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Motor system GABAergic tonic inhibition early after stroke - a pilot study

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Objectives: Stroke triggers a complex series of neurobiological events that leads to acute functional impairment and, over a longer time-frame, results in the specific functional outcome and complications for individual patients. One such event is the cortical tonic γ-aminobutyric acid (GABA) inhibition dysfunction, i.e., enhanced tonic inhibition. On a physiological level, reversing such overactivation may improve functional outcome, e.g., arm motor function. The current knowledge is derived largely from preclinical studies. We aimed to study here the GABAergic inhibition changes and their functional relevance at admission to rehabilitation in stroke survivors exhibiting arm motor impairment (n=3).

Design: Survivors of a single subcortical infarct (66.3 [10.1] years old, 2 males) with mild clinical impairment (NIHSS=6 for all) were recruited at 22.2 [2.0] days after acute event. GABAergic inhibition was measured via MR Spectroscopy (MEGA-sLASER) in 2 motor areas controlling the paretic arm function: motor (M1) and premotor (PM) cortices in injured (ipsilesional) and uninjured (contralesional) hemispheres. GABA levels in each area were compared to those in matched healthy controls (n=3). Patient recruitment ended in March 2020 due to COVID-19.

Results: Relative to controls, we found in patients a trend toward higher GABA levels across all areas, most prominent in the ipsilesional areas (ipsilesional vs. left hemisphere in controls: M1, p=0.2, PM, p=0.08; contralesional vs. right, M1, p=0.6, PM, p=0.2). Due to the small sample size and similar impairment, the relationships between GABA levels and hand impairment were not assessed.

Conclusions: Our preliminary data have shown there is a trend toward increased tonic GABAergic inhibition early after stroke. If this trend is further demonstrated in larger sample size, this knowledge will provide evidence of a robust biological substrate, possibly underlying early motor recovery, offering the basis for conducting clinical trials for mechanistic restorative therapies in this population.