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Age-ility Project
Flexible minds for life
www.age-ility.org.au
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Age related changes in white matter pathways underlying response threshold adjustment

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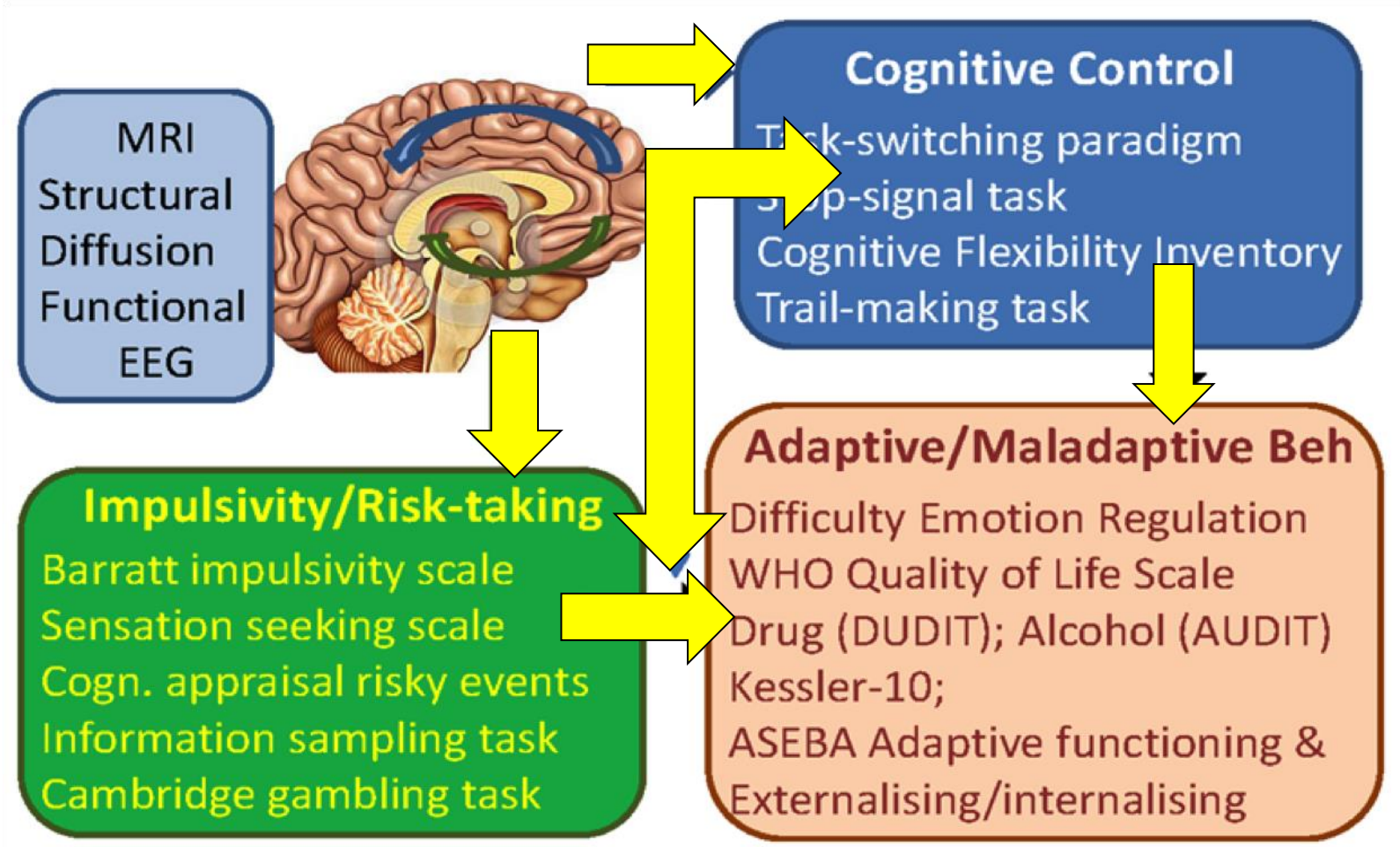
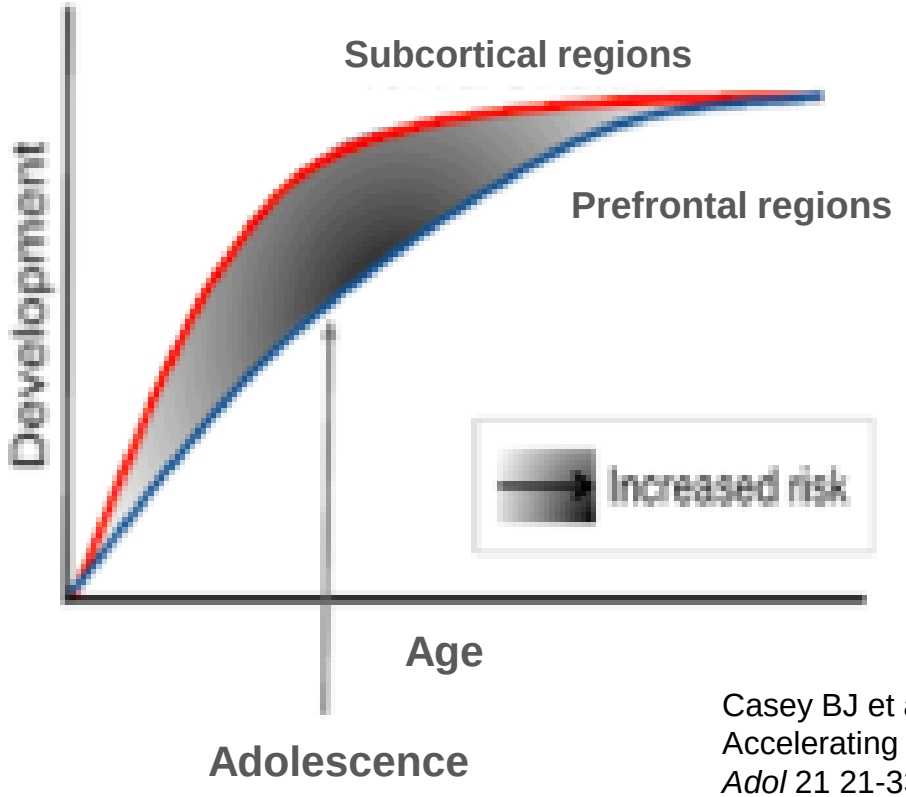
Priority Research Centre for Translational Neuroscience and Mental Health

This research is supported by:
Australian Government Australian Research Council
HMRI Hunter Medical Research Institute
In collaboration with
UNSW
Concordia University

Individual variability in healthy young adults



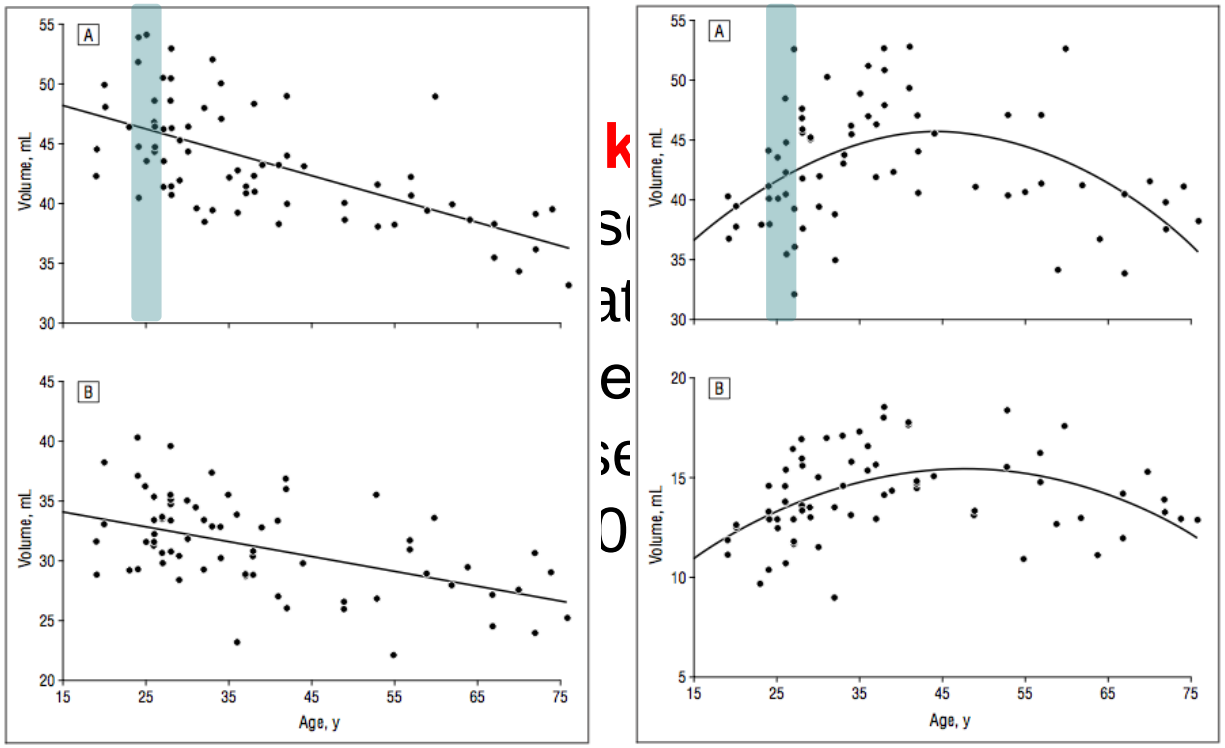
Neurobiological dual-systems model of adolescent risk-taking



Casey BJ et al. (2011) Braking and Accelerating of the Adolescent Brain. *J Res Adol* 21 21-33.

‘Top-Down Cognitive Control’: Maturation of prefrontal brain networks is protracted, with grey matter pruning and increases in myelination effecting white matter density and connectivity (Gogtay, N., Thompson P.M., 2010; Paus, T., 2010)

Grey Matter **White Matter**



‘Bot **k** ward-
sens s(nce is
cons at prefrontal
‘con e ng bottom up
cont se alvan, A. et
al., 2 0

Bartzokis et al., 2001

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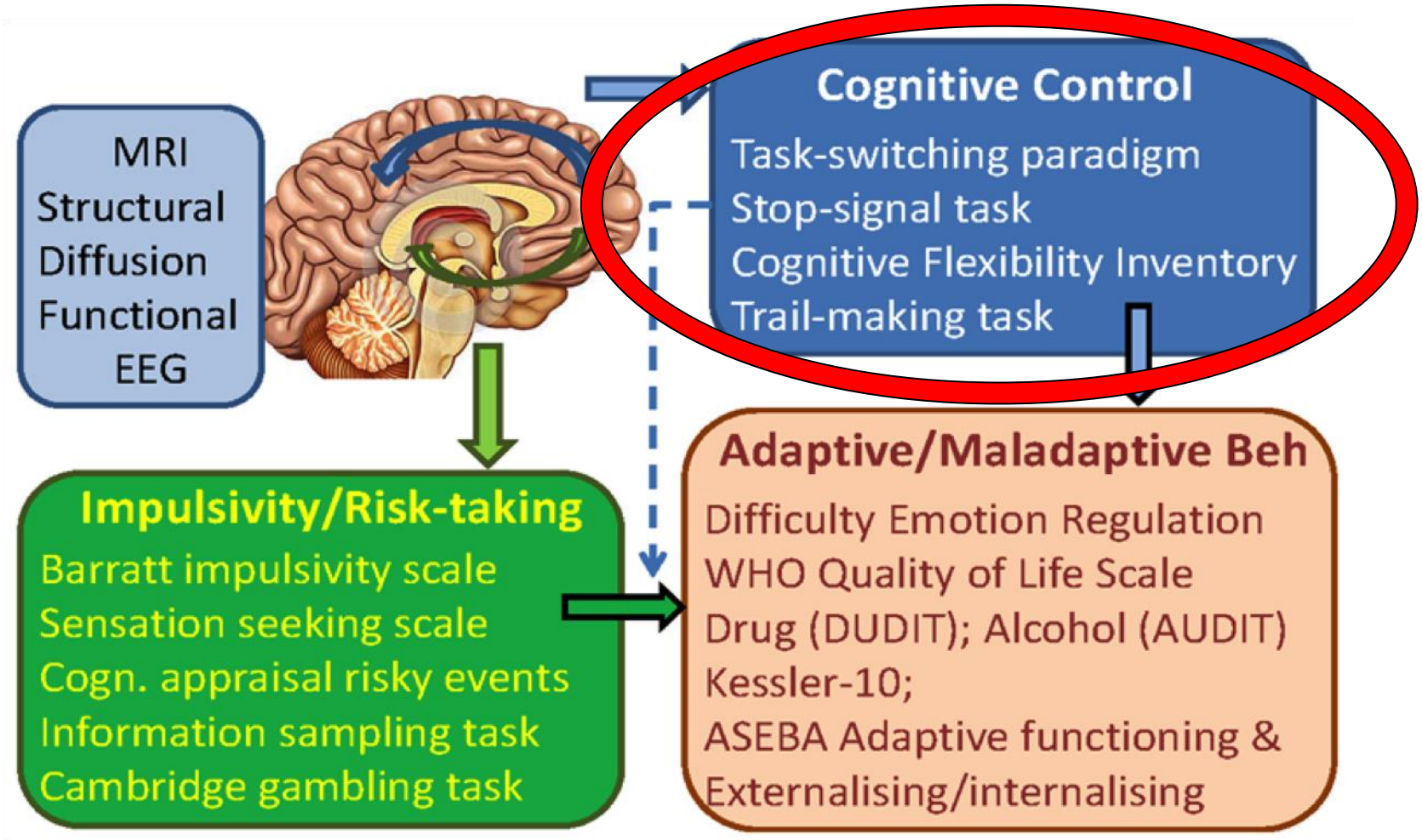
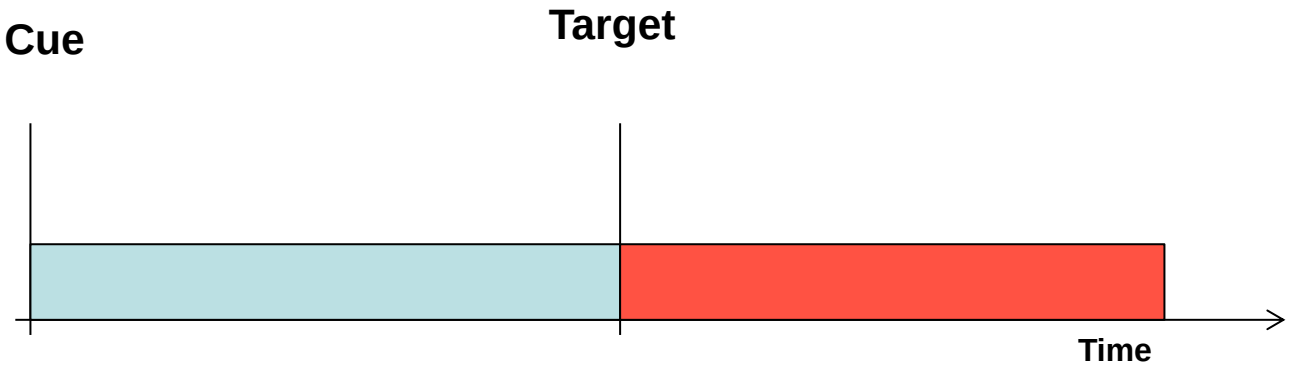


Dual mechanism of control framework - Proactive and reactive control processes in task-switching paradigms



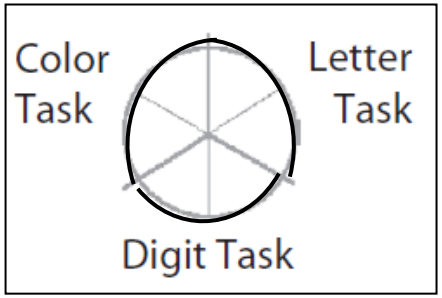
Proactive control

- advance goal setting
- task-set preparation
- WM
- Inhibition of previous task

Reactive control

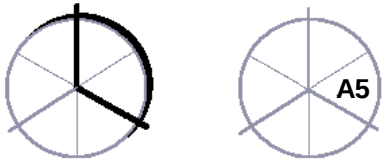
- task implementation in the presence of interference

Nicholson et al., 2006; Karayanidis et al., 2009 Mansfield et al., 2011; for review see, Karayanidis et al., 2010



TRIAL N-1

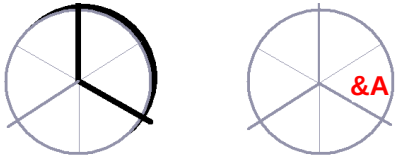
cue=letter task *vowel=left*



TRIAL N

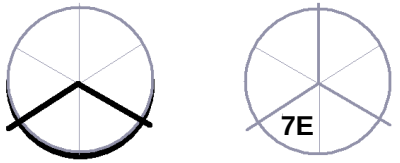
Repeat Cue

cue=letter task vowel=left



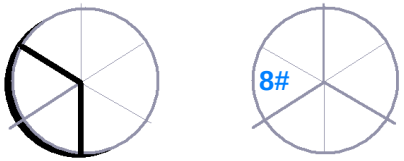
Switch-to Cue

cue=digit task odd=right



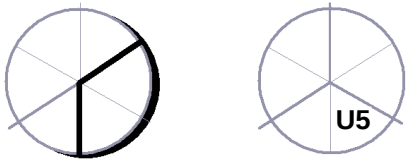
Switch-away Cue

cue=digit or color Color (green=left)



Non-informative Cue

cue=letter or digit Digit (odd=right)



Nicholson et al., 2006 Karayanidis et al., 2009 Mansfield et al., 2011

Fully vs. partially informative cues Paradigm (to/away paradigm)

MixingCosts= (WM) MixedRepeats-AllRepeats (poorer performance on repeat trials in mixed-task blocks than trials in single-task blocks (all-repeat trials))

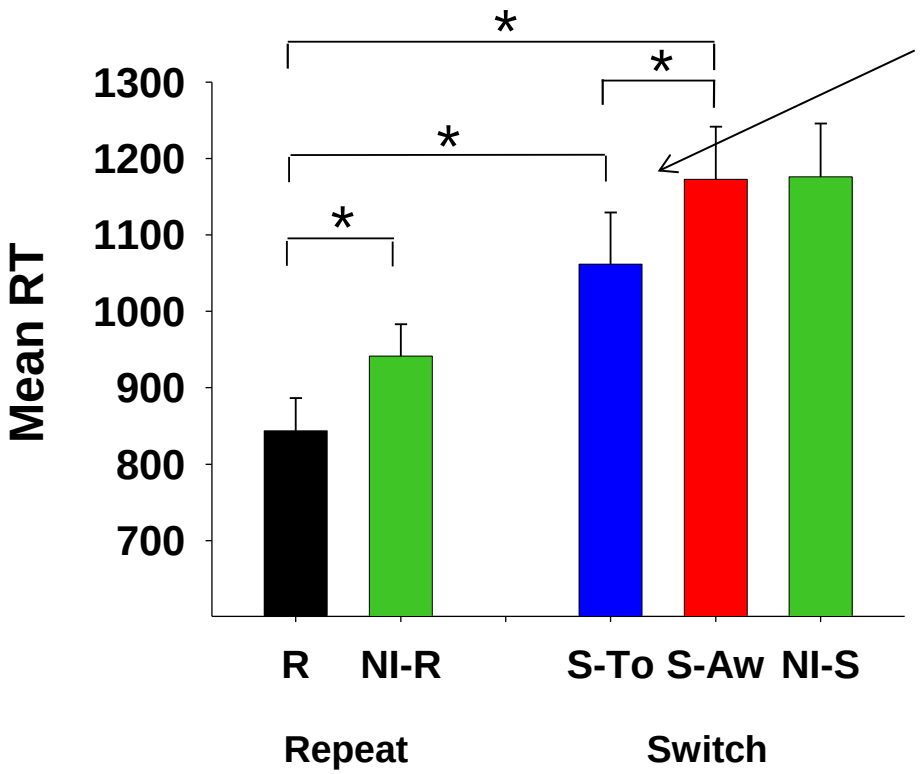
Switch to - mixed repeat = SwitchCosts (re-configuration)

Fully informative repeat
(repeat trial & task)

Fully informative switch
(switch trial & task)

Partially informative switch
(switch trial, no task info)

Non-informative
(no trial info, no task info)

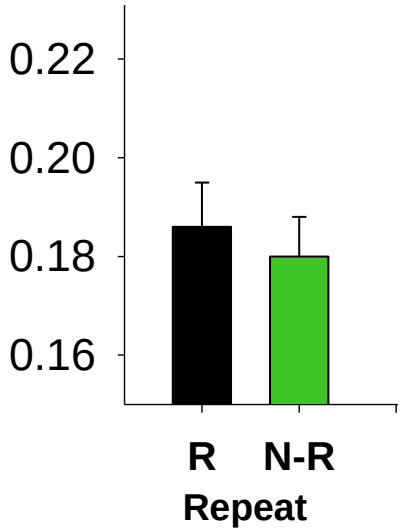


1. Switching leads to longer RTs='RT-Switchcost'
2. Informative Cues reduce this slowing

Karayanidis, Mansfield, Galloway, Smith, Provost & Heathcote 2009, *Cognitive Affective Behavioural Neuroscience*

Diffusion Model

threshold/ criterion (i.e., response caution)



iterior

ervative in switch-

erion- switch-

speed of information accumulation (i.e., drift rate)

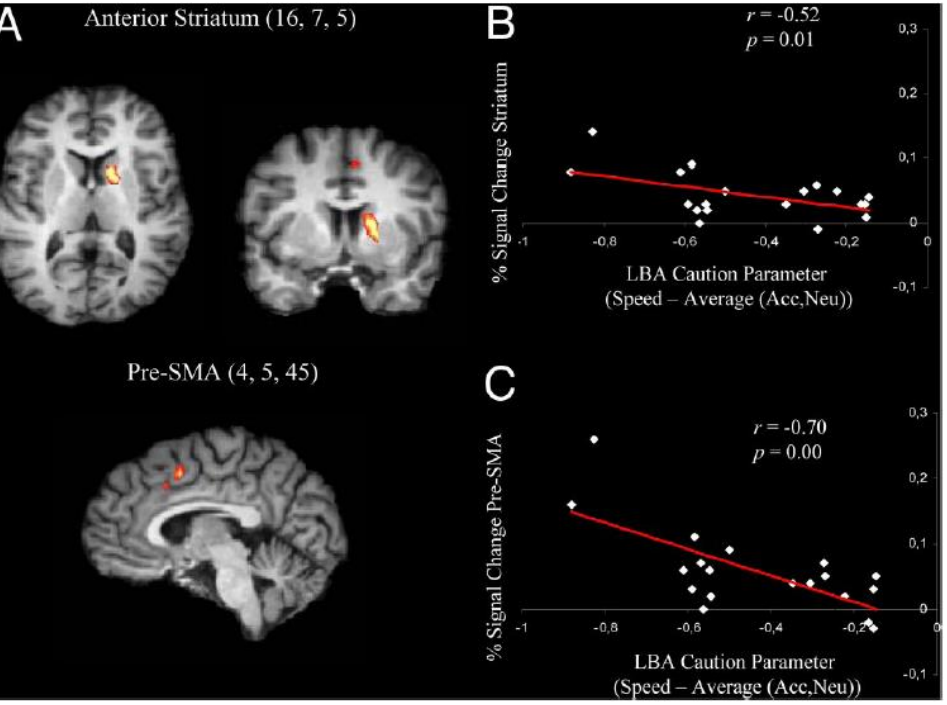
d

h

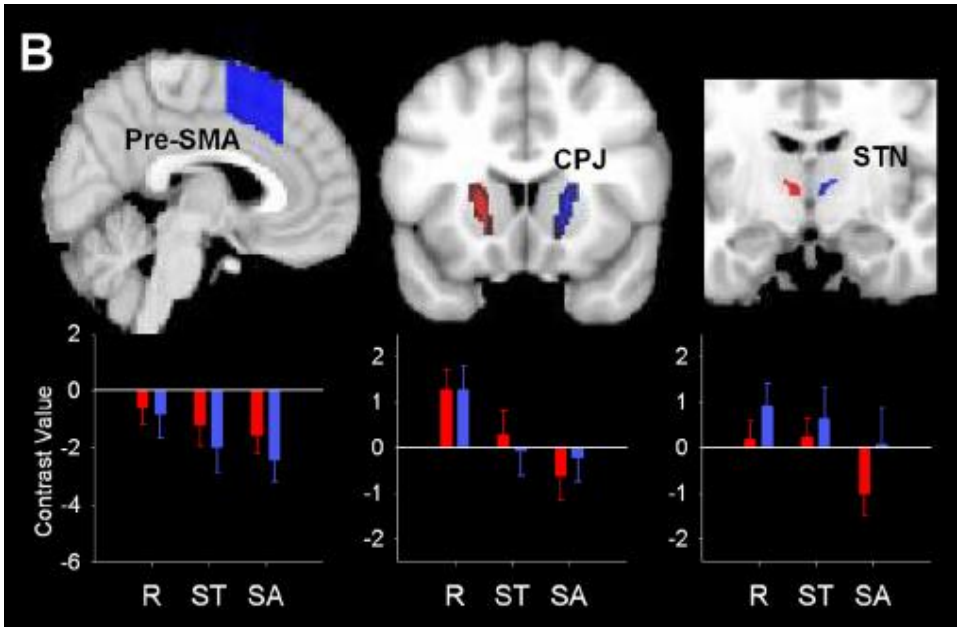
y

eld, Galloway, Smith, Provost

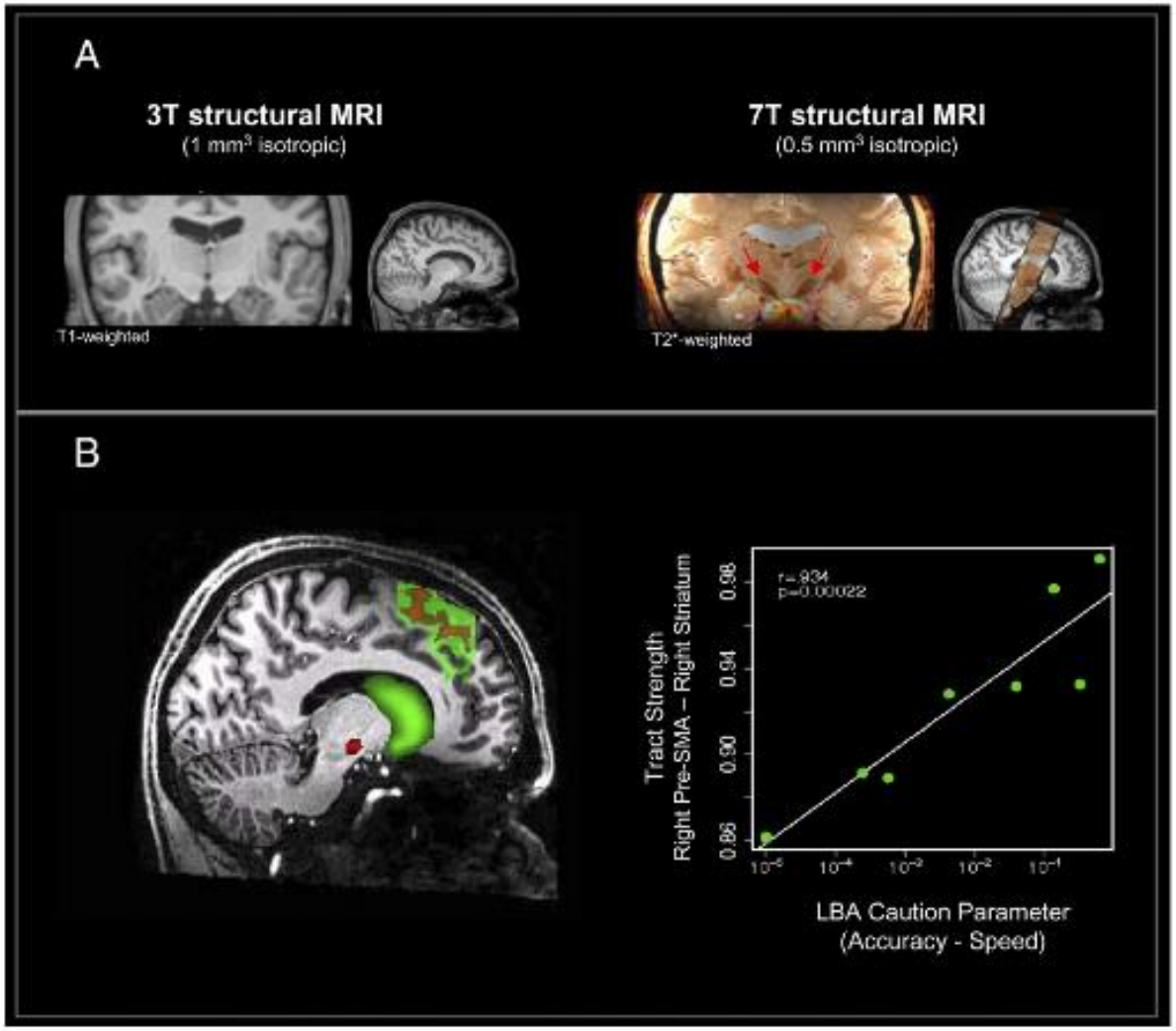
Cognitive Affective Behavioural



Forstmann et al. (2008). *Proceedings Nat Acad Sci, 105*, 17538-17542.



Mansfield et al. (2011). *The Jn of Neurosci., 31:41*, 14688-14692.



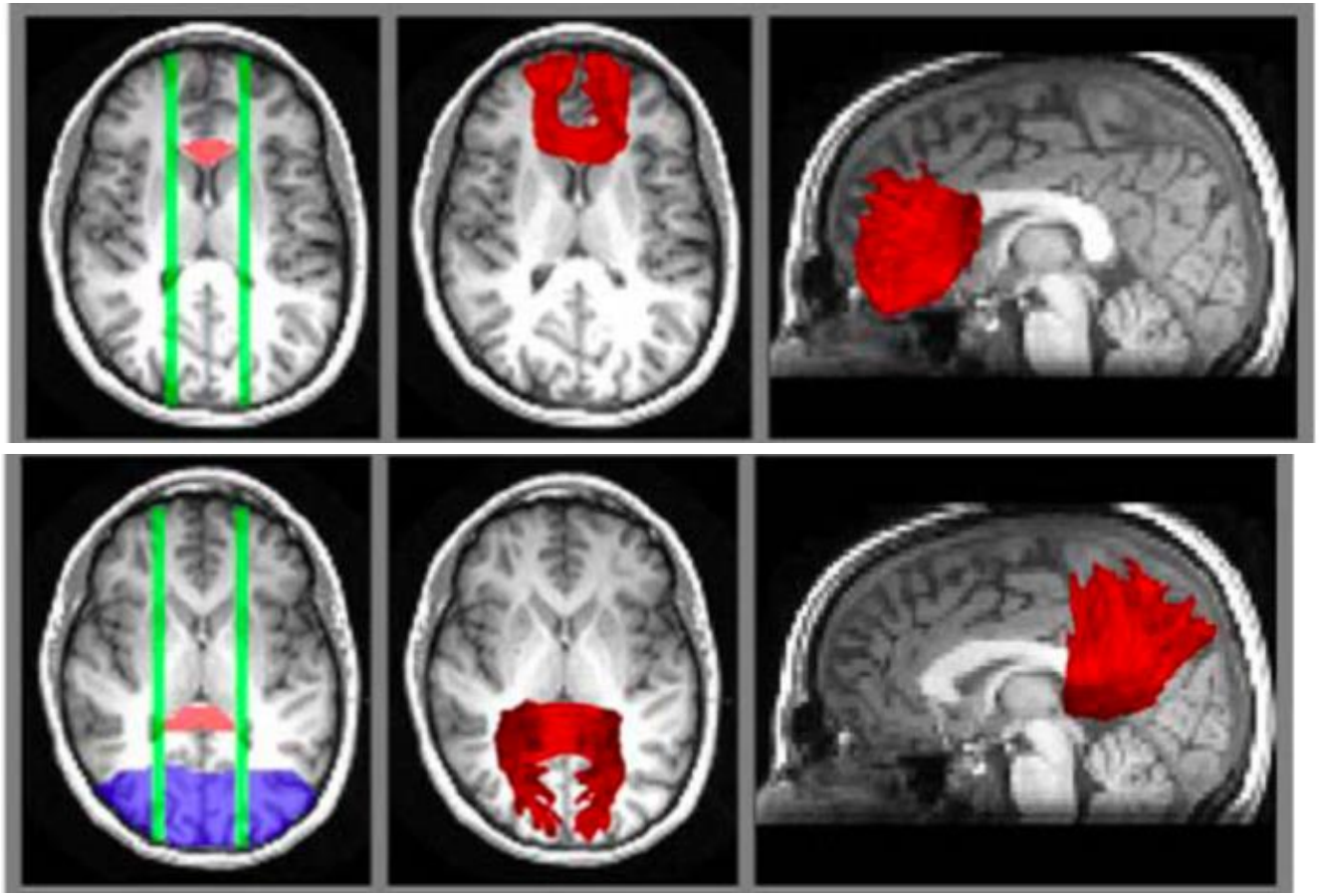
Connectivity-based seed classification:

pre-SMA projecting into the striatum (green) and STN (red)

Individual differences in tract strength between right pre-SMA and right striatum are associated with flexible adjustments of SAT.

Forstmann et al., 2010, PNAS, 107 (36):15916-20

Age-related decline in task-switching



mediated by FA in task-relevant pathways:

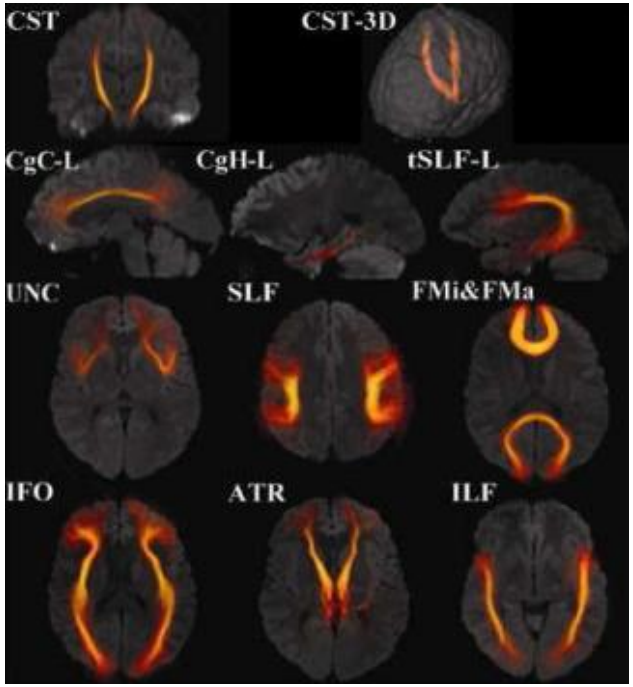
- parts of the inferior-fronto-occipital fasc.

- and inferior longitudinal fascic.

Madden et al., 2009, *J Cogn Neurosci*. 289-302.

Subsample with imaging data: N=39, 20 female, 23.85 ±5.71 yrs, **DWI Data:** 3T Siemens Skyra, b3000s/mm^2, 64 directions, (TR = 15300, TE = 108ms, FoV = 240mm, 120x120 matrix, 70 slices, 2mm, no gap). MRtrix-whole brain tractography, restricted to 18 white matter tracts* used as ROIs for calculation of DTI measures (FA, MD, RaD, Ax)

Special thanks to Todd Jolly for MRtrix-scripting!



Hua, K., et al., 2008.** ***NeuroImage 39, 336–347

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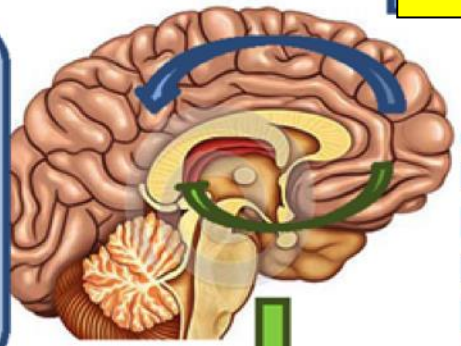
MRI
Structural
Diffusion
Functional
EEG



Cognitive Control

Task-switching paradigm
Stop-signal task
Cognitive Flexibility Inventory
Trail-making task

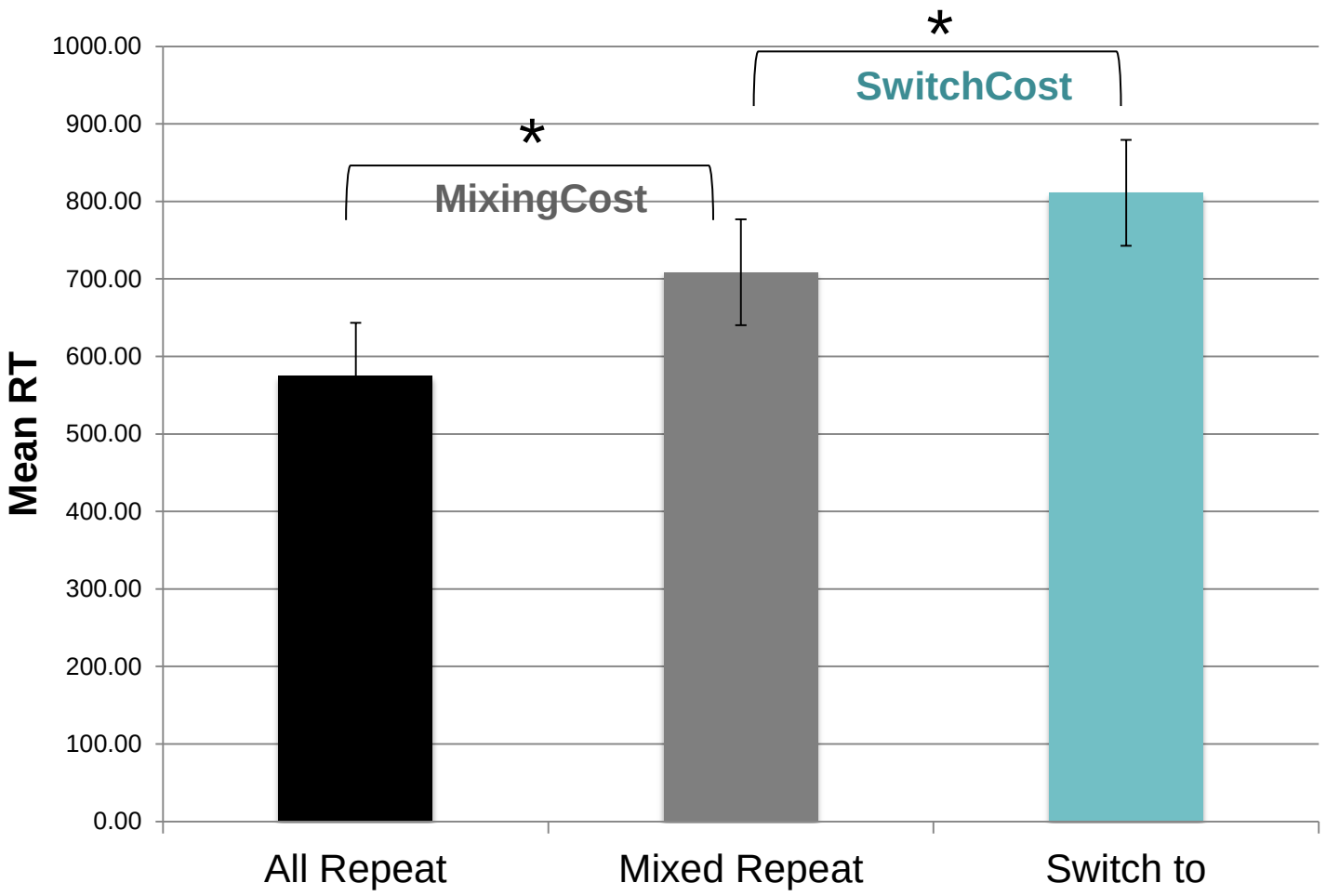
Impulsivity/Risk-taking

Barratt impulsivity scale
Sensation seeking scale
Cogn. appraisal risky events
Information sampling task
Cambridge gambling task

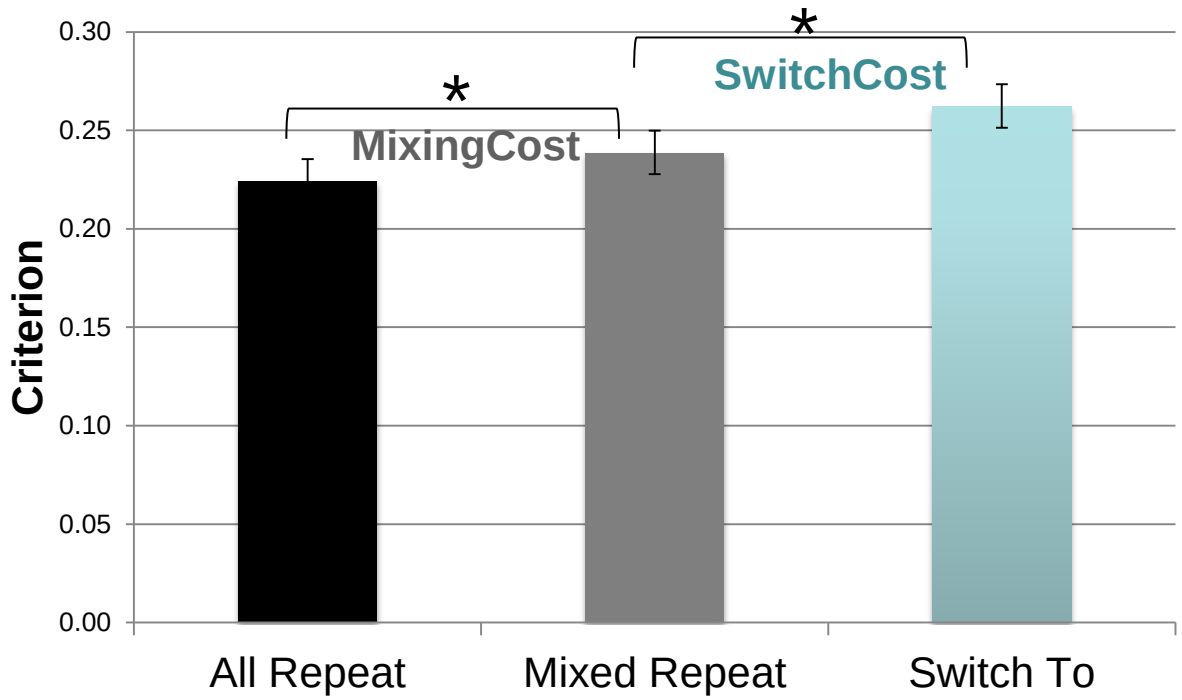
Adaptive/Maladaptive Beh

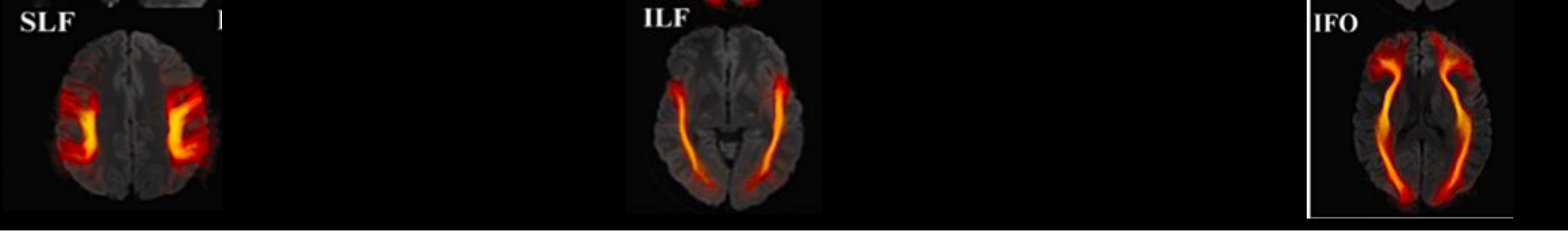
Difficulty Emotion Regulation
WHO Quality of Life Scale
Drug (DUDIT); Alcohol (AUDIT)
Kessler-10;
ASEBA Adaptive functioning &
Externalising/internalising

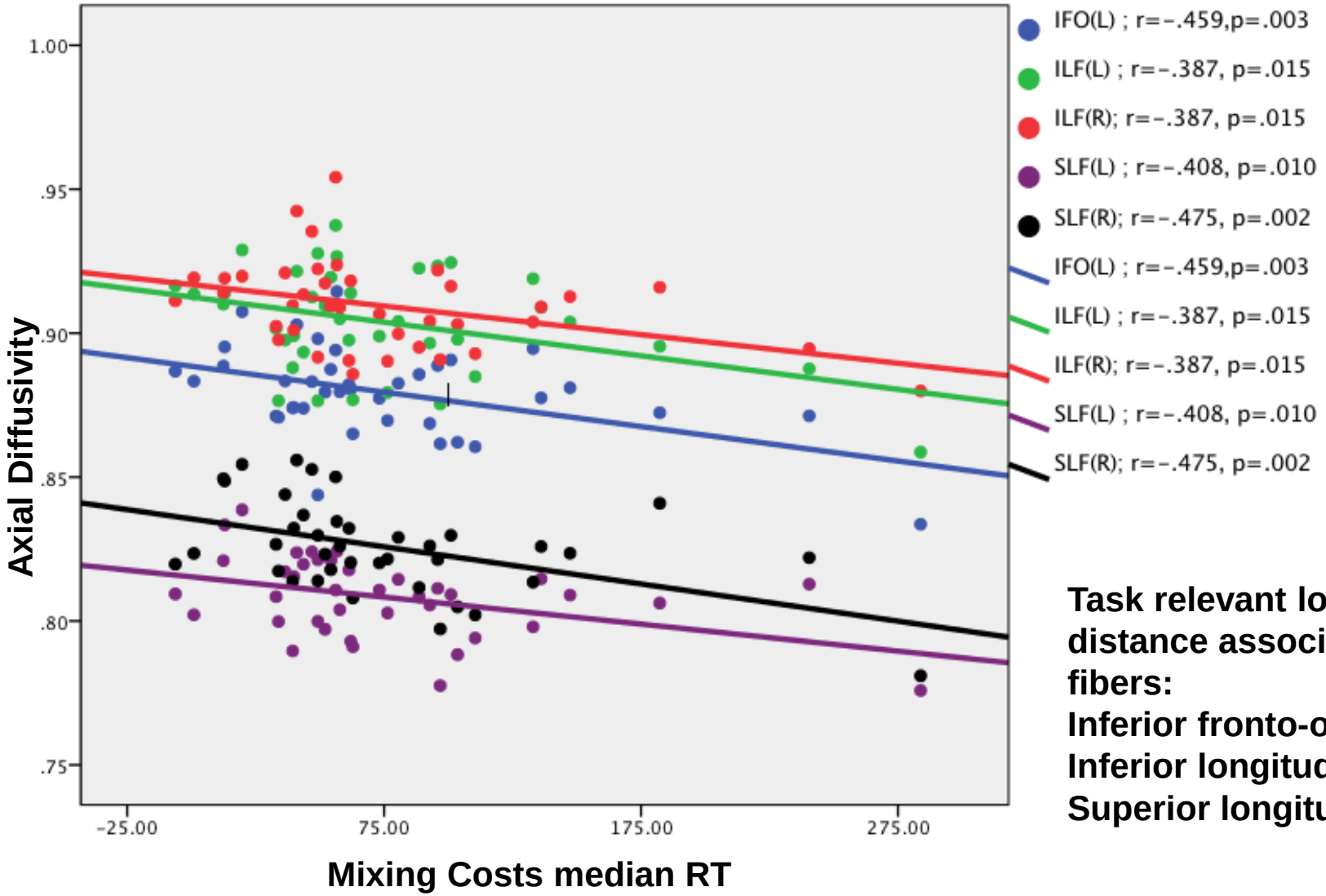
RT increases with mixing (WM) and switching (reconfiguration)



Threshold increases with mixing (WM) and switching (reconfiguration)

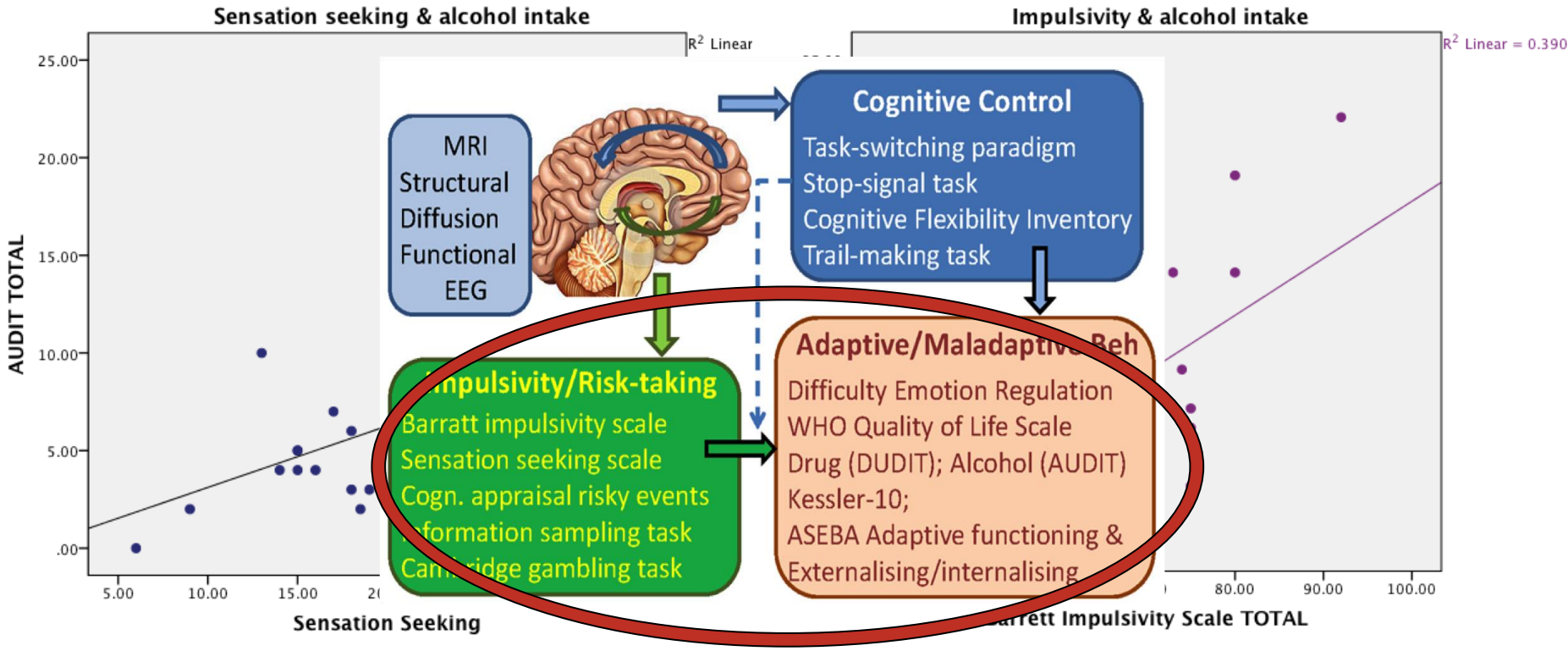






Task relevant long distance association fibers:
Inferior fronto-occipital
Inferior longitudinal
Superior longitudinal

➢ Effect of Impulsivity & Sensation Seeking on adaptive/maladaptive behaviours



r= .372, p=.030; t(29)=-2.2, p<.05

r= .624, p<.000; t(30)=-2.6, p<0.5

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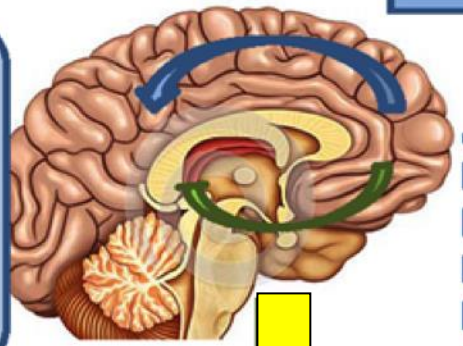

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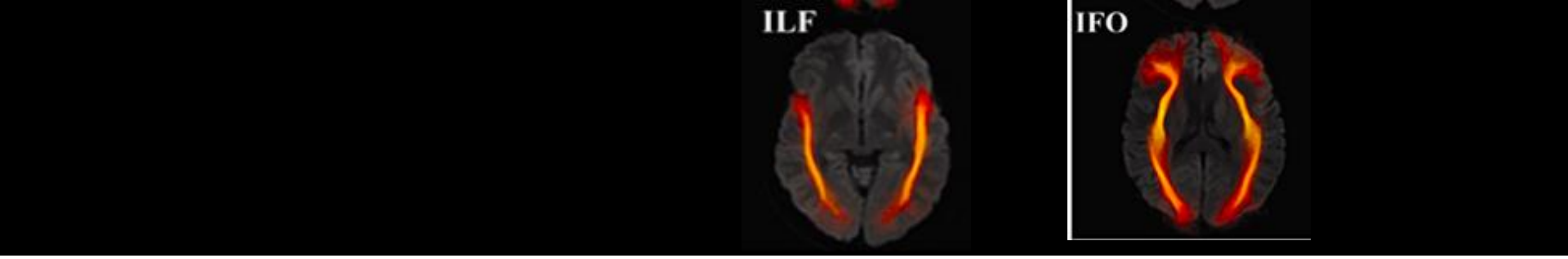
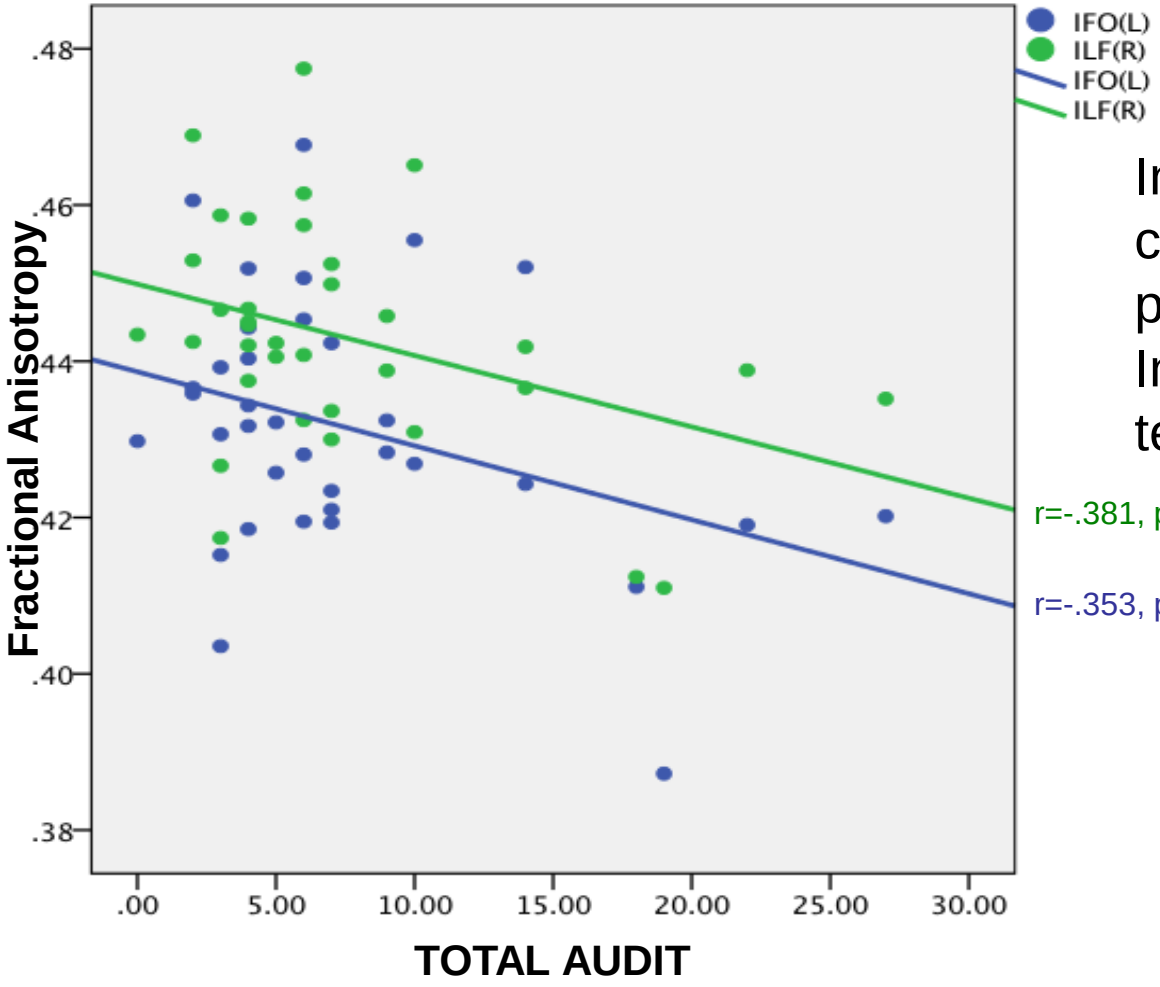


High alcohol intake is associated with low FA

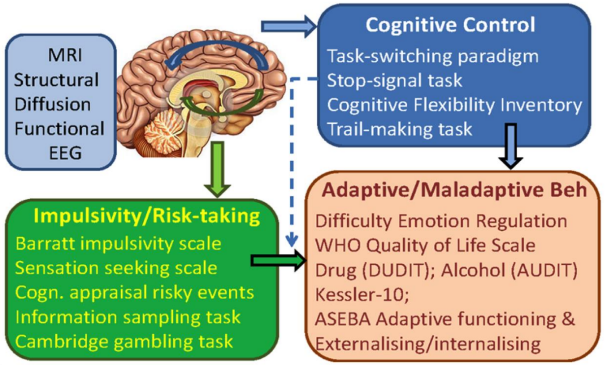


Inferior-fronto-occipital: connects frontal & posterior parts of the brain

Inferior longitudinal: connects temporo-occipital regions

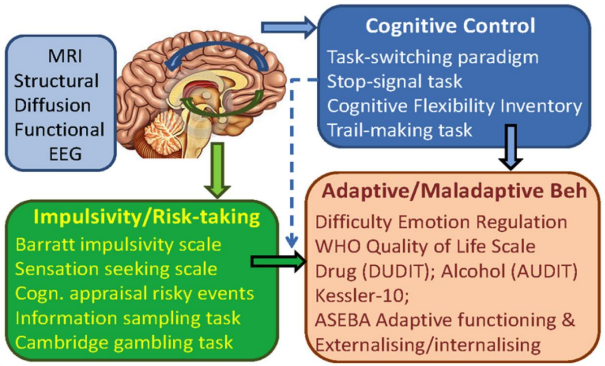
r=-.381, p=.024

r=-.353, p=.038



Preliminary conclusions

- **Mixing Costs are related to axonal orientation (Ax) in the inferior-fronto-occipital fasciculus, as well as superior longitudinal fasciculus**
- **High alcohol intake is associated with low degree of diffusion directionality (FA) in the same tracts**
- **Both sensation seeking and impulsivity are associated with high alcohol intake**



Outlook

- At this stage we cannot speculate about causality
- Increase of sample size with spread of age range
- Future analysis with structural equation, maximum-likelihood and Bayesian approaches applying mixed-effects models, and regression models
- Voxel based analysis of DWI data
- Integration with other MRI measures such as resting state, including the use of graph theory incorporating theories of highly connected nodes (hubs, rich clubs)
- Longitudinal arm-trajectory analysis

Thank You

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