Neural Correlates of Reward and Punishment after Tyrosine and Tryptophan Depletion

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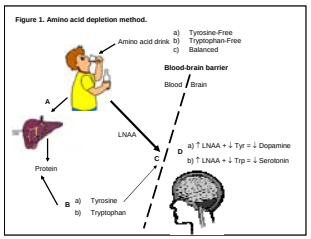
Introduction

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

Method

- 27 participants (14 male, 13 female; mean age 25 years) were randomised to one of 3 amino acid drinks
  - a) Tyrosine-free (TyrD)
  - b) Tryptophan-free (TrpD)
  - c) Balanced (Bal)
- **Amino acid depletion**
- Amino acid depletion works via a two-fold method (Figure 1) e.g. given for tyrosine depletion
  1. An oral amino acid load induces synthesis of proteins by the liver (A) reducing circulating tyrosine in the blood (B).
  2. Large neutral amino acids (LNAA) compete with tyrosine at the blood brain barrier (C) lowering tyrosine in the brain, reducing dopamine synthesis (D).
- Plasma amino acid concentrations were measured before and 4 hours post drink



Results – Biochemical Measures

- **Tyrosine Depletion (TyrD)**
- Tyrosine decreased by 66.1%
- The ratio of tyrosine to LNAA decreased by 91.8%
- **Tryptophan Depletion (TrpD)**
- Tryptophan decreased by 89.5%
- The ratio of tryptophan to LNAA decreased by 94.6%

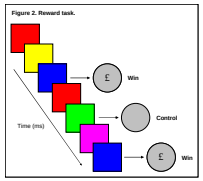
Imaging

Participants completed two tasks (Figures 2 and 3) in a Phillips 1.5T Gyroscan scanner, which required responses to certain stimuli in order to win (Reward task) and to not lose (Loss task).

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.

Results – Reward Task

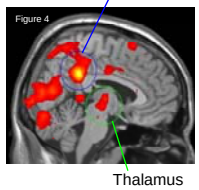


Responses to both blue and green squares were required.

Participants were told to respond quickly to blue squares to win money.

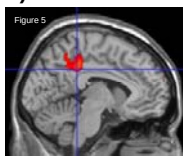
Main effect of Reward (Figure 4)

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



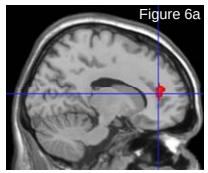
Tyrosine Depletion (Figure 5)

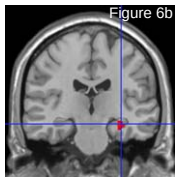
Attenuated BOLD signal in right posterior cingulate cortex.



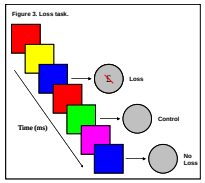
Tryptophan Depletion (Figure 6)

Increased BOLD signal in left medial prefrontal cortex (a) and right hippocampus (b).





Results – Loss Task

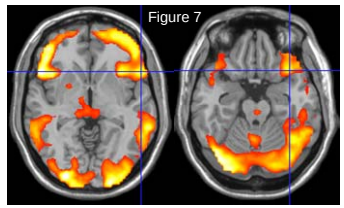


Responses to both blue and green squares were required.

Participants were told to respond quickly to blue squares to avoid losing money.

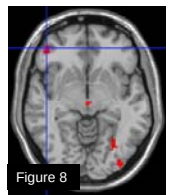
Main effect of Loss (Figure 7)

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



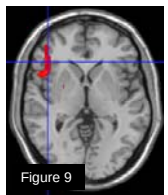
Tyrosine Depletion (Figure 8)

Increased BOLD signal in left lateral orbitofrontal cortex.



Tryptophan Depletion (Figure 9)

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.

Conclusions

- 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 response in left lateral orbitofrontal cortex during loss, after both TyrD and TrpD, suggests a similar role for serotonin and dopamine in this region during negative reinforcement.
- Amino acid depletion in conjunction with functional magnetic resonance imaging is a useful tool for examining neurotransmitter modulation of neuronal responses.

Acknowledgements

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