Neuroimaging Biomarkers for Predicting Substance Use Trajectories in Adolescents: Insights from the ABCD Study

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Introduction

Substance use disorders (SUDs) are the most prevalent and deadly forms of psychopathology with a heavy societal burden[1].

More than half of substance use begins in adolescence, with a considerable proportion of users transitioning to higher levels of use or developing dependencies[2].

Early identification of individuals at risk for escalating substance use is crucial for preventative interventions.

Studies have found imaging evidence related to the initiation and abuse of drugs[3]. However, little research focuses on the transition between the key stage of SUDs, for example escalation to problem use.

The Adolescent Brain Cognitive Development (ABCD) study is a large-scale, long-term investigation of brain development and child health in the United States[4].

It provides a range of data types, including multimodal brain imaging and a comprehensive battery of behavioural assessments.

Adolescent Brain Cognitive Development®
Teen Brains. Today's Science. Brighter Future.

Aim

Using longitudinal neuroimaging data from the ABCD study, this study aims to identify neuroimaging biomarkers that could potentially predict substance use trajectories following initial exposure at a young age.

Method

- We established a cohort of adolescents with a history of substance use from the ABCD database.
- The cohort is comprised of adolescents with no initial substance use at baseline (ages 9-10) and their substance use was tracked across four years from the ABCD database.
- Demographic variables were compared at baseline to control for potential confounders.
- The cohort was categorised into low-risk, mild escalation, and severe escalation groups based on their consumption patterns for alcohol, nicotine, cannabis, and other substances.

	Low-risk (LR)	Mild escalation (ME)	Severe escalation (SE)
Alcohol	≥ 1 standard drink + ≤ 2/year & ≤ 1 maximum	≥ 4/year | > 2 maximum	≥ 12/year | > 2 on average | > 4 maximum
Nicotine	≥ 1 full cig + ≤ 2 occasions per year & ≤ 1 maximum	≥ 12/year | > 2 on average | > 2 maximum	≥ 52 occasions per year (weekly)
Cannabis	≥ 1 full unit + ≤ 2 occasions per year & ≤ 1 maximum	≥ 4/year | > 2 on average | > 2 maximum	≥ 12 occasions per year
Other	Ever use +≤ 1 occasions per year & ≤ 1 maximum	≥ 2 occasions per year | > 1 maximum	≥ 4 occasions per year

- Multimodal neuroimaging data, including structural and functional metrics from T1 imaging, resting-state fMRI, and diffusion tensor imaging, were analysed with one-way ANOVA tests with post-hoc Tukey corrections.
- Additionally, topological analyses of brain networks were conducted to assess global and nodal network properties.

Results

The cohort included 319 subjects (130 LR, 96 ME and 93 SE), with no baseline demographic differences found among the groups.

Comparative neuroimaging analyses identified several brain regions related to substance use trajectories in each imaging mode.

Substructural changes, such as increased fractional anisotropy and longitudinal diffusivity of the left superior parietal lobule, were found in SE individuals compared to LR ones. However, no significant alteration was observed in the comparison of ME and SE.

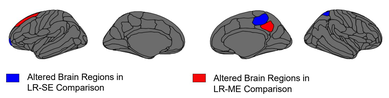

Figure 1. *Brian regions exhibiting differences in LR-ME and LR- SE DTI comparisons*

Significant structural differences in critical brain regions such as the orbital and occipital lobe were observed in three comparisons. Particularly, alterations such as the cortical area of the **right lateral orbital sulcus** and sulcal depth of the **right precuneus** were observed when comparing the ME and SE groups to the LR group, suggesting fundamental changes associated with the escalation of substance use.

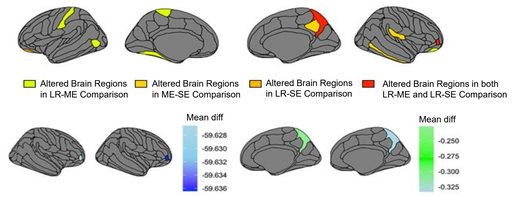

Figure 2. *Brian regions exhibiting structural differences in three pairwise comparisons*

In the meantime, reduced functional connectivity was observed between the salience and default networks when comparing the escalation groups to the LR. While strengthened connections were exhibited not only within the interaction of the cingulo-parietal, dorsal attention and sensorimotor hand networks, as well as their connection with subcortical areas. Among these differences, the stronger connectivity between **salience network and left caudate** was uniquely observed in both escalation groups.

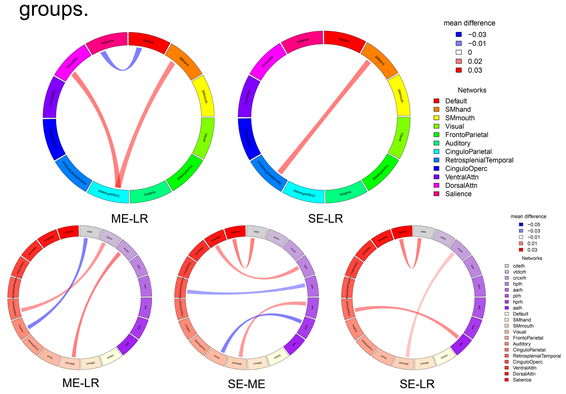

Figure 3. *Altered functional connectivity within large-scale networks (top) and between networks and subcortical areas (bottom) in three pairwise comparisons*

Further topological analysis on the large-scale networks also demonstrated significant changes, indicating potential biomarkers for substance use severity. As was the case with the connectivity findings, the salience network, cingulo-parietal and dorsal attention networks demonstrated dysfunction in the escalation groups. Of particular note was the **retrosplenial temporal network**, which exhibited a unique pattern, with its BC significantly increased in severe escalation but controversial alterations of NCP and NLE in the first two transitions. This could suggest an increasingly significant role of this network as substance use escalates, though its efficiency may not necessarily improve.

Comparison	Network	Metric	Meandiff	p-Value
Mild Escalation – Low Risk	ad	DC	0.043	0.0174
		NE	0.0226	0.0284
	ca	DC	0.0405	0.0197
		NE	0.0237	0.02
	dla	BC	-0.02	0.0304
	rspltp	NLE	0.0756	0.0084
		NCP	0.0598	0.0068
Severe Escalation – Mild Escalation	rspltp	NLE	-0.0802	0.0091
		BC	0.0212	0.0083
		NCP	-0.06	0.0098
	sa	NE	-0.0208	0.0314
Severe Escalation – Low Risk	sa	BC	-0.02	0.0305

Conclusion

This study identifies potential neuroimaging biomarkers that could predict adolescent substance use trajectories.

Early alterations in specific brain areas and networks, including the precuneus and salience network, may precede and potentially influence escalating substance use.

These biomarkers can inform targeted interventions to mitigate the progression of substance use in high-risk individuals.

References

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