



The Neural Correlates of Reduced Dopamine and Serotonin on Mood and Reinforcement

[Link to publication record in Manchester Research Explorer](#)

Citation for published version (APA):

Lythe, KE., Elliott, R., Anderson, IM., & Deakin, JFW. (2007). *The Neural Correlates of Reduced Dopamine and Serotonin on Mood and Reinforcement*. Poster session presented at European College of Neuropsychopharmacology 2007 Congress, Vienna.

Citing this paper

Please note that where the full-text provided on Manchester Research Explorer is the Author Accepted Manuscript or Proof version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version.

General rights

Copyright and moral rights for the publications made accessible in the Research Explorer are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Takedown policy

If you believe that this document breaches copyright please refer to the University of Manchester's Takedown Procedures [<http://man.ac.uk/04Y6Bo>] or contact uml.scholarlycommunications@manchester.ac.uk providing relevant details, so we can investigate your claim.



The Neural Correlates of Reduced Dopamine and Serotonin on Mood and Reinforcement

Lythe KE, Elliott R, Anderson IM, and Deakin JFW

Neuroscience and Psychiatry Unit, The University of Manchester

Introduction

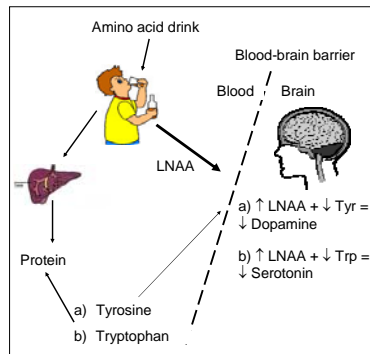
- The brain reward system includes striatum, thalamus, midbrain, amygdala, and regions of the prefrontal cortex
- Dopamine and serotonin influence reward processing
- Does a reduction in brain dopamine and serotonin through dietary amino acid depletion alter neuronal activity during reinforcement processing?

Participants

- No history of physical or psychiatric illness
- 14 male, 13 female (mean age 25 years) were randomised to one of 3 amino acid drinks
 - Tyrosine-free (TyrD)
 - Tryptophan-free (TrpD)
 - Balanced (Bal)
- Plasma amino acid concentrations were measured before and 4 hours post-drink.

Amino Acid Depletion

- Amino acid depletion works via a two-fold method
- E.g. for tyrosine depletion (Figure 1)
 - An oral amino acid load induces synthesis of proteins by the liver (A) reducing circulating tyrosine in the blood (B).
 - Large neutral amino acids (LNAA) compete with tyrosine at the blood-brain barrier (C) lowering tyrosine in the brain, thus reducing dopamine synthesis (D).



Imaging

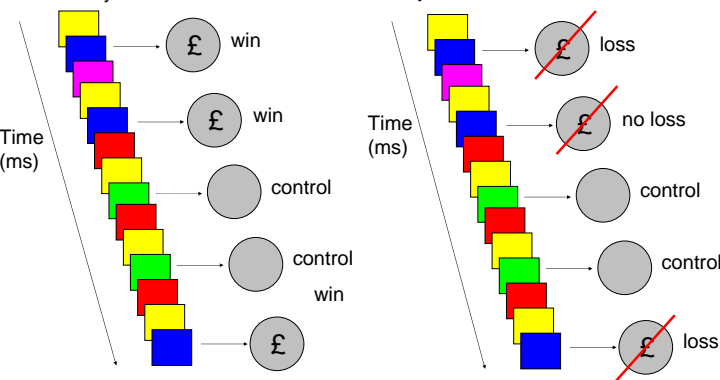
- Participants completed two tasks in a Phillips 1.5T Gyroscan scanner.
- Participants were shown a series of coloured squares and were required to respond to blue (B: active condition) and green (A: control condition) squares.
- Tasks were blocked ABABAB design.
- Both tasks lasted 6 minutes during which 72 volumes were acquired each of 40 slices, with a slice thickness of 3.5mm.
- Data were analysed using SPM2.
- Significance level uncorrected $p < 0.001$.

Reward Task

- Responses to both blue and green squares were required.
- Participants were told to respond quickly to blue squares in order to win money.

Loss Task

- Responses to both blue and green squares were required.
- Participants were told to respond quickly to blue squares to avoid losing money.



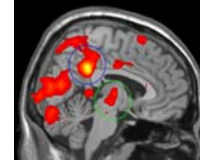
Results: Biochemical Measures

- Tyrosine Depletion
 - Tyrosine decreased by 66.1%
 - The ratio of tyrosine to LNAA decreased by 91.8%
- Tryptophan Depletion
 - Tryptophan decreased by 89.5%
 - The ratio of tryptophan to LNAA decreased by 94.6%

Results: Reward Task

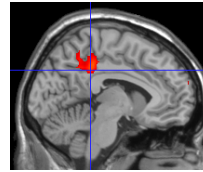
Main effect of Reward

- Significant BOLD responses were observed in right medial orbitofrontal cortex, left posterior cingulate cortex, right thalamus and left midbrain.



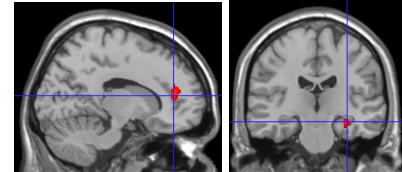
Tyrosine Depletion

- Attenuated BOLD signal in right posterior cingulate cortex.



Tryptophan Depletion

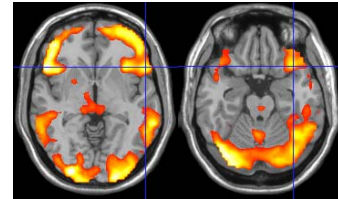
- Increased BOLD signal in left medial prefrontal cortex and right hippocampus.



Results: Loss Task

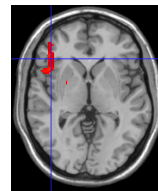
Main effect of Loss

- Significant BOLD responses were observed in bilateral ventrolateral prefrontal cortices extending down to lateral orbitofrontal cortices, left dorsomedial prefrontal cortex, bilateral putamen, left caudate and left thalamus.



Tyrosine Depletion

- Increased BOLD signal in left lateral orbitofrontal cortex.



Tryptophan Depletion

- Increased BOLD signal in left lateral orbitofrontal cortex.



Discussion

- In line with previous research we observed significant decreases in plasma tyrosine after TyrD and in plasma tryptophan after TrpD.
- The present study observed a dissociation between medial and lateral orbitofrontal cortices for reward and loss, respectively.
- As predicted, there were no increases in BOLD signal after TyrD observed during the Reward Task

Conclusion

- The attenuated BOLD response with TyrD in posterior cingulate after reward may reflect less salience of reward due to lower dopamine function.
- Results suggest that increased BOLD in medial prefrontal cortex and hippocampus with TrpD after reward perhaps indicates increased neuronal recruitment.
- Increased BOLD responses in left lateral orbitofrontal cortex during loss, after both TyrD and TrpD, suggests a similar role for serotonin and dopamine in this region during loss.
- Amino acid depletion in conjunction with functional magnetic resonance imaging is a useful tool for examining neurotransmitter modulation of neuronal responses.

Acknowledgements

- Thanks to the participants who took part in this study.
- Many thanks to the Translational Imaging Unit at the Wellcome Trust Clinical Research Facility, Manchester, UK
- This research was supported by the Medical Research Council and contributes to the NEWMOOD EU Integrated Programme LSHM-CT-2004-503474