

## ***Supplementary Material***

### **Interactive effects of locus coeruleus structure and catecholamine synthesis capacity on cognitive function**

Hsiang-Yu Chen\*, Jourdan H. Parent, Claire J. Ciampa, Martin J. Dahl, Dorothea Hämmerer, Anne Maass, Joseph R. Winer, Renat Yakupov, Ben Inglis, Matthew J. Betts and Anne S. Berry

\*Corresponding author: Hsiang-Yu Chen (hsiangyuchen@brandeis.edu)

#### **1 Analyses and results of the PLSC analysis on the datasets of LC-MRI contrast ratios and [<sup>18</sup>F]FMT PET Ki<sub>vis</sub> at the voxel-wise whole brain level or within 36 regions of interest.**

An equivalent PLSC analysis was applied to the correlation matrix between LC-MRI contrast ratios and [<sup>18</sup>F]FMT Ki<sub>vis</sub> measures at the voxel-wise whole brain level or between LC-MRI contrast ratios and [<sup>18</sup>F]FMT Ki<sub>vis</sub> within 36 ROIs (Desikan et al., 2006). The SVD is formulated as follows.

$$SVD[R_{(LC-MRI, FMT)}] = U_{FMT} S V_{LC-MRI} \quad (\text{Eq. S1a})$$

$$LV_{LC-MRI} = X_{LC-MRI} V_{LC-MRI} \quad (\text{Eq. S1b})$$

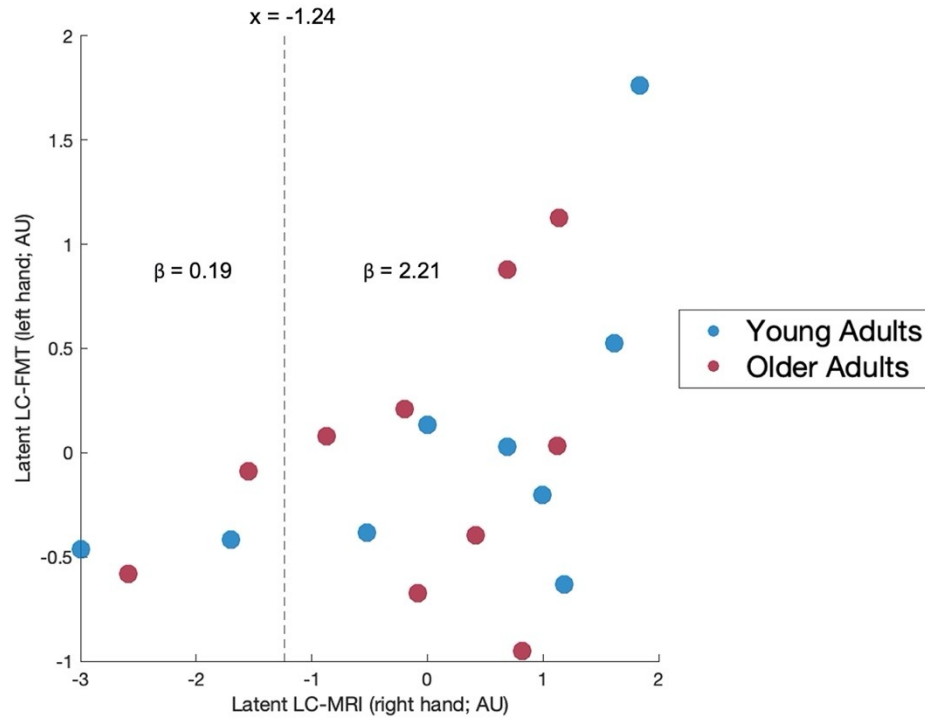
$$LV_{FMT} = Y_{FMT} U_{FMT} \quad (\text{Eq. S1c})$$

where  $R$  indicates Pearson's correlation matrix between LC-MRI contrast ratios and [<sup>18</sup>F]FMT Ki<sub>vis</sub> at the voxel-wise whole brain level or between LC-MRI contrast ratios and [<sup>18</sup>F]FMT Ki<sub>vis</sub> within Desikan's 36 ROIs (Eq. S1a) subjected to SVD.  $U$  and  $V$  are the singular vectors (the saliences) that represent the profiles of LC-MRI contrast and [<sup>18</sup>F]FMT weights at the voxel-wise or ROI level, respectively, to best characterize  $R$ .

Based on the matrix decomposition, a latent variable ( $LV$ ) was extracted to denote a linear combination of each original dataset (i.e.,  $X_{LC-MRI}$  or  $Y_{FMT}$ ) and its correspondingly singular vector (i.e.,  $V_{LC-MRI}$  or  $U_{FMT}$  in Eq. S1b or S1c). The association between the two latent variables optimally expresses (in the least squares sense) the pattern of interindividual differences in LC-MRI contrast ratios that shares the largest amount of variance with interindividual differences in overall [ $^{18}F$ ]FMT  $Ki_{vis}$  at voxel-wise or ROI level. We found no association between the LC-MRI contrast ratios and [ $^{18}F$ ]FMT  $Ki_{vis}$  at the voxel-wise or ROI level ( $ps > 0.09$ )

## **2 Analyses and results of the piecewise regression on the latent variables of LC-MRI contrast ratios and [ $^{18}F$ ]FMT PET $Ki_{vis}$ extracted by PLSC.**

A piecewise regression was performed to determine a breakpoint in the association between the LC structural integrity and LC catecholamine synthesis capacity across our 19 participants (9 young adults: 20-29 years [mean  $\pm$  SD = 24.78  $\pm$  2.21]; 10 older adults: 65-84 years [mean  $\pm$  SD = 77.4  $\pm$  5.76]). Although we did find a breakpoint (-1.24 in the LC-MRI contrast ratios; dashed line in Fig. S1), both segments showed positive trend-wise associations (correlation coefficient  $\beta_s = 0.19$  and 2.21) and were not clustered by age groups (Fig. S1).



**Fig. S1. Piecewise regression results in 19 participants.** The breakpoint at  $x = -1.24$  on the latent LC-MRI variable was determined, but both segments showed positive trend-wise associations between LC-MRI and LC-FMT (correlation coefficient  $\beta_s = 0.19$  and 2.21) and did not suggest associations between LC-MRI and LC-FMT measures differed based on age groups.