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A CLINICAL GENETIC STUDY OF ADULT OBSESSIVE COMPULSIVE DISORDER FROM INDIA

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ABSTRACT

Objective: The current study aims to replicate western reports of a familial excess of syndromal and sub-syndromal Obsessive Compulsive Disorder (OCD) in OCD probands in an Indian population. Method: 148 relatives of OCD probands were compared with 151 normal subjects, based on evaluation on Schedule for Clinical Assessment for Neuropsychiatry (SCAN). Results: There were no clinically significant differences in the prevalence of psychiatric disorders between the two samples. Conclusion: In an Indian setting, the absence of familial loading in adult OCD is being reported. Whether subgroups of OCD are familial, or other factors play a role in the pathogenesis of OCD in India needs to be explored.

Key words: Genetics, Adult Obsessive Compulsive Diorder, India

While many reports in the past have reported that OCD is a familial disorder, this has to a large extent been confirmed by methodologically robust studies conducted in last decade (Black et al,1992; Yang & Liu,1998; Nestadt et al.,2000; Lougee et al.,2000; Bienvenu et al.,2000; Nestadt et al.,2001). They have reported a higher prevalence of variety of psychiatric disorders including OCD, OC Spectrum Disorders, Obsessional Traits, other Anxiety Disorders, Mood Disorders, Psychotic Disorders and Personality Disorders in the relatives of OCD probands. On other hand there have been a few studies which report almost equal prevalence or low prevalence in the general population (Rosenberg, 1967; Insel et al.,1983; McKeon & Murray,1987). Some of the limitations in earlier studies include usage of different criteria, absence of or usage of different assessment techniques for probands and relatives, lack of controls and lack of blinded assessments.

One of the risk factors which have been implicated in familial transmission of OCD is the presence of comorbid Tic Disorder (Comings & Comings 1985). However, in India, Tourette's syndrome (GTS) is infrequently encountered. This may mean absence of a significant genetic pool in India for OCD (Khanna, unpublished observations). It may be one of the reasons for a lower prevalence rate of OCD in India as compared to USA (0.6 vs 2.6%) (Khanna, unpublished observations).

Hence the current study aimed to explore whether familial transmission of adult OCD was similar to that reported by the western studies.

MATERIAL AND METHODS

Thirty -three subjects who met ICD-10 (World Health Organisation,1994) criteria for OCD and were first time attendees at Psychiatric facility at NIMHANS, Bangalore, India were recruited for this study. The subjects were recruited over a period of 1 year. Subjects who had comorbid

psychosis, Epilepsy, Bipolar disorder or Drug or Alcohol Dependence were excluded from study. The subjects were all self referred. An experienced psychiatrist initially assessed the probands to confirm the diagnosis using Schedule for Clinical Assessment in Neuropsychiatry (SCAN) (World Health Organisation, 1991). A control group of 32 families making a population of 215 (including children) was taken from a small village about 150 kilometers from Bangalore city. The control subjects were similar to index patients as per mean family size, age and sex distribution. The probands and adult first-degree relatives formed the universe of study group. The assessment of OCD probands and control subjects was carried out only after obtaining informed consent.

Procedure for Assessment of Relatives: Informed consent was taken from all the relatives who were assessed. 27 of 299 first degree relatives had already died so information regarding them was collected from a close relative. In total 283 relatives could be assessed out of the 299. The consent for relatives who had died was taken from the relative from whom information was gathered. All the available subjects were interviewed using schedule for clinical assessment in neuropsychiatry (SCAN). No interviews were conducted by telephone. In case relatives could not be interviewed directly, information regarding their mental health was ascertained using format of SCAN, and if necessary the Symptom Checklist, from adult relatives. Questionnaire for Tic Disorder (Black et al.,1992) was applied to the probands and relatives because SCAN does not assess the diagnosis of Tic Disorder.

All interviews were conducted by the same qualified psychiatrist. The information obtained from relatives was analyzed, and consensual diagnoses were determined by 2 qualified psychiatrists according to ICD-10 criteria.

The diagnostic criteria for sub syndromal OCD were as follows: the individual 1) met all criteria for OCD, except that symptoms were reported to occur for less than 1 hour per day; 2) met all the criteria for OCD, except for ego dystonicity and insight; or 3) met all criteria for OCD, except for interference and distress.

Data Analyses: The comparisons were done for prevalence of psychiatric morbidity between groups. Socio-demographic variables were compared between two groups, using chi-square with Yates correction and t-test, wherever appropriate. Families with or without a family history of OCD were compared.

RESULTS

The sample included 33 OCD probands, 32 matched unaffected control subjects and 299 first-degree relatives. The clinical characteristics of OCD probands are given in Table 1.

TABLE 1
CLINICAL CHARACTERISTICS OF OCD PROBANDS

Total number of subjects(n)	33
Mean (SD) age, years	27.33(9.09)
Number (%) male subjects	22(66.7)
Number(%)female subjects	11(33.3)
Mean(SD) age at onset,year	22.18(8.18)
Mean (SD) duration of illness, months	48.61(43.67)
Characteristics of OCD (n,%)	
Checking rituals	19(57.6)
Orderliness related compulsions	17(51.5)
Obsessive fear of harm	16(48.5)
Checking compulsions	14(42.4)
Comorbidity (n,%)	
Depressive Disorder	10(30)
Anxiety Disorder	
Phobia	2(6.1)
Panic Disorder	2(6.1)
Tic Disorder	2(6.1)
Neurasthenia	3(9.1)
Somatoform Disorder	3(9.1)
Non Organic Insomnia	15(45.5)
Any comorbidity	18(54.5)

The demographic characteristics of the probands and their relatives are given in table 2. Relatives of OCD probands and control group did not differ significantly with regard to sex ratio and age. Information about psychiatric morbidity was obtained from 283 (94.6%) relatives out of a total of 299 first degree relatives of both OCD probands and control subjects. Of 283 relatives interviewed, 173(61%) were assessed in person. Details of assessment of relatives are provided in Table 2.

The psychiatric morbidity profile of first-degree relatives is summarized in table 3. The 2 groups did not show any significant difference in occurrence of OCD or sub syndromal OCD (X^2=0.19, p=0.66).None of the relatives of either probands or control subjects received a diagnosis of TS, although 6.1% of OCD probands had chronic motor tic disorder((X^2=0.19, p=0.66). One relative each from both the groups of relatives had chronic motor tic disorder. The prevalence of other psychiatric disorders did not differ significantly in both the groups except for non-organic insomnia, which was found to be more prevalent in relatives of control group.

TABLE 2
CLINICAL CHARACTERISTICS OF OCD PROBANDS

	Relatives of OCD Probands	Relatives of Control Subject
Total number of relatives (*n*=299)[a]	148	151
Parents	66	65
Siblings	75	86
Children	7	0
Sex of relatives[b]		
Males	78	73
Females	70	78
Number of relatives[c]		
Live	130	142
Dead	18	9
Number (%) of relatives assessed (n=283)	135(91)	148(98)
Mean (SD) age, year of relatives[d]	39.29(15.53)	36.85(15.45)
Number(%) of relatives assessed		
Directly	61(45)	112(76)
Indirectly	74(55)	36(24)

[a] Chi-square=9.24, P>0.01, [b] Chi-square=0.57, P>0.01, [c] Chi-square=3.50, P>0.01, [d] t=1.29, P>0.01

DISCUSSION

Although studies over last 50 years have suggested that OCD is transmitted familialy, the methodologies used in earlier studies did not allow for conclusive results. Most of them were retrospective analyses, using imprecise diagnostic terminology. However our study had two major findings. Firstly, the prevalence of OCD and subsyndromal OCD in relatives of OCD probands was equal to the prevalence in relatives of control subjects. Secondly, Tourette's Syndrome was absent in relatives of both groups.

There was male preponderance in the subjects (male: female=2:1), which is not in concordance with earlier studies (Black et al.,1992; Nestadt et al.,2000; Karno et al.,1988) but it is almost similar to another report on juvenile OCD from India (Reddy et al.,2001). While a younger age at onset is associated with an excess of familial OCD (Reddy et al.,2001), no effect of gender has so far emerged. If genetic transmission is mediated by female gender of OCD probands, that can perhaps account for low heritability observed in this study. Evidence for such a speculation is however lacking.

Earlier studies have reported higher morbid risk in relatives of OCD probands (Nestadt et al.,2000, Comings & Comins 1985, Reddy et al.,2001, Riddle et al.,1990, Leonard et al.,1992, Bellodi et al.,1992, Pauls et al.,1995). These studies focus more on OCD probands of child and adolescent age group or adult OCD probands with childhood onset of illness. However, the current sample comprises largely of adult onset disorder. The obvious inference is that OCD in juveniles is perhaps a more familial form of illness. This stands true in light of recent study who could not find a case of OCD symptoms in relatives of probands whose age at onset of symptoms was 18 years or older (Nestadt et al.,2000).

Over half of relatives of OCD probands in the study by Black et al.(1992) were psychiatrically ill; the corresponding rate in this study was only 15%. If overall rates for psychiatric morbidity are considered there was no difference between the two groups. But it was noticed that non-organic insomnia was much more frequently noticed in the general population. The relative lack of this in the OCD group is difficult to speculate on. It is probable that this is an artifact of the SCAN computer algorithms, as a very high rate was also observed as a comorbid diagnosis in OCD probands, where such a dysfunction was

TABLE 3
LIFETIME PREVALENCE OF DSM-III-R DISORDERS IN INTERVIEWED OCD AND CONTROL RELATIVES

Diagnosis	Relative OCD probands (n=135) n(%)	Relatives of controls (n=148) n(%)	Chi-Square with Yates correction Chi-Square	P
Mood Disorder				
Depressive Episode	1(0.74)	1(0.68)	0.00	1.00
Dysthymia	2(1.48)	0(0)	0.60	0.44
Suicide	2(1.48)	1(0.68)	0.006	0.54
Anxiety Disorder				
OCD	2(1.48)	5(3.38)	0.41	0.52
Sub syndromal OCD	7(5.19)	8(5.41)	0.00	1.00
Combined	9(6.67)	13(8.78)	0.19	0.66
Schizophrenia	2(1.48)	1(0.68)	0.006	0.94
Alcohol Dependence	3(2.22)	2(1.35)	0.01	0.92
Mental Retardation	1(0.74)	0(0)	0.002	0.96
Chronic motor tic	1(0..74)	1(0.68)	0.00	1.00
Non Organic Insomnia	0(0)	13(8.78)	10.51	0.001
Neurasthenia	0(0)	2(1.35)	0.42	0.52
Any mental illness	20(14.81)	21(13.51)	0.04	0.84

more likely to have been secondary to OCD.

Comparable rates of tic disorders were observed between the 2 populations studied. No case of GTS was identified. It seems that a sub group of OCD subjects with comorbid tic disorders form a genetic subgroup in whom tic disorders are more frequently encountered in families. Various reports suggesting an OCD- tics genetic conglomeration (Leonard et al.,1992; Pauls et al.,1995; Commings et al.,1989; Pauls,1992) were thus not supported by the current report.

Tic disorders are infrequently encountered in India. While this has often been thought to be due to decreased sensitivity to the disorder, or lack of consultation by affected clients, but in current study this aspect was specifically looked for. The data of this study suggest that while tics may be genetically transmitted, their association with OCD in our setting is not sufficiently well established. The similar finding of lack of familial relation between OCD and tics has been reported in juvenile OCD in India (Reddy et al.,2001).

The current study was unable to replicate various western reports suggesting a genetic diathesis for adult OCD. There was a suggestion that tics, even though rarely encountered, may be genetically transmitted, but there was no evidence to suggest that tics- OCD shared a common genetic diathesis (Pauls et al.,1995). In only 6% of OCD probands was there a family history of OCD, as compared to figures around 50% in earlier studies. There are suggestions that other non-genetic etiological factors such as streptococcal infections (Lougee et al.,2000) and Herpes Simplex virus infections (Khanna et al.,1997) may play an important role. At a different level, the suggestion that different phenotypes of OCD may have differential genetic mediation (Alsbrook et al.,1998) is an area which the current study has not explored.

The most obvious conclusion from these finding would support the hypothesis that pool of genetically transmitted OCD seen in Western settings is largely, if not totally absent in an Indian setting. This would suggest that cases of OCD arise in India, in genetic parlance, due to mutations, rather than due to genetic transmission across generations. Thus, a lower prevalence of OCD in Indian situation would be predicted and the familial risk of the disorder needs to be adapted to the results from this study. The possibility that there are differences in the genetic pools for certain common psychiatric disorders is a promising area for cross-cultural research, in this era where

globalistaion is a norm.

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