Anhedonia is Associated with Altered Striatal Neurophysiology and Function in Adolescents Varying in Levels of Depression

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BACKGROUND

- Anhedonia—the reduced capacity for pleasure—is a common[1] and debilitating[2] feature of adolescent depression.
- Previous work has implicated altered reward circuitry[3], which undergoes protracted maturation through adolescence[4], in anhedonia; however, the role of striatal neurophysiology in remains unclear.
- Measures derived from resting-state functional magnetic resonance imaging (rsfMRI) can non-invasively provide *in vivo* measurements of various aspects of striatal neurophysiology.

Hypotheses: (1) Lower striatal regional homogeneity (ReHo) (Fig. 1, path b) and lower dopamine function (T2*) intensity (Fig. 1, path c) will be associated with higher levels of anhedonia. (2) Striatal tissue iron will moderate this relationship, such that lower ReHo will be most strongly linked to high levels of anhedonia at low level of tissue iron.

METHODS

- Sample: 75 adolescents (M age = 15.30 (1.50), 46 F) participated in the study, of whom 56 scored ≥ 40 on the Children's Depression Rating Scale-Revised (CDRS-R)[5] and 19 reported no current/past self/parent psychiatric diagnosis.
- Anhedonia was assessed using the Snaith-Hamilton Pleasure Scale (SHAPS)[6] and other depressive symptoms using the Mood and Feelings Questionnaire (MFQ)[7].
- We derived two measures from two 6-minute resting-state functional magnetic resonance imaging (rsfMRI) scans:
  - ReHo to assess regional voxel synchronization[8]
  - Normalized T2* signal to assess tissue iron[9]
- Data were preprocessed using *fmriprep*[10].
- We used a voxel-wise moderated mediation approach to examine the relationships between T2* intensity, ReHo, and anhedonia severity, controlling for age, sex, and depressive symptoms besides anhedonia (**Fig. 1**).
- Clusterwise permutation testing accounted for multiple comparison corrections.

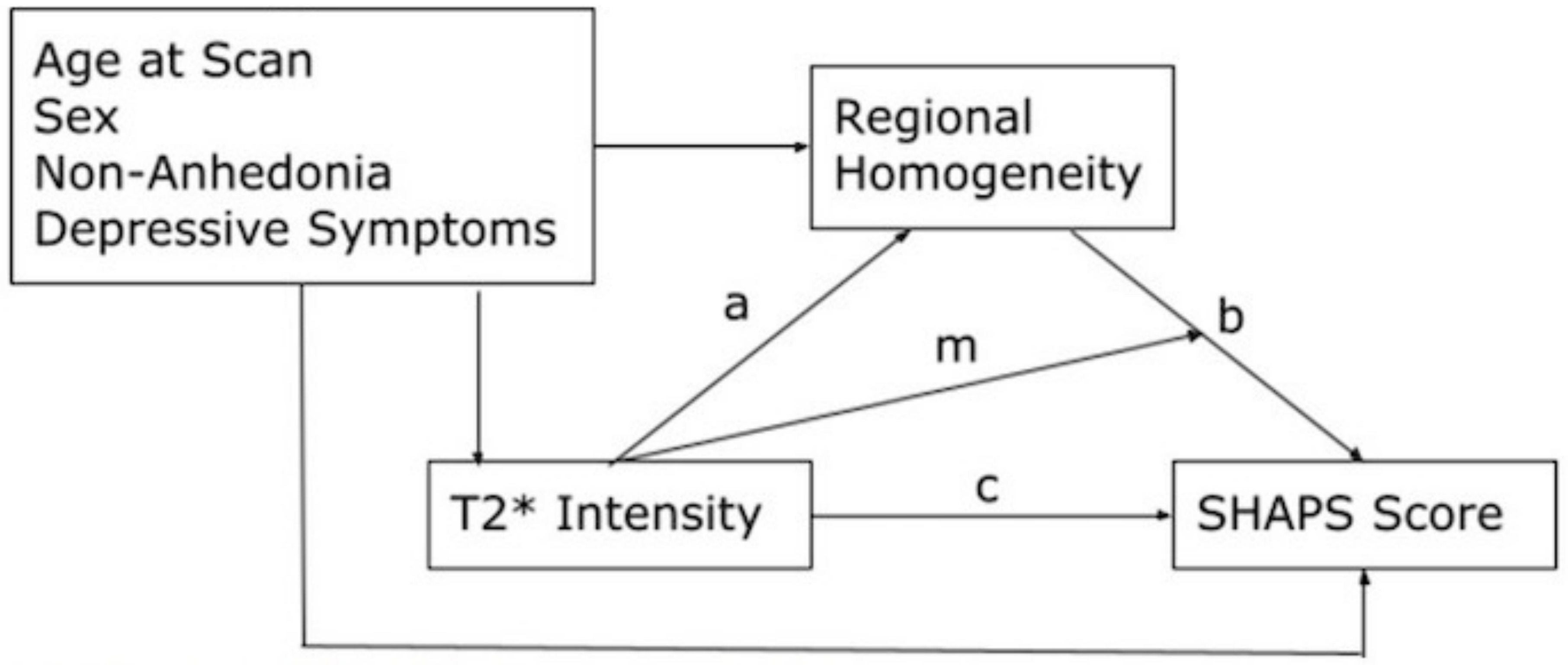
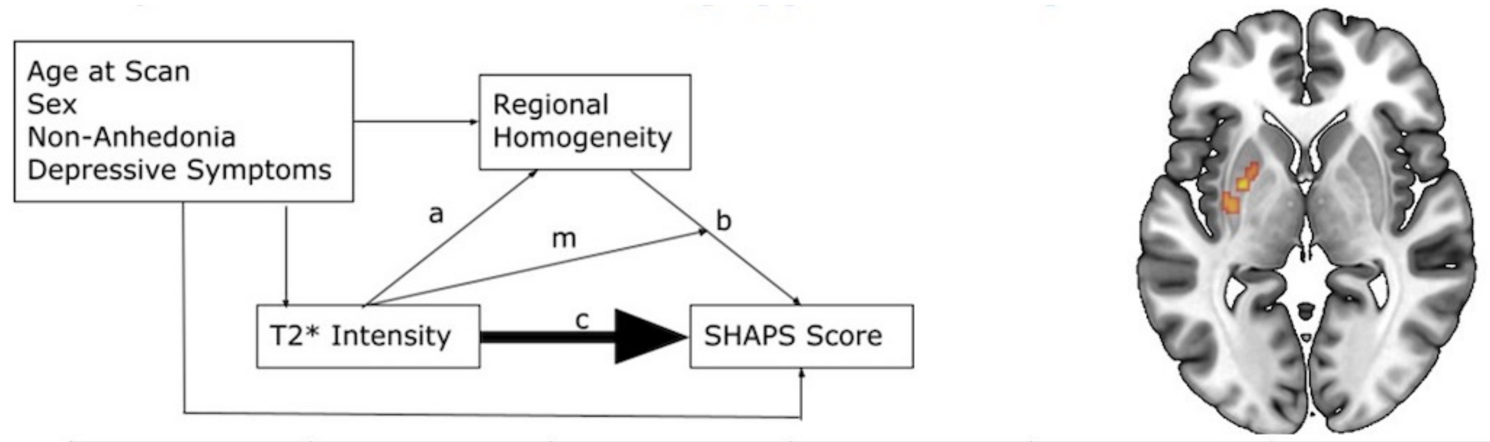


Figure 1. Path diagram for moderated mediation model.

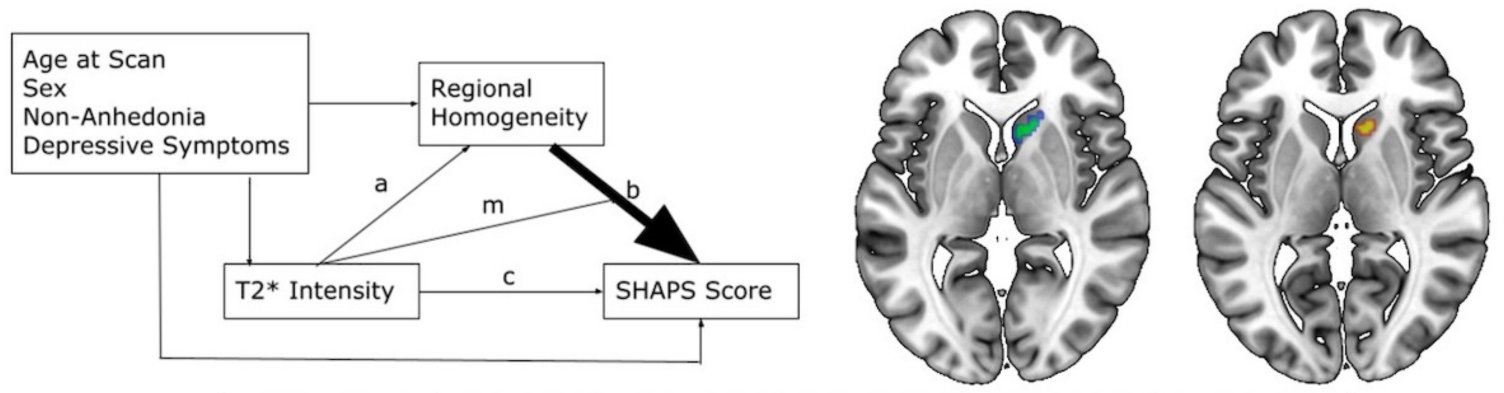
RESULTS

- Reduced striatal tissue iron in the left putamen was associated with higher levels of anhedonia (**Fig. 2**).
- Reduced ReHo was associated with higher levels of anhedonia in adolescents with higher striatal tissue iron in the right caudate, and with lower levels of anhedonia in adolescents with lower levels of tissue iron.



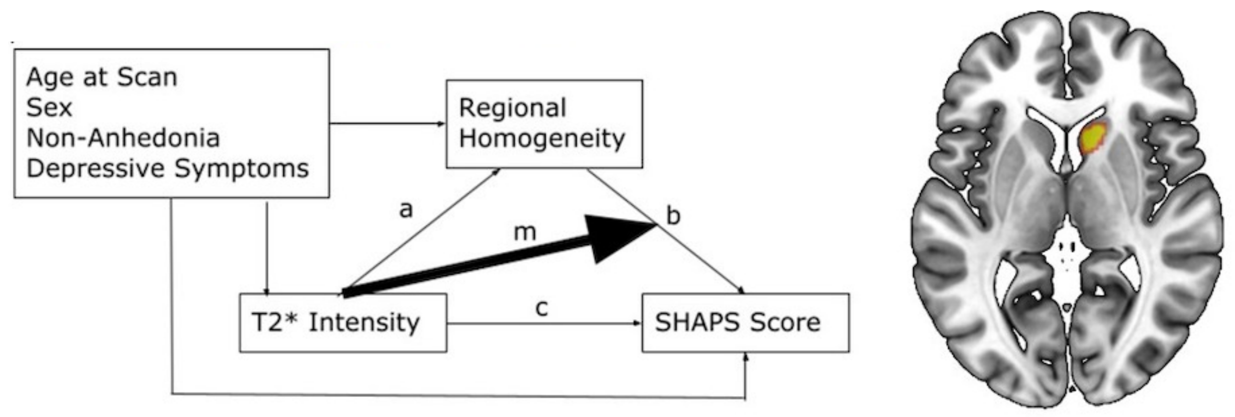
Cluster	N Voxels	Peak T Value	Peak X (MNI)	Peak Y (MNI)	Peak Z (MNI)
Left Putamen	40	2.795	34.735	-7.322	-0.5

Figure 2. Simple slopes for T2* intensity effect on SHAPS score (**Hypothesis 1**)



Cluster	N Voxels	Peak T Value	Peak X (MNI)	Peak Y (MNI)	Peak Z (MNI)
Right Caudate (Low T2*)	49	-3.646	-7.664	18.925	3.5
Right Caudate (High T2*)	27	2.783	-7.664	16.906	5.5

Figure 3. Simple slopes for ReHo effect on SHAPS score (**Hypotheses 1 + 2**)



Cluster	N Voxels	Peak T Value	Peak X (MNI)	Peak Y (MNI)	Peak Z (MNI)
Right Caudate (High T2*)	78	4.169	-9.683	18.925	5.5

Figure 4. Moderating effect of T2* intensity on ReHo-SHAPS score simple slopes (**Hypothesis 2**)

CONCLUSIONS

- Both lower striatal ReHo and striatal tissue iron were associated with anhedonia beyond other depressive symptoms.
- However, these effects were specific to the dorsal striatum and the direction of this relationship was contingent upon levels of striatal tissue iron.
- Future research is needed to determine the effectiveness of dopamine-targeted pharmacotherapy for adolescents with anhedonia and particularly those with altered dopaminergic functioning.

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