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Progression of age-related decline in task-switching performance and white matter microstructure: A longitudinal study

Frini Karayanidis, Todd Jolly,
Jaime Rennie, Rhoshel Lenroot, Pat Michie,
Mark Parsons, Christopher Levi

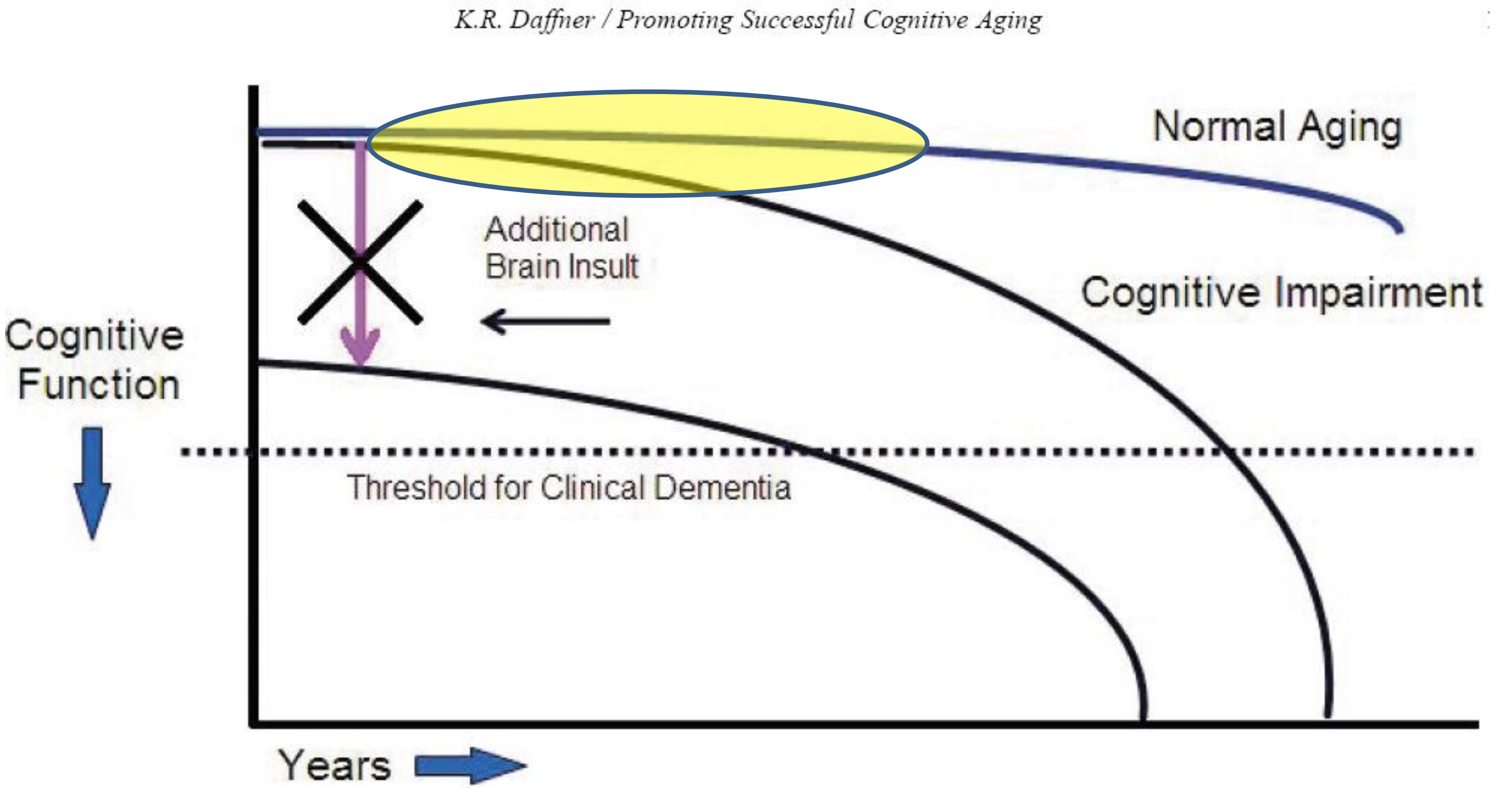
Functional Neuroimaging Laboratory
School of Psychology
University of Newcastle

Health NSW Government
Hunter New England Local Health District

HMRI Hunter Medical Research Institute

ICON-2014 Brisbane

Cognitive changes in healthy ageing vs. dementia



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Age-related cognitive decline

- Cognitive decline in "healthy older adults" is well-documented
- Large variability across areas of cognition (e.g., *Goh et al 2012 Psychol Aging*)
- Greater effects on higher order cognitive control processes (i.e., last-in, first-out)
- More prominent structural decline in frontal networks

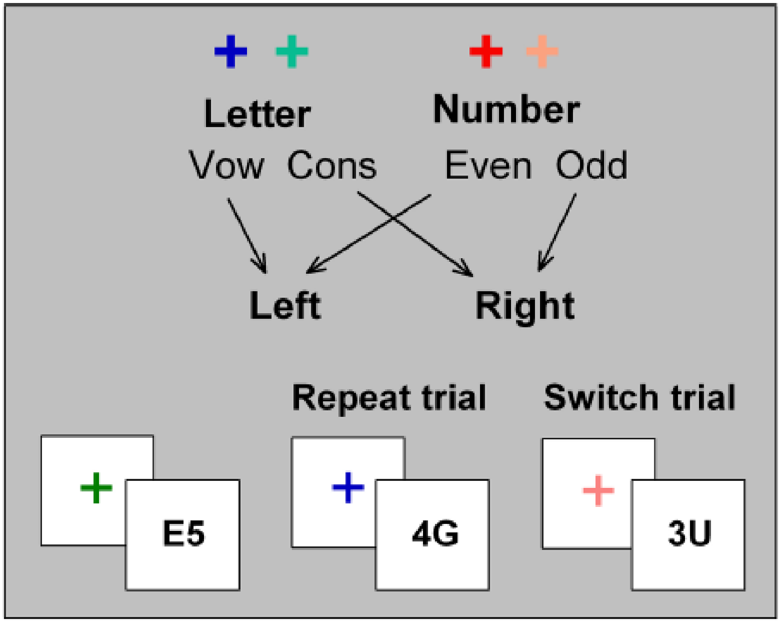
The present study

In "cognitively intact older" adults, is decline in cognitive control over time associated with changes in microstructure in frontal/parietal WM tracts or diffuse changes across the entire WM?

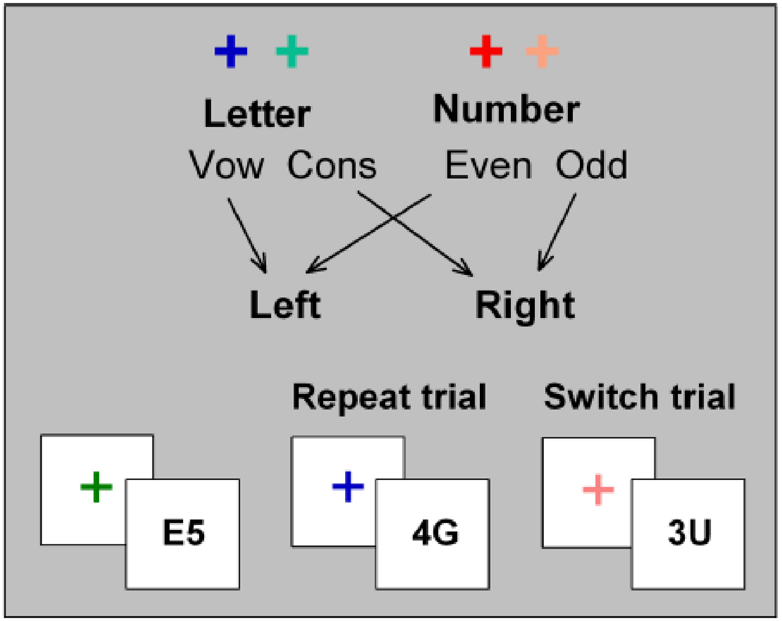
Proactive and reactive control processes in task-switching paradigms

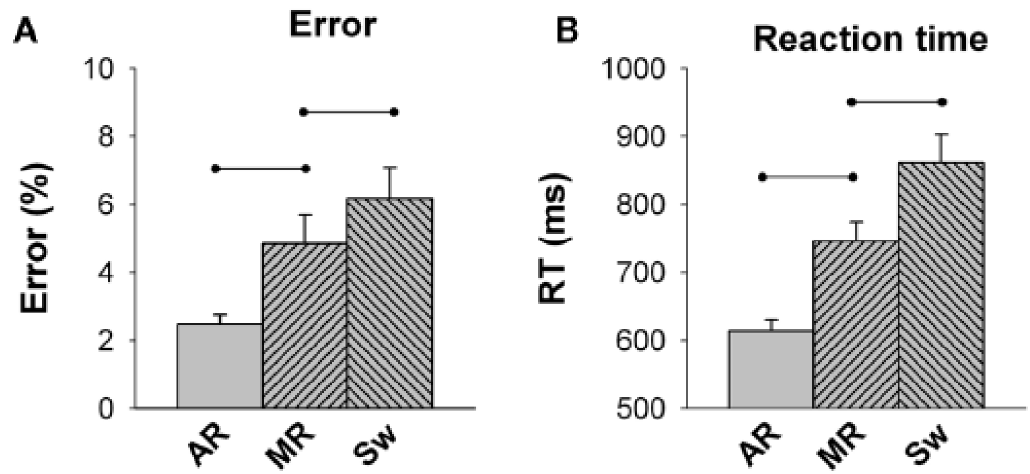
Use of contextual cues to flexibly alternate between task-sets

- **Proactive control** - advance goal setting and task-set preparation
- **Reactive control** – task implementation in the presence of interference



Task-switching paradigm





Mixing Cost =

AR= all-repeat: Letter – *Letter* – *Letter* – *Letter*

MR= mixed-repeat

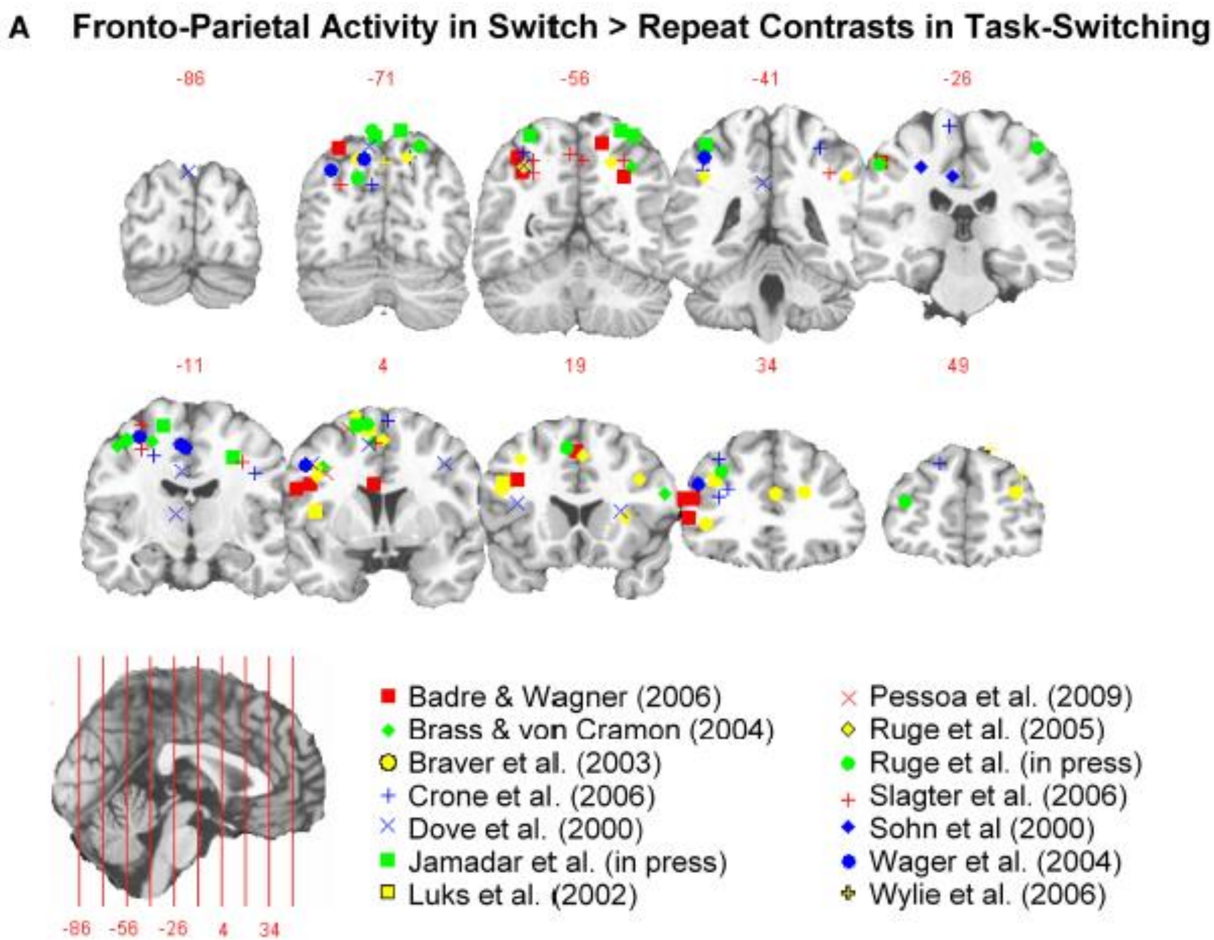
Switch Cost =

: Letter – *Letter* – *Number* – *Letter* – *Number* - *Number*

Sw = Switch

Networks involved in switching-related control

Ruge, Jamadar, Zimmerman, Karayanidis, HBM, 2013

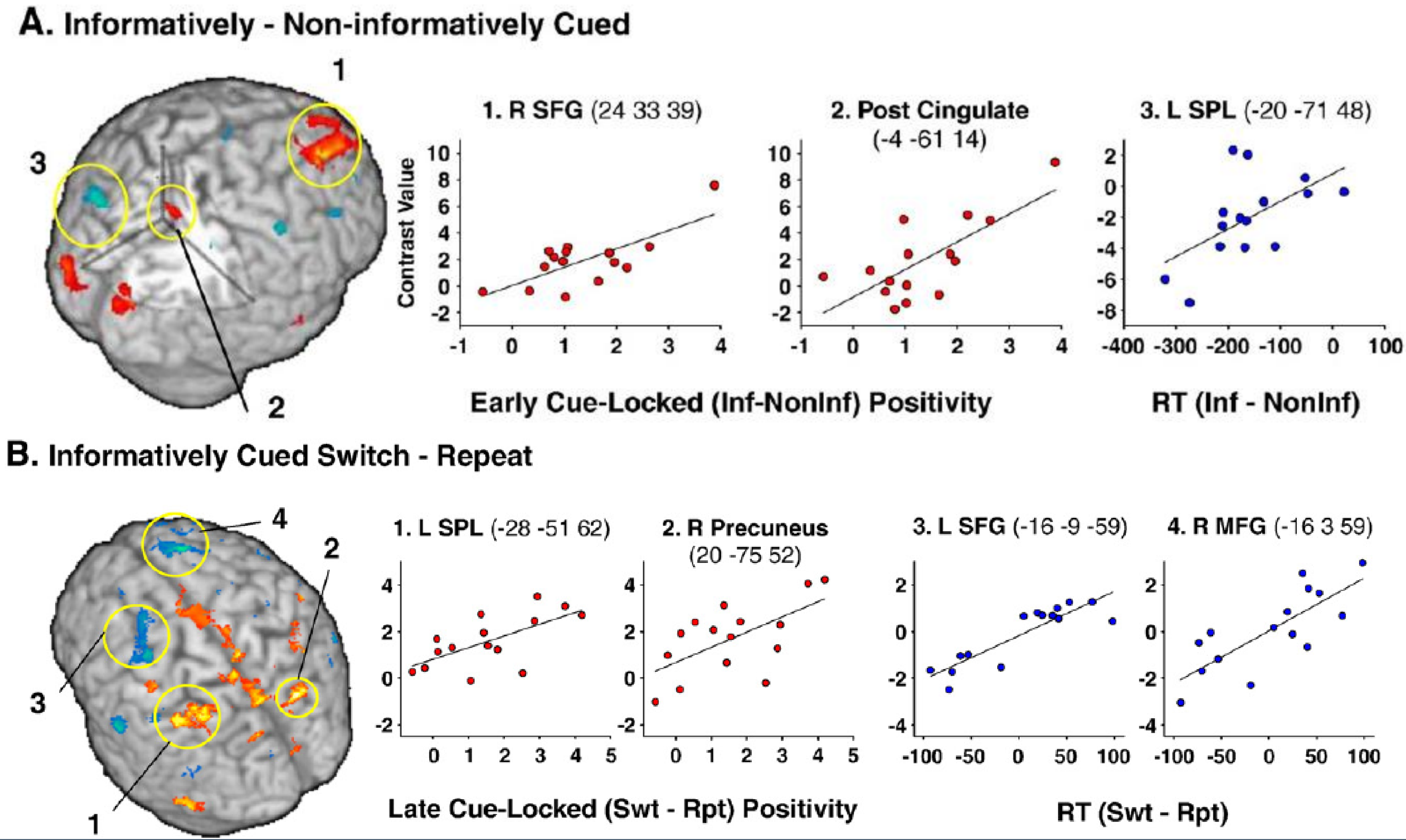


Richter & Yeung, in press

BA6, Medial Frontal Gyrus;
BA40, IPL;
BA40/7, SPL;
BA7, Precuneus;
BA32, Cingulate Cortex;
BA9/6, Middle Frontal Gyrus;
BA19, Precuneus;
BA9, Middle Frontal Gyrus;
BA7/31, Precuneus;
BA46, Middle Frontal Gyrus;
BA31, Precuneus;
BA39, Middle Temporal gyrus;
BA13, Insula;
BA13/47, Insula;
BA18, Middle Occipital Gyrus;
BA19, Inferior Occipital Gyrus/Fusiform Gyrus

Task-switching and fMRI activation

Jamadar et al. 2010 Neuroimage



Ageing effects in task-switching

Older adults

- Larger switch cost early in task exposure
- Slower to develop advance preparation to switch
- Sustained mixing cost even after extensive task practice
- Greater engagement of proactive control for switch and repeat trials
- Greater target-driven interference for switch trials

E.g., Karayanidis et al., Frontiers in Psychology 2011; Kray et al., Psychophysiology 2005
Kray et al., Acta Psychologica 2004; Whitson et al., Acta Psychologica 2012

Present study

Characterise change over 2y in healthy older adults

- in WM organisation change
- overall cognitive performance
- specific aspects of task-switching performance

Are changes in cognition associated with deterioration of specific WM tracts or global WM changes?

Fronto-parietal involvement in ageing-related task switching changes

Madden et al., *Neuropsychol Rev 2009;* Gold et al., *Neurobiology of Aging*

- Frontoparietal white matter changes linked to age-related differences in task-switching
- However, did not examine whether diffuse white matter differences could account for effect

Role of white matter microstructure in age-related cognitive decline

Jolly, Michie, Bateman, Fulham, Cooper, Levi, Parsons, Rennie, Karayanidis.

Participants

- 35 Healthy older adults
- 35 Mild ischaemic attack

Expt tasks with ERPs

- **Cued-trials task-switching**
- Stop-signal

Imaging

Siemens 3T Verio

- T1 structural (MPRAGE)
- Fluid Attenuated Inversion Recovery (FLAIR)
- **Diffusion Weighted Imaging (DWI) sequence**

Neuropsych measures

- WASI, MoCA
- WMS – LM
- Digit Span
- CANTAB (IED, SWM, Stockings, SSP, PRM)

Functional Measures

- Functional Assessment Questionnaire
- Geriatric Depression Scale
- SF-36
- DASS-42

- **Test**
- Re-test @ 20-24mo

Role of white matter microstructure in age-related cognitive decline

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Measure	Mean (SD)
Age (yrs)	66.79 (9.54)
FSIQ	111.64 (14.60)
MoCA	25.97 (3.11)

Clinical profile	Yes	No
Vascular risk factors present	39 (56%)	31 (44%)
Hypertension	27 (39%)	
Hypercholesterolemia	21 (30%)	
Atrial fibrillation	11 (16%)	
Multiple vascular risk factors	24 (34%)	

Cognitive domains

Working memory

Digit span (WAIS-IV)

Spatial span (CANTAB)

Spatial working (CANTAB)

Episodic memory

Logical memory (WMS-IV)

Pattern Recognition memory (CANTAB)

Executive Function

Stockings of Cambridge (CANTAB)

Intra-extra dimensional set shift (CANTAB)

Processing speed

Choice RT

Letter classification task

Number classification task

White matter tractography

- Siemens 3T Verio with 32 channel head coil, b = 3000, 64 directions
- Probabilistic whole brain tractography using MRTrix software to derive tractogram
- Tractogram was filtered into 18 separate white matter pathways using constraint ROI’s derived from a DTI tract atlas from John Hopkins University (JHU).

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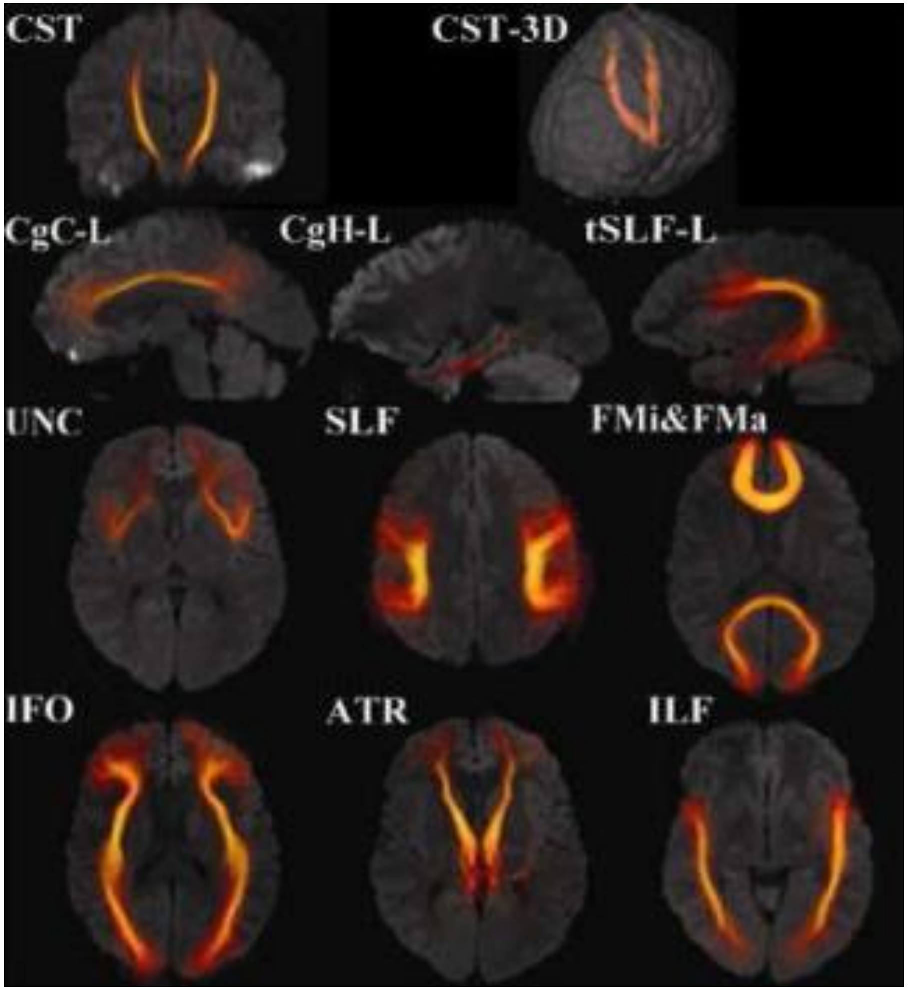


Fractional Anisotropy
directional diffusion

Mean Diffusivity
magnitude of diffusion, regardless of direction

Radial Diffusivity
Diffusion perpendicular to main fibre orientation

Axial Diffusivity
Diffusion along the main fibre orientation

Hua et al., *Neuroimage* 2008

Correlations between neuropsychological measures and age / WM

	Age	WM RaD
Working memory	**-.365*** **	**-.367*** **
Episodic memory	**-.265***	**-.411*** **
Executive function	**-.430*** **	**-.468*** **
Processing speed	**-.494*** **	**-.676*** **

*p<.05, **p<.01, ***p<.001

Eliminated when partialling WM Rad

Retained when partialling Age

- Performance in all cognitive domains was associated with both age and all WM measures
- Strongest effects with Radial Diffusivity

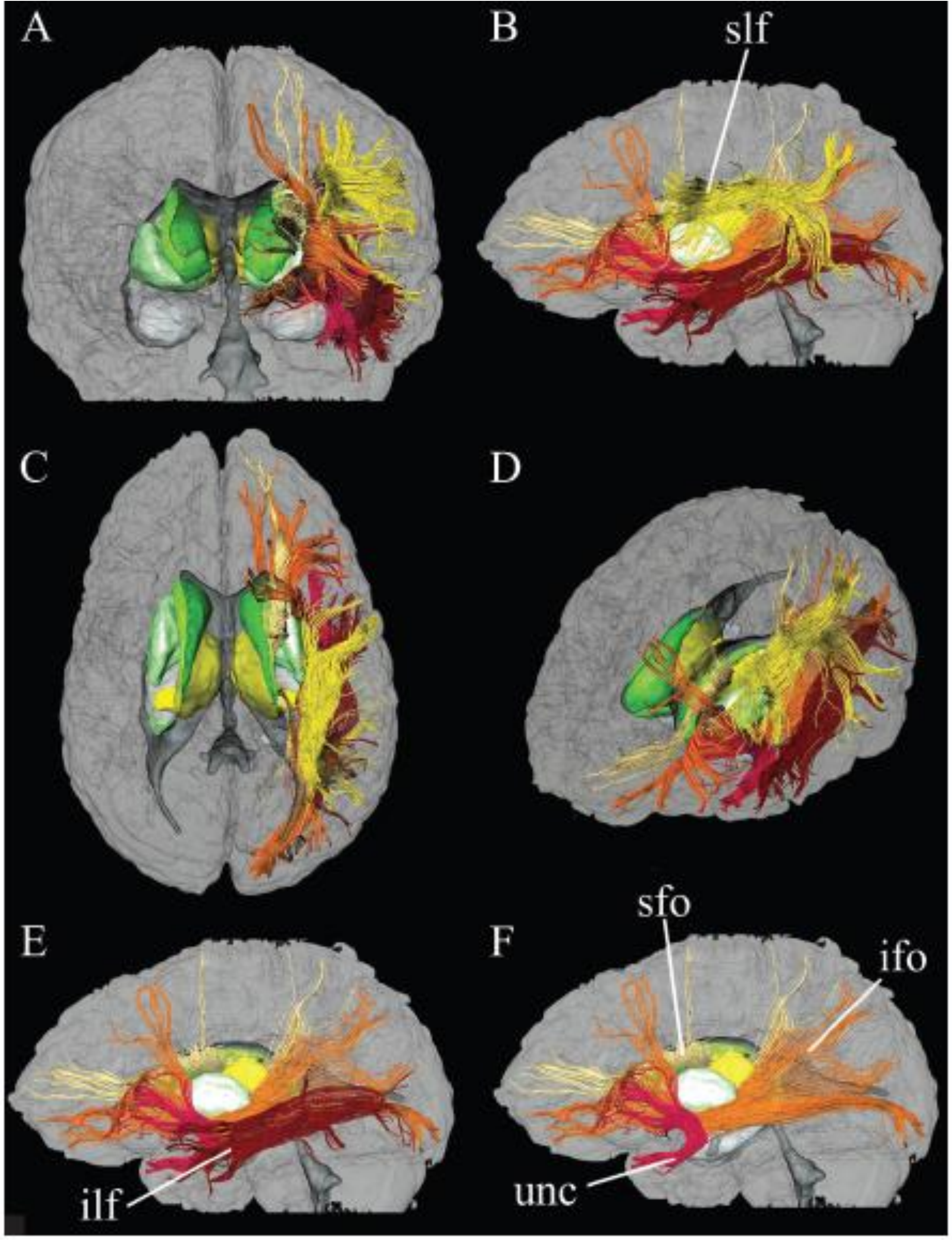
Influence of diffuse vs regional white matter on mixing-cost

Strongest effects in

MIXING COST	Total WM	IFOL	ILFL	SLFL
Error (incongruent)	.503***	.520***	.534***	.523***
Error (neutral)	.351**	.350**	.343**	.336**
RT (incongruent)	.290**	.339**	.365**	.341**
RT (neutral)	.415***	.470***	.489***	.466***

***p<.01, ***p<.001*

IFOL = Inferior fronto-occipital fasciculus – left
ILFL = Inferior longitudinal fasciculus – left
SLFL = Superior longitudinal fasciculus – left



Wakana et al., Radiology 2005

IFO: Inferior fronto-occipital fasciculus

direct pathway connecting occipital, posterior temporal, and orbito-frontal areas

ILF: Inferior longitudinal fasciculus

long association fibres running the length of occipital and temporal lobes

SLF: Superior longitudinal fasciculus

long association fibres connecting frontal and parietal lobes

Influence of diffuse vs regional white matter on mixing-cost

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RT mixing cost effects remained significant when controlling for total WM

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Conclusions

- Age-related decline in task switching performance is mediated by changes in white matter microstructure
- Stronger associations between RaD in IFO, ILF, SLF pathways and mixing cost
- RaD variability in older samples is consistent with demyelination changes
- These WM changes
  - Mediate relationship between age and task-switching performance
  - Remain significant even when controlling for total WML volume
  - Are associated with variability in intracranial arterial pulsatility, especially in the presence of cardiovascular risk factors *(Jolly et al, Frontiers Hum Neurosci 2013)*

Is the rate of age-related decline of cognitive control ability related to changes in structural integrity of white matter

Karayanidis, Jolly, Rennie, Michie, Bateman, Fulham, Cooper, Levi, Parsons

Participants

- 20 Healthy older adults
- 8 Mild ischaemic attack

Expt tasks with ERPs

- **Cued-trials task-switching**
- Stop-signal

Imaging

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Functional Measures

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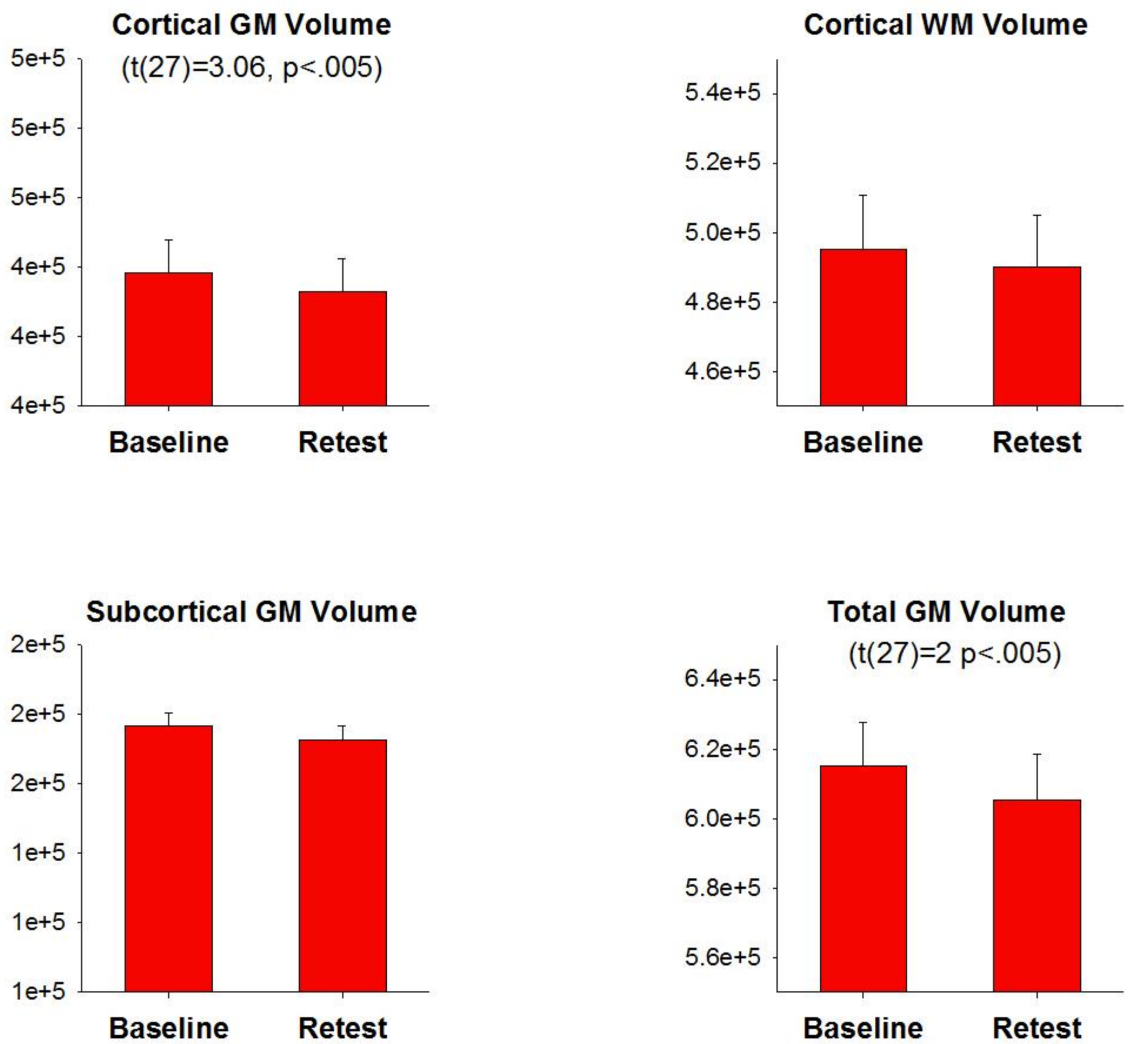
- **Test**
- **Re-test** @ 20-24mo

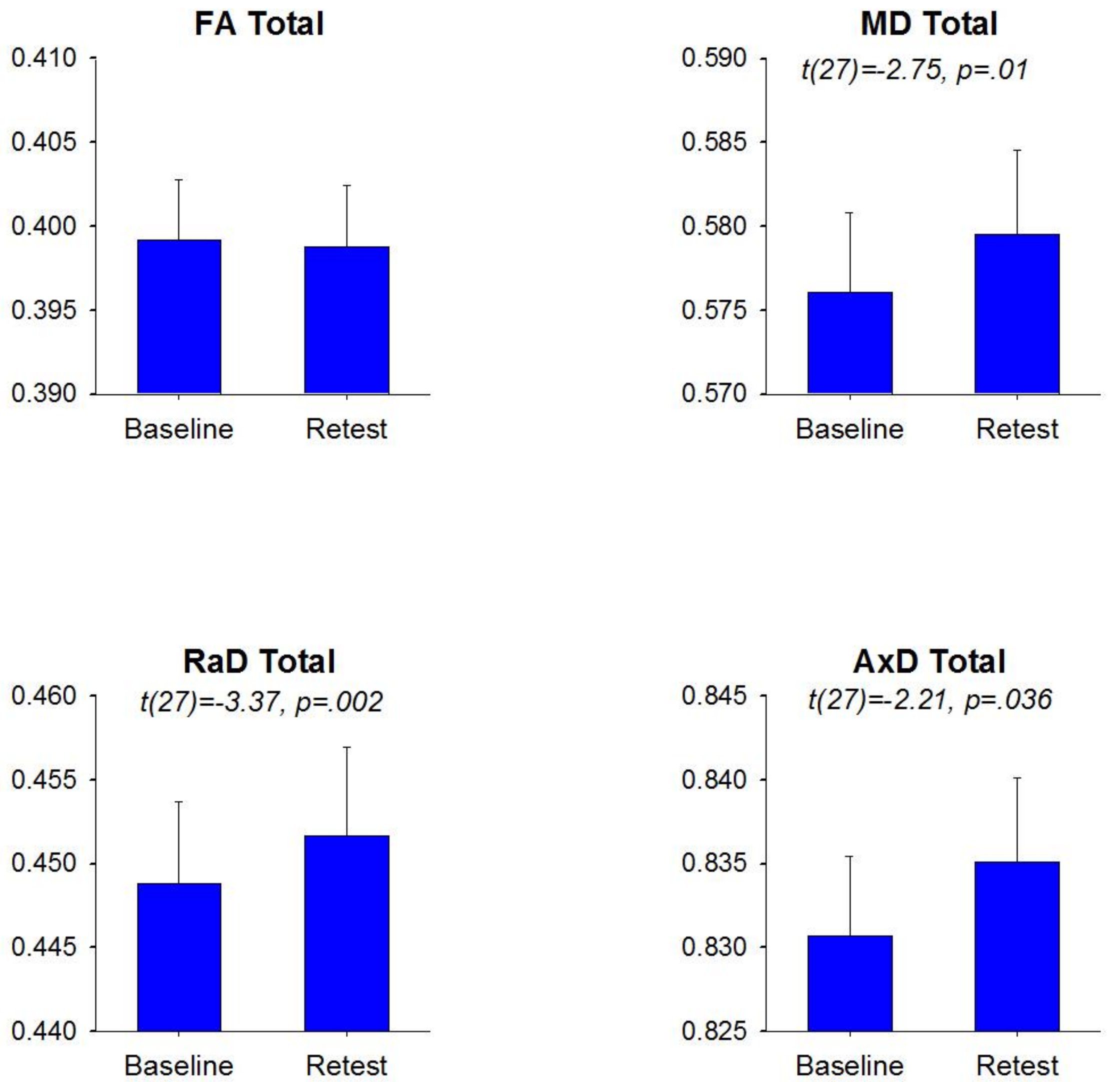
Participants

	Full Sample	Time 1
n	70	28
Female	35	12
Age	65.7 +/- 9.3 y	65.4 +/- 8.9
MoCA	25.97 (3.11)	27.0 +/- 2.5
FA WMTotal	0.398 +/- 0.02	0.399 +/- 0.02
RaD WMTotal	0.451 +/- 0.03	0.448 +/- 0.03

Brain volumes



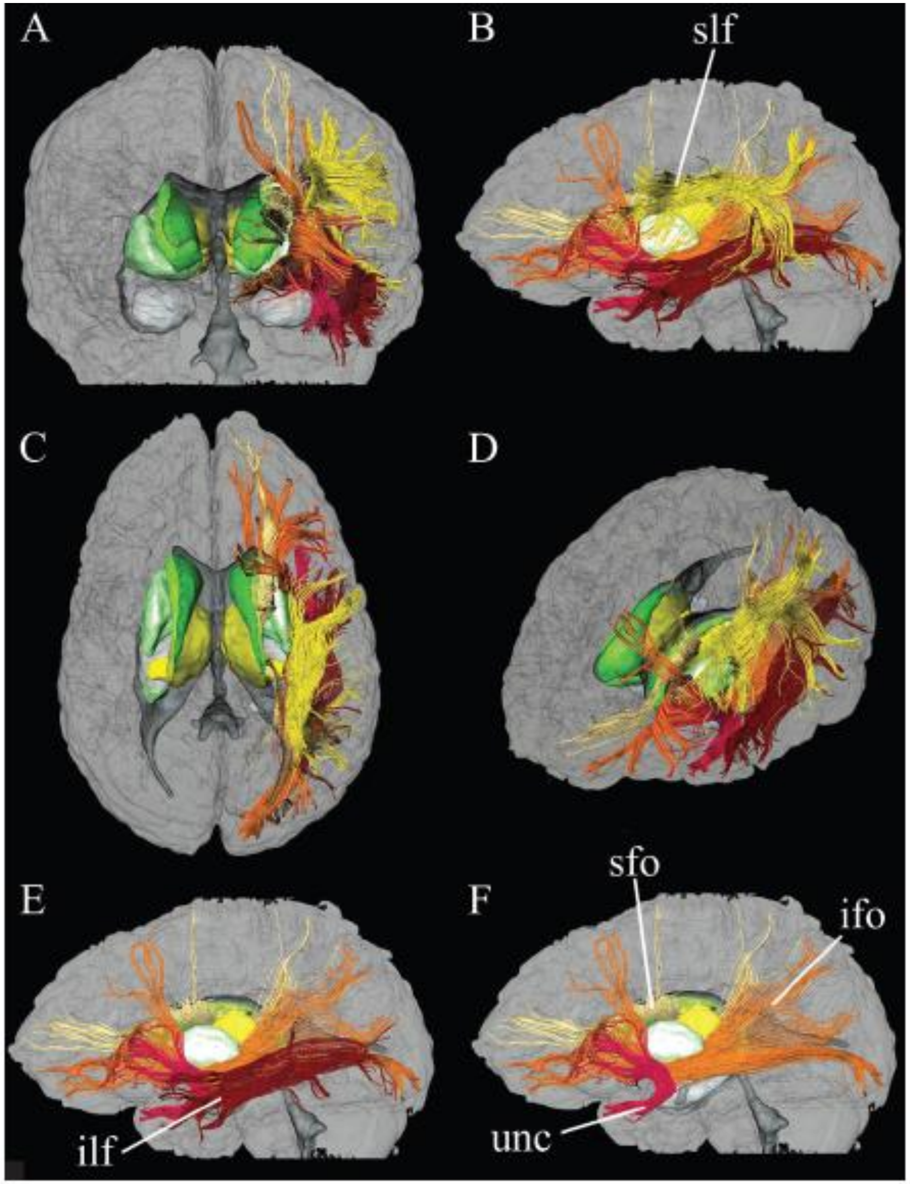
Whole brain DTI measures



Pathway-specific DTI measures

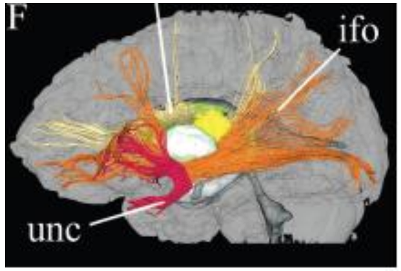
Changes from Baseline to Retest

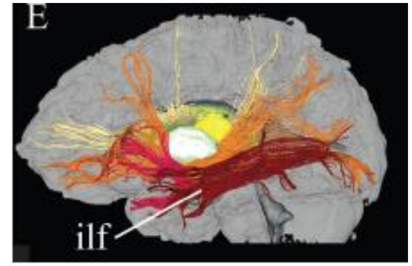
0.01		FA	MD	Ax	RaD
ATR	L				
ATR	R				
CCFma			**0.007**	0.036	0.054
CCFmi					
CST	L				
CST	R				
CgCin	L		0.015	0.015	
CgCin	R			0.048	
CgHi	L				
CgHi	R				
IFO	L		**0.001**	**0.002**	**0.005**
IFO	R		**0.001**	**0.001**	**0.001**
ILF	L		**0.005**	**0.012**	0.029
ILF	R		**0.002**	**0.001**	0.021
SLF	L		0.011	**0.003**	
SLF	R		0.015	**0.001**	
UNC	L		0.024	0.014	
UNC	R				
TOTAL			**0.010**	**0.002**	0.036

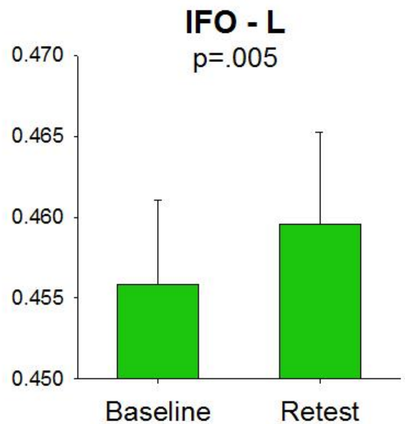


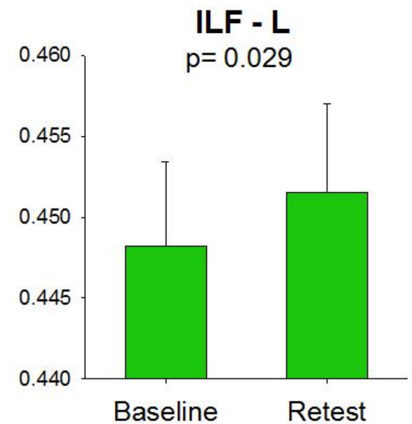
Wakana et al., Radiology 2005

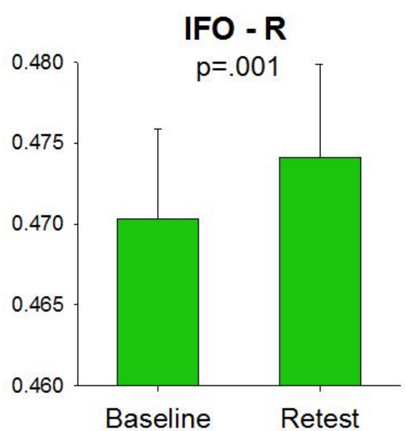
Radial Diffusivity

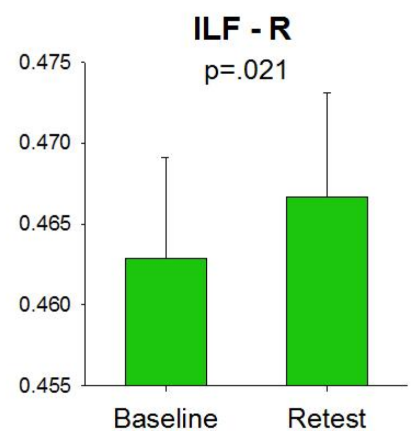




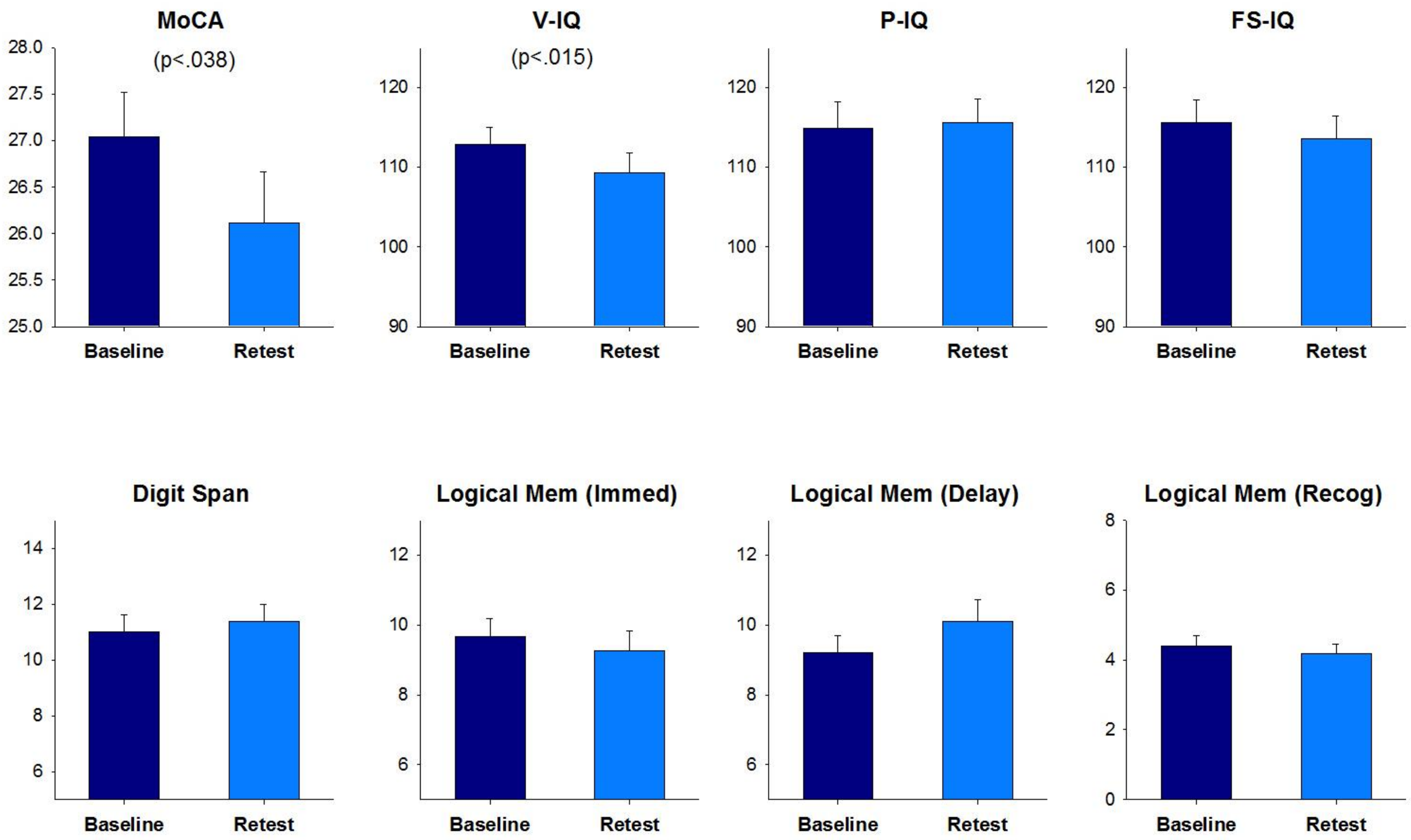




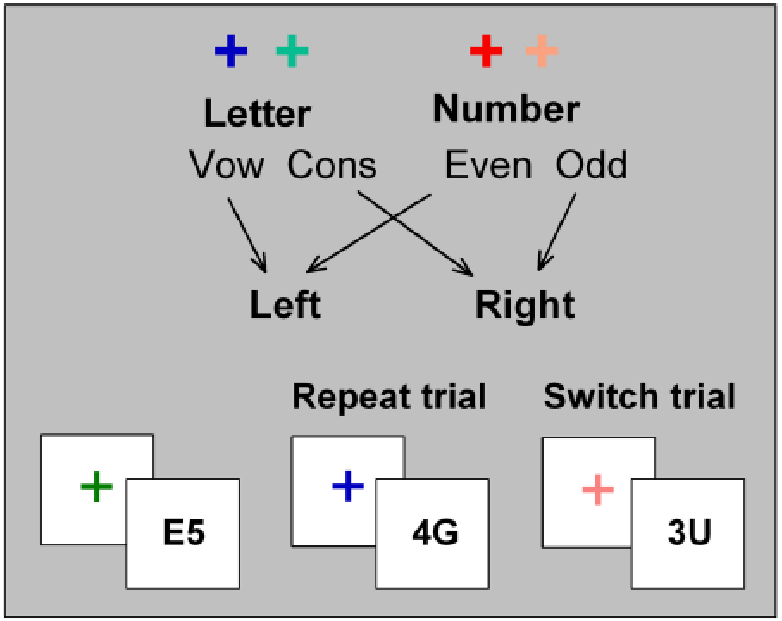


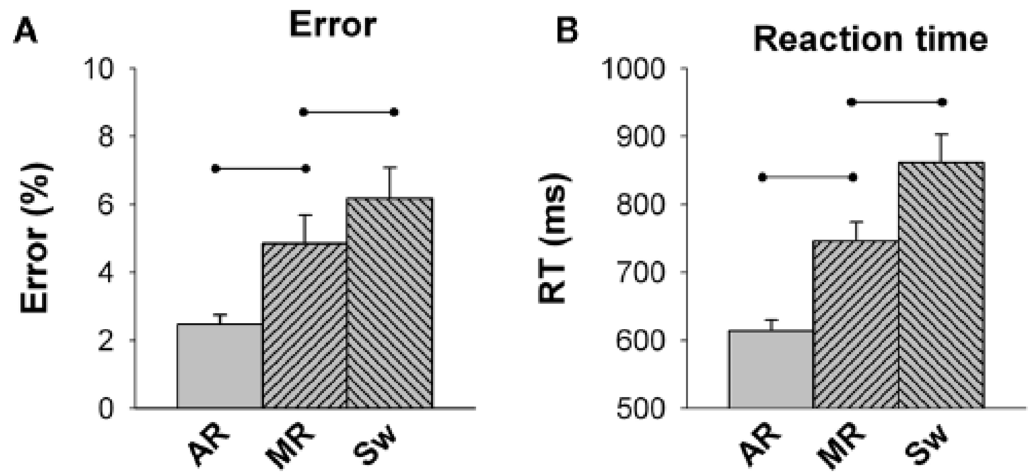


General Functioning



Task-switching paradigm





Mixing Cost =

AR= all-repeat: Letter – *Letter* – *Letter* – *Letter*

MR= mixed-repeat

Switch Cost =

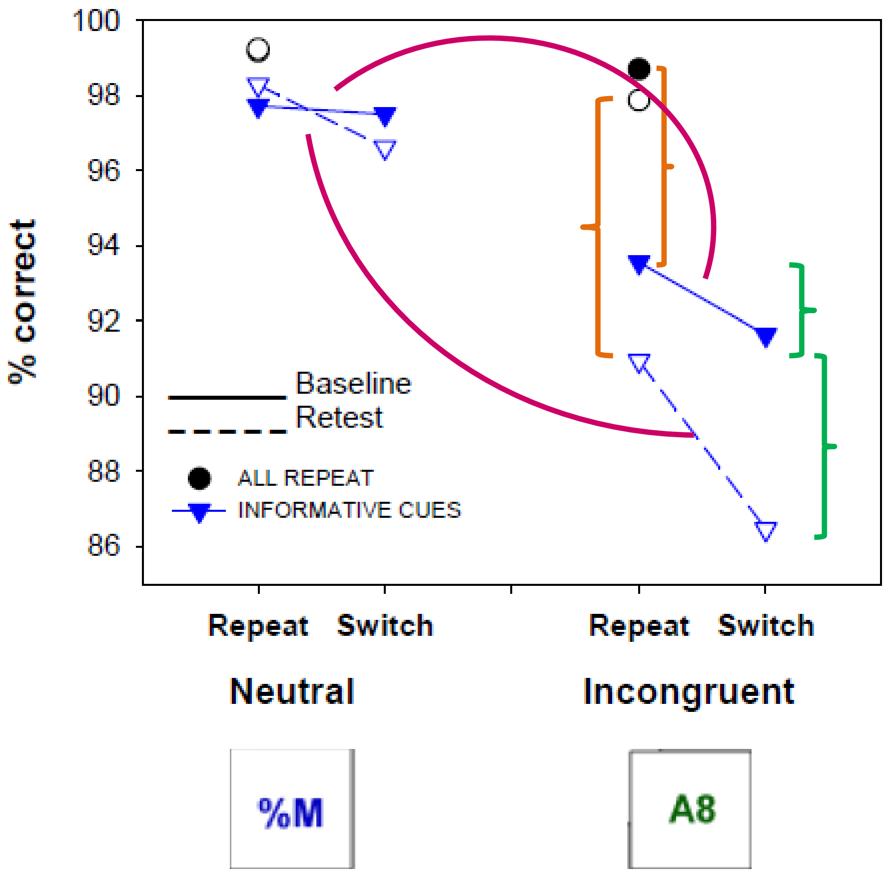
: Letter – *Letter* – *Number* – *Letter* – *Number* - *Number*

Sw = Switch

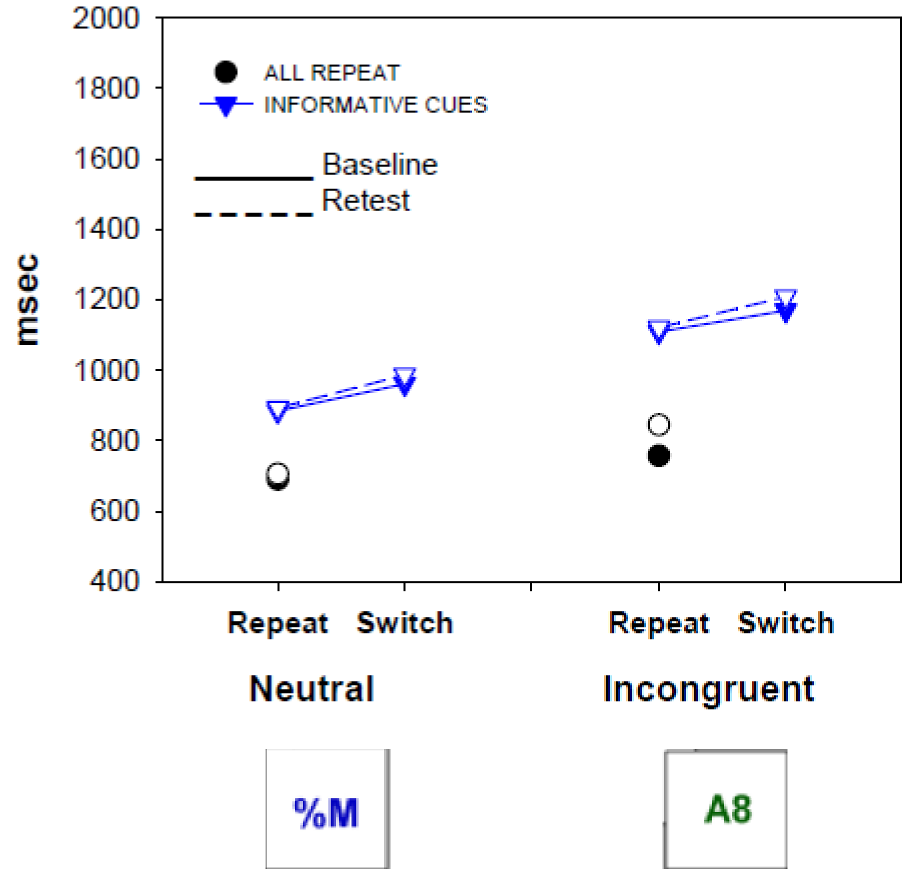
Task-switching: *Informative Cues (prepared)*

1. Greater mixing cost | **2. Greater switch cost** | **3. Greater congruence cost**

Accuracy: Informative Cues



RT: Informative Cues



Correlations between cost and WM RaD measure

Error Cost	Baseline			Retest		
RaD	Mixing	Incongr	Switch	Mixing	Incongr	Switch
TotalWM						
IFO-L	.457**			.468**	.444*	
IOF-R	.503**			.435*		
ILF-L	.475**			.435*		
ILF-R	.531**					
SLF-L						
SLF-R						

** p<.01; all remain significant when controlling for total WM FA or age

Correlations between mixing cost and WM RaD measure

Error Cost	Baseline	Retest	Change
RaD	Mixing	Mixing	Mixing
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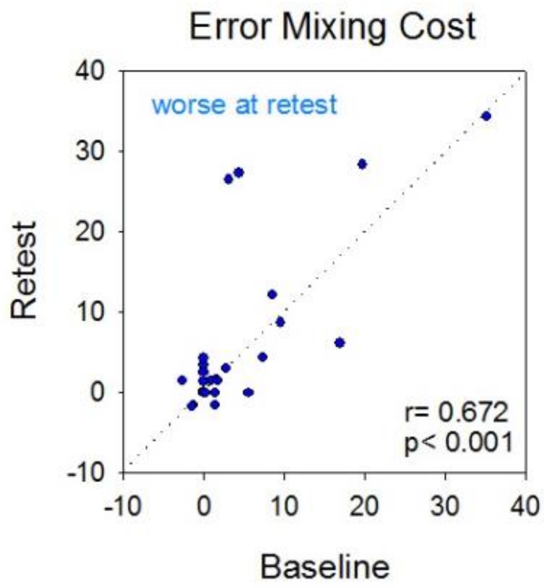
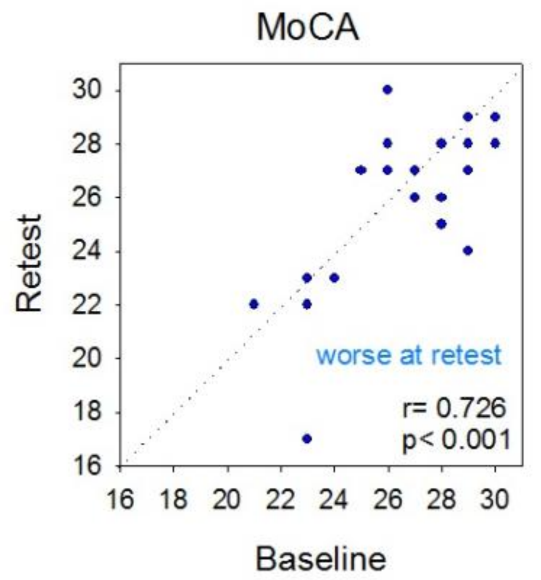
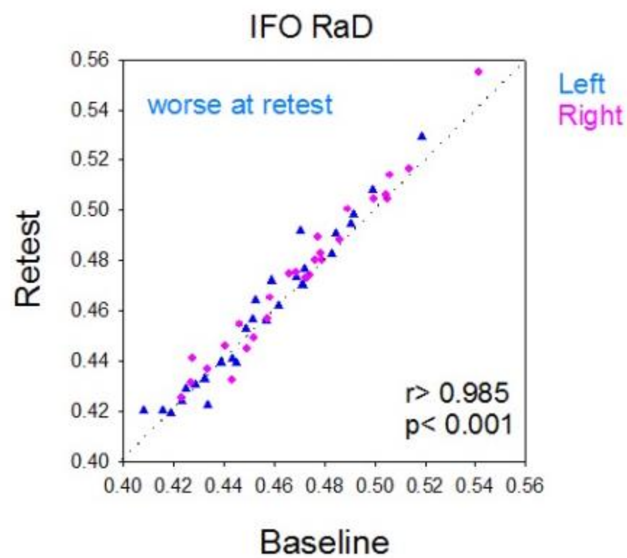
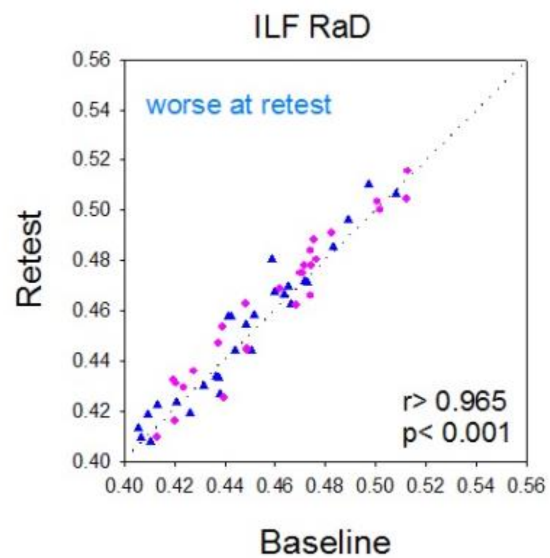
Baseline to Re-test

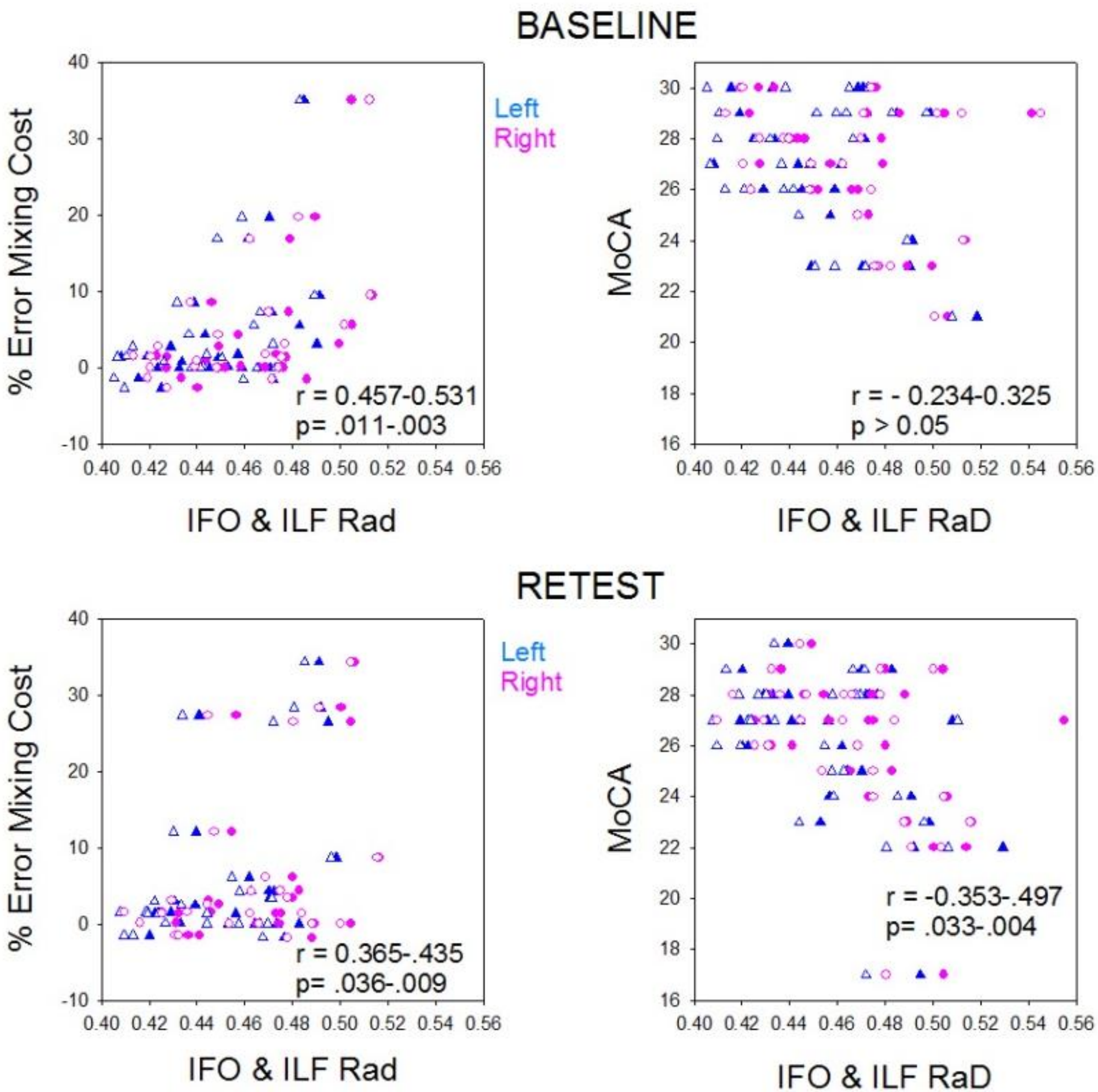








WM RaD with MoCA / Mixing Cost



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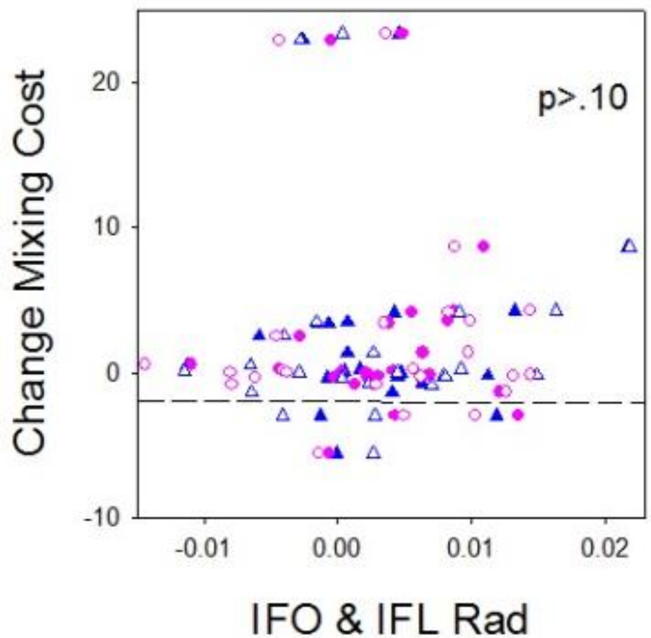

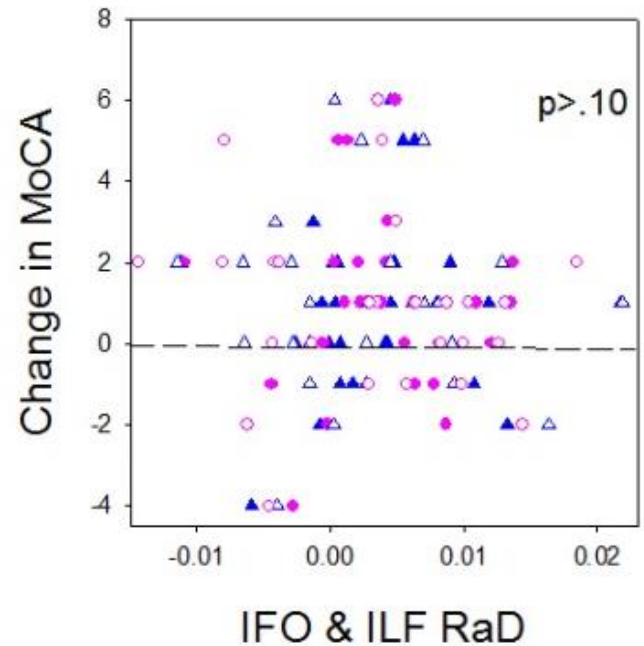

Summary

Over 24 months:

- Significant decline in global functioning measures (MoCA), but not in IQ / Memory / WM
- Under prepared task conditions (Informative cues) and with incongruent stimuli, baseline to retest showed
  - Reduced sustained control (mixing cost)
  - Reduced proactive control (switch cost for informative cues)
  - Reduced reactive control (congruence cost for informative cues)

  All affecting primarily response accuracy.
- Substantial variability in size of change across participants

Summary

Over 24 months:

- Reduced WM organisation in pathways connecting occipito-temporal-frontal and parieto-frontal areas
  - Effects larger for RaD consistent with myelination changes
  - Measure very consistent within individuals across time (baseline to retest)

Summary

At each test time:

- RaD in these long anterior-posterior tract consistently correlated with error mixing cost and less so with MoCA

BUT:

No correlation between change in MixCost/MoCA and change in WM RaD

- Obvious culprit – sample size?
- Alternative more sensitive behavioural measures – latent parameters to differentiate between drift rate (Madden) and threshold (Ratcliff) changes?

PRIORITY RESEARCH CENTRE
TRANSLATIONAL NEUROSCIENCE AND MENTAL HEALTH

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NSW GOVERNMENT Health Hunter New England Local Health District

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ILF-R	-.575**					
SLF-L						
SLF-R						

** p<.01; all remain significant when controlling for total WM FA or age

Stronger pattern consistent with RaD;