University of Zurich[UZH] | ETH Eidgenössische Technische Hochschule Zürich Swiss Federal Institute of Technology Zurich

Translational Neuromodeling Unit

Timing of prediction error signaling in reward learning: A computational trial-by-trial EEG analysis

S. Tomiello[1], D. Schöbi[1], L. A. E. Weber[1], K. Wellstein[1], G. Stefanics[1], H. Haker[1], S. Iglesias[1], K. E. Stephan[1, 2, 3]

[1] Translational Neuromodeling Unit (TNU), UZH & ETH Zurich, Switzerland

[2] Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, London, UK

[3] Max Planck Institute for Metabolism Research, Cologne; Germany

Introduction

In reward learning, action optimization relies on the success of past decisions and on accumulated knowledge about the (in)stability of the environment [1]. Consequently, belief updating is informed by **multiple prediction errors (PEs) that are related hierarchically** [2].

Recent work linked these computational quantities to fMRI data [3], implying that hierarchically different precision-weighted PEs may be encoded by specific neurotransmitters such as dopamine (DA) and acetylcholine (ACh). By contrast, the **timing** of these different PEs is **poorly understood**.

Using a reward-based associative learning task in which the contingency between cues and rewards changed over time, we inferred, from subject-specific behavioral data, a low-level choice PE ($c\delta_1$) about the reward outcome, a high-level PE (δ_2) about the probability of the outcome and the respective precision-weights and related them, **trial-by-trial**, to the EEG signal.

Furthermore, the current study employed **pharmacological interventions to probe DA and ACh modulation** of these quantities.

The aberrant modulation by DA and ACh of N-methyl-D-aspartate receptors (NMDARs) dependent plasticity is a **central mechanisms in many psychiatric disease** [4], as for example in schizophrenia.

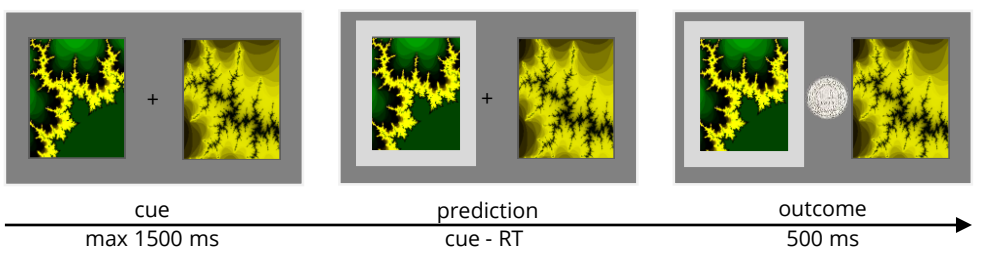
Experimental Procedure & Analyses

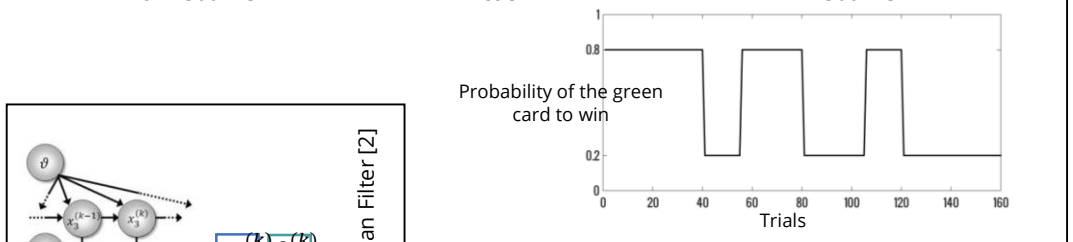
Sample: 68 healthy, male volunteers.

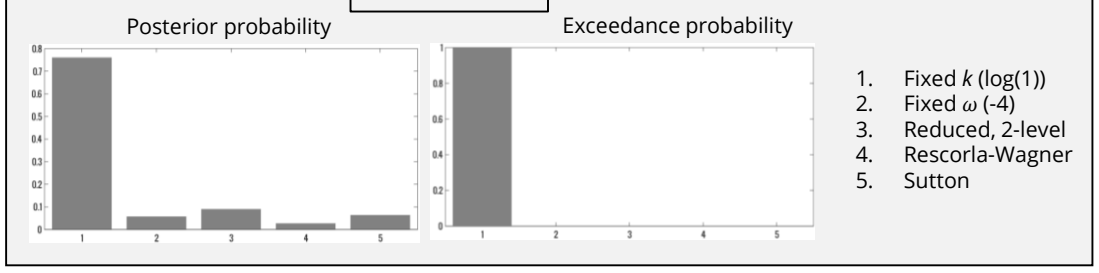
Pharmacological Interventions:
- Amisulpride: antagonistic effects on D2/D3 dopaminergic receptors
- Biperiden: antagonistic effects on M1 cholinergic muscarinic receptors
- Placebo

Double-blind, between-subject, placebo-controlled design

EEG data acquisition: 64-channels cap (EASYCAP GmbH), 10-20 system. Subject-specific electrode positions.

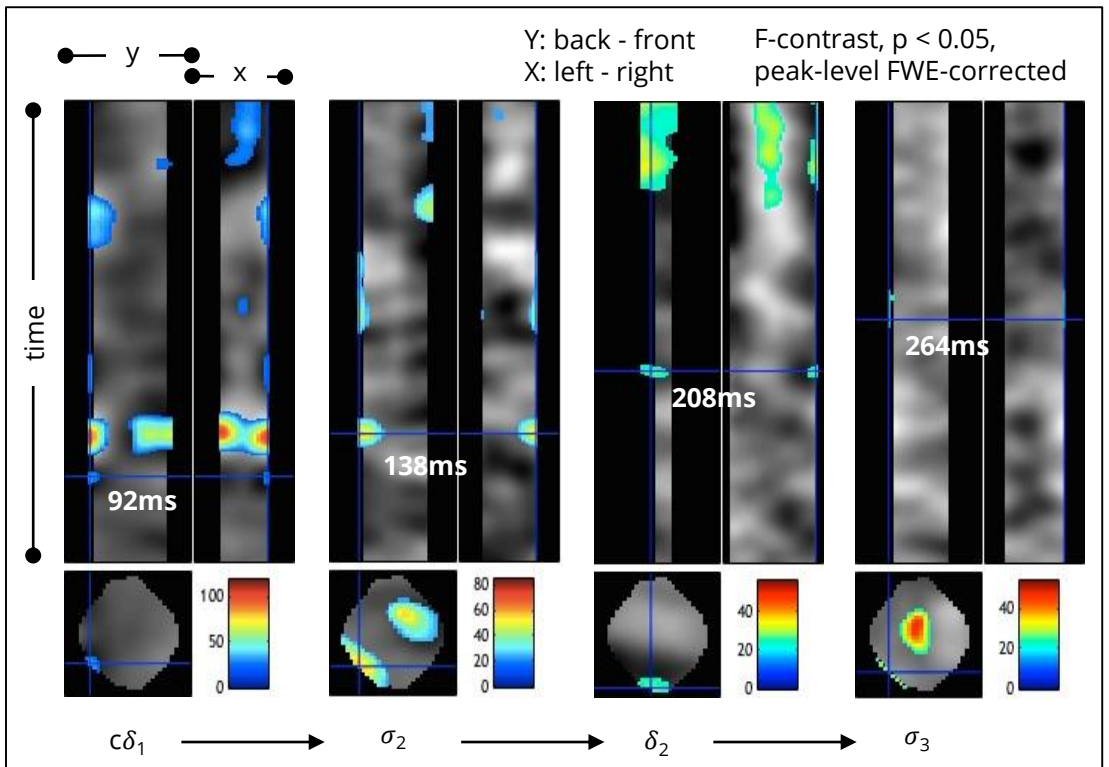


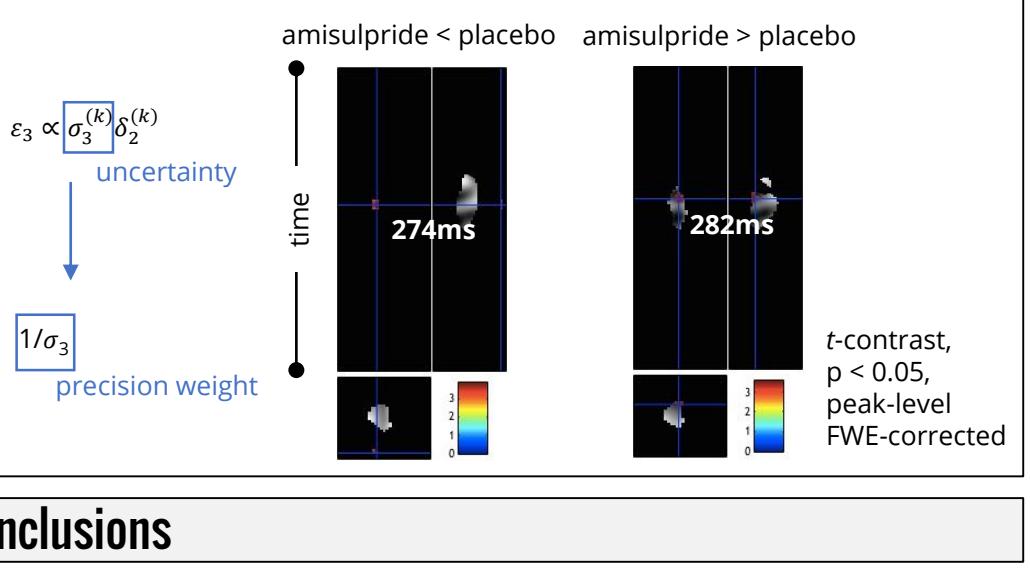




1. Fixed k (log(1))
2. Fixed ω (-4)
3. Reduced, 2-level
4. Rescorla-Wagner
5. Sutton

Results





Conclusions

Our computational trial-wise EEG analysis captures learning dynamics and allows for examining the temporal relation of different computational quantities. We find that hierarchically related PEs are expressed at different time points. Notably, the temporal profile of activity is consistent with the computational sequence or hierarchy postulated by our hierarchical Bayesian model.

Concerning pharmacological effects, we find that the D2/D3 dopamine receptor antagonist amisulpride modulates the electrophysiological expression of the third-level precision-weight ($1/\sigma_3$), i.e. the precision of the subject's belief about environmental volatility, at 274 and 282 ms after trial outcome. Given the previous results by Iglesias et al. (2013), it is possible (but presently speculative) that this effect may arise from interactions between dopaminergic and cholinergic nuclei in the brainstem.

Future analyses will focus on biophysical models for discriminating between DA and ACh effects on synaptic plasticity in individual subjects. In clinical studies, this may prove useful for **detecting pathophysiological subgroups** (e.g. within the schizophrenia spectrum) and to generate **individual treatment predictions**.

References

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