## Theme: Imaging Research in Basic and Clinical Science: Neuroscience, Cardiology and Oncology

## The role of impaired metabolic control in decision-making under uncertainty in the diabetic brain: an fMRI study

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## Abstract:

Type 2 diabetes mellitus (T2DM) has been associated with impaired cognition and brain function. We hypothesize that metabolic deregulation impacts mesocorticolimbic circuitry, which mediates decision-making processes. In this context, task-related functional magnetic resonance imaging (fMRI) studies are scarce, and evidence on such mechanisms remains fragmentary. Moreover, beyond economic choices, health-related decision-making is pivotal in the daily life of these patients, who are required to make constant decisions related to therapy compliance and healthy lifestyle habits. We employed a comprehensive fMRI protocol to investigate self-consequential decision-making in T2DM (N=17) and healthy controls (N=18) in the economic and health domains. fMRI data were analyzed using BrainVoyager, with cluster-level correction (p<0.05). Correlation analysis between the BOLD signal and metabolic control, expressed as glycated hemoglobin (HbA1c) levels, was also performed within the diabetic group.

Our results revealed that healthy controls have greater BOLD activation in dopaminerich regions related to risk encoding and reward processing in both domains, specifically in the orbitofrontal and ventromedial cortices. This is suggestive of impaired substrates of choice in T2DM individuals, particularly in goal-directed behavior related to appetite regulation and reward value representation. The correlation analysis showed contextdependent results: higher BOLD variations were positively correlated with higher HbA1c levels in the health domain, an effect not observed in the economic domain.

We found evidence of impaired neural correlates of decision-making closely linked to metabolic deregulation, which might underly T2DM-associated behavioral changes and poor self-regulation. Such findings may help to predict treatment responses, impact patient compliance and guide new pharmacological approaches.

**Keywords:** Type 2 diabetes mellitus, decision-making, metabolic control, magnetic resonance imaging