# Dopamine transporter concentration is reduced in asymptomatic Machado-Joseph disease gene carriers

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摘要

**Abstract**

Dopamine transporter (DAT) binding is decreased in Machado-Joseph disease (MJD) patients. To further investigate the DAT activity in asymptomatic MJD (aMJD) gene carriers, we performed this prospective study using 99mTc-TRODAT-1 ([99mTc][2[[2-[[[3-(4-chlorophenyl)-8-methyl-8-azabicyclo[3,2,1]oct-2-yl]-methyl](2-mercaptoethyl)amino]ethyl]amino]ethane-thiolato(3-)-N2,N2',S2,S2]oxo-[1R-(exo-exo)])) brain SPECT on 5 aMJD gene carriers, 10 age-matched MJD patients, and 10 age-matched healthy control subjects. Methods: Brain SPECT images were acquired 4 h after intravenous injection of 925 MBq (25 mCi) 99mTc-T RODAT-1, which is known to bind specifically to the DAT on the nigrostriatal terminals. By fusing these SPECT images with a striatal atlas, obtained from MRI, binding of this tracer in the entire striatum was measured and the uptake values in bilateral striatal areas were compared between these 3 groups. Results: The uptake values of the aMJD gene carriers ($P < 0.001$) and MJD patients ($P < 0.001$) displayed a significant reduction compared with those of the control subjects. The reduction was more severe in the MJD patient group ($P < 0.05$). Bilateral putamen-to-caudate ratios were significantly lower in the aMJD gene carrier and MJD patient groups ($P < 0.001$). The dopamine neuronal activity, as represented by the tracer binding, was more prominently affected in the putamen in these patients and gene carriers. Conclusion: 99mTc-TRODAT-1 brain SPECT is capable of detecting early alteration of dopamine neurons in the striatal region. Significantly, the results suggest that this impairment of presynaptic dopamine function actually occurs at an early stage, which was previously unrecognized in these aMJD gene carriers.