The role of nucleus accumbens in the perception of natural rewards

ABSTRACT:

Background
To survive, individuals must learn to associate cues in the environment with emotionally relevant outcomes. This association is partially mediated by the nucleus accumbens (NAc), a key brain region of the reward circuit that is mainly composed by GABAergic medium spiny neurons (MSNs), that express either dopamine receptor D1 or D2. Recent studies showed that both populations can drive reward and aversion, yet how distinct neuronal populations encode appetitive or aversive stimuli remains undetermined.

Aims
Determining if/how NAc D1- and D2-MSN activity mediates distinct events of cue-outcome associative learning to produce appropriate behaviour.

Method
We investigated the relevance of D1- and D2-MSNs in Pavlovian associations, by measuring calcium transients with fiber photometry during Pavlovian tasks in mice. Using microendoscopic calcium imaging, we tracked NAc D1- or D2-MSNs' activity during exposure to stimuli of opposing valence and associative learning.

Results
Our results show that D1- and D2-MSNs are similarly co-recruited during both appetitive and aversive conditioning. Their collective population activity is sufficient to encode cue-outcome associations, supporting a shared role in associative learning. However, when the contingencies change, the NAc exhibits an asymmetric response, with a more pronounced shift in D2-MSN activity. Optogenetic manipulation of D2-MSNs provided causal evidence of the necessity of this population in extinction learning.

Conclusions
These findings support a model in which D1- and D2-MSN populations are co-recruited to encode cue-outcome associations, playing complementary roles in eliciting appropriate motivated behaviors.

Keywords
Nucleus accumbens, Reward, Aversion, Associative learning

Os textos são da exclusiva responsabilidade dos autores
All texts are of the exclusive responsibility of the authors

Published Work:

Soares-Cunha, C., Domingues, A. V., Correia, R., Coimbra, B., Vieitas-Gaspar, N., Vasconcelos, N., Pinto, L., Sousa, N. & Rodrigues, A. J. (2022). Distintic role of nucleus accumbens D2-MSN projections to ventral pallidum in different phases of motivated behavior. *Cell Reports*, *38*(7), 110380. doi:10.1016/j.celrep.2022.110380

Domingues, A. V., Coimbra, B., Correia, R., Deseyve, C., Vieitas-Gaspar, N., Floresco, S., Sousa, N., Soares-Cunha, C., & Rodrigues, A. J. (2022). Prenatal dexamethasone exposure alters effort decision making and triggers nucleus accumbens and anterior cingulate cortex functional changes in male rates. *Translational Psychiatry*, *12*(1), 338. doi:10.1038/s41398-022-02043-4

Soares-Cunha, C., & Heinsbroek, J. A. (2023). Ventral pallidal regulation of motivated behaviors and reinforcement. *Frontiers in Neural Circuits*, *17*, 1086053. doi:10.3389/fncir.2023.1086053

Correia, R., Coimbra, B., Domingues, A. V., Wezik, M., Vieitas-Gaspar, N., Gaspar, R., Sousa, N., Pinto, L., Rodrigues, A. J., & Soares-Cunha, C. (2023). Involvement of nucleus accumbens D2-medium spiny neurons projecting to the ventral pallidum in anxiety-like behaviour. *Journal of Psychiatry and Neuroscience*, *48*(4), E267-E284. doi:10.1503/jpn.220111

Domingues, A. V., Rodrigues, A. J., & Soares-Cunha, C. (2023). A novel perspective on the role of nucleus accumbens neurons in encoding associative learning. *FEBS Letters*, *597*(21), 2601-2610. doi:10.1002/1873-3468.14727

Deseyve, C., Domingues, A. V., Carvalho, T. T. A., Armada, G., Correia, R., Vieitas-Gaspar, N., Wezik, M., Pinto, L., Sousa, N., Coimbra, B., Rodrigues, A. J., & Soares-Cunha, C. (2024). Nucleus accumbens neurons dynamically respond to appetitive and aversive associative learning. *Journal of Neurochemistry*, *168*(3), 312-327. doi:10.1111/jnc.16063.

Jungmann, R. M., Feliciano, T., Aguiar, L. A. A., Soares-Cunha, C., Coimbra, B., Rodrigues, A. J., Copelli, M., Matias, F. S., de Vasconcelos, N. A. P., & Carelli, P. V. (2024). State-dependent complexity of the local field potential in the primary visual cortex. *Physical Review E*, *110*(1-1):014402. doi:10.1103/PhysRevE.110.014402.

Domingues, A. V., Carvalho, T. T. A., Martins, G. J., Correia, R., Coimbra, B., Bastos-Gonçalves, R., Wezik, M., Gaspar, R., Pinto, L., Sousa, N., Costa, R. M., Soares-Cunha, C., & Rodrigues, A. J. (2025). Dynamic representation of appetitive and aversive stimuli in nucleus accumbens shell D1- and D2-medium spiny neurons. *Nature Communications*, *16*(1), 59. doi:10.1038/s41467-024-55269-9

Researcher's Contacts:

Carina Soares-Cunha
University of Minho
ICVS, School of Medicine
Campus de Gualtar
4710-057 Braga
Portugal

Phone: +351 253 604 831
Email: carinacunha@med.uminho.pt