SUPPLEMENTARY MATERIALS

RESULTS

Task-based Functional Connectivity Analysis

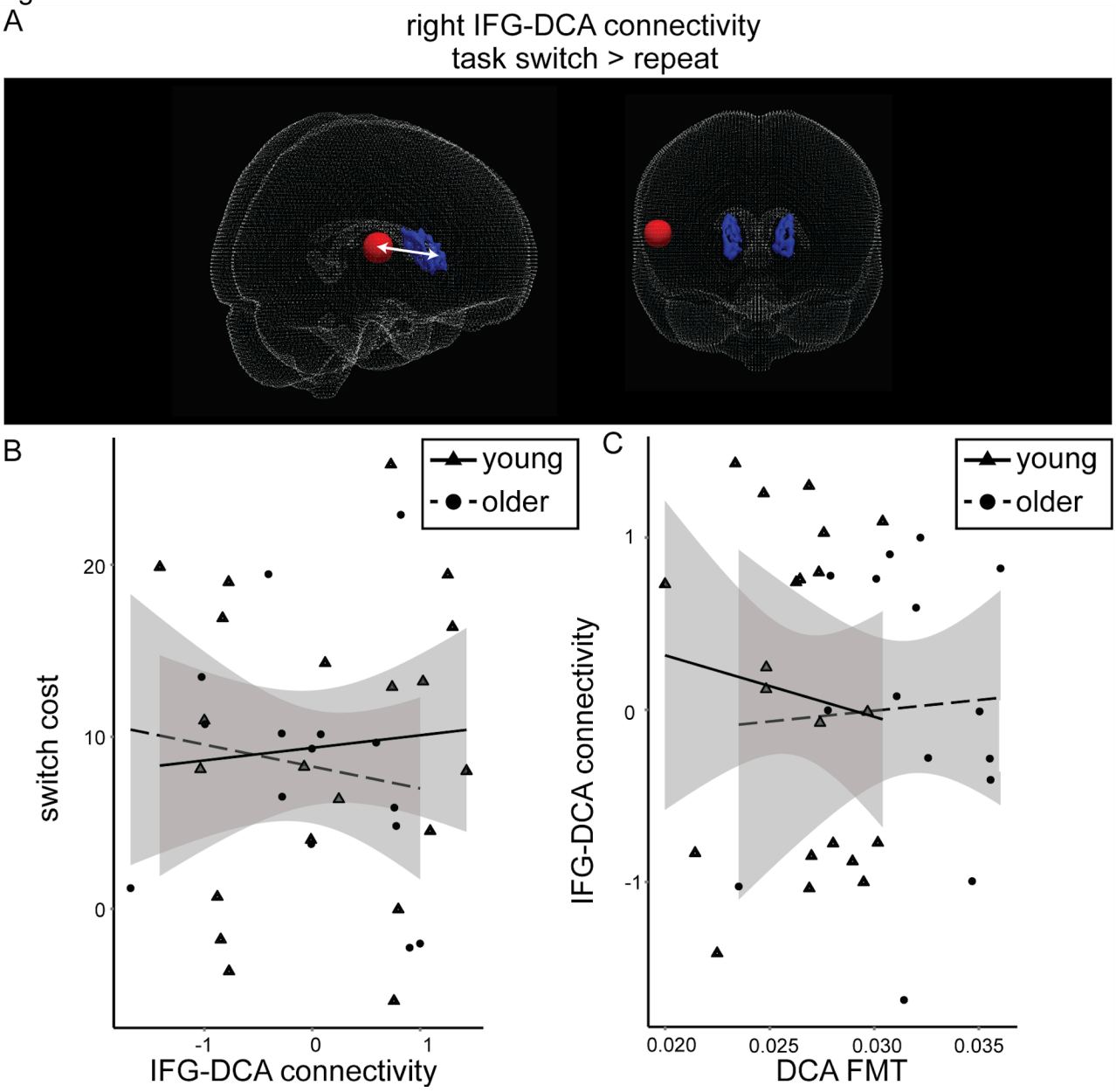
No relationship between right IFG-DCA connectivity and switch cost

We examined individual differences in functional connectivity between bilateral DCA and right IFG (8 mm sphere centered on MNI 54, 6, 10; Figure S1A) for switch relative to repeat trials. There was no significant difference in functional connectivity between age group ($t(34) < 1$). There was no correlation between switch cost and right IFG-DCA connectivity across all participants ($r = .01$, $p = .95$), or independent analysis of young ($r = .08$, $p = .73$) and older adults ($r = -.15$, $p = .59$; Figure S1B).

No relationship between right IFG-DCA connectivity and DCA dopamine synthesis capacity

There was no correlation between right IFG-DCA connectivity and DCA [^{18}F]FMT K_i across all participants ($r = .06$, $p = .73$), or independent analysis of young ($r = -.12$, $p = .60$) and older adults ($r = .03$, $p = .92$; Figure S1C).

Figure S1


A
right IFG-DCA connectivity
task switch > repeat
B
young
older
switch cost
20
10
0
-1
0
1
IFG-DCA connectivity
C
young
older
IFG-DCA connectivity
1
0
-1
0.020
0.025
0.030
0.035
DCA FMT

Mediation and Moderation Analyses

Here we present supplemental mediation and moderation analyses. Separate mediation analyses probe the mediating influence of IFG-DCA PPI connectivity and DCA-thalamic PPI connectivity independently. Additionally, separate moderation analyses probe the moderating influence of DCA [^{18}F]FMT K_i on IFG-DCA PPI connectivity and DCA-thalamic PPI connectivity independently. Overall, results were consistent with those primary analyses presented in the main manuscript for which IFG-DCA-thalamic PPI connectivity was considered together (averaged IFG-DCA and DCA-thalamic PPI connectivity for each participant). The only discrepancy in results was found for mediation analyses in young adults using IFG-DCA PPI connectivity alone as the mediating variable. We report full statistical analyses below.

Mediation Analysis

IFG-DCA PPI connectivity does not mediate striatal dopamine's influence on switch cost.

The moderated mediation was not significant as dopamine was only marginally related to IFG-DCA functional connectivity (step 2: $\beta = 97.46$, $p = .09$). Consistent with findings reported in the main manuscript, the effect of IFG-DCA functional connectivity on switch cost (accounting for dopamine) was significant (step 3: $\beta = -3.59$, $p = .05$). Though the index of moderated mediation did not indicate a significant difference in indirect effects of dopamine on switch for young and older adults (629.08 [-38.87, 1745.76]), we report conditional group effects in Supplementary Figure S2A,B for comparison to Figure 4. The indirect effect of dopamine on switch cost via functional connectivity was not significant for young (estimated indirect effect = 350.00; bootstrapped CI = [-1127.00, 80.72]) or older adults (279.08 [-132.10, 876.66]).

DCA-thalamus PPI connectivity mediates striatal dopamine's influence on switch cost in young adults.

The moderated mediation was significant and indicated that overall, the effect of dopamine on switch cost was mediated by functional connectivity, but that this relationship differed between young and older adults. Specifying the overall mediation, step 1: the direct effect of dopamine on switch cost (independent of functional connectivity) was significant (β = -1838.88, p = .002), step 2: the effect of dopamine on functional connectivity was significant (β = 74.62, p = .05), step 3: the effect of functional connectivity on switch cost (accounting for dopamine) was significant (β = -6.89, p = .01), and step 4: the effect of dopamine on switch cost was reduced when accounting for functional connectivity (β = -1325.27, p = .02).

However, age group significantly moderated these relationships. Age group interacted with dopamine to significantly moderate dopamine's direct relationship with switch cost (dopamine x age interaction: β = 2315.77, p = .005) as well as dopamine's relationship with functional connectivity (dopamine x age interaction: β = -155.57, p = .004). The index of moderated mediation was 1072.06 and bootstrapped confidence interval was entirely above zero ([123.46, 2,516.67]), indicating the indirect effect of dopamine on switch cost via functional connectivity significantly differed across groups. Indeed, the indirect effect of dopamine on switch cost was not significant for older adults (estimated indirect effect = 557.82, bootstrapped CI [-97.38, 1530.36]), though it was significant for young adults (-514.23 [-1203.08, -31.85]). These results indicate the mediation was not significant for older adults. Supplementary Figure S3A,B displays results for age-conditional effects for young and older adults generated from the moderated mediation model. Age was not included as a moderator for the path relating functional connectivity and switch cost, so those values are held constant across groups.

Moderation Analysis

Striatal dopamine and IFG-DCA PPI connectivity interact to influence cognitive flexibility in aging.

In older adults, moderation analysis indicated striatal dopamine and functional connectivity interact to produce individual differences in cognitive flexibility (Figure S2C). The two predictors (DCA [^{18}F]FMT K_i and IFG-DCA PPI connectivity) were first entered into the regression analysis to determine each predictor's effect on switch cost and the interaction term. The overall model was marginal (R^2 = .53; F(4,10) = 2.85, p = .08). For older adults, results indicated that DCA [^{18}F]FMT K_i was not a significant predictor of switch cost (b = 220.57, t(10) = 0.45, p = .66) but PPI was a significant predictor (b = 54.91, t(10) = 2.22, p = .05) of switch cost. The interaction between DCA [^{18}F]FMT K_i and connectivity was significant (b = -1887.64, t(10) = 2.44, p = .03) and explained a significant increase in variance in switch cost (change R^2 = .28, F(1,10) = 5.97, p = .03). Thus, the influence of PPI connectivity on switch cost depends on dopamine synthesis capacity.

The unstandardized simple slopes were tested for low (-1 SD), moderate and high levels (+ 1 SD) of dopamine synthesis in older adults. Different patterns in the slope of the regression line with varying levels of dopamine synthesis show that the relation between IFG-DCA PPI connectivity and switch cost is unique and depends on the level of dopamine. Results suggest that the conditional effect of PPI on switch cost was present for high dopamine synthesis capacity (1SD above the mean); t(10) = 3.03, p = .01), and was not significant for moderate levels of dopamine synthesis capacity t(10)= 1.78, p = .11, or low levels of dopamine synthesis capacity (-1SD) t(10) = 0.40, p = .70).

For young adults, moderation analysis revealed no interaction between striatal dopamine and functional connectivity in producing individual differences in cognitive flexibility (Figure S2D). The two predictors (DCA [^{18}F]FMT K_i and IFG-DCA PPI

connectivity) were first entered into the regression analysis to determine each predictor's effect on switch cost and the interaction term. The overall model explained a significant amount of variance (R^2 = .63, F(4,16) = 6.73, p < .005). Results indicated that DCA [^{18}F]FMT K_i was a significant predictor of switch cost (b = -1407.00, t(16) = 2.85, p = .01) and connectivity marginally predicted switch cost (b = -3.53, t(16) = 1.96, p = .07). The interaction between DCA [^{18}F]FMT K_i and connectivity was not significant (b = 187.02, t(16) = 0.30, p = .77). Thus, the influence of PPI connectivity on switch cost did not interact with synthesis capacity.

Striatal dopamine and DCA-thalamus PPI connectivity interact to influence cognitive flexibility in aging.

In older adults, moderation analysis indicated striatal dopamine and functional connectivity interact to produce individual differences in cognitive flexibility (Figure S3C). The two predictors (DCA [^{18}F]FMT K_i and DCA-thalamus PPI connectivity) were first entered into the regression analysis to determine each predictor's effect on switch cost and the interaction term. The overall model was marginal (R^2 = .51; F(4,10) = 2.63, p = .10). For older adults, results indicated that DCA [^{18}F]FMT K_i was not a significant predictor of switch cost (b = 662.22, t(10) = 1.10, p = .30) but PPI was a marginal predictor (b = 54.53, t(10) = 2.13, p = .06) of switch cost. The interaction between DCA [^{18}F]FMT K_i and connectivity was significant (b = -1818.80, t(10) = 2.39, p = .04) and explained a significant increase in variance in switch cost (change R^2 = .28, F(1,10) = 5.73, p = .04). Thus, the influence of PPI connectivity on switch cost depends on dopamine synthesis capacity.

The unstandardized simple slopes were tested for low (-1 SD), moderate and high levels (+ 1 SD) of dopamine synthesis in older adults. Different patterns in the slope of the regression line with varying levels of dopamine synthesis show that the relation between DCA-thalamus PPI connectivity and switch cost is unique and depends

on the level of dopamine. Results suggest that the conditional effect of PPI on switch cost was present for high dopamine synthesis capacity (1SD above the mean); $t(10) = 2.48$, $p = .03$), and was not significant for moderate levels of dopamine synthesis capacity $t(10)= 0.85$, $p = .41$, or low levels of dopamine synthesis capacity (-1SD) $t(10) = 0.60$, $p = .56$).

For young adults, moderation analysis revealed no interaction between striatal dopamine and functional connectivity in producing individual differences in cognitive flexibility (Figure S3D). The two predictors (DCA [^{18}F]FMT K_i and DCA-thalamus PPI connectivity) were first entered into the regression analysis to determine each predictor's effect on switch cost and the interaction term. The overall model explained a significant amount of variance ($R^2 = .66$, $F(4,16) = 7.88$, $p = .001$). Results indicated that DCA [^{18}F]FMT K_i was a significant predictor of switch cost ($b = -1181.19$, $t(16) = 2.32$, $p = .03$) and connectivity predicted switch cost ($b = -7.33$, $t(16) = 2.54$, $p = .02$). The interaction between DCA [^{18}F]FMT K_i and connectivity was not significant ($b = 242.65$, $t(16) = 0.21$, $p = .83$). Thus, the influence of PPI connectivity on switch cost did not interact with synthesis capacity.

Figure S2

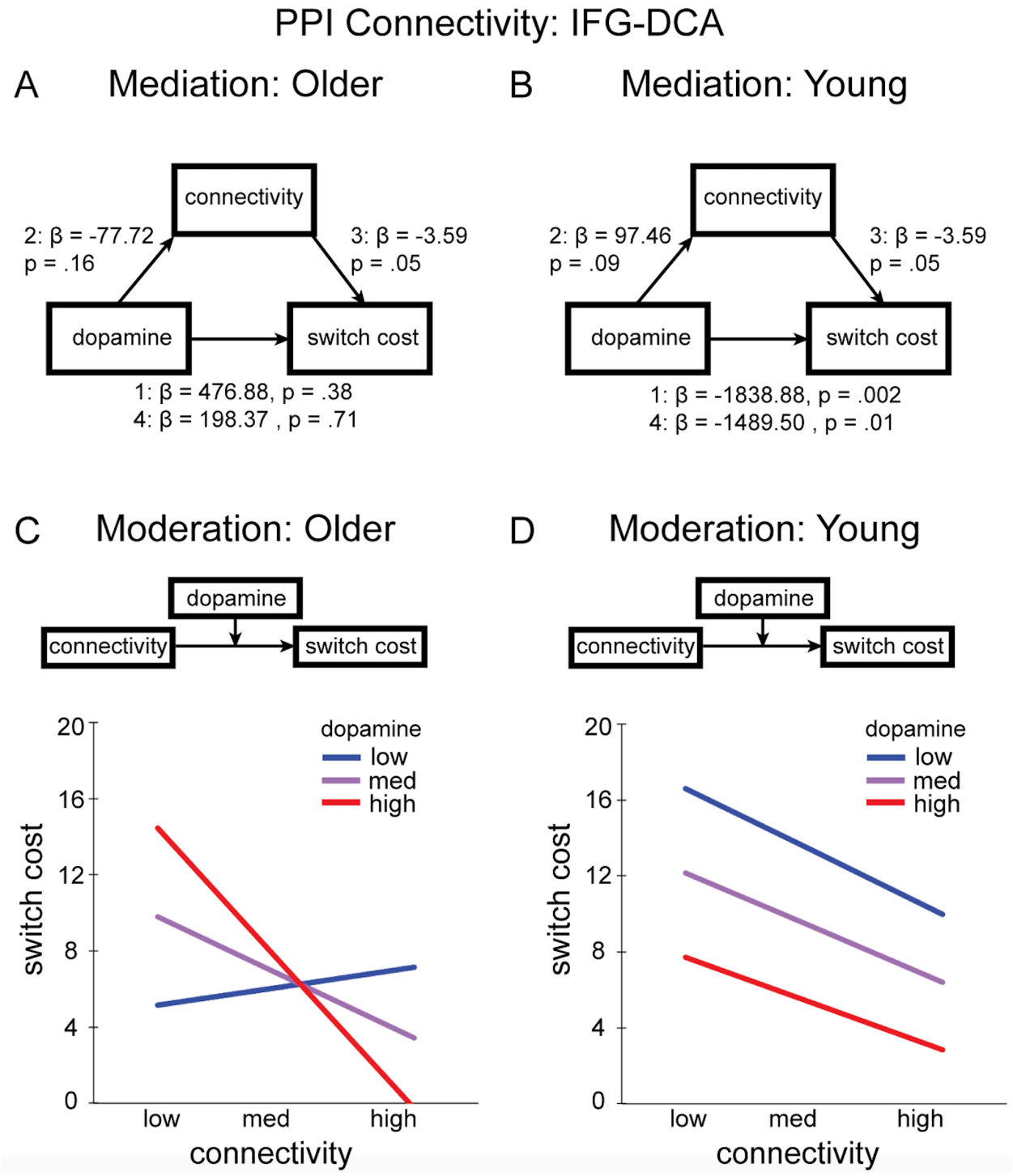
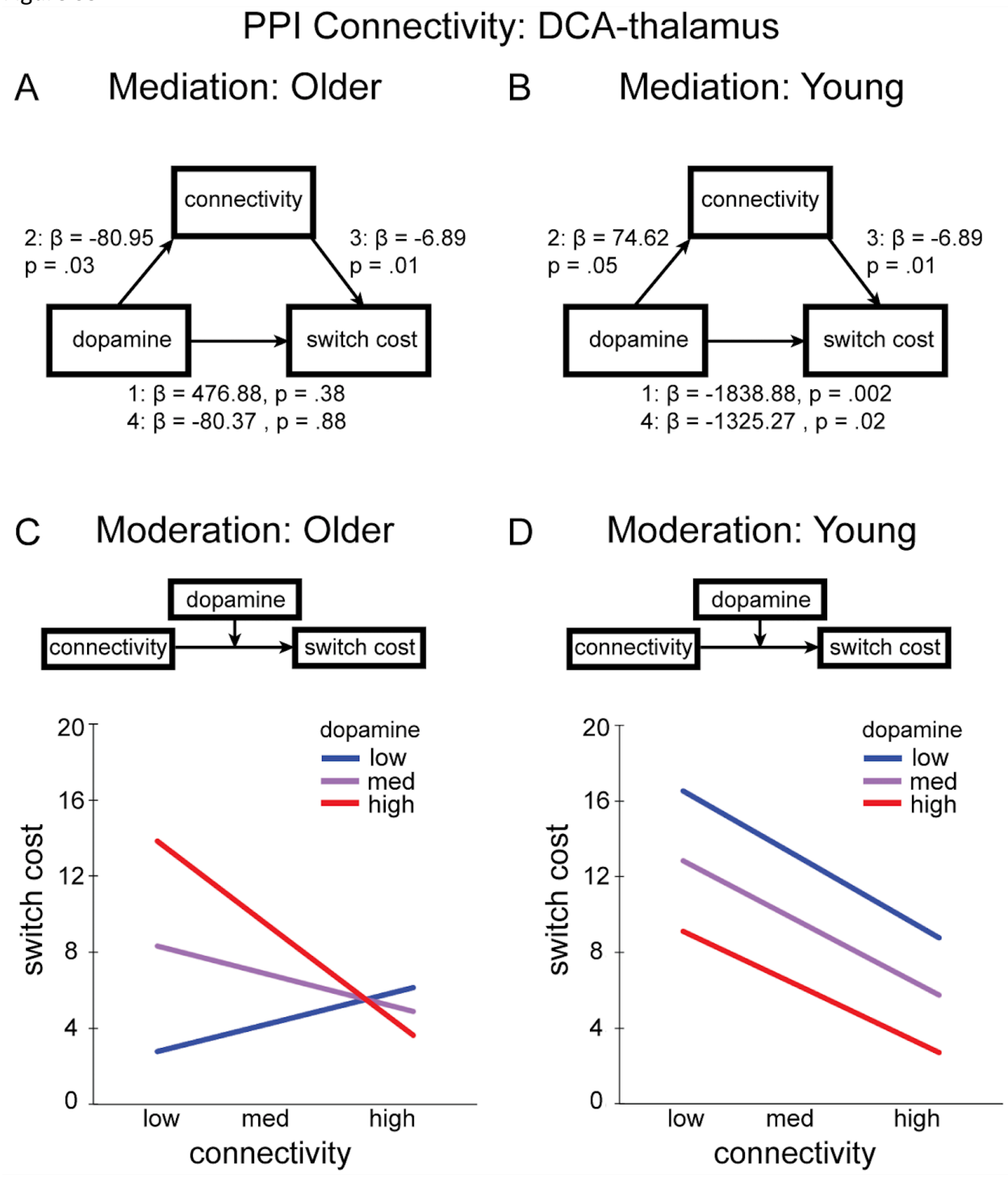

PPI Connectivity: IFG-DCA
A Mediation: Older
connectivity
2: β = -77.72
p = .16
3: β = -3.59
p = .05
dopamine
switch cost
1: β = 476.88, p = .38
4: β = 198.37 , p = .71
B Mediation: Young
connectivity
2: β = 97.46
p = .09
3: β = -3.59
p = .05
dopamine
switch cost
1: β = -1838.88, p = .002
4: β = -1489.50 , p = .01
C Moderation: Older
dopamine
connectivity
switch cost
dopamine
low
med
high
switch cost
20
16
12
8
4
0
low
med
high
connectivity
D Moderation: Young
dopamine
connectivity
switch cost
dopamine
low
med
high
switch cost
20
16
12
8
4
0
low
med
high
connectivity

Figure S3


PPI Connectivity: DCA-thalamus
A Mediation: Older
connectivity
2: β = -80.95
p = .03
3: β = -6.89
p = .01
dopamine
switch cost
1: β = 476.88, p = .38
4: β = -80.37 , p = .88
B Mediation: Young
connectivity
2: β = 74.62
p = .05
3: β = -6.89
p = .01
dopamine
switch cost
1: β = -1838.88, p = .002
4: β = -1325.27 , p = .02
C Moderation: Older
dopamine
connectivity
switch cost
dopamine
low
med
high
switch cost
20
16
12
8
4
0
low
med
high
connectivity
D Moderation: Young
dopamine
connectivity
switch cost
dopamine
low
med
high
switch cost
20
16
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connectivity