Has the Brain-Derived Neurotrophic Factor a role in influencing rhythm-dependent metaplasticity of the human primary motor cortex? A tACS-TBS study

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Introduzione

The Val66Met polymorphism in the brain derived neurotrophic factor (BDNF) has been suggested to influence memory and learning. However, its possible role in modulating long-term potentiation (LTP)/depression (LTD)-like plasticity and metaplasticity in the human primary motor cortex (M1) is highly controversial. We have recently demonstrated that theta burst stimulation (TBS)-induced LTP/LTD-like plasticity of M1 can be modulated by transcranial alternating current stimulation (tACS) at γ frequency, with mechanisms of rhythm-dependent metaplasticity. The aim of this study is to assess the effect of the Val66Met BDNF polymorphism on this specific form of metaplasticity.

Metodi

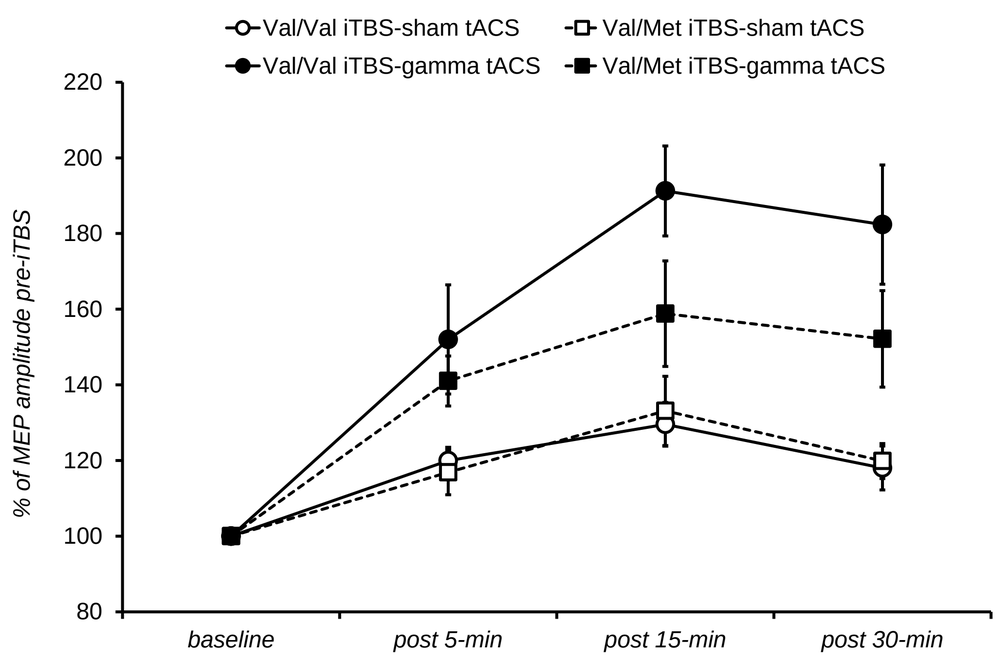
TMS was performed by MAGSTIM 200 and a figure-of-eight coil delivering monophasic magnetic pulses while intermittent (iTBS) and continuous TBS (cTBS) protocols were delivered by a biphasic magnetic stimulator (Magstim SuperRapid). tACS was delivered through conductive electrodes enclosed in saline-soaked sponges (BrainSTIM, EMS). Genotyping of the Val66Met polymorphism was performed by Sanger sequencing on DNA samples isolated from whole blood. Thirty-seven healthy subjects (18 Val66Met, 19 Val66Val carriers) participated. In a first study, a subgroup of 28 subjects (13 Val66Met carriers) underwent two randomized experimental sessions: i) iTBS delivered during γ-tACS (iTBS-γ); ii) iTBS delivered during sham-tACS (iTBS-sham). In a second study, a subgroup of 26 subjects (13 Val66Met carriers) underwent cTBS delivered during γ-tACS (cTBS-γ) and cTBS during sham-tACS (cTBS-sham). In all sessions, motor evoked potentials (MEPs) elicited by single-pulse TMS were recorded before (T0) and 5 (T1), 15 (T2) and 30 (T3) minutes after the intervention.

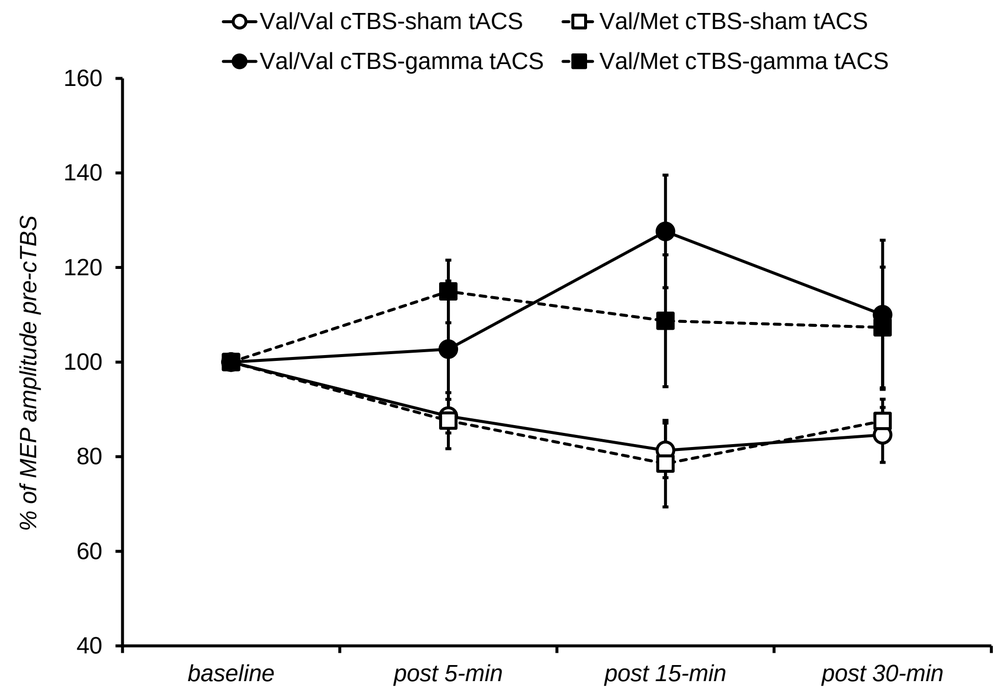
Risultati

iTBS-sham and cTBS-sham produced a significant MEPs facilitation and inhibition over time (T1-T3), respectively. No differences in MEPs changes emerged when comparing Val66Val and Val66Met carriers, both in iTBS-sham and cTBS-sham. As expected, iTBS-γ induced higher MEPs facilitation than iTBS-sham at T1-T3, whereas cTBS-γ reversed the MEPs inhibition observed in cTBS-sham into a facilitation. However, the effects produced by the combined TBS-γ-tACS stimulations were comparable in Val66Met and Val66Val carriers.

Conclusioni

We confirm that γ-tACS boosts the iTBS-induced LTP-like plasticity and reverses the cTBS-induced LTD-like plasticity of M1, as a result of rhythm-dependent metaplasticity. Our data demonstrate no influence of Val66Met BDNF polymorphism on both LTP-like and LTD-like plasticity of M1. Also, Val66Met BDNF polymorphism does not exert any relevant effect on rhythm-dependent metaplasticity phenomena. Our findings support recent studies suggesting that the Val66Met BDNF polymorphism has no significant role in influencing the LTP/LTD-like plasticity and metaplasticity mechanisms of M1.





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