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Is Obsessive–Compulsive symptomatology a risk factor for Alzheimer-type dementia?

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ABSTRACT

In the present study, we hypothesized that lifetime Obsessive–Compulsive (OC) symptomatology would be risk factors for the development of Alzheimer's disease (AD). For this aim, first we compared 39 patients with AD and 30 age and gender matched control subjects. We have found that lifetime and current OC symptoms (OCs) and comorbid diagnosis of Obsessive–Compulsive Personality Disorder in AD patients were significantly more prevalent than in control group. AD patients had more likely to have lifetime and current hoarding, and checking obsessions compared to controls. The rate of lifetime and current hoarding, and checking compulsions also appeared to be higher in AD patients in comparison to control subjects. Hoarding and checking obsessions, and compulsions seemed to proceed through the dementia in contrast to other OCs. The mean number of lifetime compulsions seemed to predict the diagnosis of AD. When we compared AD patients with and without OCs, we have found that OC symptomatology prior to AD did not cause an earlier onset of dementia and more severe cognitive impairment. Further longitudinal clinical, genetic and neuroimaging investigations are required to determine if lifetime presence of OCs would predispose to the development of later AD.

1. Introduction

Alzheimer's disease (AD) is a progressive, and irreversible neurodegenerative syndrome that is characterized by impairments in cognition and memory (Cummings 2004). Age, family history of AD, lower levels of education, female gender, and personal or family history of depression have been identified as prominent risk factors for AD.

Several neurocognitive symptoms seen in the course of AD are also characteristic of obsessive compulsive disorder (OCD). Clinical observations clearly indicate that OCD patients report memory impairments. Current models of OCD emphasize the frontal–subcortical circuit involving the orbitofrontal cortex, anterior cingulate, striatum, and thalamus that connect specific portions of the frontal lobes with subcortical structures (Cummings, 1995; Saxena et al., 2001; Cavedini et al., 1998; Menzies et al., 2008). The role of serotonin, dopamine and glutamate in relation to the pathophysiology of OCD is well known. In addition, there is some evidence that central cholinergic systems might be involved in OCD. Since orbitofrontal cortex which is one of the most involved brain areas in OCD received a substantial cholinergic innervation, cholinergic system dysfunction might be related to the physiopathology of OCD (Carlsson, 2001; Lundberg et al., 2004). If there is a real memory deficit in patients with OCD, then pre-existing Obsessive–compulsive symptoms (OCs) may predispose to AD in later ages. Previously, Frydman et al. (2010) reported a case of late-onset and treatment-refractory OCD who developed into full-blown dementia after 7-years of follow-up. They suggested that treatment refractoriness in a patient with late-onset OCD may indicate underlining organicity. Khiari et al. (2011) described a case of old woman with cognitive decline and some behavioral disturbances. She had a past history of severe OCD. Many subjects in her family had also a history of OCD and/or dementia. So, the authors proposed that OCD might be a new risk factor for AD, considering that glutamatergic dysfunction may be a common physiopathology of OCD and AD. Studies of neurologic disorders suggest that a detailed assessment of the learning and memory processes might provide a means of identifying the role of frontal–striatal systems to memory. In frontal–striatal disorders, executive dysfunction appears to be predominant, and this has a secondary impact on other functions, including memory in patients with AD and OCD. Studies also demonstrated that increased hippocampal activity in OCD patients may represent a compansatory mechanism, activating fronto-hippocampal circuitry which is responsible for conscious information processing (Van den Heuvel et al., 2005; Rauch et al., 2007; Milad and Rauch, 2012). A recent study reported that a significant reduction in the caudate volume of AD patients was observed compared to that of the healthy controls. The

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authors hypothesized that these changes can be considered as an indication of early AD (Jiji et al., 2013).

In the present study, we expected that AD patients would have more frequent lifetime OCs compared to age and gender matched control subjects. We also supposed that there might be possible relationship between lifetime Obsessive–Compulsive (OC) symptomatology and the duration of dementia and the level of memory impairments in patients with AD. Therefore, we hypothesized that lifetime OCs would be risk factors for the later development of AD.

2. Methods

2.1. Subjects

Thirty-nine subjects (25 women and 14 men) with AD were recruited consecutively from April 2012 to September 2013 at the neurology out-patient clinics of the Adnan Menderes University Hospital. The control sample included 30 individuals matched for age and sex. The all samples were screened for psychiatric or neurological illnesses. Exclusion criteria for the all participants included lifetime of current substance use disorder, psychosis, head injury, or neurologic disorder (including Tourette's syndrome). The patients except two were under antidementia treatment at the time of evaluation. The study was approved by the local ethics committee of the medical faculty of Adnan Menderes University. All participants gave their written informed consent prior to inclusion into the study.

The diagnosis of AD and neurological assessments were done by a senior neurologist. A trained psychiatrist (AD) administrated Mini Mental Status Examination (MMSE) (Folstein et al., 1975) to the all samples to assess the current cognitive status. Information on previous psychiatric symptoms and personality characteristics was avaliable from surrogate sources or first-degree relatives of the patients. Reported onset information about OCs and dementia for persons with AD is the family's best estimate of symptom onset.

To assess a possible relationship with AD, the lifetime diagnosis of major depression (MD) was obtained through the Structured Clinical Interviews for DSM-IVAxis I Disorders (SCID-I) (First et al., 1997; Ozkurkcugil et al., 1999). The Obsessive Compulsive Personality Disorder (OCPD) was determined by DSM-III-R Axis II Disorders (SCID-II) (Spitzer et al., 1990; Coskunol et al.,1994). All patients and controls were applied Yale–Brown Obsessive Compulsive Scale (Y–BOCS, Goodman et al.,1989) to determine the severity of current OCs. The types of lifetime and current OCs were identified using Y–BOCS symptom checklist. The severity of current depression and anxiety was assessed with the Hamilton Depression Rating Scales (HDRS) and Hamilton Anxiety Rating Scales (HARS). Because most of the dementia patients may give unreliable reports, we administrated these clinical scales by obtaining information directly from the patient and surrogate sources within the family, ideally those with a sufficient knowledge of the patient, as suggested some of the previous studies (Green et al., 2003; Thorpe, 2009).

After this baseline assessment, the patients who had at least one obsession or/and compulsion before the onset of AD ($n=24$); and the rest of the AD patients who had no lifetime and current OCs ($n=13$) were divided into two groups. The two patients whose OCs first emerged after the onset of AD ($n=2$) were excluded from the analyses. In consistent with some of the previous studies (Grant et al., 2007), we determined the patients whose OCs first emerged after 30 years old as late-onset patients.

These two groups were administrated ADAS-Cog Scale to evaluate the level of cognitive disturbance (Mohs et al., 1997; Mavioglu et al., 2004). Therefore, we could be able to examine the possible effects of lifetime OCs on the level of cognitive functions and the other variables in patients with AD. The ADAS-Cog subscale consists of 11 tasks measuring cognitive abilities in memory, language, orientation and praxis. The test includes seven performance items and four clinician-rated items, with a total score ranging from zero (no impairment) to 70 (severe impairment). The higher the ADAS-Cog score, the more impaired the subject.

2.2. Statistical analysis

The groups were compared using chi-square or Fisher's exact tests for categorical variables. The continuous independent data were compared using Mann–Whitney U test. The relationships between several clinical variables and the severity of ADAS-Cog scores were examined by Pearson's correlation coefficient. All statistical tests were two-tailed at $p=0.05$. We performed two logistic regression analyses to determine potential predictors of AD, one for variables related to the rate of lifetime and current OCs, and the comorbid diagnosis of OCPD, the other for variables related to the content of lifetime and current OCs. To reduce the number of independent variables used in regression analysis, potential predictors were identified from the variables that were significant ($p<0.05$). Overall percent correct classifications for regressions one and two were 73.0% and 73.9%, respectively.

3. Results

As illustrated in Table 1, there were no significant differences between the patient and control groups with respect to age, marital status, educational level, personal history of depression, and family history of dementia. AD patients had significantly higher scores of HDRS, HARS, and MMSE than control subjects.

Table 2 demonstrates that the comparisons of AD and control groups in terms of OC symptomatology. The current total and subscale scores of Y–BOCS were more likely to be higher in AD group than in controls. The mean number of lifetime ($p<0.0001$) and current obsessions ($p=0.001$) in AD group was significantly higher than control group. Also, we have found that the mean number of lifetime ($p<0.0001$), and current compulsions ($p=0.002$) were greater in patients with AD compared to control subjects.

The most prevalent lifetime and current obsessions were hoarding, contamination, symmetry, and checking among the patients with AD. The frequency of lifetime ($p<0.0001$) and current hoarding ($p<0.0001$), and checking obsessions ($p=0.03$; $p=0.01$, respectively) were more likely to be higher in AD group than in controls. The rate of lifetime symmetry obsessions ($p=0.03$) tended to be higher in the

Table 1
Comparison of patients and controls with respect to demographic and clinical variables.

	AD ($n=39$)		Control subjects ($n=30$)		Statistical analyses		
	S	%	*S*	%	χ^2	d.f.	*p*
Gender					0.394	1	0.53
Female	25	64.1	17	56.7			
Male	14	35.9	13	43.3			
Marital status					2.176	3	0.53
Married	28	71.8	25	83.3			
Single	1	2.6	0	0.0			
Divorced	1	2.6	0	0.0			
Widow	9	23.1	5	16.7			
Personal history of depression	17	43.6	13	43.3	0.000	1	0.98
Family history of dementia	14	35.9	7	23.3	1.26	1	0.26
	Ort	SS	Ort	SS	*Z*		*p*
Age	73.20	7.24	70.4	6.55	−1.83		0.06
Educational level (year)	4.48	3.42	5.44	4.55	−0.70		0.48
HDRS	12.10	5.51	5.73	4.11	−4.71		<0.0001
HARS	11.48	7.19	6.60	3.92	−2.83		0.005
MMSE	15.28	6.95	28.20	1.32	−6.92		<0.0001