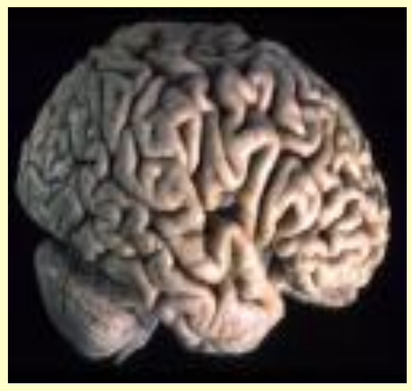
Acute administration of the anti-psychotic sulpiride modulates the neural response to chocolate in healthy volunteers.

Ciara McCabe, Anna Huber, Catherine Harmer, Philip Cowen

University of Oxford, Dept of Psychiatry, Oxford OX3 7JX



INTRODUCTION

Reduced subjective experience of reward (anhedonia) is a key symptom of major depression. Dopamine pathways are known to play a key role in reward-based mechanisms. The aim was to determine the effect of dopamine antagonism on the neural basis of reward.

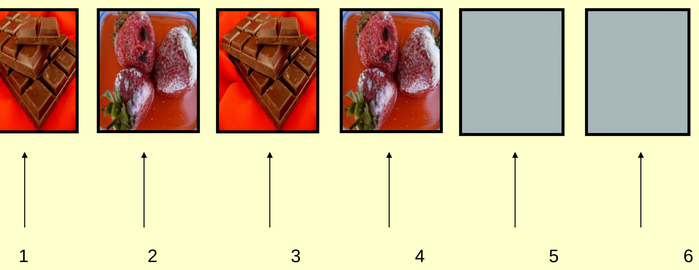
HYPOTHESES

We hypothesised that the D2 antagonist sulpiride would block the activation produced by chocolate in the nucleus accumbens.

METHODS

Design: We used functional Magnetic Resonance Imaging to measure the response to the flavour and the sight of chocolate, and to their combination, and also an unpleasant flavour and sight of an unpleasant picture.

Experimental Model:



Participants: Thirty healthy volunteers were randomised to receive sulpiride 400mg (n=15), or placebo (n=15) in a double blind between groups design.

fMRI data acquisition and analysis;

Images were acquired with a 3.0-T VARIAN/SIEMENs where 33 T2* weighted EPI slices were acquired every 2 seconds (TR=2). SPM5

RESULTS

Sulpiride reduced the neural processing of primary rewarding stimuli (chocolate taste)in the striatum (nucleus accumbens and caudate)

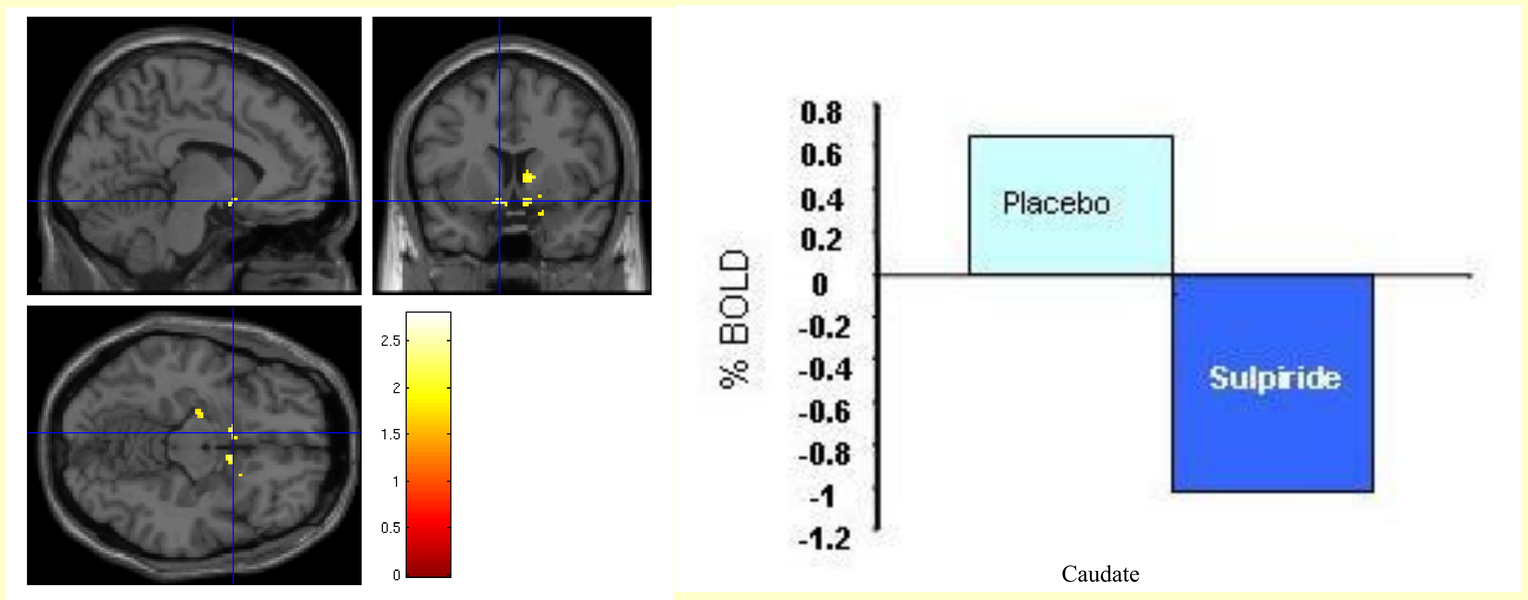


Fig 1. Chocolate in the mouth (placebo vs. sulpiride): Axial, saggital and coronal image of decreased ventral striatal activation in the sulpiride group compared to the placebo ([-8 8 -12] z = 2.6 p= 0.05 FDR svc corrected). B. Parameter estimates from 6 mm sphere centered at -8 8 -12 for sulpiride and placebo.

Yet enhanced activity in the prefrontal cortex.

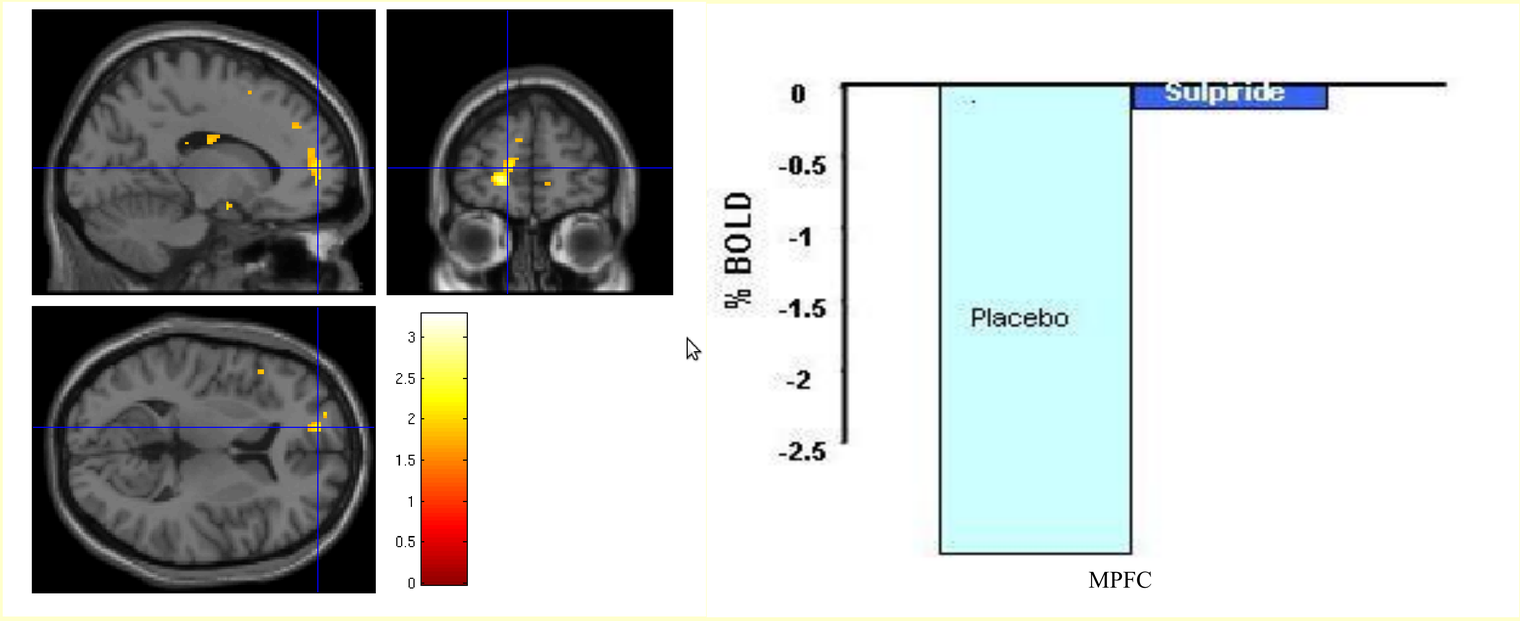


Fig 2. Chocolate in the mouth (sulpiride vs. placebo): Axial, saggital and coronal image of increased medial prefrontal cortex activation in the sulpiride group compared to the placebo ([-18 56 0] z = 2.99 p= 0.03 FDR svc corrected). B. Parameter estimates from 6 mm sphere centered at -18 56 0 for sulpiride and placebo

CONCLUSIONS

1. A single dose of 400mg of sulpiride can modulate mesolimbic-mesocortical neural activations in response to reward and aversion in our model in healthy volunteers.

2. This type of human model of reward might be useful in illuminating how medications may impact on neural processing and how these effects may correlate with their beneficial or deleterious effects on mood in patients with affective disorders.

DISCLOSURE

Dr Harmer has acted as a consultant for the following companies: Lundbeck, P1Vital, Merck, Sharpe and Dohme and has received grant income from Merck, Sharpe And Dohme. Professor Cowen has been a paid member of advisory boards of Eli Lilly, Servier, Wyeth and Xytis and has been a paid lecturer for Eli Lilly, Servier and Glaxo Smith Kline. Dr McCabe reports no biomedical financial interests or potential conflicts of interest. Miss Huber reports no biomedical financial interests or Potential conflicts of interest.