



Obsessive–compulsive behaviors in parents of multiplex autism families

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Abstract

Parents of autistic probands with high and low rates of repetitive behaviors were compared for rates of obsessive–compulsive traits and disorder. The rate of repetitive behaviors was assessed using the Autism Diagnostic Interview–Revised (ADI–R) in 176 autistic probands from 57 multiplex families. Obsessive–compulsive disorder (OCD) in parents was determined by direct interview using a parental history questionnaire, with screening for obsessive–compulsive traits using the Yale–Brown Obsessive–Compulsive Scale checklist. Children who had high total scores on the repetitive behavior domain of the ADI–R were significantly more likely to have one or both parents with obsessive–compulsive traits or disorder compared with children who had low total scores on this domain. Children with high scores on D1/D2 of the ADI–R (narrow restricted interests and rituals) were significantly more likely to have one or both parents with OCD, especially fathers, than those with low D1/D2. The occurrence of obsessive–compulsive traits or disorder in parents of autistic children in multiplex families is significantly more likely if autistic children have a high occurrence of repetitive behaviors. Dichotomizing autistic probands by severity and type of repetitive behaviors (circumscribed interests and compulsive rituals) may yield more homogenous groups, which could be helpful in genetic linkage studies.

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1. Introduction

Current research indicates that mild forms of autism-like symptomology may occur in one or both parents and/or siblings of autistic probands (Landa et al., 1992; Bradford et al., 2001). Studies

of autism spectrum disorder sibling pairs indicate familial difficulties in communication, socialization (MacLean et al., 1999; Silverman et al., 2002), and repetitive behaviors (Spiker et al., 1994; Folstein et al., 1999; Silverman et al., 2002). Szatmari et al. (1996) found a high intraclass correlation of social behavior abnormalities in first-degree relatives of autistic disorder probands. Piven et al. (1994) also identified certain personality

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characteristics in parents of autistic probands, such as aloof, unctuous, and unresponsive traits, and some Axis I disorders (Piven and Palmer, 1999) in parents of autistic probands. However, not all studies report familiarity of the repetitive behavior domain (Piven et al., 1997).

In a review, Tanguay (2000) suggested an increased loading for both autistic disorder and autism-like disorders in first-degree relatives of autistic probands. Bolton et al. (1998) found the occurrence of obsessive–compulsive disorder (OCD) was significantly more common in first-degree relatives of autistic probands (3%) compared to relatives of Down syndrome probands (0%). In addition, the authors found that family members with OCD were also more likely to exhibit autistic-like social and communication impairments (Bolton et al., 1998).

Genetic studies have identified possible links to autism. However, while several susceptibility genes have been identified, there has been limited concordance of linked loci, a finding which reflects multiple genes contributing to the disorder and/or sample heterogeneity. Buxbaum et al. (2001) examined the impact of decreasing sample heterogeneity by restricting their sample to relatives with delayed onset of phrase speech. By stratifying the sample based on this language criterion, the authors obtained a maximal LOD score (HLOD) on chromosome 2q of 2.99, in contrast to the HLOD score of 1.96 in the entire sample. Bradford et al. (2001) obtained linkage signals on chromosomes 7q and 13q in a subgroup of families in which sibling probands had language delays. Interestingly, this finding became apparent only when the parent's history of language-related difficulties was incorporated into the analysis. These findings suggest that identifying autism-like symptomatology in family members may decrease the heterogeneity of the sample and help identify genes linked to the disorder.

Studies have also attempted to link the core symptom domains of repetitive behaviors within autism to specific neurotransmitter, peptide, and immune factors. Our group demonstrated a significant correlation between the severity of repetitive behaviors in autism and one aspect of serotonin function (5-HT_{1D} sensitivity) (Hollander et al.,

2000) and a specific B cell immune marker (D8/17) (Hollander et al., 1999). These findings suggested that these factors were not linked to the severity of autism per se, but rather to one symptom domain within the disorder (repetitive behaviors). We also found that infusion of synthetic oxytocin modulated the severity of the repetitive behaviors in adult patients with autism spectrum disorders (Hollander et al., in press). These findings suggest that examining the severity of the repetitive behavior domain in autism may be helpful in reducing biological as well as genetic heterogeneity.

A goal of the current preliminary study was to identify traits of the autism phenotype, specifically obsessive–compulsive traits or a past or present diagnosis of OCD in one or both parents of autistic probands, to inform genetic studies. A criterion for autism diagnosis is marked resistance to change, as evidenced by rigid and repetitive behaviors and restricted interests. This preliminary study examined whether these OC-like symptom dimensions characterized unaffected parents in autism multiplex families in the form of OC traits or OCD. It was hypothesized that autistic probands demonstrating a high level of repetitive behaviors were more likely to have one or both parents with OC traits or OCD. Parent(s) of autistic children with low levels of repetitive behavior were expected to show less occurrence of OC traits or OCD. It was also hypothesized that specific types of repetitive and compulsive behaviors in autistic children, specifically OC-like repetitive behaviors, would be associated with higher prevalence of OC traits or OCD in a parent(s).

2. Methods

Fifty-seven families, a subgroup of US families who participated in the Family Genetics Studies Program at the Seaver Autism Research Center of the Mount Sinai School of Medicine (Silverman et al., 2002) and who had completed the perinatal questionnaire and the Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) checklist, participated in this study. After obtaining informed consent for participation from parents, parental history was taken in a face-to-face interview using a perinatal

parent interview developed by the Family Genetics Studies Program for use in their research. This interview includes history of medical disorders, developmental disorders, learning disabilities, substance abuse, and psychiatric disorders, as well as history of OCD diagnosis or OC symptoms. The interview was conducted by a trained and experienced clinical rater (C.S.) who had no access to the probands' repetitive behavior scores. Parents also completed the entire Y-BOCS checklist (Goodman et al., 1989). Parents who endorsed any checklist item(s) were included in the OC traits group.

Probands were diagnosed with autistic disorder or autism spectrum disorder by trained and reliable clinical raters using the Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994), the 'gold standard' in autism diagnosis. While autistic disorder was diagnosed using the ADI-R algorithm, the method for identifying and classifying autism-related deficits that did not meet full criteria for autistic disorder is described in another report (Silverman et al., 2002) and will be briefly summarized here. Children were included in this sample who: (1) met full criteria for autistic disorder, (2) were no more than one point short of full criteria in the social domain and either the repetitive behavior or communication domain (borderline autism), (3) did not meet full or borderline autism criteria but met DSM-IV criteria for Asperger's Disorder, or (4) met onset criteria for autistic disorder but showed marginally sub-threshold deficits in either of the three core domains.

The repetitive behaviors and stereotyped patterns domain of the ADI-R was used to determine 'high' and 'low' rates of repetitive behaviors in autistic probands. The repetitive behavior domain is characterized by four sub-domains: the first two comprise 'obsessive-compulsive-like' behaviors and the latter two comprise 'stereotypic-like' behaviors. The first sub-domain (D1) describes behaviors characterized by circumscribed interests and unusual preoccupations. The second sub-domain (D2) comprises compulsive adherences to nonfunctional nonverbal or verbal routines or rituals. The third sub-domain (D3) includes stereotyped and repetitive motor mannerisms, such as hand, finger, and complex body mannerisms. The

fourth sub-domain (D4) describes preoccupation with parts of objects or non-functional elements of materials, and unusual sensory interests. While the ADI-R was designed as a diagnostic tool for autism, researchers have found the sub-domains useful for identifying core symptom domains (Spiker et al., 1994; MacLean et al., 1999; Buxbaum et al., 2001; Silverman et al., 2002).

Children with a total repetitive behavior domain score ≥ 9 were defined as having a 'high' level of repetitive behaviors. Children with a total repetitive behavior domain score ≤ 4 were defined as having a 'low' level of repetitive behaviors. Cutoff scores were determined for the total repetitive behavior score by dividing the sample into the top and bottom thirds. Children were then divided into those with high and low levels of the more OC-like repetitive behaviors based on the ADI-R repetitive behavior sub-domains (D1) narrow interests and (D2) compulsive rituals. 'High' scores were defined as ≥ 3 on both measures and 'low' scores were defined as ≤ 2 on both measures, which were determined to be clinically significant cutoff scores by clinicians with expertise in autism (J.S., E.H., K.D.). ADI-R scores are initially coded as 0 through 3; however, in scoring the algorithm, scores of 3 are transformed to a score of 2. Therefore, the maximum score on each D1/D2 domain is 4. No proband had a high score on one domain and a low score on the other domain.

Chi-square analysis was used to compare the prevalence rates of OC traits or OCD in parents of children with high and low total repetitive behavior scores, and high and low OC-like (D1/D2) and autism-like repetitive behaviors (D3/D4). A two-tailed significance level of $P \leq 0.05$ was utilized.

3. Results

Of the 233 probands screened, 176 met either high ($n=15$) or low ($n=161$) D1/D2 cutoffs, and 92 met either high ($n=39$) or low ($n=53$) total repetitive behavior cutoffs (Table 1). Of 114 parents of these 176 probands, 44 reported the presence of one or more OC traits, and 11 reported a past diagnosis of OCD.

Table 1

Mean, standard deviation and range of the total repetitive behavior domain and D1/D2 domain scores of the proband sample ($N=176$), including the number and percent of children high and low in each domain, regardless of parent's status

Repetitive behaviors	Mean \pm S.D.	Range
Total	6.22 \pm 2.5	0–12
D1	1.8 \pm 1.2	0–4
D2	1.42 \pm 1.27	0–4

Children with 'high' total repetitive behavior scores were significantly more likely to have one or both parents with OC traits (46%) than children with 'low' total repetitive behaviors scores (25%) ($\chi^2=4.70$, $P=0.03$) (Table 2). Children with 'high' total repetitive behaviors were significantly more likely to have one or both parents with OCD (15%) than those children with 'low' total repetitive behavior scores (4%) ($\chi^2=3.81$, $P=0.05$).

To test the second hypothesis, that OC-like repetitive behaviors in autistic probands would be associated with higher prevalence of OC traits or OCD in parent(s), parents of children with high levels of narrow interests (D1) and compulsive rituals (D2) were compared to parents of children with low D1/D2 scores. Children with high scores on D1/D2 were significantly more likely than children with low scores on these sub-domains to have a parent with OC traits (42% vs. 22%) ($\chi^2=$

4.11, $P=0.04$) (Table 2). Findings were also significant for the occurrence of OCD in a parent ($\chi^2=20.53$, $P=0.00$), where children with high D1/D2 scores were nine times more likely to have a parent with OCD than children with low D1/D2 scores (34% high vs. 4% low), especially fathers (27% high vs. 2% low) (Table 2).

A final analysis compared groups based on the D3 and D4 autistic-like sub-domains of stereotypic interests and interests in parts of objects. No significant differences were found in the percentage of children with one or both parents with OCD or OC traits.

4. Discussion

Findings indicated that children with a high total score on the repetitive behavior domain of the ADI-R were significantly more likely to have parents with OC traits or OCD than children with a low total score on the repetitive behavior domain. An additional finding was that the OC-like sub-domain scores of restricted interests and repetitive behaviors (D1 and D2) were significantly related to the findings of increased OC traits and OCD in families, while the more autistic-like D3 and D4 scores were not.

These findings suggest that repetitive behaviors show familiarity between autistic probands and parents, which adds to the findings in siblings of

Table 2

Percentage of parents ($N=114$) with OC traits or OCD categorized by probands' ($N=176$) 'Low' and 'High' total repetitive behavior scores and 'Low' and 'High' OC-like (D1/D2) repetitive behavior scores

	Probands		Probands	
	Low total RB % (n)	High total RB % (n)	Low D1 and D2 % (n)	High D1 and D2 % (n)
Mo OC traits	17 (9)	21 (8)	11 (18)	20 (3)
Fa OC traits	6 (3)	10 (4)	9 (15)	7 (1)
Both OC traits	2 (1)	15 (6)	2 (4)	20 (3)
Total OC traits	25 (13)	46 (18)	22 (37)	47 (7)
Mo OCD	2 (1)	5 (2)	2 (3)	7 (1)
Fa OCD	2 (1)	10 (4)	2 (3)	27 (4)
Both OCD	0 (0)	0 (0)	0	0
Total OCD	4 (2)	15 (6)	4 (6)	34 (5)

RB, Repetitive behavior domain; D1, encompassing preoccupation/circumscribed pattern of interest; D2, compulsive adherence to nonfunctional routines or rituals; Mo, Mother; Fa, Father.

autistic probands suggesting familiarity of social and communication deficits and repetitive behaviors (Silverman et al., 2002), early history of language-related cognitive difficulties (Folstein et al., 1999), personality characteristics (Piven et al., 1994), and Axis I disorders (Piven and Palmer, 1999). The co-occurrence of OC symptoms and autism does not necessarily reflect a genetically causal link. Therefore we have cautiously interpreted the results of this pilot study as preliminary data that, upon further investigation, may provide a valuable way in which genetics researchers can decrease the heterogeneity of their samples to increase genetic loading.

The importance of these findings is highlighted by Bradford et al. (2001) and Buxbaum et al. (2001) who found stronger genetic linkage for autism after stratifying for family history of language difficulties in their analysis. Identifying traits shared by family members is useful in identifying factors associated with greater genetic loading. These traits are thought to be manifestations of a genetic liability for autism and can be incorporated into genetic studies of the disorder.

The parental questionnaire used in this study was conducted in a face-to-face interview by a trained rater. A limitation of this study is that the diagnosis of OCD using this method was overly conservative, using a past diagnosis made by a trained professional. It is likely that parents not formally diagnosed with OCD were placed in the OC traits category, which included parents who endorsed items on the Y-BOCS checklist. Bolton et al. (1998) used both face-to-face interviews and a structured interview measure (SADS-L) leading to their findings that OCD was significantly more common in relatives of autistic probands than in Down syndrome (1.4% vs. 0%) and that individuals with OCD were more likely to exhibit autistic-like social and communication impairments. However, they did not stratify their proband populations into high and low levels of severity of OC symptoms. Future studies should include structured psychiatric interview with DSM-IV criteria for OCD, which could provide greater sensitivity in diagnosing OCD. The use of the Y-BOCS checklist to probe for OC traits aided in defining the sample of parents, and should also be incor-

porated into future studies. An additional consideration for the future use of the perinatal questionnaire would be to incorporate parental history of social and communication development. This would be important to distinguish OC traits from the broader autism phenotype in parents. In addition, the parental self-ratings of behavior (and ADI-R ratings of child behavior) may contain a certain amount of reporting bias. Although parents do not cause autism, their flexibility may relate to the severity (or perceived severity) of certain behaviors within the syndrome.

In conclusion, this study found the occurrence of OC traits or OCD in one or both parents of autistic children in multiplex families to be significantly associated with high occurrence of repetitive behaviors, especially OC-like repetitive behaviors, in their autistic children. Identifying autism-like traits shared by family members of autism probands may be a valid approach toward decreasing sample heterogeneity, identifying traits that are manifestations of a genetic liability for autism, and facilitating genetic linkages to autism. Distinguishing the relationship between OC traits and the broader autism phenotype is a challenge. Further study of this relationship may incorporate data on social and language development in parents.

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