Multimodal Correlates of Adolescent Substance Use: Examining Reward-Driven Self-Regulation in Brain and Behavior

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Background

- Adolescent risk behaviors, such as substance use, are often linked to deficits in reward-related self-regulation.
- Real-time fMRI neurofeedback (rtfMRI-nf) offers a way to measure volitional control over reward-related brain activation, incuding in the nucleus accumbens (NAcc), more directly than may be possible with selfreport and neurocognitive measures.
- The goal of the current study was to evaluate whether rtfMRI-nf predicts substance use outcomes in adolescents above and beyond self-report and neurocognitive measures.

Methods

- **Participants:** N= 56; Substance -naïve adolescents aged 14–16 years from the NeuroMod study (57.1% female).
- **Self-Regulatory Inventory (SRI):** Baseline self-report 36-item measure assessing self-regulation across behavioral, attentional, emotional, and cognitive domains (Moilanen, 2007); summed across items.
- **Emotional Go/No-Go Task:** Baseline neurocognitive task measuring self-regulation across emotional-salience conditions, using happy faces as rewarding cues (Fig. 1).
- **rt-fMRI-nf:** Baseline neuroimaging task measuring ability to volitionally up- and down-regulate NAcc activity (Fig. 2). Average percent signal change was assessed across increase and decrease trials to evaluate modulation success.
- **Substance Use Questionnaire:** Follow-up RA-administered substance use assessment (Miech et al., 2024) conducted every 6-months post baseline visit over two years to measure the use of alcohol, cannabis, and other drugs; any use coded as 1 = yes, 0 = no.
- **Data Analysis:** Hierarchical logistic regression models tested whether percent signal change in NAcc activity, emotional Go/No-Go performance, and SRI scores predicted substance use over two years. Models included progressive iterations of sociodemographics, self-report, neurocognitive, and task data, across substance use outcomes (any use, alcohol, cannabis).

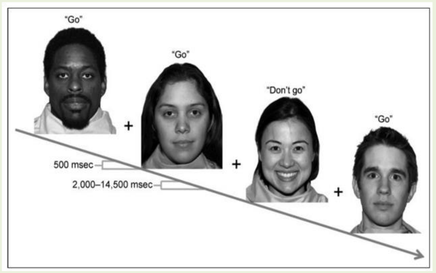


Fig 1. Example schematic of the trials that were conducted on for the Emotional Go/No-Go task

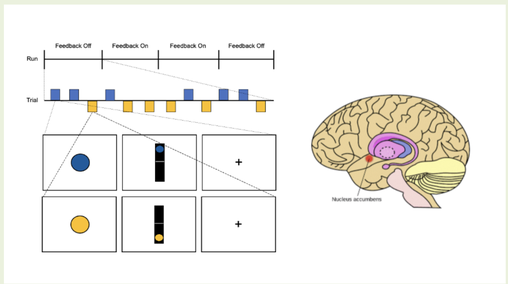


Fig 2. Real-Time fMRI Neurofeedback Paradigm on NAcc up- and down-regulation

Results

1a. Descriptive Differences by Cannabis Use

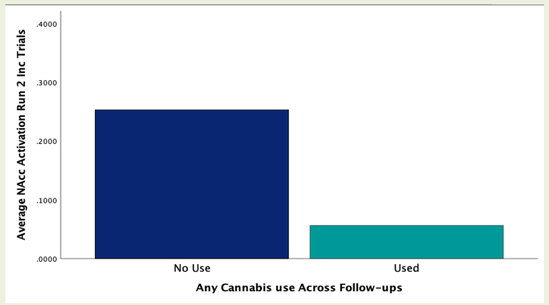
- Compared to all other substances, cannabis use showed the strongest associations and significant predictive models; analyses focus on cannabis outcomes.
- Adolescents who used cannabis were significantly less likely to be male compared to non-users ($p < .05$, Cohen's $d = 0.49$).
- Adolescents who used cannabis exhibited significantly lower NAcc activation during Run 2 feedback-increase trials compared to non users ($p = .032$, Cohen's $d = .23$)
- Youth who used cannabis also reported lower self-regulation (SRI sum scores) on average; however, the difference was not statistically significant.

Table 1. Group Comparison of Cannabis Use vs. Non-Use

Variable	Any Cannabis Use (n= 8)	No Use (n= 45)	t
	M (SD) or %	*M (SD) or %*	
Sociodemographic Characteristics (%)			
Male Sex	13.00	47.00	2.34*
White	75.00	82.22	0.47
Parent Education	100.00	97.78	-0.42
Self-Report: Self-Regulatory Inventory			
Sum SRI	123.13 (17.80)	131.36 (15.48)	1.36
Neuroimaging: Avg. NAcc Activation During rt-fMRI-NF (M)			
Run 1 NoFB Increase Trials	0.25 (.16)	0.31 (.23)	0.63
Run 1 NoFB Decrease Trials	0.09 (.33)	0.22 (.23)	1.35
Run 2 FB Increase Trials	0.06 (.31)	0.25 (.22)	2.21*
Run 2 FB Decrease Trials	0.23 (.10)	0.20 (.21)	-0.44
Run 3 FB Increase Trials	0.12 (.17)	0.17 (.23)	0.67
Run 3 FB Decrease Trials	0.25 (.23)	0.20 (.31)	-0.45
Run 4 NoFB Increase Trials	0.06 (.38)	0.15 (.22)	0.95
Run 4 NoFB Decrease Trials	0.23 (.17)	0.10 (.24)	-1.49
Neurocognitive: Emotional Go/No-Go			
Happy Face Go, Neutral Face No Go False Alarm (%)	19.71	22.38	0.43
Hit RT (M)	381.30 (44.31)	374.55 (38.83)	-0.44
False Alarm RT (M)	327.64 (55.98)	333.37 (57.49)	0.26
Happy Face No Go, Neutral Face Go False Alarm (%)	25.96	31.29	0.83
Hit RT (M)	386.22 (36.42)	380.50 (40.18)	-0.38
False Alarm RT (M)	361.69 (90.44)	338 (50.72)	-1.02

*$p < .05$

Fig 3. NAcc Activation Run 2 Increase Trial by Cannabis Use



1b. Predictive Modeling for Follow-up Cannabis Use

- Hierarchical logistic models predicting cannabis use showed moderate variance explained (Nagelkerke $R^2 \approx 0.28$), while alcohol and other substance use models were not significant.
- Predictors included in final models were selected based on theoretical relevance to self-regulation and preliminary model testing.
- Model 3 results showed a significant contribution of NAcc activation during increase trials indicating that lower activation was associated with increased odds of later cannabis use.
- Sex modestly improved model fit, but it was not a statistically significant predictor.
- Although sex significantly differed between use groups, models excluding it showed similar fit (Nagelkerke R^2) to those including it—suggesting that cognitive and neural measures contributed independently to predicting cannabis use.

Results

Table 2. Summary of Predictive Models for Cannabis Use Outcomes

Model	Predictors	Nagelkerke R^2	Significant Predictors	Notes
Model 1	Sex, SRI Sum, Happy Face No-Go False Alarm Percent, Run 2 Increase Trial	0.278	None	Best overall fit ($p = .050$), but no single significant predictor
Model 2	Sex, SRI Sum, Happy Face No-Go Hit Reaction Time, Run 2 Increase Trial	0.283	None	Highest explained variance, marginally non-significant predictors
Model 3	Sex, Happy Face No-Go Hit Reaction Time, Run 2 Increase Trial	0.258	Avg. NAcc Activation Run 2 Increase ($p = .041$, OR = 0.027, 95% CI [0.001, 0.863])	Run 2 Increase activity significantly predictive of reduced odds of cannabis use

Conclusion

- Adolescents who went on to use cannabis showed significantly lower NAcc activation during feedback-based increase trials, suggesting a weaker capacity to up-regulate reward-related brain activity.
- These findings align with prior research by Martz et al. (2016), who found that greater cannabis use was associated with later reduced NAcc activation, while our results show this blunting may be present before initiation. Together, these findings suggest altered reward processing may both predict and result from cannabis use, reinforcing its role as a key neurodevelopmental risk marker.
- Limitations include small sample size and low/no baseline substance use. While self-report data were less predictive, the findings highlight the added value of objective measures like neurocognitive and task-based indices.
- Future studies should recruit more diverse samples, including adolescents with higher and escalating patterns of substance use, to better capture the full spectrum of risk and examine how early self-regulation capacities interact with environmental factors (e.g., stress, peer influence) across development.

References

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