DOPAMINE EXCESS MAY DELAY SELECTION OF SYLLABIC MOTOR PROGRAMS: A MODELING STUDY OF STUTTERING

Oren Civier[a], *Daniel Bullock*[a,b], *Ludo Max*[d,e] *& Frank H. Guenther*[a,c,f]

[a]Department of Cognitive and Neural Systems; [b]Department of Psychology; [c]Department of Speech, Language, and Hearing Sciences, Boston University, USA;
[d]Department of Speech and Hearing Sciences, University of Washington, USA;
[e]Haskins Laboratories, USA;
[f]Division of Health Sciences and Technology, Harvard University – MIT, USA
orenciv@gmail.com

ABSTRACT

The hypothesis that stuttering partly results from dopamine excess leading to delayed selection of the motor program for the next syllable (from candidate programs for phonologically similar syllables) was investigated with a combined simulation of two neurobiological models of speech production circuits: GODIVA and DIVA. Parametric simulations showed that high dopamine levels in the GODIVA model can account for dysfluent speech. The affected neural circuit is a loop of interconnected brain regions involved in syllable sequencing and initiation: basal ganglia, thalamus, and left ventral premotor cortex.

Keywords: stuttering, neural modeling, mental syllabary, dopamine levels, basal ganglia

1. INTRODUCTION

Several lines of evidence suggest that people who stutter (PWS) have a hyperactive dopaminergic system [6, 9]. We hypothesize that this abnormality leads to an impaired ability to read out motor programs for well-learned syllables from the "mental syllabary" [7], resulting in dysfluencies.

We propose that the affected circuit is the basal ganglia (BG) - thalamus - left ventral premotor cortex (vPMC) loop, or BG-vPMC loop, whose integrity is essential for proper readout of motor programs. The circuit is a loop because the vPMC not only receives projections from the BG via the thalamus, but also sends projections back to the BG. According to our proposal, the function of the BG-vPMC loop is to decide when the conditions for program execution are satisfied, and then to facilitate fast syllable initiation by biasing cortical competition in favor of the premotor neuron population responsible for reading out the correct motor program for the next syllable.

We predict that elevated dopamine (DA) levels may disturb the BG-vPMC loop due to increased DA binding in the striatum [8]. The BG-vPMC loop will be unable then to bias cortical competition, and the resulting delayed activation of the appropriate premotor neuron population would lead to dysfluency. Here, we perform a computational simulation of a scenario in which the central nervous system (CNS) waits until the neuron population is fully activated; hence, the outcome is a prolongation of the articulatory position for the initial sound of the next syllable (we assume that without full activation, only the very beginning of the motor program can be read out properly). If the CNS tries reading out the complete motor program right away, an impaired readout is likely, resulting in production errors that can lead to sound/syllable repetitions [4].

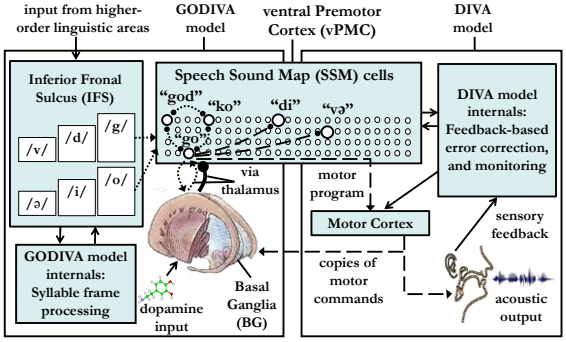
2. THE GODIVA AND DIVA MODELS

GODIVA and DIVA are biologically constrained neural circuit models capable of simulating speech development and production [2, 5]. DIVA (Directions Into Velocities of Articulators) models circuits that control articulation of sounds and well-learned syllables, whereas GODIVA (Gradient Order DIVA) models higher-level aspects of speech production, including syllable sequence planning and readout (controlled initiation) of successive plan constituents. The GODIVA model circuit outputs to the DIVA circuit through a premotor cortex stage that consists of speech sound map (SSM) cells (Fig. 1). Each SSM cell represents a premotor neuron population that encodes the motor program for a specific well-learned syllable. The GODIVA model decides which SSM cell should be active at each point, and the DIVA model controls an articulatory synthesizer (represented in the figure

by a cartoon of a vocal tract) to execute the articulatory program coded by that cell.

Fig. 1 shows the models' contribution when fluently producing the syllable "go" of the syllable sequence "go.di.və" ("go diva"). The syllables "di" and "və" are produced in a similar fashion.

Figure 1: Schematic of the GODIVA and DIVA models producing the first syllable of "go.di.və".



The order of events in Fig. 1 is as follows:

2.1. Processing of inputs

The input to the simulation is a graded set of pulses sent in parallel, assumed to arrive from higher-order linguistic areas. In the inferior frontal sulcus (IFS) stage of the GODIVA model, these inputs create an activity gradient across the /g/, /d/, and /v/ phoneme cells in the onset consonant's queue, and a gradient across the /o/, /i/, and /ə/ phoneme cells in the vowel nucleus's queue. Each phoneme cell represents an IFS neuron population that is tuned to a particular phoneme and to a particular abstract syllable position (see [2]).

2.2. Selection of "go"

Because both the /g/ and /o/ phoneme cells have the highest activity in their corresponding queues within the IFS, these cells drive initial activity in the premotor cortex. Multiple SSM cells representing motor programs for syllables become active, each partially matching the phonological sequence representation in the IFS. Three such cells are depicted in Fig. 1: "go", "god", and "ko". These cells compete with each other for a variable time interval that depends on inputs via the BG-thalamus. Under normal conditions, these inputs promote competitive selection in favor of the cell with the best match to the phonological sequence representation. In this case, the "go" SSM cell (see dotted arrows in Fig. 1. Arrowheads and circles indicate excitation and inhibition, respectively).

2.3. Execution of "go"

After competitive selection, the SSM cell for "go" reads out the motor program for that syllable, while inhibiting other SSM cells (e.g., the cells for "di" and "və"). The motor cortex stage of the DIVA model articulates the commands of the program, sending to the BG a copy of each executed command (see dashed arrows in Fig. 1).

2.4. Termination of "go"

When the BG receive a copy of a command that executes toward the end of the syllable "go" (e.g., the command to fully round the lips), they act (based on prior experience) to terminate the syllable by inhibiting the "go" SSM cell (see thick arrow from the BG to the "go" SSM cell in Fig. 1).

3. RESULTS

Computer simulations of the combined models producing "go.di.və" were performed to test mechanisms by which elevated DA levels could lead to stuttering. The first simulation used normal DA levels (β_{D1}=100%), and served as a baseline (Fig. 2). In the second simulation, we raised the parameter for DA tone (β_{D1}=175%), while keeping other parameter values constant (Fig. 3). Before the simulations, the motor programs for the 300 most frequent syllables from the CELEX database were acquired by the DIVA model.

The time course of activity in key cell types of the BG-vPMC loop is shown in Fig. 2(b) and 3(b). Each plotted line shows the activity of a single cell representing a neuron population. The figures include the activity of premotor planning cells, premotor SSM cells, thalamic cells, and putamen cells that express D1 dopamine receptors (D1 cells). The vertical dotted lines mark the baseline initiation time of the syllable "go", and Fig. 2(a) and 3(a) show snapshots of the BG-vPMC loop at that point. The bars in these figures represent cells, with bar height indicating the neural activation level of the cell. Notice that the cells are organized in columns; the cells of each column pertain to control of the syllable indicated above the column. For clarity, the diagrams only include the cells for "go" and "god". The arrows represent projection fibers, or for the arrows from the D1 cells to the thalamus, net effect. Arrow thickness indicates the strength of excitation (arrowhead) or inhibition (circle).

Figure 2 (below): Activities in key cell types of the BG-vPMC loop during fluent production of "go.di.və" with normal dopamine levels. (a) Snapshot at t=585 ms. (b) Time course of activities at the four loop stages shown in (a).

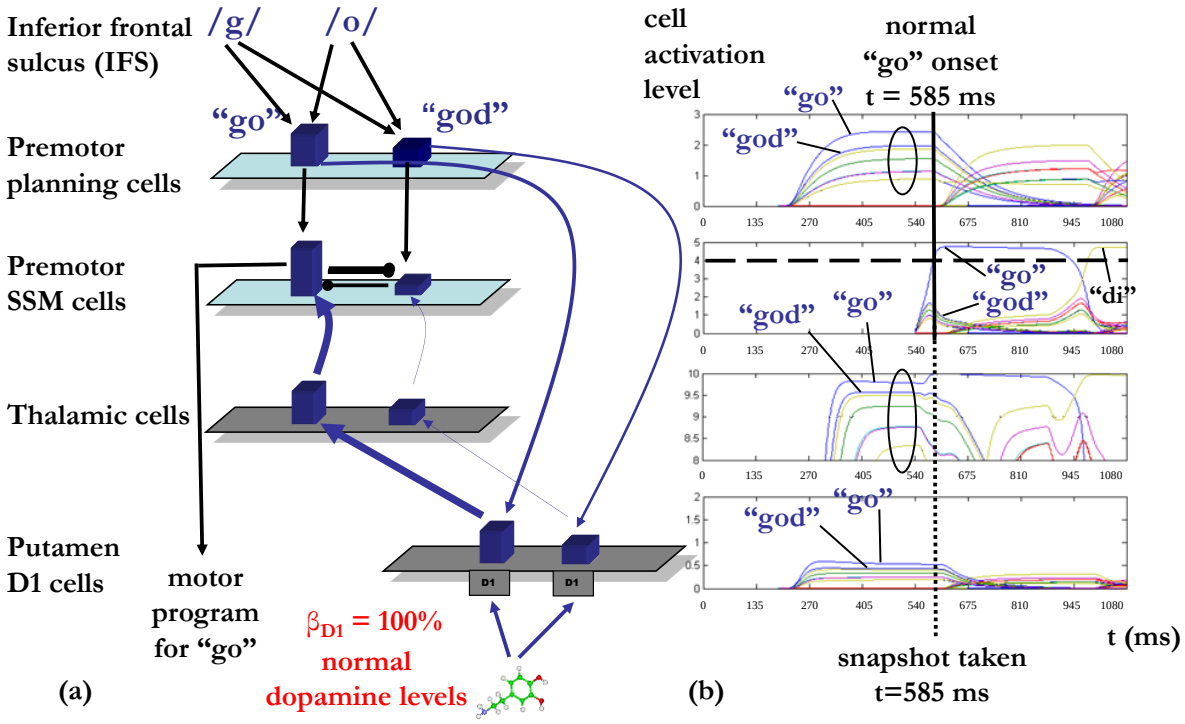
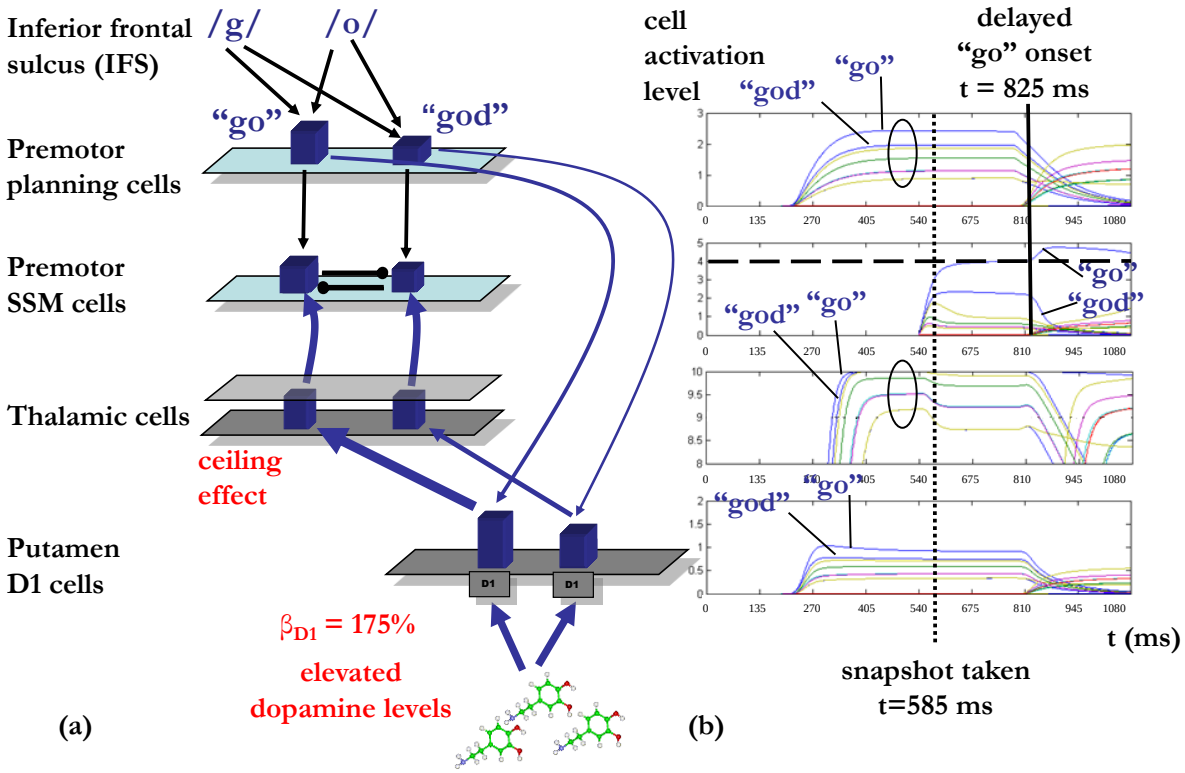


Figure 3 (below): Activities in key cell types of the BG-vPMC loop during dysfluent production of "go.di.və" due to elevated dopamine levels. (a) Snapshot at t=585 ms. (b) Time course of activities at the four loop stages shown in (a).



Next we describe the behavioral outcomes and neural dynamics in each of the two simulations.

3.1. Normal dopamine levels – Fluent Speech

Fig. 2(a) and (b) show results from a simulation of the combined models using normal DA levels. As described in Section 2.2., the BG-vPMC loop facilitates fast selection of the best-matching syllable ("go") by biasing the competition in favor of that syllable's SSM cell. To this end, the D1 cells enhance the contrast of their inputs regarding the phonological match of the competing syllables, exciting the SSM cell for "go" (via the thalamus) much more than the cell for "god". The production of the "go" syllable starts when the activity of the "go" SSM cell exceeds at t=585 ms the threshold marked by the dashed line in Fig. 2(b), row two.

It is vital to note that SSM and D1 cells receive information regarding phonological matching not directly from the IFS, but via premotor planning cells. Each planning cell is activated according to the degree of phonological match between its corresponding syllable and the IFS's phonological sequence representation. For fluent production, the activation level differences among planning cells must be correctly registered at the thalamic stage of the GODIVA model (see ellipses in Fig. 2(b)).

3.2. Dopamine excess – Dysfluent speech

Fig. 3(a) and (b) show results from a simulation of the combined models using elevated DA levels. In contrast to the simulation using normal DA levels, the production of "go" starts too late (the SSM cell for "go" exceeds threshold only at t=825 ms). The behavioral correlate is a prolonged initial articulatory position, adding 240 ms to word onset.

The reason for the dysfluency is that the active D1 cells are over-excited due to DA excess. Downstream, this enables the activation of the thalamic cell for the desired syllable ("go") to reach its highest possible level. However, the same occurs for cells of similar syllables (e.g., "god"). If the competing activations are regarded as noise, this situation amounts to strong compression of the signal-to-noise ratio at thalamus, relative to the ratio among premotor planning cells (see ellipses in Fig. 3(b)). The "go" thalamic cell still receives stronger net excitation than its competitors, but its activation cannot rise above theirs; hence, a ceiling effect. Although the SSM cell for "go" retains a competitive advantage, without normal assistance from BG-thalamus it needs more time to overcome the other SSM cells and to eventually exceed the activation threshold (marked by the dashed line). Thus, selection of the syllable "go" is delayed.

4. CONCLUSIONS

Simulations of the GODIVA and DIVA models show that elevated dopamine levels can account for stuttering. Abnormal excitation of putamen neurons that express D1 dopamine receptors leads to over-excitation of the thalamus and a ceiling effect (cf. [1]). As a result, the basal ganglia – thalamus – left ventral premotor cortex loop cannot facilitate fast competitive selection of the next syllable's motor program, and dysfluency occurs. In support of the models' prediction, an imaging study of stuttering showed that thalamic activity is positively correlated with dysfluency [3].

5. ACKNOWLEDGMENTS

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