

Abstract

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Cholinergic activity in autism: abnormalities in the cerebral cortex and basal forebrain.

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OBJECTIVE: Measures of cholinergic transmitter activity were investigated in patients with autism because of reported neuropathological abnormalities in cholinergic nuclei in the basal forebrain.

METHOD: Levels of cholinergic enzyme and receptor activity were measured in the frontal and parietal cerebral cortex of deceased autistic adults, similarly aged normal adults without mental retardation, and nonautistic mentally retarded adults. The immunoreactivity levels of brain-derived neurotrophic factor and nerve growth factor were measured in the basal forebrain.

RESULTS: There were no differences between the autistic and comparison groups in choline acetyltransferase or acetylcholinesterase activity in the cerebral cortex and basal forebrain or in muscarinic M(2) receptor or alpha-bungarotoxin binding within the cortex. Cortical M(1) receptor binding was up to 30% lower than normal in the autistic subjects, and the difference reached significance in the parietal cortex. In both the parietal and frontal cortices, differences in nicotinic receptors assessed by [(3)H]epibatidine binding were significant and extensive (65%-73% lower in the autistic group than in the normal subjects); there were no differences in nicotine binding in the basal forebrain. Immunochemical analysis indicated lower levels of both the alpha(4) and beta(2) nicotinic receptor subunits in the parietal cortex. The M(1) receptor abnormality was not evident in the nonautistic group with mental retardation, although the lower [(3)H]epibatidine binding was apparent. In the basal forebrain, the level of brain-derived neurotrophic factor in the autistic group was three times as high as the level of the normal group.

CONCLUSIONS: These neurochemical abnormalities implicate the cholinergic system in developmental disorders such as autism and suggest the potential for intervention based on cholinergic receptor modulation.

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