Introducing the novel combination therapy of TMS with ketamine (CTK) for treatment-resistant depression: A long-term, retrospective review of clinical use

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Key Points:

- **CTK:** A novel combination therapy of Transcranial Magnetic Stimulation (TMS) administered simultaneously with intravenous ketamine (CTK)
- **The retrospective review:** CTK therapy was used for 28 patients with Treatment-Resistant Depression.
- **Statistically significant improvement:** Reduction in CGI-S for all patients following CTK therapy.
  CGI-S reduced from 5.7 to 1.7 (σ=0.8).
- **Long-term remission:** CGI-S remained at same reduced level for over 2 years post-treatment.
- **Improved regional brain perfusion** observed using SPECT imaging following CTK therapy (in cases where applied).
- **Advantages**:
  - Successful long-term outcomes, where other treatments failed.
  - Higher intensities of TMS were achievable due to moderate anesthesia resulting from the ketamine infusion
  - Lower doses of ketamine and fewer TMS sessions required vs. monotherapy.
  - Fewer side-effects and improved treatment adherence

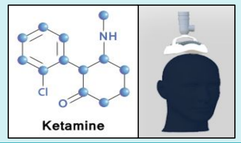
1. The Problem:

- Treatment-resistant neuropsychiatric conditions
- Putatively related to a thalamocortical dysrhythmia
- Abnormal function of the anterior cingulate cortex (ACC) and remaining limbic system
- Ketamine and TMS recognized treatments for MDD, but typically short-term relief for patients

2. The Hypothesis:

Combination Therapy of TMS & Ketamine (CTK)

TMS temporarily interferes with pathologic synchronisation of ACC function, while **ketamine** affects neurotransmission.

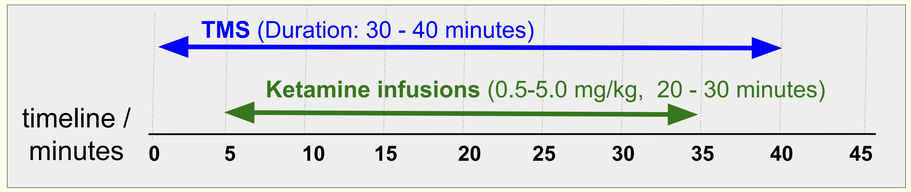


→ Higher intensities of TMS achievable due to moderate anesthesia resulting from the ketamine infusion
→ Enhanced response to treatment vs monotherapy
→ Synergistic effect that improves normal function

3. The Study:

Patients: 28 TRD patients
CGI-Severity measured for all patients at times:
T1: Pre-treatment
T2: Post-treatment
T3: 2 years following treatment
Brain SPECT Imaging measured in some cases

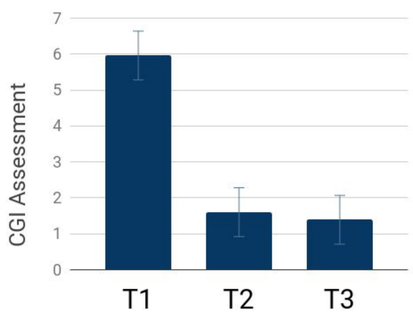
4. The CTK Therapy:



Dosing: Gradually titrated upward until patient enters mildly cataleptic state
Frequency: Illness severity dependent. Start with 3 sessions / week before tapering
Mild cases: 10-20 sessions Severe cases:~30 sessions

Pre-Treatment:
Depending on illness severity, patients may undergo pre-treatment of TMS alone:
- 3-14 days
- 3 sessions daily

Clinical Global Impression (CGI)



- Following CTK therapy mean CGI-S reduced from 5.7 to 1.7 (σ = 0.8)
- This reduction in CGI-S was sustained for 2 more years following CTK therapy completion.

Fig. 1: Mean CGI-Severity score of sample group (N=28) at different times. T1 = Pre-Treatment, T2 = Post-Treatment T3 = 2 years following treatment completion. Bars represent standard deviation.

Example of SPECT Imaging of Brain

- Single Photon Emission Computed Tomography
- Depicts regional cerebral perfusion

Pre - CTK Therapy

5 months Post - CTK therapy

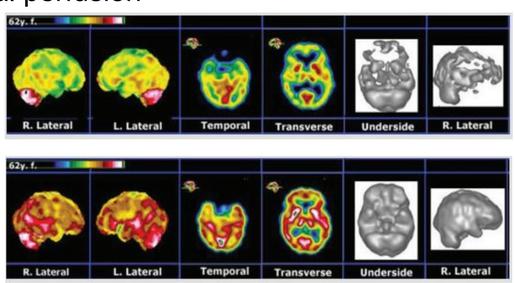


Fig. 2: SPECT brain images before and after CTK therapy. Five months after CTK therapy (30 sessions) a marked improvement in perfusion across all cortical and subcortical structures. This corresponded to a dramatic clinical improvement sustained at 3-year follow up.

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