

RESEARCH ON AUTISM SUBTYPES: AN URGENT NEED THAT THE AUTISM COMMUNITY MUST SUPPORT AS A HIGH PRIORITY

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Remarks by

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Background: Autism spectrum conditions are currently included under the category of Pervasive Developmental Disorders (PDDs) in the *Diagnostic and Statistical Manual IV* of the American Psychiatric Association. The three most frequently encountered conditions in the autism community are Autistic Disorder, Asperger's Syndrome (AS), and Pervasive Developmental Disorder—Not Otherwise Specified (PDD/NOS). Rett's Syndrome, another condition in the PDD category, is typically not well represented at autism conferences, perhaps because of the severe physiological impairments that tend to be associated with this condition. Childhood Disintegrate Disorder, a fifth condition, is believed to be quite rare.

The problem: Current diagnostic standards separating individuals into the categories of autism, AS, and PDD/NOS are controversial. Some research—albeit controversial at this point—suggests that a continuous autism spectrum may be more meaningful than the current PDD categories. Differences *within* each group are frequently larger than the average differences *between* groups. Further, it is by now evident that a larger number of subtypes of autism are likely to exist and that *members of each subgroup may differ significantly among each other—both in symptoms experienced and response to various kinds of treatments*. Regardless of their specific diagnostic category, some individuals appear to be especially vulnerable to gastrointestinal problems while certain others will be more vulnerable to anxiety and/or tendencies toward self-injurious behavior. Thus, although there are important differences among individuals falling on the larger autism spectrum, the current PDD categories do not adequately distinguish among individuals showing highly diverse symptoms.

Our current inability to establish meaningful subtypes of autism results in several complications:

- **Heterogeneity among the autism population may *obscure results of research*.** That is, results may suggest that no relationship exists between variables when the reality is that a *more complicated relationship exists*. Two problems are evident:
 - *Masking of true effect sizes “cancelled out” by heterogeneous response*. It is known that many individuals affected with autism will often tend to “gravitate” toward one extreme or the other in various domains—e.g., a tendency to be either hyper- or hypo-sensitive to certain stimuli. This reality results in *very large within-group variances* when comparing treatment groups. For example, if an intervention is helpful for some individuals and actively harmful for others, average results may misleadingly suggest that no statistically significant effect exists.
 - *Aggregation bias*. When results of disparate group observations are averaged together, meaningless and very misleading results may appear. For complicated statistical reasons, even if two populations individually show the same relationship between two

variables (e.g., a positive response to Vitamin C treatment), the *aggregated result* for the two populations may show the *opposite* effect! Aggregating results from disparate groups may also suggest effects that, in truth are spurious.¹

- **Difficulty in identifying the more promising treatments for an individual** . Since there is such a large variation among individuals on the autism spectrum, appropriate interventions and supports *will depend on the specifics of each individual* . Currently, a considerable amount of experimentation is generally needed, both in terms of behavioral and pharmaceutical interventions, before an effective method without unacceptable side effects is found. This is problematic for several reasons:
 - *Delay in the identification of effective treatments* . An individual’s prognosis is likely to be significantly improved when an effective intervention is started early on. Although interventions may still show some effectiveness if started later, the opportunity to take advantage of a critical period of development is lost if the most appropriate treatment is not selected early on. Many symptoms that occur on the autism spectrum—e.g., severe anxiety and difficulty in communication—arguably result in a significant reduction in the quality of life. More urgently, certain symptoms such as self-injurious behavior represent an immediate danger of serious harm.
 - *Harm from attempted interventions that turn out to be unsuitable* .
 - *Stress experienced by individuals vulnerable to sensory and emotional overload in the course of undergoing several varied treatment experiences* .
 - *Verbal limitations that prevent many individuals on the autism spectrum from articulating felt experiences, thus complicating the evaluation of a treatment* .
 - *Costs associated with ineffective interventions performed under institutional resource limitations and/or limited insurance coverage* .

Obstacles to subtype research in the academic setting. A researcher’s opportunities for retention, promotion, tenure, and future funding are highly dependent on “peer” evaluation of his or her research. Although many biomedical fields have found it necessary to be somewhat more flexible, there is generally a strong preference in the social sciences for research that tests specific hypotheses predicted by clear theory.² Since the genetics of autism and other causal factors are not yet clearly understood, much research at this phase will unavoidably have to be more “data driven.” It will likely be a long time before research in the area of the autism spectrum advances enough to significantly reduce this problem. **Given the urgency of identifying autism subtypes, it is important that the autism community lobby funding organizations and institutional evaluators to favorably consider and encourage research that would be risky under standards of review common in more “mature” academic fields.**

¹ Research in marketing is illustrative. Data indicate that an individual who bought a given brand on sale on the last “purchase occasion” is *less* likely to repurchase that same brand when it is no longer available on “deal.” For many years, this was interpreted to mean that buying a product on sale would condition consumers to expect lower prices—a conclusion that seems to make theoretical sense. Only later was it discovered that this effect actually results from “brand switchers” who always tend to buy the lower priced brand. “Brand loyal” customers who consistently buy their preferred brand are generally not greatly affected by temporary promotions. However, because the group of switchers attracted to the deal is much larger, this group will dominate the results, suggesting an effect that in truth does not exist. **Note that autism research, with our current state of knowledge, is often based on much less explicit theory, and thus we are considerably more vulnerable to such confounds here.**

² Findings that confirm a previously hypothesized result are considered more reliable because such findings are less likely to have resulted from “chance.” If you make enough observations, something highly unusual will happen at some point. When numerous variables or groups are considered simultaneously without reference to predicted outcomes, it is more likely that that seeming effects will result from chance (a “Type I” error in statistical jargon). With tens, or even hundreds, of other variables considered, it might be found, for example, that a particular theory of mind development program is much more effective if administered on Tuesday as opposed to other days of the week. Thus, some judgment must be exercised in interpreting more data when no clear hypotheses are made in advance. It is also important that attempts be made to *replicate* these findings in new, independent studies. Here, the prior results may serve as a basis for explicit hypotheses that may be tested.