

# Neuroimaging and clinical features in adults with a 22q11.2 deletion at risk of Parkinson's disease.

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## Abstract

The recurrent 22q11.2 deletion is a genetic risk factor for early-onset Parkinson's disease. Adults with the associated 22q11.2 deletion syndrome (22q11.2DS) may exhibit phenotypes that could help identify those at highest risk and reveal disease trajectories. We investigated clinical and neuroimaging features relevant to Parkinson's disease in 26 adults: 13 with 22q11.2DS at genetic risk of Parkinson's disease (mean age = 41.5 years, standard deviation = 9.7), 12 healthy age and sex-matched controls, and a 22q11.2DS patient with l-DOPA-responsive early-onset Parkinson's disease. Neuroimaging included transcranial sonography and positron emission tomography using 11C-dihydrotetrabenazine (11C-DTBZ), a radioligand that binds to the presynaptic vesicular monoamine transporter. The 22q11.2DS group without Parkinson's disease demonstrated significant motor and olfactory deficits relative to controls. Eight (61.5%) were clinically classified with parkinsonism. Transcranial sonography showed a significantly larger mean area of substantia nigra echogenicity in the 22q11.2DS risk group compared with controls ( $P = 0.03$ ). The 22q11.2DS patient with Parkinson's disease showed the expected pattern of severely reduced striatal 11C-DTBZ binding. The 22q11.2DS group without Parkinson's disease however showed significantly elevated striatal 11C-DTBZ binding relative to controls ( $\sim 33\%$ ;  $P < 0.01$ ). Results were similar within the 22q11.2DS group for those with ( $n = 7$ ) and without ( $n = 6$ ) psychotic illness. These findings suggest that manifestations of parkinsonism and/or evolution to Parkinson's disease in this genetic at-risk population may include a hyperdopaminergic mechanism. Adequately powered longitudinal studies and animal models are needed to evaluate the relevance of the observed clinical and imaging phenotypes to Parkinson's disease and other disorders that are more prevalent in 22q11.2DS, such as schizophrenia.