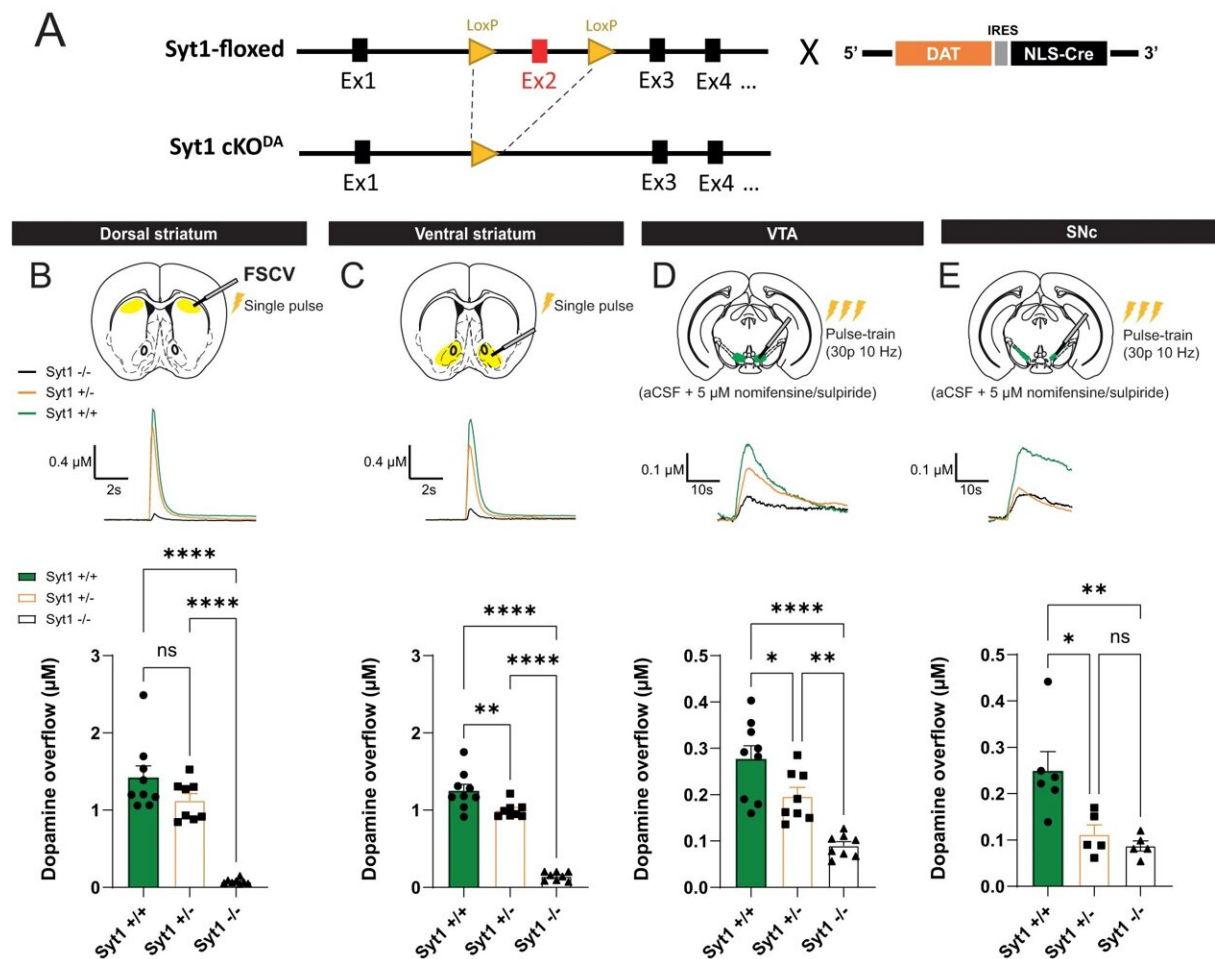


Study shows how Parkinson's disease can quietly progress undetected for years

July 18 2023



Syt1 is the main calcium sensor for fast axonal dopamine release. **A** Generation of conditional knockout of Syt1 in DA neurons by crossing Syt1-floxed mice ($Syt1^{lox/lox}$) with $DAT^{IRESCre}$ mice. **B** Fast-scan cyclic voltammetry recording of Syt1 cKO^{DA} mice in the dorsal striatum. Representative traces (top) and quantification of peak amplitude (bottom) obtained with single-pulse electrical

stimulation (1 ms, 400 μ A) in Syt1^{+/+} ($n = 18$ slices/9 mice), Syt^{+/-} ($n = 16/8$) and Syt1^{-/-} mice ($n = 16/8$). **C** Same, but in the ventral striatum (NAc core and shell, $n = 18$ slices/9 mice in Syt1^{+/+}, $n = 16/8$ in Syt^{+/-} and $n = 16/8$ in Syt1^{-/-}). **D** Representative traces (top) and quantification of peak amplitude (bottom) obtained in the VTA ($n = 16$ slices/9 mice in Syt1^{+/+}, $n = 14/8$ in Syt^{+/-} and $n = 16/8$ in Syt1^{-/-}) with aCSF containing nomifensine (DAT blocker) and sulpiride (D2 antagonist) (both at 5 μ M), and pulse-train stimulation (30 pulses of 1 ms at 10 Hz, 400 μ A). **E** Same for the SNc ($n = 11$ slices/6 mice in Syt1^{+/+}, $n = 10/5$ in Syt^{+/-} and $n = 9/5$ in Syt1^{-/-}). Error bars represent \pm SEM and the statistical analysis was carried out by one-way ANOVAs followed by Tukey tests (ns, non-significant; * P)

Citation: Study shows how Parkinson's disease can quietly progress undetected for years (2023, July 18) retrieved 3 May 2024 from <https://medicalxpress.com/news/2023-07-parkinson-disease-quietly-undetected-years.html>

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