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### **Assessing Autism, A Disorder of Social Cognition**

Major issues in the neuropsychological assessment of autism will be discussed, including general testing issues, areas to be assessed, and some available tools for the assessment of social cognition. Data will be presented on language, social cognition, and attention in children who are essentially 'recovered' from autism.

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### **Widespread findings and systems considerations in autism neuroimaging**

Autism is a syndrome defined only behaviorally, through carefully characterized deficits in three domains (language, social interaction, desire for sameness/repetitive or ritualistic behaviors). This definition has oriented researchers toward seeking genes and brain regions that might be associated with these deficits. This has also contributed to the presumption that autism is constituted by an aggregation of three distinct and independent genetically shaped brain abnormalities, and that comorbidities may be related to sharing of some portion of these genetic brain deficits or of others associated with so-called "secondary" features of autism. In this setting, the most replicated finding in autism neuroanatomy—a tendency to unusually large brains—has seemed paradoxical, and has posed challenges regarding how to understand its functional significance. We now know a range of things about this phenomenon of large brains, including that brains in autism have a growth spurt shortly after birth and then slow in growth a few short years afterward, that only younger but not older brains are larger in autism than in controls, that white matter contributes disproportionately to this volume increase and in a nonuniform pattern suggesting postnatal pathology, that functional connectivity among regions of autistic brains is diminished, and that neuroinflammation (including microgliosis and astrogliosis) appears to be present in autistic brain tissue (in at least some individuals) from childhood through adulthood. We also have documentation of many similar volumetric features (additionally including widespread asymmetry differences from controls) in a cohort of non-autistic children with developmental language disorder. Alongside these pervasive brain tissue and functional abnormalities, there have arisen theories of pervasive or widespread neural information processing or signal coordination abnormalities (such as weak central coherence, impaired complex processing, and underconnectivity), which are argued to underlie the specific observable behavioral features of autism; in this framework specific deficits would occur in domains most vulnerable to changes whose impact was more widely distributed. Parallels can be drawn to theories of rapid temporal processing impairments as well as to immune issues in language disorders. This convergence of findings and models suggests that a systems- and chronic disease–based reformulation of function and pathophysiology in autism needs to be considered. Further research will be needed, oriented toward testing specific features of this model to see if findings across multiple structural, functional, medical and treatment intervention domains are consistent with this framing of autism.

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### **Oxytocin Increases Social Cognition in Autism**

Oxytocin dysfunction may contribute to the development of social deficits in autism, a core symptom domain and potential target for intervention. This study explored the relationship between increasing oxytocin levels and social information processing. Oxytocin and placebo challenges were administered to fifteen adult subjects diagnosed with autism or Asperger disorder, and comprehension of affective speech (happy, indifferent, angry, and sad) in neutral content sentences was tested. The outcome measure (Comprehension of Affective Speech) was scored dichotomously and mixed regression analyses was used to model the change in comprehension scores over time. Subjects who received the oxytocin infusion first showed increased levels of retention in comprehension of affective speech when retested after a delay, whereas subjects who received placebo first showed lower levels of retention. The mean delay between infusions was  $16.067 \pm 14.26$  days. There was a significant three-way interaction of time X treatment X order for the dichotomous comprehension of affected speech ( $z=2.134$ ,  $p=0.033$ , estimate=0.170). Subjects showed pretest to posttest improvement for 3 of the 4 treatment x order conditions (Oxytocin First, Placebo First, Oxytocin Second). For the Placebo Second condition, there was a slight drop in comprehension of affective speech from pretest to posttest (.958 to .898). This inconsistent pattern is most clearly driven by the finding that the second infusion placebo baseline scores were already high. Thus, subjects who received oxytocin first showed increased levels of retention in the task and did not show a tendency to revert to baseline when retested after a delay. In contrast, subjects who received placebo first did show a tendency to revert to baseline. The difference between the predicted pretest scores for subjects who received placebo second (0.958) and placebo first (0.712) is 0.246, which corresponds to a medium to large effect size ( $d$ ) of 0.66. These results indicate that oxytocin may facilitate the retention of social information, and suggest a possible benefit of oxytocin in the treatment of social deficits in autism.