Quadripulse stimulation (QPS): a new protocol for plasticity induction in humans
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I will introduce a new protocol of transcranial magnetic stimulation (TMS) for plasticity induction in human brain.

What's QPS?
There are several stimulation methods to induce plastic changes in human brain. QPS must be most powerful and reliable one for human plasticity induction. One stimulation burst consisting of four monophasic pulses is given every five seconds for 30 minutes. It finally gives 360 bursts (1440 pulses) in one session. After QPS the stimulated cortical area excitability is bidirectionally modulated depending on the interval of magnetic pulses in one burst. Short interval QPS potentiates the excitability and longer interval QPS depressed the target area. QPS at interval of 5ms (QPS5) induces LTP most efficiently and QPS50 LTD most effectively in the human primary motor cortex (M1). Their physiological characteristics, bidirectional modulation, dependence on the interval of pulses, spatial specificity are all compatible with the plasticity reported previously. We conclude that QPS is able to induce neuronal plasticity in human brain.

Mechanisms underlying QPS
To elucidate mechanisms for QPS, we compared several physiological features between baseline (before QPS) and after QPS. No changes were found in the threshold, GABAergic function of M1, Acetylcholine function. In contrast, EPSP summation and sharpness of IO curve are bidirectionally modulated by QPS. These indicate that excitatory synaptic efficacy is bidirectionally modulated by QPS. The effect is specific to the activated neurons. These all are consistent with synaptic LTP/TLD.

Meta-plasticity of QPS
To overcome some exaggerated plasticity, meta-plasticity (plasticity of plasticity) regulates plastic changes. Namely, some weak priming stimulation given before the main plasticity induction stimulation weakens the main effect to get rid of abnormally enhanced plasticity. We studied metaplasticity in QPS by comparing the amount of effect between usual QPS and QPS primed by some short duration QPS. We demonstrated that priming stimulation modulated the conventional QPS effects to a stable direction. In addition to homotopic metaplasticity (M1 to M1), priming stimulation over supplemental motor area (SMA) has also metaplastic influence on M1 plasticity (heterotopic plasticity). These all are consistent with classical knowledge.

Dopamine and plasticity
It is well known that dopamine enhances both LTP and LTD, and the former is one of D1 effects and the latter is a kind of D2 effects. To study the relation between dopamine and QPS, we compared LTP/LTD effect between baseline condition and the condition after L-Dopa intake in normal volunteers. Dopamine enhanced both LTP of QPS5 and LTD of QPS50. It is again compatible with plasticity induction in animals.

QPS stimulation steadily induces LTP and LTD like effects in human brain.

References
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Key words
Transcranial magnetic stimulation (TMS), synaptic plasticity, primary motor cortex