Supplemental Appendix

It is possible to simulate the amount of total striatal signal that originates from the SERT binding as a function of DAT density. In the case of the current DAT radioligands, BP_{ND} is equal to the product of the free fraction of ligand in the nondisplaceable tissue compartment (f_{ND}) and the sum of available monoamine transporters in the tissue of interest (B_{avail}) divided by the affinities for the individual monoamine transporters (K_d) for each radioligand.

$$BP_{ND} = f_{ND}\left(\frac{B_{avail,SERT}}{K_{d,SERT}} + \frac{B_{avail,DAT}}{K_{d,DAT}} + \left(\frac{B_{avail,NET}}{K_{d,NET}}\right)\right)$$

As mentioned in the "Discussion" section of the article, the in vitro $B_{avail,\ DAT}$-to-$B_{avail,\ SERT}$ ratio in the putamen is 20:1 but highly variable within individuals, so it may also be 10:1. The literature suggests that in contrast to DAT, SERT binding is less affected with age (*1–3*). If $B_{avail,\ SERT}$ remains unchanged in healthy volunteers, we can estimate SERT signal as a function of $B_{avail,\ DAT}$:

$$\frac{\text{SERTsignal}}{\text{TOTALsignal}}\left(B_{avail,DAT}\right) = \frac{B_{avail,SERT}}{B_{avail,SERT} + \frac{K_{d,SERT}}{K_{d,DAT}} \times B_{avail,DAT}}$$

$\text{SERTsignal} = B_{avail,SERT}/K_{d,SERT}$, $\text{TOTALsignal} = B_{avail,SERT}/K_{d,SERT} + B_{avail,DAT}/K_{d,DAT}$.

The binding of the radioligand to NET is neglected. Since K_d values are not available, K_i are used instead and the ratio of K_i values are comparable to that of the K_d ratio.

The equation is presented in Supplemental Appendix Figures 1A and 1B. As one can appreciate from the figures, in ^{123}I-FP-CIT SPECT, the SERT signal may contribute to 20% of total striatal signal when $B_{avail,\ DAT}$ is between 60% and 40% of normal; the opposite is true in ^{123}I-PE2I SPECT, where the SERT signal is below 5% (60%–40% of normal $B_{avail,\ DAT}$ is typical what is present of $B_{avail,\ DAT}$ when PD patients experience their first Parkinson symptoms and is referred to a DAT SPECT scanning).

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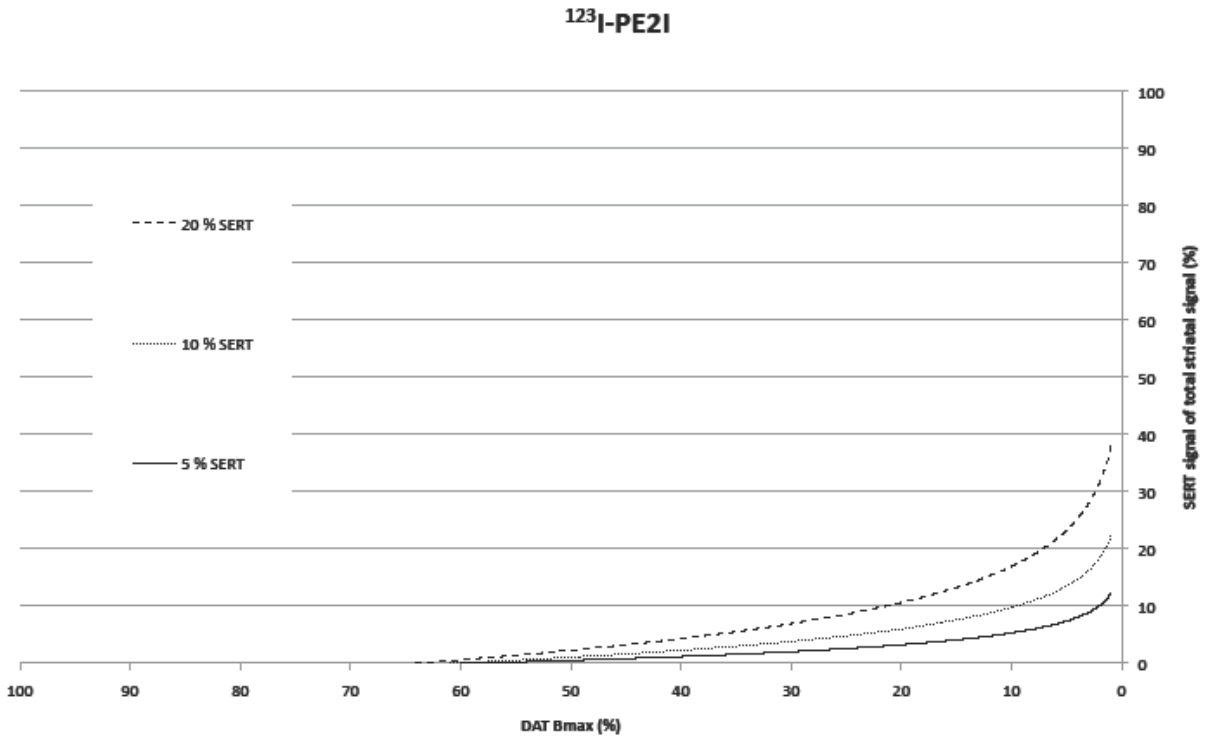
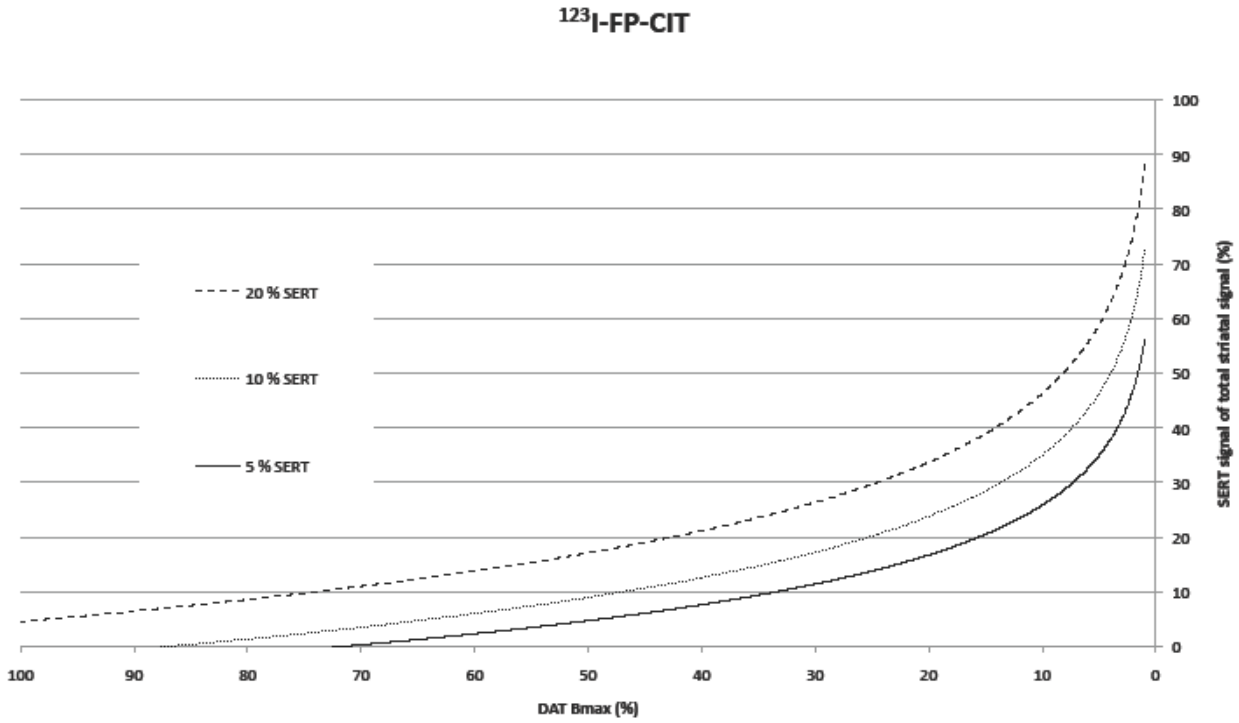


Supplemental Appendix Figure 1. The theoretical proportion of SERT signal of total striatal signal in ^{123}I-PE2I in a 20/1, 10/1 and 5/1 ratio of DAT/SERT distribution.



Supplemental Appendix Figure 2. The theoretical proportion of SERT signal of total striatal signal in ^{123}I-FP-CIT in a 20/1, 10/1 and 5/1 ratio of DAT/SERT distribution.