# StrokeNetProject

May 24, 2019

## 1 Analysis summary, figures and results

### 1.1 Summary

Measuring associations between localized brain lesions and cognitive impairments in stroke patients is a powerful approach for establishing brain-behaviour relationships. However, the distal effects of such lesions on brain connectivity and behaviour are not well understood. In the current study we hypothesized that damage to white matter tracts and highly connected cortical regions would result in widespread connectivity deficits related to multiple, correlated behaviours. We investigated this hypothesis by modelling white matter damage within a stroke patient cohort (N = 80) and related these 'lesion-connectivity patterns' to a broad range of behavioural impairments in the domains of visual perception, attention, reasoning, language and IQ, all within a multivariate statistical framework. Using canonical correlation analysis we found that a single principle axis relating behavioural deficits and lesion damage. Consistent with previous work this pattern conformed to a left-right hemispheric bias for language, on the one hand, and attention, on the other. More specifically, the predictive connections associated with language were dominated by highly weighted subcortical connections, whereas the attention-related was dominated by damage the fronto-parietal "control" network. Critically, using this low-dimensional approach single-subject behavioural scores could be predicted in a leave-one-out fashion across multiple behaviours. Our findings highlight the importance of lesion-network approaches in explaining complex clusters of behavioural deficits following stroke, and the potential for predicting recovery and optimizing rehabilitative interventions in the future.

<IPython.core.display.HTML object>

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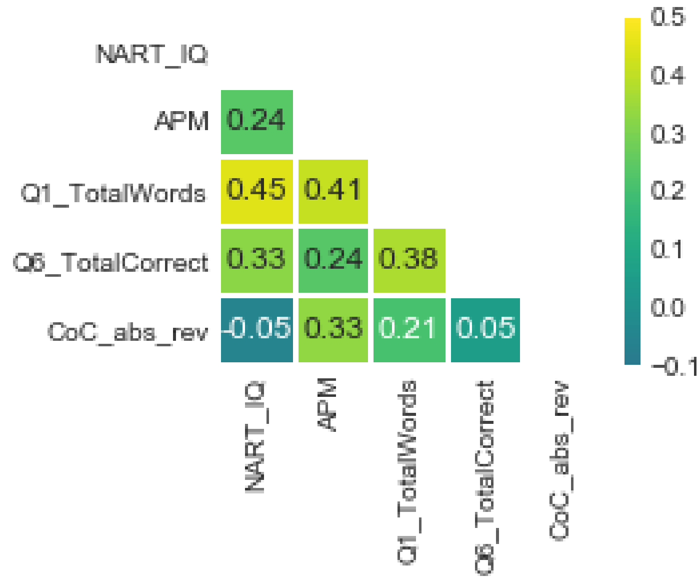
/anaconda3/lib/python3.7/importlib/_bootstrap.py:219: ImportWarning: can't resolve package fron
  return f(*args, **kwds)
/anaconda3/lib/python3.7/importlib/_bootstrap.py:219: ImportWarning: can't resolve package fron
  return f(*args, **kwds)
```

### 1.2 Lesions, connectivity lesion-mapping and behaviour

Post-stroke behaviour is generally correlated. We used five different measures of interest: - NART_IQ: IQ score based on the National Adult Reading Test (NART). We *wouldn't* expect this to change with stroke damage considering it is often used as a "premorbid IQ" measure. - APM: The first set of the Raven's Advanced Progressive Matrices. - Q1_TotalWords: Language measure - Q6_TotalCorrect: Verbal fluency language measure - CoC_abs_rev: Spatial Neglect cancellation task absolute value.

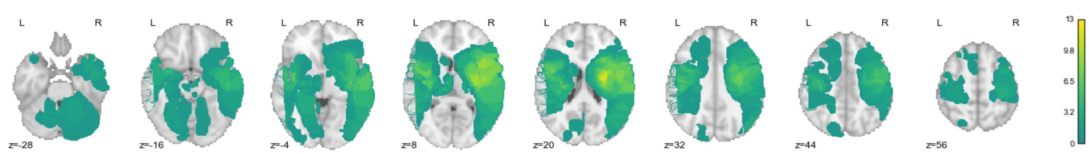
Previous work has shown that post-stroke behaviour is correlated and has a simple three factor solution [**?**] Unfortunately we don't have enough breadth of behavioural variables to show this.




### 1.2.1 Lesion density plot

Our stroke locations are typical for the literature. Usually, this map would be thresholded for a VLSM analysis (~10% of the sample), meaning that only regions around the insula would be tested.

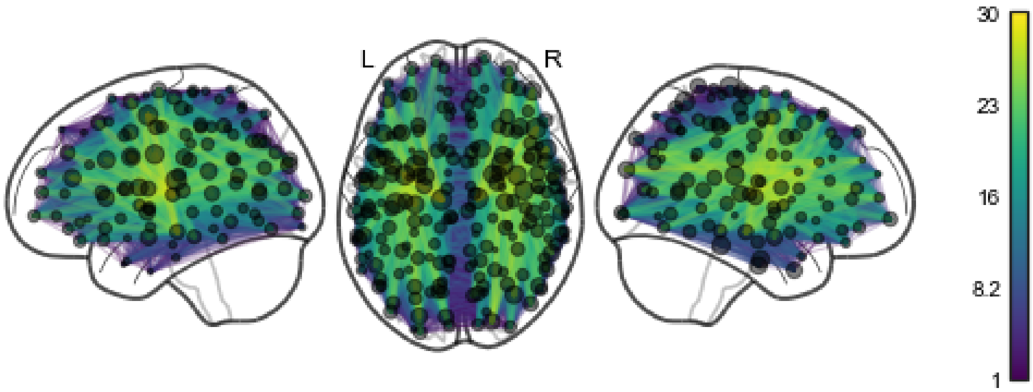
Colourbar indicates overlap across participants. The strange wispy lines are from changing the MNI space of the images (it doesn't affect the lesion-network mapping).




### 1.2.2 Lesion-connectivity mapping density plot

These are the estimated lesioned connections based on 20 similarly aged and gender matched controls from the NKI database. Nearly every connection is implicated across participants.

Colourbar indicates overlap across participants

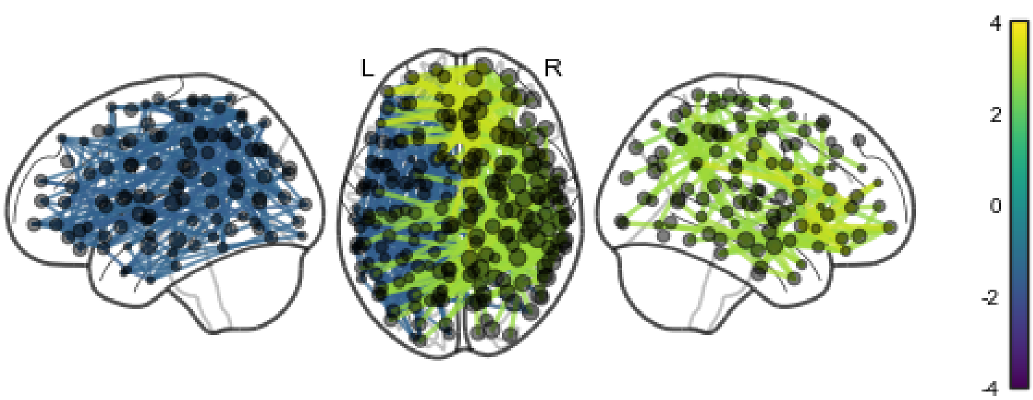


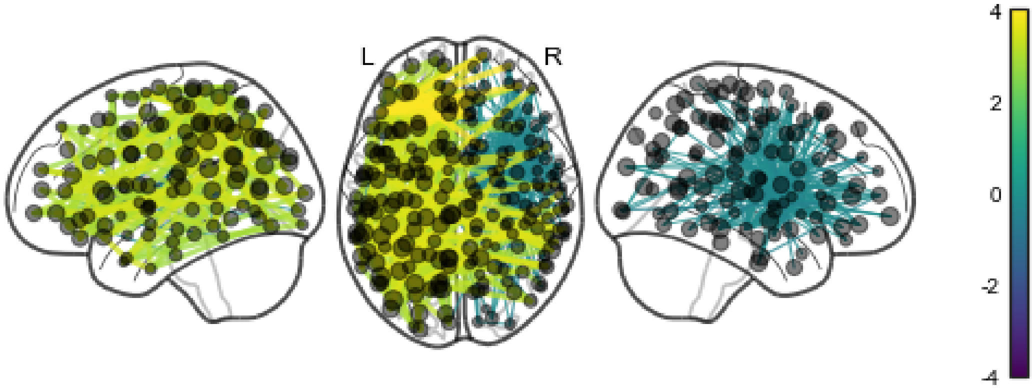

### 1.3 Dimensionality reduction: multiple correspondance analysis (MCA) results

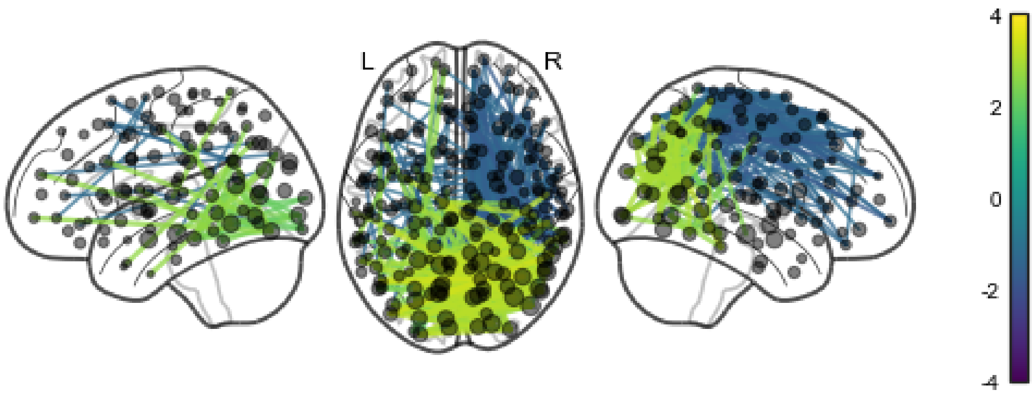
We used MCA to reduce the potential edges used in the CCA (~10,000) to a smaller number of components (tested from 7 - 20). MCA can be thought of as a alternative to PCA for data that is binary. In our case, a PCA is inappropriate because a vector of connections would include many 0's (not damaged connections) and a few weighted connections, resulting in a non-normal distribution. As an added bonus, using binary data lends itself to comparison with the raw lesion maps (which are also binary).

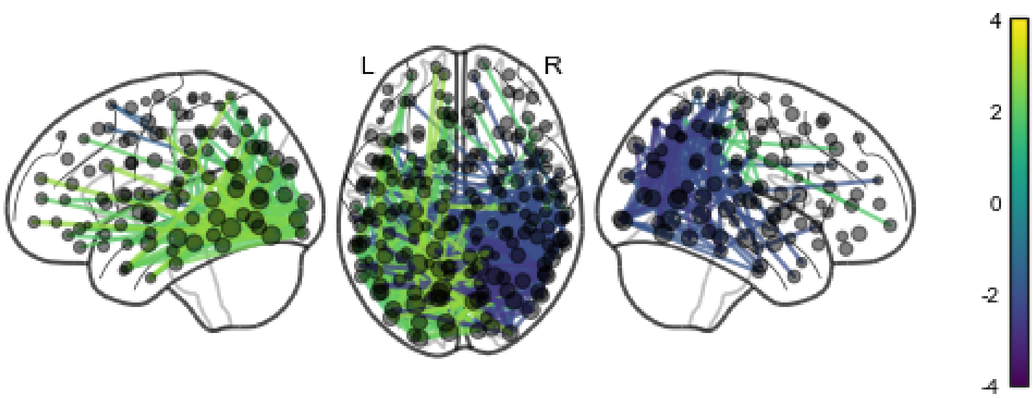
These maps can be interpreted as the patterns of damage and undamaged connectivity that account for the most variance across participants, i.e. "common lesion connectivity damage patterns". The first two, perhaps not surprisingly are left and right hemisphere damage stemming from the insula.

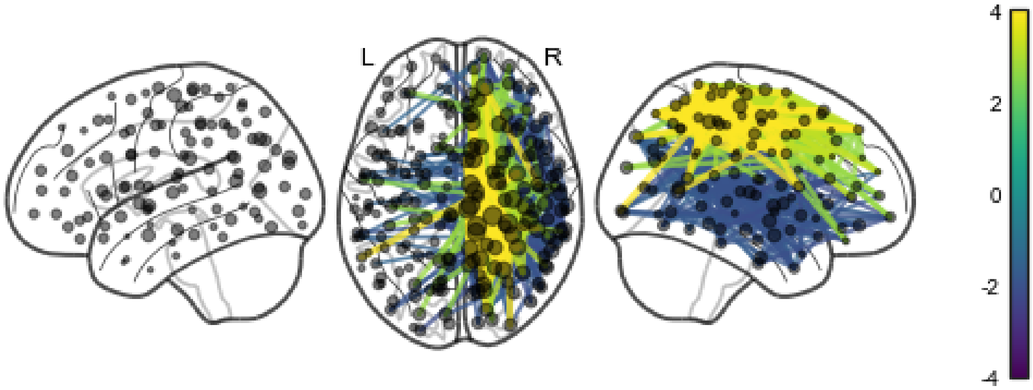
```
Mean variance explained for components (%) [20.51294935  9.69037583  5.13592384  4.66652438  4
  3.10184957  2.75664116  2.58948542  2.4559511 ]
```




L
R
4
2
0
-2
-4


L
R
4
2
0
-2
-4

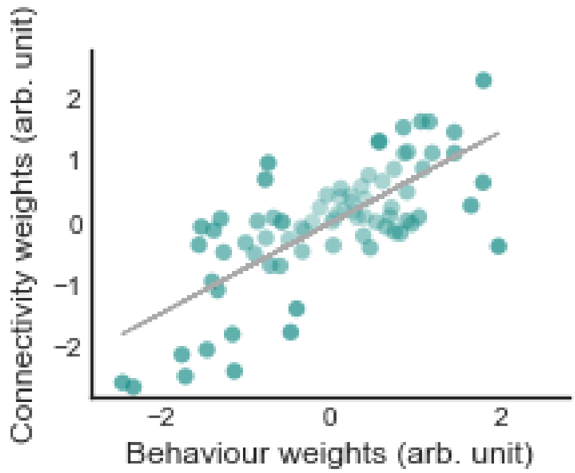

L
R
4
2
0
-2
-4



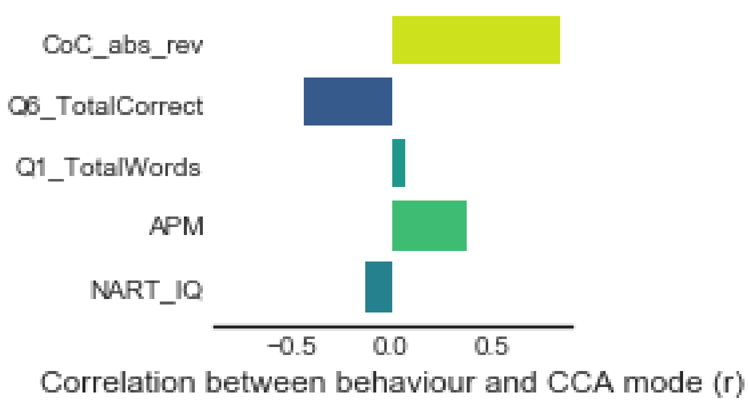

## 1.4 CCA Results

Only one mode is significant after correcting via permutations. It loads positively onto the APM and Spatial Neglect, and neglativly onto verbal fluency. The connectivity is pretty clearly determined by damage on the left associated with language and the right associated with spatial neglect/APM.

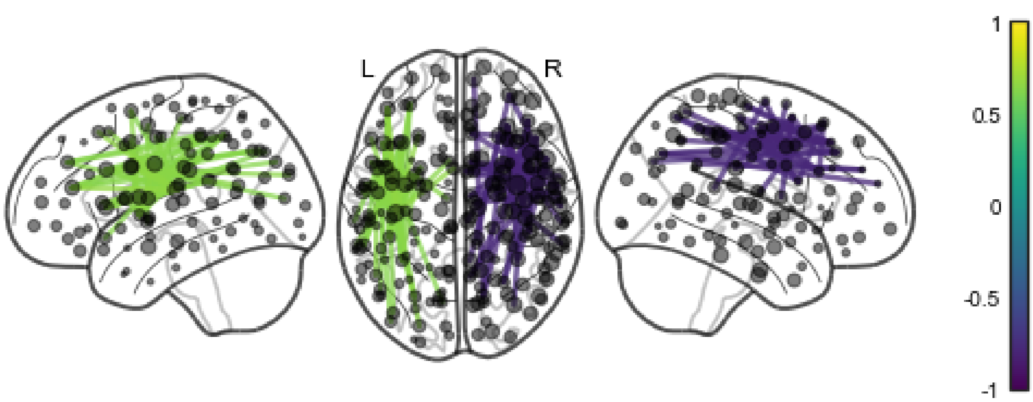
When investigating the associted networks a fairly clear patterns emerges whereby the APM/spatial neglect/ right hemisphere damage is associated with control and attention networks - makes sense! The left-hemisphere /verbal fluency damage is associated with more diffuse, potentially subcortical connection damage.



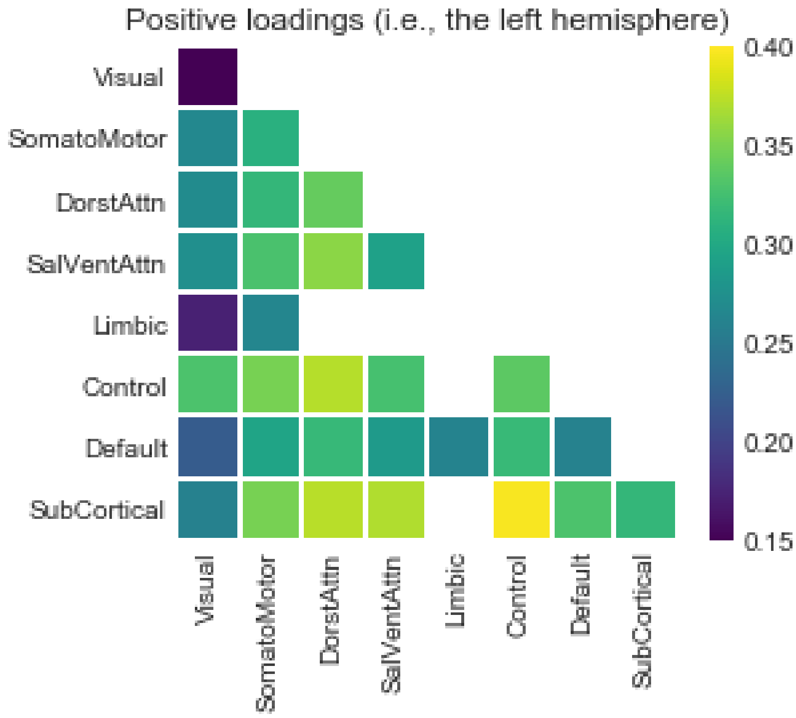
Connectivity weights (arb. unit)
Behaviour weights (arb. unit)
2
1
0
−1
−2
−2
0
2

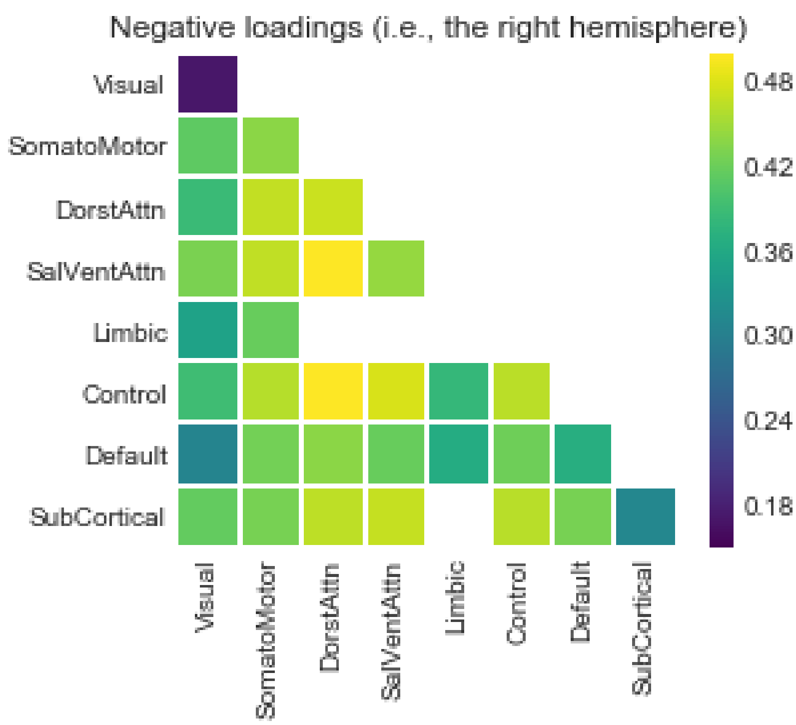
CoC_abs_rev
Q6_TotalCorrect
Q1_TotalWords
APM
NART_IQ
−0.5
0.0
0.5
Correlation between behaviour and CCA mode (r)

L
R
1
0.5
0
-0.5
-1



Positive loadings (i.e., the left hemisphere)
Visual
SomatoMotor
DorstAttn
SalVentAttn
Limbic
Control
Default
SubCortical
0.40
0.35
0.30
0.25
0.20
0.15

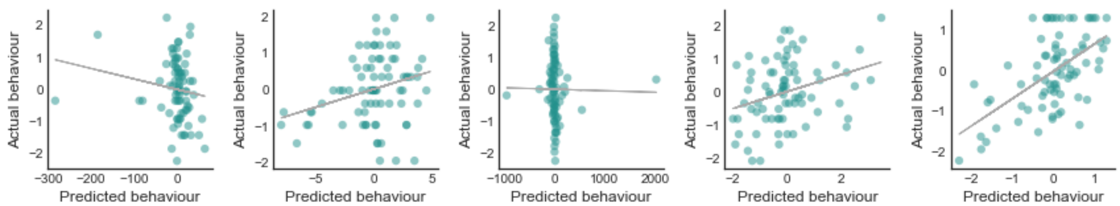
Negative loadings (i.e., the right hemisphere)
Visual
SomatoMotor
DorstAttn
SalVentAttn
Limbic
Control
Default
SubCortical
0.48
0.42
0.36
0.30
0.24
0.18

### 1.4.1 Leave-one-out prediction of behavioural scores

The CCA can predict 3/5 behaviours (in line with the behavioural loadings above).

Remember that we wouldn't expect it to predict the NART (so, 3/4).

This is kind of impressive because it is distilling each individual into a single value + a simple transformation for each behaviour to acheive this level of accuracy. Suggests that a low dimensional description is quite useful for predicting a left out individual's cognitive scores (on some tasks).

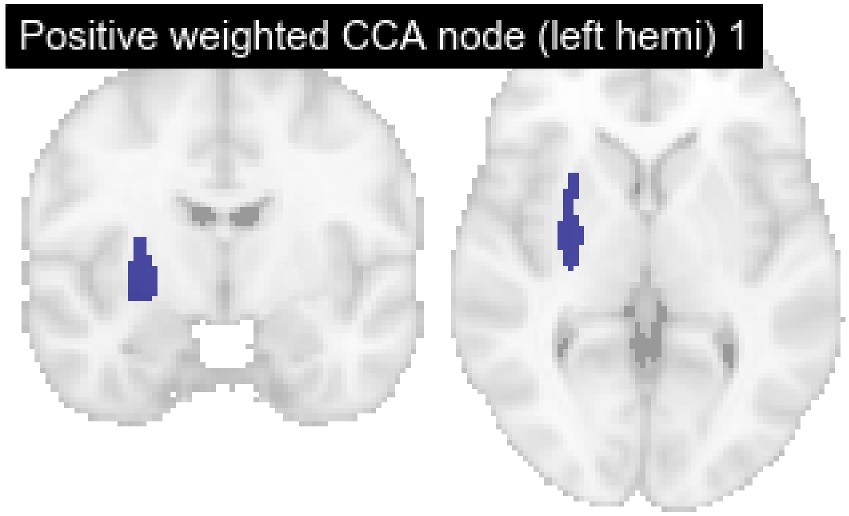




## 1.5 Neurosynth reverse inference analysis

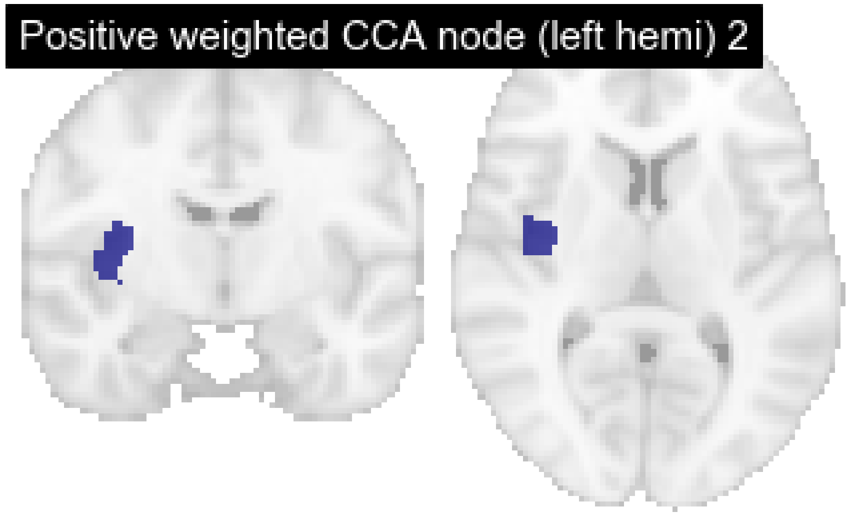
The last analysis I have done is using neurosynth to conduct a meta-analysis on the top five positive and negatively weighted regions from the CCA.

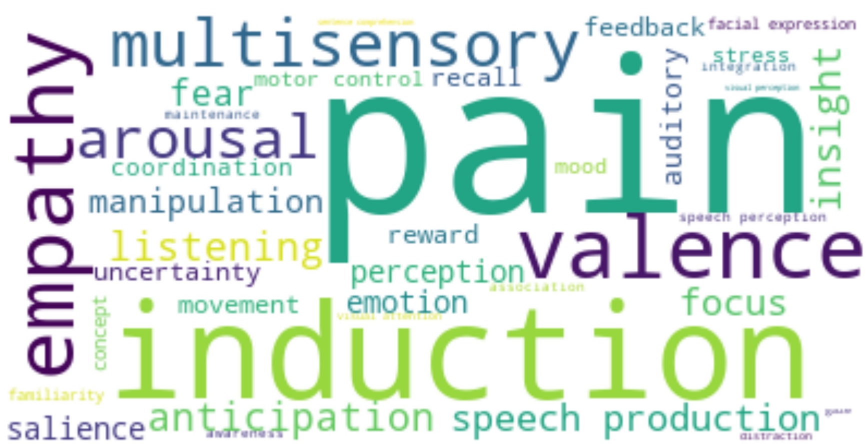
This method is relatively simple, for each roi it does a meta-analytic comparison of all studies that activate within the region versus all the ones that don't. The final result is a set of labels associated with the activated studies.

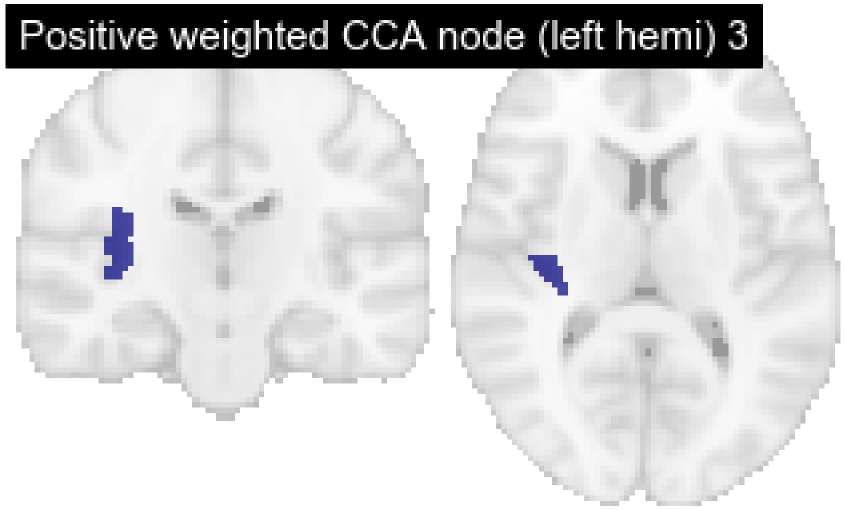
I'm interpreting the results in the following way: - We only measure five behavioural variables, but it is likely that our results extend beyond these cognitive faculties. i.e., this is weak (reverse inference based) evidence for generalization. - The most 'interesting' effects tend to occur away from the Insula, suggesting that connections, rather than localised damage might be a key factor.


Positive weighted CCA node (left hemi) 1

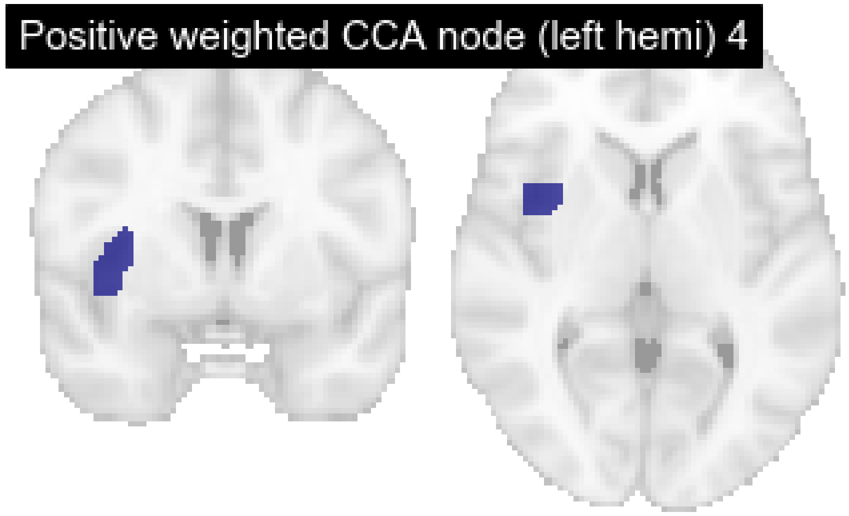

movement
motor control
learning
coordination
feedback
speech production
imagery
pain
reward
valence
arousal
response selection
inhibition
skill
listening
insight
search
rhythm
planning
recall
speech perception
strategy
expectancy
remembering
stress
anticipation
episodic memory
rehearsal
response inhibition
empathy
focus
goal
encoding
consolidation
interference
monitoring
uncertainty
association
auditory
action

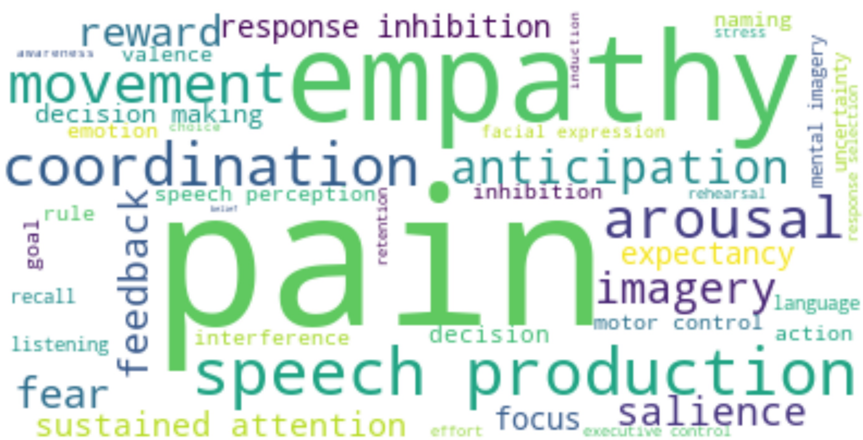

Positive weighted CCA node (left hemi) 2

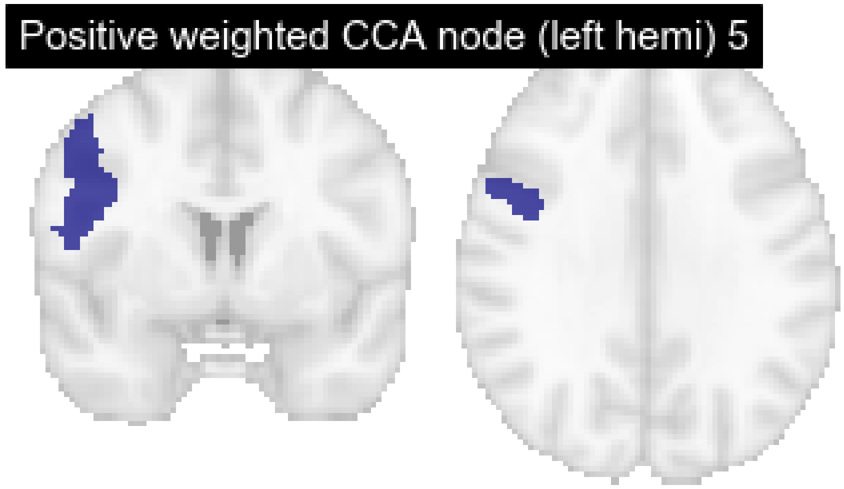

pain
induction
empathy
valence
multisensory
arousal
feedback
facial expression
stress
integration
auditory
insight
fear
motor control
recall
maintenance
coordination
mood
manipulation
speech perception
listening
reward
uncertainty
perception
association
movement
emotion
focus
concept
familiarity
salience
anticipation
speech production
awareness
distraction

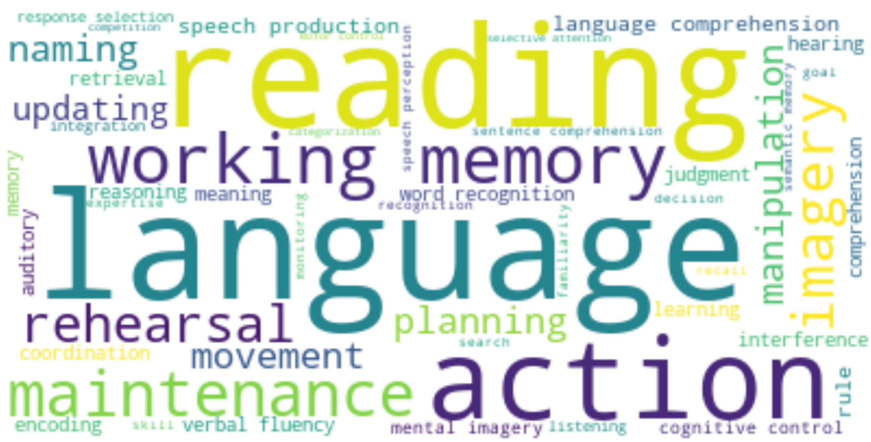

Positive weighted CCA node (left hemi) 3

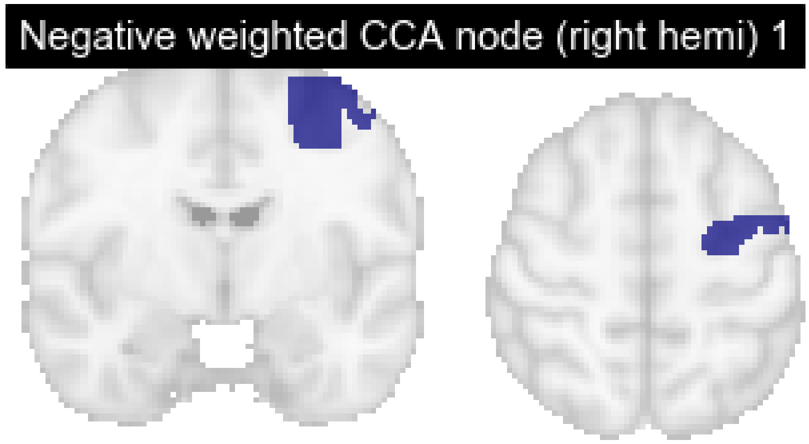

auditory
pain
listening
multisensory
speech perception
speech production
visual perception
consciousness
concept
arousal
remembering
empathy
context
rhythm
meaning
consolidation
hearing
fear
feedback
valence
encoding
integration
competition
induction
word recognition
fixation
skill
emotion
decision making
perception
movement
motor control
visual attention
coordination
distraction
learning
insight
anticipation
belief
recall
effort
stress
sustained attention
awareness
reading


Positive weighted CCA node (left hemi) 4

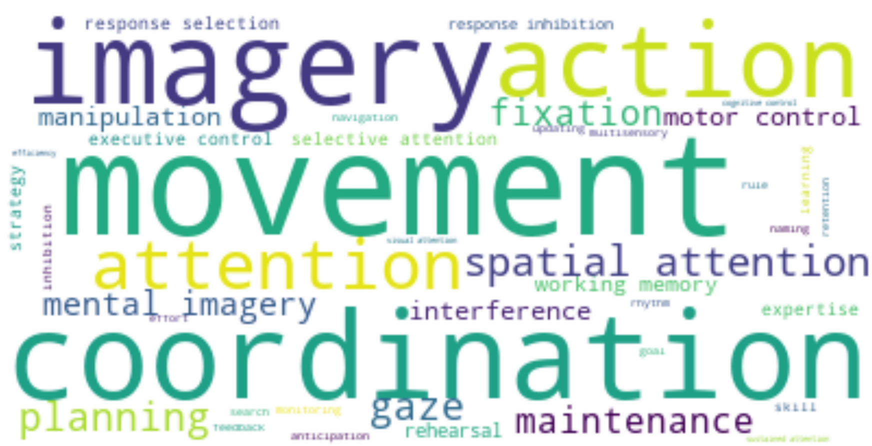

reward
response inhibition
naming
stress
valence
movement
empathy
induction
mental imagery
uncertainty
response selection
decision making
emotion
facial expression
coordination
anticipation
speech perception
inhibition
rehearsal
rule
goal
feedback
pain
retention
arousal
expectancy
recall
imagery
language
motor control
listening
interference
decision
action
speech production
fear
focus
salience
sustained attention
effort
executive control


Positive weighted CCA node (left hemi) 5

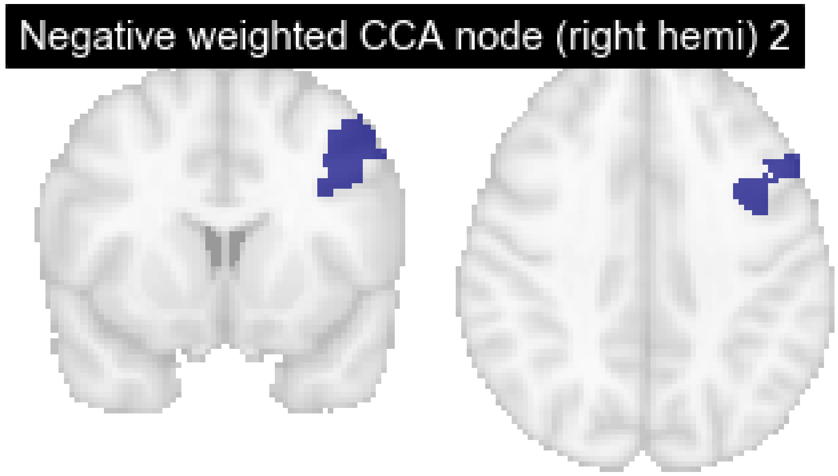

response selection
speech production
language comprehension
naming
reading
hearing
retrieval
updating
integration
working memory
manipulation
imagery
judgment
comprehension
memory
reasoning
meaning
word recognition
decision
language
auditory
rehearsal
planning
learning
interference
coordination
movement
maintenance
action
rule
encoding
verbal fluency
mental imagery
listening
cognitive control



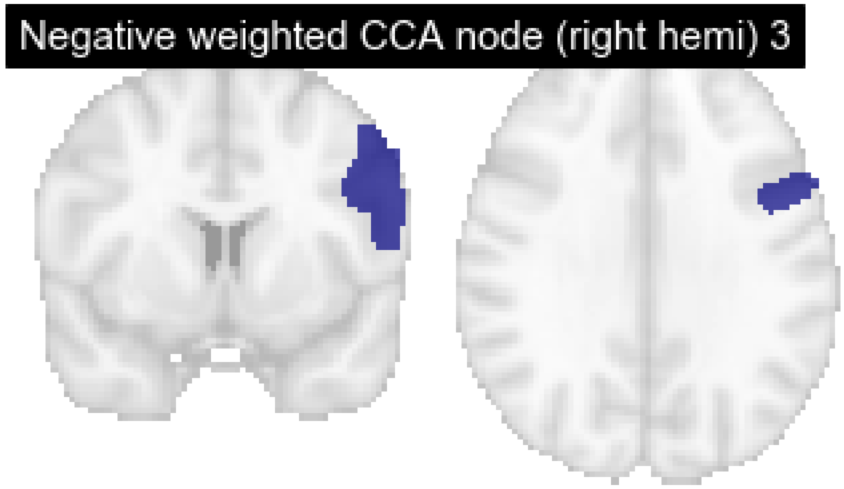
Negative weighted CCA node (right hemi) 1

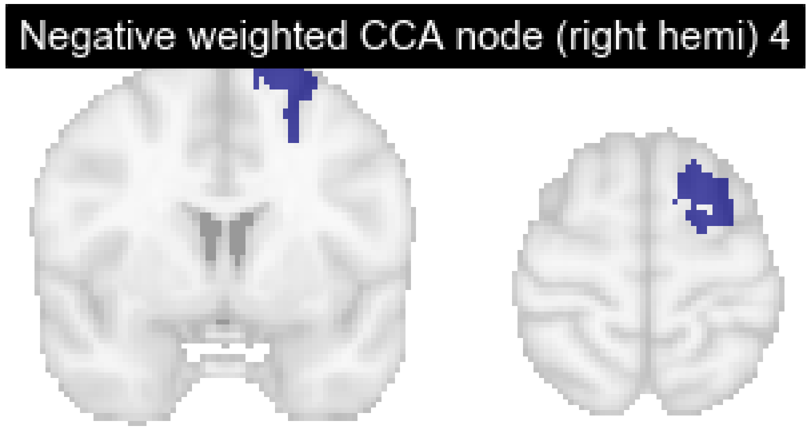
response selection
response inhibition
imagery
action
manipulation
fixation
motor control
executive control
selective attention
movement
strategy
inhibition
attention
spatial attention
working memory
mental imagery
interference
expertise
coordination
planning
gaze
rehearsal
maintenance


Negative weighted CCA node (right hemi) 2

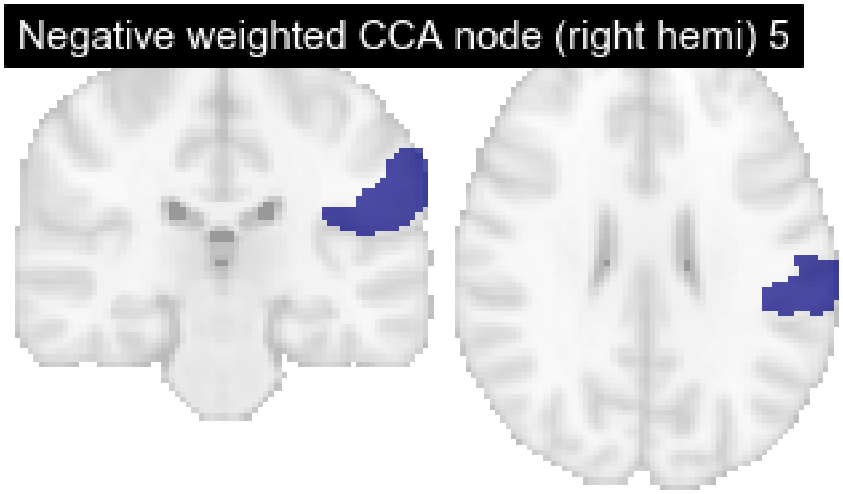

monitoring
maintenance
manipulation
executive control
mental imagery
retrieval
remembering
memory
inhibition
uncertainty
attention
recall
interference
response
inhibition
listening
expectancy
spatial attention
memory retrieval
working memory
categorization
executive function
strategy
imagery
cognitive control
action
sustained attention
distraction


Negative weighted CCA node (right hemi) 3


coordination
imagery
action
working memory
movement
manipulation
attention
maintenance
empathy
interference
response inhibition
planning
reading
perception
skill
spatial attention
encoding
selective attention
cognitive control
inhibition
motor control
executive control
hearing
response selection


Negative weighted CCA node (right hemi) 4


response inhibition
goal
efficiency
imagery
manipulation
retention
executive control
navigation
cognitive control
working memory
maintenance
interference
empathy
movement
inhibition
updating
executive function
mental imagery
competition
learning
attention
uncertainty
visual attention
monitoring
spatial attention
memory
motor control
effort
rule
gaze
decision
planning
remembering
action
fixation
choice
decision making
coordination
response selection





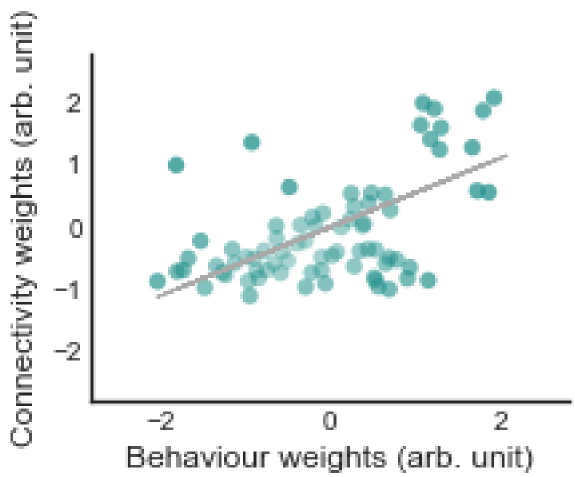
## 2 Supplementary figures and analysis

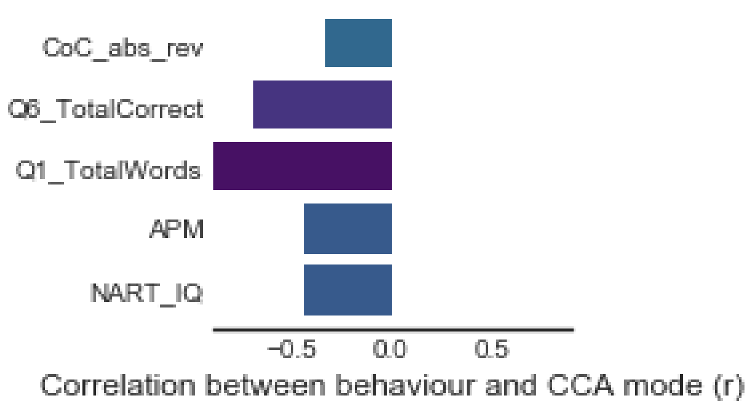
Various supplemental analyses.

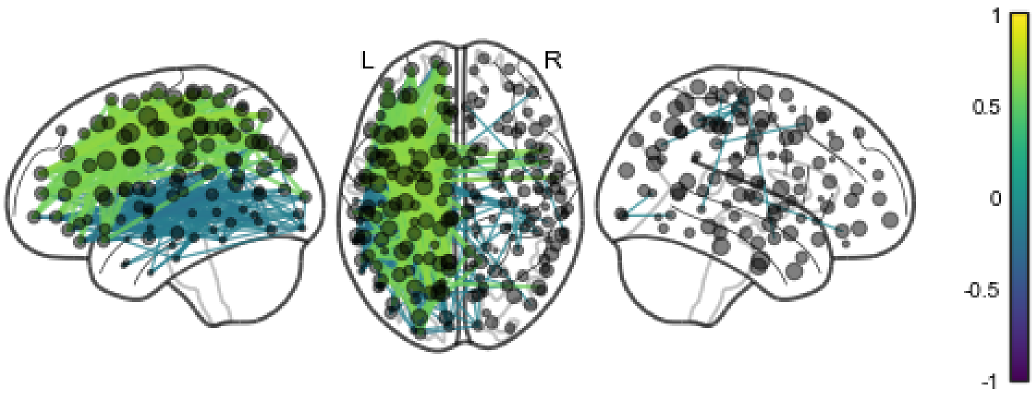
## 2.1 Mode 2?

Arguably the permutation approach taken [?] is a harsh on canonical variates beyond the first. Is Mode 2 interesting and or helpful to interpet?

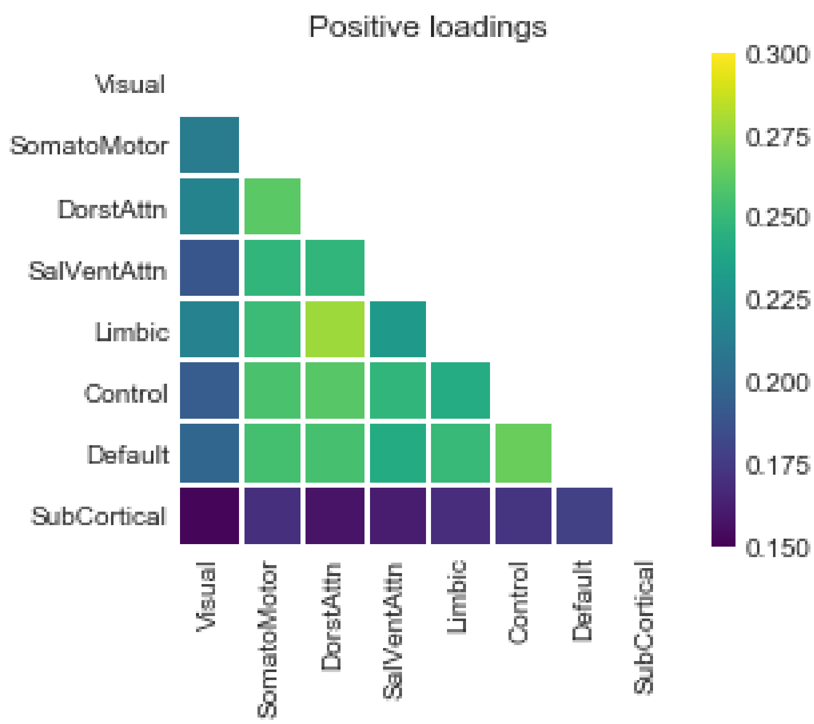
Maybe yes! It predicts the language task that could not be predicted in mode 1 reasonably well. It is associated with damage to a left-hemisphere superior network. Need to think what this might mean in terms of localisation.

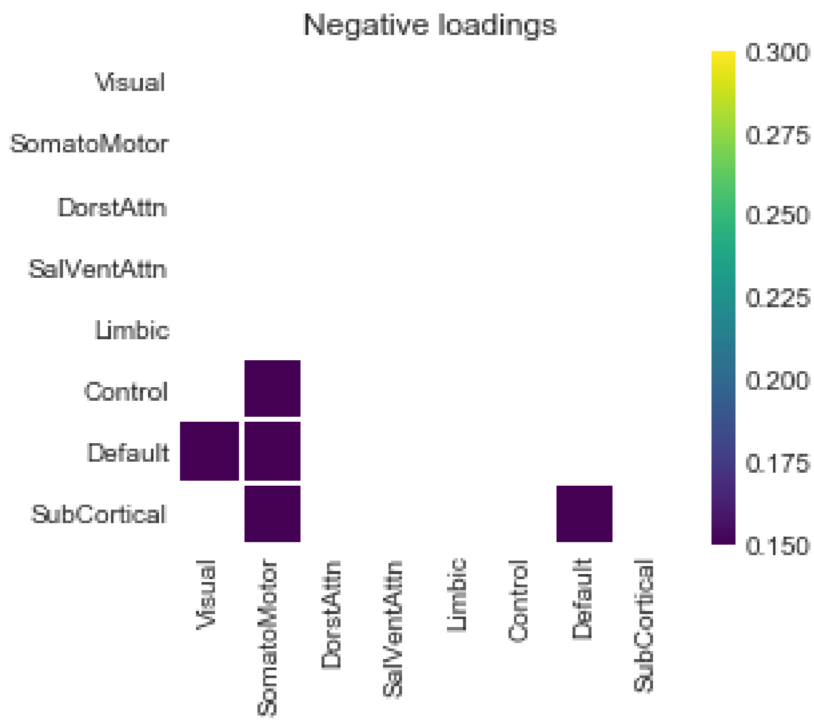



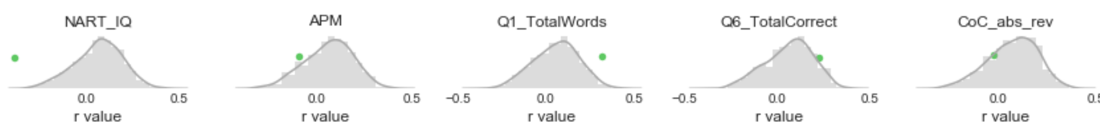


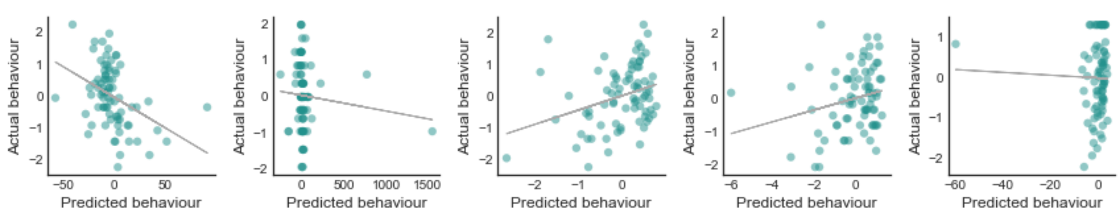
L
R
1
0.5
0
-0.5
-1

Positive loadings
Visual
SomatoMotor
DorstAttn
SalVentAttn
Limbic
Control
Default
SubCortical
0.300
0.275
0.250
0.225
0.200
0.175
0.150

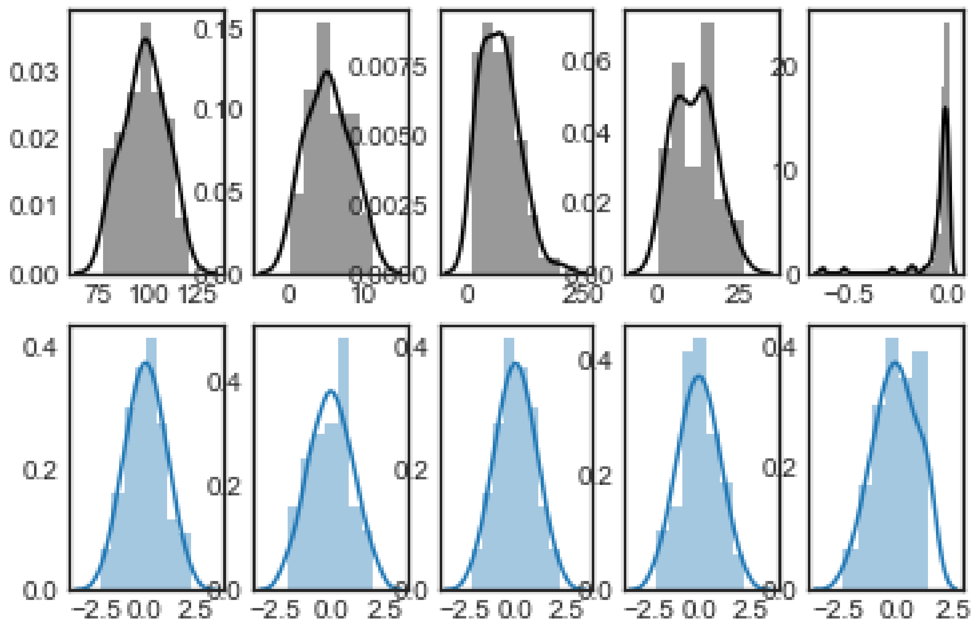


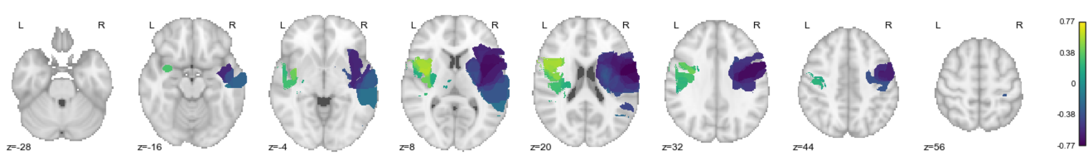

## 2.2 Behavioural data transform

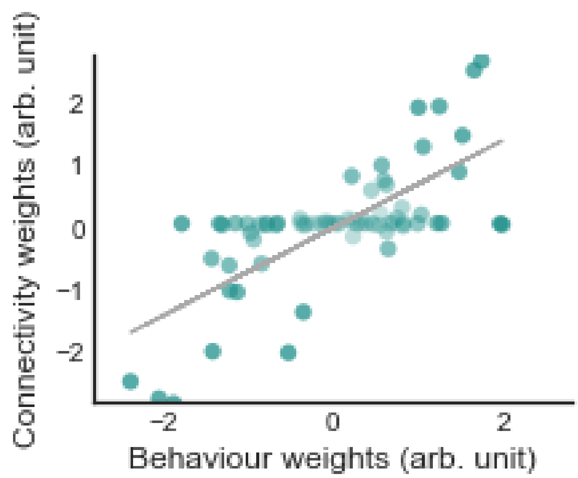
After the transform no behavioural data violates normality assumptions

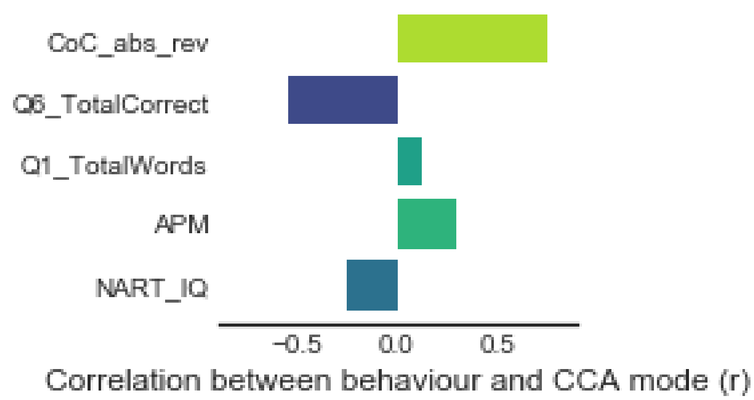


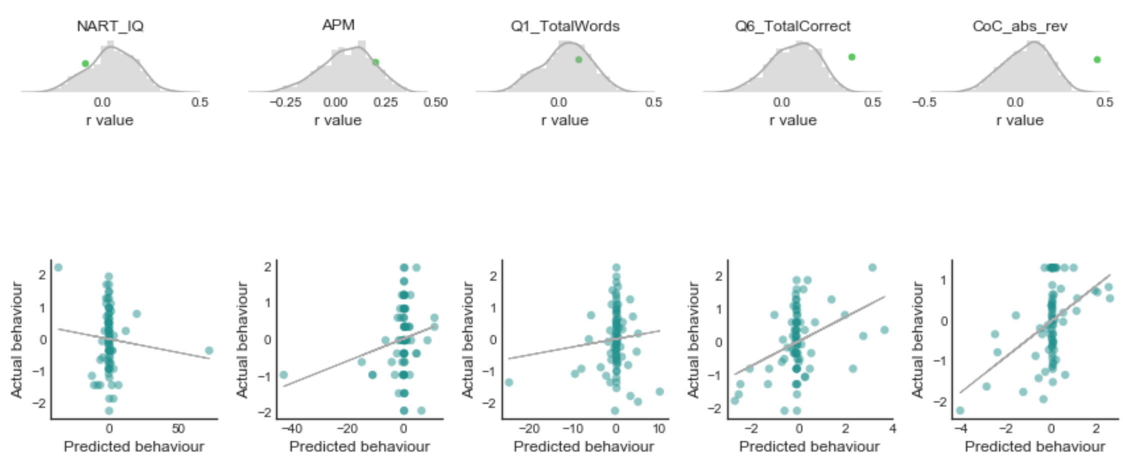
## 2.3 What happens if you perform the CCA on the voxels?

- 1) Left - right axis is the same.
- 2) Predictions are not as impressive. Presumably because it doesn't seem to capture as many subject's data (many 0-loadings)




Connectivity weights (arb. unit)
Behaviour weights (arb. unit)

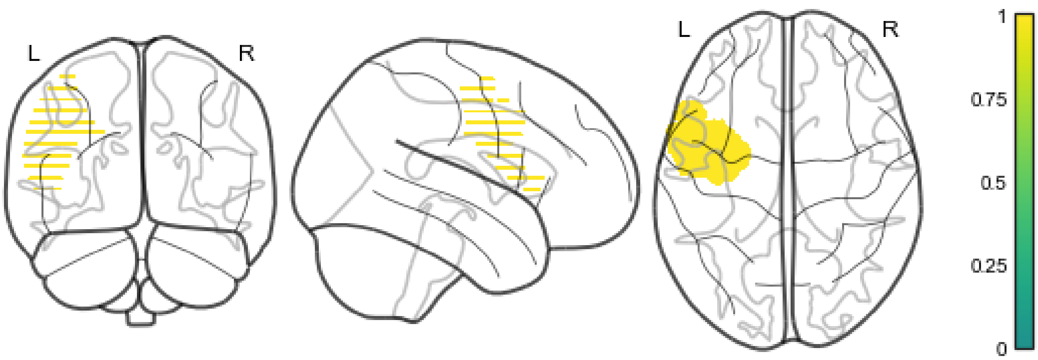

CoC_abs_rev
Q6_TotalCorrect
Q1_TotalWords
APM
NART_IQ
Correlation between behaviour and CCA mode (r)

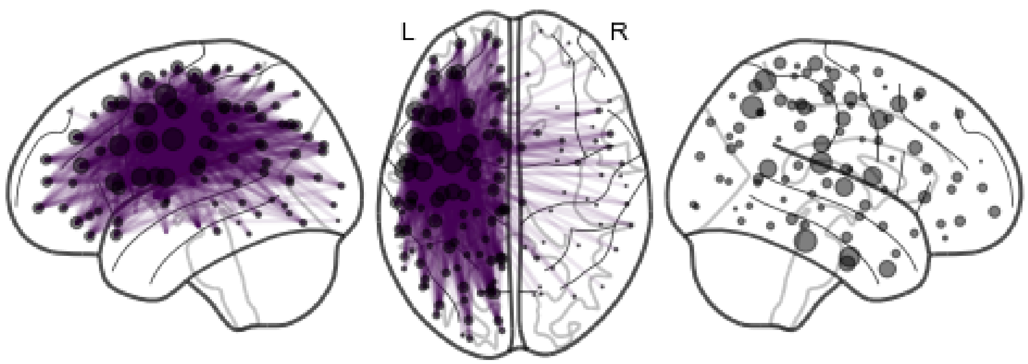

NART_IQ
APM
Q1_TotalWords
Q6_TotalCorrect
CoC_abs_rev
r value
Actual behaviour
Predicted behaviour

### 2.3.1 Empirical comparison to connectivity based CCA

## 2.4 Single example lesion subject

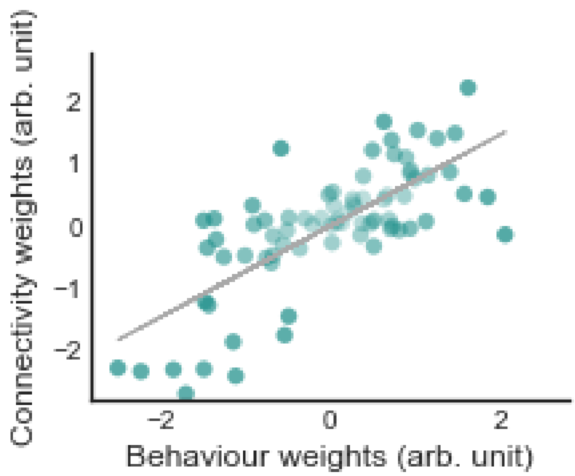
Note the widespread effects of a lesion

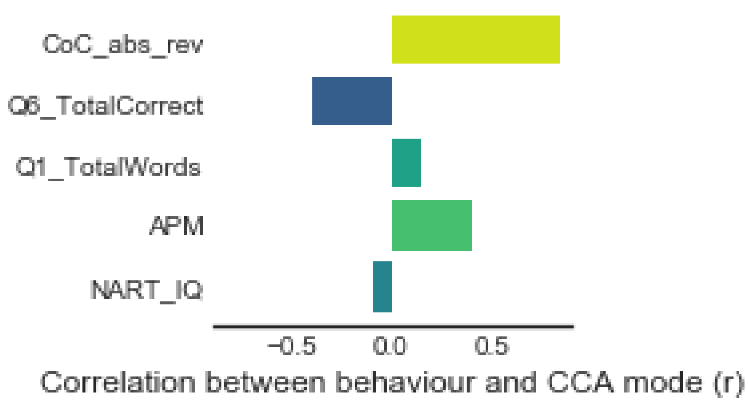


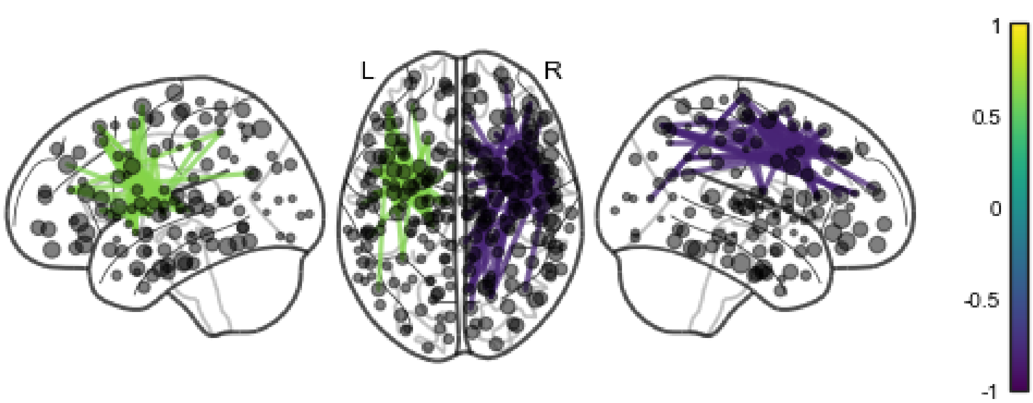



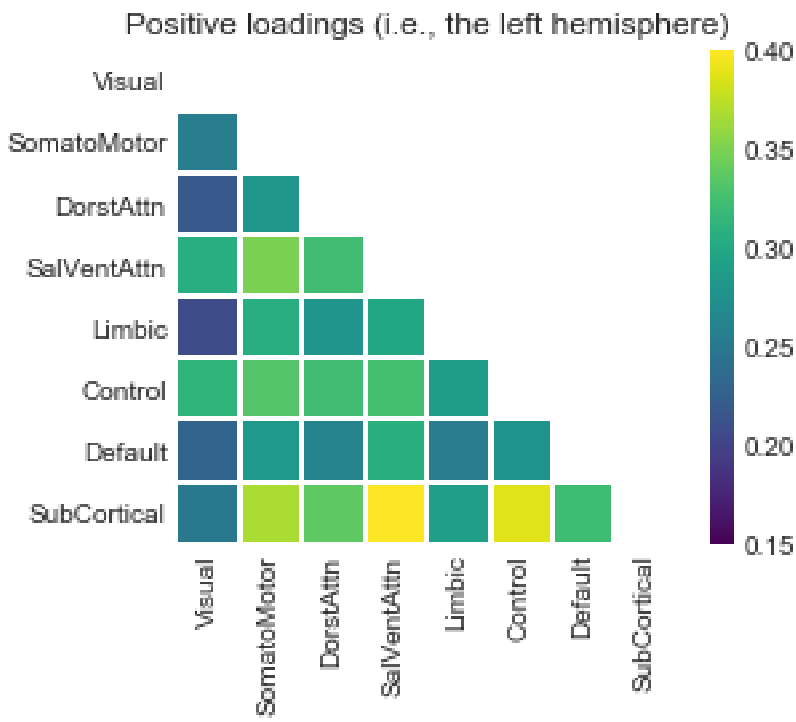

## 2.5 Replication in another parcellation

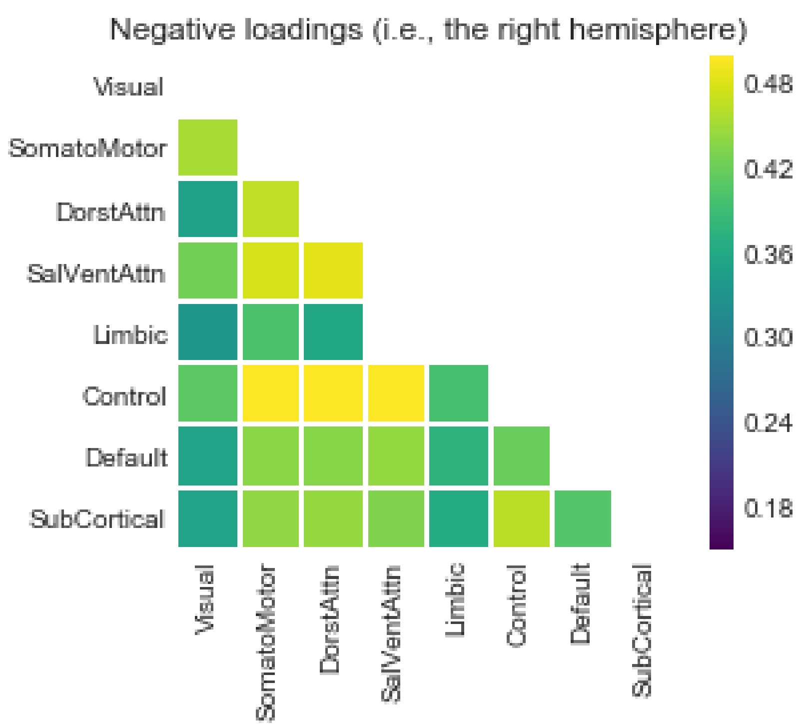
Results look very similar.

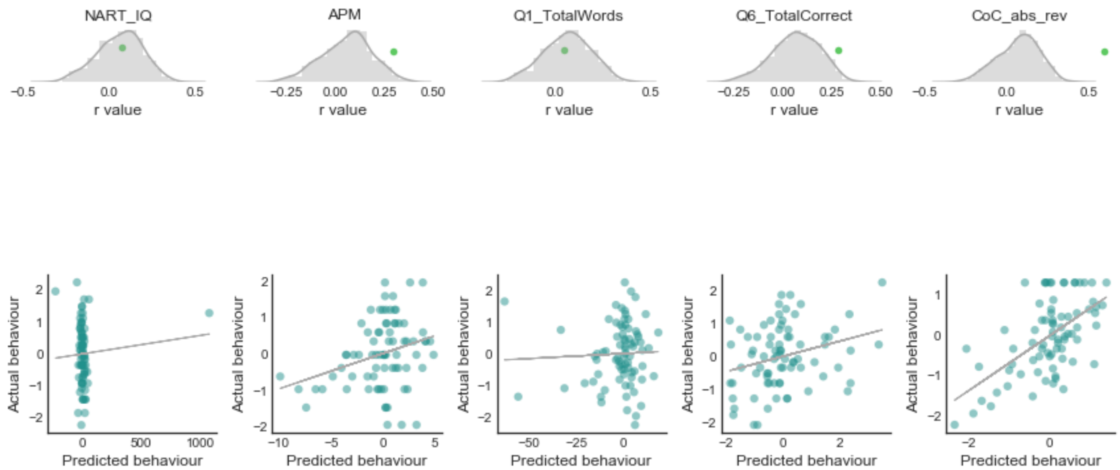

Connectivity weights (arb. unit)
2
1
0
−1
−2
−2
0
2
Behaviour weights (arb. unit)


CoC_abs_rev
Q6_TotalCorrect
Q1_TotalWords
APM
NART_IQ
−0.5
0.0
0.5
Correlation between behaviour and CCA mode (r)


L
R
1
0.5
0
-0.5
-1


Positive loadings (i.e., the left hemisphere)
Visual
SomatoMotor
DorstAttn
SalVentAttn
Limbic
Control
Default
SubCortical
0.40
0.35
0.30
0.25
0.20
0.15


Negative loadings (i.e., the right hemisphere)
Visual
SomatoMotor
DorstAttn
SalVentAttn
Limbic
Control
Default
SubCortical
0.48
0.42
0.36
0.30
0.24
0.18


NART_IQ
APM
Q1_TotalWords
Q6_TotalCorrect
CoC_abs_rev
r value
r value
r value
r value
r value
Actual behaviour
Predicted behaviour
Actual behaviour
Predicted behaviour
Actual behaviour
Predicted behaviour
Actual behaviour
Predicted behaviour
Actual behaviour
Predicted behaviour