A dynamic [18F]fallypride PET study: Measuring dopamine neuromodulation in the extrastriatal reward circuit

E. Vrieele, J. Ceccarinig, D. Pizzagallil, G. Bormans2, K Van Laere2, K. Demyttenaere1, S. Claes1

1 Department of Psychiatry, University hospital Leuven, Belgium
2 Department of nuclear medicine, University hospital Leuven, Belgium
3Department of Psychology, Harvard University, Cambridge, Massachusetts

ABSTRACT

Introduction: Animal research indicates the mesocorticolumbic pathway as the central circuit of the brain reward system, with dopamine (DA) as the most important neurotransmitter (1). Previous studies propose that the extrastriatal part of the reward circuit plays a role in the ability to experience pleasure (liking the reward), but also in behaviours like motivation and drive (wanting the reward and learning). It is hypothesized that these psychological subcomponents of reward correspond with specific neural areas in the extrastriatal reward pathway in the brain.

Purpose: The purpose of this study was first to examine presynaptic DA release in extrastriatal regions of the reward circuit, in particular the prefrontal cortex (PFC) and anterior cingulate cortex (ACC), by measuring the high affinity D1/D2 radioligand [18F]-fallypride binding potential in response to a monetary reward challenge and second to identify the specific neural subcomponents in this part of the reward system in the brain.

Methods: 10 healthy volunteers underwent a single [18F]-fallypride injection Postion Emission tomography imaging session (2) while executing a computerised probabilistic reward task (3). DA-release in the extrastriatal reward areas of the brain was statistically tested by measuring time-dependent alterations in the kinetics of [18F]-fallypride using the linearized simplified reference region model (LSRRM). Statistical images, reflecting DA changes, were calculated and correlated with reward responsiveness, and feedback-related behaviour (learning and reward anticipation) by trail by trail probabilistic reward analysis.

Results: Voxel-based analysis revealed a significant inverse correlation between reward capacity and DA-release in the ventrolateral PFC (BA 10), orbitofrontal PFC (BA 11) and ACC (BA 32) Furthermore, the ACC and thalamic DA-displacement showed a significant positive correlation with the impaired tendency to modulate behavior as a function of prior reinforcements.

Conclusion: These findings support the hypothesis that several extrastriatal areas of the brain are involved in reward capacity. Individuals with a lower reward responsiveness show a higher DA release in prefrontal areas and the ACC during a reward challenge. Furthermore, integration of reinforcement history over time inversely correlates with thalamic and ACC DA release.

RESULTS

- Voxel-based analysis (statistical parametric mapping SPM2; phight=0.001), revealing a significant inverse correlation between reward sensitivity and DA-release in the ventralmedial prefrontal (PFC) (BA 10), orbitofrontal PFC (BA 11) and Anterior Cingulate Cortex (ACC) (BA 32).

Subjects with lower reward response show a higher DA release in the orbitoprefrontal cortex and the ACC.

- Trail by trail probabilistic reward analysis was used to analyse modulation of behavior as a function of prior reinforcements, revealing a significant positive correlation with the ACC and thalamic DA-displacement.

Subjects with impaired modulation of behavior after reinforcement show a lower DA release in the thalamus.

CONCLUSIONS

- Individuals with a lower reward responsiveness show a higher DA-release in prefrontal areas and the ACC during a reward challenge, implicating a greater attendance to the reward context of potential rewarding stimuli in less reward sensitive individuals.

Furthermore, the impaired ability to modulate behaviour as a function of prior reinforcements inversely correlates with thalamic and ACC DA-release, but not with PFC DA release, supporting the hypothesis that the ACC and thalamus play a role in learning and reward anticipation, in contrast to the PFC (which probably mediates the consumption of a reward).

REFERENCES

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