Inactivation of the subcallosal anterior cingulate cortex Area 25 increases reward-related behaviour and motivation in the common marmoset

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- Caudal aspects of subcallosal cingulate cortex, including area 25, is overactive in depressed patients (1)
- First causal evidence for primate area 25's involvement in anhedonia showed that area 25 overactivation in the marmoset induced anticipatory and motivational but not consummatory anhedonia (2). Conversely, it heightened threat-induced arousal.
- Under normal test conditions, area 25 does not appear to contribute to appetitive anticipatory arousal as area 25 inactivation had no effect on cardiovascular or behavioural arousal measures. Only when area 25 was over activated did blunting occur
- However, the effect of area 25 inactivation on motivational and consummatory reward processes has not been determined.

Here we use a touchscreen progressive ratio (PR) task and sucrose preference test (SPT) to determine whether area 25 contributes to motivational and consummatory aspects of reward, by investigating the behavioural effects of inactivation of area 25 in the common marmoset.

Methods

Motivational arousal: Progressive ratio task (n = 7)

The progressive ratio schedule: response increment of 1 for the first 9 trials. Increments doubled every 9 trials. Maximum session time of 30 mins with a cut-off point following 2 minutes of inactivity

Consummatory arousal: Sucrose preference test (n = 8)

Sucrose preference test carried out over 120 mins and the first 30 mins analysed. Two sucrose solution concentrations of 6% and 10%.

$$\% \text{ Preference} = \frac{\text{sucrose consumption (g)}}{(\text{sucrose} + \text{water consumption})(g)} \times 100$$

Drugs:

- Area 25 Inactivation: GABA_{A/B} agonists, Muscimol/Baclofen (MB)
- Vehicle (0.9% saline)
- Area 25 Overactivation: EAAT₂ inhibitor, Dihydrokainic acid (DHK)

Results

Motivational arousal: Progressive ratio task

Inactivation of area 25 increased total number of reponses at breakpoint compared to saline (whereas overactivation decreased it). Inactivation increased time spent licking the spout outside of reward delivery

Consummatory arousal: Sucrose preference test

Inactivation of area 25 increased sucrose consumption compared to saline and DHK, (the latter two not differing from one another), but had no effect on sucrose preference.

Conclusion

- Under normal test conditions area 25 was previously shown not to contribute to appetitive anticipatory Pavlovian arousal but here we show that it does contribute to motivational and consummatory arousal.
- Specifically, inactivation of area 25 resulted in increased responding for reward and increased overall reward consumption.
- In line with our previous findings area 25 overactivation blunted willingness to work for reward but had no impact on consummatory behaviours.
- We hypothesise that activity in area 25 in an appetitive context normally acts to prevent the over-expression of responses to unconditioned rewarding stimuli but when over-activated as, for example following stress, this tips the balance, suppressing anticipatory and motivational responses in favour of enhanced threat reactivity.

References:

1. Mayberg HS et al. (2005) Neuron, 45:651-660

2. Alexander L et al. (2019) Neuron 101:307-320