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# Large-scale, multimodal, open imaging: the CamCAN example

Rik Henson

MRC CBU

Cognestic Summer School, Sep 2023

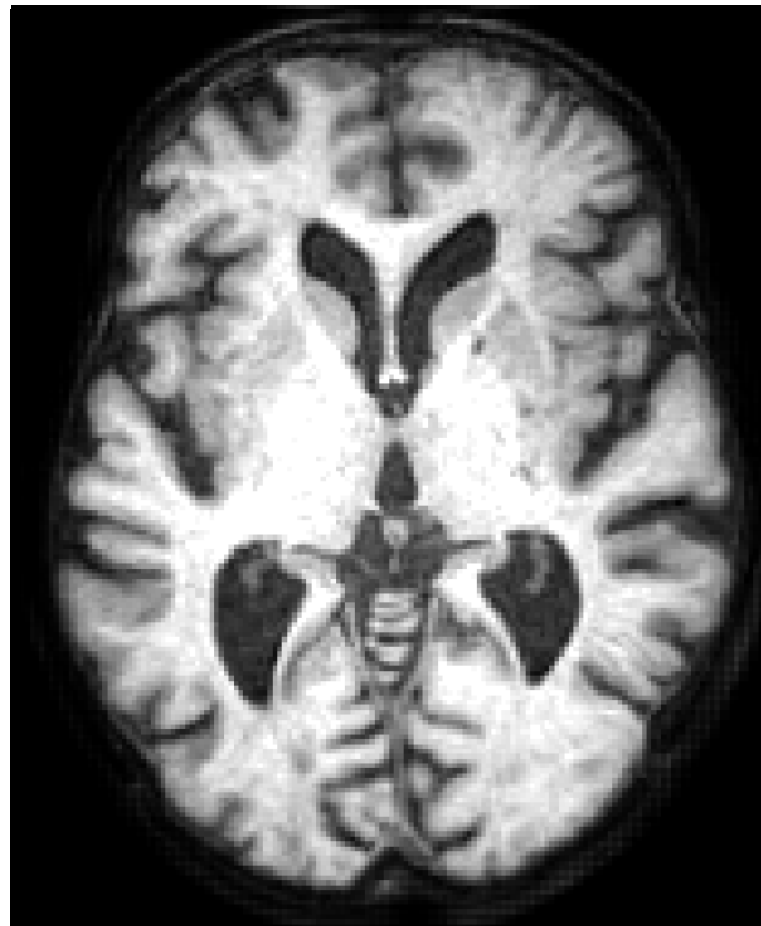


- People are living longer, and the proportion of most world populations that are in “old age” is increasing
- Ageing brings cognitive problems, owing to brain changes, so understanding how ageing of the brain affects cognition might help us maintain cognitive abilities for longer, and so help people function independently for longer
- Brain structure and function can be measured in many ways (sMRI, fMRI, DTI, MEG...) and relating to individual differences requires large samples...

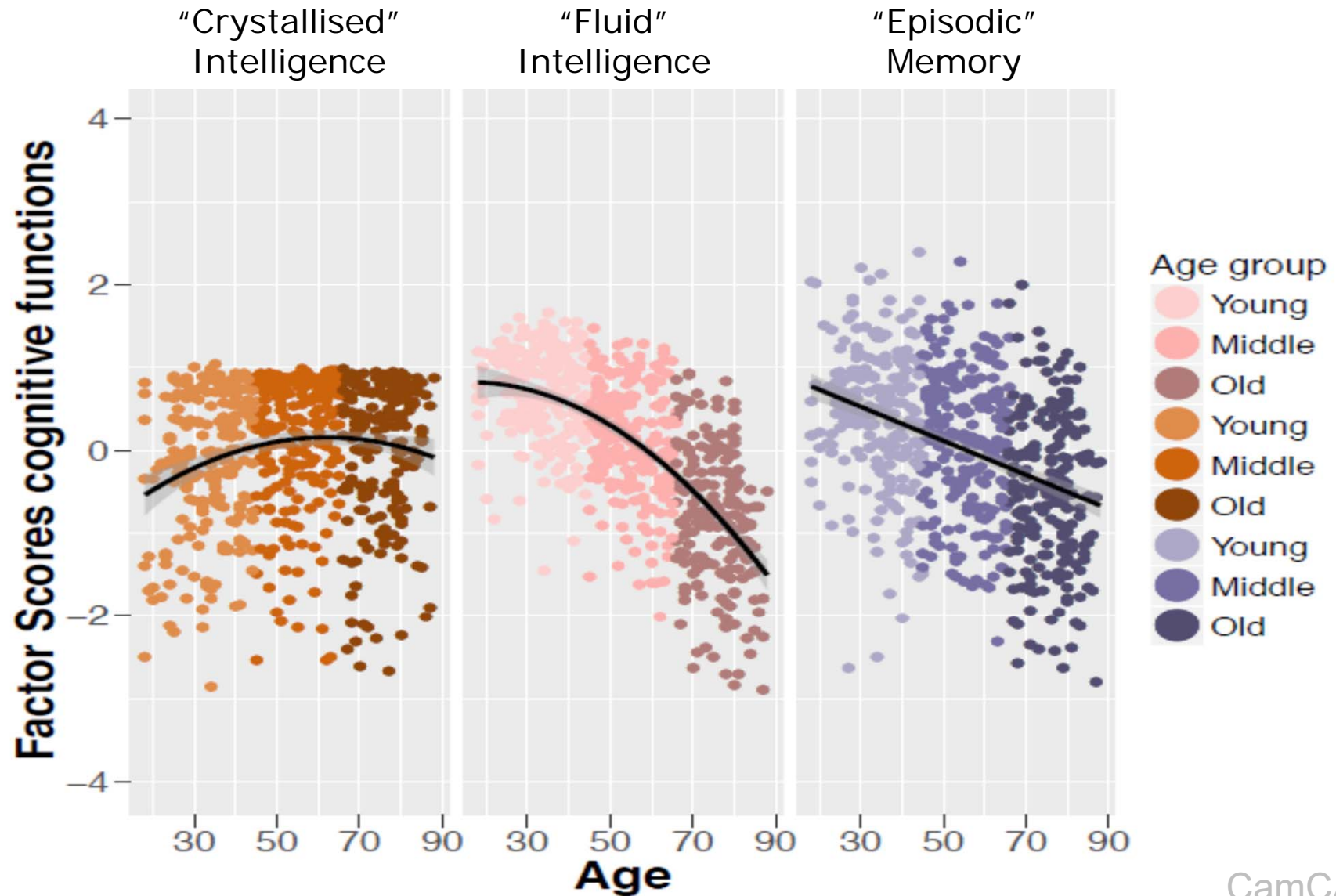
... a “large-scale, multi-modal” approach...

# Ageing Brains (MRI)

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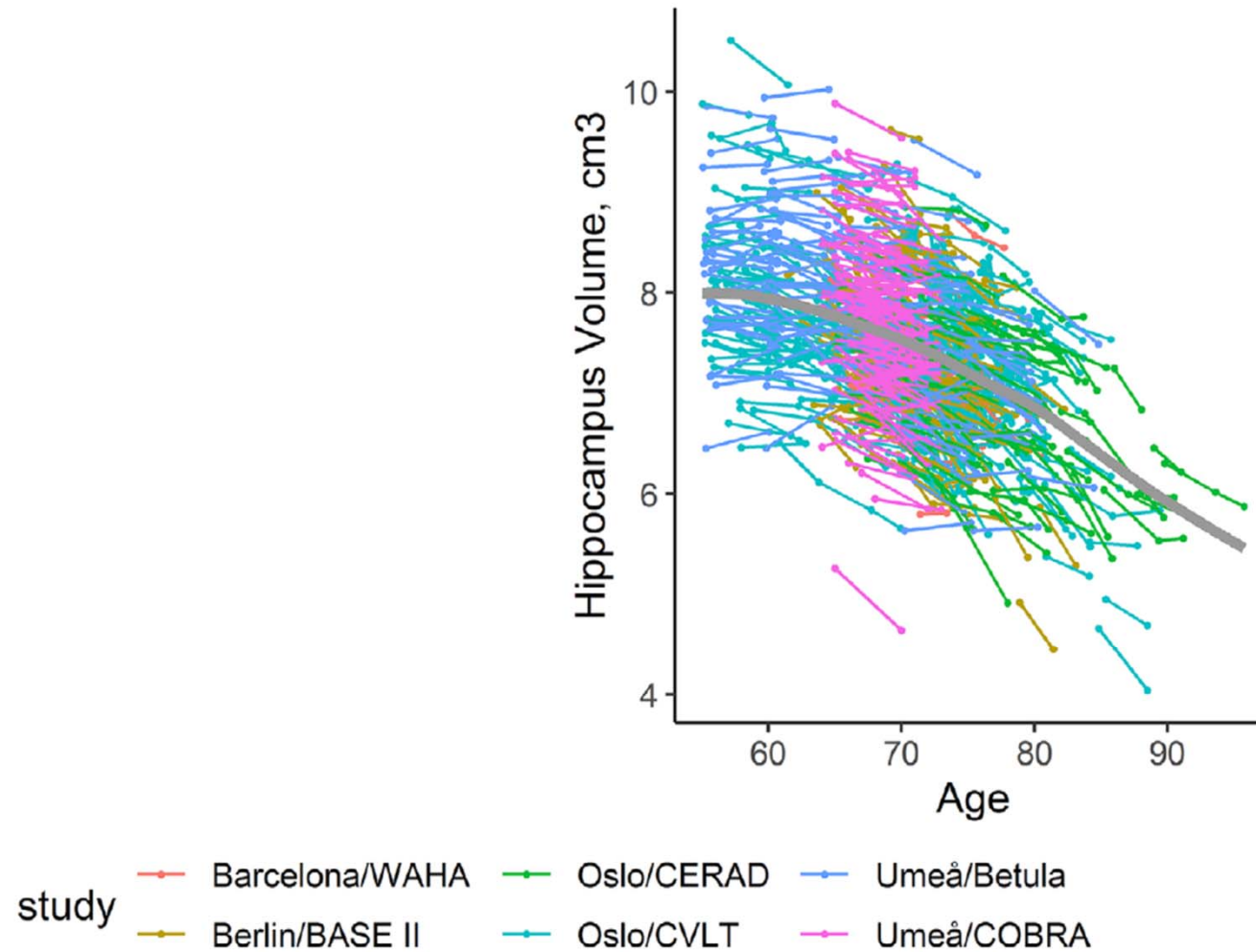


# Ageing Cognition



# More than Brain Structure?

=> **functional** connectivity/reorganisation/compensation...?



- MRI has been used for many years to study brain ageing
- **Structural** MRI (sMRI) measures (static) brain anatomy
- **Functional** MRI (fMRI) measures dynamic activity / connectivity, eg related to specific cognitive functions
- However, fMRI response is a function of 1) **neural** and 2) **haemodynamic** characteristics (vasculature)...
- ...and ageing likely to affect **both**
- Furthermore, haemodynamics are **slow** (seconds)...
- MEG (and EEG) provide direct measure of **neural** activity...
- ... at millisecond resolution, revealing rich repertoire of oscillatory activity above 0.1Hz (fMRI)
- MEG has greater spatial degrees of freedom than EEG, ie., can resolve more nodes/states





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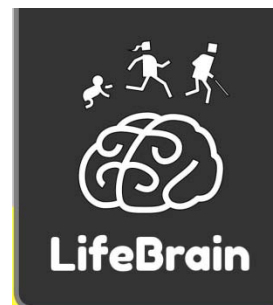
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## Cambridge Centre for Ageing & Neuroscience (CamCAN)



<http://www.cam-can.org/>

- 2010: ~2700 recruited after ~9000 calls (opt-out), so population-derived  
2-hour home interview (eg, lifestyle)
- 2011: 100 per decade 18-88, from 3000  
~7 hours of cognitive tests  
1 hour MRI (T1, T2, DTI, MTR, fMRI)  
0.5 hour of MEG
- 2016: data released – over 2000  
downloads, over 100 publications:  
<https://camcan-archive.mrc-cbu.cam.ac.uk/dataaccess/>
- (2023: repeat imaging and cognition)







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Cam-CAN

cam-can.org/index.php?content=dataset



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THE SCIENCE OF AGEING

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## Cam-CAN Data Repository

The data repository for the **Cambridge Centre for Ageing and Neuroscience (Cam-CAN) dataset** can be found here

Data Access Portal

## Worldwide Usage

The CamCAN dataset has been requested by over 1000 researchers worldwide (number last updated 26/01/2022; map last updated 11/05/2020).







## CamCAN Data Use Agreement

I request access to data collected by the Cambridge Centre for Ageing Neuroscience (CamCAN) for the purpose of scientific investigation, teaching or the planning of clinical research studies and agree to the following terms:

1. I will receive access to de-identified data and will not attempt to establish the identity of, or attempt to contact, any of the CamCAN participants.
2. I will not further disclose these data beyond the uses outlined in this agreement.
3. I will use the data only for the purposes of non-commercial, ethical research or teaching specified in this application and to seek the approval of CamCAN (via the CamCAN Administrator) for any other proposed use.
4. I will require anyone on my team who utilizes these data, or anyone with whom I share these data, to comply with this data use agreement. Note, for this reason, students should ask their supervisors to apply on their behalf.
5. I will not copy data to external storage locations (such as dropbox, google drive or external harddrives) and understand data must remain on my institution's server.
6. I will respond promptly and accurately to requests to update this information.
7. I will comply with any rules and regulations imposed by my institution and its institutional review board in requesting these data.
8. I understand that it is my responsibility to check data for errors, and that CamCAN is not responsible for the consequences of unreported errors in the data. I also agree to make any such errors known to CamCAN as soon as possible.
9. I understand that CamCAN cannot guarantee exclusive use of these data or police potential overlaps of interest with other researchers.
10. I agree to make any publications that arise from use of CamCAN data open-access. Any derived data and processing scripts used to produce those derived data will also be made available on a suitable open-access data repository.
11. I will acknowledge the CamCAN project as a source of data and include language similar to the following:  
"Data collection and sharing for this project was provided by the Cambridge Centre for Ageing and Neuroscience (CamCAN). CamCAN funding was provided by the UK Biotechnology and Biological Sciences Research Council (grant number BB/H008217/1), together with support from the UK Medical Research Council and University of Cambridge, UK."
12. I will include language similar to the following in the methods section of my manuscripts in order to accurately acknowledge data gathering by the CamCAN investigators. Depending upon the length and focus of the article, it may be appropriate to include more or less than the example below. However, inclusion of some variation of the language shown below is mandatory.  
"Data used in the preparation of this work were obtained from the CamCAN repository (available at <http://www.mrc-cbu.cam.ac.uk/datasets/camcan/>), (Taylor et al., 2016, Shaf to et al., 2015). Citation:

**Taylor, J.R., Williams, N., Cusack, R., Auer, T., Shaf to, M.A., Dixon, M., Tyler, L.K., CamCAN, Henson, R.N.** (2016). The Cambridge Centre for Ageing and Neuroscience (CamCAN) data repository: Structural and functional MRI, MEG, and cognitive data from a cross-sectional adult lifespan sample. *NeuroImage*. doi: 10.1016/j.neuroimage.2015.09.018.

**Shaf to, M.A., Tyler, L.K., Dixon, M., Taylor, J.R., Rowe, J.B., Cusack, R., Calder, A.J., Marslen-Wilson, W.D., Duncan, J., Dalgleish, T., Henson, R.N., Brayne, C., CamCAN, & Matthews, F.E.** (2014). The Cambridge Centre for Ageing and Neuroscience (CamCAN) study protocol: a cross-sectional, lifespan, multidisciplinary examination of healthy cognitive ageing. *BMC Neurology*, 14(204). doi:10.1186/s12883-014-0204-1.

I understand that failure to abide by these guidelines will result in termination of my privileges to access CamCAN data.

I understand that any details I enter on this website and any other communication I have with the CamCAN team will be handled according to our [data use policy](#), and I agree for my data to be stored and used in this way

☐ I agree to the above terms and conditions

submit



for each dataset requested. Cognitive data will also appear separate directories. For physiological and demographic data (homeint\_\*, epaq\_\*, scq\_\*, additional\_\*), a tab-delimited text file will be added to your home space containing the approved variables.

Raw MRI data and all MEG conform to BIDS standard. Pre-processed MRI data are stored in aa folders for each stage in the pipeline. MRI and MEG pre-processing scripts are also available:

[Automatic Analysis \(aa\) User Master Script \(UMS\) for MRI](#)

[Automatic Analysis \(aa\) Recipe \(XML\) for MRI](#)

[Automatic Analysis \(aa\) User Master Script \(UMS\) for MEG](#)

[Automatic Analysis \(aa\) Recipe \(XML\) for MEG](#)

[MindBoggle Docker Shell Script](#)

Mindboggle docker image installation instructions: <https://mindboggle.readthedocs.io/en/latest>

You will automatically get a file in your home directory called "standard\_data.csv", which contains, for each of the N=2681 unique CamCAN IDs (CCID) who took the Home Interview: the participant's Age (at time of Home Interview, in years), biological Sex (Male/Female), Handedness (on Edinburgh scale from -100 to +100), whether any MRI data were acquired before or after the scanner coil change (see Data Issues tab at top of webpage) and finally what MTI TR was used (50ms or 30ms). (There are additional "participant\_data.tsv" files within the BIDS folders for each imaging modality of raw data, which will contain a subset of participants who had valid data for that modality.)

The demographic data are from Stage I (Home Interview), and includes a range of interview and self-completion questionnaires designed to collect lifestyle variables, demographic data, physical and social activity etc. The lists are divided into four categories: Home Interview (homeint\_ prefix), Electronic Personal Assessment Questionnaire (epaq\_ prefix), Self-Completion Questionnaire (scq\_ prefix), Additional Scores (additional\_ prefix).

Please select the datasets and variables you would like to use from the following list:

Variable Name	Description
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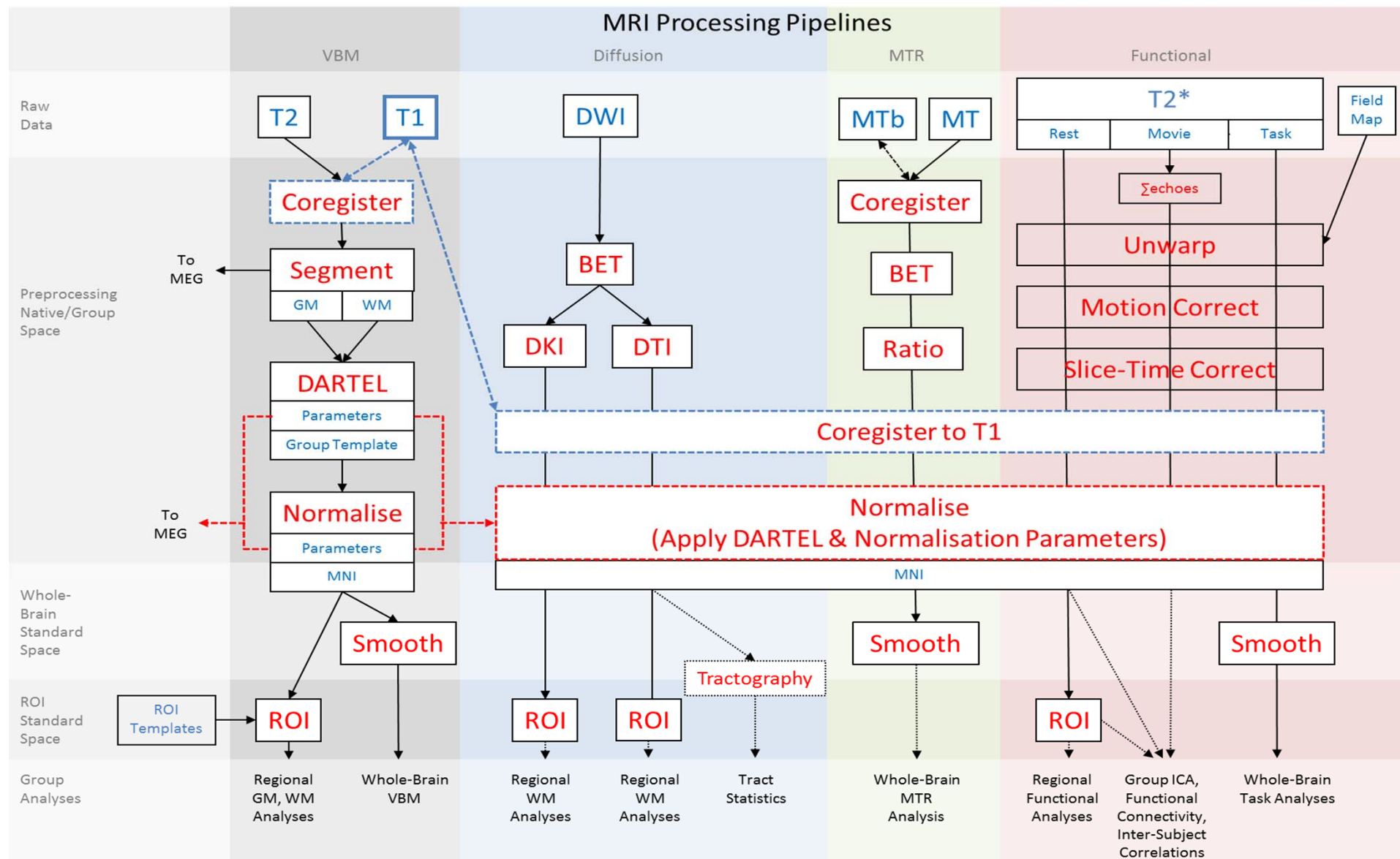
MEG	
Maxfiltered	
No movement compensation	
imaging_meg_mf_nomc_rest	Imaging Data: MEG Resting state from phase II
imaging_meg_mf_nomc_smt	Imaging Data: MEG active Sensorimotor task from phase II
imaging_meg_mf_nomc_pass	Imaging Data: MEG passive Sensory (audiovisual) from phase II
With movement compensation	
imaging_meg_mf_rest	Imaging Data: MEG Resting state from phase II
imaging_meg_mf_smt	Imaging Data: MEG active Sensorimotor task from phase II
imaging_meg_mf_passive	Imaging Data: MEG passive Sensory (audiovisual) from phase II
Transformed to default space	
imaging_meg_rest_transdef_mf	Imaging Data: MEG Resting state from phase II

Requested Variables

Submit

# Pipelines

*Taylor et al. (2017), Neuroimage*



- [Scientific summary of recent CamCAN findings](#)

## Scientific Publications

For CamCAN members and affiliates with approved projects, please refer to this page for [publication conditions](#); for non-CamCAN researchers with approved access via the data-sharing portal, please refer to this page for [publication conditions](#).

### Preprints

- **Henson, R.N., Olszowy, W., Tsvetanov, K.A., Cam-CAN, Zeidman, P.** Evaluating models of the ageing BOLD response. *BioRxiv*. [[Cam-CAN Author list 14](#)] [Open Access Preprint](#)
- **Bingjiang, L., Tsvetanov, K.A., Tyler, L.K., Clarke, A., Cam-CAN, Amos, W.** Genetic signatures of human brain structure: A comparison between GWAS and relatedness-based regression. *BioRxiv*. [[Cam-CAN Author list 13](#)] [Open Access Preprint](#)

### In press

#### 2024

- **Knights, E., Henson, R.N., Morcom, A.M, Mitchell, D.J. & Tsvetanov, K.A.** (2024). Neural Evidence of Functional Compensation for Fluid Intelligence in Healthy Ageing. [[Cam-CAN Author list 15](#)] [Elife](#)
- **Raykov, P., Knights, E., Cam-CAN, Henson, R.N.** (2024). Does functional system segregation mediate the effects of lifestyle on cognition in older adults? *Neurobiology of Aging*, 134, 126-134. [[Cam-CAN Author list 15](#)] [DOI](#)

#### 2023

- **Henriques, R.N., Henson, R.N., Cam-CAN, Correia, M.M.** (2023). Unique information from common diffusion MRI models about white-matter differences across the human adult lifespan. *Imaging Neuroscience*, 1. [[Cam-CAN Author list 15](#)] [DOI](#)
- **McCormick, E.M., Cam-CAN, Kievit, R.A.** (2023). Poorer White Matter Microstructure Predicts Slower and More Variable Reaction Time Performance: Evidence for a Neural Noise Hypothesis in a Large Lifespan Cohort. *Journal of Neuroscience*, 43. [[Cam-CAN Author list 15](#)] [DOI](#)
- **Lugtmeijer, S., Geerligs, L., Tsvetanov, K.A., Mitchell, D.J., Cam-CAN & Campbell, K.L.** (2023). Lifespan differences in visual short-term memory load-modulated functional connectivity. *Neuroimage*, 270, 119982. [[Cam-CAN Author list 14](#)] [DOI](#)
- **King, D.L.O., Henson, R.N., Kievit, R., Wolpe, N., Brayne, C., Tyler, L.K., Rowe, J.B., Cam-CAN & Tsvetanov, K.A.** (2023). Distinct components of cardiovascular health are linked with age-related differences in cognitive abilities. *Scientific Reports*, 13:978. [[Cam-CAN Author list 14](#)] [DOI](#)
- **Mitchell, D., Mousley, A., Shafto, M., Cam-CAN, Duncan, J.** (2023). Neural contributions to reduced fluid intelligence across the adult lifespan. *Journal of Neuroscience* [[Cam-CAN Author list 14](#)] [DOI](#)
- **Liu, X., Tyler, L.K., Cam-CAN, Davis, S.W., Rowe, J.B., Tsvetanov, K.A.** (2023). Cognition's dependence on functional network integrity with age is conditional on structural network integrity. *Neurobiology of Aging*, 129, 195-208 [[Cam-CAN Author list 14](#)] [DOI](#)



- Vascular changes (fMRI+MEG)
- Latency effects (MEG+DTI)
- Effects of APO-E (sMRI+fMRI+MEG)
- Cognitive Reserve (sMRI+fMRI)

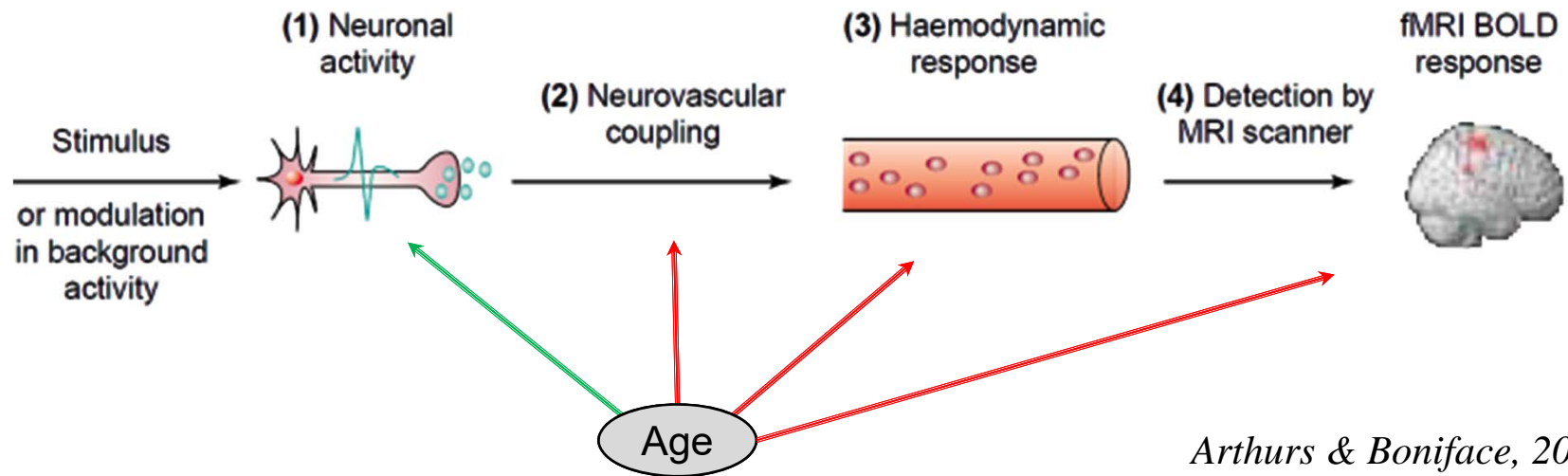




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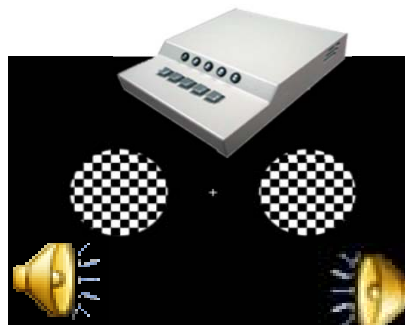


1. Adjust data... e.g, adjust BOLD activation by RSFA (Tsvetanov et al., 2015)



# The Effect of Ageing on fMRI: Correction for the Confounding Effects of Vascular Reactivity Evaluated by Joint fMRI and MEG in 335 Adults

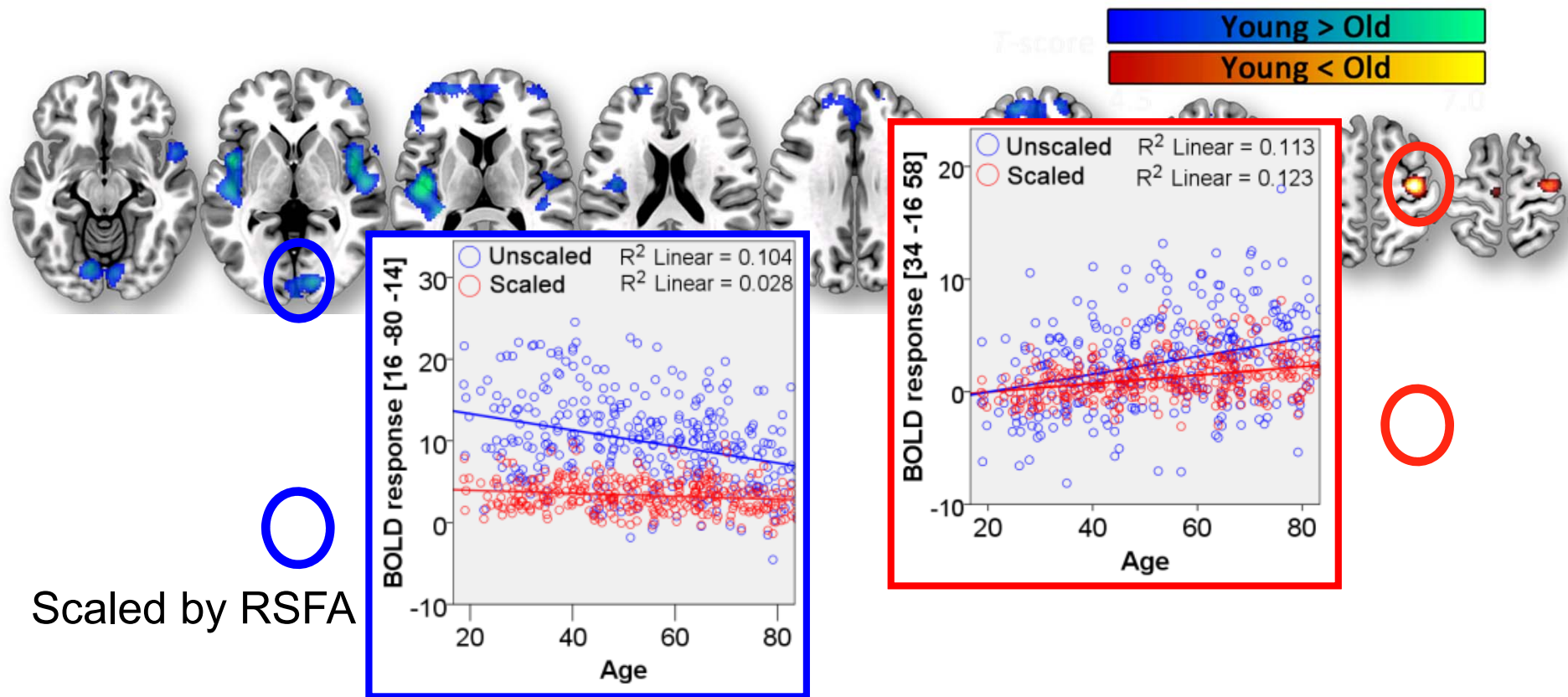
Kamen A. Tsvetanov,<sup>1\*</sup> Richard N. A. Henson,<sup>2</sup> Lorraine K. Tyler,<sup>1</sup>  
Simon W. Davis,<sup>1</sup> Meredith A. Shafto,<sup>1</sup> Jason R. Taylor,<sup>2,3</sup> Nitin Williams,<sup>2</sup>  
Cam-CAN,<sup>4</sup> and James B. Rowe<sup>2,5</sup>



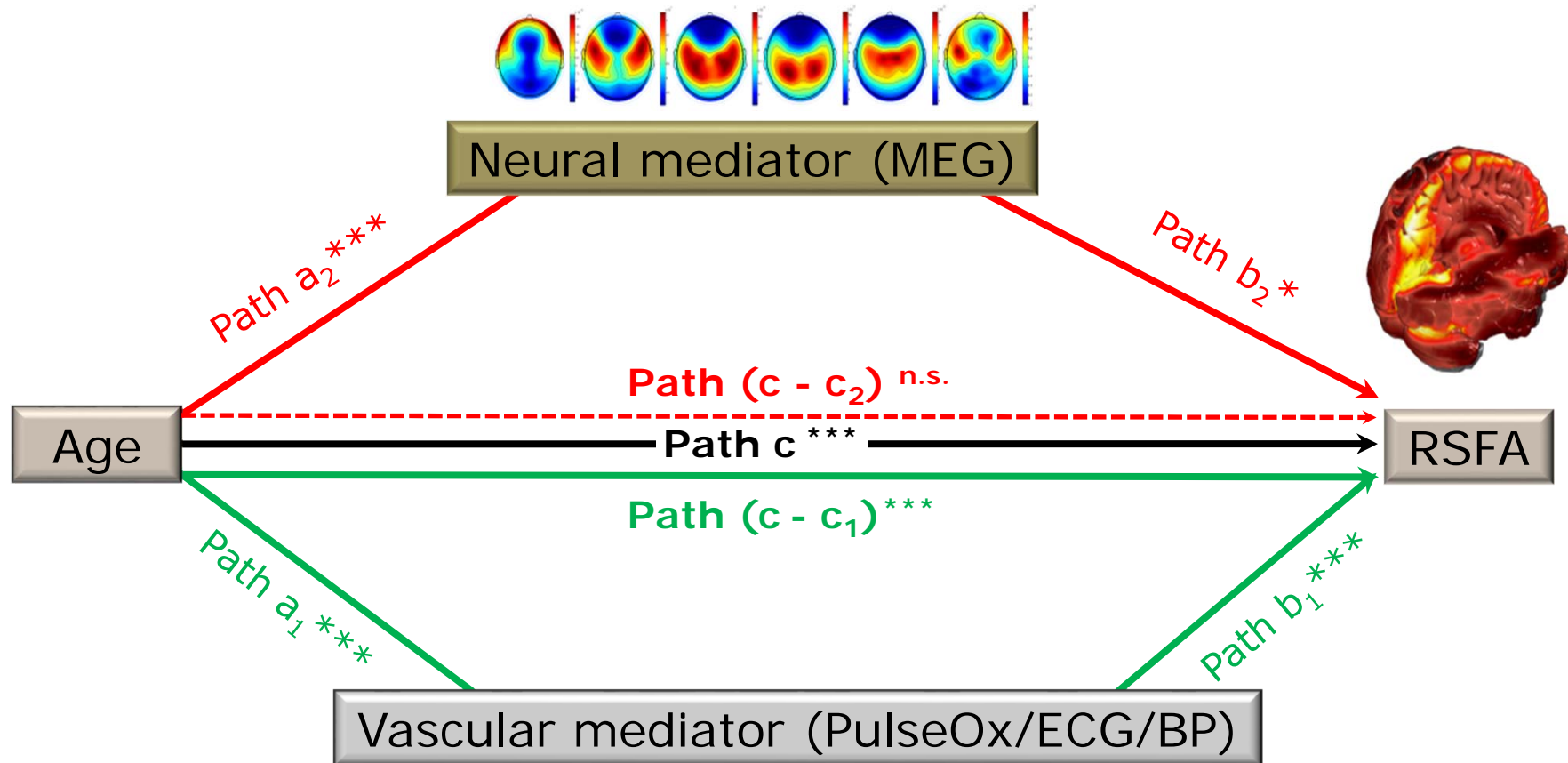
Kamen Tsvetanov

# Sensory Evoked Responses in fMRI

## Effect of Age, unscaled by RSFA



## Is RSFA scaling fair?



- Many age-related fMRI (de)activations are likely to reflect vascular rather than neural changes...  
*Tsevtanov et al (2015), Hum. Brain. Mapping*
- ...specifically in vasodilatory signal decay and haemodynamic transit time (though not in all brain regions, eg right motor cortex)  
*Henson et al (preprint), BioRxiv*
- ... but what about functional connectivity? Surely Pearson correlation coefficient independent of (eg RSFA) scaling...?





Linda Geerligs

♦ **Human Brain Mapping** 38:4125–4156 (2017)

## **Challenges in Measuring Individual Differences in Functional Connectivity Using fMRI: The Case of Healthy Aging**

**Linda Geerligs** <sup>1,2,3\*</sup> **Kamen A. Tsvetanov**<sup>2,4,5</sup> **Cam-CAN**<sup>2</sup> and  
**Richard N. Henson**<sup>1,2</sup>

<sup>1</sup>*MRC Cognition and Brain Sciences Unit, Cambridge, United Kingdom*

<sup>2</sup>*Cambridge Centre for Ageing and Neuroscience (Cam-CAN), University of Cambridge and  
MRC Cognition and Brain Sciences Unit, Cambridge, United Kingdom*

<sup>3</sup>*Donders Institute for Brain, Cognition and Behaviour, Radboud University, the Netherlands*

<sup>4</sup>*Centre for Speech, Language and the Brain, Department of Psychology, University of  
Cambridge, Cambridge, United Kingdom*

<sup>5</sup>*Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom*





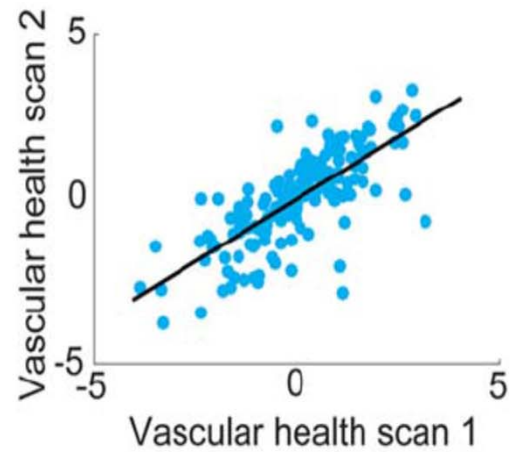
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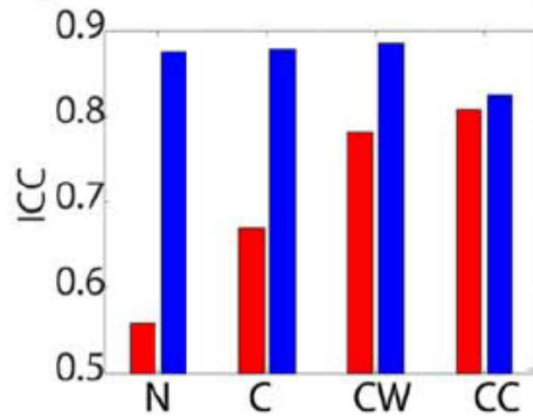
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## Vascular Health – fMRI functional connectivity

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A. Reliability of the relation between age and functional connectivity



■ No mean regression  
■ Mean regression



- Difficult to assess whether a method “improves” FC estimation, but regressing out mean FC at least appears to improve:
  - Intra-Class Correlation (ICC) of Age effects across Sessions
  - ICC of individual Connectivity Matrices
  - Similarity between Age-matched individuals
- *Note: lose ability to detect effects of Age on mean connectivity and ~50% connections become negative (ie, only relative connection strengths remain)*



# Vascular Conclusions

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- Many age-related fMRI (de)activations are likely to reflect vascular rather than neural changes...  
*Tsevtanov et al (2015), Hum. Brain. Mapping*
- ...specifically in vasodilatory signal decay and haemodynamic transit time (though not in all brain regions, eg right motor cortex)  
*Henson et al (preprint), BioRxiv*
- Not just (de)activations, but even fMRI functional connectivity (FC) is influenced by vascular health...  
*Geerligs et al (2017), Hum. Brain. Mapping*



- Vascular changes (fMRI+MEG)
- Latency effects (MEG+DTI)
- Effects of APO-E (sMRI+fMRI+MEG)
- Cognitive Reserve (sMRI+fMRI)



## ARTICLE

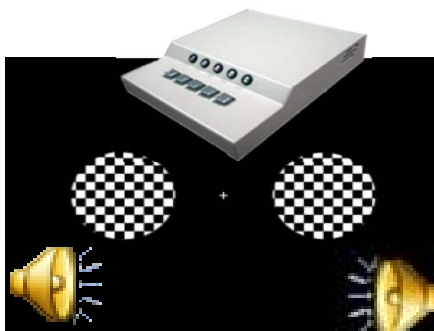
Received 24 May 2016 | Accepted 18 Apr 2017 | Published 9 Jun 2017

DOI: [10.1038/ncomms15671](https://doi.org/10.1038/ncomms15671)

**OPEN**

# Age-related delay in visual and auditory evoked responses is mediated by white- and grey-matter differences

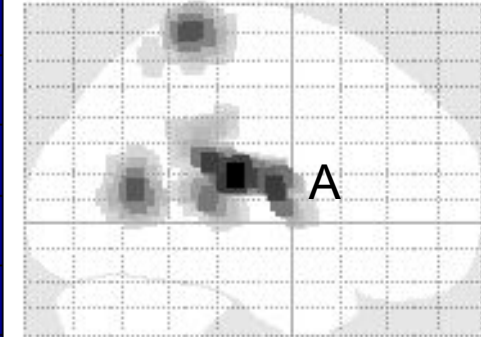
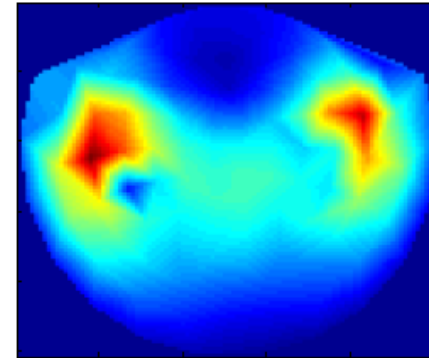
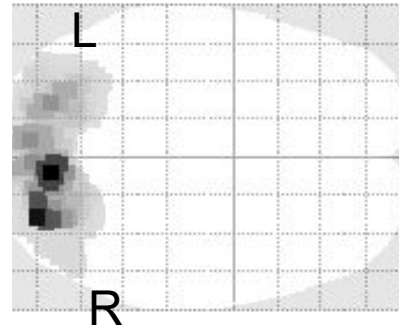
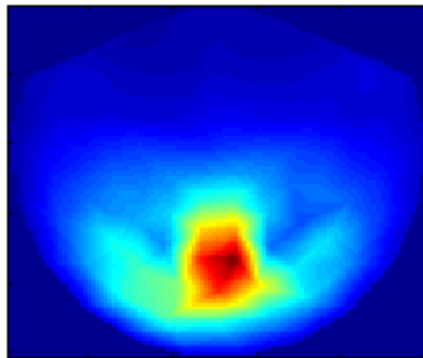
D. Price<sup>1</sup>, L.K. Tyler<sup>2</sup>, R. Neto Henriques<sup>1</sup>, K.L. Campbell<sup>3</sup>, N. Williams<sup>4</sup>, M.S. Treder<sup>2</sup>, J.R. Taylor<sup>5</sup>, Cam-CAN<sup>†</sup> & R.N.A. Henson<sup>1</sup>



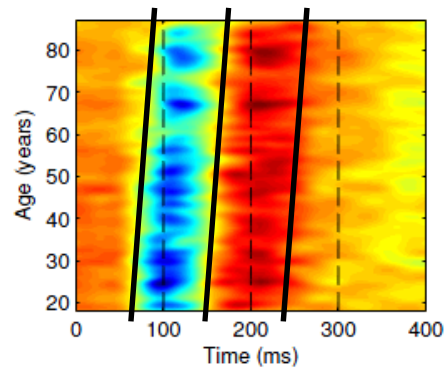
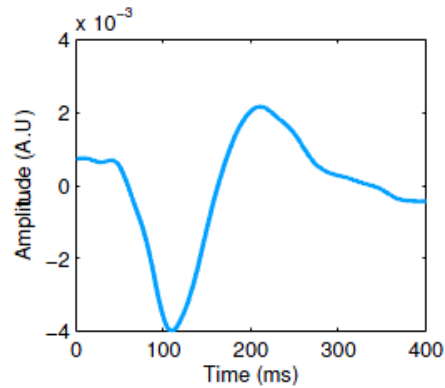
Darren Price



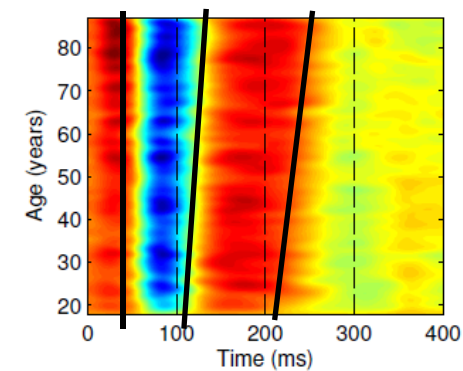
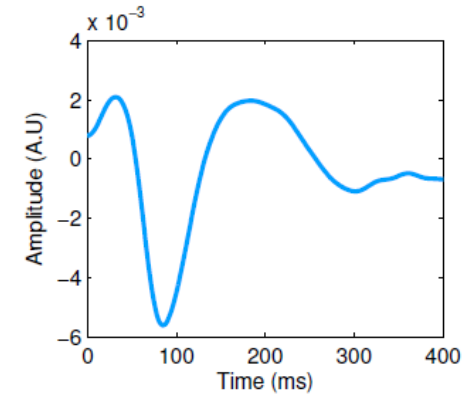
# Sensory Evoked Responses in MEG

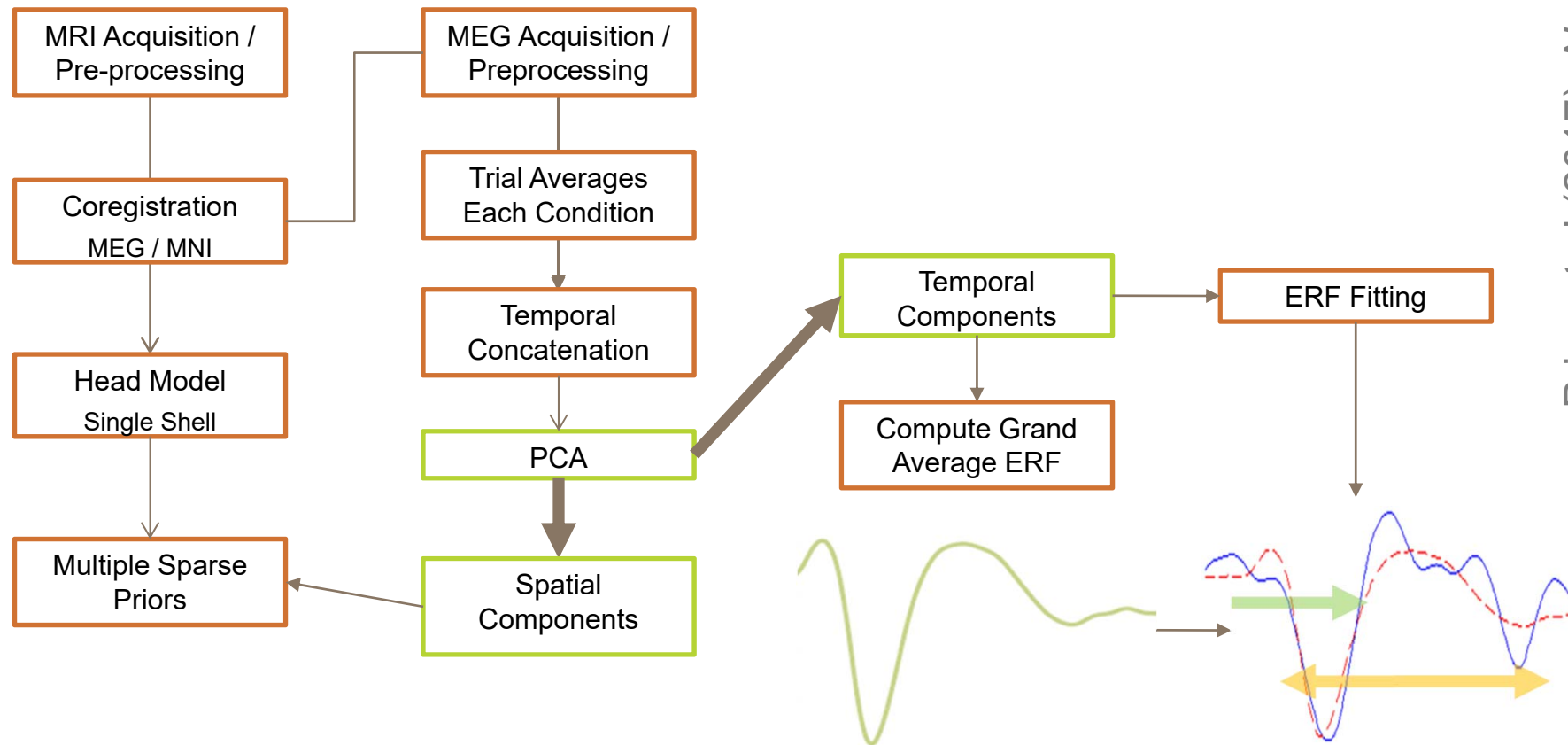


Visual ERFs



Auditory ERFs





Price et al (2017), Nat Com

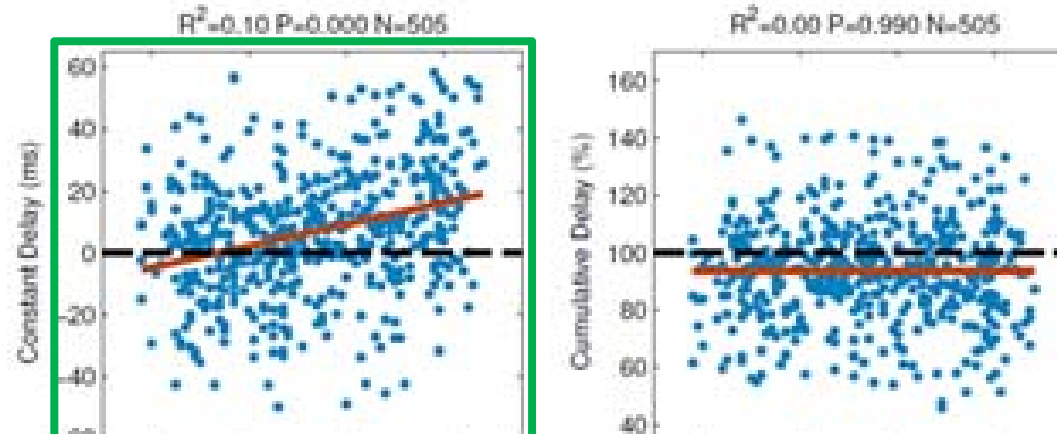
**2 Delay Parameters:**  
**Constant** + **Cumulative**

# Sensory Evoked Responses in MEG

## Constant Delay

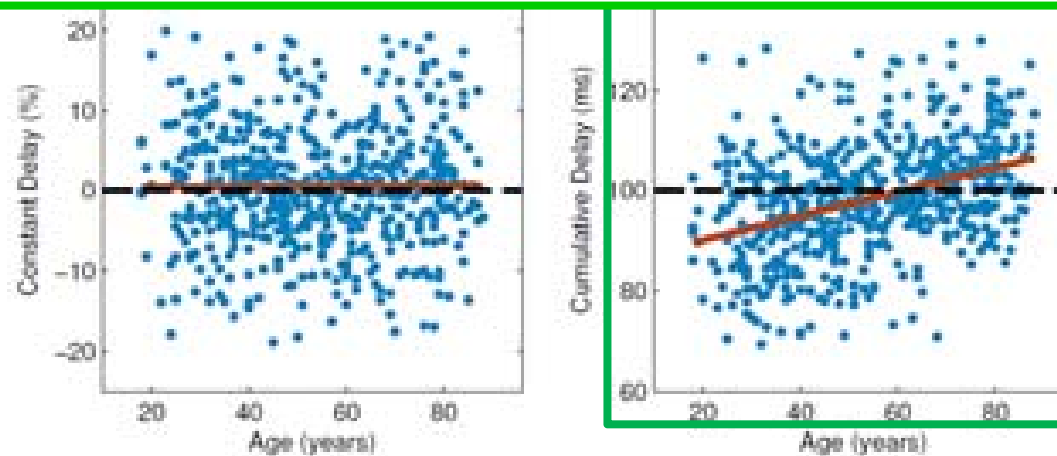
## Cumulative Delay

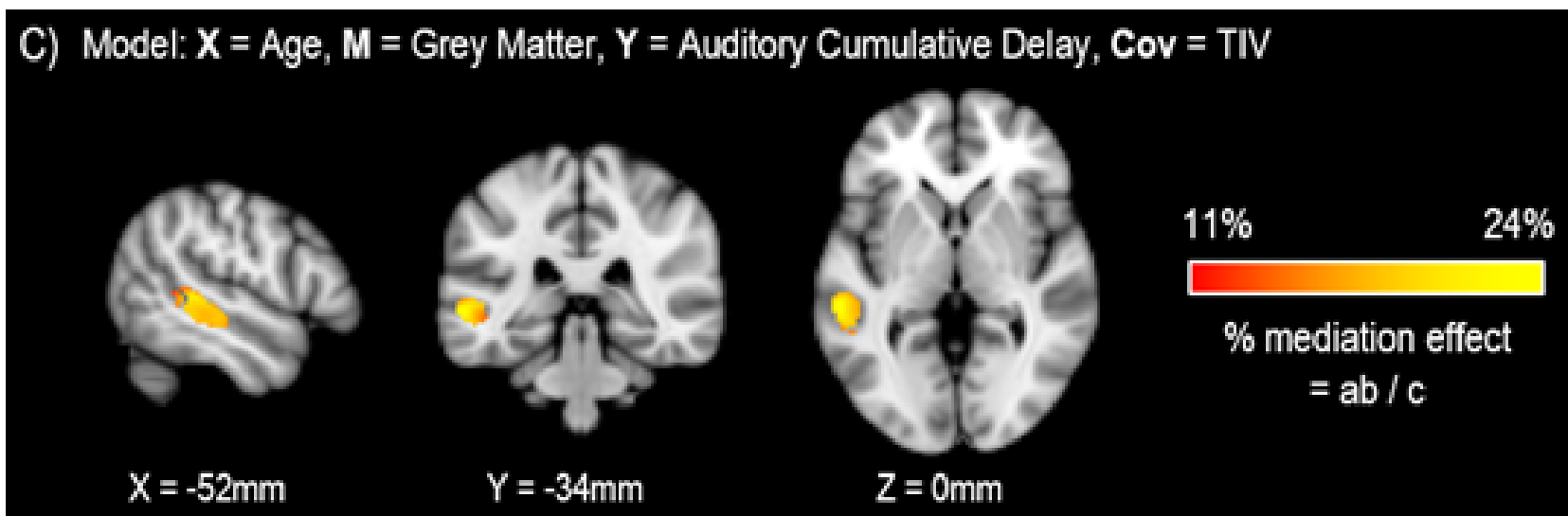
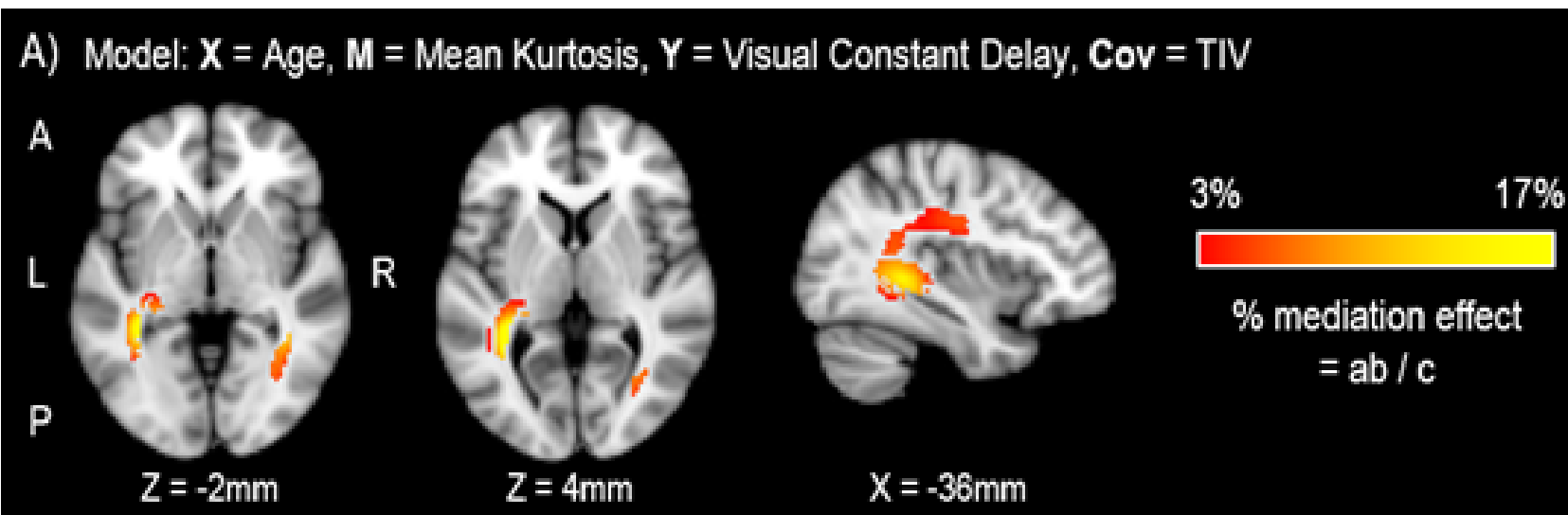
Visual



Correlation of Visual Constant delay and Auditory Cumulative delay surprisingly low,  $R^2(504) < 1\%$ , disappearing after adjusting for age...

Auditory





- Age exerts differential and uncorrelated effects on visual evoked latency (constant delay) and auditory evoked latency (cumulative delay)
- White Matter integrity (MK) in optic radiation mediates effect of Age on Visual Constant delay
  - *delayed transmission?*
- Grey-Matter Volume (GMV) within auditory cortex mediates effect of Age on Auditory Cumulative delay
  - *local computation?*
- MEG reveals multiple contributions to age-related neural slowing



- Vascular changes (fMRI+MEG)
- Latency effects (MEG+DTI)
- **Effects of APO-E (sMRI+fMRI+MEG)**
- Cognitive Reserve (sMRI+fMRI)





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# Genetics

*Registered Report*

Brain and  
Neuroscience  
Advances

## Effect of apolipoprotein E polymorphism on cognition and brain in the Cambridge Centre for Ageing and Neuroscience cohort

Richard N. Henson<sup>1,2</sup> , Sana Suri<sup>3,4</sup>, Ethan Knights<sup>1</sup>, James B. Rowe<sup>1,5</sup>,  
Rogier A. Kievit<sup>1</sup>, Donald M. Lyall<sup>6</sup>, Dennis Chan<sup>7</sup>, Else Eising<sup>8</sup>  
and Simon E. Fisher<sup>8,9</sup>

*Brain and Neuroscience Advances*

Volume 4: 1–12

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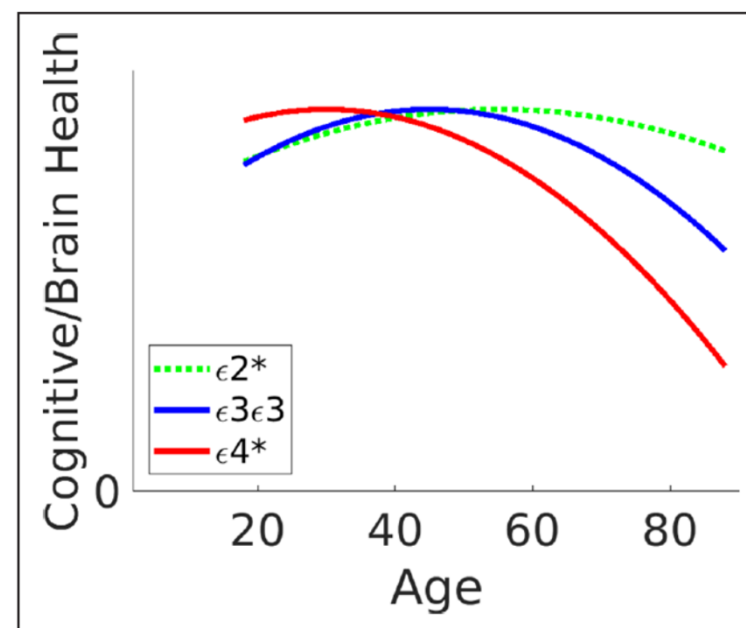
DOI: 10.1177/2398212820961704

[journals.sagepub.com/home/bna](https://journals.sagepub.com/home/bna)

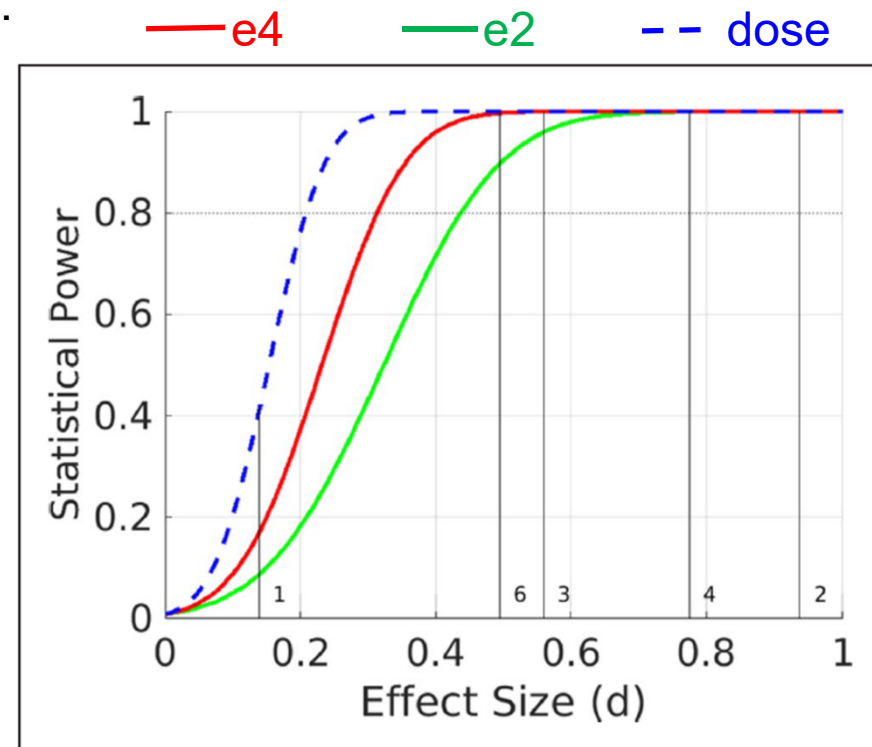


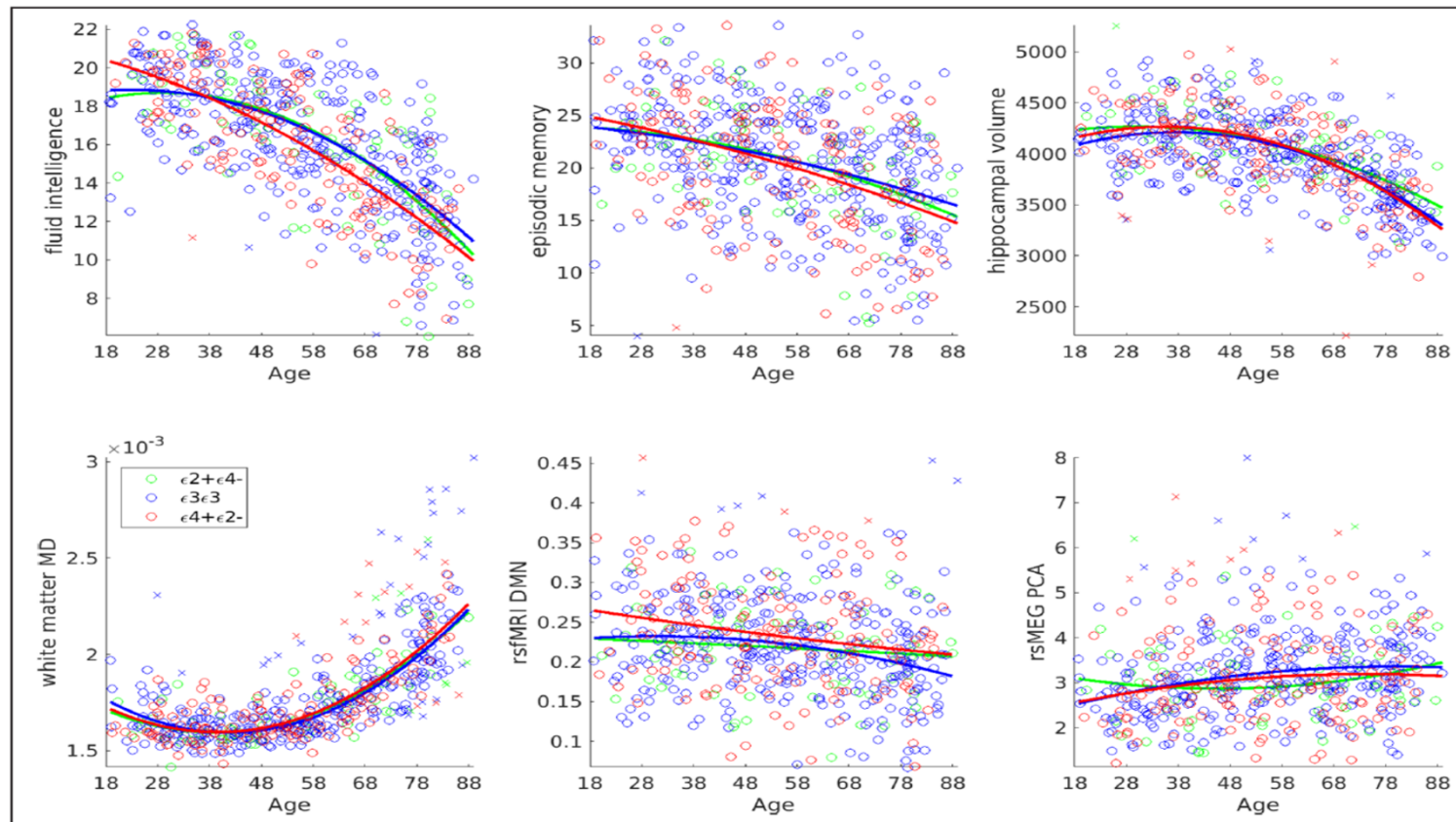
*Henson et al (2020) Brain Neuro Advances*

- Presence of an **e4** allele (relative to more common **e3**) in APOE gene is associated with cognitive decline in old age, specifically Alzheimer's Disease
- The “Antagonistic Pleiotropy” hypothesis claims that **e4** offers benefits earlier in life (which could contribute to its prevalence in population)
- The **e2** polymorphism, on other hand, is claimed to be neuroprotective in old age



- We published a Registered Report (i.e., APOE status de-blinded after acceptance) to test Antagonistic Pleiotropy hypothesis, in terms of a (quadratic) Age X APOE interaction
- We tested interaction on 6 outcomes:
  1. Fluid Intelligence
  2. Episodic Memory
  3. Hippocampal Volume
  4. White Matter FA
  5. DMN FC from fMRI
  6. FC from MEG
- Though small N for genetic study (N~600), prior APOE effect sizes so large that should be detectable





- In no case was there a significant Age-by-APOE interaction for either  $\epsilon 4$  or  $\epsilon 2$  (or dose effect), and Bayes Factors favoured the null...  
... i.e., evidence **against** the Antagonistic Pleiotropy hypothesis



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## Outline

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- Vascular changes (fMRI+MEG)
- Latency effects (MEG+DTI)
- Effects of APO-E (sMRI+fMRI+MEG)
- Cognitive Reserve (sMRI+fMRI)



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# Cognitive Reserve

Neurobiology of Aging 70 (2018) 180–183

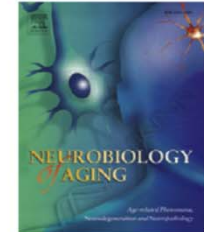


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## Neurobiology of Aging

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Brief communication

Lifestyle activities in mid-life contribute to cognitive reserve in late-life, independent of education, occupation, and late-life activities



Dennis Chan<sup>a,\*</sup>, Meredith Shafto<sup>b</sup>, Rogier Kievit<sup>b</sup>, Fiona Matthews<sup>c</sup>, Molly Spink<sup>b</sup>, Michael Valenzuela<sup>d,e</sup>, Cam-CAN, Rik N. Henson<sup>b</sup>



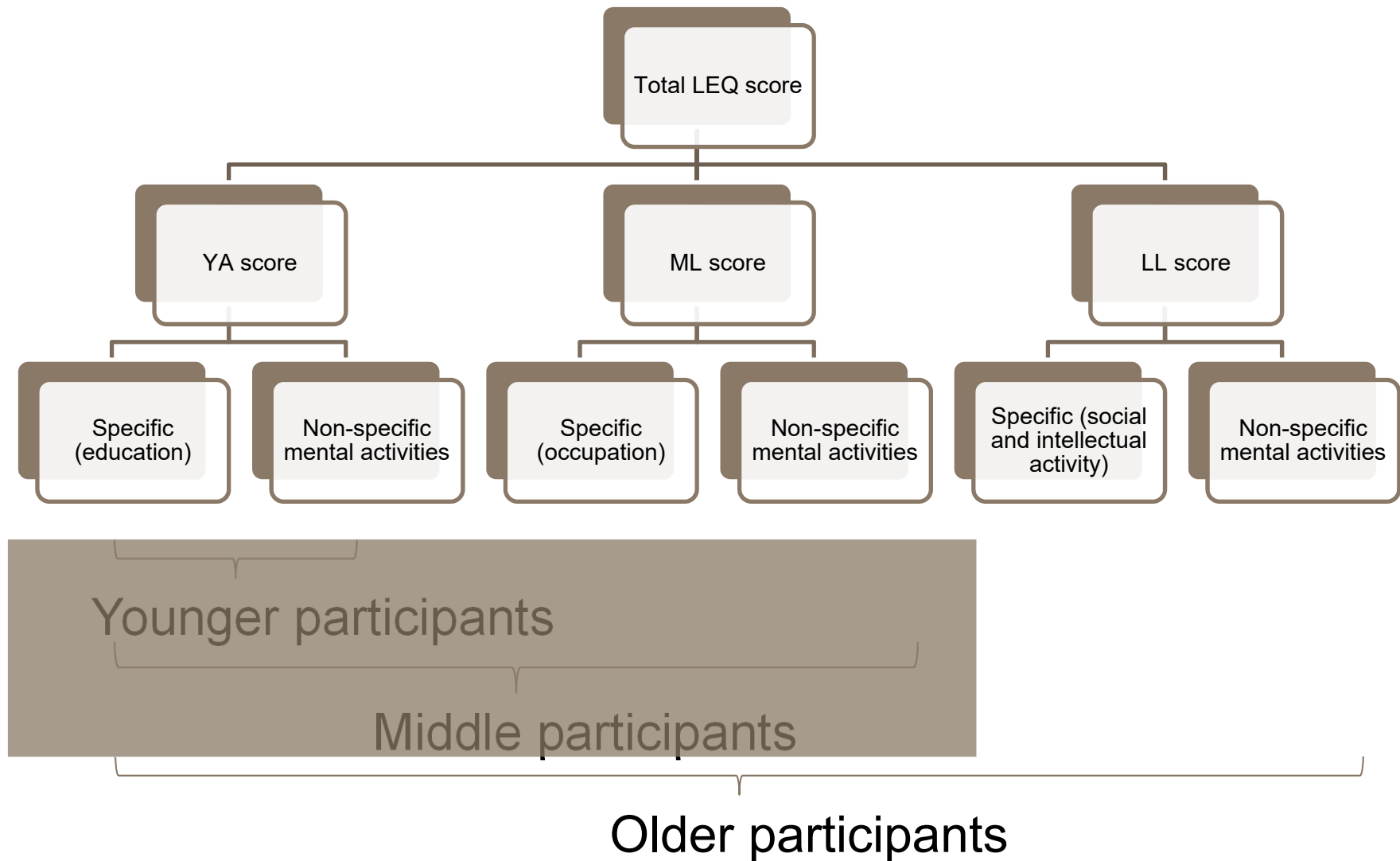
Dennis Chan



- Cognitive Reserve (CR) is used to explain why some people maintain cognitive health despite brain changes owing to, e.g, ageing and dementia (Stern, 2002).
- One factor commonly associated with CR is level of education.
- Here, we explore more *modifiable* factors, such as mid-life activities.
- Identifying such factors will enable public health strategies for maintaining cognitive health in old age and dementia (Gow et al., 2017).



- We analysed data from the “Lifetime Experience Questionnaire” (LEQ; Valenzuela & Sachdev, 2007)
- N=205 population-derived healthy individuals >65 years of age in CC700 phase of CamCAN
- We defined Cognitive Health by the Cattell test of fluid intelligence (similar results obtained when taking the first principal component across 12 more specialised cognitive tests.)



6 LEQ Variables		
Young Adult (18-29)	Specific	<b>Education</b> (national careers service, level multiplied by number of years)
	Non-specific	Eg family outings, musical instrument, physical activity, board games
Mid-Life (30-65)	Specific	<b>Occupation</b> (standard occupational scores, multiplied by number of years)
	Non-specific	Eg family outings, musical instrument, physical activity, board games
Late-Life (66-88)	Specific	<b>Other roles</b> (social, charity, family, etc, summed score)
	Non-specific	Eg family outings, musical instrument, physical activity, board games

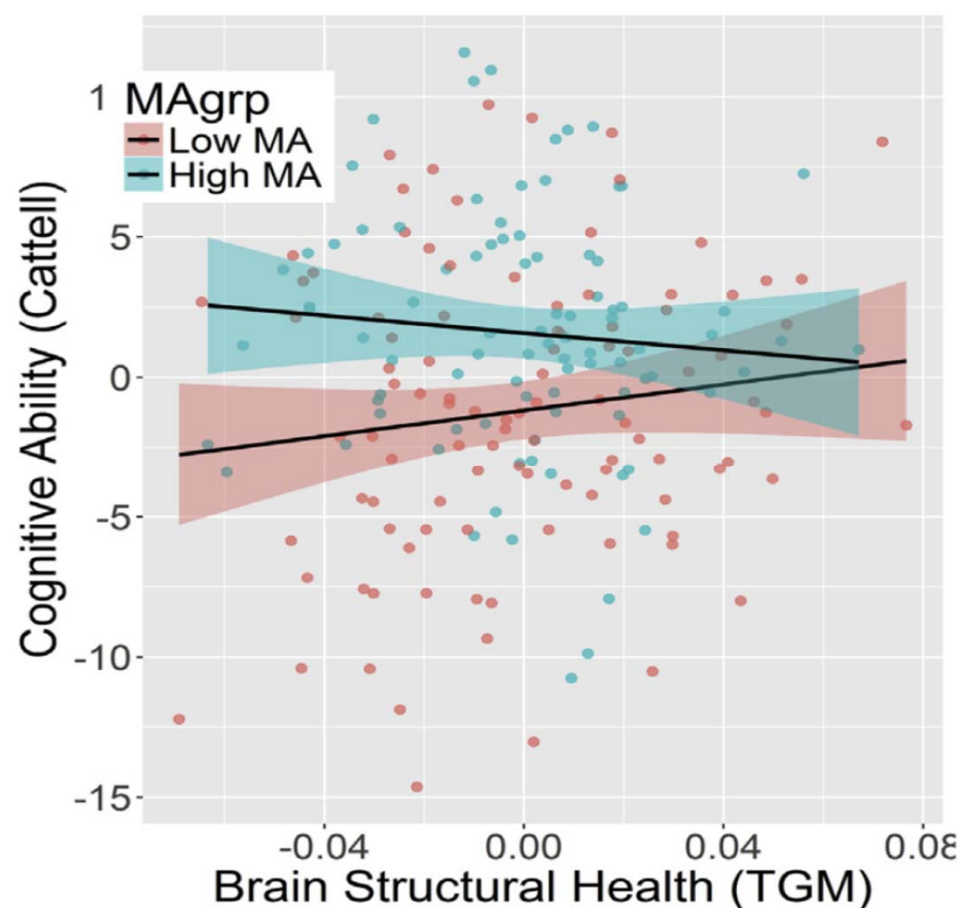
- (All LEQ scores positively related to Cognition in separate regressions)
- **Multiple** linear regression of the LEQ scores, together with age and sex, revealed unique contributions of:

Variable	Normalised Coefficient	Percentage Variance	P-value (df=196)
Young Adult Specific	+0.259	6.70	3.58e-4
Young Adult Non-specific	+0.027	0.08	.723
Mid-Life Specific	+0.096	0.93	.164
Mid-Life Non-specific	+0.324	10.50	2.53e-5
Late-Life Specific	+0.010	0.99	.110
Late-Life Non-specific	-0.098	0.96	.195
Age	-0.287	8.26	1.93e-6
Sex	-0.082	0.67	.201



- While mid-life activities may help preserve cognition in old age, to qualify for Cognitive Reserve, these activities need to **moderate** the relationship between Cognition and Brain
- On n=195 individuals, Brain health was estimated from T1+T2-weighted MRIs as Total Gray Matter, adjusted for head size (aTGM)
- Tested for the interaction (moderation) between Mid-Life Non-specific Activities and aTGM in predicting Cognition  
(for visualisation purposes, split the group into High (n=103) and Low (n=92) levels of Mid-Life Non-specific activities)

- Significant linear interaction (adjusting for education, age, sex), in that Cognition was less related to (structural) Brain health when Mid-Life Nonspecific Activities were high...
- ...as expected if Mid-Life activity is a form of Cognitive Reserve



- We identified a type of Cognitive Reserve – Mid-Life Nonspecific activity (i.e, beyond occupation) – which:
  - 1) predicted Cognition years later in old age, over and above Education in youth and current activities in old age
  - 2) reduced the dependency of Cognition on Brain Structure
  - 3) is potentially modifiable by simple interventions (perhaps easier than for other determinants of Cognitive Reserve like Education)



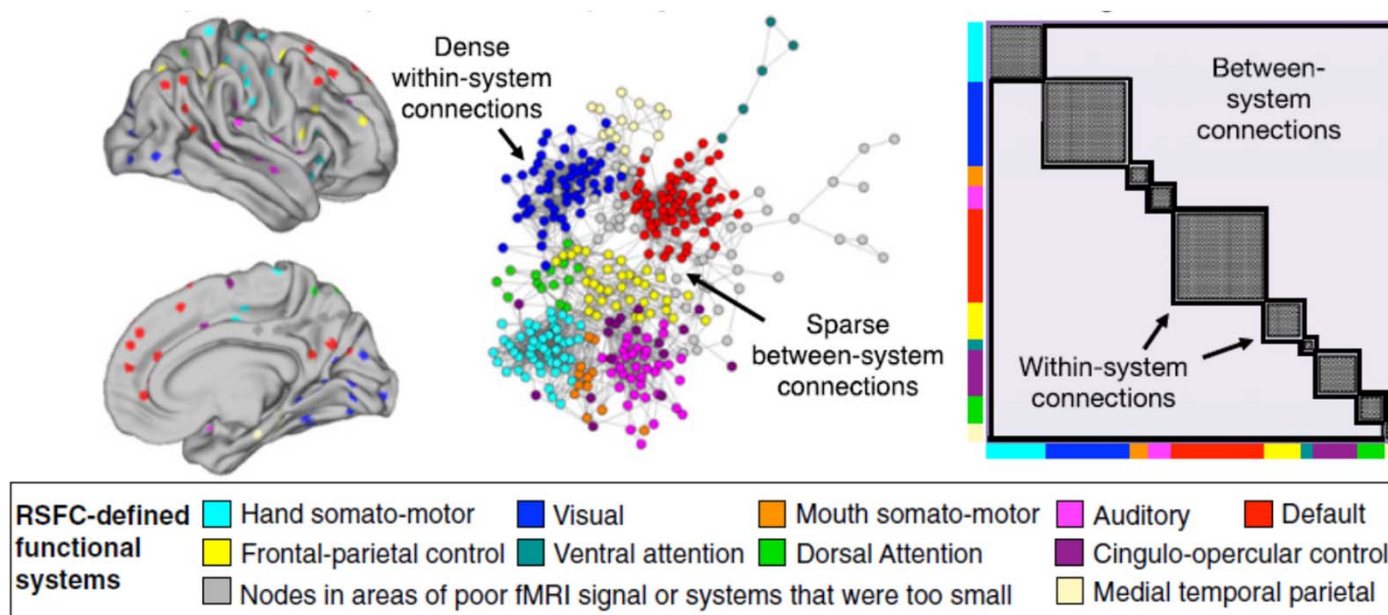
- Apart from being beyond occupation, we could not distinguish whether key mid-life activities are physical, intellectual and/or social
- Warning: “reverse causation” still possible (i.e, cognition caused lifestyle):
  - Lifestyle could be influenced by past (stable) cognitive ability (no direct childhood measure of cognition like Gow et al, 2017)
    - Though childhood cognition likely to correlate with education?
  - Lifestyle Reporting could be affected by current cognitive ability
    - Though autobiographical memory not severely affected in healthy ageing?
- Prospective studies, with *objective* measures of mid-life physical / social / intellectual activity will need to replicate in future...

(which is why longitudinal cohorts are vital, and need funding, eg CamCAN...)



- But Cognitive Reserve must have some brain correlate (even if not Brain Structure).... what about Brain Function?
- Functional segregation of large-scale networks may be key....

- Functional connectivity can be measured while recording brain activity during rest, leading to a number of large-scale “networks”
- Functional segregation refers to how well those networks are separated (within-network minus between-network connectivity)



- Do individuals with high Mid-Life Activities have higher functional segregation in old age (that compensates for structural loss)...?

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Neurobiology of Aging

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Does functional system segregation mediate the effects of lifestyle on cognition in older adults?

Petar P. Raykov<sup>a,\*</sup>, Ethan Knights<sup>a</sup>, Cam-CAN<sup>a,b,1</sup>, Richard N. Henson<sup>a,b</sup>

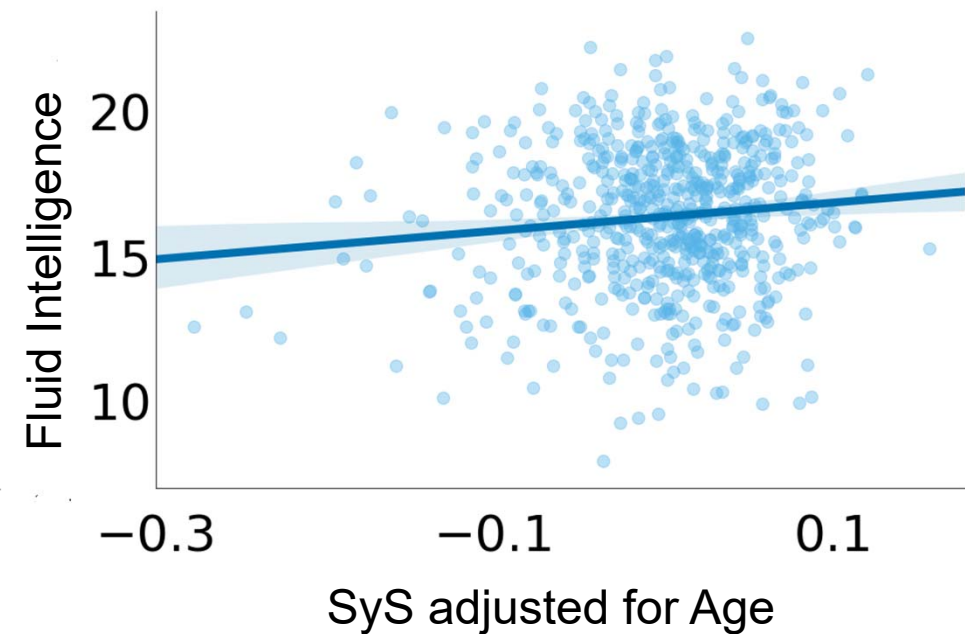
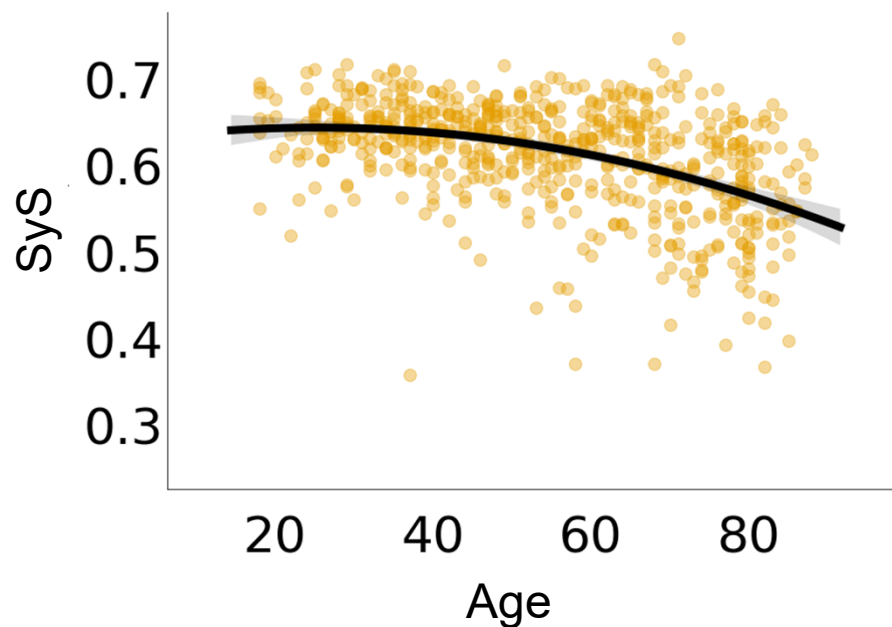
<sup>a</sup> Medical Research Council Cognition and Brain Sciences Unit, University of Cambridge, UK

<sup>b</sup> Department of Psychiatry, University of Cambridge, UK

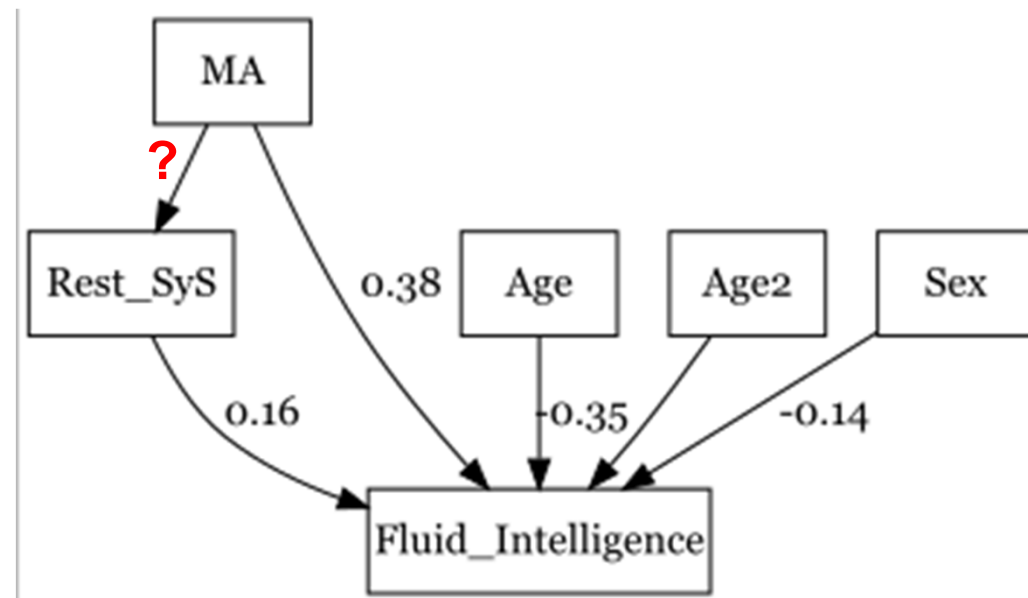


Petar Raykov

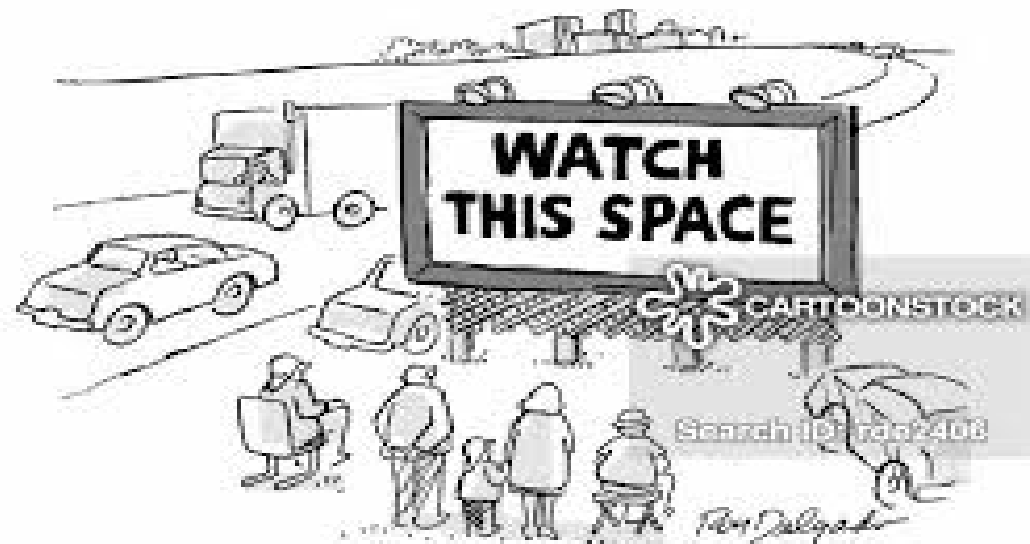
- Pre-registered procedure for “Functional System Segregation” (SyS)
- Replicated effect of Age on SyS...
- ...and effect of SyS on Cognition above Age...



- Pre-registered procedure for “Functional System Segregation” (SyS)
- Replicated effect of Age on SyS...
- ...and effect of SyS on Cognition above Age...
- ...but SyS did **not** mediate effects of Mid-life Activities (MA) on Cognition (largely because no relationship between MA and current SyS)



- Functional (system) segregation (SyS) does not seem to be neural correlate of Cognitive Reserve, at least that part of reserve related to mid-life activities (or education)
- Other possible neural correlates:
  - more specific functional connections?
  - **white matter structural connectivity?**







MRC Cognition  
and Brain  
Sciences Unit



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CAMBRIDGE

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- Many age-related fMRI (de)activations are likely to reflect vascular rather than neural changes...  
*Tsevtanov et al (2015), Hum. Brain. Mapping*
- So either:
  1. Adjust data... e.g, adjust BOLD activation by RSFA
  2. ...or have more complex model, e.g, HaemoDynamic Modelling, HDM...



New Results

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## Evaluating models of the ageing BOLD response

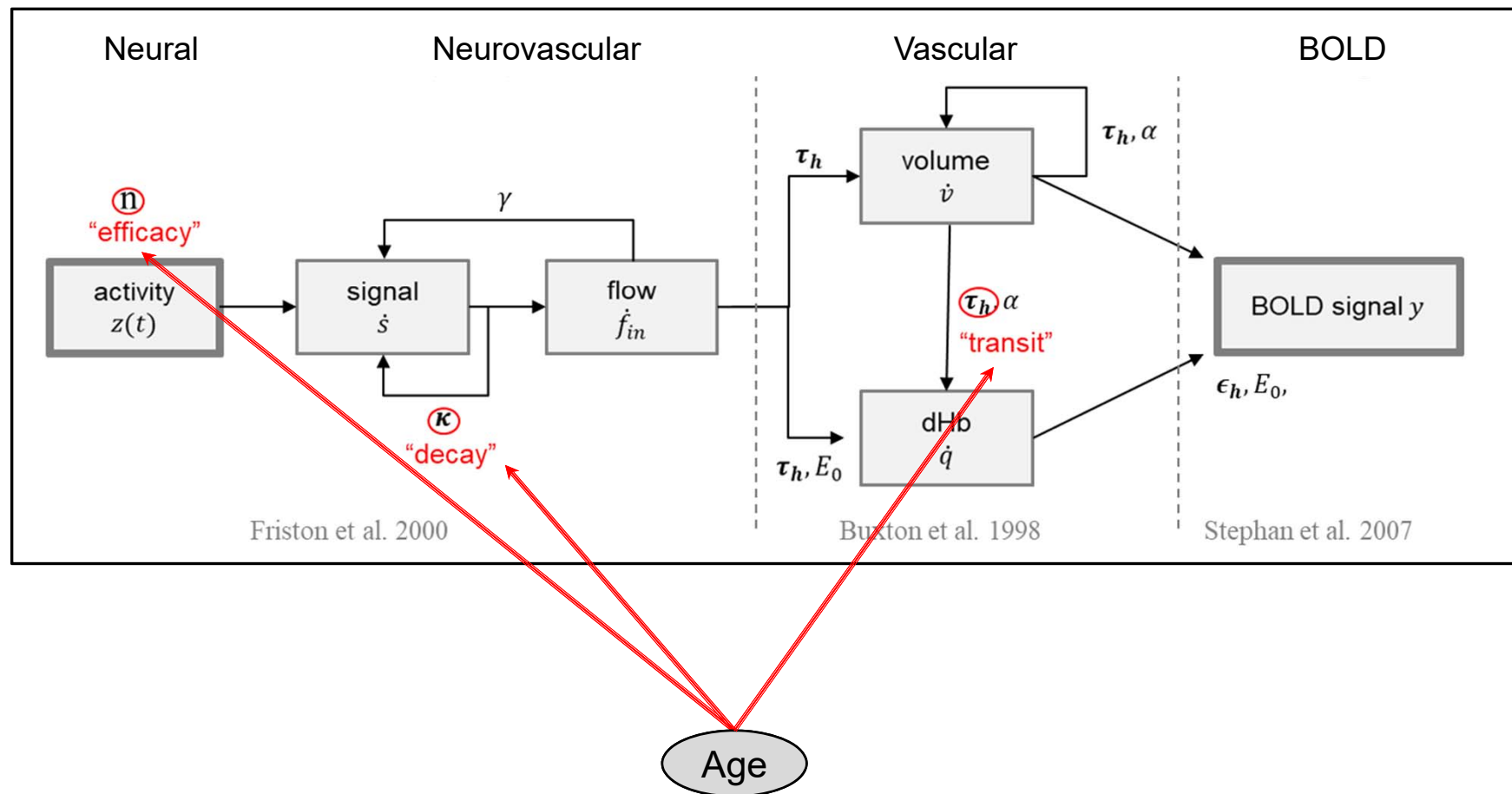
 R.N. Henson, W. Olszowy, K.A. Tsevtanov, Cam-CAN, P. Zeidman

doi: <https://doi.org/10.1101/2023.08.24.554634>

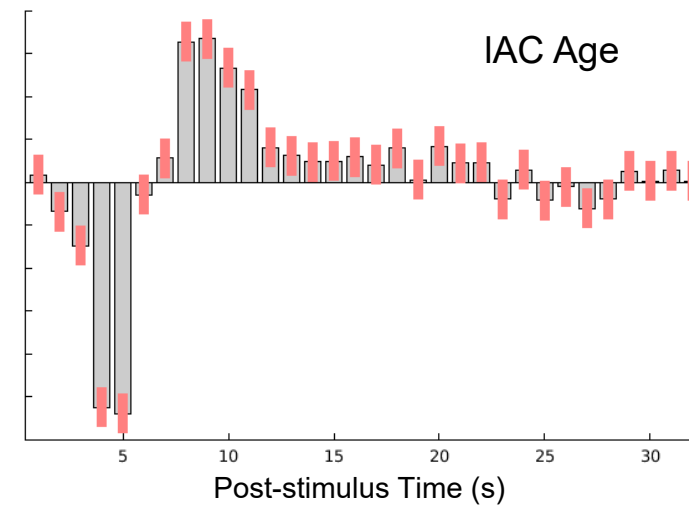
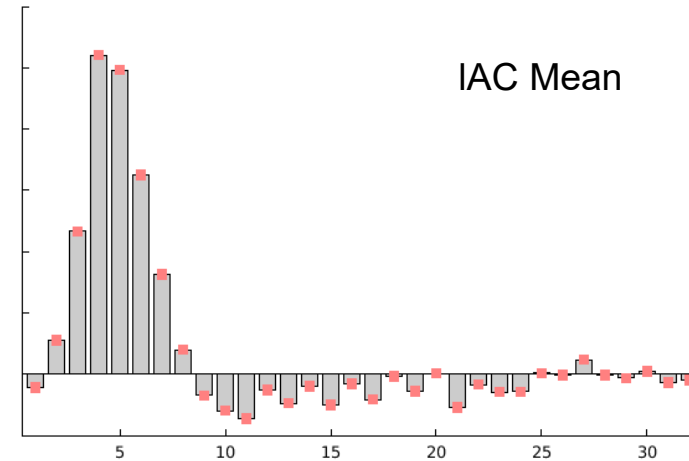
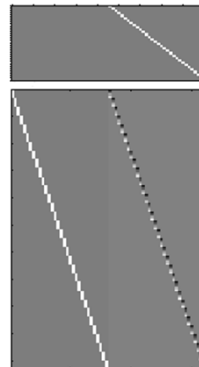
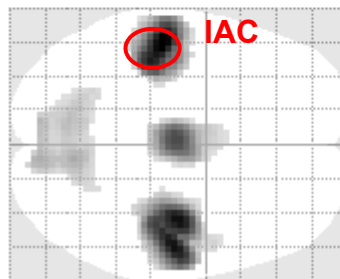
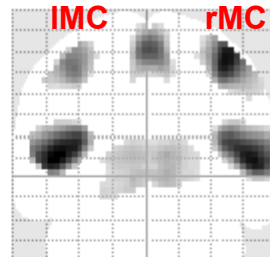
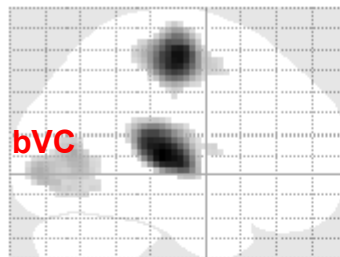
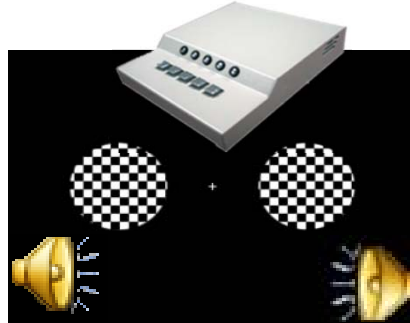
This article is a preprint and has not been certified by peer review [what does this mean?].



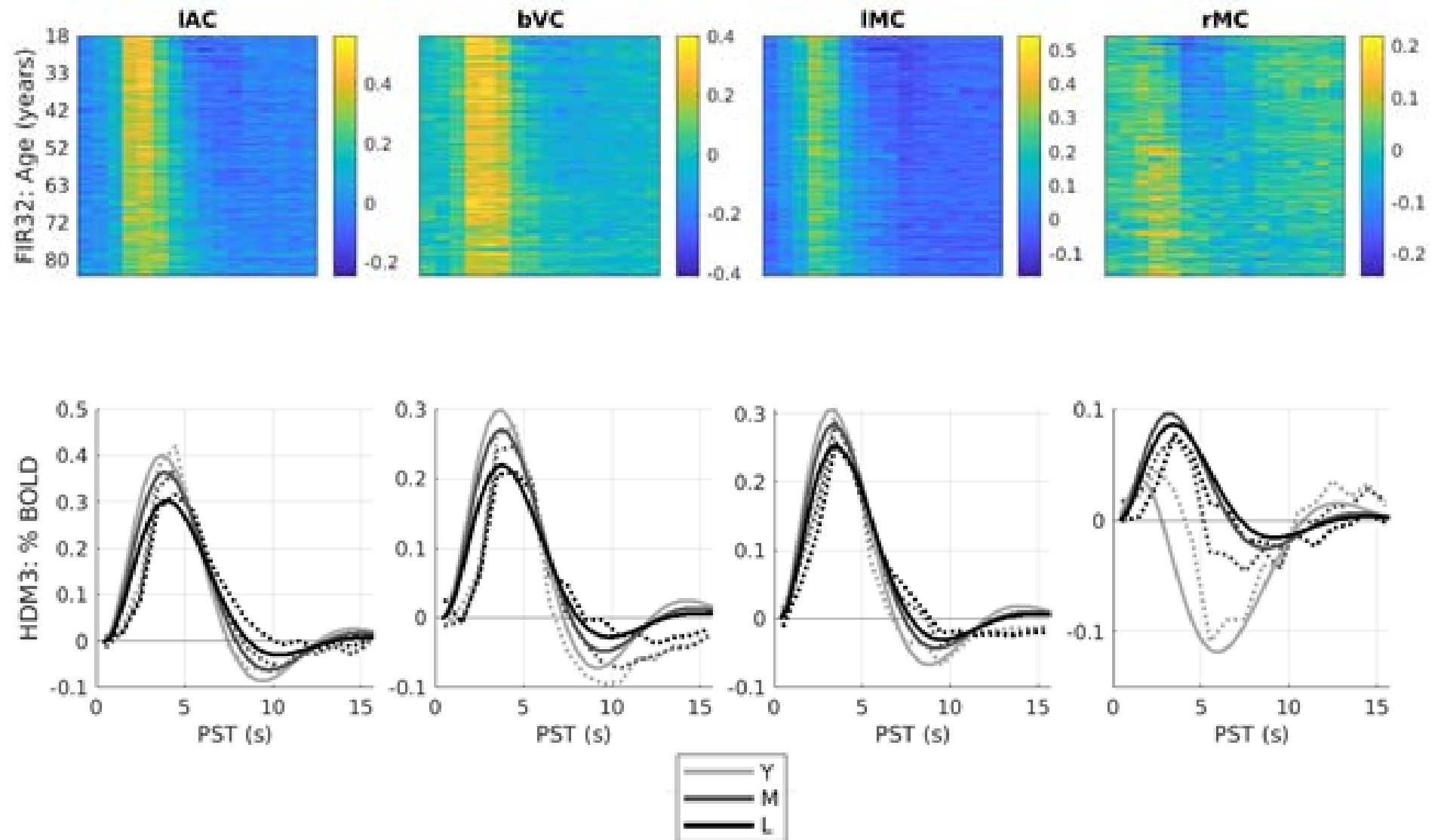
# Haemodynamic Modelling (HDM)



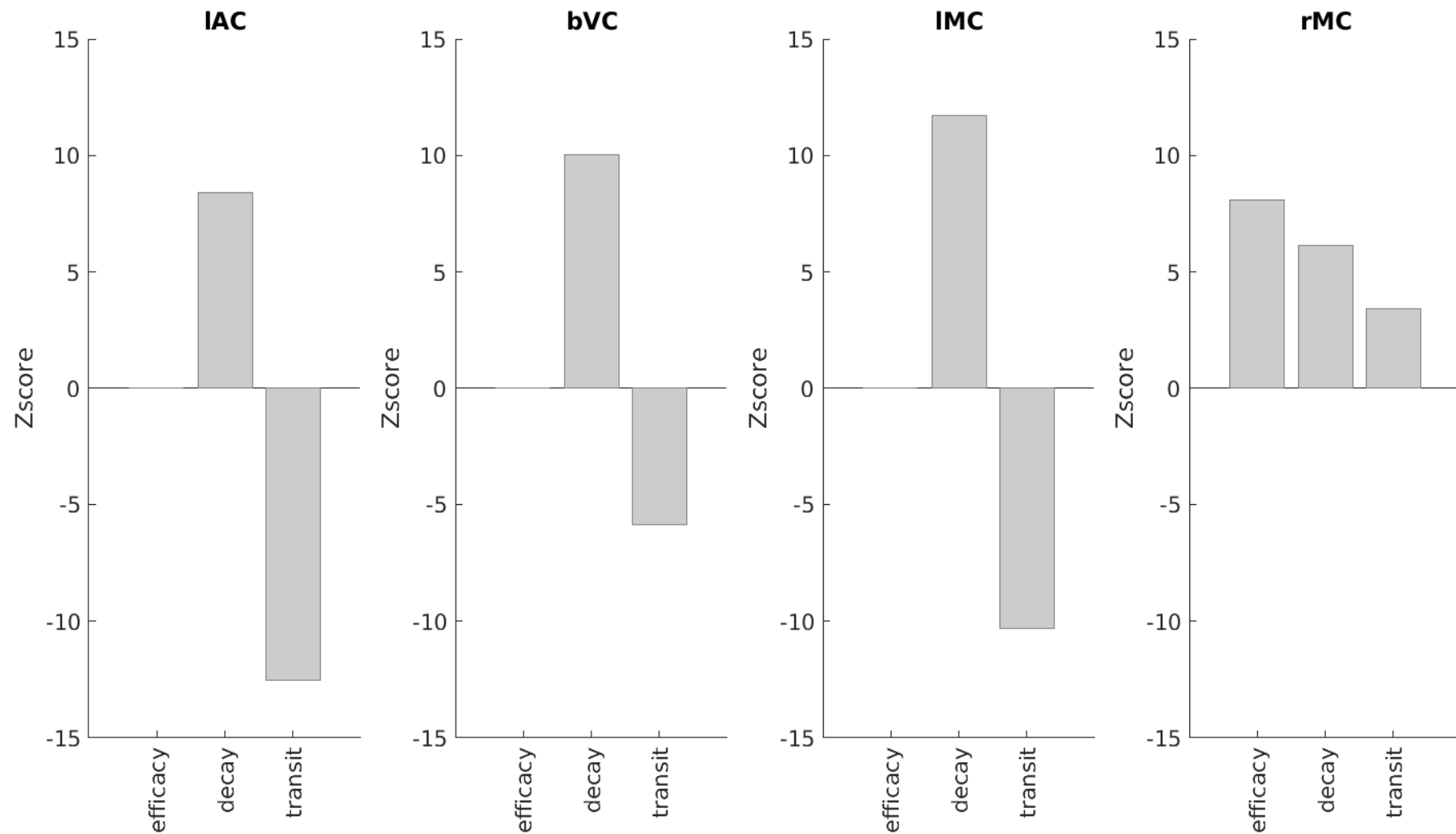
# Haemodynamic Modelling (HDM)



# Haemodynamic Modelling (HDM)



## Effect of Age (PEB)




1. Adjust data... e.g, adjust BOLD activation by RSFA (Tsvetanov et al., 2015)  
or BOLD connectivity by mean FC (Geerligs et al., 2017)
2. ...or have more complex model, e.g, HaemoDynamic Modelling, HDM,  
Dynamic Causal Modelling, DCM...

The Journal of Neuroscience, March 16, 2016 • 36(11):3115–3126 • 3115

Behavioral/Cognitive

## Extrinsic and Intrinsic Brain Network Connectivity Maintains Cognition across the Lifespan Despite Accelerated Decay of Regional Brain Activation

 Kamen A. Tsvetanov,<sup>1,7</sup> Richard N.A. Henson,<sup>2,7</sup> Lorraine K. Tyler,<sup>1,7</sup> Adeel Razi,<sup>3,4</sup> Linda Geerligs,<sup>2,7</sup> Timothy E. Ham,<sup>5</sup>  
James B. Rowe,<sup>2,5,6,7</sup> and Cambridge Centre for Ageing and Neuroscience<sup>7</sup>

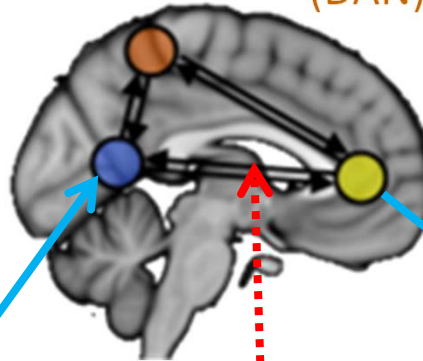


# Resting state DCM

## Connectivity Model Dorsal Attention Network (DAN)

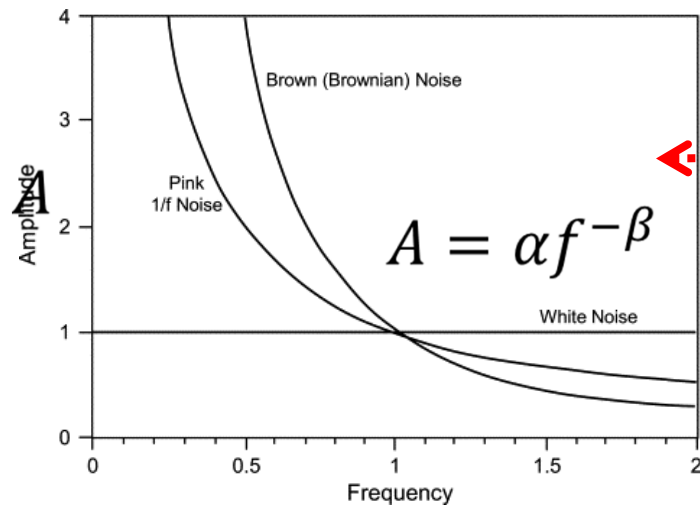
Default Mode  
Network (DMN)

Saliency Network  
(SN)

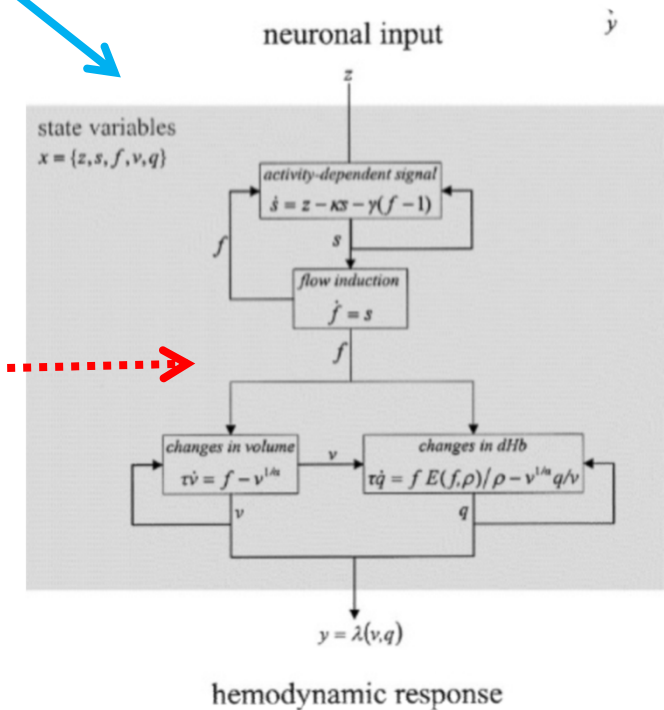


## Haemodynamic Model

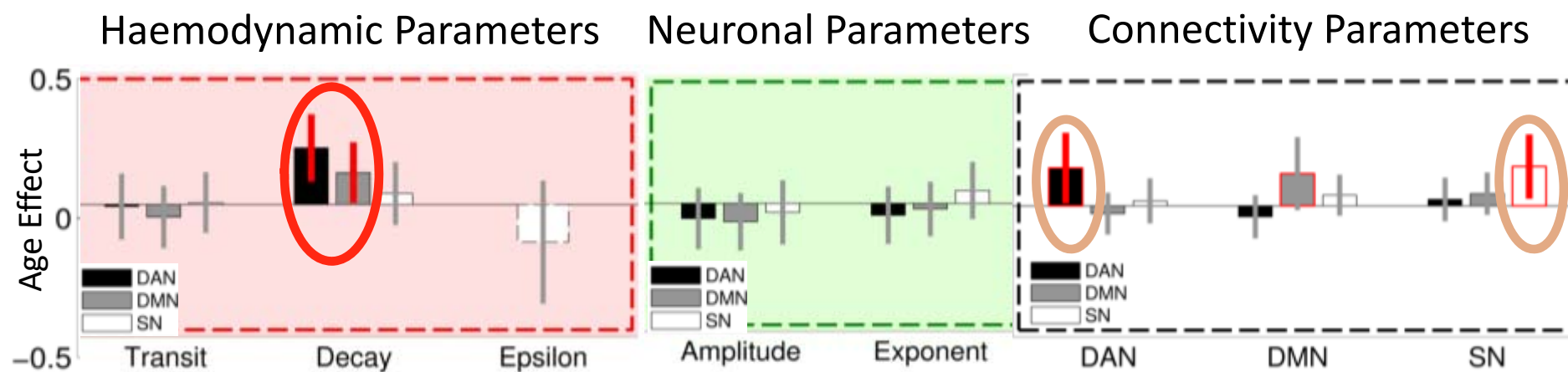
## Activity Model



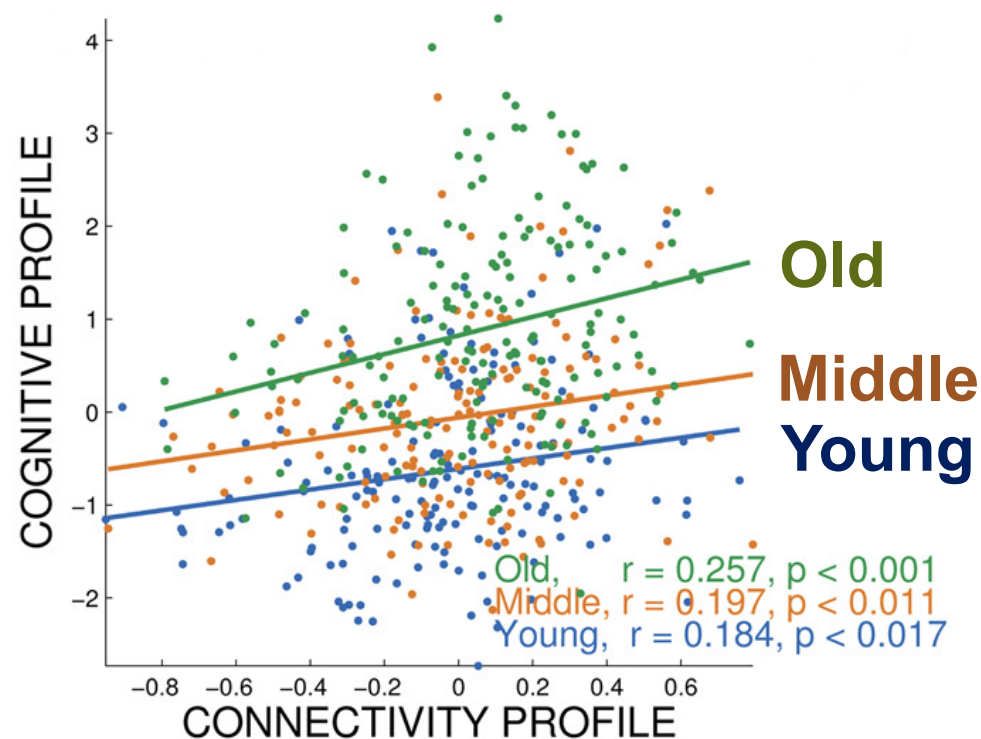
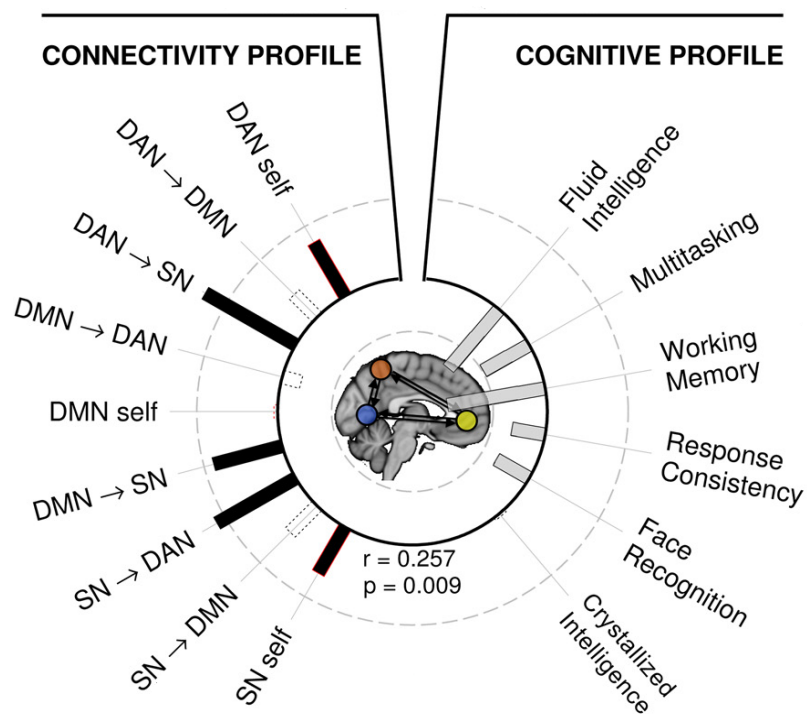
Age



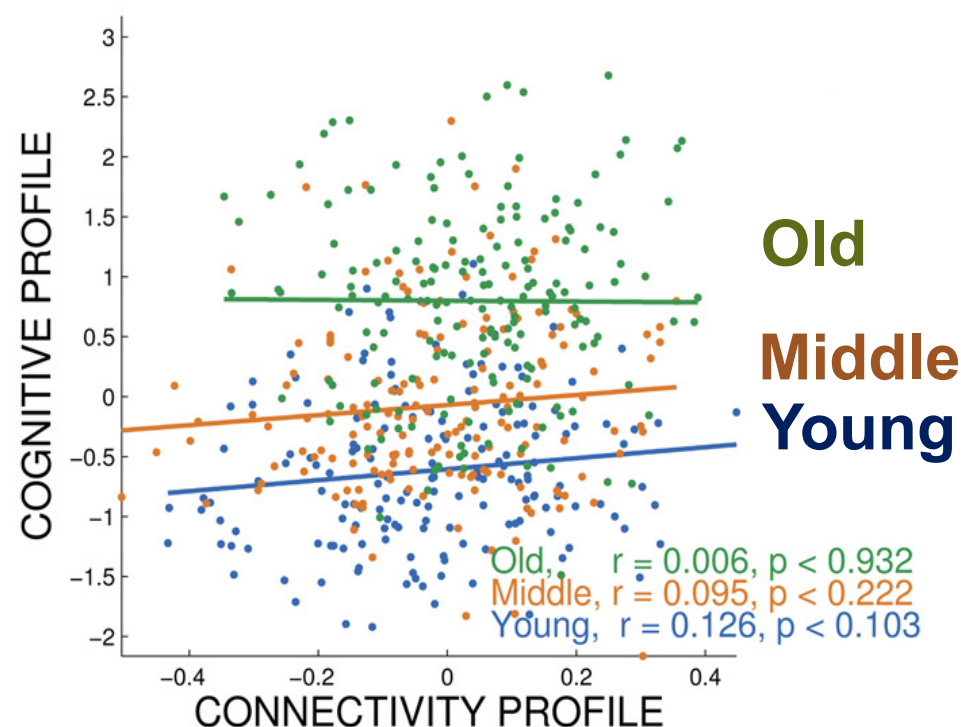
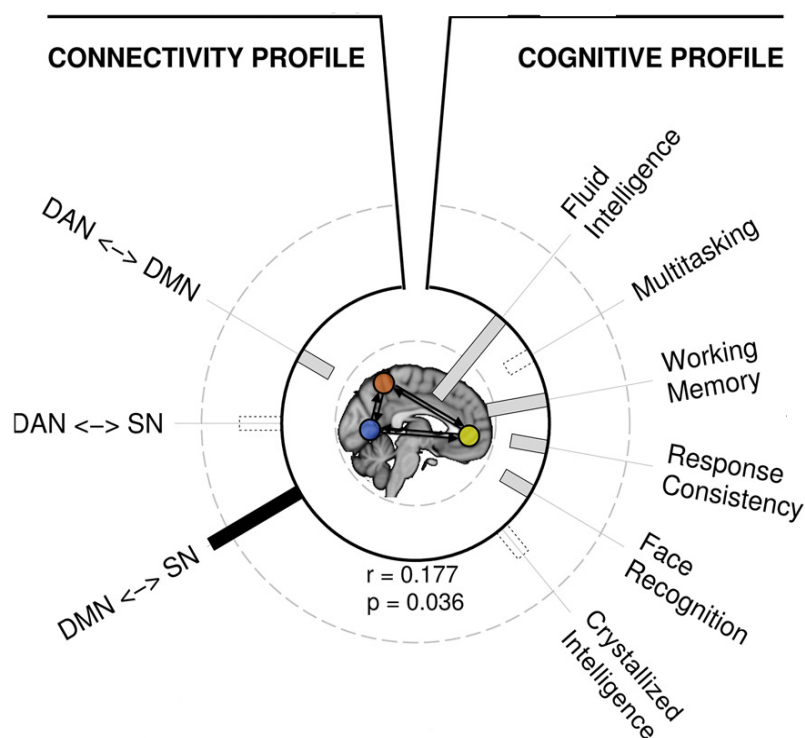
## Effects of Age on DCM parameters:



## Canonical Correlation Analysis (CCA):



## Canonical Correlation Analysis (CCA):



- Many age-related fMRI (de)activations are likely to reflect vascular rather than neural changes...  
*Tsevtanov et al (2015), Hum. Brain. Mapping*
- ...specifically in vasodilatory signal decay and haemodynamic transit time (though not in all brain regions, eg right motor cortex)  
*Henson et al (preprint), BioRxiv*
- Not just (de)activations, but even fMRI functional connectivity (FC) is influenced by vascular health...  
*Geerligs et al (2017), Hum. Brain. Mapping*
- ...and once you allow for vascular contributions, relationship of (neural) FC with cognition gets stronger...  
*Tsvetanov et al (2016), Journal of Neuroscience*
- So if you want to study age effects on fMRI, either:
  - Adjust data by RSFA, mean FC, or independent vascular measures (BP, ECG)...
  - ...or separate neural and vascular components with a model (eg DCM)
  - ...or use an non-haemodynamic measure, eg MEG...  
*Price et al (2016), Nat Comms...*