TRANSCRANEAL PULSE STIMULATION FOR THE TREATMENT OF MILD COGNITIVE IMPAIRMENT AND EARLY ALZHEIMER'S DISEASE

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Brain stimulation techniques based on the delivery of transcranial shockwaves are a novel tool for treating patients with cognitive impairment with increasing popularity. It is an interesting approach to modulate the human brain in a focal and targeted manner.

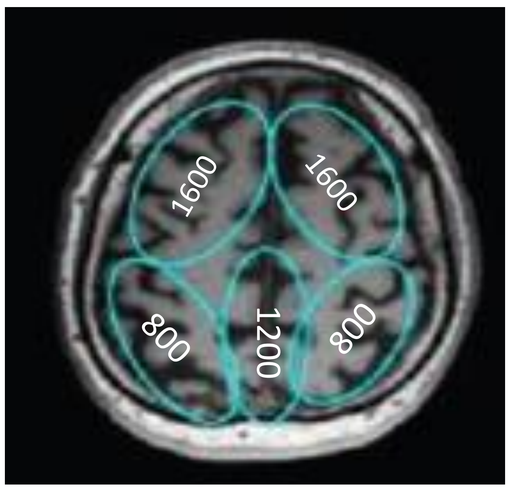
Transcraneal pulse stimulation (TPS) is based on single ultrashort ultrasound pulses that can stimulate up to 8cm into the brain, reaching deep brain structures. With short duration and low frecuency pulses we are able to stimulate the brain without heating risk.

TPS has the following demonstrated <u>biological effects</u>:

- Blood-brain barrier opening
- Increased serotonin and dopamin, BDNF and VEGF and NO.
- Reduction of GABA levels
- Pore formation, transendothelial openings, better molecules passing-through
- Microglia activation and Amyloid Beta plaque reduction

Here we present our experience with TPS. We share our results regarding **16 patients** with mild or moderate Alzheimers Disease (AD) treated with **Neurolith®**.

All patients received 6000 pulses/session: 1600 pulses in both frontal areas, 800 pulses on each parietal area and 1200 pulses on the precunean area (short pulses of 3 microseconds, 0.2-0.3 mJ/mm3). The session duration is 25 minutes. Subjects received 6 sessions delivered over 2 weeks on alternate days, and a reinforcement session was administrated 10 weeks after the initiation of the treatment.



All patients underwent a cognitive evaluation pre and post treatment. The time elapsed between pre- and post-treatment assessments was **three months**.

From a total of 16 patients treated, we have been able to verify during the follow-up that TPS produces not only a **stabilization of the clinical profile of our patients**, but also results show an overall cognitive improvement three months after treatment with TPS ($p<0.05$). There is also a significant **improvement in both temporal orientation** ($p<0.05$) **and immediate story recall** ($p<0.05$). No significant side effects were observed.

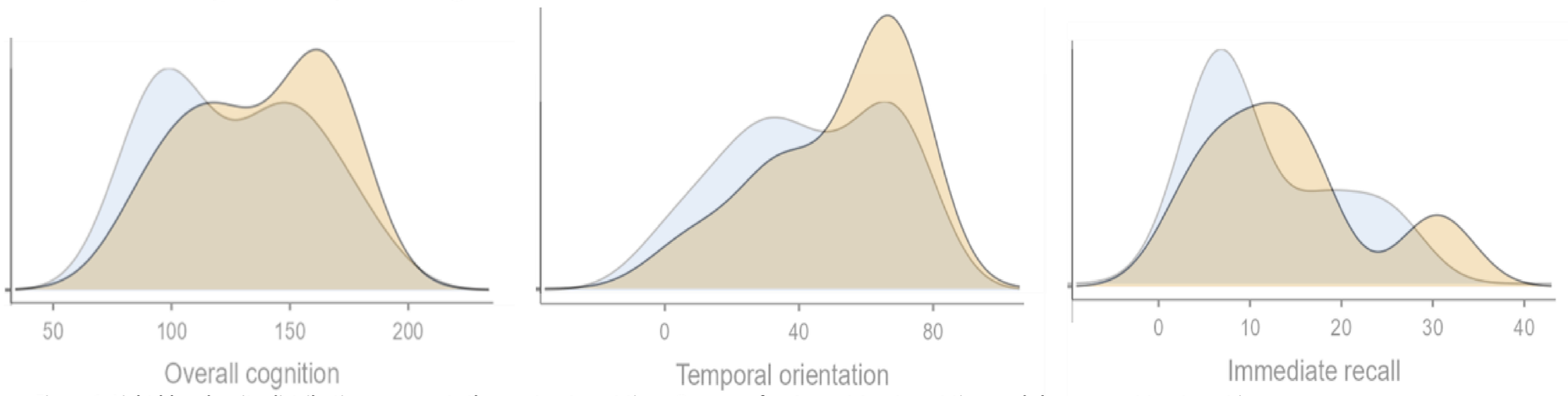


Figure 1. Light blue density distribution represents the pre-treatment time. Orange refers to post-treatment time and shows a post treatment increase.

Table 1. Cognitive results after TPS intervention.

	Pre-treatment		Post-treatment		W	p
	Median	IQR	Median	IQR		
Orientation: temporal	42.00	44.75	62.00	35.00	10.00	0.023
Immediate recall	8.00	10.50	14.00	8.50	13.00	0.040
OVERAL COGNITION	124.50	51.00	141.50	47.00	10.50	0.046

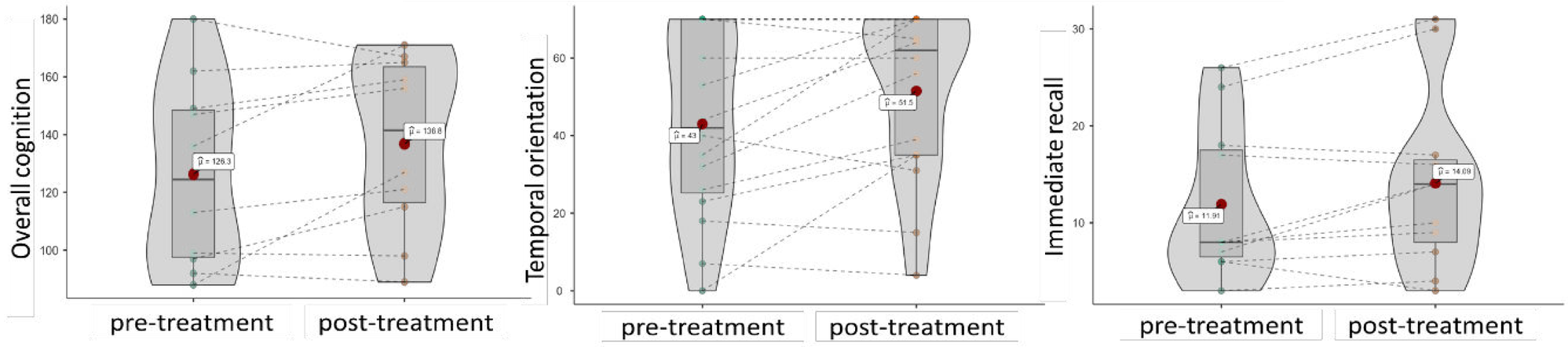


Figure 2. Each line represents a patient. Red dot representes mean value and shows an improvement post-treatment.

<u>Treatment with TPS produces significant improvements in overall cognition, temporal orientation and immediate recall</u>. We can conclude that TPS is an excellent and safe therapeutic option for AD that accompanies currently available treatments and complements them, helping to maintain **greater stability of the disease and slowing its progression**.

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