REVERSIBLE DOPAMINE TRANSPORTER REDUCTION IN DRUG-INDUCED PARKINSONISM

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BACKGROUND-AIM
To describe a patient with drug-induced parkinsonism whose baseline dopamine transporter SPECT resulted abnormal, but whose dopaminergic neuronal density was normal.

Background: In vivo imaging techniques investigating presynaptic nigrostriatal function using dopamine transporter (DAT) SPECT or 18F-Dopa PET are currently considered to reliably distinguish a degenerative parkinsonism from a iatrogenic disorder.

METHODS
The patient performed a DAT-SPECT and 18F-Dopa-PET while on lithium therapy (baseline). All SPECT scans onto a FP-CIT template and used an automated software including age-adjusted normal binding cut-off for analysis. DAT-SPECT and 18F-Dopa PET were performed in a healthy subject and a patient with idiopathic PD for comparison.

RESULTS
A 71-year-old female patient presented with a 4-year history of bilateral hand tremor and gait instability with freezing and unbalance leading to frequent falling, worsened further over the last 6 months. She had an 8-year history of bipolar disorder, treated with lithium carbonate. Serum lithium level was normal. Global cognition was normal but frontal lobe executive functions were mildly impaired. Brain MRI showed mild cortico-subcortical atrophy. Baseline FP-CIT SPECT showed significant decrease of DAT uptake; at that time, 18F-Dopa PET revealed normal nigrostriatal terminal density. After one month after switching lithium to low-dose aripiprazole, her motor symptoms greatly improved and all borderline cognitive testing scores reversed to normal. A 9-month follow-up SPECT scan showed an increase in binding values within the normal range. A subsequent 24-month follow-up scan showed a further increase in DAT density and no remarkable clinical sign of parkinsonism.

CONCLUSION
We demonstrated for the first time that membrane DAT density may undergo reversible down-regulation, using two complementary approaches: (1) an alternative presynaptic intraneuronal tracer, such as 18F-Dopa; (2) two follow-up SPECT scans. In agreement with previous findings, we speculate that chronic lithium administration impaired DA transmission and led to functional reduction of membrane DAT in presence of normal DA nerve terminals, as compensatory attempt to increase of synaptic DA availability by reducing DA reuptake.