

## **DaTSCAN imaging in p.A53T $\alpha$ -synuclein-associated Parkinson's disease: comparison with sporadic Parkinson's disease**

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**Objective:** The objective of this study was to assess striatal dopaminergic denervation in a cohort of symptomatic carriers of the p.A53T  $\alpha$ -synuclein (SNCA) mutation as compared to sporadic PD (sPD). **Methods:** DaTSCAN SPECT imaging was acquired at Parkinson's Progression Markers Initiative (PPMI) imaging centers as part of the PPMI imaging protocol and sent to imaging core for processing and calculation of striatal binding ratios. Data from the PPMI database of 10 symptomatic p.A53T SNCA mutation carriers who underwent DaTSCAN at our site, were compared to those of 21 age-, gender- and disease duration-matched sPD patients. **Results:** The striatal dopaminergic denervation was so severe in 3/10 p.A53T mutation carriers, that corresponding binding ratios were unmeasurable. The remaining 7 p.A53T mutation carriers had significantly lower left caudate nucleus binding ratio ( $p=0,01$ ), and a similar trend for the right caudate, compared to sPD patients. There was no difference in the putaminal binding ratios. The caudate / putamen signal ratio was significantly lower bilaterally in the p.A53T cohort (Right side  $p=0,028$ , Left side  $p=0,018$ ). A similar degree of striatal asymmetry was observed in both the p.A53T and sPD subgroups.

**Conclusions:** PD patients harboring the p.A53T SNCA mutation show evidence of a more severe, albeit variable, dopaminergic nigrostriatal denervation, mainly involving the caudate nucleus. This finding possibly reflects a more rapid disease progression, as well as a differential topography of nigrostriatal degeneration in the mutation carriers compared to sPD.