# DRD2 polymorphism and sensitivity to losses during value-based decision-making

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Background

- Dopamine receptor subtypes respond differently to gains and losses
- Dopamine receptor D2 (DRD2) -141C Ins/Del genetic variant associates with lower levels of D2 receptor density
- DRD2 variant carriers may be less sensitive to losses during feedback learning
- It remains unclear how phasic dopamine is modulated by the opposing influences on the direct and indirect striatal pathways in feedback learning
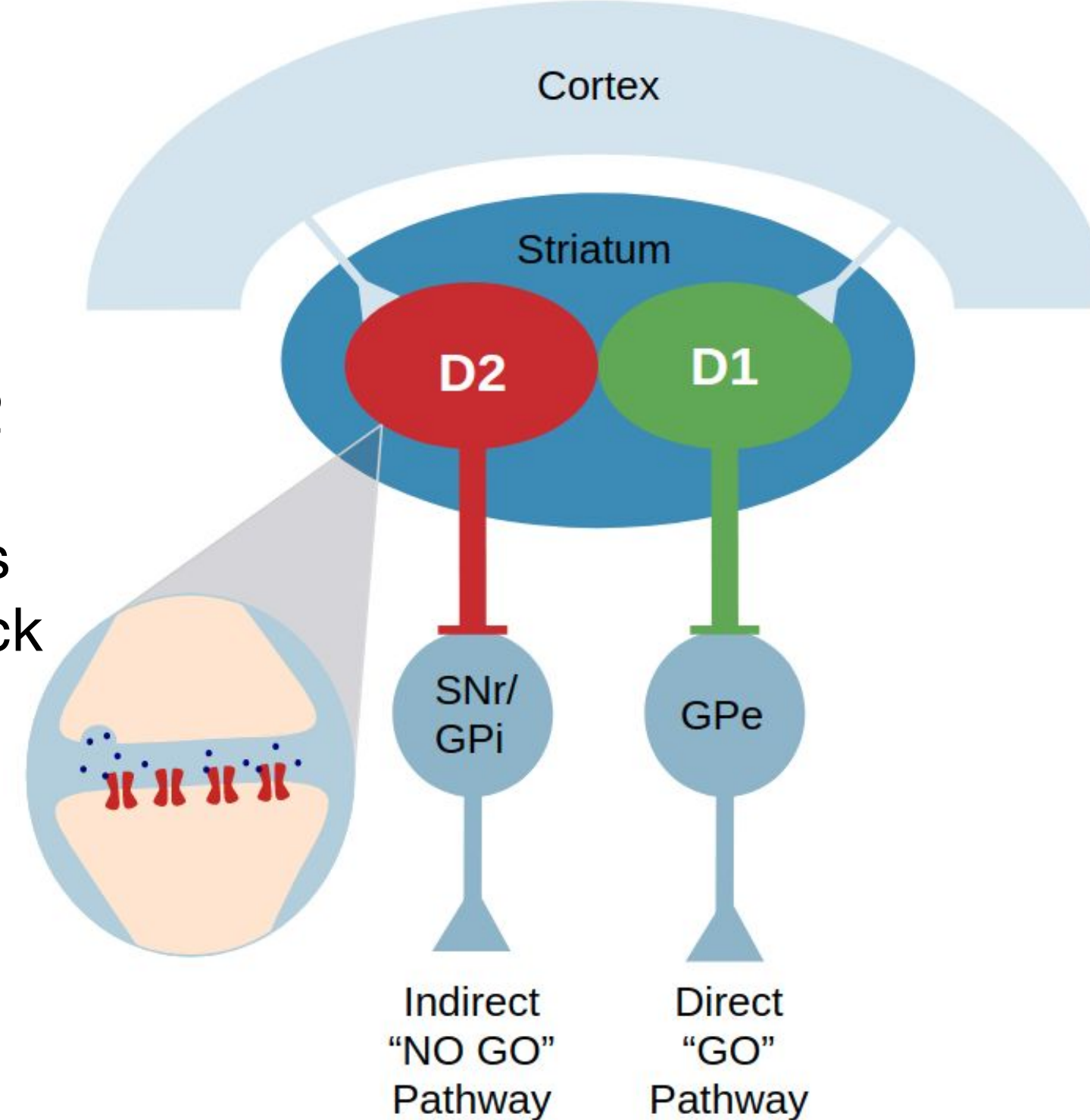

Hypothesis

- Ventral striatal reactivity to rewards interacts with the presence of the DRD2 -141C Ins/Del variant to impact sensitivity to gains and losses

Methods

Participants

- Neurologically healthy adults from southwestern Pennsylvania from University of Pittsburgh's Adult Health And Behavior project, Phase II
- 438 participants (228 females, 210 males) between the ages of 30 and 54 (M=42.67, SD=7.36)
- Participant's blood was drawn for genotyping for the DRD2 -141C Ins/Del variant (119 carriers, 319 non-carriers) (1)
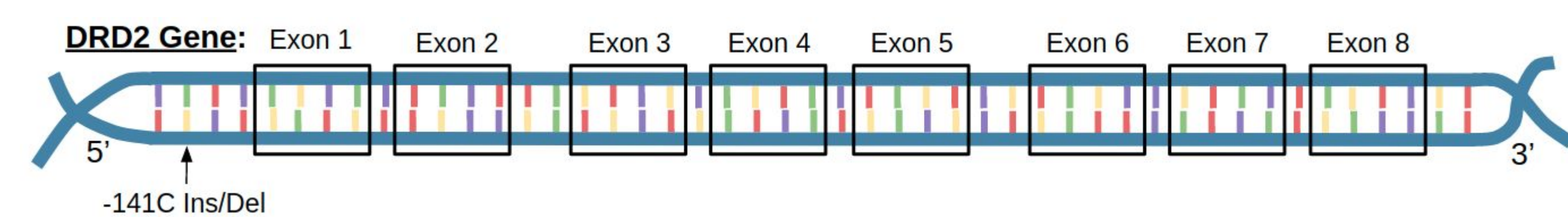
Iowa Gambling Task (IGT)

- Maximize profit with a set amount of number of draws possible from 4 decks of cards
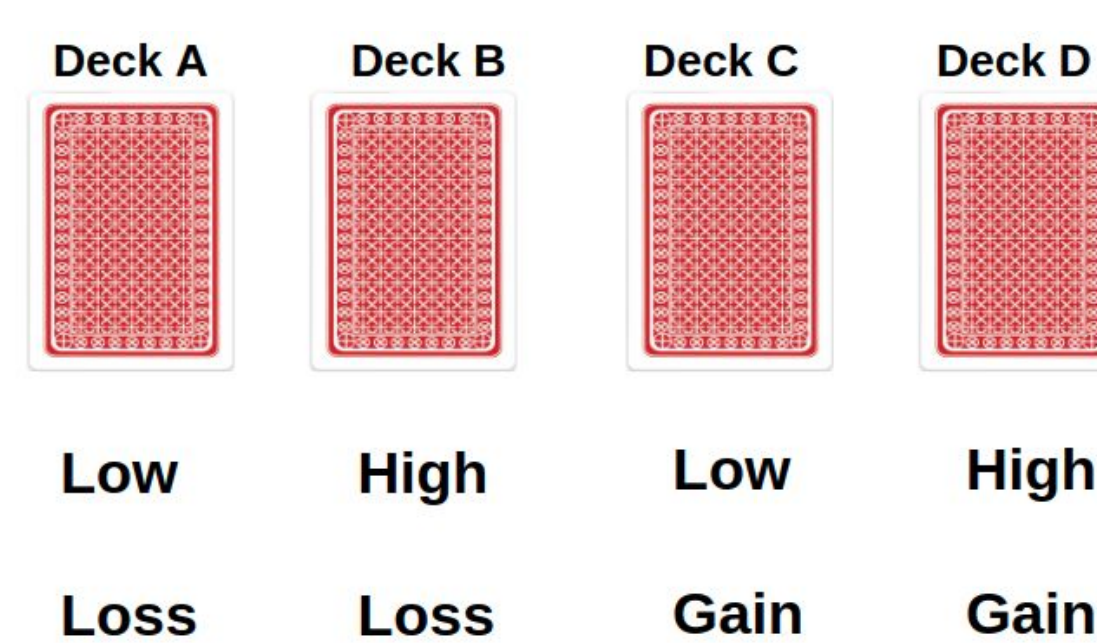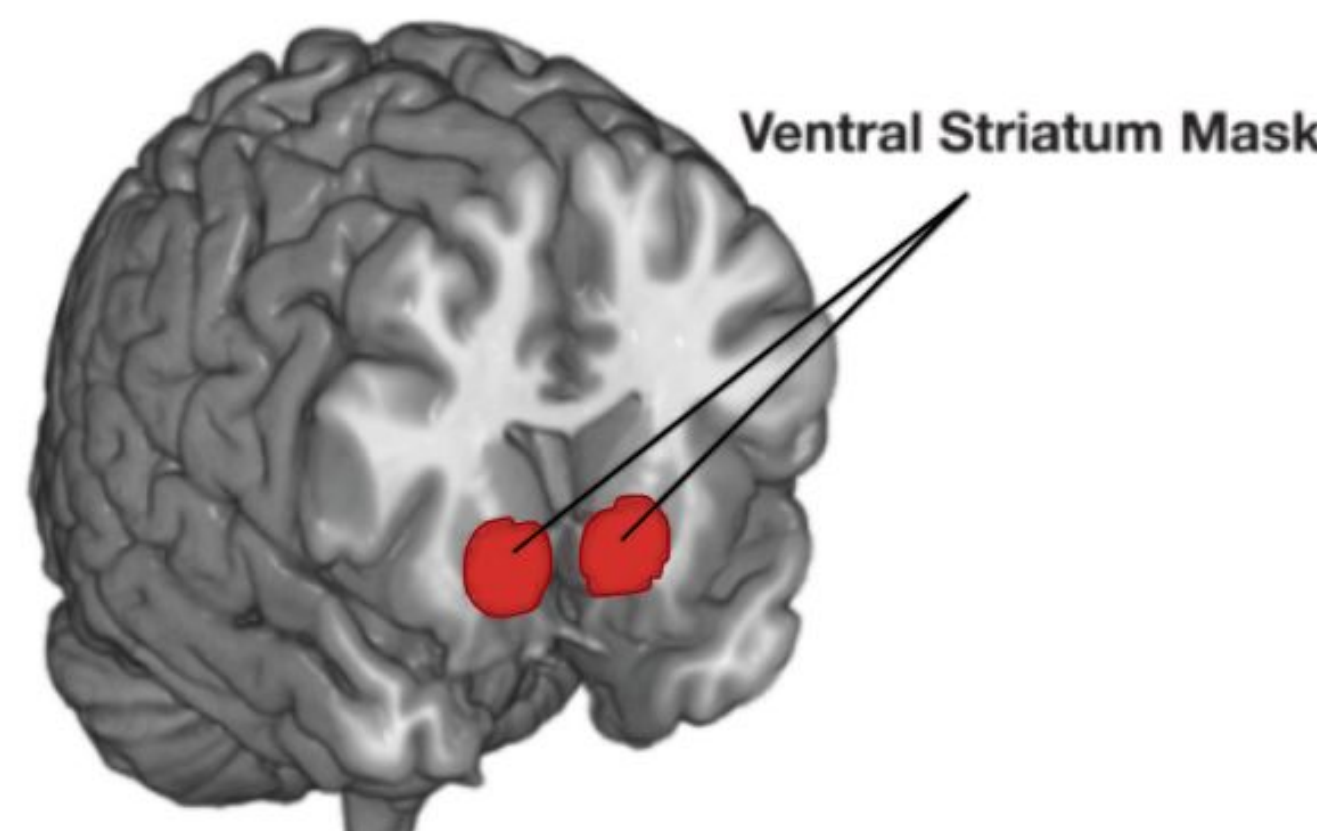

Payoff:

$$P = (C + D) - (A + B)$$

Sensitivity to high frequency rewards:

$$Q = (B + D) - (A + C)$$

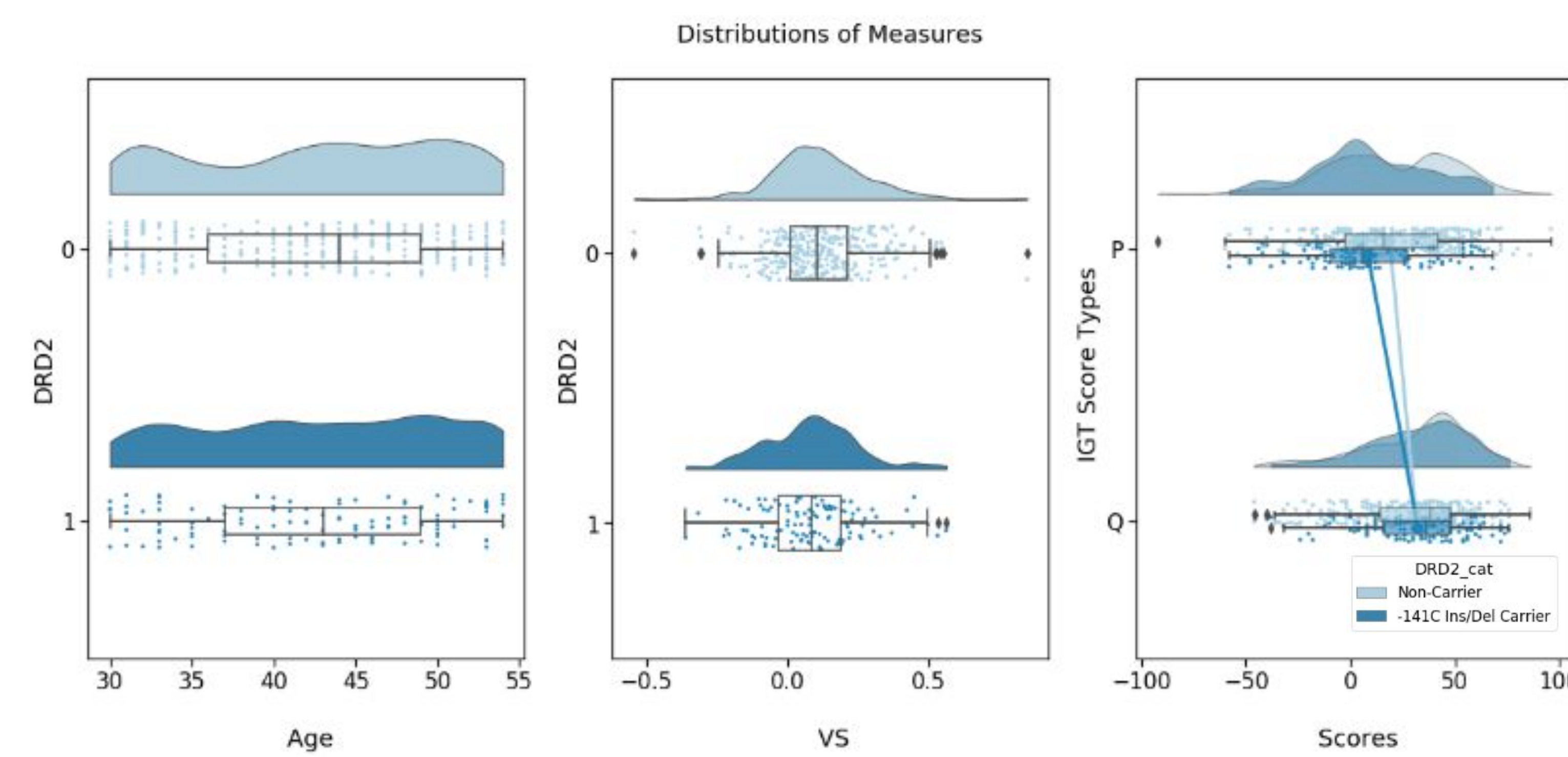|	Deck A	Deck B	Deck C	Deck D
Frequency of Reward:	Low	High	Low	High
Net Yield:	Loss	Loss	Gain	Gain

Ventral Striatal (VS) Reactivity Task

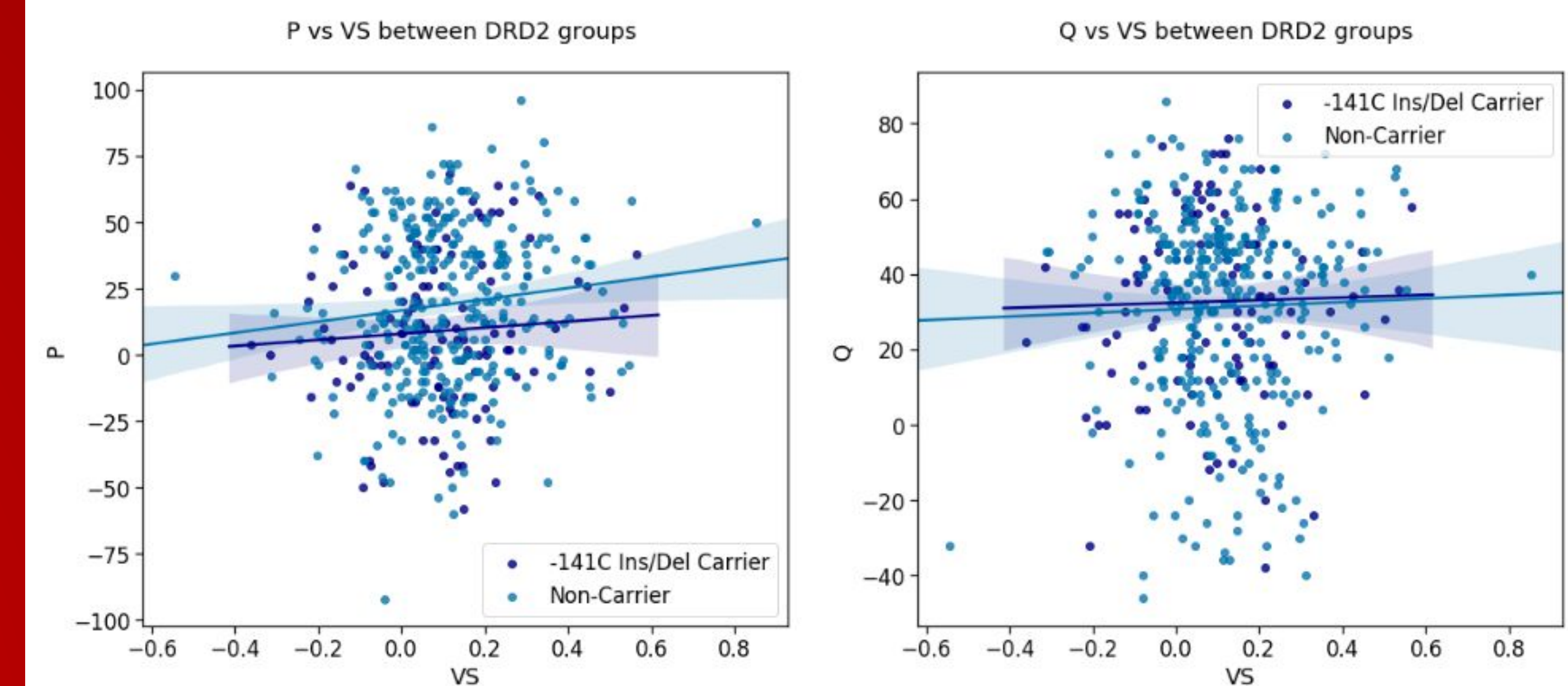- Assess the VS reactivity to negative and positive feedback cues associated with monetary gain (2 & 3)

Results: Distribution of Measures

- Distributions of Age, VS reactivity and IGT scores by DRD2 group are not normal

Results: Main Effects and Interactions

Payoff Analysis

- Significant effects from the DRD2 variant and for VS reactivity, but not for the interaction
- Carriers scored almost 9 points lower on Payoff compared to the non-carriers
- Strong evidence against the alternate model

Payoff Models

Bayes Factor: 18.37

$$H_0 : Y_P = \hat{\beta}_0 + \hat{\beta}_1 X_{DRD2} + \hat{\beta}_2 X_{VS}$$
$$H_A : Y_P = \hat{\beta}_0 + \hat{\beta}_1 X_{DRD2} + \hat{\beta}_2 X_{VS} + \hat{\beta}_3 X_{DRD2} \times X_{VS}$$

Payoff Linear Regression:

	coef	std err	t	P>|t|	[0.025	0.975]
Intercept	16.7039	2.020	8.269	0.000	12.733	20.674
DRD2	-8.7905	3.634	-2.419	0.016	-15.932	-1.649
VS	21.1400	10.020	2.110	0.035	1.447	40.833
DRD2:VS	-9.5730	18.830	-0.508	0.611	-46.582	27.436

Sensitivity Linear Regression:

	coef	std err	t	P>|t|	[0.025	0.975]
Intercept	30.6606	1.746	17.563	0.000	27.230	34.092
DRD2	1.7348	3.140	0.553	0.581	-4.437	7.906
VS	4.7830	8.658	0.552	0.581	-12.234	21.801
DRD2:VS	-1.3082	16.272	-0.080	0.936	-33.289	30.673

Sensitivity Analysis

- No significant effects from the DRD2 variant, for VS reactivity, nor for the interaction
- Strong evidence against the alternate model

Sensitivity Models

Bayes Factor: 20.86

$$H_0 : Y_Q = \hat{\beta}_0 + \hat{\beta}_1 X_{DRD2} + \hat{\beta}_2 X_{VS}$$
$$H_A : Y_Q = \hat{\beta}_0 + \hat{\beta}_1 X_{DRD2} + \hat{\beta}_2 X_{VS} + \hat{\beta}_3 X_{DRD2} \times X_{VS}$$

Results: VS Reactivity between Groups

- DRD2 variant carriers had generally lower performance in IGT than non-carriers for Payoff (t = 3.23, p = 0.001), but not for Sensitivity (t = 0.54, p = 0.590), and lower VS reactivity (t = -1.77, p = 0.077)

Conclusion

Summary

- Lower D2 receptor density, and lower dopamine release associates with sub-optimal value-based decision-making
- The interaction between D2 receptor density and dopamine release does not associate with differences in value-based decision-making
- No significant effects were found for sensitivity to high frequency rewards

Take Home Message

- Strong evidence that lower available D2 receptors, and lower dopamine release associates with a lower sensitivity to gains and losses in feedback learning
- Inconclusive evidence for the mechanistic role of the D2 pathway in using feedback effectively during value-based decision-making

Future Directions

Theoretical Directions

- Simulations of the D1 and D2 pathways in order to test other possible mechanistic roles of the D2 pathway in feedback learning

Experimental Directions

- Another feedback learning measure that separates between sensitivity to losses and gains

References

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2. Hariri, A. R., Brown, S. M., Williamson, D. E., Flory, J. D., De Wit, H., & Manuck, S. B. (2006). Preference for immediate over delayed rewards is associated with magnitude of ventral striatal activity. Journal of Neuroscience, 26(51), 13213-13217.
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