Exploring the effects of selective dropout in longitudinal fMRI studies

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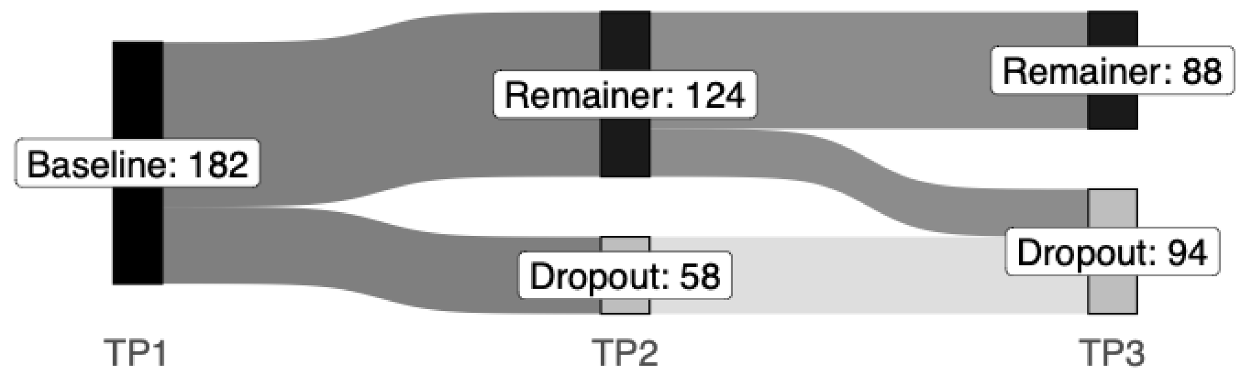
BACKGROUND

- Participant dropout poses a significant challenge to longitudinal aging studies, particularly if directly related to the outcome of interest.[1,2]
- Evidence of task-based fMRI sensitivity to dropout (i.e., dropouts showing higher/lower activation than returnees), but baseline differences have primarily been assessed.[3,4]
- While past work in cognition shows attrition to be selective to level and not change, older adults did display differences in slopes based on the number of available timepoints.[5]
- It is thus be of interest to assess whether attrition effects in fMRI may be selective to **level or change.**

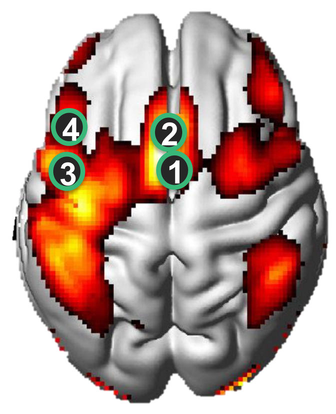
SAMPLE & METHODS

182 older adults from the Cognition, Brain and Aging (COBRA) study.[6]

Dropouts: N=94, M_{age}=66.20 (SD=1.16)
Remainers: N=88, M_{age}=66.13 (SD=1.26)



Task fMRI during n-back. Reanalysis of four regions showing differences between working memory decliners and maintainers from Nyberg et al.[7]

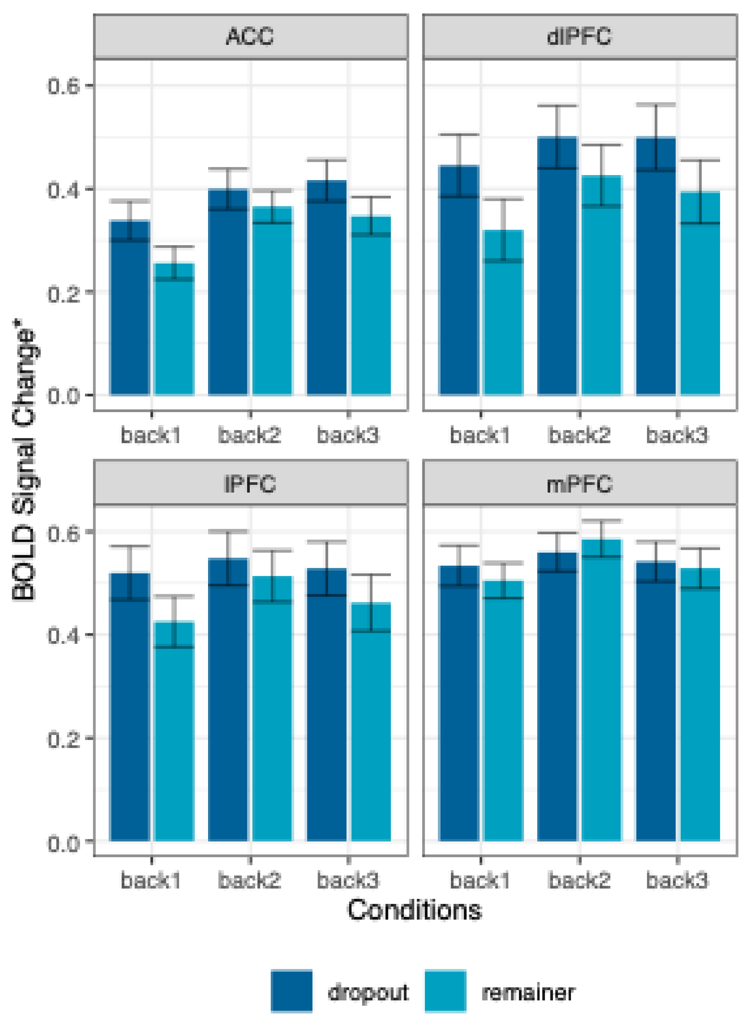


1. **medial frontal** [-4 6 54]
2. **ACC** [-6 20 46]
3. **lateral frontal** [-52 4 44]
4. **DLPFC** [-52 24 32]

Figure from Nyberg et al.[7]

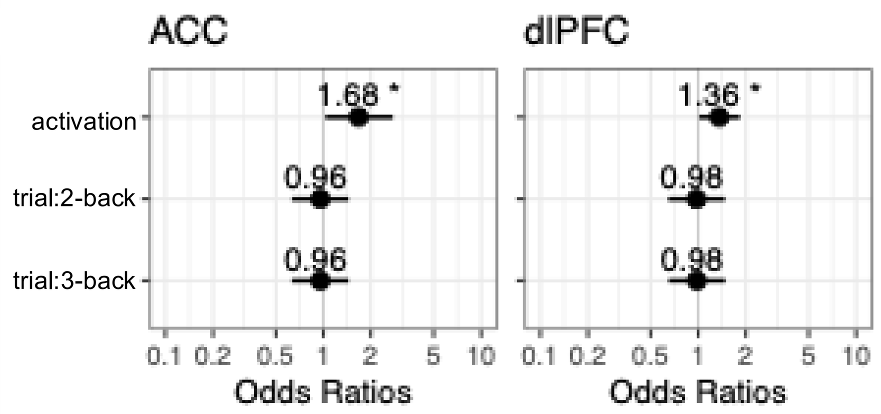
BASELINE ACTIVITY DIFFERENCES

All Dropouts vs. Remainers



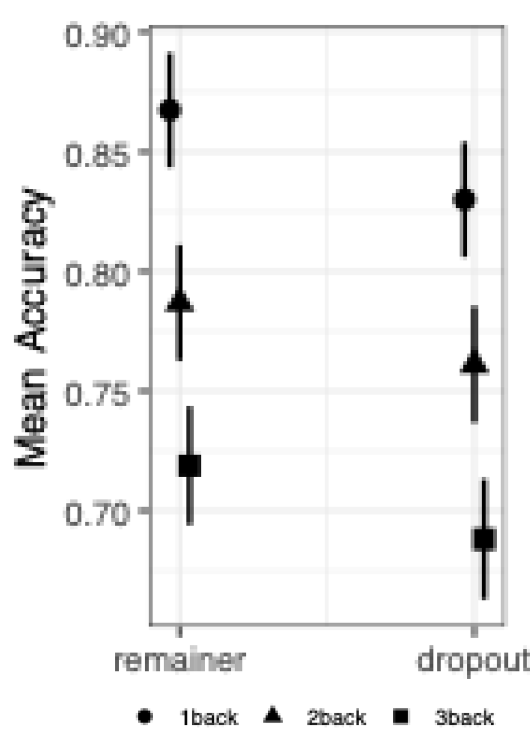
ACC and DLPFC activity were significant predictors of dropout status.

Higher baseline activity increased odds of belonging to the dropout group.



ACC: OR=1.68, 95% CI: [1.03, 2.76], p=.039.
DLPFC: OR=1.36, 95% CI: [1.01, 1.84], p=.042.
No significant effects on outcome for trial type.

Dropouts had lower accuracy, most salient for 1-back.



Group: F(1,157)=4.24, p=.04
Condition: F(2,299.79)=177, p<.001
Group*Condition: F(1,299.79)=.3, p=.7

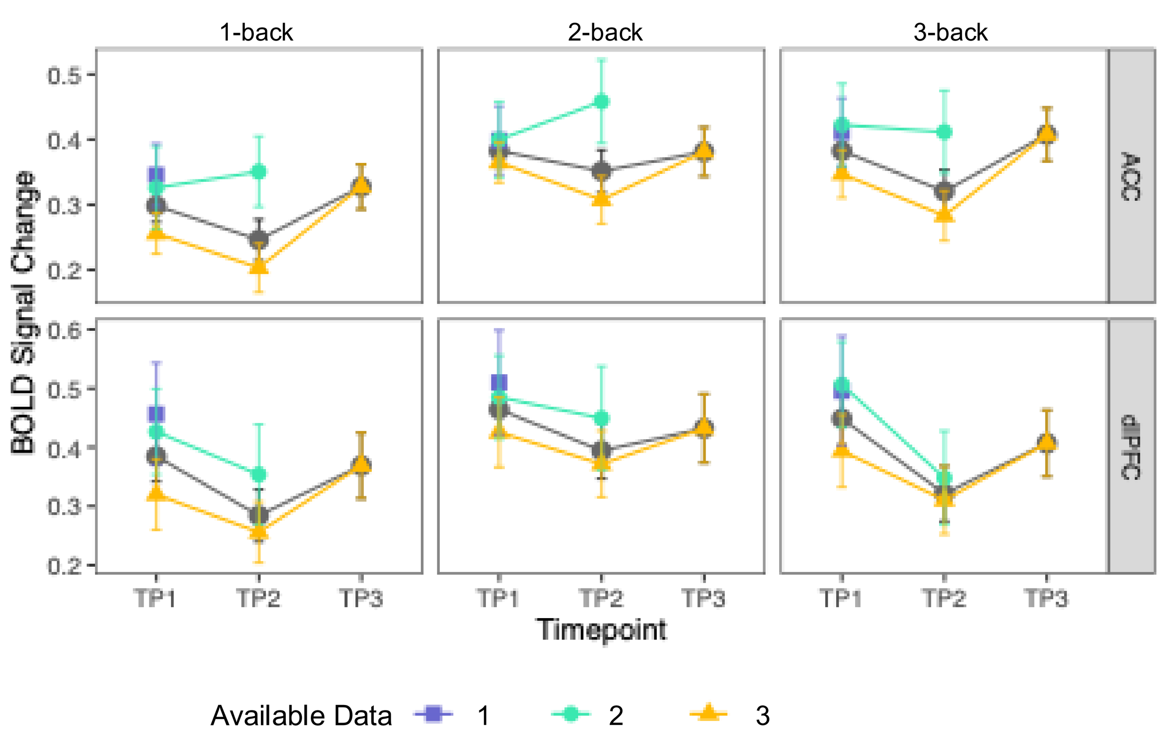
SAMPLE SELECTIVITY

Total selectivity: extent individuals measured at a given occasion differ from parent sample.[2]

Region	N-back trial	Parent (M)	Parent (SD)	Returnees (M)	Returnees (SD)	Selectivity
ACC	**1-back**	**0.30**	**0.34**	**0.26**	**0.29**	**-0.13**
ACC	2-back	0.38	0.34	0.36	0.29	-0.05
ACC	**3-back**	**0.38**	**0.37**	**0.35**	**0.34**	**-0.10**
dlPFC	**1-back**	**0.38**	**0.58**	**0.32**	**0.56**	**-0.11**
dlPFC	2-back	0.46	0.57	0.43	0.56	-0.07
dlPFC	**3-back**	**0.45**	**0.60**	**0.39**	**0.58**	**-0.09**
lPFC	**1-back**	**0.47**	**0.48**	**0.43**	**0.46**	**-0.10**
lPFC	2-back	0.53	0.49	0.51	0.47	-0.04
lPFC	3-back	0.50	0.51	0.46	0.51	-0.07
mPFC	1-back	0.52	0.35	0.51	0.32	-0.04
mPFC	2-back	0.57	0.35	0.59	0.33	0.04
mPFC	3-back	0.54	0.37	0.53	0.36	-0.02

$$Selectivity = \frac{Mean_{returnees} - Mean_{parent\_sample}}{SD_{parent\_sample}}$$

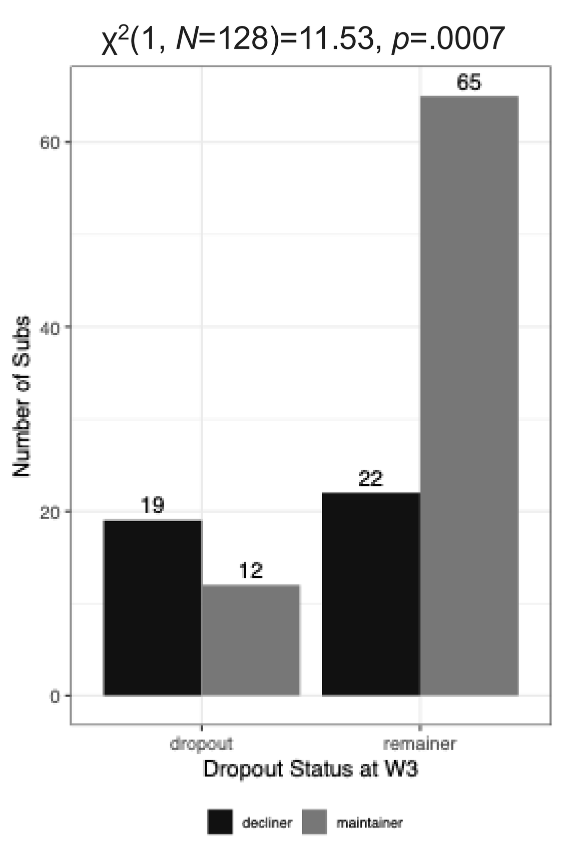
EFFECTS ON SLOPES



ACC: Overall appearance of declines in activation (grey). Disaggregating slopes based on available timepoints shows increasing activation over time for TP3 dropouts compared to those who T3 remainers (green and yellow).

COGNITIVE CHANGE

Working memory decliners more likely to dropout.



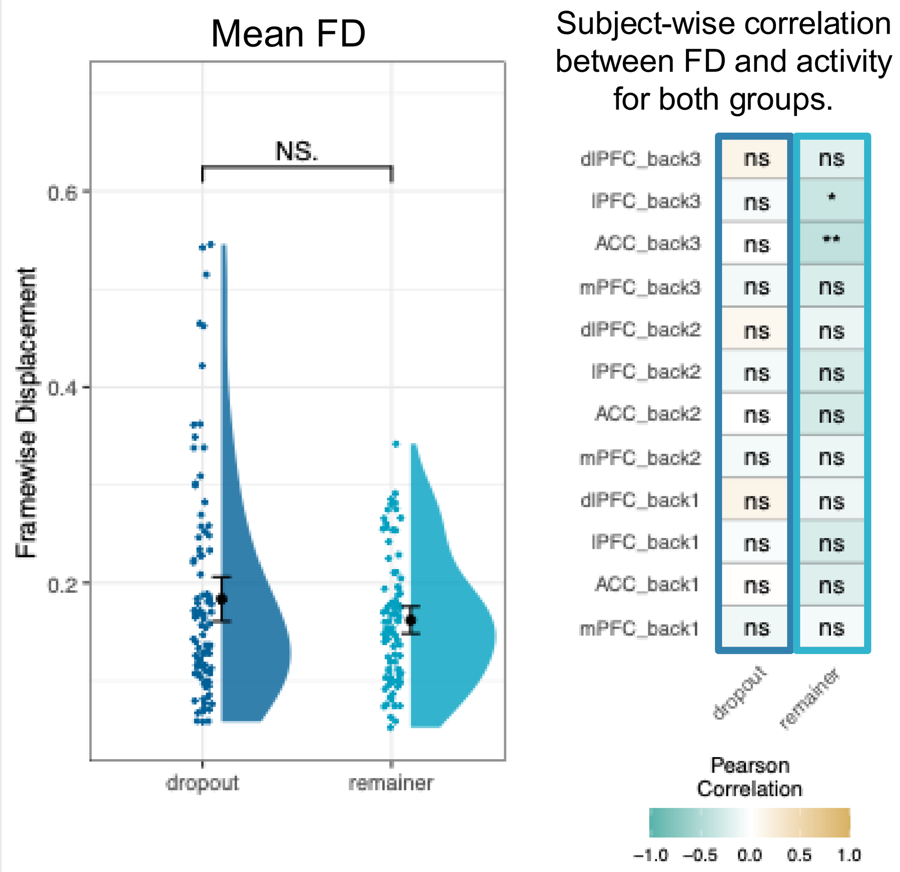
→ working memory change between T1 and T2, grouping from[7]

→ dropout status T3

~60% of dropouts were cognitive decliners

CONFOUNDS?

No motion differences between dropouts and returnees.



SUMMARY & NEXT STEPS

- Dropouts showed greater activation and lower cognitive performance at baseline, indicating greater neural resource requirement.
- Restricting fMRI analyses to subjects with complete data across timepoints may bias estimates of level and directions of change of functional brain activity in aging, resulting in trends of diverging or higher functioning to be missed.
- These findings confirm past work (e.g., Nyberg et al.[3]), that dropout effects, with a trend to elevated activity, risk biasing cross-sectional analyses towards over-recruitment in aging.
- Next steps: assessing methods to correct fMRI analyses for such effects.

References:
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[6] Nevalainen et al. (2015). COBRA: A prospective multimodal imaging study of dopamine, brain structure and function, and cognition. *Brain Research.*
[7] Nyberg et al. (2022). Longitudinal stability in working memory and frontal activity in relation to general brain maintenance. *Scientific Reports.*