Indirect influence of medial orbitostriatal projections on response selection: Check yourself before you rectus yourself

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Background

- The integration of task goals (prefrontal areas) and reinforcement history (orbitofrontal cortex) is thought to be integrated via corticostriatal pathways (Frank & Claus, 2006).

- We previously found that obesity-related changes in the connectivity of orbitofrontal-striatal circuits predict ineffient conflict processing in the Stroop Task (Verstynen et al. 2012).

Goals

1) Is the orbitofrontal cortex associated with response selection in a task without explicit reinforcement structure?

2) Does this response updating happen via integration at the corticostriatal pathways?

Methods

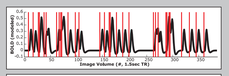
Participants

Neurologically healthy adults (N=28; 19 male; ages = 19-45; 4 left handed) were recruited from the local Pittsburgh population and the Army Research Laboratory in Aberdeen Maryland.

Run 1: Color-Word Stroop Task (fMRI)

Task: Report the color of the letters, ignoring the words. Rapid event-related design.

Params: Siemens Verio 3T, TE=20 ms; TR=1500 ms; Flip Angle=90°, 3.2 mm x 3.2 mm x 4 mm voxels, 30 slices. All 370 EPI volumes were motion corrected, slice-time corrected, smoothed (4mm FWHM), and normalized to MNI space (EPI template) using SPM8.



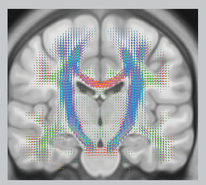
Analysis: General Linear Model (GLM)

Condition 1: Congruent Trials
Condition 2: Neutral Trials
Condition 3: Incongruent Trials

Interference Effect = $\beta_{Incon} - \beta_{Neutral}$

Run 2: Diffusion Spectrum Imaging (DSI)

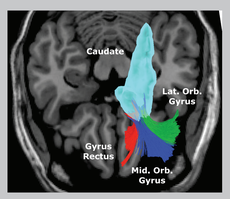
Params: TR=9916 ms, TE=157 ms, voxel size=2.4x2.4x2.4 mm, FoV=231x231mm, b-max=5000 s/mm^2, 257-directions, 5 shells.



Reconstruction: Orientation diffusion functions (ODFs) were reconstructed into MNI space using a Q-space Diffeomorphic Reconstruction approach (Yeh & Tseng, 2011) in DSI Studio (http://dsi-studio.labsolver.org).

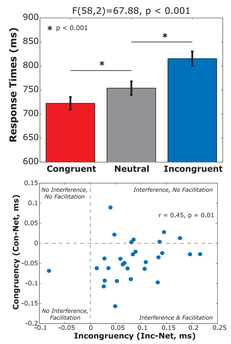
Fiber Tracking: An ODF-streamlined version of the FACT algorithm was used to map fiber connections from targeted cortical regions to the striatum. A random seeding approach was used with every white matter voxel in the brain having a probability of being seeded 300 times.

Analysis: Anatomically defined regions of interest (ROIs) were extracted from the AAL template and coregistered to the space of the MNI template. Statistical parametric analysis was performed by using one-sample t-tests on the fiber density maps, across subjects, to identify significant endpoint fields in the striatum.



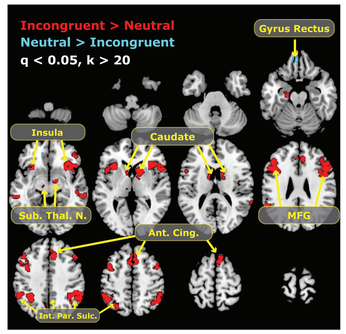
I. Dynamics of response selection

Behavior



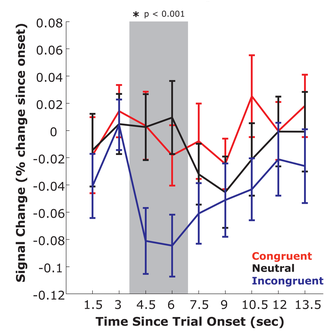
Responses were slower during Incongruent trials (Interference) and faster on Congruent trials (Facilitation). Subjects with better Facilitation also had less Interference.

Random Effects Analysis



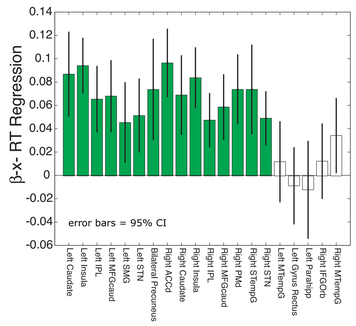
Of the 20 distinct clusters with significant Intereference responses at the group level, only the Gyrus Rectus (GR) showed a significant negative BOLD response.

Evoked GR Responses



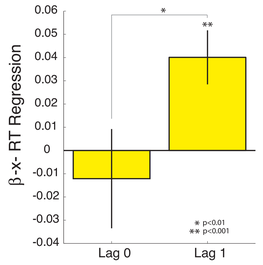
The negative BOLD response in the GR was reflected as a dip in evoked activity during Incongruent trials, rather than increased BOLD during Neutral trials.

II. Predicting single-trial response times (RT)



Current Trial

Single-trial BOLD responses were correlated with single-trial RTs (across all trials) in 15 out of the 20 Interference-related ROIs.



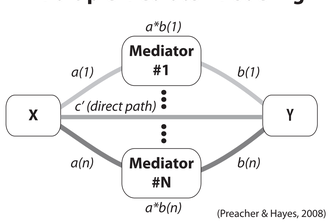
Subsequent Trial

While GR responses were not correlated with RTs on the current trial, they were significantly correlated with the next trial's RT.

Only two other ROIs showed this lag-1 correlation (Right ACC and Right MFG).

III. Indirect network mediating GR-RT associations

Multiple Mediator Modeling



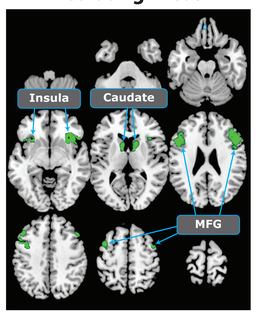
(Preacher & Hayes, 2008)

$$Y = [c_1' \dots c_N']X + [b_1 \dots b_N]M + \eta$$

$$M = [m_1 \dots m_N] = [a_1 \dots a_N]X + \eta$$

We used a permutation-based multiple mediator model to identify the the brain regions that could serve as indirect (*a*b*) pathways linking GR responses (**X**) and RT (**Y**) on the current trial.

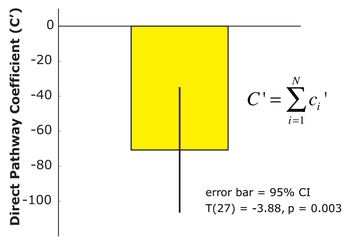
Mediating Areas



Three bilateral regions were found to be significant indirect mediators of GR-RT interactions:

1) Caudate Nucleus
2) Insula
3) Middle Frontal Gyrus (MFG)

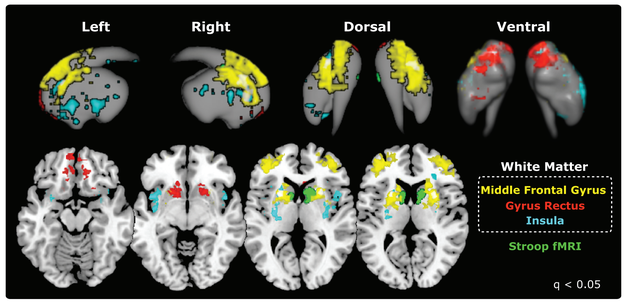
Recovered GR-RT Relationship



$$C' = \sum_{i=1}^{N} c_i'$$

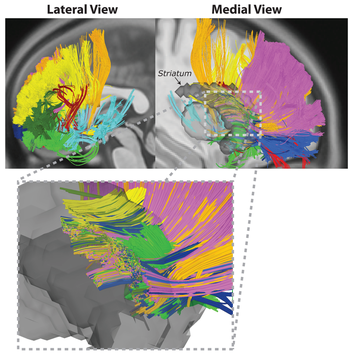
Accounting for the interaction of the indirect pathways revealed a signifcant negative association between GR responses and RT speed on the current trial.

IV. White matter networks predict functional relationships

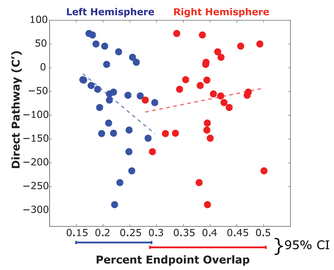


Caudate activity during Incongruent trials is situated between the endpoint fields of white matter projections from the MFG and GR.

Overlapping Rostral Frontal-Striatal Projections



$$overlap(s) = \frac{1}{2N_{ROIs} - 1} \sum_{i=1}^{N_{ROIs}-1} \sum_{j=i+1}^{N_{ROIs}} \left(\frac{1}{N_{vox}} \sum_{v=1}^{Nvox} P(f_i \cap f_j) \right)$$



The right corticostriatal pathways had more overlapping projections than the left.

The degree of overlap in the left hemisphere correlated with the magnitude of the direct pathway coefficient (C'; r(27) = -0.36, p = 0.029). This was not observed in the right hemisphere (r(27) = 0.13, p = 0.239).

Summary

1) The orbitofrontal cortex has a negative BOLD response during Incongruent trials.

2) Orbitofrontal activity predicts the response speed on the next trial.

3) A network of lateral prefrontal & striatal regions indirectly mediates the relationship between orbitofrontal activity and single-trial response speeds on the current trial.

4) The degree of overlap of frontal-striatal projections in the left hemisphere predicts the magnitude of the residual orbitofrontal-response speed association.

Conclusion

Rapid updating of trial-by-trial responses in the Stroop Task relies on a network of *physically overlapping* executive control & reward pathways through the striatum.

References

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Frank MJ & Claus ED (2006) Anatomy of a decision: striato-orbitofrontal interactions in reinforcement learning, decision making, and reversal. Psychol Rev. 2006 Apr;113(2):300-26.

Preacher KJ & Hayes AF (2008) Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behav Res Methods.40(3):879-91.