is an endogenous inhibitor of nitric oxide synthase and binds to imidazoline-binding sites, α_2-adrenoreceptors and blocks N-methyl-D-aspartate receptors and other ligand-gated cationic channels including nicotinic and serotonin 5-HT$_3$ receptors. When exogenously administered, agmatine has been shown to exert a variety of pharmacological effects improving a wide spectrum of central nervous system pathologies. Growing number of studies suggest that agmatine may be a potent antidepressant molecule; however, the exact mechanism underlying this effect remains to be unclear. Recently, agmatine's anti-depressant effect was also proposed in a pilot clinical study with a small sample size. Interestingly, the anti-depressant effect produced by agmatine in MDD patients was reported to be independent from serotonergic mechanisms [4].

Up to the present, several line of evidence suggests that agmatine by reducing inflammatory mediators has beneficial effects in certain inflammatory conditions including acute lung injury, pulmonary fibrosis or neuronal injury highlighting its anti-inflammatory properties. At present, there are few but encouraging reports suggest that agmatine might also have therapeutic potential for inflammation aspect of depression. We recently demonstrated for the first time that acute agmatine administration reversed sub-chronic stress-induced inflammatory mediators via mechanism at least partially mediated by inflammasome formation in rats [5].

The mentioned findings and the literature therefore, provided basis for the present study in which we aimed to examine the therapeutic potential of agmatine in inflammatory aspect of depression. To accomplish this, we addressed the effect of chronically administered agmatine as a potent antidepressant molecule on certain indicators of neuroinflammation induced by chronic unpredictable mild stress (CUMS), a well-validated animal model of depression, with regard to behavioral alterations in rats.

Methods

Male adult Sprague-Dawley rats (290-320 g) were used (Marmara University, Experimental Animal Implementation and Research Center) and housed in groups under standard laboratory conditions except stress sessions. Food and water were provided *ad libitum* except the duration of CUMS. The study was approved by the Animal Ethics and Care Committee of Marmara University. Rats were divided into 4 experimental groups (n=11-12/each) as Control (saline; non-stressed), CUMS (saline), CUMS+Imipramine (10 mg/kg; i.p. for 21 days) and CUMS+Agmatine (40 mg/kg; i.p. for 21 days) (n=10-12 in each).

Rats underwent CUMS, a well-validated animal model of depression, for 6 weeks in order to produce depression-like state. In CUMS model, various stressors were applied such as tail pinch (1 min), cage tilting (24 h), wet bedding (24 h), swimming in cold/hot water (5 min), paired caging (48 h), level shaking (10 min), light/dark cycle reversal (24 h) and food deprivation (24 h) for 6 weeks. Rats received one or two of these stressors per day and the same stressor was not applied in subsequent days in order to prevent anticipation. Non-stressed control animals were kept in a different room where they had no contact with CUMS groups. Treatments were started at 3rd week and continued for 21 days along with the CUMS. Anhedonia and despair-like behaviors were assessed as reflections of depressive state of animals by using sucrose preference test (SPT) and forced swim (FS) test, respectively. Body weights of rats were recorded weekly. SPT was applied in every two weeks throughout CUMS as depicted in Figure 1. FS test was conducted at 6th week before sacrification. In FS test, rats were allowed to swim for 15 min in Plexiglas cylinders (40×14 cm) filled with tap water (30-31 cm height; 25 ± 1°C) for habituation. The next day, rats underwent FS test for 5 min under the same conditions. The swimming sessions were recorded by a video camera. The immobility time was scored by an experienced researcher.

After FS test, rats were sacrificed, the brains were dissected and prefrontal cortex (PFC) and hippocampal tissues were collected. Tissue samples were stored at -80 ℃ until molecular analysis. All experimental procedures conducted on animals were depicted in Figure 2.

Real-time polymerase chain reaction (PCR) was conducted for gene expression assays for IL-1β, IL-6, caspase-1 and two inflammasome forming proteins;
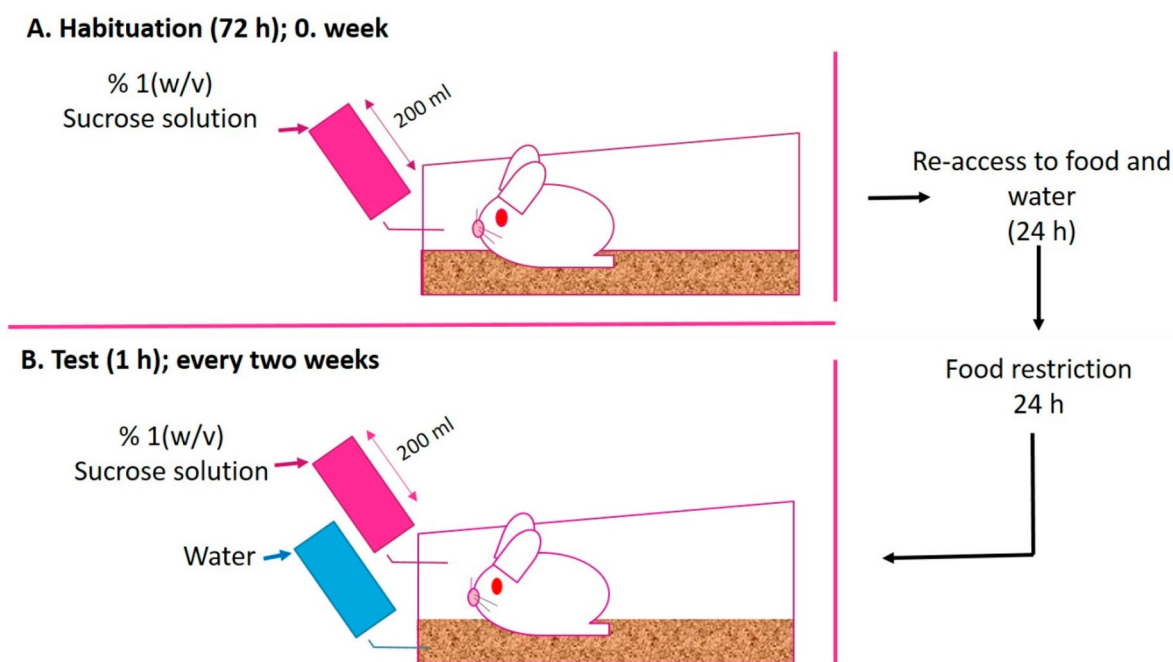
A. Habituation (72 h); 0. week

% 1(w/v)
Sucrose solution

200 ml

Re-access to food and
water
(24 h)

B. Test (1 h); every two weeks

% 1(w/v)
Sucrose solution

200 ml

Water

Food restriction
24 h

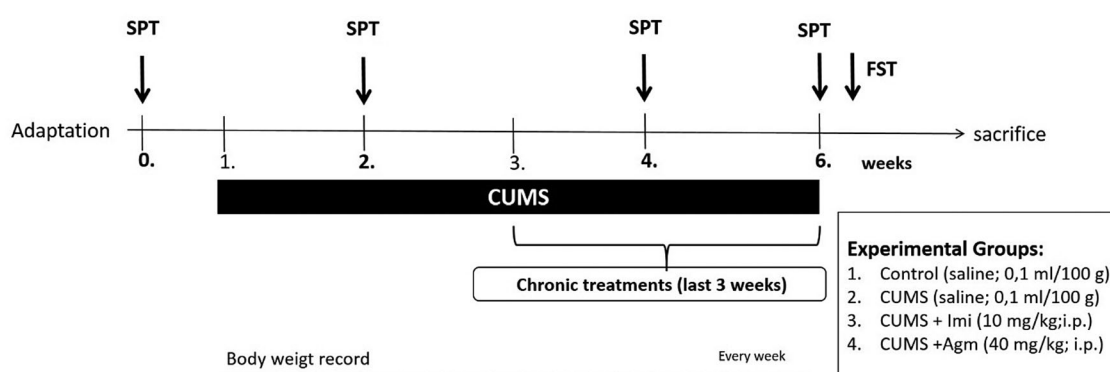**Figure 1.** Schematic diagram of sucrose preference test.

Figure 2. Schematic diagram of the experimental design. CUMS; chronic unpredictable mild stress, Imi; imipramine, Agm; agmatine, FST; forced swim test, SPT; sucrose preference test.

Nod-like receptor 3 (NLRP3) and NLRP1. The data was normalized to Beta-catenin Cycle Threshold and it was calculated and quantified by 2^{-ddCT} relative quantification method. As a marker of microglial activation, Iba-1 was assessed by immunohistochemical analysis in hippocampus.

Statistical analyses were performed using GraphPad Prism 5 program. Data were presented as the means ± SEMs. The one-way analysis of variance (ANOVA) test followed by Tukey's HSD test was used for FST and gene expression analysis of statistics. Two-way ANOVA was used for SPT and body weight results. A $p < 0.05$ was considered to be statistically significant.

Results

In SPT, 6 weeks of CUMS procedure induced anhedonia behavior as sucrose preference was significantly reduced in CUMS exposed rats compared to control group ($p < 0.01$). Imipramine ($p < 0.05$) and agmatine ($p < 0.01$) treatments started at 3rd week of CUMS, significantly ameliorated anhedonia behavior at 6th week compared to CUMS group (Figure 3). In FS test, immobility time as reflection of despair behavior was significantly elevated in CUMS group ($p < 0.001$) compared to control group while imipramine ($p < 0.001$) and agmatine ($p < 0.001$) treatments caused significant reductions of immobility time compared to CUMS group (Figure 4). Body weight was recorded weekly through the entire experiment. No significant changes were found between the groups (data not shown here).

In immunohistochemical experiments Iba-1 was overexpressed in hippocampus of CUMS group ($p < 0.01$) and agmatine significantly reduced the Iba-1 immunoreactivity ($p < 0.01$) (Figure 5). Gene expression analysis in PFC revealed that CUMS exposure for 6
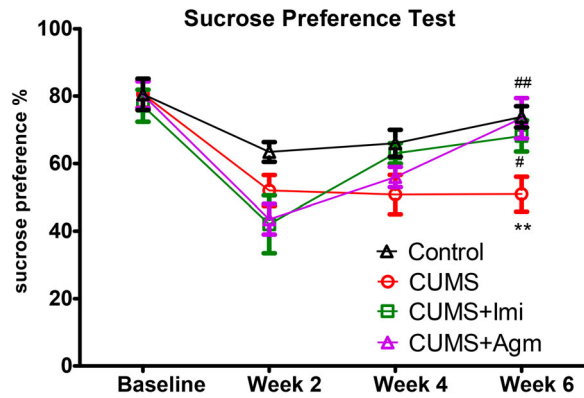
Figure 3. Sucrose Preference Test (SPT). All data are expressed as mean ± S.E.M. **$p<0.001$ versus control, ##$p<0.01$, #$p<0.05$ versus CUMS.
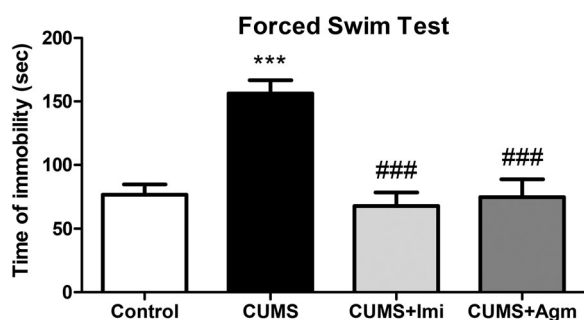

Figure 4. Forced Swim Test (FST). FST was conducted at 6th week after CUMS and treatment schedule. All data are expressed as mean ± S.E.M. ***$p<0.001$ versus control, ###$p<0.001$ versus CUMS.

weeks caused significant elevations in mRNA levels of IL-1β ($p<0.05$), IL-6 ($p<0.05$) two major pro-inflammatory cytokines involved in depression (Figure 6). In addition to cytokines, two members of inflammasome forming NLR proteins and caspase-1 which are responsible for initiating cytokine-mediated inflammatory responses were examined in this present study. In CUMS group NLRP1 ($p<0.01$), caspase-1 ($p<0.05$) but not NLRP3 levels were significantly higher compared to control. Unlike imipramine, chronic agmatine treatment for 3 weeks caused significant reductions in CUMS-induced inflammatory mediators, IL-1β ($p<0.05$), IL-6 ($p<0.05$), NLRP1 ($p<0.05$) and caspase-1 ($p<0.05$) compared to CUMS alone (Figure 6).

Conclusions

In conclusion, our initial findings presented here clearly demonstrate that agmatine as a potent antidepressant molecule comparable to imipramine might have therapeutic potential in inflammation-associated depression. It is of note that agmatine's anti-inflammatory actions are not only restricted to reducing pro-inflammatory cytokine response but also comprehends modulation of innate immune activation regarding its effects on inflammasome forming protein NLRP1 and caspase-1 and reduction in microglial activation. A recent meta-analysis revealed that there was a correlation between antidepressant
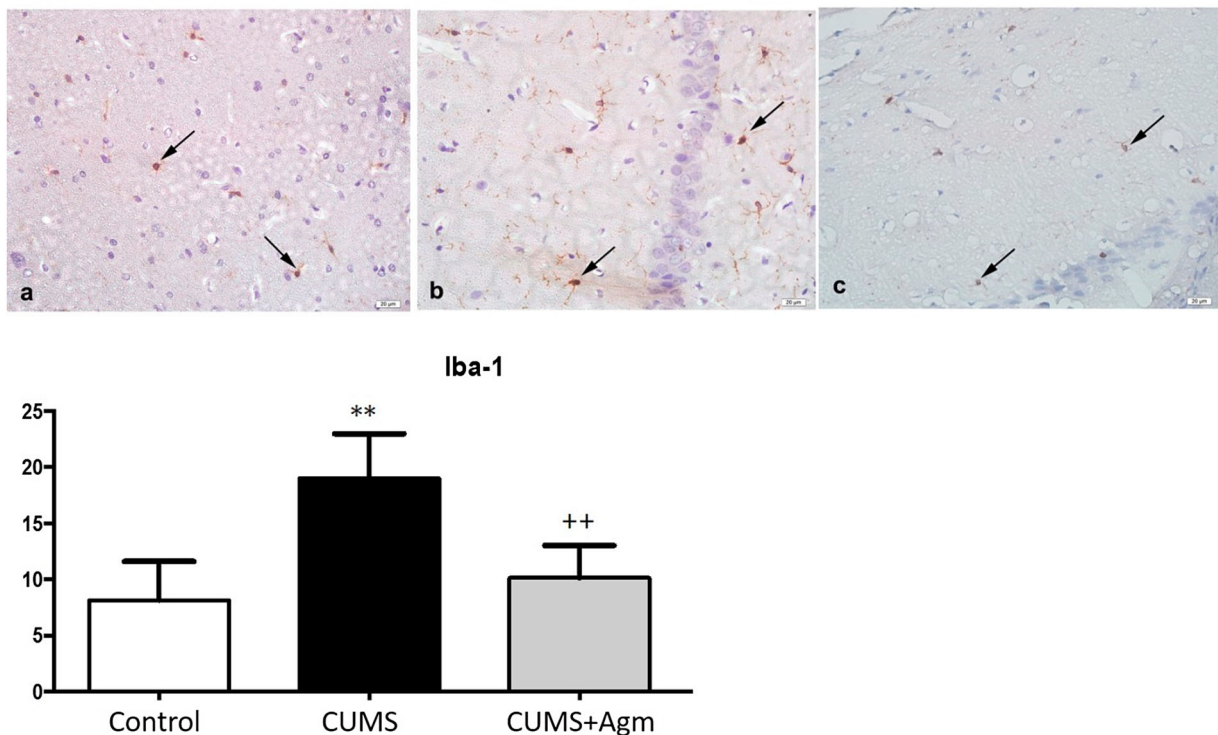

Figure 5. The effect of CUMS and agmatine treatment of Iba-1 immunoreactivity in hippocampus of rats. (a) Control, (b) CUMS, (c) CUMS+Agmatine Bar: 20 cm. Original magnification: x400. **$p<0.01$, versus control, ++$p<0.01$ versus CUMS. All data are expressed as mean ± S.E.M.
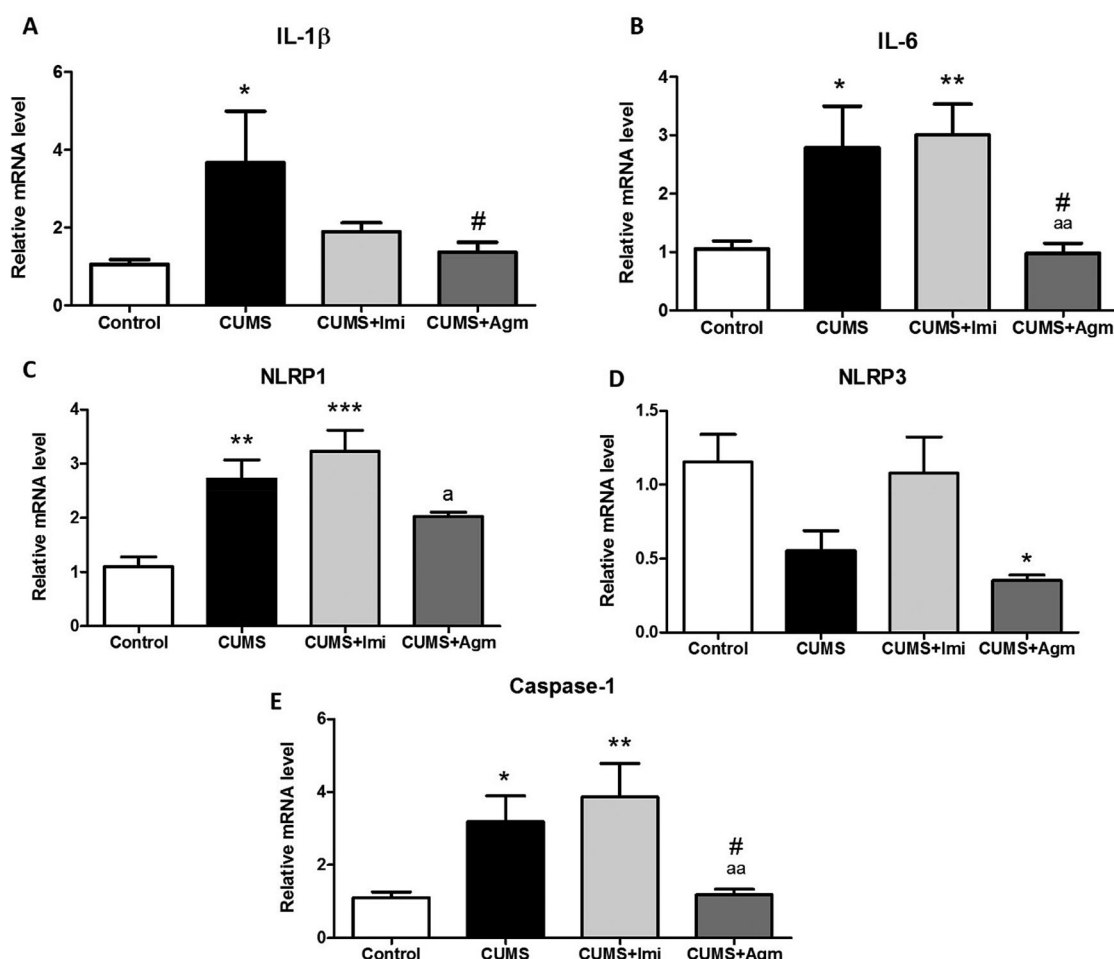
Figure 6. The effect of CUMS and treatments of relative mRNA levels of inflammatory mediators in PFC of rats. *$p<0.05$, **$p<0.01$, ***$p<0.001$ versus control, #$p<0.05$ versus CUMS, a$p<0.05$, aa$p<0.01$ versus CUMS+Imi. All data are expressed as mean ± S.E.M. and represented as fold change relative to control.

treatment resistance and increased inflammation in MDD patients [6]. Therefore, inflammation aspect of depression holds promise for predicting antidepressant treatment response and possible significance of utilizing novel therapeutics having anti-inflammatory properties in the treatment of depression. Our preliminary findings could provide novel insights for future clinical studies addressing agmatine as a potent antidepressant candidate for treatment-resistant depression with elevated inflammation.

Source of Funding

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Neural Stem Cell Treatment Prevents Neuroinflammation and Increases Hippocampal BDNF Levels in Genetic Absence Epileptic WAG/Rij Rats

Tijen Utkan[a], Tuğçe Demirtaş Şahin[a], Yusufhan Yazir[b], Zehra Seda Halbutoğulları[c], Semil Selcen Gocmez[a] and Feyza Arıcıoğlu[d]

[a]Department of Pharmacology, School of Medicine, Kocaeli University, Kocaeli, Turkey; [b]Department of Histology and Embryology, School of Medicine, Kocaeli University, Kocaeli, Turkey; [c]Stem Cell and Gene Therapies Research & Applied Center, Kocaeli University, Kocaeli, Turkey; [d]Department of Pharmacology and Psychopharmacology Research Unit, School of Pharmacy, Marmara University, Istanbul, Turkey

E-mail address: tugcemedusa@gmail.com

ABSTRACT

Objective: Studies have revealed cognitive impairments in absence epileptic patients and animal models of absence epilepsy. WAG/Rij rats, a strain of Wistar origin, is a valid genetic model of generalized absence epilepsy. We previously reported that neural stem cell (NSC) treatment ameliorated cognitive dysfunctions in WAG/Rij rats. In this study we examined in WAG/Rij rats whether NSC treatment reduces both neuroinflammation and hippocampal BDNF levels.

Methods: Two-month old Wistar and WAG/Rij rats were divided into three subgroups: Control, NSC and Sham (n=10 in each). NSCs taken from fetal medial ganglionic eminence were transplanted into perioral regions of the primary somatosensory cortex of the NSC groups and we waited for 3 months for cell differentiation. After 3 months, hippocampal BDNF expression was assessed by immunohistochemically. Hippocampal TNF-α and IL-1β levels were evaluated by ELISA. One-way ANOVA and Tukey's post hoc test used for statistical analysis. The immunoreactivity scores were compared by the Kruskal–Wallis test following Dunn's multiple comparison test. The alpha level of 0.05 was set up to indicate statistical significance.

Results: We found reduced hippocampal BDNF immunoreactivity and increased hippocampal TNF-α and IL-1β levels in WAG/Rij control group compared to Wistar control group, while these values were similar in all Wistar groups. However, NSC treatment in WAG/Rij rats significantly enhanced BDNF immunoreactivity and decreased hippocampal TNF-α and IL-1β levels compared to WAG/Rij control group. In WAG/Rij sham group, both BDNF immunoreactivity and TNF-α and IL-1β levels were similar to that of the WAG/Rij control group.

Conclusions: The findings of this study showed that NSC treatment enhanced BDNF expression and decreased TNF-α and IL-1β levels in the hippocampus of genetic absence epileptic WAG/Rij rats. These actions of NSC treatment may be responsible, at least in part, for its preventive effect on cognitive impairment in absence epilepsy in humans.

Introduction

Absence epilepsy is characterized by a brief loss and return of consciousness with bilateral synchronous spike wave discharges on the EEG. Wistar Albino Glaxo/Rijswijk (WAG/Rij) rats, a strain of Wistar origin, is a valid genetic model of generalized absence epilepsy. Electrophysiologically and behaviorally well-defined absence seizures occur in every member of WAG/Rij rats (Coenen and Van Luijtelaar, 2003). Several studies have focused on cognitive impairments in absence epileptic patients and animal models of absence epilepsy. We previously reported decreased learning and memory ability in WAG/Rij rats compared to aged-matched Wistar rats. In the same study, we also found that neural stem cell (NSC) treatment significantly improved cognitive functions of genetic absence epileptic WAG/Rij rats in passive avoidance and Morris Water maze tests and ameliorated emotional and spatial learning and memory impairment (Utkan, Sahin, Karson, Gocmez, 2016). On the other hand, several studies suggested an important role of neuroinflammation in the development of absence seizures in animal models

of absence epilepsy. A previous study revealed that lipopolysaccharide injection increased spike wave discharges in genetic absence epileptic WAG/Rij rats parallel with the peripheral proinflammatory cytokine responses (Kovacs, Czurko, Kekesi & Juhasz, 2011). Another study also demonstrated that long term treatment with a selective COX-2 inhibitor, etoricoxib, decreased the development of absence seizures in WAG/Rij rats (Citraro, Leo, Marra, De Sarro & Russo, 2015). However, we previously showed significantly reduced number, mean duration and total duration of spike-wave discharges in WAG/Rij rats compared to control and sham groups (Utkan, Şahin, Karson, & Halbutoğulları, 2016). Based on this background, we hypothesized that there may be a relationship between cognitive dysfunctions and neuroinflammation in absence epilesy, and examined whether NSC treatment reduces both hippocampal neuroinflammation and neurogenesis in WAG/Rij rats. So, we analyzed proinflammatory cytokine levels (TNF-α and IL-1β) and BDNF expression in hippocampal tissues.

Methods

Animal preparation and experimental design

Male Wistar albino and WAG/Rij rats (2-month-old, weighing 180-220 g) obtained from Kocaeli University, Experimental Medical Research and Application Center, Kocaeli, Turkey, were used in the present study. Rats were housed in an animal colony ($\sim$ 5 to 6 per cage) for 2 weeks before the start of the experiments. All behavioral tests were carried out between 9:00 a.m. and 12:00 p.m. under standard laboratory conditions (12-h light/dark cycle with lights on at 07:00 a.m., 22±2°C room temperature). Tap water and foot pellets were provided without restrictions. All the animals were naïve for the experimental tests.

This study conformed to the Rules of Animal Research Ethics Committee in Turkey (No: 26220, July 6, 2006) for the animal care and the experimental protocol in the current study was approved by Kocaeli University Animal Research Ethics Committee. Wistar and WAG/Rij rats were divided to the following groups (n=10 in each group): Wistar control, Wistar NSC, Wistar sham, WAG/Rij control, WAG/Rij NSC and WAG/Rij sham. Wistar and WAG/Rij control groups received no treatment. NSCs taken from fetal medial ganglionic eminence were transplanted into perioral regions of the primary somatosensory cortex of the Wistar and WAG/Rij NSC groups. The sham groups were exposed to the same surgical procedure as the NSC groups but they only received the differentiation medium without NSC. We transplanted undifferentiated NSCs and waited 3 months for cell differentiation after transplantation. At the end of 3-month period, rats were decapitated under ketamine/xylazine (90 mg/kg/10 mg/kg) anesthesia and, brain tissues were removed for the immunohistochemical and biochemical analyses.

Animal Surgery and NSC Transplantation

Rats were anesthetized with ketamine/xylazine (90/10 mg/kg) mixture and placed in a stereotaxic frame. Their heads were firmly fixed with ear bars and the scalp was opened. Stainless-steel guide cannulas were bilaterally implanted into the perioral region of the primary somatosensory cortex (AP -1,4 mm, L ± 4,7 mm; AP -2.1 mm, L ± 4,7 mm: V -2 mm from the surface of the cortex). The coordinates were obtained from stereotaxic atlas of Paxinos and Watson with bregma as the reference point. Microinjections were made at two different sites in each hemisphere. The cortices were bilaterally injected with 10^5 cells in each point (total volume 1 µl per injection). The concentration of viable cells was adjusted to a density of 10^5 cells /µl in a differentiation medium. Intracortical injections were made with a Hamilton syringe at a flow rate of 0.5 µl min^{-1}. Following the surgery, rats were placed under a heating lamp until actively breathing and then returned to their cage.

Immunohistochemistry

Paraffin sections were prepared from rat hippocampi that were fixed with 10% neutral buffered formalin. Sections were deparaffinized in xylene, rehydrated through a graded alcohol series and they were washed with phosphate-buffered saline (PBS). Following these procedures, an antigen retrieval procedure was performed by treating the samples in 10 mM citrate buffer (pH 6.0) in a microwave oven at 600 W for 5 min two times. The samples were allowed to cool for 20 min at room temperature and incubated in 3% H_2O_2 for 15 min. In order to block nonspecific bindings, the sections were then incubated in a blocking serum (Histostain-Plus Kit, Broad Spectrum, Invitrogen, and Carlsbad, CA, USA) for 10 min at room temperature to block specific binding. The primary rabbit polyclonal anti-BDNF antibody (Santa Cruz Biotechnology, Santa Cruz, CA, USA) was applied overnight at a 1:100 dilution at room temperature. The negative control samples were prepared by replacing the primary antibody with the antibody diluent solution (Ab-diluent reagent solution, Invitrogen, Carlsbad, CA, USA) at the same concentration. After a number of washes, the slides were incubated with a biotinylated secondary antibody (Histostain-Plus Kit, Broad Spectrum, Invitrogen, and Carlsbad, CA, USA) for 20 min at room temperature, and diaminobenzidine (DAB) (DAB Substrate Kit, Invitrogen, Carlsbad, CA, USA) was applied for visualization. The sections were briefly counterstained with Mayer's hematoxylin (Invitrogen, Carlsbad, CA, USA) and they were mounted with ClearMount (Invitrogen, Carlsbad, CA, USA) on glass slides. The slides were examined under a light microscope (Olympus BX 50, Tokyo, Japan), and photomicrographs were taken with a Leica DM 100 system (Leica DFC 290HD, Wetzlar, Hessen, Germany). The same protocol was used to treat all the samples. Two independent observers who were blinded to the groups in this study graded the immunohistochemical staining intensity on a semi-quantitative scale ranging from no (−), very weak (+), moderate (++), strong (+++) and very strong (++++) expression. Scores were assigned based on percentage of positive cells as follows: 0, <5%; 1, 6-15%; 2, 16-50%; 3, 51-80; and 4, >80%.

Biochemical measurements of proinflammatory cytokines

For hippocampal cytokine measurements, the hippocampi were dissected out from the rat brains, rinsed with cold 0.9% saline, weighed and stored at -80°C

until processing. Samples were collected in microfuge tubes, homogenized and spun down. We measured the hippocampal TNF-α and IL-1β levels to evaluate the effects of NSC treatment on neuroinflammation in WAG/Rij rats. Quantification of cytokine levels were assessed with an ELISA kit (Biosource, Invitrogen, Carlsbad, CA) according to the manufacturer's instructions. The absorbance was measured at 450 nm using a microtiter ELISA reader (VERSAmax Molecular Devices, Sunnyvale, CA, USA).

Statistical analysis

All of the data were expressed as the mean value ± standard error of the mean. Significance was tested by one-way analysis of variance (ANOVA) with a post hoc Tukey-Kramer's test. Immunoreactivity scores were evaluated by Kruskal-Wallis test followed by Dunn's multiple comparison test as a post hoc testing. Probabilities of less than 5% (p<0.05) were assumed to be statistically significant.

Results

The Kruskal-Wallis test showed that hippocampal BDNF levels differed significantly between six groups (p<0.05). We then followed these significant overall effects with multiple comparisons. Dunn's test showed that BDNF immunoreactivity in the hippocampal tissues was markedly decreased in WAG/Rij control group compared to Wistar control group (p<0.05), while these values were similar in all Wistar groups (p>0.05). However, NSC treatment in WAG/Rij rats significantly enhanced BDNF immunoreactivity compared to WAG/Rij control group (p<0.05). In WAG/Rij sham group, BDNF immunoreactivity was similar to that of the WAG/Rij control group (p>0.05).

There was a significant overall difference between six groups in terms of the hippocampal TNF-α and IL-1β levels (p<0.05). We found significantly increased TNF-α and IL-1β levels in WAG/Rij control group compared to Wistar control group (p<0.05), while there were no differences between all Wistar groups (p>0.05). In treated WAG/Rij rats, NSC treatment significantly decreased hippocampal TNF-α and IL-1β

levels compared to WAG/Rij control group (p<0.05). In WAG/Rij sham group, TNF-α and IL-1β levels were similar with the WAG/Rij control group (p>0.05).

Conclusions

The results of the current study showed reduced BDNF expression and increased proinflammatory cytokine levels in the hippocampi of WAG/Rij rats, indicating neuroinflammation and decreased neurogenesis in absence epilepsy. However, NSC treatment significantly enhanced BDNF expression and decreased TNF-α and IL-1β levels in the hippocampi of WAG/Rij rats. These actions of NSC treatment may be responsible, at least in part, for its preventive effect on cognitive impairment in absence epilepsy in humans.

Source of Funding

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The Effects of Cardiovascular Diseases and Medications on Structural Brain Outcomes

Övgü Sinem Buğan Gülbahar[a], Abda Mahmood[b], Enikő Zsoldos[b], Charlotte L. Allan[b], Anya Topiwala[b] and Klaus P. Ebmeier[b]

[a]Department of Psychiatry, Istanbul University School of Medicine, Istanbul, Turkey; [b]Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford, UK

E-mail address: osbugan@hotmail.com

ABSTRACT

Objective: The aim of this study was to examine the effects of cardiovascular medications and diseases on white matter volume (WMV), gray matter volume (GMV), and global white matter fractional anisotropy (FA) and mean diffusivity ($\bar{D}$) as measures of white matter integrity measured with magnetic resonance imaging (MRI).

Methods: A random sample of 552 of Whitehall II Phase 10 and 11 participants; gave informed consent to attend the imaging sub-study at the Oxford Centre for Functional MRI of the Brain (FMRIB). Sociodemographic information, the medical history and medication data were collected between April 2012 and February 2014. Multivariate linear regression analyses were used to evaluate the effects of cardiovascular medications, age and gender and cardiovascular diseases separately on WMV, GMV, FA and $\bar{D}$ measures.

Results: Totally, 552 participants were recruited to the study, 444 (80.4%) were men, the mean age of the participants was 69.5 (SD=5.3) years. In the crude models, GMV, FA and $\bar{D}$ were highly related to how many different cardiovascular medications participants took. This did not change after correcting for age and gender and for cardiovascular diseases. In contrast, WMV was not associated with the number of cardiovascular medications in the crude model or after correction for age, sex and cardiovascular illness. In the fully corrected models; cardiovascular diseases made a significant contribution to WMV, but not to GMV or FA and $\bar{D}$ independent of medication.

Conclusions: The results suggest that number of cardiovascular medications had an effect on gray matter volume and white matter integrity, independent of age, gender, and number of cardiovascular diagnoses. So intensity of treatment may be related to the architecture of gray and white matter, while it had no effect on white matter volume. However, the number of cardiovascular diagnoses had a direct effect on WMV, which was not mediated by number of medications.

Introduction

The aim of this study was to examine the effects of cardiovascular medications and diseases on various structural brain outcomes, such as percentage of white matter (PWM), percentage of gray matter (PGM), fractional anisotropy (FA) and mean diffusivity ($\bar{D}$) on brain magnetic resonance imaging (MRI).

Methods

The Whitehall II (WHII) study with a sample size of 10,308 British civil servants provides to explore factors hypothesized to affect brain health and cognitive ageing [1]. The cohort was established in 1985 at University College London (UCL) and the study had acquired nearly thirty years at Phase 11 [2]. A random sample of 552 WHII Phase 10 and 11 participants; willing and able to give informed consent were invited to attend the imaging sub-study at the Oxford Centre for Functional MRI of the Brain (FMRIB). We excluded participants with contraindications to MRI scanning or who were unable to travel to Oxford without assistance.

Informed consents were obtained according to ethical approval granted by the University of Oxford Central University/Medical Science Division Interdisciplinary Research Ethics Committee (CUREC/MSD-IDREC) for the "Protocol for non-invasive magnetic resonance investigations in healthy volunteers" (MSD/IDREC/2010/P17.2) and the specific protocol: "Predicting MRI abnormalities with longitudinal data of the Whitehall II sub-study" (MSD-IDREC-C1-2011-71). Demographics, the medical history and medication data were collected in a questionnaire that the participants filled out no longer than a week before their imaging appointment. Cardiovascular diseases were identified by the International Classification of Diseases 10th Revision (ICD-10) and the cardiovascular medications were classified by the British National Formulary (BNF). Data collection of this sub-study was conducted between April 2012 and February 2014.

MRI scanning was carried out at the FMRIB by a 3 T Siemens Magnetom Verio (Erlangen, Germany) Scanner with a 32-channel receive head coil. Brain tissues were segmented to grey matter (GM) and white matter (WM) using FMRIB's Automated Segmentation Tool (FAST). FA and $\bar{D}$ maps were generated with DTIFit which is a part of FMRIB's Diffusion Toolbox (http://fsl.fmrib.ox.ac.uk/fsl/fdt).

Statistical analyses were performed using IBM SPSS Statistics version 21 (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as frequencies with percentages and age as a continuous variable was presented as the mean ± standard deviation (SD). Multivariate linear regression analyses were used to evaluate the effects of cardiovascular diseases and cardiovascular medications on PWM, PGM, FA and $\bar{D}$ using enter method in three different models. In model 1, only cardiovascular system medication was added to model. However, age and gender were added to the model in addition to the model 1, in model 2. Finally, cardiovascular system disease was added to the model, in model 3. P value <0.05 defined statistical significance.

Results

Totally, 552 participants were recruited to the study during the study period. Of the participants, 444 (80.4%) were men, the mean age of the study group was 69.5 (SD=5.3) years. While, nearly the half of the participants (n=272) had no cardiovascular disease, 194 (35.1%) had one disease, 70 (12.7%) had two, 10 (1.8%) had three, and 6 (1.1%) had four or more cardiovascular diseases. The median number of cardiovascular disease was 1 with a range of 0–5. However, 242 participants (43.8%) did not use any cardiovascular medication, 104 (18.8%) had one medication, 85 (15.4%) had two, 64 (11.6%) had three, and 57 had four or more cardiovascular medications. The median number of cardiovascular medication was 1 with a range of 0–9 (Table 1).

Structural brain outcomes were shown at Table 2. While the mean of the PGM of the brain of the participants was 36.95% (S.D.=2.19%), the mean of the PWM of the brain was 37.05% (S.D.=1.69%). The mean of the FA was 0.479 (S.D.=0.018), and the mean of the $\bar{D}$ was 0.682 $mm^2.s^{-1}.10^{-3}$ (S.D.=0.025 $mm^2.s^{-1}.10^{-3}$) (Table 2).

We found that model 1 for PGM was statistically significant ($p<0.001$) with an R^2 of 0.096. Participants' PGM decreased 0.4% for each number of the cardiovascular system medication in model 1. Also the model 2 was found statistically significant ($p<0.001$) with an R^2 of 0.364. Participants' PGM decreased 0.2% for each number of the cardiovascular system medication and year in age, and females had 1.2% of PGM more than males in model 2. In addition to variables in model 2, cardiovascular disease number was added to the model 3. But it is found that the model 3 was not statistically significant, and explanation of the model did not differ from model 2 (Table 3).

It was found that the model 1 for PWM was not statistically significant. However, model 2 and model 3 were found statistically significant ($R^2=0.125$, $p<0.001$; $R^2=0.133$, $p=0.020$, respectively). Cardiovascular system medication did not have any statistically significant effect on PWM in both of model 2 and model 3. Participants' PWM decreased 0.1% for each year of age, and females had 0.4% of PGM less than males in model 2. Also their PWM decreased 0.1% for each year of age and 0.02% for each number of cardiovascular diseases, and females had 0.4% of PGM less than males in model 3 (Table 3).

Table 1. Demographics and clinical characteristics of study group (n=552).

Demographics	
Gender, n (%)	
Men	444 (80.4)
Women	108 (19.6)
Age, years, mean (S.D.)	69.5 (5.3)
Clinical characteristics	
Cardiovascular diseases, n (%)	
0	272 (49.3)
1	194 (35.1)
2	70 (12.7)
3	10 (1.8)
4 or more	6 (1.1)
Median (Q1-Q3)	1.0 (0.0–1.0)
Range (min-max)	0–5
Cardiovascular medications, n (%)	
0	242 (43.8)
1	104 (18.8)
2	85 (15.4)
3	64 (11.6)
4 or more	57 (10.4)
Median (Q1-Q3)	1.0 (0.0–2.0)
Range (min-max)	0–9

S.D., standard deviation; Q1, first quartile; Q3, third quartile.

Table 2. Structural brain outcomes on brain magnetic resonance imaging (n=552).

Structural brain outcomes	
Percentage of grey matter, mean (S.D.)	36.95 (2.19)
Percentage of white matter, mean (S.D.)	37.05 (1.69)
Fractional anisotropy, mean (S.D.)*	0.479 (0.018)
Mean diffusivity, mean (S.D.)*	0.682 (0.025)

*n=537.

Table 3. Multivariate linear regression analysis of the effects of cardiovascular diseases and medication on structural brain outcomes.

Models	PGM		PWM		FA		$\bar{D}$	
	B	p	B	p	B	p	B	p
1	($R^2=0.096$)*		($R^2=0.003$)		($R^2=0.018$) †		($R^2=0.028$)*	
(Constant)	0.375	<0.001	0.371	0.000	0.481	<0.001	0.679	<0.001
Cardiovascular system medication	-0.004	<0.001	-0.001	0.199	-0.002	0.002	0.003	<0.001
2	($R^2=0.364$)*		($R^2=0.125$)*		($R^2=0.135$)*		($R^2=0.181$)*	
(Constant)	0.497	<0.001	0.452	<0.001	0.563	<0.001	0.546	<0.001
Cardiovascular system medication	-0.002	<0.001	0.000	0.654	-0.001	0.074	0.002	<0.001
Age	-0.002	<0.001	-0.001	<0.001	-0.001	<0.001	0.002	0.001
Gender	0.012	<0.001	-0.004	0.014	-0.007	<0.001	0.009	0.021
3	($R^2=0.365$)		($R^2=0.133$) ‡		($R^2=0.136$)		($R^2=0.183$)	
(Constant)	0.497	<0.001	0.453	<0.001	0.564	<0.001	0.545	<0.001
Cardiovascular system medication	-0.002	0.001	-0.001	0.307	-0.001	0.054	0.002	0.001
Age	-0.002	<0.001	-0.001	<0.001	-0.001	<0.001	0.002	<0.001
Gender	0.012	<0.001	-0.004	0.010	-0.007	<0.001	0.009	0.008
Cardiovascular disease	-0.001	0.597	-0.002	0.020	0.001	0.399	0.002	0.166

PGM, percentage of grey matter; PWM, percentage of white matter; FA, fractional anisotropy; $\bar{D}$, mean diffusivity.
*p<0.001, †p<0.01, ‡p<0.05.

For FA, while model 1 and model 2 were statistically significant (R^2=0.018, p=0.002; R^2=0.135, $p<0.001$, respectively), model 3 was not statistically significant. In model 1, cardiovascular system medication had a significantly effect on FA, but it was found that there was no statistically significant effect in model 2. However, neither the number of cardiovascular system medication nor the number of cardiovascular disease had any significant effect on FA in model 3 (Table 3).

It was found that the model 1 and model 2 for $\overline{D}$ were statistically significant with R^2 of 0.028 and 0.181, respectively ($p<0.001$ for both two models). Cardiovascular system medication had positively effect on $\overline{D}$ in model 1 and model 2. Participants' $\overline{D}$ increased 0.003 $mm^2.s^{-1}.10^{-3}$ in model 1 and 0.002 $mm^2.s^{-1}.10^{-3}$ in model 2 for each number of the cardiovascular system medication. We found that the model 3 for $\overline{D}$ was not statistically significant, and explanation of the model did not differ from model 2 (Table 3).

Conclusions

Grey matter percentage, FA and $\overline{D}$ seem to be related to how many cardiovascular system medication participants take, and those did not depend on the number of cardiovascular diseases they had. These results suggest that the number of the cardiovascular disease did not have direct effect on those outcomes, but had indirect effect through the number of cardiovascular medication. So it may actually be a measure of the severity of structural changes of brain.

In contrast of these results, the number of cardiovascular system medication seems not to be related to white matter percentage, but the number of cardiovascular disease was related to PWM. This made us think that cardiovascular disease had direct effect on PWM, not through the number of medication. The other probable conclusion is that although participants were optimally treated still had abnormal brain changes.

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Normative Data and Factorial Structure of the Turkish Version of the Borderline Personality Questionnaire (Turkish BPQ)

Vedat Ceylan[a], Samet Kose MD, PhD[a,b], Ercan Akin[a] and Mehmet Hakan Turkcapar[a]

[a]Hasan Kalyoncu University Department of Psychology, Gaziantep, Turkey; [b]University of Texas Medical School of Houston, TX, USA and Center for Neurobehavioral Research on Addictions, Houston, TX, USA.

E-mail address: sametkose@gmail.com

ABSTRACT

Objective: Borderline personality disorder is a psychiatric pattern that begins with early adulthood and characterized by impulsivity and instability in self-image, interpersonal relationships, and affection. Borderline personality disorder is seen by 2% in the general population, 10% in the emergency service, and 20% in the inpatient. Within personality disorders, borderline personality disorders are seen at a rate of 30–60%. Specific measures of Borderline Personality were adapted to a multidimensional approach to measure borderline personality. In this study, we aimed to examine the validity, reliability, and factor structure of the Borderline Personality Questionnaire in a Turkish sample.

Methods: Participants were 306 (201 female, 105 male) college students at the Hasan Kalyoncu University in Gaziantep, Turkey. The study protocol was approved by the Ethics Committee of Hasan Kalyoncu University. Sociodemographic information of the participants was collected and Turkish version of the Turkish version of the Borderline Personality Questionnaire (BPQ), Borderline Evaluation of Severity over Time (BEST), Beck Depression Inventory (BDI), Personality Belief Questionnaire (PBQ), and State-Trait Anxiety scales were administered. All statistical analyses were performed by using SPSS version 23 for Windows.

Results: The Cronbach alpha coefficient for the Turkish BPQ was found as 0.89. The test-retest correlation coefficient for Impulsivity, Affective Instability, Abandonment, Relationships, Self-Image, Suicide, Self-Mutilation, Emptiness, Intense Anger and Quasi Psychotic States were 0.50, 0.77, 0.40, 0.68, 0.72, 0.48, 0.73, 0.74, and 0.62, respectively. A positive and statistically significant correlation was found between the Turkish BPQ and BEST (r=0.337, p<0.01), BDI (r=0.375, p<0.01), PBQ (r=0. 322, r<0.01), State Anxiety (r=0.299, p<0.01) and Trait Anxiety (r=0.306, p<0.01) scales. Principal axis factor analyses with Oblimin rotations were performed and two-factor structure was observed.

Conclusions: Our results suggested that Turkish BPQ was a valid and reliable tool with a robust factorial structure for use in clinical population in Turkey.

Introduction

Borderline Personality Disorder is a psychiatric condition, which is characterized by unstable interpersonal relationships, fear of abandonment, difficulties in regulating emotions, feeling of emptiness, chronic dysphoria and depression, and impulsivity and increased risk-taking behaviors. Furthermore, recurring self-injurious and suicidal behaviors are also features of Borderline Personality Disorder. It starts with early adulthood [1].

Previously although there are plenty inventories to assess borderline personality disorder abroad none of them was completely related to DSM-IV and/or DSM-5 BPD criteria. In this inventory, using DSM-IV/ DSM-5 criteria for the borderline personality disorder, Poreh et al. have formed separate subscales for each characteristic that identifies borderline personality disorder. BPQ was developed by Poreh et al. in 2006 [2]. The BPD criterions were self-evaluated by answering 80 items, which are in "True" or "False" format. The inventory has a separate subscale for each BPD criterion and validity and reliability of the inventory were studied on 763 college students in total [2].

In this present study, we aimed to translate and establish psychometric properties and factorial validity of the Borderline Personality Questionnaire (BPQ) in a representative Turkish university students sample and obtain normative data for future epidemiological and clinical studies in Turkey.

Methods

Participants were 306 (201 female, 105 male) college students at the Hasan Kalyoncu University in Gaziantep, Turkey. The study protocol was approved by the University's Ethics Committee. The Turkish BPQ has been translated into Turkish by Samet Kose, and back-translated into English by Ercan Akin who was blinded to the original items. After establishing semantic equivalence of the BPQ items, the content equivalence of all items was examined, and no items were excluded as being irrelevant to Turkish culture. Final version was approved by Amir Poreh.

Sociodemographic information of the participants was collected and the Turkish version of the Borderline Personality Questionnaire (BPQ),Turkish version of the Borderline Evaluation of Severity over Time (BEST), Beck Depression Inventory (BDI), Personality Belief Questionnaire (PBQ), and State-Trait Anxiety scales were administered. To examine test-retest reliability, the Borderline Personality Questionnaire (BPQ) was readministered to 50 students selected from 325 students participating in the study 4 weeks after the initial application. All statistical analyses were performed by using SPSS version 23 for Windows.

Results

The average age of 306 participants in the study was 21.19 with a standard deviation of 2.85 and it ranged from 18 to 49. The sample consisted of 201 female (65.7%) and 105 male (34.3%) students. The majority of the students participated in the study were single (96.4%) and 10 (3.3%) were married and one student was divorced.

The correlation coefficients between Emptiness and Relationships (r=0.42, p<0.01) and Emptiness and Abandonment (r=0.45, p<0.01) were higher than the correlations between other subscales (r<0.39, p <0.01). In terms of correlation coefficients between the Turkish BPQ subscales; the correlation coefficients between Emptiness and Self-Image (r=0.55, p<0.01) between Relationships and Abandonment (r=0.53, p<0.01), between Emptiness and Affective Instability (r=0.49, p <0.01) and between Intense Anger and Affective Instability (r=0.47, p<0.01) were higher than the correlation coefficients between other subscales. On the other hand, there were no statistically significant differences between age and subscales of the Turkish BPQ except for Suicide/ Self-Mutilation (r=0.18, p<0.05).

The Cronbach's alpha coefficients for the Turkish BPQ were ranging from 0.46 to 0.81. The lowest alpha values were observed for the Abandonment (0.46). For the whole scale, Cronbach's alpha coefficient was found to be 0.89. The Cronbach's alpha coefficients for the Turkish BPQ subscales were relatively consistent within each of the scales.

The test-retest correlation coefficient for Impulsivity, Affective Instability, Abandonment, Relationships, Self-Image, Suicide/ Self-Mutilation, Emptiness, Intense Anger and Quasi-Psychotic States were found to be 0.50, 0.77, 0.40, 0.68, 0.72, 0.48, 0.73, 0.74, and 0.62, respectively. There were no significant differences between the mean scores of the Turkish BPQ across the 1-month test-retest period.

Convergent and Discriminant validity were examined by correlation between the BPQ scores and BEST, BDI, PBQ, State-Trait Anxiety scales scores. A positive and statistically significant correlation was found between the Turkish BPQ and BEST (r=0.337, p<0.01), BDI (r=0.375, p<0.01), PBQ (r=0.322, r<0.01), State Anxiety (r=0.299, p<0.01) and Trait Anxiety (r=0.306, p<0.01) scales.

Principal axis factor analyses with Promax rotations were performed and two-factor structure was observed. Factor 1 included Affective Instability, Abandonment, Relationships, Self-Image, Suicide/ Self-Mutilation, Emptiness, Intense Anger and Factor 2 included Impulsivity, Quasi-Psychotic States. These two factors

Table 1. BPQ Scales and subscales, Mean and SD, and Cronbach's alpha values, and test-retest correlations.

	Turkish (n=306)			
	M	SD	α	rtt
Impulsivity	1.4	1.4	0.53	0.504**
Affective Instability	4	5.2	0.68	0.774**
Abandonment	2.5	1.6	0.46	0.398**
Relationships	2.9	2	0.65	0.683**
Self-Image	1.4	1.6	0.65	0.718**
Suicide/ Self-Mutilation	0.6	1.1	0.68	0.484**
Emptiness	3	2.1	0.63	0.734**
Intense Anger	4	2.8	0.81	0.739**
Quasi-Psychotic States	2.5	1.8	0.65	0.623**
Total BPQ	22.8	10.7	0.89	0.672**

rtt, test-retest correlation coefficient.
**p<0.01.

accounted for 39.40% and %10.63 of the variance (50.03% cumulatively).

Discussion

In this study, we aimed to examine the validity, reliability, and factor structure of the Borderline Personality Questionnaire in a Turkish sample. The main results of the study confirmed that the Turkish BPQ was observed to have stable and reliable psychometric properties.

The internal consistency coefficients of the Turkish BPQ scale and subscales showed that the scale was reliable. The Cronbach's alpha coefficients for the Turkish BPQ were ranging from 0.46 to 0.89. The lowest alpha values were observed for the Abandonment subscale and the highest Cronbach's alpha coefficient were observed for the Intense Anger. Cronbach's alpha coefficient for the total scale was found to be 0.89. These results showed the internal consistency of the scale was reliable. The reason why Abandonment subscale had the lowest Cronbach's alpha coefficient might have been due to factorial structure of the borderline personality, translation problems, or sample size. Additionally, the positive correlation coefficient between the first and the second administration of the Turkish BPQ revealed high test-retest reliability.

Both Cronbach's alpha coefficients and test-retest correlation coefficients showed that Turkish BPQ was a reliable scale. The positive correlation between Turkish BPQ, BEST, BDI, PBQ, and STAI further gave support to the validity of the scale.

Initially, to examine the factorial structure of the Turkish BPQ at the subscale level, we used unrotated principal component analysis. Results showed one-dimensional structure using a condition of Eigenvalues greater than 1 rule for retaining factors. However, this factor solution did not provide a strong fit and the study of original scale has used a two dimensional structure and this two-factor solution showed a better factor orientation. Then, using a Promax rotation and a principal component method for extraction, the results yielded a two factor solution. Results showed that the first factor consisted of Affective Instability, Relationships, Self-Image, Suicide/Self-Mutilation, Emptiness and Intense Anger subscales and the second factor consisted of Impulsiveness and Quasi-Psychotic States subscales. These two factors explained 50.03% of the total variance. Previous studies that examined the factor structure of borderline personality indicated that the structure of BPD in non-clinical and clinical samples can range from a one-factor to a six-factor solutions [3,4]. Poreh et al. [2] conducted a Principal Component Analysis of the BPQ subscales and found both a single borderline factor and a 2-factor solution. In this present study, we also found a one-dimensional solution and a 2-factor solution. Impulsivity did not show highest loading on Factor 1 and Self-Image and Emptiness did not show highest loading on the same factor, which is Factor 2. These three subscales were also unambigiously related to Factor 1 and Factor 2 in all samples, respectively (see Table 6). Our results provided support to Poreh et al.'s findings. [2] Furthermore, we also conducted Partial Confirmatory Factor Analysis (PCFA), which sits somewhere between exploratory factor analysis (EFA) and confirmatory factor analysis (PCFA) by using Maximum Likelihood as an Extraction Method. In this analysis,

Table 2. The first unrotated factor (PC1) and pattern matrix following principal components analysis and Promax rotation of two factors (F1 and F2), for the Turkish, United States, English, and Australian Samples.

BPQ Sub-scale	Turkish sample			U.S sample			Australian sample			English Sample		
	PC1	F1	F2	PC1	F1	F2	PC1	F1	F2	PC1	F1	F2
Impulsivity	0.47	---	0.73	0.54	---	0.71	---	---	0.94	---	---	0.83
Affective Instability	0.71	0.67	0.52	0.81	0.51	0.43	0.80	0.79	---	0.77	0.67	---
Abandonment	0.70	0.67	0.50	0.73	0.75	---	0.73	0.84	---	0.73	0.76	---
Relationships	0.68	0.65	0.49	0.78	0.74	---	0.76	0.73	---	0.75	0.71	---
Self-Image	0.61	0.73	---	0.58	0.79	---	0.79	0.82	---	0.73	0.87	---
Suicide/Self-Mutilation	0.60	0.54	0.49	0.40	---	0.77	0.59	0.37	0.51	0.53	0.37	0.31
Emptiness	0.74	0.83	---	0.76	0.86	---	0.83	0.86	---	0.84	0.88	---
Intense Anger	0.55	0.51	0.44	0.55	---	0.71	0.68	0.57	---	0.56	---	0.62
Quasi-Psychotic States	0.48	0.30	0.70	0.68	0.64	---	0.57	0.46	---	0.37	---	0.52
% Variance		39.40	10.63		43.62	12.34		46.95			41.05	13.23

Note: Scores below 0.30 were replaced with blanks.

the Residuals are computed between observed and reproduced correlations. The adequacy of sample size was verified using the Bartlett's test of sphericity and the Keiser-Meyer-Olkin (KMO) measurement of sampling adequacy. Bartlett's test of sphericity was significant (Chi Square=7766.169, df=3160, p=0.000) for the BPQ and the KMO measure of sampling adequacy was acceptable at 0.739. There were 1328 (42.0%) non-redundant residuals with absolute values greater than 0.05. Goodness-of-fit test was also significant (Chi-Square=4971.099, df=3001, p=0.000). The PCFA yielded with 2-factor solution in consistent with Poreh et al.'s [2] and our PCA analysis. We agree with Cabrera-Nguyen's (2010) [5] approach that the EFA should be followed by CFA using a different sample (or samples) to evaluate the EFA-informed a priori theory about the measure's factor-structure and psychometric properties. This is what we plan to perform in conducting our clinical studies using the Turkish BPQ in BPD patients and BPD patients who are comorbid with depression.

In conclusion, the Turkish version of the BPQ had sound psychometric properties in our sample of Turkish healthy volunteers, including its internal consistency, test-retest reliability, concurrent validity, and factorial structure. The Turkish BPQ will be useful for future studies in different countries to help better understanding normalcy, psychopathology, and personality disorder and to examine the biological, social, and psychological differences in people from different cultures.

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Normative Data and Factorial Structure of the Turkish Version of the Borderline Evaluation of Severity Over Time (Turkish BEST)

Ercan Akin[a], Samet Kose MD, PhD[a,b], Vedat Ceylan[a], Gulizer Temel[a] and Mehmet Hakan Turkcapar MD[a]

[a]Hasan Kalyoncu University Department of Psychology, Gaziantep, Turkey; [b]University of Texas Medical School of Houston, TX, Department of Psychiatry and Center for Neurobehavioral Research on Addictions, Houston, TX, USA.

E-mail address: sametkose@gmail.com

ABSTRACT

Objective: Borderline Personality Disorder is a psychiatric condition, which is characterized by unstable interpersonal relationships, difficulties in regulating emotions, fear of abandonment, feeling of emptiness, chronic dysphoria and depression, and impulsivity and increased risk-taking behaviors. Several specific measures of Borderline Personality were adapted to a multidimensional approach to measure borderline personality. In this study, we aimed to examine the validity, reliability, and factor structure of the Borderline Evaluation of Severity Over Time scale (Pfhol et al., 2009) in a Turkish sample.

Methods: Participants were 306 (201 female, 105 male) college students at the Hasan Kalyoncu University in Gaziantep, Turkey. The study protocol was approved by the University's Ethics Committee. Sociodemographic information of the participants was collected and Turkish version of the Borderline Evaluation of Severity over Time (BEST), the Turkish version of the Borderline Personality Questionnaire (BPQ), Beck Depression Inventory (BDI), Personality Belief Questionnaire (PBQ), and State-Trait Anxiety scales were administered. All statistical analyses were performed by using SPSS version 23 for Windows.

Results: The Cronbach's alpha coefficients for the Thoughts and Feelings, Negative Behaviors, and Positive Behaviors subscales were 0.80, 0.65, and 0.67, respectively. For the whole scale, the Cronbach's alpha coefficient was 0.75. The test-retest correlation coefficients for Thoughts and Feelings, Negative Behaviors and Positive Behaviors were 0.61, 0.50, and 0.51, respectively (Table 1). A positive and statistically significant correlation was found between the Turkish BEST and BPQ (r=0.337, p<0.01), BDI (r=0.460, p<0.01), PBQ (r=0.337, p<0.01), State Anxiety (r=0.351, p<0.01) and Trait Anxiety (r=0.387, p<0.01) scales (Table 2). A two-factor solution

that accounted for 87.81% of the variance observed. The first two subscales of the BEST formed Factor 1 and the last subscale formed Factor 2.
Conclusions: Our results suggested that Turkish BEST was a valid and reliable tool with a robust factorial structure to use in clinical population in Turkey.

Introduction

Borderline Personality Disorder is a psychiatric condition, which is characterized by unstable interpersonal relationships, fear of abandonment, difficulties in regulating emotions, feeling of emptiness, chronic dysphoria and depression, and impulsivity and increased risk-taking behaviors [1].

Borderline Evaluation of Severity over Time (BEST) is a 15-item self-report Likert-style scale, which is developed by Pfhol and Blum [2] and composed of three subscales. The purpose of the development of this scale is to measure the severity and variation of the Borderline personality in response to treatment. The scale consists of items that measure feelings, thoughts, and behaviors and it is used to measure the severity of Borderline personality rather than to diagnose it [2].

The first 8 items of the scale form subscale A (Thoughts and Emotions). This subscale includes assessment of mood reactivity, identity disorder, unstable relationships, paranoia, space, and suicidal thinking. The next 4 items form subscale B (Behaviors-Negative) and assess negative behaviors like self-injury. In both these two subscales, Items are rated from 1 (None/Slight) to 5 (Extreme). The last 3 items form subscale C (Behaviors- Positive) and assess positive behaviors like continuing to therapy. These 3 items are rated from 5 (Almost Always) to 1 (Almost Never) [2].

To the best of our knowledge, no study has been conducted with Borderline Evaluation of Severity over Time (BEST) in a different language. In the present study, we aimed to translate and establish psychometric properties and factorial validity of the Borderline Evaluation of Severity over Time (BEST) in a representative Turkish university students sample and obtain normative data for future epidemiological and clinical studies in Turkey.

Methods

Participants were 306 (201 female, 105 male) college students at the Hasan Kalyoncu University in Gaziantep, Turkey. The study protocol was approved by the University's Ethics Committee. The Turkish BEST has been translated into Turkish by SK, and back-translated into English by EA who was blinded to the original items. After establishing the semantic equivalence of the BEST items, the content equivalence of all items was examined, and no items were

excluded as being irrelevant to Turkish culture. Final version was approved by Pfhol and Blum. Sociodemographic information of the participants was collected and Turkish version of the Borderline Evaluation of Severity over Time (BEST), the Turkish version of the Borderline Personality Questionnaire (BPQ), Beck Depression Inventory (BDI), Personality Belief Questionnaire (PBQ), and State-Trait Anxiety scales were administered. To examine test-retest reliability, the Borderline Evaluation of Severity over Time (BEST) was readministered to 50 students selected from 325 students participating in the study 4 weeks after the initial application. All statistical analyses were performed by using SPSS version 23 for Windows.

Results

The average age of 306 participants in the study was 21.19 with a standard deviation of 2.85 and it ranged from 18 to 49. The sample consisted of 201 female (65.7%) and 105 male (34.3%) students. The majority of the students participated in the study were single (96.4%) and 10 (3.3%) were married and one student was divorced.

In our sample the number of female participants was nearly two times greater than male participants (201 female, 65.7%, 105 male, 34.3%). To compare mean scores of females and males, we used Independent sample t-test and compared the means of both groups. A statistically significant difference was found between male and female participants regarding Negative Behaviors scale. The mean score of Negative Behaviors (μ=6.552, t= -2.556, df=304, p<0.05) were significantly higher in males than females.

The Cronbach's alpha coefficients for the Thoughts and Feelings, Negative Behaviors and Positive Behaviors subscales were 0.80, 0.65, and 0.67, respectively. For the whole scale, the Cronbach's alpha coefficient was 0.75. The Cronbach's alpha coefficients for BPQ (0.89), STAI-State Anxiety (0.91), STAI-Trait Anxiety (0.84), BDI (0.89) and BPQ (0.94) were all sufficient. Mean and SD, and Cronbach's alpha values of Scales Used in Turkish Sample in Table 1.

The test-retest correlation coefficients for Thoughts and Feelings, Negative Behaviors, and Positive Behaviors were 0.61, 0.50, and 0.51, respectively. Positive and statistically significant correlations were found between the Turkish BEST and BPQ (r=0.337,

Table 1. Mean and SD, Cronbach's alpha values, and test-retest values.

	M	SD	α	r_{tt}
BEST	25.7	8.9	0.75	0.666**
Thoughts and Feelings	15.7	5.9	0.80	0.606**
Negative Behaviors	6.0	2.6	0.65	0.509**
Positive Behaviors	11.1	3.0	0.67	0.503**
BPQ	22.9	10.8	0.89	
STAI-State Anxiety	36.6	10.4	0.91	
STAI-Trait Anxiety	42.5	8.6	0.84	
BDI	10.0	8.6	0.89	
PBQ	87.7	34.7	0.94	

rtt, test-retest correlation coefficient.
**p<0.01.

p<0.01), BDI (r=0.460, p<0.01), PBQ (r=0.337, p<0.01), State Anxiety (r=0.351, p<0.01) and Trait Anxiety (r=0.387, p<0.01) scales.

Convergent and Discriminant validity were examined by correlations between the BEST scale scores and BPQ, BDI, PBQ, State-Trait Anxiety scales scores. Positive and statistically significant correlations were found between the Turkish BEST and BPQ (r=0.337, p<0.01), BDI (r=0.460, p<0.01), PBQ (r=0.337, r<0.01), State Anxiety (r=0.351, p<0.01) and Trait Anxiety (r=0.357, p<0.01) scales. Correlations between the Turkish BEST and other scales and subscales were presented in Table 2.

The correlation coefficients between the BEST subscales and BPQ and PBQ subscales were also examined. There were statistically significant and positive correlation coefficients between Thoughts and Feelings and Negative Behaviors subscales of the BEST and all subscales of the PBQ. The Highest correlation was found between Thoughts and Feeling subscale of the BEST and Avoidant subscale of PBQ (r=0.349, p<0.01). Negative and statistically significant

correlations were found between Positive Behaviors subscale of the BEST and Passive-Aggressive and Narcissistic subscales of PBQ (r=-0.152, p<0.01; r=-0.158, p<0.05, respectively). The lowest correlation coefficient was found between Thoughts and Feeling subscale of the BEST and Histrionic subscale of the PBQ (r=0.141, p<0.05).

To examine the factor structural validity of the BEST scale, exploratory factor analysis has been performed by various methods. Kaiser-Meyer-Olkin Measure of Sampling Adequacy (KMO) and Barlett's test of Sphericity were performed. In this study, KMO Sampling Adequacy was found to be 0.53 and Barlett's test of Sphericity X^2 was found as 165.074. Factor structure of the BEST scales was explored with an exploratory factor analysis using a condition of Eigenvalues greater than 1 rule for retaining factors. A two-factor solution showed a better factor distribution. The first two subscales of the BEST loaded on factor 1 and the last subscale Positive Behaviors loaded on factor 2, as expected. These two factors accounted for 56.76% and 31.35% of the variance (87.81% cumulatively).

Discussion

Cronbach's alpha coefficients of the Turkish BEST for both the scale and subscales were high enough as in Pfhol et al.'s original study [2]. Due to fact that Cronbach's alpha coefficients were high enough (>0.60) in both main scale and subscales, the internal consistency of the Turkish BEST was considered to be sufficient. The present study also confirmed that the Turkish BEST has good test-retest reliability due to fact that

Table 2. Correlations between the Turkish BEST, age, and other scales.

Scales	BEST	Thoughts and Feelings	Negative Behaviors	Positive Behaviors
BPQ	0.261**	0.342**	0.261**	NS
Impulsivity	0.330**	0.120*	0.156**	NS
Affective Instability	0.256**	0.241**	0.156**	NS
Abandonment	0.350**	0.286**	0.202**	NS
Relationships	0.157**	0.186**	NS	NS
Self-Image	0.255**	0.165**	0.124*	NS
Suicide-Self Mutilation	0.317**	0.232**	0.208**	NS
Emptiness	0.155**	0.234**	0.201**	-0.150**
Intense Anger	0.244**	0.231**	0.182**	NS
Quasi-Psychotic-States	0.299**	0.218**	0.151**	NS
STAI-State Anxiety	0.351**	0.315**	0.195**	-0.248**
STAI-Trait Anxiety	0.357**	0.404**	0.180**	-0.193**
BDI	0.460**	0.449**	0.253**	0.257**
PBQ	0.337**	0.346**	0.257**	NS
Avoidant	0.330**	0.349**	0.214**	NS
Dependent	0.256**	0.240**	0.218**	NS
Passive Aggressive	0.350**	0.332**	0.263**	-0.152**
Obsessive Compulsive	0.157**	0.202**	0.156**	NS
Antisocial	0.255**	0.262**	0.194**	NS
Narcissistic	0.317**	0.282**	0.257**	-0.158**
Histrionic	0.155**	0.141**	0.142*	NS
Schizoid	0.244**	0.297**	0.173**	NS
Paranoid	0.299**	0.317**	0.176**	NS
Borderline	0.261**	0.265**	0.204**	NS

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).
NS: Not Significant.

similar correlations were observed across a one-month interval, indicating stability of the measure over time.

Borderline personality disorder mostly has comorbidity with especially accompanied mostly by depression, anxiety, substance abuse, and eating disorders [3]. In our sample, Turkish BEST was found to be positively correlated with Turkish BPQ, PBQ, BDI, and STAI scores. The participants who received higher scores in Turkish BEST also received higher scores in these personality, depression, and anxiety scales. In the original study Pfhol et al. [2] reported that at the screening visit, the BEST is strongly correlated with the ZAN-BPD score, SCL-90-R total score, the SAS total score, the CGI severity score, and both the GAS and BDI scores.

The first factor consisted of 12 items predicting symptoms of borderline personality. The second factor is just about following the STEPPS program, change in negative behaviors, and mood regulation [2]. For this reason it was an expected result that the first two subscales factored into symptoms of borderline personality and the last three items of scale which comprise the third subscale named Positive Behaviors would have not factored into a separate factor. In other words, our data indicated a two-factor structure, which would have fitted borderline personality symptoms outlined by the items in the BEST. First, predicting the symptoms of borderline personality, and the second is examining the effectiveness of the therapy program. Therefore, the results of this study are consistent with the one dimensional structure found in both non-clinical [4] and clinical samples [5].

Although the BEST subscales may not possess high reliability in other languages, the BEST might be more practical when used as screening measure for BPD as it has fewer items and possesses overall reasonable reliability and in clinical settings they would provide diagnostic suggestions that could be followed by a more in-depth clinical interview. The Turkish BEST will be useful for future studies in different countries to help better understanding normalcy, psychopathology, and personality disorder and to examine the biological, social, and psychological differences in people from different cultures.

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Normative Data and Factorial Structure of the Turkish version of the Temperament and Character Inventory-Revised (Turkish TCI-R)

Samet Kose MD, PhD[a,b], Mehmet Yalcin[a], Ercan Akin[a], Vedat Ceylan[a] and Hakan Turkcapar MD, PhD[a]

[a]Hasan Kalyoncu University Department of Psychology, Gaziantep, Turkey; [b]University of Texas Medical School of Houston, TX, Department of Psychiatry and Center for Neurobehavioral Research on Addictions, Houston, TX, USA

E-mail address: sametkose@gmail.com

ABSTRACT

Objective: Cloninger proposed a revised version of the Temperament and Character Inventory (TCI-R) in 1999, which uses a five-point-Likert format to provide more variability and includes subscales for persistence to improve its scale construct. In this study, we aimed to examine the reliability, validity, and factor structure of the TCI-R in a Turkish sample.

Methods: Participants were 1026 (786 female, 240 male) college students at various universities in Turkey. The study protocol was approved by the local Ethics Committee. Sociodemographic information of the participants was collected and the TCI-R, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Personality Belief Questionnaire (PBQ) were administered. All statistical analyses were performed by using SPSS version 23 for Windows.

Results: The internal consistency was satisfactory for all dimensions (Cronbach alpha coefficients above 0.7). The highest Cronbach alpha was found for Persistence Dimension (0.92) and the lowest Cronbach alpha was found for Novelty Seeking Dimension (0.73) and

test-retest correlation coefficients for all dimensions were relatively high and statistically significant (Table 1). TCI-R temperament and character scales were found significantly correlated with the BDI, the BAI, and the PBQ total scores (Table 2). A principal-components analysis with Promax rotation yielded 4 factors with an Eigenvalue greater than one, representing 63% of the total variance for temperament dimension. A principal-components analysis with Promax rotation yielded 3 factors with an Eigenvalue greater than one, representing 56.14% of the total variance for character dimension. The addition of 4 new subscales to the original scale for Persistence has produced a very reliable dimension in the TCI-R with the loadings ranging from 0.816 to 0.856.

Conclusions: Our preliminary findings suggested that Turkish TCI-R was a valid and reliable tool with a robust factorial structure for further use in in the assessing of personality psychopathology in clinical populations in Turkey.

Introduction

According to Cloninger's psychobiological model of personality; personality consists of two dimensions, temperament and character. Temperament refers to individual differences in basic emotional reactions that are inherited and mostly stable. It is seen as the biological aspect of personality [1,2]. The character reflects one's life goals, value system, self, and conscious feelings. Character, which is influenced by our life experiences, learning, and insight, is a structure that is unique to each individual and develop gradually over time [1,2]. Based on this theory, seven dimensions of personality are defined. These are four major temperament dimensions: Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), and Persistence (P) and also three major character dimensions: Self-directedness (SD), Cooperativeness (C) and Self-transcendence [1,2]. Cloninger's personality theory provides us with broad insight in order to understand human personality. Moreover, this theory is important because it is a model that is supported by long-term follow-up studies, neuropharmacological and neurobehavioral learning studies, twin and family studies, and psychometric studies [2,3].

Cloninger proposed a revised version of the scale in 1999 (TCI-R). The revised form of Temperament and Character Inventory (TCI-R) also assesses the same temperament and character dimensions of personality as TCI. In TCI-R, the Persistence (P) scale of temperament was improved, and it is divided into four dimensions consisting of 35 items. Another change made in TCI-R is that the participants must respond to 240 items on a 5-point Likert scale ranging from 1 (definitively false) to 5 (definitively true) rather than responding as true or false [4].

In the current study, we aimed to translate and establish the psychometric properties and factorial validity of the Temperament and Character Inventory-Revised (TCI-R) in a representative Turkish university students sample and obtain normative data for future epidemiological and clinical studies in Turkey.

Methods

Participants were 1026 (786 female, 240 male) college students at various universities in Turkey. The study protocol was approved by the Hasan Kalyoncu University's Ethics Committee. The Turkish TCI-R has been translated into Turkish by Samet Kose and back-translated into English by Ercan Akin who was blinded to the original items. After establishing the semantic equivalence of the TCI-R items, the content equivalence of all items was examined, and no items were excluded as being irrelevant to Turkish culture. Final version was approved by Cloninger. Sociodemographic information of the participants was collected and Turkish version of the Temperament and Character Inventory-Revised, the Beck Depression Inventory (BDI), Beck Anxiety Inventory and Personality Belief Questionnaire (PBQ), were administered. To examine test-retest reliability at 4-weeks, the TCI-R was readministered to a subsample of 100 participants, but only 84 filled out the TCI-R for a second time. All statistical analyses were performed by using SPSS version 23 for Windows.

Results

The average age of 1026 participants in the study was 21.54 with a standard deviation of 3.44, and it ranged from 18 to 51. The sample consisted of 786 female (76.6%) and 240 male (23.4%) students. The majority of the students participated in the study were single (95.6%), 33 (3.2%) were married, and eight students were divorced.

The mean scores for TCI–R scales and their subscales are presented in Table 1. Multivariate analysis showed that women exhibited significantly higher scores for HA, RD, SD, C, and ST dimensions than men. For the C dimension, all the subscale scores were higher in women, whereas for the HA and ST dimensions, one subscale did not differ between the two groups (respectively HA3 and ST2). For the HA and ST dimensions, all of other subscales scores were higher in women. Moreover, NS4, PS2, PS4, and SD3 subscale scores were lower in women, whereas RD1 and SD5 were higher.

Table 1. TCI–R Scale and Subscale Means, Standard Deviations, Cronbach alpha Among the Sample.

	Total			Women		Men			
	M	SD	α	M	SD	M	SD	F(df= 1024)	p
NS1 (exploratory excitability)	31.8	4.0	0.46	31.7	4.1	32.1	3.8	1.53	0.21
NS2 (impulsiveness)	24.4	3.9	0.51	24.4	4.0	24.3	3.9	0.48	0.69
NS3 (extravagance)	27.9	6.0	0.78	27.9	6.2	27.9	5.6	2.74	0.95
NS4 (disorderliness)	20.0	3.5	0.45	19.8	3.3	20.6	4.0	6.41	<0.01
Novelty seeking (NS)	104.0	11.3	0.73	103.8	11.3	104.8	11.3	0.09	0.21
HA1 (anticipatory worry)	32.9	6.2	0.77	32.6	6.2	31.2	6.0	1.87	<0.01
HA2 (fear of uncertain)	21.9	4.6	0.69	22.3	4.5	20.7	4.5	0.02	<0.001
HA3 (shyness with strangers)	19.8	5.0	0.80	20.0	5.0	19.4	4.9	0.08	0.14
HA4 (fatigability)	23.3	5.1	0.76	23.6	5.1	22.3	5.0	0.25	<0.005
Harm avoidance (HA)	97.3	16.2	0.89	98.5	16.1	93.7	16.1	0.97	<0.001
RD1 (sentimentality)	28.4	4.4	0.58	28.9	4.3	26.8	4.3	0.01	<0.001
RD2 (open to warm communication)	34.6	5.6	0.70	34.7	5.7	34.4	5.3	5.55	0.057
RD3 (attachment)	18.9	4.3	0.72	18.9	4.5	18.6	3.7	8.95	0.026
RD4 (dependence)	16.9	3.1	0.47	17.0	3.1	16.6	3.2	0.04	0.08
Reward dependence (RD)	98.8	12.3	0.80	99.5	12.8	96.5	10.1	15.28	<0.001
PS1 (eagerness of effort)	31.1	4.9	0.73	31.2	4.9	30.9	4.8	0.01	0.46
PS2 (work hardened)	27.9	4.6	0.75	27.7	4.6	28.5	4.5	0.34	0.01
PS3 (ambitious)	35.9	5.4	0.80	35.8	5.5	36.1	5.3	1.02	0.46
PS4 (perfectionist)	25.9	5.1	0.78	25.7	5.2	26.5	4.9	2.91	0.04
Persistence (PS)	120.8	17.6	0.92	120.4	17.7	122.0	17.3	0.64	0.20
SD1 (responsibility)	26.8	4.5	0.72	26.8	4.5	26.7	4.7	0.90	0.66
SD2 (purposefulness)	22.1	3.8	0.69	22.1	3.7	22.2	4.0	0.59	0.79
SD3 (resourcefulness)	17.3	3.2	0.61	17.2	3.1	17.8	3.2	0.00	<0.01
SD4 (self-acceptance)	27.5	5.9	0.73	27.6	6.0	27.3	5.7	2.33	0.49
SD5 (congruent second nature)	38.6	4.9	0.61	38.9	4.8	37.6	5.0	1.74	<0.005
Self-directedness (SD)	132.3	15.3	0.84	132.5	15.2	131.6	15.6	0.57	0.39
C1 (social acceptance)	29.0	4.4	0.75	29.3	4.4	28.2	4.4	0.25	<0.005
C2 (empathy)	18.8	2.7	0.53	19.0	2.5	18.0	2.9	6.35	<0.001
C3 (helpfulness)	25.4	3.2	0.39	25.5	3.2	25.1	3.0	3.77	0.09
C4 (compassion)	24.3	6.2	0.88	24.8	6.1	22.6	6.1	0.13	<0.001
C5 (principled)	30.0	4.1	0.57	30.4	3.8	29.0	4.8	15.19	<0.001
Cooperativeness (C)	127.6	14.8	0.86	129.0	14.5	123.0	15.0	1.17	<0.001
ST1 (self-forgetfulness)	32.2	4.9	0.65	32.5	4.9	31.3	4.8	1.00	<0.005
ST2 (transpersonal identification)	26.2	4.5	0.66	26.1	4.5	26.4	4.4	0.00	0.45
ST3 (spiritual acceptance)	27.5	5.6	0.78	27.8	5.5	26.3	5.8	0.15	<0.001
Self-transcendence (ST)	85.9	11.2	0.80	86.4	11.1	84.0	11.4	0.11	<0.005

The internal consistency was satisfactory for all dimensions (Cronbach alpha coefficients above 0.7). The highest Cronbach alpha coefficient was found for Persistence Dimension (0.92), and the lowest Cronbach alpha coefficient was found for Novelty Seeking Dimension (0.73). For the whole scale, the Cronbach's alpha coefficient was 0.85.

The test-retest correlation coefficients for all dimensions were relatively high and statistically significant. The test-retest correlation coefficients for NS, HA, RD, and PS scales of Temperament dimension were 0.72, 0.74, 0.61, and 0.84, respectively; for SD, C, and ST of Character dimension were 0.77, 0.58, and 0.78, respectively. All of the correlations were significant at 0.01 level. Therefore, there were no significant differences between the mean scores of the Turkish TCI-R across the 4-weeks test-retest period.

The correlations among the four dimensions of temperament and the three dimensions of character were also statistically significant. The highest positive correlation coefficients were between SD and C (r=0.456, p<0.001), PS and SD (r=0.443, p<0.001) RD and C (r=0.387, p<0.001). The highest negative correlation coefficients were found between HA and SD (r=−0.469, p<0.001), HA and PS (r=−0.432, p<0.001), and NS and HA (r=-0.226, p<0.001).

The factorial structure of the TCI-R was examined by exploratory factor analysis for temperament and character separately. Kaiser-Meyer-Olkin Measure of Sampling Adequacy (KMO) and Barlett's test of Sphericity were performed. In this study, KMO Sampling Adequacy was found to be 0.83, Barlett's test of Sphericity X^2 was found as 6398.710 for Temperament dimension, Sampling Adequacy was found to be 0.78, and Barlett's test of Sphericity X^2 was found as 3941.901 for Character dimension.

Factor structure of the Temperament dimension scales was explored with an exploratory factor analysis using a condition of Eigenvalues greater than 1 rule for retaining factors. The initial results indicated a four-factor solution not providing a strong fit. On the other hand, following Promax rotation, a four-factor solution showed a better factor distribution. The four factors accounted for 28%, 16%, 12%, and 7% of the variances observed (63% cumulatively). The standardized factor loading following Promax rotation showed that in the four-factor solution, PS, HA, RD, and NS factors were robust. The subscale NS1 also loaded negatively on Factor 2 (HA) and positively on factor 3 (RD).

Factor structure of the Character dimension scales was explored with an exploratory factor analysis using

a condition of Eigenvalues greater than 1 rule for retaining factors. The results indicated a three-factor solution not providing a strong fit. On the other hand, following Promax rotation, a four-factor solution showed a better factor distribution. The three factors accounted for 29.6%, 14.3%, and 12.3% of the variance (56.14% cumulatively). The standardized factor loading following Promax rotation showed that in the four-factor solution, C and ST factors were robust. For SD, SD1, SD2, SD3, and SD5, subscales loaded consistently, whereas SD4 subscale did not load on factor 2 (SD) but loaded more strongly on Factor 1 (C) and factor 3 (ST).

BDI was positively correlated with Novelty Seeking (r=0.116, p<0.01), Harm Avoidance (r=0.261, p<0.01) and Self-Transcendence (r=0.079, p<0.05) and negatively correlated with Self-Directedness (r=-0.410, p<0.01), Persistence (r=−0.140, p<0.01), Cooperativeness (r=−0.181, p<0.01). BAI was positively correlated with Novelty Seeking (r=0.068, p<0.05), Harm Avoidance (r=0.237, p<0.01), Self-Transcendence (r=0.143, p<0.01) and negatively correlated with Persistence (r=−0.083, p<0.01), Self-Directedness (r=−0.340, p<0.01), Cooperativeness (r=−0.176, p<0.01) and PBQ was positively correlated with Harm Avoidance (r=0.133, p<0.01), Self-Transcendence (r=0.156, p<0.01) and negatively correlated with Self-Directedness (r=−0.379, p<0.01), Cooperativeness (r=−0.439, p<0.01).

Discussion

Cronbach's alpha coefficients of the Turkish TCI-R for both the scale and subscales were high enough as in the previous studies [4,5]. Due to the fact that Cronbach's alpha coefficients for TCI-R scale and many subscales were high enough (>0.60) in both main scale and subscales, the internal consistency of the Turkish TCI-R was considered to be sufficient. The present study also confirmed that the Turkish TCI-R has a good test-retest reliability due to the fact that similar correlations were observed across a one-month interval, indicating stability of the measure over time.

The results of factor analysis in the present study were very similar to the previous study conducted by Hansenne and colleagues [4]. They have reported that the standardized factor loading with Promax rotation showed that in the four-factor solution, PS, HA, RD, and NS factors were robust and only the subscale NS1 also loaded negatively on Factor 2 (HA). Moreover, as partly similar with our results, in their study, the standardized factor loading with Promax rotation showed that C and ST factors were robust. For SD, SD1, SD2, SD3, and SD5, subscales loaded consistently. However, SD4 subscale has been found relatively problematic because of loading more strongly on Factor 1 (C).

In conclusion, this study confirmed that the Turkish TCI-R displayed good psychometric properties. Particularly, the Persistence dimension appears to be a robust dimension that is well measured by the TCI–R and robust test-retest correlations at 4-weeks. These psychometric properties support the clinical usefulness of the TCI-R in the process of personality psychopathology assessment.

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Rational Use of Controlled Drugs in Umraniye District of Istanbul

Isa Badur PhD, MPharm[a] and Naciye Bilgin Badur[a,b]

[a]Department of Clinical Pharmacy, Istanbul Medipol University, Istanbul, Turkey; [b]Department of Neuroscience, Istanbul Medipol University, Istanbul, Turkey

E-mail address: isabadur@st.medipol.edu.tr

ABSTRACT
Objective: In this pharmacoepidemiological study, the prescriptions of controlled drugs were evaluated from the perspective of rational drug use.
Methods: In this cross-sectional, observational study, drug usage was examined retrospectively. Prescriptions written in last three months of 2014 from the archives Local Directorate of Health were examined and the prescripitons were chosen randomly from pharmacies.
Results: 416 (25% of three months) red colored controlled drug prescriptions were

retrospectively evaluated and 48 patients' drug history examined from the perspectives of drug-drug interaction, overdose, psychiatry consultation frequency, and birth month and demographic data. 144 (70%) of the pharmacist were women. There was an increase in prescriptions compared to past years. It was found that women use more tramadol and alprazolam; less biperiden than men. The green colored controlled drug prescriptions per pharmacy in Umraniye was 5.66 (vs. Istanbul 6.28) and the mean of drug box per prescription was 8.45. Results of 48 prescriptions of methylphenidate: overdosed (60 mg) was 45.2%; drug-drug interaction was 35.4%; overdosed and drug-drug interaction have not determined were 17%; daily doses were between 10 mg to 108 mg. Most of the prescriptions were written for males (71%). 44.12% of these males were born in the months of June, July and August. There was positive correlation (r=0.302; p=0.042); between frequency of psychiatric visits of by men and their birth months. It was found that 357 (86%) of the 416 red prescriptions contain methylphenydate, 37 prescription were of phentanyl. There was a positive correlation between the total number of prescriptions and the variety of the doctors. **Conclusions:** In this observational psycho-pharmacoepidemiological study, the results confirmed the occurence of irrational use of certain drugs and series of inadequate practices related to medication.

Introduction

In this study, the controlled drugs prescriptions in Umraniye district of İstanbul were evaluated retrospectively from the aspect of consumers, prescribing and distributions by pharmacy pharmacoepidemiologically and to develop the rational use of drug was aimed by detecting the irrational use of drug. Distribution and production of benzodiazepines are under control in many developed countries but they are not controlled in developing countries [1]. In Turkey, the rational drug use has special importance in red prescription and green prescription which has been controlled by the Ministry of Health. Those drugs have the potential of drug dependency and drug abuse.

Methods

This is a cross-sectional, observational pharmacoepidemiological study in which the prescriptions that are given by pharmacies in between the dates of October 2014 and January 2015 in Umraniye district of Istanbul were evaluated retrospectively. The total number of red and green prescriptions that were given by the pharmacies in the districts of Istanbul (n=39) and the demographic data based on age groups were examined.

The sample was evaluated in terms of drug-drug interactions, drug overdoses, ratio of psychiatrist visits among the other specialist visit frequencies in 2014-2015, and birth dates in months and demographic data of the patients. All statistical analyses were performed by using SPSS version 23 for Windows. The data was defined as means, standard deviations, and percentages. The relationship between variables was evaluated by Spearman's or Pearson's correlation analyses. The differences between nominal variables were analyzed by *chi-square test*. The $p<0.05$ probability value was accepted as statistically significant.

Results

There was a positive correlation between green prescription drug and the gender of the patients. It was found that the female patients used tramadol hydrochloride 37.5 mg + paracetamol 325 mg 20 tablets and alprazolam 0.5 mg 30 tablets more than male patients. The correlation between districts of Istanbul (n=39) population data according to age groups; and the total numbers of red and green prescriptions and total number of pharmacies in the districts (n=39) in October through December 2014 were examined. Green prescriptions have been found to correlate significantly with the ages of 20–24 (Pearson's rho=0.359) in both males and females. The correlation was determined that the red scripts started at an older age. A significant positive correlation (Pearson's rho=0.322) in the red prescriptions was found in females aged 40–44 years and a significant correlation was found in males (Pearson's rho=0.323) later (Figure 2). The correlations between both female and male age groups and both green and red

Table 1. Descriptive Statistics of Red Prescriptions in October 2014.

|	n	Minimum	Maximum	Mean	Standard deviation
Age	48	7	19	11.69	3.026
Gender	48	29% Female	71% Male		
Onset of drug (Age)	48	5	17	9.10	3.005
Drug usage duration (Year)	48	2	5	2.58	1.048
Overdose (60 mg)	31	0 (there is not)	1 (there is)	0.45	0.506
Drug interaction	48	0 (there is not)	1 (there is)	0.35	0.483
Interaction and overdose (together)	31	0 (none)	2 (both)	0.97	0.706
Number of psychiatric examinations (2014–2015)	46	0	23	6.61	4.942
Percent of psychiatric examinations (2014–2015)	45	0	100	58.55	29.383
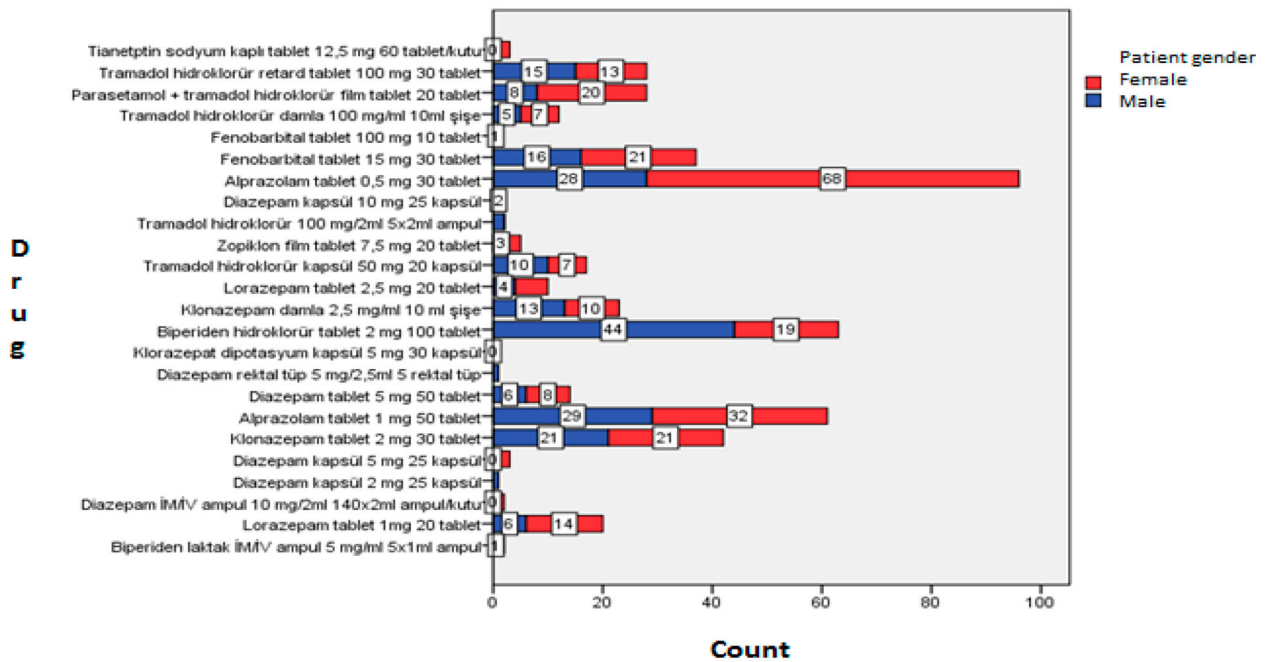
Figure 1. The distribution of sample according to the gender of patient in green prescriptions (per drug box)

prescription increased in numbers with increasing age. The number of pharmacies in districts had significant positive correlations with all age groups but it was not the case for the prescriptions (Figure 2). In the above table 60 red prescriptions (20 prescriptions per each month of the last 3 months of 2014) were chosen randomly and the methylphenidate containing ones were studied in detail. The past medical history of 48 patients who were prescribed methylphenidate was studied detailed retrospectively in 2014 and 2015.

Discussion

The total green prescription ratio for 3 months during 6 years (2008–2014) was 1.13 and the total red prescription ratio for 3 months during 6 years (2008–2014) was 3.12. Green prescription number was almost same during 6 years, the red prescription number was increased by 3 fold. The dramatical increase in red prescriptions compared to green prescriptions has to be examined from the perspective of rational drug use.
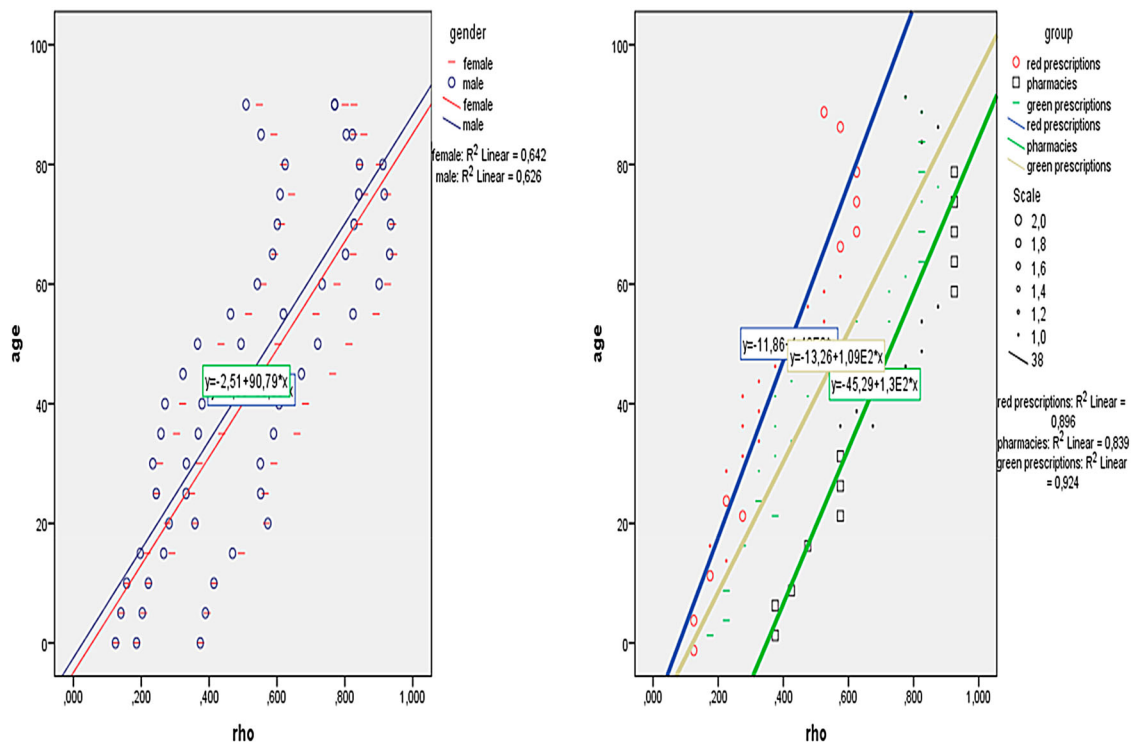

Figure 2. The correlation between districts of Istanbul (n=39) population data according to age groups; and the total number of red and green prescriptions and total number of pharmacies in the districts (n=39) in October, November, and December 2014.
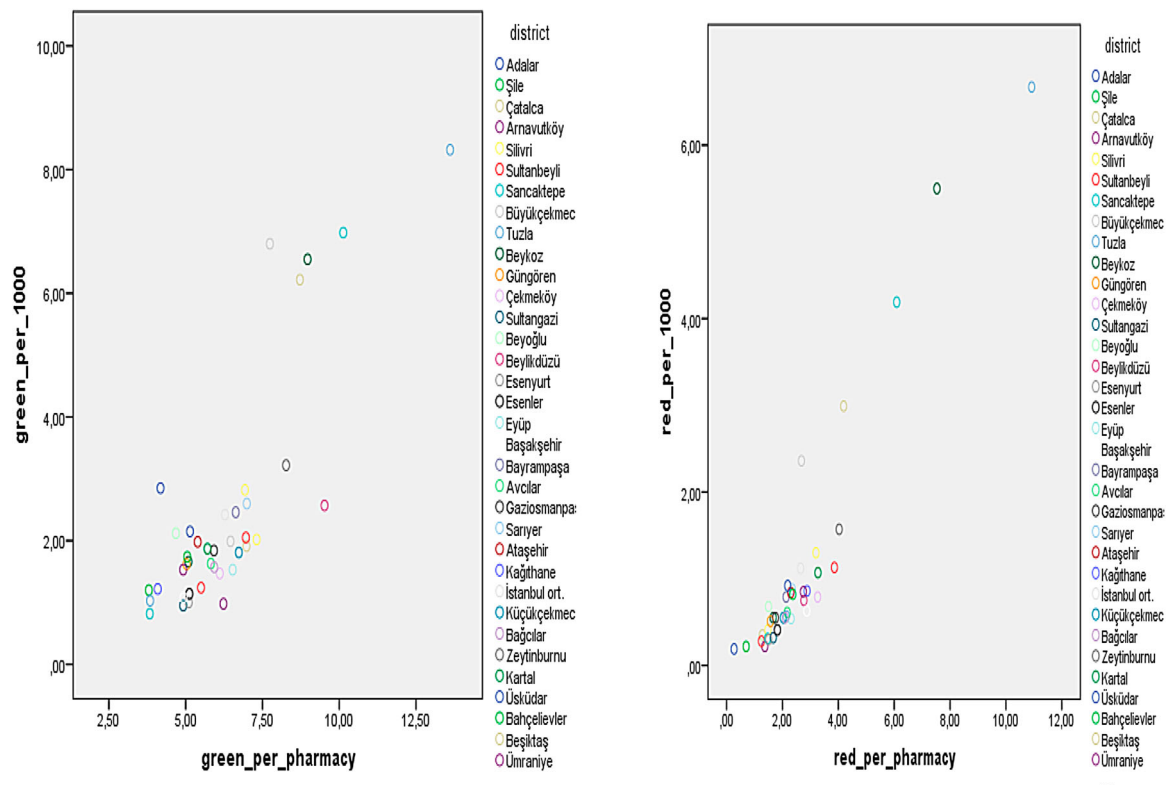
Figure 3. The data of the red and green prescriptions mean monthly, prescription per pharmacy monthly, per 1000 ppl monthly of the districts of Istanbul.

The relationship between green prescription brand name and patient gender was examined by Spearman's correlation analysis and significant correlation was found (p=0.000). We have to consider the effect of gender difference in this group of drugs. It was found that the female patients use tramadol hydrochloride 37.5 mg + paracetamol 325 mg 20 tablets and alprazolam 0.5 mg 30 tablets more than male patients. The male patients used biperidene hydrochloride 2 mg 100 tablets brand names more than female patients (Figure 1). Methylphenidate was the mostly prescribed drug during October, November, and December 2014. Almost all of the red prescriptions of these 3 months (1685) were composed of methylphenidate which has to be accepted as irrational drug use. When the number of doses per box of methylphenidate was listed in descending order, the order was by

Figure 4. Birth month and psychiatric examination percentage.

female doctor for female patient, by female doctor for male patient, by male doctor for female patient, by male doctor for male patient (21.9 mg / box>20.8 mg / box> 19.2 mg / box> 17.0 mg / box). We could speculate that both female and male doctors were more generous in prescribing methylphenidate to female patients. There are similar studies in the literature [2]. The number of psychiatric examinations was examined for two years as 304 (one patient averaged 6.33 visits), 26 as urgent (0.54 per patient) and 551 (one patient with a mean of 11.46) in all departments. The situation gets even worse when we think that there are unrecorded examinations (Table 1). According to data from the General Directorate of Health Services of the Public Health Authority of Turkey, number of presentations per person for 2nd and 3rd grade hospitals in 2014 was 5.5. There was a positive correlation between the number of psychiatric examinations and the interaction (Spearman's rho=0.440; p=0.000). There was positive correlation; between male psychiatric examination percent and month of birth June-July-August (Spearman's rho=0.302; p=0.042). With both male and female age groups; the correlation coefficients between both green and red prescriptions were increasing with increasing ages. In other words, the power of correlation increased with age.

It is observed that the number of red and green prescriptions increased in 2014 compared to previous years and this increase was seen in red
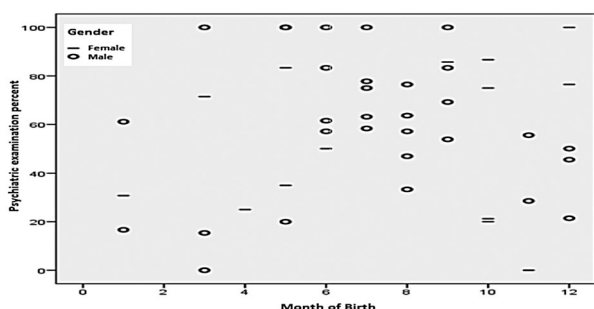
prescriptions. This finding was consistent with Turkey's increasing consumption of drugs compared to previous years [3].

Similar studies have shown that female patients clearly used more benzodiazepines in almost all benzodiazepine use [4]. With patient gender; there was no significant relationship between the prescription drug (Spearman's rho=0.030; p=0.530). This can be considered as an irrational drug use, because ADHD, an indication for methylphenidate, is more common in male patients [5].

There is inevitable partnership involvement in the community for rational drug use. However, sometimes the doctor's prescription of certain drugs can be manipulated by the patients who knew the doctor from the community [6]. The ADHD guide in the UK, which is almost the same guidelines in Europe and America, suggests parental education programs and behavioral strategies [7]. However, in severe ADHD, medication is recommended along with "psychosocial recommendations" only for patients over 6 years of age [7,8]. The maximum dose of methylphenidate is 60 mg per day [8–11]. The drug should be periodically discontinued and stopped after puberty [11]. It can be said that both the female doctor and the male doctor are more generous in terms of the methylphenidate intake of the female patient. Similar studies in the literature are available [2]. Methylphenidate is known to be used especially in children [12]. The FDA also has a number of safety precautions to be aware of in this regard [13]. To reduce the overuse of psychostimulants such as methylphenidate, psychotherapeutic approaches are needed before drug treatment.

Conclusions

In this observational psycho-pharmacoepidemiological study, our results confirmed the occurrence of irrational use of some drugs and series of inadequate practices related to medications.

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Hidden Details in Patients with Palpitation Complaints: Type D Personality, Depression, and Anxiety

Yüksel Kıvrak[a], Yasin Taşdelen[b], İbrahim Yağcı[c] and Fatih Aydın[d]

[a]Department of Psychiatry, Kafkas University, Kars,Turkey; [b]Department of Psychiatry, Edremit State Hospital, Balıkesir,Turkey; [c]Department of Psychiatry, Kars Harakani State Hospital, Kars, Turkey; [d]Department of Cardiology, Eskişehir State Hospital, Eskişehir, Turkey

E-mail address: ykivrak21@gmail.com

ABSTRACT

Objective: Even though palpitations are a very common disorder, neither the etiology nor the treatment could be fully elaborated. Type D personality is associated with being highly negatively affected and socially inhibited. It is known that cardiac disorders are more frequent in these people as well as those with depression and anxiety. The rate of type D personality depression and anxiety scores are unknown in patients with complaints of palpitation where an organic cause could not be determined. Knowing these can contribute to understanding the etiology of palpitations and its treatment.

Methods: 50 patients who were admitted to the Cardiology Outpatient Clinic with palpitations and no other cardiovascular disorders and 50 patients who were not diagnosed with no medical illnesses were included in the study. Type D Personality Scale, Hospital Anxiety and Depression Scale (HADS) were administered. Statistical significance level was accepted as p<0.05.

Results: When the patient and control groups were compared, there was no significant difference in terms of age, gender, education, marital status, and anxiety scores. Type D personality was found in 60% of the patients group and 22% of the control group.In addition, the depression scores of the patient group were higher than the control group (p<0.05). There was a positive correlation between type D personality scale score and depression and anxiety scores in both patient and control groups (p<0.05).

Conclusions: Both type D personality rates and depression scores were higher in those who have palpitations. Type D personality and depression relationship may contribute to the understanding of palpitation etiology and its treatment.

Introduction

Type D personality was defined as a personality disorder associated with high levels of negative affectivity (presence of depressive feelings, anxiety, anger, and hostility feelings) and social inhibition [1]. Patients with type D personality disorder are seen to have anxiety, depressive symptoms, somatic complaints, and suicidal thoughts. In addition, cardiac disease is common in patients with type D personality disorder which is an independent predictor of cardiac symptoms. The association between Type D personality and cardiovascular disease was examined and type D personality was found to be independently associated with coronary heart disease and hypertension [2]. Palpitations are defined as rapid, strong or irregular pulses that are felt on the chest and are a common symptom among outpatients. Cardiovascular diseases (43%), psychiatric causes (31%), other causes (10%) and unknown causes (16%) were listed in the aetiology of palpitations [3]. Panic disorder and anxiety are the most common psychiatric disorders that would lead to palpitations [4]. In patients with complaints of palpitations where an organic cause cannot be determined, the rate of type D personality and depression and anxiety scores are unknown. Knowing these can contribute to the treatment of palpitations and understanding of its etiology.

Methods

Kocaeli Government Hospital Cardiology Outpatient Clinic patients complaining of palpitations who were aged over 18 were included in the study. During the study, patients with anemia, hypothyroidism, hyperthyroidism, arrhythmias and patients with pathological findings from Echocardiogram, ECG, and 24-hour ECG holter recordings were excluded. Patients under psychiatric treatment were also excluded from the study. Patients were requested to fill the sociodemographic data form, Type D Personality Scale, and the Hospital Anxiety and Depression Scale (HADS).

Sociodemographic Data Form

Thesociodemographic data form is a form prepared by the researchers which includes demographic parameters such as age, gender, marital status, educational status, chronic illness history, smoking, and alcohol use.

Type D Personality Scale DS-14

Type D scale-14 (DS-14) was developed to evaluate Negative Affectivity (NA), Social Inhibition (SI), and Type D. The DS-14 scale includes a total of 14 items and consisted of two subscales measuring NA and SI. Each item is a Likert-type scale scored between 0–4. Both subscales also have a cut-off point of $\geq$ 10. Test-retest validity is good and internal validity is high in both subscales. The Cronbach's α values were 0.88 for NA and 0.86 for SI. The psychometric quality and prognostic power of the scale were statistically proven in Belgian cardiac patients. Structural and internal consistency of the NA and SI subscales were confirmed in studies conducted in Danish and German cardiac patients.

Hospital Anxiety and Depression Scale (HADS)

The HADS is a self-evaluation scale developed by Zigmond et al. in order to measure the level of risk and change of violence in terms of anxiety and depression

in the patient. The validity and reliability of the Turkish form was created by Aydemir et al.

Statistical Analysis

SPSS version 15.0 was used for statistical analysis of the data. Pearson's Chi-Square and Fisher's Exact tests were used to compare categorical data among the groups, independent samples t-test was used when comparing continuous data among the groups with normal data distribution and Mann-Whitney U test was used for non-normal distribution data. The relationship between type D presence and other variables were assessed by using Spearman's correlation analyses. A p <0.05 was considered statistically significant.

Results

There were 31 female and 19 male volunteers in the patient group and 22 male and 22 female volunteers in the control group. The mean age of the patient group was 38.8 ± 10.77 and the mean age of the control group was 39.9 ± 11.2. There were no significant differences between the mean age of the patients and control group (p>0.05) (Table 1). There were also no significant differences between the groups in terms of gender, education, and marital status (p>0.05).

When the Hospital Anxiety and Depression Scale scores of the groups were examined, there were no significant differences between male and female depression scores (p>0.05). The depression scores of the patient group were significantly higher than the depression scores of the control group (p<0.05). When the mean distribution of anxiety scores according to gender of patient and control group were examined, there were no significant differences between the groups (p>0.05) (Table 2).

D type personality was found in 60% of the patients and 22% of the control group. When the results of the Spearman's correlation analysis were examined to determine the relationship between type D personality presence and patients' age, gender, marital status, depression, and anxiety scores; there was a negative and significant relationship between type D personality

Table 1. Sociodemographic characteristics of the participants.

		Patient (n=50)	Control (n=50)	p
Age (Mean±SD)		38.8±10.77	39.9±11.2	0.618
Gender	Female	31	28	0.542
	Male	19	22	
Marital status	Married	35	38	0.499
	Not married	15	12	
Education level	Elementary	24	26	0.938
	High school	22	22	
	College	2	2	
Type D personality	Present	30	11	0.000
	Absent	20	39	

SD, Standard Deviation.

Table 2. Comparison of depression and anxiety scores per HADS.

	Patient	Control	p
Depression scores	6.06±2.67	4.46±2.62	0.003
Anxiety scores	6.1±3.13	4.98±2.78	0.121

SD, Standard Deviation; HADS, Hospital Anxiety and Depression Scale.

Table 3. Correlations of Type D personality with Sociodemographic variables and HADS scores.

	Patient Type D r	Patient Type D p	Control Type D r	Control Type D p
Age	0.188	0.190	0.095	0.510
Gender	0.135	0.351	0.113	0.435
Education status	-0.285	0.045	-0.046	0.753
Marital status	0.089	0.538	-0.041	0.779
Depression	0.773	0.000	0.655	0.000
Anxiety	0.683	0.000	0.674	0.000

HADS; Hospital Anxiety and Depression Scale.

presence and educational status in the patient group of this present study (p<0.05). There was a strong positive correlation between D type presence and depression and anxiety scores in the patient and control group (p<0.05) (Table 3).

Discussion

Personality is considered a strong predictor of medical outcomes of cardiac diseases. Type D individuals were reported to be particularly prone to heart disease. Type D personality has been shown to have an effect on the cardiac disease predisposition independent of the person's emotional state at that time. Type D personality is characterized by a tendency to negative emotions and by suppressing these emotions by staying away from social relations. Putting emotions under pressure has been found to be associated with decreased cardiac rate change by increased cardiovascular reactivity. From this point of view, we thought that the underlying cause of cardiology outpatient clinic patients complaining of palpitations with no apparent cause should be examined for Type D personality. We found that the rate of type D personality was significantly higher in the study group compared to the control group and that the palpitation complaint and Type D personality were strongly related. Studies have shown that the prevalence of type D personality in healthy groups have reached up to 32%. In the control group of this present study this rate was 22% and in the study group it was 60%.

When the relationship between personality type and gender is examined; some studies indicated that type D personality was more often seen in women, while others claim that there was no significant relationship between type D personality and gender. In this present study, type D personality was seen to be higher among

women within the study group and men among the control group; however, overall there was no statistically significant relationship found between gender and type D personality.

This present study showed that type D personality may have been an independent risk factor for palpitations. Type D personality increased the level of cortisone and alertness in the individual. It was also observed that there was an increase in proinflammatory cytokine levels, their activities and disorders in cytokine network in individuals with type D personality [5]. Elevated cytokines, increased levels of cortisol, and high cardiac oxidative stresses that they have been exposed to lead to imbalances in heart rate and rhythm which further lead to tachycardia and bradycardia or increased cardiac output independent of heart rate which are called palpitations (also known as patient feeling a his/her heart beat strongly) in type D individuals.

There are also studies showing that individuals with type D personality have increased heart rates, increased ventricular arrhythmia and cardiac output. Our results are consistent with these earlier reports. When the Hospital Anxiety and Depression Scale scores were examined, the depression score of the study group was found to be higher than the control group and this was statistically significant. Anxiety scores were not significantly different between the two groups. In the study group, there was a weak and statistically significant negative correlation in terms of education status; which means that the type D personality decreases as the level of education increases. To support this hypothesis, further studies are needed to identify the relationship between education and type D personality using larger sample size populations. The present study has certain limitations. One of the main limitations is the fact that lacking electrophysiological examinations which detect rare causes of palpitations due to their being invasive methods which are not routinely used techniques to illuminate the etiology of palpitations.

In sum, in addition to the fact that type D individuals worsen the prognosis and increase the risk of organic heart problems such as heart failure, atrial fibrillation and coronary heart disease, type D personality also negatively affects life quality by increasing complaints of palpitations and possibly arrhythmia in individuals without any organic heart complaints. We think that the type D person should be kept in mind as an independent cause in palpitations etiology and should be considered when approaching palpitations. In those who have palpitations, both D type personality ratios and depression scores are higher. Knowing that type D personality and depression, which are known to be effective in many cardiovascular diseases, are also high in cases of palpitations may contribute to the understanding of palpitation etiology and its treatment.

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How Trait Impulsivity Associated with Creativity?

Ayca Idil Aytekin[a], Melek Saka[a], Sule Aydin[a], Beyazit Garip[b] and Hakan Kayir[c]

[a]Bilfen Cayyolu Science College, Ankara, Turkey; [b]Department of Psychiatry, Gulhane Training and Research Hospital, Ankara, Turkey; [c]Commat Ltd., Ankara, Turkey

E-mail address: aytekinayceidil@gmail.com

ABSTRACT

Objective: Creativity becomes a more prominent skill in today's world that innovation is highly important in every area. A 50-year follow-up study showed that creative thinking score obtained during elementary school was positively correlated with lifetime achievements. Creativity has been tended to see as an innate ability and sometimes related with several mental disorders such as bipolar disorder and some personality traits such as impulsivity. In this present study, we examined a possible relationship between creativity and impulsive choices using objective tools.

Methods: The high school students from 9th and 10th grades (20 girls and 20 boys) completed the Iowa Gambling Task (IGT) which was based on choosing cards from the decks bring less reward but also less penalty. The creativity was evaluated using two different tests; Torrance

Drawing Completion Test for visual creativity and Duncker's candle problem for verbal creativity. The drawings were scored for fluency, flexibility, originality, and elaboration by blind observes. The candle problem was asked to volunteers using a standard form with an answering time limit of 3 min. The latency for correct answer was recorded. The relationships between the variables were examined by using correlation analyses.

Results: The visual creativity score was positively correlated with card selecting duration at 3rd, 4th and 5th bins (r= 0.470, r=0.425, and r=0.387; $p<0.05$, respectively). The correct answer latency in the candle test was negatively correlated with the total monetary reward at IGT (r=-0.573, $p<0.05$).

Conclusions: The present results indicated that the individuals with higher visual creativity scores spent more time while selecting the cards during the last three bins of IGT, indicating they made their decisions less impulsively. Moreover the individuals solved the candle problem faster earned more reward in IGT test. These results indicated that trait impulsivity is a negative factor for visual and verbal creativity.

Introduction

Creativity is the ability of producing something original and worthwhile. Creativity needs courage of following different or discrete ways and breaking the ordinary patterns, elastic thinking ability to connect ideas seemed irrelevant, and being open to the new ideas. Creativity is not a sole ability but it consists of many different skills. At least four different measures were described for creative action. 1) Flexibility: The ability to cross boundaries and make remote associations. It can be evaluated by number of different categories of ideas generated. 2) Originality: Producing ideas significantly different or novel compared to a general population. It can be evaluated as the number of novel ideas generated. 3) Fluency: The ability to come up with many diverse ideas quickly. It can be evaluated by the total number of ideas generated in a given time period. 4) Elaboration: The amount of details associated with the ideas. Elaboration reflects the ability of focusing on each solution/idea and developing it further. Moreover in different individuals, these abilities may be differentially expressed, such as verbally or visually. Thus at least verbal and visual creative thinking abilities should be evaluated individually. Creativity becomes a more prominent skill in today's world that innovation is highly important in every area. A 50-year follow-up study started by Paul Torrence in 1950 showed that creative thinking score obtained during elementary school was positively correlated with lifetime personal achievements [1]. Runcoa et al. [1] impressed those public achievements were more related with the interaction of creativity scores and intelligence. Creativity has been tended to be seen as an innate ability and sometimes related with several mental disorders such as bipolar disorder [2] and some personality traits such as impulsivity. Impulsivity can be defined as doing actions without enough considering the situations. It leads risky actions or choices in general. For example selecting small but immediate rewards over big and long-term rewards is a typical impulsive choice behavior. Trait impulsivity has both positive and negative facets for creative thinking. The positive facets may include boldness, risk-taking behavior driven by sensation and seeking novelty. Conversely, the negative facets may be acting without thinking, deliberation, or reflection [3].

In the present study, we aimed to examine possible relationships between creative thinking and impulsivity. In particular we aimed to use more objective tools to measure creative thinking ability and impulsivity. Unfortunately many previous studies examining such a relationship [2] used questionable criteria especially for creativity such as being an artist, novelist or having an art course. Here, we evaluated creative thinking ability with well-documented and evidenced tests, such as Torrance Drawing Completion Test for visual creativity and Duncker's candle problem for verbal creativity.

Methods

The high school students from 9th and 10th grades (20 girls and 20 boys) who are blind to the study completed the Iowa Gambling Task (IGT) using a free application running on an Android tablet. The application starts with $2000 credit and the aim is wining the highest amount by choosing cards from four decks. Choosing the cards from decks A and B provide more monetary reward than the cards from C and D, but the cards A and B also bring higher unexpected monetary loses. Choices, deciding latency, card selecting duration, and total money earned were recorded in five bins. The percentage of card selection from A + B to C + D decks indicates impulsive choices and immediacy of card selecting duration indicates impulsive action.

The creativity was evaluated two different tests, Torrance Drawing Completion Test for visual creativity and Duncker's candle problem for verbal creativity. The volunteers individually seated in a classroom and first a white paper containing 30 circles (r=2 cm) was given them and asked to make drawings as they wished in 3 min time. Then the candle problem was asked to volunteers using a standard forms with an answering time limit of 3 min. The test presents the participant

with the following task: You have a book of matches and a box of thumbtacks. By using them how to fix and light a candle on a wall in a way so the candle wax won't drip onto the table below. The solution is to empty the box of thumbtacks, use the thumbtacks to nail the box to the wall, put the candle into the box, and light the candle with the match. The concept of functional fixedness predicts that the participant will only see the box as a device to hold the thumbtacks and not immediately perceive it as a separate and functional component available to be used in solving the task. To find the correct solution volunteers need to overcome functional fixedness. The latency for correct answer was recorded. At the end of all the tests the drawings were scored (10 points Likert scale for each measure) for fluency, flexibility, originality, and elaboration by blind observes. The relationships between the variables were examined with correlation analyses.

Results

The study participants randomly selected the cards from decks during the first two bins of the IGT, and with the 3rd bin they began selecting from the advantageous decks showing that they discovered the rules. The mean (±S.E.M.) total visual creativity score was 26.6±1.97 (range: 10–59). One of the volunteers was excluded from the verbal creativity test because she knew the Duncker's candle problem already. Eighteen of the 39 volunteers correctly answered that problem with a mean (±S.E.M.) correct answering time of 75.1 ±13.11 s. The visual creativity score was positively correlated with card selecting duration at 3rd, 4th and 5th bins (Figure 1A-1C; r^2=0.470, 0.425, and 0.387, respectively; p<0.05). The correct answer latency in the candle test was negatively correlated with the total monetary reward at IGT, which indicates the successful performance in IGT (Figure 2; r^2=−0.573, p<0.05).

Discussion

The present results indicated that the individuals with higher visual creativity scores spent more time while selecting the cards during the last three bins of IGT, indicating they decide less impulsively. Furthermore, the individuals solved the candle problem faster earned more reward in IGT test. These results indicated that trait impulsivity was a negative factor for visual and verbal creativity. The most important aspect of the present study was evaluating the creativity by using objective tests. Although it is a highly important area of research there are a few validated tests for measuring creativity. Torrance Drawing Completion Test is one of the well-studied tests for visual creativity assessments. There are several different versions of that test, and we preferred the one with regular circles. This test allowed us to score fluency, elaboration,

originality and flexibility of the drawings created by the volunteers. Two different creativity areas, visual and verbal, were also evaluated by different tests. The importance of separately testing these two areas was evidenced in the present study by showing there was no statistically significant correlation among the outcomes of Torrance Drawing Completion Test and Duncker's candle problem.

It has been showed that the healthy functioning of the frontal cortex was very important for successfully performing IGT. The mean (±S.E.M) of our volunteer group was 14.7±0.12 years that they have not fully completed the frontal cortex development yet. However, the card selection patterns over five bins were comparable to the previous studies on adults. A previous study indicated that during early adolescence (at age of 12) IGT score was significantly disrupted, but after age 13 IGT scores were very close to the range in the adults. Therefore, our data were consistent with that study. A similar study with different age groups (including 12 years of age) would be helpful to understand whether the change in IGT performance may have an effect on creativity scores. Future studies could be performed by measuring impulsive action or impulsive choice, such as stop signal task or delay discounting models, because these entire tests might measure different aspects of impulsivity. Other measures of IGT, such as decision making latency or card selecting duration have not been studied as much as advantageous/ disadvantageous card selection. In this present study, we used the advantage of performing the IGT on a touch screen device and easily measured these parameters. Additionally, we found a significant correlation with creativity score, which indicated that these timing parameters should have been evaluated in studies performing IGT.

In conclusion, we showed that both visual and verbal creativity may have decreased in individuals with trait impulsivity. During the adolescence, such individuals may be advised to have courses or practices, such as art or sport classes, to lower their trait impulsivity. Hence, they may have more chance to unleash their creative thinking ability.

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Comparison of Obsessive-Compulsive Disorder Patients with Healthy Volunteers in Terms of Neurocognitive Functions, Risk Taking, and Impulsivity

Pelin Öztürk[a], Serkan Zincir[b], Cihad Yükselir[c], Feyza Ersan Unal[a], Şakir Gıca[d] and Aytül Gürsu Hariri[e]

[a]Department of Psychiatry, Erenkoy Training and Research Hospital for Psychiatric and Neurological Diseases, Istanbul; [b]Department of Psychiatry, Golcuk Necatı Celık State Hospital, Kocaeli; [c]Department of Psychiatry, Ataturk State Hospital, Balıkesir; [d]Department of Psychiatry, Bakırkoy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Education and Research Hospital, Istanbul; [e]Department of Psychiatry, Maltepe University School of Medicine, Istanbul

E-mail address: kartalpelin@yahoo.com

ABSTRACT

Objective: There is growing evidence for neuropsychological dysfunction in obsessive-compulsive disorder (OCD) regarding to an underlying frontal lobe and basal ganglia dysfunction. Although specific prefrontal-striatal-thalamic dysfunction is proposed in obsessive-compulsive disorder (OCD), this is not sustained by neuropsychological studies.
Methods: Thirty adult OCD patients who were diagnosed according to DSM-5 and 30 healthy controls matched on age, gender, educational level are included in the study. All participants were administered the SCID-I, Yale-Brown Obsessive Compulsive Scale, and the Barratt Impulsivity Scale (BSI-11). Trail Making Test, Controlled Oral Word Association Test, Categorical Verbal Fluency Test, Stroop Task, Balloon Analogue Risk Task, Stop Signal Task, Digit Span Test, Digit Symbol Test, Auditory Consonant Trigrams Test, Rey Auditory Verbal Learning Test, Visual Reproduction Test on the Wechsler Memory Scale-Revised, Wisconsin Card Sorting Test have been used for neurocognitive assessment.
Results: In terms of cognitive functions and impulsivity, significant differences were found between the OCD patients and controls.
Conclusions: Prospective studies with larger sample sizes are required to replicate our findings and elucidate neuropsychological dysfunctions seen in OCD patients.

KEYWORDS

Obsessive-compulsive disorder; Barratt Impulsivity Scale; Balloon Analogue Risk Task; neurocognitive functions

Introduction

Obsessive-compulsive disorder (OCD) is a chronic disease characterized by repetitive, unwanted intrusive thoughts and ritualistic behaviors. Studies of the neuropsychological functions in OCD have documented deficits in several cognitive domains, particularly with respect to visual-spatial abilities, executive functioning, motor speed, and impulsivity.

Many studies have examined cognitive functions in OCD, frequently with contradicting results. Several studies have suggested that OCD patients have selective neuropsychological deficits in attention, executive functions, verbal memory, non-verbal memory and visuospatial skills. However, a number of studies have also examined the correlations between different neuropsychological variables in OCD and these have found that impaired use of organization strategies may also contribute to memory dysfunction. The objective of the present study was to examine systematically the cognitive functioning of OCD patients who were taking medication and the effect of impulsivity on neurobiological tests. A total of 30 medicated OCD patients were compared with 30 healthy control subjects in respect of performance in a comprehensive battery of neuropsychological tests. The OCD patients and healthy volunteers were compared in respect of the cognitive functions such as attention, short and long term memory, verbal fluency, concentration and the impulsivity.

Methods

The study included 30 adults who met the OCD diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, fifth Edition, and 30 healthy, age, gender, and education -matched control subjects. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and Barratt Impulsivity Scale (BIS) were administered to all participants. A comprehensive battery of neuropsychological tests comprising the Turkish adaptations of well-established neuropsychological tests was administered in a separate session lasting approximately 2 hours. The Trail Making Test, Controlled Oral Word Association Test, Categorical Verbal Fluency Test, Stroop Task, Balloon Analogue Risk Task, Stop Signal Task,Barratt impulsiveness scale, Digit Span Test, Digit Symbol Test, Rey Auditory Verbal Learning Test, Visual Reproduction Test, and the Wisconsin Card Sorting Test were used for neurocognitive evaluation. Statistical analyses were performed by using the SPSS 20 for Windows.

Results

The 30 OCD patients comprised 15 males and 15 females with a mean age of 40.6±10 years and mean number of years in education of 11.6±4.2 years. The 30 control subjects comprised 15 males and 15 females with a mean age of 41.1±10 years and mean number of years in education of 12.5±4.7 years. No difference was

determined between the groups in respect of age (t test, p=0.880), gender (χ^2=0.018, p=0.890) and years in education (t test, p=0.013).

The mean age at onset of the disease was 18.5±8.2 years. The mean duration of the disease was 8.1±6.2 years, and the mean duration of the treatment was 10.2 years. The mean Y-BOCS score was 27.7±5.1, the mean obsession subscale score was 14.1±3.0 and the mean compulsion subscale score was 13.7±2. Statistically significant differences were determined between the OCD patients and the control group in respect of cognitive functions. In the tests comparing attention functions, in respect of interference errors in the Stroop test, values were determined as 2.2±2.8 in the OCD group and 0.8±0.8 in the control group. This difference was found to be statistically significant (p=0.002). In the digital span test and the Trail Making test, no statistically significant difference was determined between the groups. (p>0.05). The performance of functional memory, which is important in decision-making, problem solving, abstract thinking, classification, cognitive functionality, cognitive flexibility and judgement was measured in the Wisconsin Card Sorting Test. The number of categories completed was less in the OCD group than in the control group (p=0.000), the number of total correct was lower (p=0.000), the total incorrect (p=0.000) and the perseverative error percentages were higher (p=0.005).

Categorical Verbal Fluency Test: this is a test which measures the ability of an individual to organise their thoughts and manage their behaviour. Fewer words were counted by the OCD group than by the control group (36.2±12.2 *vs.* 48.6±11.3) and there was greater perseverative word counting in the OCD group (p=0.000).

Visual Reproduction: points are awarded for immediate recall. The test results were determined as 33.3±5.0 in the OCD group and 33.5±4.3 in the control group (p>0.05). In the delayed recall test the results were 29.4±6.9 in the OCD group and 29.9±6.5 in the control group (p>0.05)

Rey Auditory Verbal Learning Test: The number of words remembered at the first attempt (OCD: 6.7 ±2.0, control: 9.4±1.4) and the total number of words remembered in 5 attempts (OCD: 52.0±8.4, control: 58.8±6.0) were lower in the OCD group than in the control group (p=0.000, p=0.010, respectively).

Stop Signal Task: In the comparison of the Stop Signal Reaction time (SSRT) values, the mean values of the OCD group of 480.4±64.5 were determined to be lower than those of the control group at 425.1±52.1 (p=0.001). In other words, the SSRTs of the OCD group were longer than those of the control group.

Barratt Impulsiveness Scale: The total points were 64.9±6.9 in the OCD group and 53.4±8.0 in the control group (p=0.000). Due to attention impulsivity and being unplanned in the OCD group, they could not

be sure of tight control and what they had done and motor impulsivity resulted in not being able to inhibit the inappropriate stiumulus

Balloon Analogue Risk Task (BART): in the results of this test, which evaluates risk-taking behaviour, the number of balloons burst was mean 12.4±3.4 in the OCD group and 9.5±2.4 in the control group (p=0.000).

Discussion

The results of this study determined differences in respect of cognitive functions between the OCD patients and the control group. That there was no difference between the groups in the attention functions test suggested that there was no basic attention function deficit in the OCD patients but that there could be selective attention response. In the interference section of the Stroop test, the higher results of the OCD patients in not resisting an inappropriate response is highly consistent with the pathophysiology of the disease.

The Wisconsin Card Sorting Test (WCST) demonstrates the ability of the person to direct attention away from a stimulus while maintaining a task. It is thought that a higher number of perseverative responses reflects the inability to inhibit a previous incorrect response and this results in the person continuing to maintain the old behaviour. In the current study, it was observed that the OCD patients were forced to change old behaviours and they made more perseverative errors. It has been reported in literature that verbal fluency is affected in OCD patients [1]. In the controlled word recall test of the current study, the perseverative word count in the OCD group was found to be greater. Perseverative word count in the test indicates inhibition weakness. Due to insufficient organisation of thought and inhibition weakness in OCD patients, this is consistent with the pattern of maintaining the same behaviour.

Visual-spatial ability demonstrates the person's capacity to perceive, use and manage spatial objects. In studies which have researched cognitive functions related to OCD, the most agreement has been that there is impairment in vision, visual-spatial skills and visual memory functions. Similar to a study by Kang et al. [2], in the current study there was no difference between the OCD group and the control group in the Visual Reproduction Test suggesting that the medication used by the patients could have been the reason for the improvement in the test. While this gives rise to the conclusion that the medication of the patients could have had an improving effect on the cognitive structure, there was also the side-effect of the medication seen in the results of the Stop Signal Test that response inhibition times were prolonged and the reaction times of the patients were slowed down. In other

words there was a slowing down of the obsessive and compulsive reactions of the patients. This effect is greater in tricyclic anti-depressants and anxiolytic drugs which have more anticholinergic side-effects.

As the number of words remembered in the Rey Auditory Verbal Learning Test results was lower in the OCD group than the control group, this showed a greater inadequacy in immediate recall, verbal skills and learning points of the OCD group. Focussing on details by delaying attention directed to general information can reduce recall. Impulsivity has been associated with compulsive behaviours in OCD. Impulsivity is thought to be related to the cognitive processes such as being unplanned, risk-taking, extroversion, thrill-seeking, response inhibition and decision-making. Impulsivity is evaluated by examining the reaction times in the responses given and response inhibitions in the Stop Signal Task with Response Inhibition. In the current study, the SSRT values were prolonged in the OCD group compared to the control group. The OCD patients were found to be more inadequate in the inhibition of motor responses compared to the control group. Generally, it has been noticeable that in studies of medicated OCD patients, the response rate has been slowed and in studies of unmedicated OCD patients, the response rate has been normal [3].

In the Barrat Impulsivity Scale, the OCD group had higher points than the control group in respect of attention, motor rate, being unplanned and total points. Due to attention impulsivity and being unplanned in the OCD group, they could not be sure

of tight control and what they had done and motor impulsivity resulted in not being able to inhibit the inappropriate stimulus.

In the current study, as the years of treatment increased, so the attention subscale points decreased. In other words, it could be concluded that the treatment decreased impulsive inattention. Risk-taking or making risky decisions can be said to be one of the signs of impulsivity. A person showing impulsive characteristics has reduced control over their own behaviours and as a result may take risky decisions and put themselves at greater risk than other people. There has been reported to be an increase in risk-taking behavior in OCD patients in the long-term as a response to immediate gain. In the current study, the OCD group were determined to take more risks than the control group.

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