Enhanced Brainstem Cerebral Blood Flow Accompanies Symptoms of Anhedonia in Young Adults

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BACKGROUND

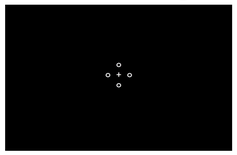
- Midbrain monoaminergic projections – including dorsal raphe nucleus (DRN), locus coeruleus (LC)[1], and ventral tegmental area (VTA) are of crucial theoretical significance for mood disorders
- Learned helplessness associated with enhanced metabolic activity in the midbrain (dorsal raphe) of rodents[2]
- However, little human neuroimaging evidence supports involvement of monoaminergic projections in illness severity prediction
- Present study: Arterial Spin Labelling (ASL) measure of cerebral blood flow (CBF) within whole brain during period of rest in distressed and healthy young adults varying on anxiety/anhedonia dimensions

METHODS

Participants

36 distressed (DS) and 34 healthy controls (HC)

Resting State Acquisition



Participants told to relax and watch fixation cross for six minutes

Neural Measures

- Blood flow was measured via multiband pseudo continuous ASL sequence
- Regional cerebral perfusion data was collected with 25 slices, multiband factor=5, 4mm slice thickness, FA=90, 64x64 resolution FOV=192x912, TR/TE=3.5s/19ms, labeling time=1.5s and postlabeling delay=1.7s.
- Data was processed using Statistical Parametric Mapping (SPM)

METHODS

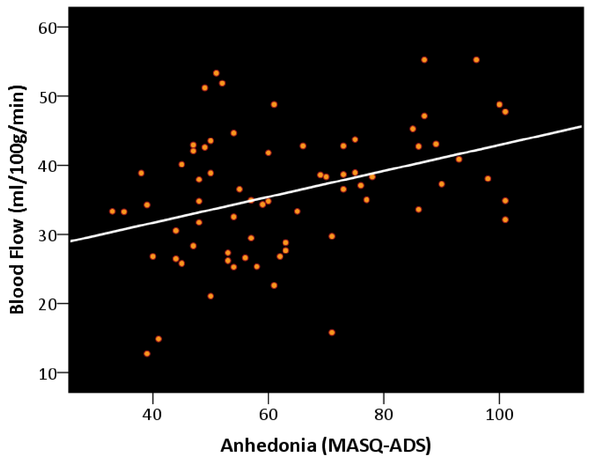
Clinical Measures

- *Anhedonia* measured via : Mood and Anxiety Symptom Questionnaire Anhedonic Depression Scale (**MASQ-ADS**) and Snaith–Hamilton Pleasure Scale (**SHAPS**) as a secondary measure
- *Anxiety* measured via: Mood and Anxiety Symptom Questionnaire General Distress Anxious Symptoms Scale (**MASQ GD-A**)

Demographics	DS	HC	Statistics
Age (years)	22.2 ± 2.1	21.5 ± 1.8	T<1
Sex (M/F)	9/27	15/19	X^2=2.84, p=0.092
SES	5.3 ± 1.1	5.5 ± 1.1	T<1
Clinical Measures			
MASQ-AD	75.6 ± 16.6	50.3 ± 9.1	t(68)=-7.9; p<.001
SHAPS	27.8 ± 7.8	18.9 ± 5.2	t(68)=-6.7; p<.001
MASQ GD-A	28.0 + 10.1	13.5 + 2.1	t(68)=-8.2; p<.001

Mean ± SD (Range) or Proportion

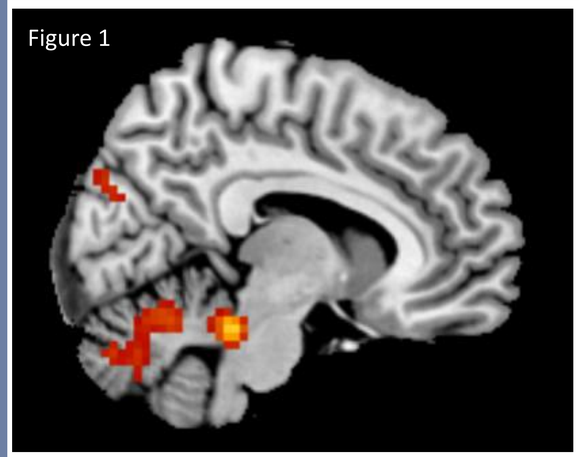
RESULTS



Association between anhedonia and midbrain CBF, with increasing endorsement of anhedonic symptoms predicting enhanced CBF

RESULTS

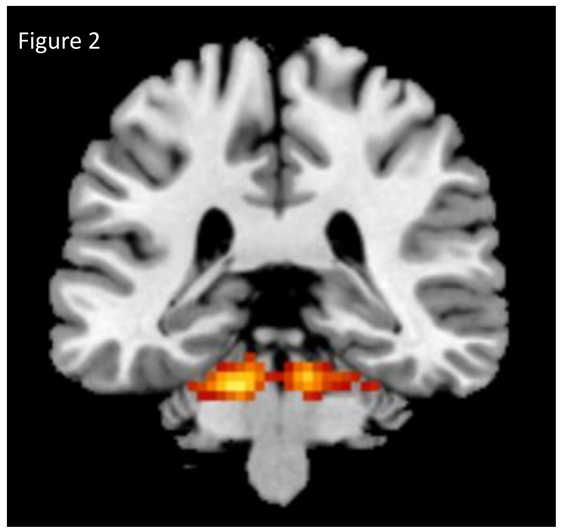
Figure 1



Figures 1 and 2 show regions positively correlating with individual differences in anhedonia (threshold uncorrected p<0.001).

Peak voxels within the midbrain located bilaterally (left: T=5.24, p_FWE=.033, x=-12, y=-34, z=-26; right: T=4.96, p_FWE=.080, x=9, y=-34, z=-23).

Figure 2



CONCLUSION

- Anhedonia associated with altered CBF in the midbrain in a young adult population showing heterogeneous symptoms of distress.
- Anhedonia associated with increased CBF in midbrain, possibly the LC[1]
- If key region is in fact LC, current findings link noradrenergic projections and anhedonia in humans, consistent with prior experimental studies of the effect of noradrenergic agents on the human reward system[3].

Future Directions

- ASL promising tool to examine enhanced local perfusion, potentially reflecting underlying midbrain serotonergic activity
- Learned helplessness studies in rodents show similar findings[2], but has thus far been difficult to investigate in humans.

Limitations

- Better resolution is needed to differentiate between relatively small midbrain structures
- No behavioral measure of anhedonia to link with animal work

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2. Christianson JP, Paul ED, Irani M, et al. The role of prior stressor controllability and the dorsal raphe nucleus in sucrose preference and social exploration. Behavioral brain research. 2008;193: 87-93.
3. Pringle A, McCabe C, Cowen PJ, Harmer CJ. Antidepressant treatment and emotional processing: can we dissociate the roles of serotonin and noradrenaline. Journal of psychopharmacology. 2013; 27(8): 719–731.

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