Nutrition, Nicotinamide Adenine Dinucleotide (NAD) in the Striatum and motivated behaviour

Project 607

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Background and aims: Previous results within the team have shown how brain metabolites play a crucial role in motivated behavior (Strasser et al., 2020; Zalachoras & Ramos-Fernández et al., 2022). These results point towards a direct link between the metabolism of specific brain structures and motivated behavior. Based on this result, we expect that other metabolites, which are fundamental for neuronal metabolism, and more specifically to mitochondrial functioning, including Nicotinamide Adenine Dinucleotide (NAD), should also play a major role in motivational capacities in humans. NAD in the body mostly comes from nutrition, through niacin (vitamin B3) and through the kynurenine pathway after transforming tryptophan (Braidy et al., 2018).

Methods: Two brain regions tightly linked to motivational processes, the dorsomedial prefrontal cortex/dorsal anterior cingulate cortex (dmPFC/dACC) and the anterior insula, were studied with 1H-MRS. We acquired a dataset of 75 healthy human participants aged between 25 and 40 years old who filled behavioral and nutritional questionnaires, including the Food-Frequency Questionnaire (FFQ). These participants also performed a behavioral task aiming at assessing their level of motivation and we also measured whole blood, plasma and brain metabolites. We then studied the relationship between nutrition-, blood- and brain-related measures and motivated behavior.

Results: The study revealed that baseline brain metabolism, particularly in the dmPFC/dACC, was associated with inter-individual differences in physical (Clairis & Barakat et al., 2024) and mental (Barakat & Clairis et al., 2025) motivation. However, only a few plasma metabolites correlated between the periphery and the brain (mostly plasma levels of glutamine and lactate), while most of NAD-related metabolites did not correlate between the periphery and the brain, supporting the view that nutrition and blood metabolism only had a marginal influence on our results.

Conclusion: Our results highlight the complexity of the interactions between nutrition, blood metabolism, brain metabolism and behavior and pave the way for future investigations targeting the link between nutritional interventions aiming at influencing dmPFC/dACC metabolism and motivation.

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Barakat A*, Clairis N*, Brochard J, Pessiglione M, Godin JP, Cuenoud B, Xin L, Sandi C (2024) A neurometabolic signature in the frontal cortex predicts individual differences in effort-based decision-making, *bioRxiv*, doi: 10.1101/2024.01.23.576854. (*co-first authors)

Clairis N*, Barakat A*, Brochard J, Xin L, Sandi C (2024) A neurometabolic mechanism involving dmPFC/dACC lactate in physical effort-based decision-making, *Molecular Psychiatry*, doi: 10.1038/s41380-024-02726-y. (*co-first authors)