

# [Psychiatry] Antidepressant Efficacy of Intermittent Theta-Burst Stimulation is Similar to Low-Dose Ketamine & Mechanisms Involve BDNF

## Theta波叢集式磁刺激(TBS)的抗鬱療效近似於低劑量K他命且機轉牽涉BDNF

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### Introduction:

1. Major depressive disorder (MDD) is a chronic and deteriorating illness.
2. A great number of patients with MDD who do not improve appreciably despite of the sufficient medication trials are defined as medication-resistant depression, which is associated with poor clinical and psychosocial outcomes.
3. **Theta-burst stimulation (TBS)** is a new form of **repetitive transcranial magnetic stimulation (rTMS)** that is an effective method in treating treatment-resistant depression (TRD)
4. **Our previous study** reported that **prolonged intermittent TBS (iTBS) for 10 sessions (2 weeks)** is **effective** for medication-resistant depression (Li et al., Brain, 2014).
5. **Treatment guideline** suggests the duration of rTMS or iTBS treatment is **at least 20 sessions (CANMAT2016)**.
6. Low-dose ketamine is also approved to be effective for treating TRD.
7. However, there is **no randomized controlled trial (RCT)** investigating
  - (1) the comparative effectiveness between the prolonged iTBS monotherapy and **high-frequency (10Hz) rTMS** for TRD.
  - (2) the effectiveness between **iTBS, 10-Hz rTMS** and **low-dose ketamine** for TRD.
  - (3) the antidepressant efficacy and mechanisms of **“standard-dose (20 sessions)” iTBS** and rTMS for TRD.

### Materials and Methods:

1. A RCT of iTBS vs 10-Hz rTMS vs. sham (10 sessions/2 weeks) for 21-70 y/o MDD patients with poor response to at least one antidepressant trial in the current episode and at least Hamilton Depression Rating Scale (HDRS-17)  $\geq 18$  (n=105)
2. Comparing antidepressant effects between the above RCT and a RCT using low-dose ketamine (0.5 mg/day) vs. normal saline for TRD (n=72)
3. A RCT of iTBS vs 10-Hz rTMS vs. sham (20 sessions/2 weeks) for TRD with poor response to  $\geq 2$  antidepressant trials in the current episode and at least HDRS-17  $\geq 18$  (n=56)
4. EEG, MRI, and 18F FDG PET would be applied for investigating central mechanisms of iTBS. (study in still in process)

### Results & Figures

Fig 1. Results for iTBS vs. rTMS vs. sham (10 sessions/2 weeks)

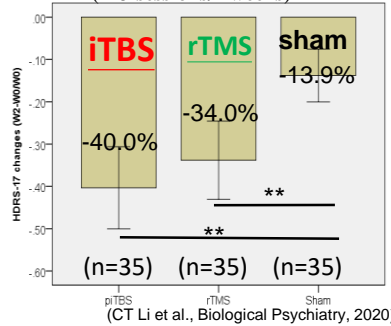
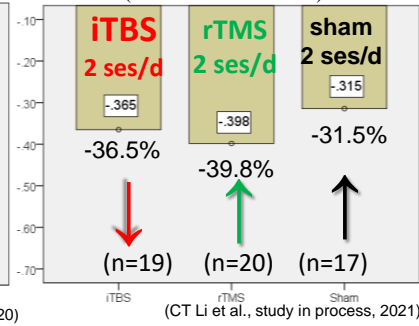


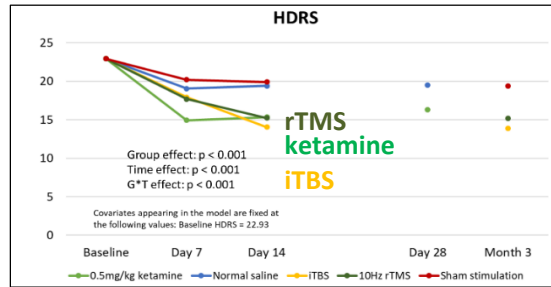
Fig 2. Results for iTBS vs. rTMS vs. sham (20 sessions/2 weeks)



#### Results:

1. iTBS and rTMS are more effective than sham for MDD (Fig. 1)
2. iTBS (2 sessions/d) is not better than iTBS (1 session/d), while rTMS and sham seems to be better effects when double doses were applied per session, as shown by preliminary data (Fig. 3).

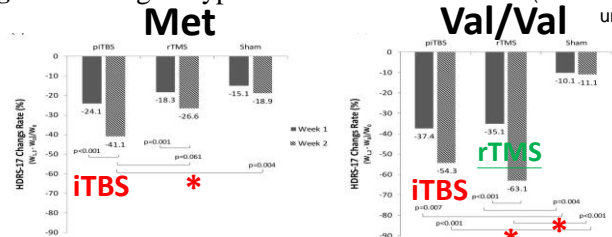
Fig 3. Left-prefrontal iTBS (yellow line) and rTMS (green line) were not inferior to low-dose ketamine (light green line) for treating TRD



Results: iTBS, rTMS and ketamine are effective, but ketamine is faster, effective in 1<sup>st</sup> week

(MH Chen and CT Li et al., under review, 2021)

Fig 4. BDNF genotypes & iTBS/rTMS effects (CM Cheng and CT Li et al., under review, 2021)



- Results: In Va/Val homozygote, iTBS and rTMS both exhibited significantly greater %HDRS reduction than sham at week-2, while in Met carriers, only piTBS showed better efficacy

### Conclusions:

1. Left prefrontal iTBS is effective in treating TRD and is not inferior to 10-Hz rTMS and low-dose ketamine.
2. iTBS seems to have NO dose-dependent effects and consistent antidepressant efficacy regardless of BDNF polymorphism

### References:

1. Li CT et al. Antidepressant Efficacy of Prolonged Intermittent Theta Burst Stimulation Monotherapy for Recurrent Depression and Comparison of Methods for Coil Positioning: A Randomized, Double-Blind, Sham-Controlled Study. Biological Psychiatry. 2020.