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Reduction of dopamine in basal ganglia and its effects on syllable sequencing in speech: A computer simulation study

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ABSTRACT

Background: Reduction of dopamine in basal ganglia is a common cause of Parkinson's disease (PD). If dopamine-producing cells die in the substantia nigra, as seen in PD, a typical symptom is freezing of articulatory movements during speech production.
Goal: It is the goal of this study to simulate syllable sequencing tasks by computer modelling of the cortico-basal ganglia-thalamus-cortical action selection loop using different levels of dopamine in order to investigate the freezing effect in more detail.
Method: This simulation was done using the Neural Engineering Object (Nengo) software tool. In the simulation, two dopamine level parameters (lg and le), representing the effect of D1 and D2 receptors, and therefore the level of dopamine in striatum respectively, can be differentiated and modified.
Results: By a decrease of the dopamine level parameters lg and le to 50% we replicated a freezing effect after less than 5 syllable productions. Furthermore freezing of action selection in speech was greater for dopamine level reduction in D1 than D2 receptors.
Conclusions: In this study using a neuro-functional brain model, the speech freezing effect results from simulating a reduction of dopamine level in striatum.

1. Introduction

In a specific contextual situation (e.g., reading silently, speaking aloud, being involved in a communication process etc.), a specific number of actions are available for cortex to perform such as activation of a cognitive representation of a word in the mental lexicon [32,33,26] or activation of cognitive, auditory, somatosensory, and motor representations of a word or syllable at hyper- and unimodal cortical levels [19,17,9,31,30]. All of these actions are represented as potentially available cognitive, sensory, or motor actions to the basal ganglia and thalamus. Due to the specific situational context, one of these actions can then be selected by the basal ganglia-thalamus system (e.g., [7,20]).

Two pathways define action selection within the basal ganglia, often referred to as the direct and indirect pathways. However, we adopt the analysis of Gurney at al. [20,21], which suggests that there is rather a "selection pathway" and a regulating or modulation pathway, called the "control pathway". In both pathways all neural activity starts with the cortex stimulating the striatum (see also Fig. 1). The striatum inhibits both the substantia nigra (SN) and the globus pallidus (GP). Both the SN and the GP consists of two parts. There is the substantia nigra pars compacta (SNc) and pars reticularis (SNr), as well as the globus pallidus pars externa (GPe) and pars interna (GPi). When the striatum inhibits the SN and the GP, SNr and GPi themselves cannot continue inhibiting the thalamus. This is the selection pathway, which largely relies on mechanisms of disinhibition. In addition, the GPe inhibits the GPi and the subthalamic nucleus (STN), which in turn reduce their excitatory input into the GPe, GPi and the SNr. As mentioned above, a less active SNr and GPi positively influence the neural activity of the thalamus (i.e., via disinhibition). This is the control pathway. Both the control and selection pathways are modulated by the SNc, which effects the striatum by modulating the dopamine level. Activation of the dopamine D1 receptor results in the inhibition of the SN and the GPi by the striatum, and activation of the D2 receptor results in the inhibition of the inhibition (i.e., disinhibition) of the GPe by the striatum. In both cases, dopamine influences result in increased thalamic activity, suggesting that the pathways work synergistically.

This process of action selection is highly dependent on the dopamine level in the striatum [15]. Following Gurney et al.

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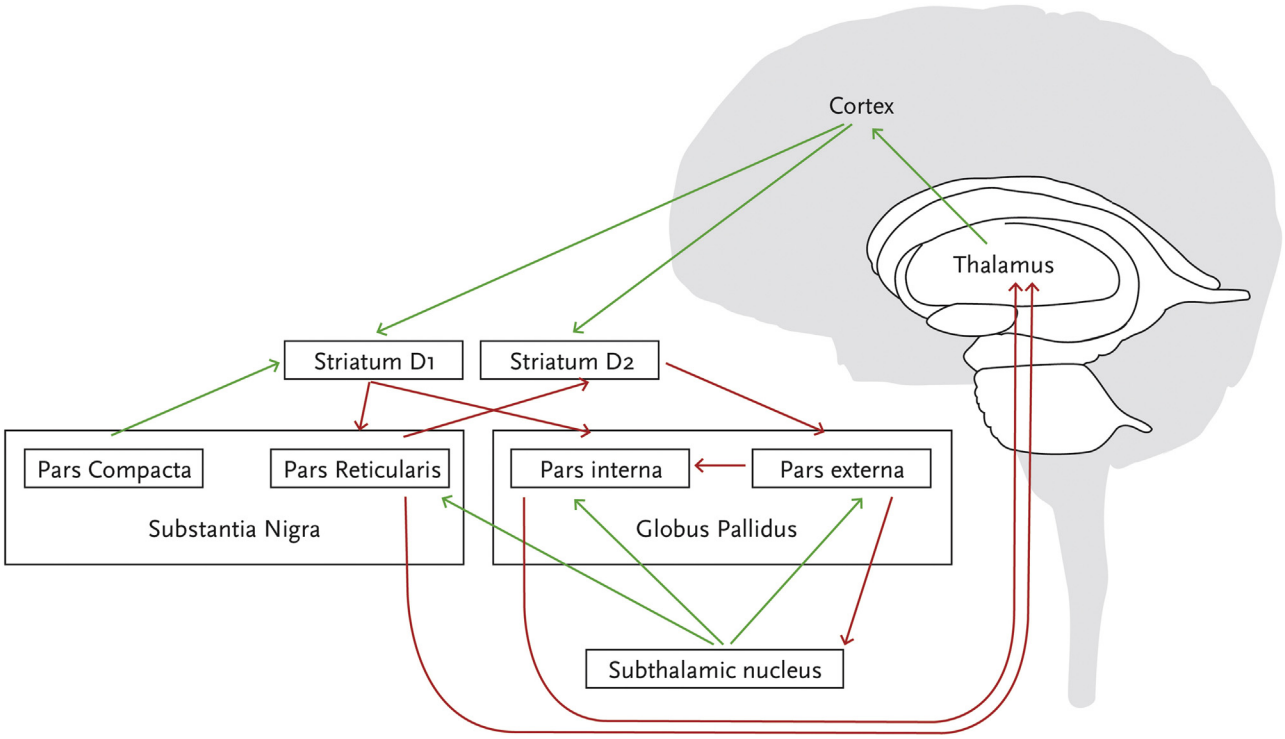

Fig. 1. Model of the cortico-basal ganglia-thalamus-cortical circuit following 9 [20,21]. The green lines symbolize excitatory pathways, the red lines inhibitory pathways.

[20,21], in our basal gangli-thalamus action selection model two parameters can be introduced in order to describe the dopamine level in striatum. The lg parameter affects the selection pathway and modulates the stimulating influence of the SNc on the striatum. Specifically, it determines the amount of dopamine, which interacts with the D1 receptor. The second parameter is the le parameter, which reflects the amount of dopamine from the SNc binding to the D2 receptor. The D2 receptor results in an inhibitory effect on the parts of the striatum which inhibit the GPe causing this inhibitory effect on GPe to decrease (disinhibition). The result is a more active GPe now inhibiting the GPi and the STN which then decreases excitatory influence on the SNr and the GPi so that both of these structures decrease their inhibitory effect on the thalamus. The D1 receptor, however, has an excitatory effect on the striatum, so the striatum itself can inhibit the SN and the GP, which subsequently cannot inhibit the thalamus (disinhibition).

Because of this complexity, an imbalanced dopamine system is thought to cause different neuropsychiatric disorders, such as the Parkinson's disease (PD) (e.g., [14]), schizophrenia (e.g., [39]) or AD/HD (e.g., [28]). In the case of PD, both the degeneration of dopaminergic cells within the substantia nigra and the resulting loss of dopamine in the striatum result in Parkinsonian symptoms such as tremor, bradykinesia, rigidity and difficulty with walking and gait [16]. More than a third of PD patients also suffer from a so-called freezing effect [18,43]. During freezing, patients suddenly interrupt an action which is already under execution, or interrupt an action sequence. This can occur in tasks like walking, reaching or speaking. In the case of walking, freezing may lead to falling, resulting in a loss of independence for these patients [35].

Patients suffering from Parkinson's disease typically produce specific symptoms in speech production like reduced loudness, poor voice quality, voice tremor, reduced prosodic variability in pitch and loudness, unprecise or reduced articulation of consonants and vowels, short rushes of speech, hesitations, and passages of dysfluency. These symptoms can be subsumed as hypokinetic dysarthria [8,38]. When confronted with a syllable repetition task in speech (rapid repetition of one syllable or of an ordered sequence of syllables) in addition speech freezing can be observed in Parkinsonian patients [1,14]. Erro et al. [14] (p. 561) described freezing of speech seen in Parkinsonian patients as "a brief, episodic absence or marked reduction of forward progression of the speech, despite the intention to speak, bearing resemblance with FoG" (freezing of gait). While other symptoms of hypokinetic dysarthria are well investigated, this does not hold for the symptom complex of hesitations, dysfluency, and freezing of speech. Freezing of speech (FoS) can be interpreted as a subform of repetitive speech in Parkinson's disease [14,4] and in its extreme form leads to a stoppage of articulation or at least to a break of articulation for a duration of a couple of syllables. Ziegler [44] reports that he excluded all trials in an endless syllable repetition task (oral diadochokinesis), which comprised less than eight produced syllables ([44] p. 561). Thus, we are unable to compare the freezing phenomena presented here with quantitative human data, and instead focus on reproducing the effect qualitatively and investigating the neural mechanisms that may be involved.

In past work, it was shown via simulation experiments by using a neurocomputational model of cortical and subcortical parts of the brain that pathological dopamine levels within basal ganglia can result in dysfluencies in speech [5]. In that work, data were gathered with the neurocomputational speech production model GO-DIVA, containing basal ganglia, thalamus and left ventral premotor cortex, which is assumed to simulate the syllable-sequencing circuit. It was shown that an elevated dopamine level in striatum disturbs normal thalamus activity and leads to a stuttering effect (repetition of a sound or syllable following a complete stop of articulation during a first production trial of that sound or syllable). Civier [5] (p. 264) confirms as well, that an imbalanced dopamine system is associated with disorders of movement and decision making.

It is our hypothesis that speech freezing in Parkinson's disease [1,43] results from dysfunctions in syllable repetition or syllable sequencing as well. It will be shown in this paper on the basis of