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**Title**

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**Permalink**

<https://escholarship.org/uc/item/85f9h1c3>

**Journal**

Annals of the New York Academy of Sciences, 615(1)

**ISSN**

0077-8923

**Authors**

SMALLEY, SUSAN

SMITH, M

TANGUAY, P

**Publication Date**

1991-04-01

**DOI**

10.1111/j.1749-6632.1991.tb37789.x

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# Autism and Psychiatric Disorders in Tuberous Sclerosis

SUSAN SMALLEY,<sup>a</sup> M. SMITH,<sup>b</sup> AND P. TANGUAY<sup>a</sup>

<sup>a</sup>*University of California, Los Angeles  
Los Angeles, California 90024*

<sup>b</sup>*University of California, Irvine  
Irvine, California 92717*

An association of tuberous sclerosis (TSC) and autism is based on the joint occurrence of these two relatively rare disorders and on one systematic study of autism in patients with TSC.<sup>1</sup> The cause of this association remains unknown. It may occur purely at the behavioral level so that autistic-like behavior is a final common pathway for different pathologic processes. The behavior associations may reflect similar brain functioning such as cognitive deficits in speech, language, or social communication. Similar brain organization or structure may be responsible for the observed association, potentially reflected in MRI scans and/or seizures. Lastly there may be an association at the gene/DNA level so that two closely linked genes account for the observed association.

In the study conducted by us, mothers of 24 subjects with TSC completed behavior checklists on their offspring. In addition, 32 adults completed questionnaires on psychopathology. Ten were considered affected with TSC based on Wood's light examinations and medical records.

The autism behavior checklist (ABC) of Krug *et al.*<sup>2</sup> was used to obtain parental information on nonadaptive behaviors. The ABC is used extensively as a screening checklist for identifying children who may be autistic. Examples of some items include: child frequently does not attend to social or environmental stimuli; child has no social smile; and child's speech is atonal or arrhythmic. A score of 67 is considered a valid cut-off score for autism, because 90% of the subjects with scores above 67 meet clinical criteria for autism. Within a score range of 58–67 points on the ABC, differential diagnoses are more difficult; however, 95% of children scoring below 57 do not meet criteria for autism.

A Millon Clinical Multiaxial Inventory<sup>3</sup> questionnaire was used to assess psychiatric status among subjects with TSC 18 years or older. The Millon consists of 175 true-false statements such as the following: (1) I have always avoided getting involved with people socially; (2) I have begun to feel like a failure in recent weeks; and (3) I am so quiet and withdrawn most people do not even know I exist.

Responses to the 175 items generate 20 clinical scales that correspond to eight DSMIII Axis II personality disorders, three pathologic personality disorders (schizotypal, borderline, and paranoid), and nine clinical syndromes (Axis I). Scores of 75 or higher on any MCMI scale indicate the presence of a disorder. The specificities for the various clinical scales range from 85–97%.

Results of our analyses using the ABC scale revealed that 5 of 24 (21%) subjects with TSC scored above 67. All five were mentally retarded and four also experienced infantile onset seizures. The seizure-free subjects had the highest IQ, it being 62. Clinical evaluations of four of these subjects, conducted by one of the authors (P.T.) using a semistructured interview, confirmed a diagnosis of autism based on the DSMIII-R criteria.<sup>4</sup> The evaluator was blind to the medical diagnosis

of the proband before the interview. A fifth child with TSC (aged 3 years) also met the criteria for autism from the clinical evaluation, although she received a score of 61 on the ABC, 6 points below the cut-off value.

In addition to autism in subjects with TSC, we observed an increased frequency of borderline personality disorder (chi-square 6.7, *df* 1; *p* = 0.009) in adult subjects with TSC. We are currently conducting psychiatric evaluations to confirm these preliminary findings.

These initial data support the previous observations of an association between autism and TSC. At this time we do not have enough data to investigate the cause of this association. Some questions we intend to address, in addition to identifying the source of this association, are:

1. Are there qualitative differences in autism co-occurring with TSC compared with autism without TSC?
2. What is the correlation of clinical severity and behavioral severity?
3. Are autism and/or psychiatric sequelae expressions of the TSC gene, and hence should these be included in the phenotypic definition?
4. Are there behavioral, psychiatric, and/or cognitive differences between families in whom the TSC gene is located on chromosome 9 versus those in whom this gene is located on chromosome 11?

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