

Brain-predicted age difference score and cognitive function: A multi-site analysis



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The aging brain

- Decrease in volume & weight
- Ventricular system enlarges
- Brain generates fewer neurotransmitters

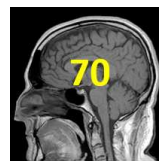


BrainPAD = Brain Predicted Age-Difference

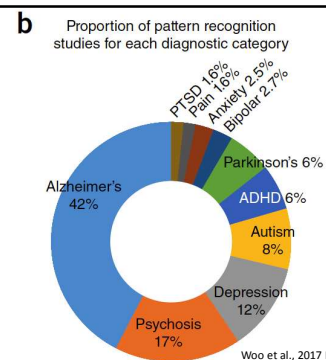
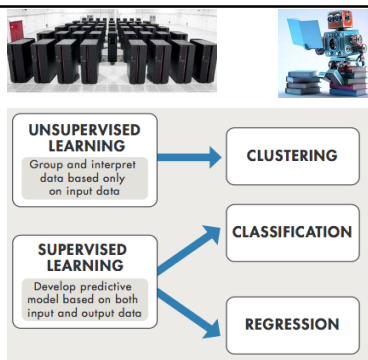


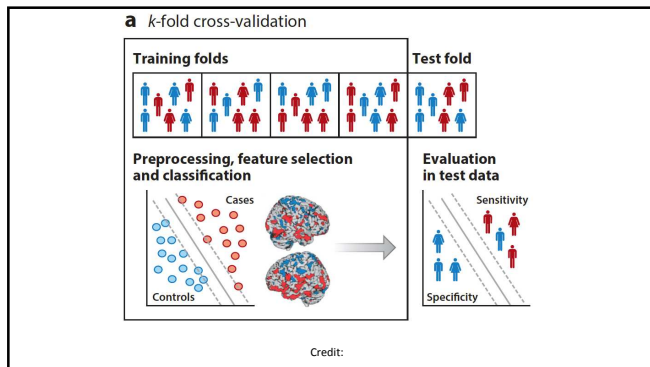
+10 years brainPAD
(‘older’ brain)

- **Intuitive:** positive brainPAD score → ‘older’ brain → poor ageing
- **Predictive:** linked with higher early mortality risk, poorer physical + cognitive ageing
- **Relevant:** higher brainPAD in Alzheimer’s Disease, MCI, TBI
- **Objective:** no practice effects etc.



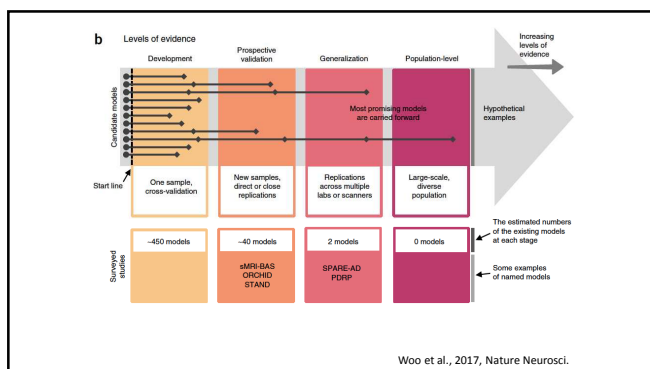
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But...

- Current models rely on data reduction → difficult to interpret results
 - Don't tell us what, or how, specific brain areas contribute to older brain age
- Not yet known what specific cognitive functions are related to brainPAD in non-clinical and older populations
 - Important if brainPAD is to be used as a cognitive ageing biomarker



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nature human behaviour

PERSPECTIVE

PUBLISHED: 10 JANUARY 2017 | VOLUME: 1 | ARTICLE NUMBER: 0021

OPEN

A manifesto for reproducible science

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Collaboration and team science

Creating the training set

- 1,359 T1-weighted MRIs from open-access repositories

IXI Dataset

Our brainPAD model

- Preprocessed and segmented into GM images
- Extracted GM voxels > 0.2 → created matrix
- Elastic Net ML
 - Run 25 times (50% males, 50% females each time) → remove gender effects
- Apply model coefficients to external datasets: TILDA, DEU, COLUMBIA
 - Test relationship between brainPAD & cognitive function

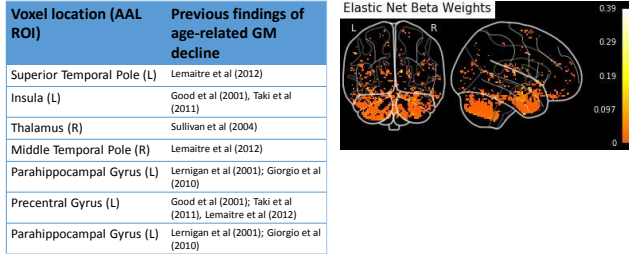
Voxels (54,869)

	1	2
1	0.5682	0.7134
2	0.4730	0.5876
3	0.4645	0.5831
4	0.4558	0.5604
5	0.6012	0.7464

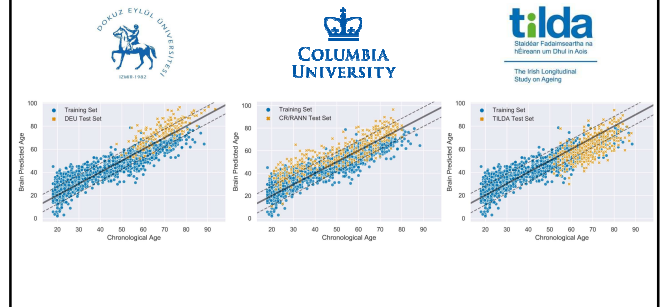
Participants (1,359)

Training Set Results

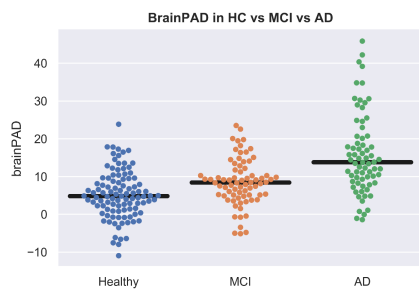
- Elastic Net significantly predicted age in training set ($r = 0.85$, $p < 0.0001$, $MAE = 7.28$ years)



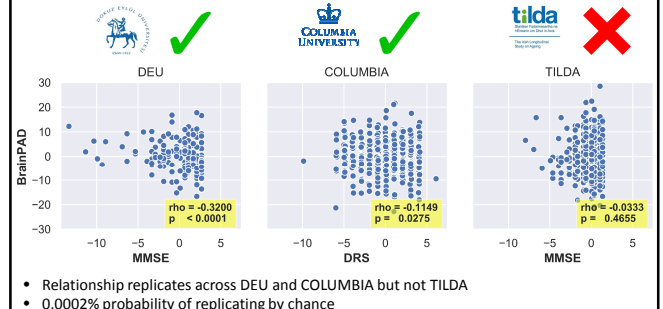
Test Sets – TILDA, DEU, COLUMBIA



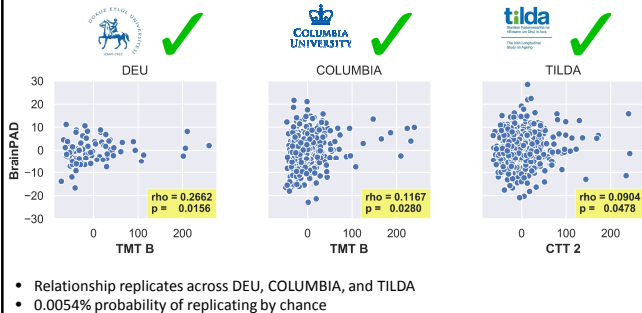
BrainPAD differences between Healthy vs MCI vs AD



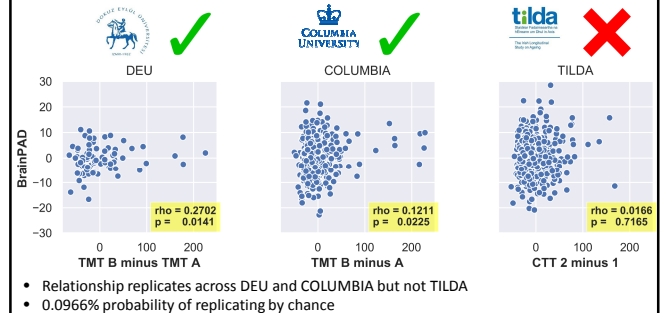
BrainPAD & General Cognitive Status

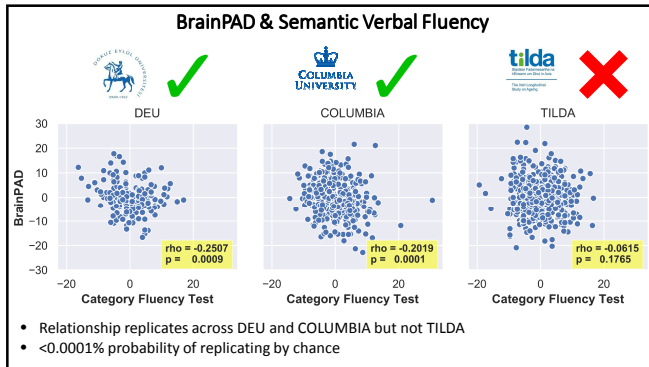


BrainPAD & Processing Speed, Visual Attention, and Cognitive Flexibility



BrainPAD & Visual Attention and Cognitive Flexibility

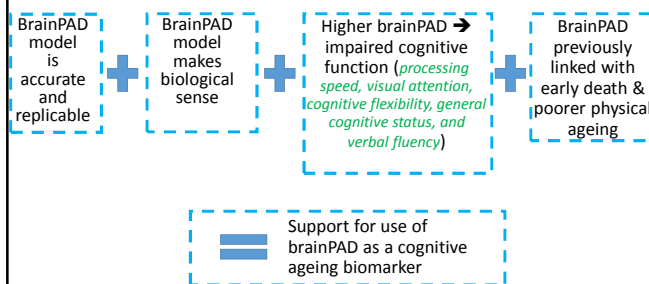




Cognitive functions not correlated with brainPAD

- **Simple processing speed**
 - TMT A/CTT 1
- **Response Inhibition/Selective Attention**
 - Stroop Colour Word Test
- **Verbal Episodic Memory**
 - Immediate & Delayed Recall
- **Sustained attention**
 - SART & PVT

Summary



Thank you

- Special thanks to Rory Boyle, PhD candidate

Significant results that aren't replicated across datasets

