Supplementary Material

Altered Cerebro-Cerebellar Dynamic Functional Connectivity in Alcohol Use Disorder: A Resting-State fMRI Study

Abdallah et al.

1 Validation Analyses

Given that dynamic FC estimates can be affected by changes in window length (Leonardi and Van De Ville, 2015), we repeated our analysis with different window lengths: 15 TR ($\approx$ 40 s) and 25 TR ($\approx$ 70 s). Then, we tested for group differences in cerebro-cerebellar FC temporal variability, flexibility, and integration in each case.

2 Results

Results obtained using 15 TR ($\approx$ 40 seconds) and 25 TR ($\approx$ 70 seconds) windows revealed qualitatively similar patterns of group differences as those obtained in the main analysis using 20 TR windows, however, with few exceptions. Particularly, we observed significant FC hypervariability between the cerebellum and both the FPN and the VAN in the AUD group when using 25 TR windows. However, when using 15 TR windows, we found significant FC hypervariability between the cerebellum and the FPN only. In addition, we observed significantly less cerebellar flexibility in the AUD group relative to controls when using 15 TR and 25 TR windows. However, while we found significant group differences in network flexibility in the SAN, CON, VAN, and DMN in the case of 15 TR windows, no significant group difference in network flexibility were observed in the case of 25 TR windows. This is consistent with previous studies showing that shorter windows are more sensitive to individual differences in flexibility, whereas longer windows are more sensitive to inter-regional variations, rather than inter-individual differences, in flexibility (Telesford et al., 2016). Finally, while we observed significantly greater cerebellar and FPN integration in the AUD

group relative to controls when using 25 TR windows, no significant group differences in cerebellar and FPN integration were detected in the case of 15 TR windows. Results are summarized below in Supplementary Tables S1-S4 and illustrated in Supplementary Figures S1-S3. We did not correct for multiple comparisons in the supplementary analysis.

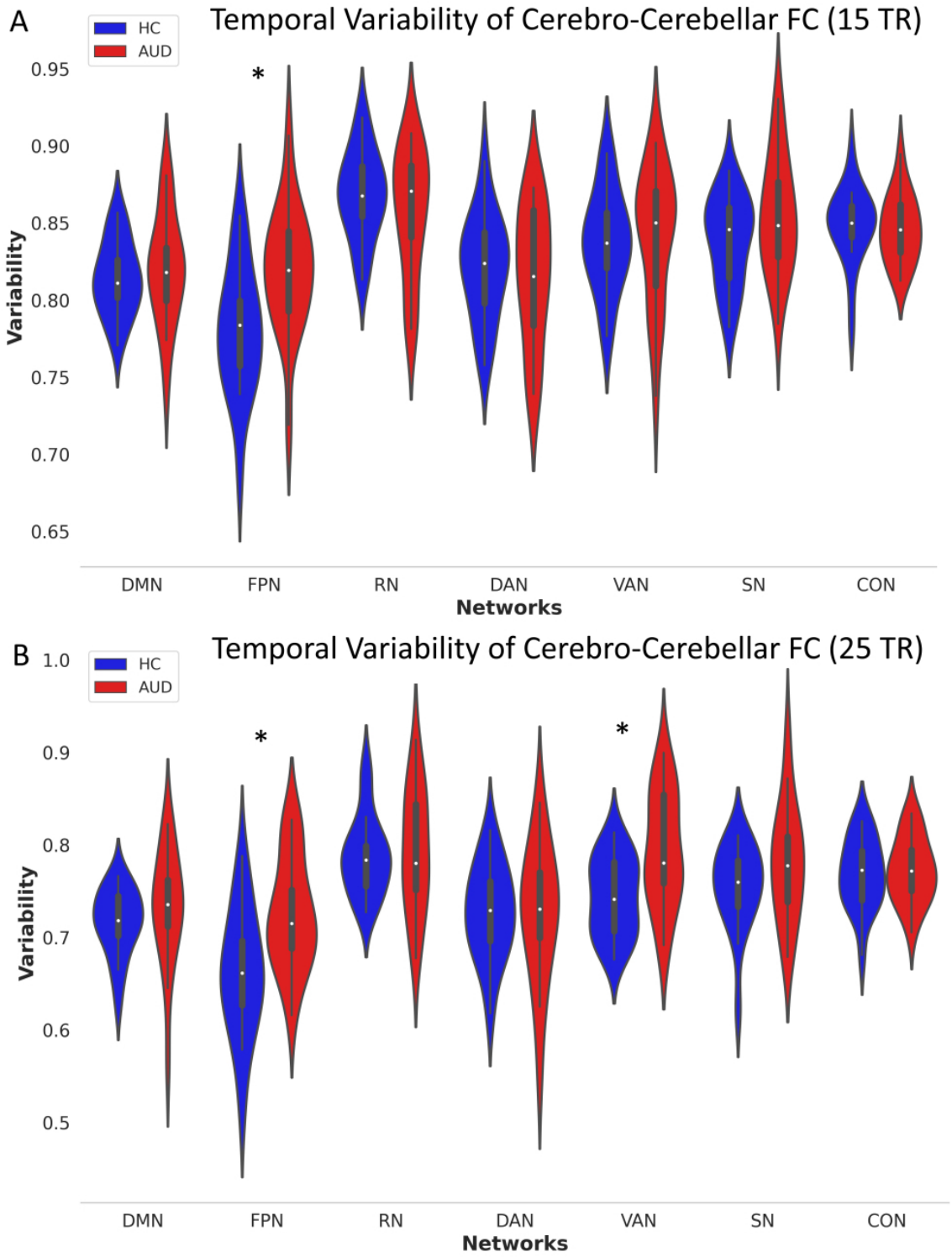

Figure 1: Violin plots of temporal variability of FC between the cerebellum and seven large-scale cognitive networks for the AUD group and HCs obtained using **(A)** 15 TR and **(B)** 25 TR windows. Asterisk indicates $p < 0.05$ (uncorrected) for group differences

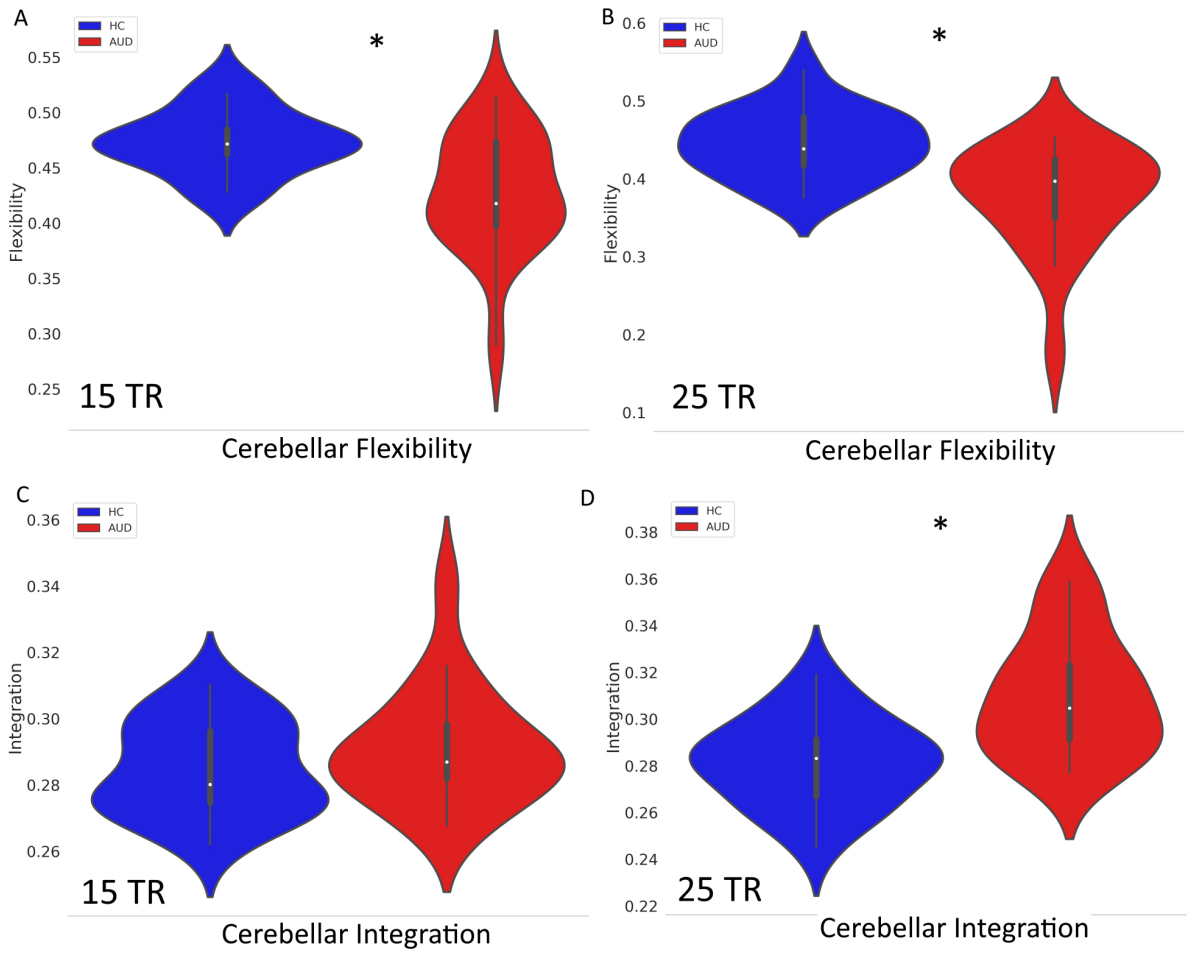

Figure 2: Violin plots of cerebellar flexibility and integration for the AUD group and HCs obtained using **(A)**, **(C)** 15 TR and **(B)**, **(D)** 25 TR windows. Asterisk indicates $p < 0.05$ (uncorrected) for group differences.

Table 1: Group comparisons in cerebro-cerebellar FC temporal variability (**15 TR**)

Network	HC mean(SD)	AUD mean(SD)	$F_{1,31}$	p-value	η_p^2
DMN	0.81(0.023)	0.82(0.034)	0.02	0.84	< 0.0001
FPN	**0.78(0.04)**	**0.82(0.04)**	**7.21**	**0.012**	**0.19**
RN	0.86(0.03)	0.86(0.04)	2.48	0.125	0.07
DAN	0.82(0.04)	0.81(0.07)	0.25	0.62	0.06
VAN	0.84(0.03)	0.85(0.04)	2.55	0.12	0.07
SN	0.84(0.03)	0.85(0.04)	0.74	0.4	0.02
CON	0.85(0.02)	0.85(0.02)	0.15	0.71	0.005

Note: **HC**= Healthy controls, **AUD**= Alcohol Use Disorder, **SD**=Standard Deviation, **F**= F-statistic, η_p^2= Partial eta-squared effect size

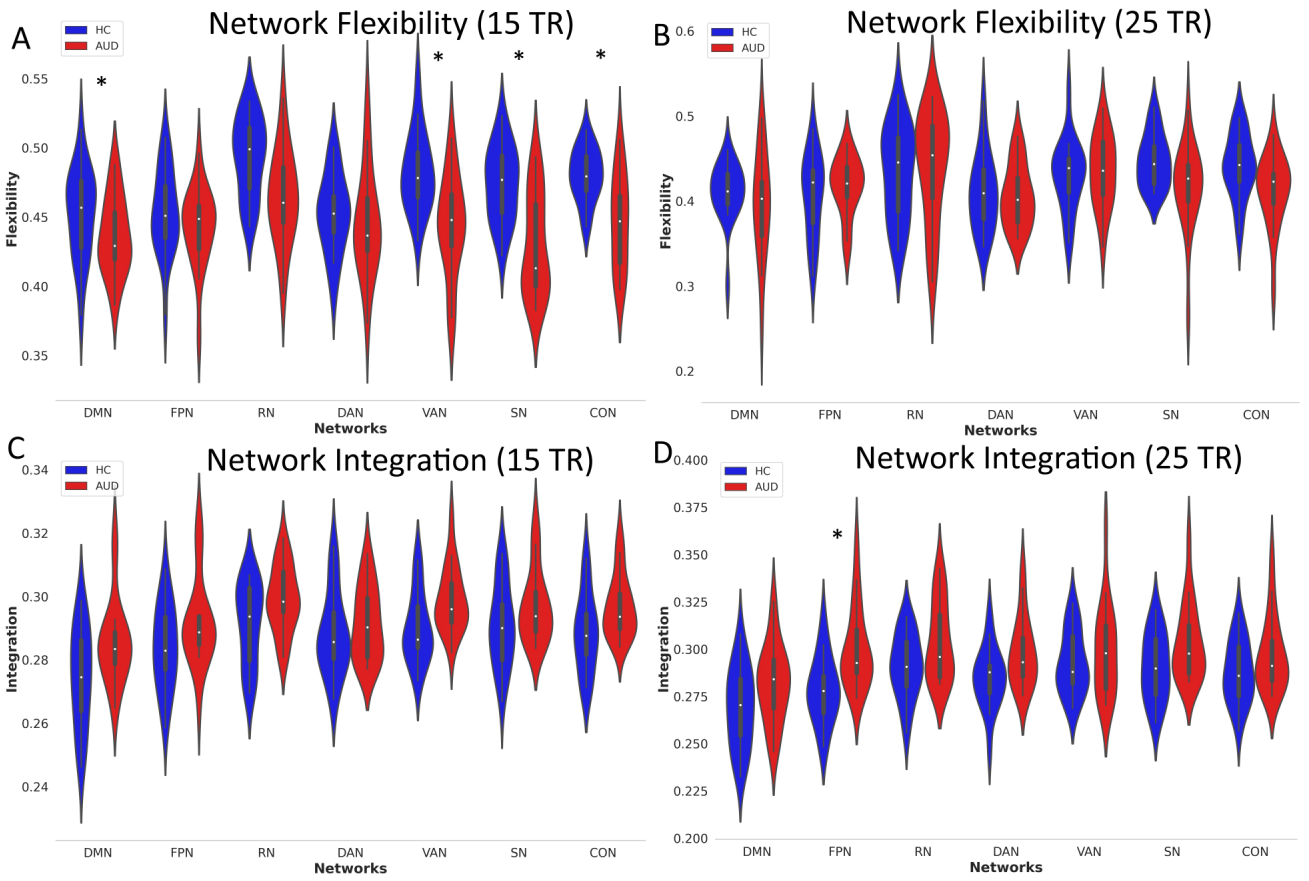

Figure 3: Violin plots of network flexibility and integration coefficients for the AUD group and HCs obtained using **(A)**, **(C)** 15 TR and **(B)**, **(D)** 25 TR windows. Asterisk indicates $p < 0.05$ (uncorrected) for group differences

Table 2: Results of group comparisons in cerebro-cerebellar FC temporal variability (**25 TR**)

Network	HC mean(SD)	AUD mean(SD)	$F_{1,31}$	p-value	η_p^2
DMN	0.72(0.04)	0.73(0.06)	0.61	0.44	0.02
FPN	**0.66(0.07)**	**0.71(0.06)**	**6.18**	**0.018**	**0.17**
RN	0.79(0.04)	0.79(0.07)	0.29	0.6	0.009
DAN	0.73(0.05)	0.72(0.07)	0.08	0.77	< 0.0001
VAN	**0.74(0.04)**	**0.78(0.06)**	**7.75**	**0.009**	**0.2**
SN	0.75(0.04)	0.78(0.06)	0.62	0.43	0.02
CON	0.77(0.04)	0.77(0.03)	0.28	0.6	0.008

Note: **HC**= Healthy Controls, **AUD**= Alcohol Use Disorder, **SD**=Standard Deviation, **F**= F-statistic, η_p^2= Partial eta-squared effect size.

Bold indicates significant group difference

Table 3: Significant Group Differences in flexibility and integration (**15 TR**)

System	Score	HC mean(SD)	AUD mean(SD)	$F_{1,31}$	p-value	η_p^2
Cerebellum	Flexibility	0.47(0.03)	0.43(0.05)	10.4	0.003	0.25
	Integration	0.28(0.014)	0.29(0.017)	2.7	0.11	0.08
DMN	Flexibility	0.45(0.03)	0.43(0.02)	5.3	0.03	0.14
VAN	Flexibility	0.48(0.03)	0.45(0.035)	11.85	0.002	0.27
SN	Flexibility	0.47(0.025)	0.44(0.035)	10.5	0.003	0.25
CON	Flexibility	0.48(0.02)	0.45(0.03)	13.8	< 0.001	0.3

Note: **HC**= Healthy controls, **AUD**= Alcohol Use Disorder, **SD**=Standard Deviation, **F**= F-statistic, η^2= Partial eta-squared effect size

Table 4: Significant group differences in flexibility and integration (**25 TR**)

System	Score	HC mean(SD)	AUD mean(SD)	$F_{1,31}$	p-value	η_p^2
Cerebellum	Flexibility	0.43(0.04)	0.39(0.07)	11.1	0.002	0.26
	Integration	0.28(0.018)	0.3(0.025)	7.85	0.009	0.2
FPN	Integration	0.28(0.017)	0.3(0.02)	5.2	0.03	0.14

Note: **HC**= Healthy controls, **AUD**= Alcohol Use Disorder, **SD**=Standard Deviation, **F**= F-statistic, η^2= Partial eta-squared effect size

References

Leonardi, N. and Van De Ville, D. (2015). On spurious and real fluctuations of dynamic functional connectivity during rest. *Neuroimage*, 104:430–436.

Telesford, Q. K., Lynall, M.-E., Vettel, J., Miller, M. B., Grafton, S. T., and Bassett, D. S. (2016). Detection of functional brain network reconfiguration during task-driven cognitive states. *NeuroImage*, 142:198–210.