

Higher Striatal GABA Relates To A More Serial And Efficient Mode Of Action Cascading And Stronger Attentional Gating In Airplane Pilots

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Purpose: Action cascading is necessary when faced with multiple response options. The mechanism of action cascading may be either serial or parallel¹. Certain professions, like being an airplane pilot, place a demand on the neuronal systems for faster response times in action cascading. The basal ganglia and GABAergic striatal medium spiny neurons (MSNs) play an important role in the selection and coordination between different actions². To better understand the neuronal mechanisms governing action control and mediating superior performance above the normal level, striatal GABAergic neural transmission was examined using gamma-aminobutyric acid (GABA) MRS in airplane pilot trainees (APTs) and controls.

Methods: 20 APTs (age: 23.18±1.97 y) and 18 controls (age 24.94±2.82 y) were recruited. All subjects underwent single voxel MRS on a 3 T Philips Achieva scanner. MEGA-PRESS³ GABA (TE/TR=68/2000 ms, 256 averages) spectra were acquired from 30×30×25 mm³ volumes of interest (VOIs) placed in the left and right striatum (fig. 1). A reference scan without water suppression was acquired for frequency and phase correction. LCModel (v6.2-0R) was used for MRS quantification. Additionally, a stop-change (SC) paradigm¹ was implemented and behavioral and electroencephalography (EEG) data were collected. During the task the subjects had to provide simple responses as fast as possible. On some trials,

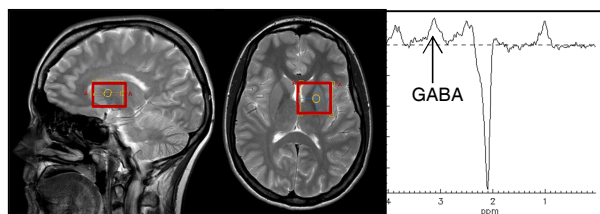


Figure 1. Representative left striatum VOI and GABA spectrum.

movement execution was interrupted by a Stop stimulus, which was followed by a stimulus signaling to change to an alternative response. In half of these trials, there was a stop-change delay (SCD) with a stimulus onset asynchrony (SOA) of 300 ms between the STOP and the CHANGE signal (“SCD300” condition), while in the other half of the SC trials, the two stimuli were presented simultaneously (SOA of 0 ms, “SCD0” condition). This data was analyzed along mathematical constraints to classify subjects as a “serial mode group” and a “parallel mode group” of action cascading and integrated with GABA levels measured using MRS. The degree of overlap between the stop and change processes was estimated by calculating the slope of the SOA-reaction times (RTs) function, that is, the function that describes how the RT on the change stimulus varies depending on the delay between SC stimuli. The event related potentials (ERPs) selected were visual P1 and N1, auditory N1 and P3 and were quantified in a peak-to-baseline manner. To integrate the model-based behavioral and electrophysiological data with the MRS data, a regression was done on the slope of the SCD-RT2 function or the amplitude of the auditory P1 in the SCD0 condition and striatal GABA/tCr ratio for both groups.

Results and Discussion: The regression model was significant ($F(2,35) = 12.38$; $p < .001$) for the slope of the SCD-RT2 function and both, GABA/tCr ($\beta = 0.47$; $t = 3.62$; $p = 0.001$) and the factor group were significant ($\beta = 0.49$; $t = 3.76$; $p = 0.001$). A correlation was present between SCT-RT2 and GABA/tCr in APTs ($r = 0.74$; $R^2 = 0.53$; $p < 0.001$) as well as controls ($r = 0.44$; $R^2 = 0.17$; $p = 0.02$). However, the slope of the regression line relating SCD-RT2 with GABA/tCr was steeper in APTs than in controls (Fig. 2), showing that similar increases in GABA/tCr have stronger effects in APTs than in controls. The regression model was also significant for the amplitude of the auditory P1 in the SCD0 condition ($F(2,35) = 25.46$; $p < 0.001$) and both, GABA/tCr ($\beta = 0.38$; $t = 3.48$; $p = 0.001$) and the factor group were significant ($\beta = 0.71$; $t = 6.54$; $p < .001$). A correlation was present between SCT-RT2 and GABA/tCr in APTs ($r = 0.59$; $R^2 = 0.33$; $p = 0.003$), as well as in controls ($r = 0.49$; $R^2 = 0.23$; $p = 0.02$). However, the behavioral data revealed a flatter slope of the SCD-RT2 function, suggesting for a more serial mode action cascading in APTs compared to controls.

Conclusion: Similar increases in GABA-levels led to stronger effects in APTs compared to controls, which suggests that the neurobiochemical-electrophysiological coupling is stronger in APTs than in controls, leading to superior action control in situations requiring a cascading of actions. The results indicate that higher striatal GABA concentrations relate to a more serial and efficient mode of action cascading and stronger attention gating.

References: 1. Mückschel M, Stock A, Beste C. Psychophysiological Mechanisms of Interindividual Differences in Goal Activation Modes During Action Cascading. *Cereb. Cortex* doi: 10.1093/cercor/bht066 2013; 2.Bar-Gad I, Heimer G, Ritov Y, Bergman H. Functional correlations between neighboring neurons in the primate globus pallidus are weak or nonexistent. *J Neurosci.* 2003 May 15;23(10):4012-6; 3. Mescher M, Merkle H, Kirsch J, et al. Simultaneous in vivo spectral editing and water suppression. *NMR in Biomedicine* 1998;11(6):266-272

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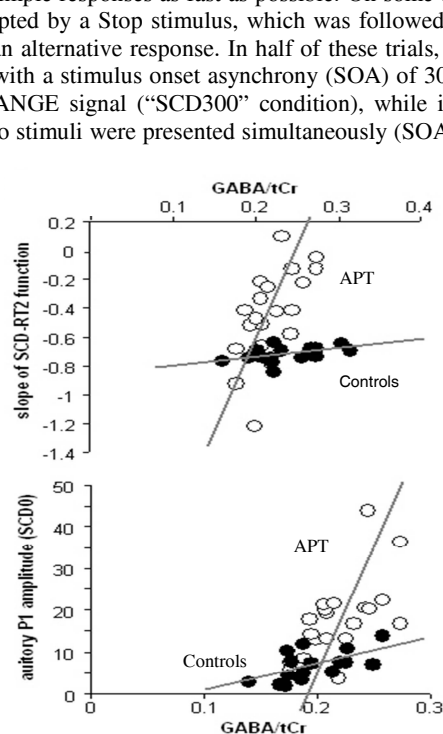


Figure 2. Regression analysis of GABA/tCr with slope of SCD-RT2 function (top) and amplitude of auditory P1 in the SCD0 condition (bottom).