

Update on Theta burst TMS June 2013

Theta waves and Theta Burst historically

Theta waves have been known and studied since the late 1970ties where Theta waves were studied in rodents and humans using EEG. The use of Theta Burst (a form of patterned rTMS) has not gained widespread use until recent years with continuous and intermittent TBS being defined in 2005. TBS refers to rTMS protocols where pulses are applied in bursts of three. The bursts are typically delivered at a frequency of 50 Hz (inter-PULSE interval=20ms), with an inter-BURST interval of 200 ms (Burst frequency=5 Hz); a presentation largely based on the limitations inherent in the first available devices on the market that were capable of delivering TBS. These parameters were originally developed after studies in both the rodent and human brain indicated that theta rhythms are associated with long term potentiation¹.

MagVenture X100 instrumentation

MagVenture X100 stimulators are able to vary the Theta Burst considerably compared to the above mentioned treatment regime. X100 can deliver up to 5 burst pulses with a biphasic burst inter pulse interval down to 0.5 ms.

Theta Burst patterns

There are two commonly used patterns of TBS, continuous (cTBS) which is inhibitory, and intermittent (iTBS) which is excitatory. cTBS consists of bursts of 3 pulses at 50 Hz (sometimes modified to 30Hz) applied at a frequency of 5 Hz for either 20 seconds (100 bursts) or 40 seconds (200 bursts). In iTBS, 2 second trains of bursts (10 bursts) of TBS are delivered with an inter train interval of 8 seconds between each train. Trains are typically repeated twenty times, for a total of 600 pulses per treatment.

Safety of Theta Burst

Use of Theta Burst TMS in the year span from 2004 – 2009 have been reviewed with emphasis put on safety and adverse events induced by TBS¹. In short TBS has been deemed to be as safe as, or safer than conventional rTMS as TBS employs fewer stimuli per treatment, see figure 1.

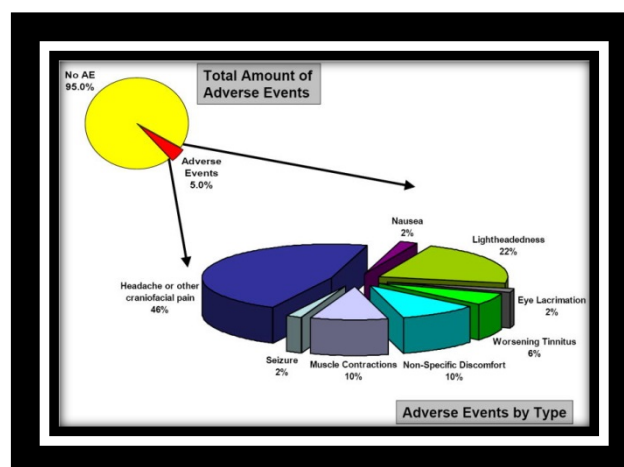


Figure 1. Adverse events in TBS. From ¹Oberman et al. 2012

Treatment regimens and study distribution

Currently there are two schools in TBS treatment, one doing the traditional triple stimuli @ 50Hz and the other doing a modified version employing triple stimuli @ 30Hz. Looking at TBS studies from 2012-2013, the majority of studies conducted with MagPro devices have employed the 30Hz protocol. (NOTE**** there is a tendency towards European researchers using the 30Hz TBS protocols, whereas in the US we do not see anyone suggesting that TBS should be delivered with bursts at 30Hz, but always defined as 50Hz bursts). Published studies from the last two years are as follows:

- MagPro
 - 2 x Auditory hallucinations, triple pulse @30Hz
 - Spatial neglect, triple pulse @ 30Hz &
 - 2 x Aphasia, triple pulse @ 30Hz/50Hz
- Competitor (all triple pulse @ 50Hz)
 - 2 x Tinnitus
 - 2 x spatial awareness
 - 1 x lazy eye
 - 1 x ALS (new treatment but no real result)
 - 1 x Rehab after stroke

Auditory hallucinations

In recent years cTBS has been used by MagPro users for treatment of auditory hallucinations in schizophrenia with effects similar to those seen with 1Hz conventional TMS treatments. TBS has been found to be as safe as conventional rTMS for treatment of auditory hallucinations with stimulation over left temporal cortex^{2,3}.

Rehabilitation after stroke

TBS studies have been conducted with various deficiencies in stroke patients as possible treatments to speed rehabilitation after stroke. cTBS/iTBS appears to be promising as a treatment regime for aphasia and improvement in naming, and speech repetition accuracy have been noted after experimental treatment of aphasic stroke patients with TBS. Treatment stimulation was located to either the inferior frontal gyrus in the left hemisphere or to the right Broca's homologue^{4,5}. Spatial neglect is another area where post stroke treatment with TBS has shown promising results. Results indicate that continuous TBS may accelerate the recovery from spatial neglect after stroke. Stimulation was located to the posterior parietal cortex^{6,12}. Another study focused on post stroke plasticity and studied effects of intermittent TBS to patients in subacute ischemic stroke patients. This smaller pilot study showed iTBS to have positive effects in the areas of post stroke plasticity and recovery when stimulation was applied over ipsilesional primary motor cortex⁹.

Traumatic Brain Injury

A case study of a younger male with Traumatic Brain Injury suggests clinical efficacy of cTBS as a treatment to improve symptoms of neglect. Considerable improvements were seen in Behavioral Inattention Test (BIT) after only 2 weeks of cTBS, stimulation was applied over the left posterior parietal cortex⁷.

Lazy eye

A smaller study treating patients having Amblyopia (lazy eye) with cTBS over the visual cortex, have shown promising results. Contrast sensitivity improvements were noted to last more than 78 days after only 5 sessions of cTBS over the visual cortex⁸.

Amyotrophic Lateral Sclerosis

cTBS has been employed for the treatment of the neurodegenerative disease Amyotrophic Lateral Sclerosis (ALS). After 5 daily treatments for 5 days, the study concludes that cTBS treatments have a cumulative depressive effect on corticospinal excitability and that repetitive sessions are needed to maintain the effect in patients. Stimulation was applied to abductor pollicis brevis¹⁰.

Tinnitus

Continuous TBS has been used for treatment of tinnitus with mixed results. One study suggests that cTBS offers a method for modulation of tinnitus where patients can benefit from emotional improvements when stimulation is applied over the auditory cortex¹³. Another study concludes that cTBS is safe when applied to either temporal or temporoparietal cortex, but that this treatment is only as effective as sham treatment¹¹.

Depression

Currently there are studies underway employing Theta Burst for the treatment of depression. Especially interesting are two studies undertaken in Germany by highly skilled depression treatment centers. One study looks at the effects of long-term bilateral Theta Burst stimulation (NCT01153139) applying bilateral TBS to the dorsolateral frontal cortex, and the other study investigating the effectiveness of Theta Burst treatment (NCT01240083) applying stimulation over the dorsolateral prefrontal cortex.

Abbreviations:

ALS	Amyotrophic Lateral Sclerosis
BIT	Behavioral Inattention Test
cTBS	continuous Theta Burst Stimulation
iTBS	intermittent Theta Burst Stimulation
rTMS	repetitive Transcranial Magnetic Stimulation

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