Psychiatry Research 240 (2016) 110–117

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Neuropsychological, electrophysiological and neurological impairments in patients with obsessive compulsive disorder, their healthy siblings and healthy controls: Identifying potential endophenotype(s)

Halil Ozcan [a,b,*], Suzan Ozer [b], Suha Yagcioglu [c]

[a] Ataturk University, Medical Faculty, Department of Psychiatry, Erzurum, Turkey
[b] Hacettepe University, Medical Faculty, Department of Psychiatry, Ankara, Turkey
[c] Hacettepe University, Medical Faculty, Department of Biophysics, Ankara, Turkey

ARTICLE INFO

Article history:
Received 6 April 2015
Received in revised form
15 February 2016
Accepted 6 April 2016
Available online 7 April 2016

Keywords:
OCD
Cognitive functions
AERP
P300
Neurological soft signs
Endophenotype

ABSTRACT

The etiology of obsessive-compulsive disorder (OCD) has not been clarified. This study aimed to investigate the cognitive, neurological, electrophysiological functions which are reflected in executive functions, memory, visuospatial integration; neurological examination and auditory event related potentials (AERP) (N100, N200, P200 and P300) in patients with OCD, their siblings, and control subjects and to determine potential endophenotypic markers. Thirty-three patients with OCD, 18 siblings and 21 controls; matched for age, gender and years of education were included. Yale Brown Obsessive Compulsive Symptoms Checklist Scale, Hamilton Depression-Rating Scale, an exhaustive neuropscyhological test battery and Neurological Evaluation Scale were administered. Their AERP recordings were obtained. Executive functions and visuospatial integration were highly impaired in patients and slightly in their siblings compared to controls. P200 amplitude was sorted as siblings > patients > controls. P300 amplitude was sorted as patients < siblings < controls. Neurological Evaluation Scale scores were lower in patients compared to siblings and controls. The logistic regression analysis showed that, higher P300 amplitude, better performance on block design test and faster completion of Stroop test would predict being in the control group, whereas higher P200 amplitude would predict being in the case (patient and sibling) groups. We suggest that these seem to be the potential endophenotypes of OCD.

1. Introduction

The etiology of obsessive-compulsive disorder (OCD) is not fully clarified. Genetics, environmental factors, functional abnormalities in brain neurotransmitter systems could lead to OCD. The rate of incidence of OCD among first-degree relatives of OCD patients is 3-12 folds more than the community incidence (Grados et al., 2003). Many studies have found neuropsychological and electrophysiological abnormalities in patients with OCD (Stein, 2000; Kuelz et al., 2004). Deficits in executive functions (selective and sustained attention, decision making, planning, problem-solving, response inhibition to irrelevant stimuli), visuospatial abilities, verbal and visual memory have been found in patients and these neuropsychological deteriorations have been suggested to be related with the neurobiology of OCD (Christensen et al., 1992; Purcell et al., 1998; Okasha et al., 2000; Evans et al., 2004; Kuelz et al., 2004; Tukel et al., 2012). The latencies and amplitudes of brain waves, those occurring during a stimuli are used to understand the electrophysiological state of the brain. In OCD, auditory event related potentials (AERP) including N100, N200, P200 and P300 which reflects neurodysfunction are studied.

Longer N100, P200, and shorter N200 latencies reflecting cortical arousal, inhibited response given to a minimal stimuli that is higher than expected, also, acceleration of information processing and memory decoding is frequently detected in patients with OCD (Towey et al., 1990; Towey et al., 1993; Okasha et al., 2000; Dayan et al., 2014). Contradictory results about P300 latency and amplitude as the most investigated potential in patients with OCD (including both auditory and visual evoked potentials) compared to controls were reported (Di Russo et al., 2000; Sanz et al., 2001; Mavrogiorgou et al., 2002; Gohle et al., 2008; Pallanti et al., 2009; Andreou et al., 2013). Shorter P300 latency related to the duration of recognizing target stimuli was reported as well (Mataix-Cols

* Correspondence to: Ataturk University, Medical Faculty, Yakutiye Research Hospital, Department of Psychiatry, Erzurum 25040, Turkey.
E-mail address: halilozcan23@yahoo.com (H. Ozcan).

http://dx.doi.org/10.1016/j.psychres.2016.04.013
0165-1781/

et al., 2002; Watkins et al., 2005; Tukel et al., 2012). Neurological soft signs were defined in different neuropsychiatric disorders including OCD, schizophrenia, bipolar disorder and others (Yazici et al., 2002; Nielen and Den Boer, 2003; Hollander et al., 2005) previously declared as potential endophenotypes in schizophrenia (Negash et al., 2004). Also, in a recent study, it was suggested that familial OCD may have distinctive clinical features, as it has been indicated that symptom features may have a genetic base (Peng et al., 2012).

Endophenotypes are indicators of susceptibility to disorders, that are state-independent (evident in a patient whether or not illness is active) and may help in understanding genetic underpinnings of OCD (Kaluzynska and Rabe-Jablonska, 2014). OCD has been conceptualized as a disorder in which failures of behavioral (cognitive and motor) inhibition constitute a key characteristic. The identity of OCD may be better understood by exploring the key endophenotypic domains, such as neurocognition, brain imaging, and molecular mechanisms.

In this study, neuropsychological, electrophysiological and neurological abnormalities were chosen to determine the candidate endophenotypes in OCD (Morault et al., 1997; Peng et al., 2012; Arumugham et al., 2014). Several endophenotypes based on neuropsychological findings, (particularly executive functions, such as decision making and planning, inhibitory function), neurological abnormalities, structural and functional imaging findings have been proposed for OCD (Donchin and Cols, 1988; Chamberlain et al., 2005; Hollander et al., 2005; Menzies et al., 2007; Hoexter et al., 2009; Viswanath et al., 2009). The results of a study which explored medicated and drug-naive patients (Hollander et al., 2005) and another which evaluated patients before and after fluoxetine treatment (Cavedini et al., 2010) suggest that executive functions may represent candidate endophenotypes of OCD. Neurological soft signs are defined as potential endophenotypes in OCD as well (Zhang et al., 2015). There have been very limited numbers of studies including unaffected first-degree relatives of patients and controls. We found only one family study assessing impulsivity in relatives of patients (Li et al., 2012) in which most of the studies have included more than one generation (other relatives, mother, father, child, sibling) as subjects. Sampling different relative groups lead to a bias because of different neurodevelopment stages. To the best of our knowledge, only two aforementioned studies (Morault et al., 1997; Li et al., 2012) and our study include siblings of patients.

Here, our primary aim was to analyze the deficits in executive functions, visuospatial abilities, verbal and visual memory, N100, N200, P200, P300 and neurological soft signs between three groups: OCD patients, siblings of the patients and healthy controls. We hypothesized that similar deficits in patients and siblings (without OCD symptoms) may be potential endophenotypes and shed light to understand the genetic and neurobiological underpinnings of OCD.

2. Materials and methods

2.1. Settings, inclusion and exclusion criteria

This study was carried out between September 2009 and May 2010, in Hacettepe University Medical Faculty Department of Psychiatry. Thirty-three patients, diagnosed with OCD, 18 siblings of patients and 21 healthy controls matched for age and education levels (referring to averages) between 18 and 65 years participated in the study. Siblings chosen were at the closest age to the patients and came from a total of 14 families. The controls constituted of the hospital staff and the acquaintances of the participants. Written informed consents were obtained from all subjects prior to commencement of the study. The study was designed in accordance with the Declaration of Helsinki and approved by Hacettepe University Ethics Committee. Mental retardation, having loss of vision or hearing, color blindness, major component of a neurological disorder, severe physical illness, history of head trauma with loss of consciousness that lasted more than five minutes and less than 5 years of formal education were the exclusion criteria for all the participants. IQ level was not formally tested as inclusion criterion of at least 5 years of formal education was considered a predictor of normal IQ level (Shaw et al., 2014). Of 23 female patients, 1 had trichotillomania, of 10 male patients, 1 had tic disorder also. Six patients had more than one OCD symptom. Eleven patients (33.3%) had a family history of OCD. For patients, age of disease onset was 22.5 ± 5.7, disease duration was 12.5 ± 9.7 years. Drug taking patients (sixteen SSRIs; two sertaline average dosage of 125 mg/day, five paroxetine average dosage of 46 mg/day, nine paroxetine average dosage of 66 mg/day, eight clomipramine in average dosage of 162.5 mg/day) were taken for the study because of the limited numbers of drug-naive patients. Four patients were under the administration of atypic antipsychotics in daily dosages of (aripiprazole 10 mg, risperidone 1 mg, amisulpiride 200 mg, olanzapine 5 mg and quetiapine 25 mg), two were taking haloperidol 1 mg per/day for strengthening treatment and symptoms like insomnia. Nine were drug-naive, seven had never used medication for OCD.

Comorbid patients, except depression, including attention-deficit and hyperactivity disorder from medical history according to DSM-IV TR criteria were excluded. Siblings and controls, having a psychiatric disorder according to DSM-IV TR criteria, controls having a family history of psychiatric disease for a lifetime, siblings with a family history of psychiatric disease except OCD were excluded. In the morning hours at first, the diagnosis of OCD and assessing the severity of symptoms after that neuropsychological evaluations, neurological evaluation and at last electrophysiological evaluations were performed. All participants were trained for an adequate time in order to follow the instructions of the study. All evaluations took almost 3–3.5 h for each participant.

2.2. Clinical assessment

Patients were evaluated with DSM-IV, Structured Interview for DSM Axis I (SCID-I) for diagnosis of psychiatric disorders (Ettelt et al., 2007; de Vries et al., 2013) and Yale Brown Obsessive Compulsive Rating Scale (Y-BOCS) for scanning OCD symptoms and disease severity (Barber, 2005), Hamilton Depression Rating Scale (HDRS) was used for detecting comorbid depression (APA, 1994). Clinical Global Impression Scale (CGIS) for the severity of the disease (First et al., 2002) and Global Assessment of Functioning Scale (GAF) for the assessment of functioning (Goodman et al., 1989) were applied to patients. A socio-demographic questionnaire was applied to all participants. SCID-I was administered to rule out any Axis I disorder in the siblings and controls.

2.3. Neuropsychological assessment

A neuropsychological test battery reported to be valid and reliable for use in Turkey was administered to all participants.

Rey Auditory Verbal Learning and Memory Test (RAVLT): A list of 15 unrelated words repeated over five consecutive trials were asked to be repeated. Another list of 15 unrelated words were asked to be repeated, then the participant were asked to repeat the first list of 15 words and then again, after 30 minutes. Short-term auditory-verbal memory, rate of learning, learning strategies, interference and retention of information were evaluated (Hamilton, 1960; Beneke and Rasmus, 1992). Three tests (Digit span forward, backward tests and figural memory test) from Wechsler