The role of dopamine for semantic prediction errors and adaptation as reflected in N400 amplitudes

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What is the relation between the semantic prediction error suggested to underlie N400 amplitudes[1] and the dopaminergic reward prediction error[2]? In a neural network model of sentence comprehension, an update of a probabilistic representation of sentence meaning was suggested to underlie N400 amplitude. The change in activation induced by a word was proposed to reflect a semantic prediction error that drives adaptation of the model's connections and estimates[1]. In reinforcement learning research, dopamine transients (phasic increases of dopamine) have long been viewed as specifically encoding reward prediction errors. Recently, however, efforts have been made to establish a framework of dopamine as a generalized prediction error[3]. Based on this view, dopamine might be expected to contribute to semantic prediction error and adaptation. Thus, increasing the availability of (phasic) dopamine might enhance semantic prediction error as reflected in the N400 and induce stronger adaptation as indicated e.g. by long term repetition effects (reduction of N400 amplitude with delayed repetition[4]). Interestingly, independent lines of research have demonstrated effects that seem consistent with this hypothesis: (1) dopamine improved implicit learning in artificial grammar[5] and word learning[6] paradigms (2) studies of individuals with schizophrenia - characterized by hyperactive dopaminergic transmission - suggest abnormal N400 activity[7,8] (3) NMDA receptor (essential for phasic dopamine bursts[9,10]) antagonists reduced N400 amplitudes at the initial presentation of words and eliminated repetition effects[11].

To directly address the relationship between dopamine, N400, and adaptation, we will administer levodopa/bensarazid (100/25mg) to 32 participants (based on a 90% power simulation in R) in a double-blind placebo-controlled cross-over design. As a dopamine precursor, levodopa is especially suited for the manipulation of dopamine levels in regard to our research question, because it not only increases tonic but also phasic dopamine transmission. We will measure EEG while the participants read 80 German sentences word-by-word, which will each be repeated in a second experimental block (position: first vs. second). Sentences are manipulated regarding their cloze probabilities (expectancy: expected vs. unexpected).

We will fit a linear mixed-effects model with random by-subject and by-item effects to single trial N400 amplitudes and focus on the following research questions:

(1) *The effect of dopamine on the semantic prediction error:* If dopamine contributes to the semantic prediction error assumed to underlie the N400, manipulating dopamine levels will induce changes in N400 amplitude. As we expect increased dopamine levels to enhance a prediction error, N400 amplitudes should be more negative at the first stimulus presentation in the dopamine compared to the placebo condition. The effect of dopamine on the N400 will be compared to its effect on the N1 visual onset response to control for general effects of dopamine on the ERP.

(2) *The effect of dopamine on adaptation:* We see N400 repetition effects as the result of model adaptation. We therefore expect Levodopa to increase the N400 repetition effect and lead to a stronger reduction in N400 amplitude compared to placebo.

(3) *The nature of the prediction error:* We will investigate whether expectancy is modulating effect (1) and (2). This will give insights into how neurotransmitters are released in the context of a semantic prediction error, specifically the quantitative relation between expectancy and phasic dopamine transmission.

This study will contribute to a better understanding of the neurocognitive basis of N400 amplitudes. It can further help to clarify the role dopamine transients play in error signaling beyond reward and places the N400 and implicit language learning within the scope of current theories on dopamine as a more general sensory prediction error.

Examples of sentences used with expected/unexpected nouns:

1 exp) Der Zauberer holte ein Kaninchen aus seinem Hut
(The magician took a rabbit out of his hat)
1 unexp) Der Tierwärter holte ein Kaninchen aus seinem Hut
(The zoo keeper took a rabbit out of his hat)

2 exp) In Bayern angekommen, aß der Tourist eine frisch gebackene Brezel
(After arriving in Bavaria the tourist ate a freshly baked pretzel)
2 unexp) In Italien angekommen, aß der Tourist eine frisch gebackene Brezel
(After arriving in Italy the tourist ate a freshly baked pretzel)

Sentences were created in pairs with a minimal difference that creates different expectations. Sentences were divided into 4 lists that were controlled for sentence length, as well as length, frequency and orthographic neighborhood of the target noun.

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