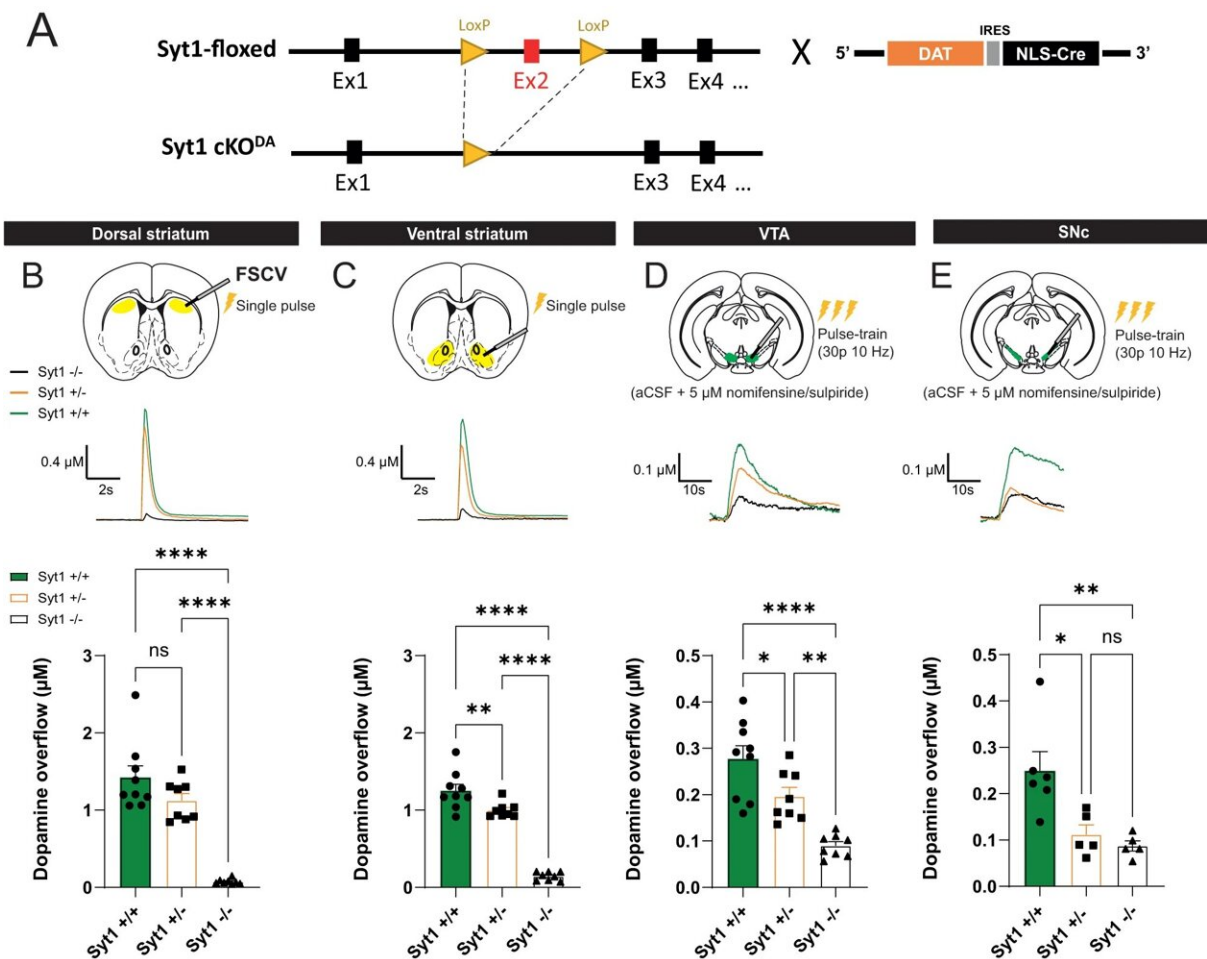


# Study shows how Parkinson's disease can quietly progress undetected for years

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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<sup>DA</sup> mice in the dorsal striatum. Representative traces (top) and quantification of peak amplitude (bottom) obtained with single-pulse electrical

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

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