

# Long-term real world data on Transcranial Pulse Stimulation in Alzheimer's patients



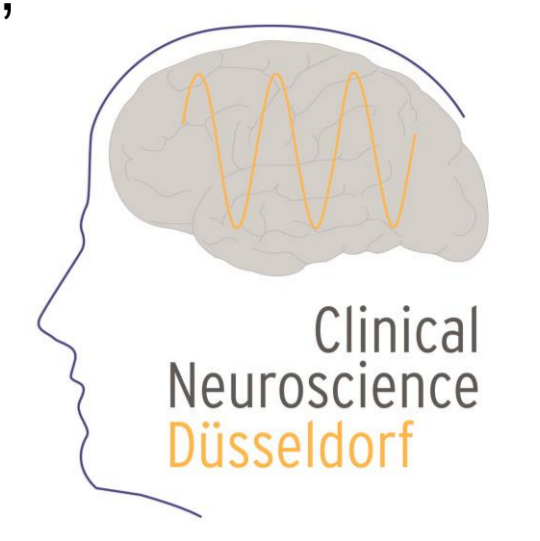
Celine Cont<sup>1,2</sup>, Jessica Schirmeisen<sup>1</sup>, Nathalie Stute<sup>1</sup>, Anastasia Galli<sup>1</sup>, Christina Schulte<sup>1</sup>, Kazimierz Logmin<sup>1</sup>, Lars Wojtecki<sup>1,2</sup>



<sup>1</sup>Clinic for Neurology and Neurorehabilitation, Hospital zum Heiligen Geist, Academic Teaching Hospital of the Heinrich-Heine-University Duesseldorf, Kempen, Germany



<sup>2</sup>Institute of Clinical Neuroscience and Medical Psychology, Medical Faculty, Heinrich-Heine-University Düsseldorf, Germany

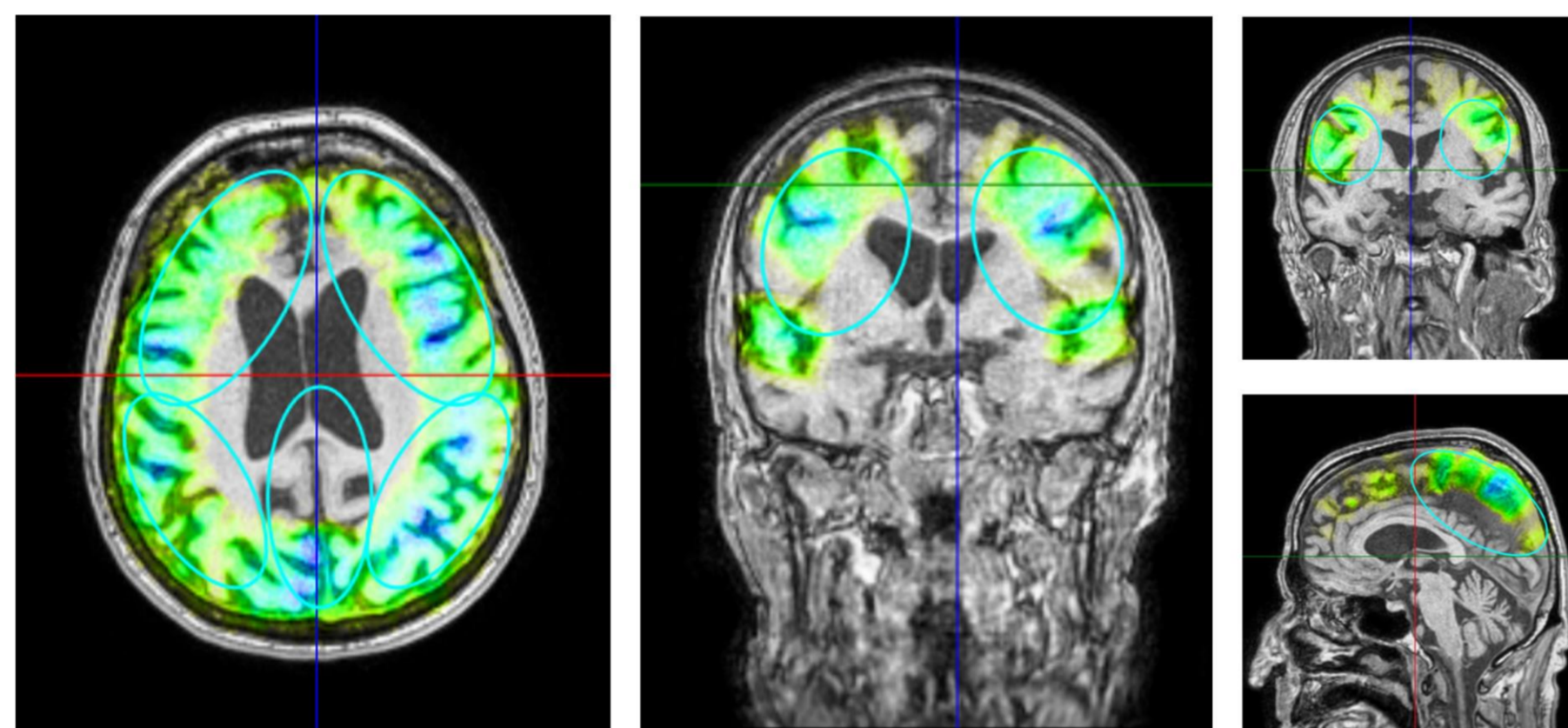


## Introduction

Transcranial Pulse Stimulation (TPS) is a new non-invasive neuromodulation therapy that uses shockwaves for the treatment of Alzheimer's Disease (AD). Recently, our group published short term clinical results after the first treatment cycle of 2 weeks (Cont et al., 2022). We found a significant improvement in the Alzheimer Disease Assessment Scale (ADAS) and in affective scores. Yet, no long-term results have been reported. Here we show first results after one stimulation cycle, 3 months, 6 months and up to 12 months.

## Methods

- A consecutive number of 24 pilot TPS-treated Alzheimer patients was examined retrospectively
- From these 24 patients we tested:
  - 24 patients before (T0) and after 1st treatment cycle (post)
  - 8 patients after 3 months (T3)
  - 10 patients after 6 months (T6)
  - 5 patients after 12 months (T12)
- For exploratory reasons: a heterogeneous group with MMST range from 2 to 27
- 4-12 sessions of 3000-6000 pulses of 4Hz TPS over two weeks with a booster session every four weeks, 0.2 mJ/mm<sup>2</sup> (navigated bifrontally, biparietally, bitemporally and praecuneus) using the Neurolith System (Storz Medical), see **Figure 1**:



- Numerous cognitive scores were assessed (ADAS, MMST, MoCA) and AE, ADE monitored
- Short term results were analyzed using an one-sided t-test with  $\alpha \leq 0.05$  for significance
- Long term performance was summarized descriptively and an overall Pearson correlation was calculated for MMST to test the stability of the scores

## Results

Treatment was well tolerable with low number of ADE. From 250 stimulation sessions totally administered: 1.6% drowsiness, 0.8% nausea and headache, and 0.4% jaw pain and earache.

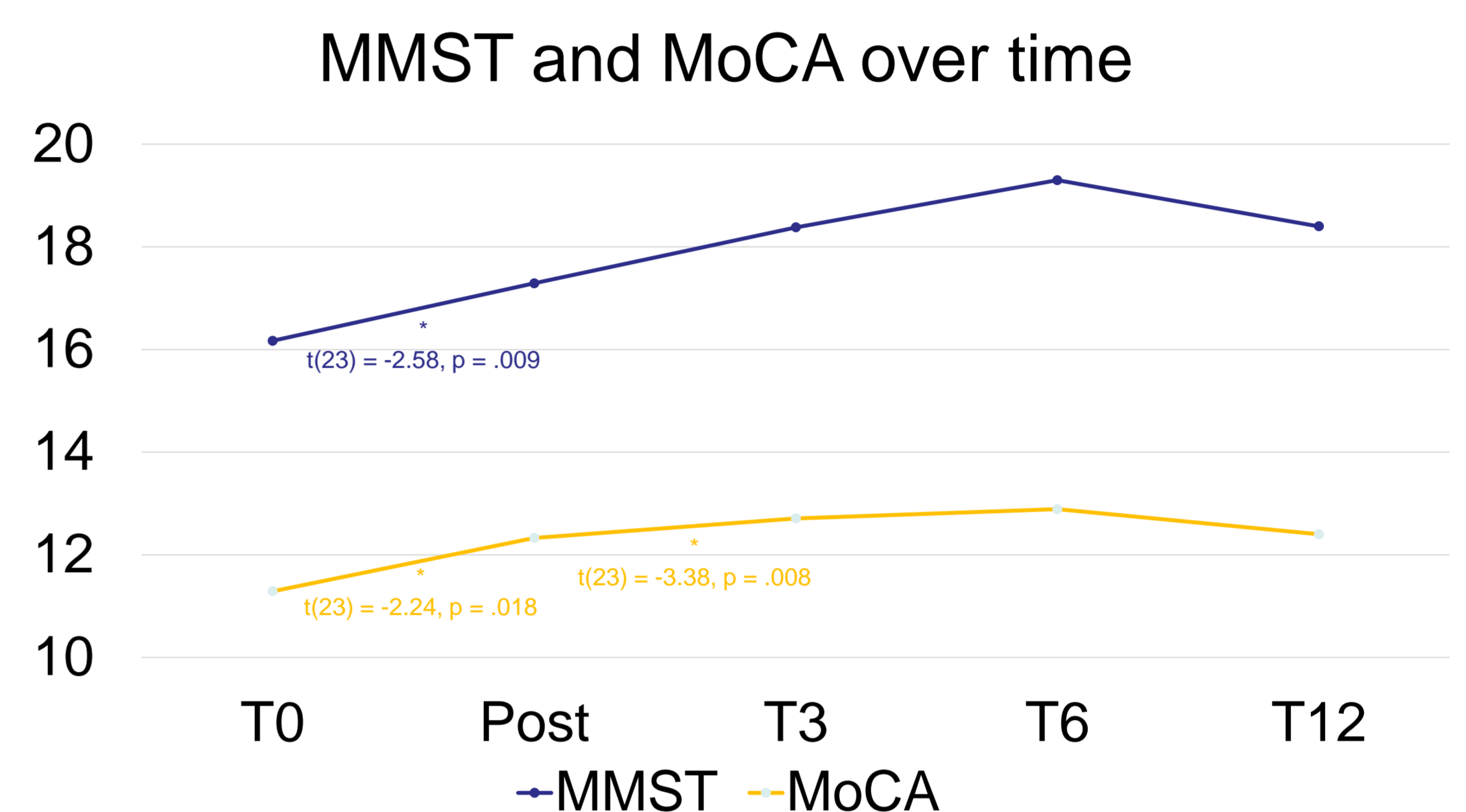
### Short-Term Results

A significant improvement in cognitive scores was detected in all neuropsychological tests:

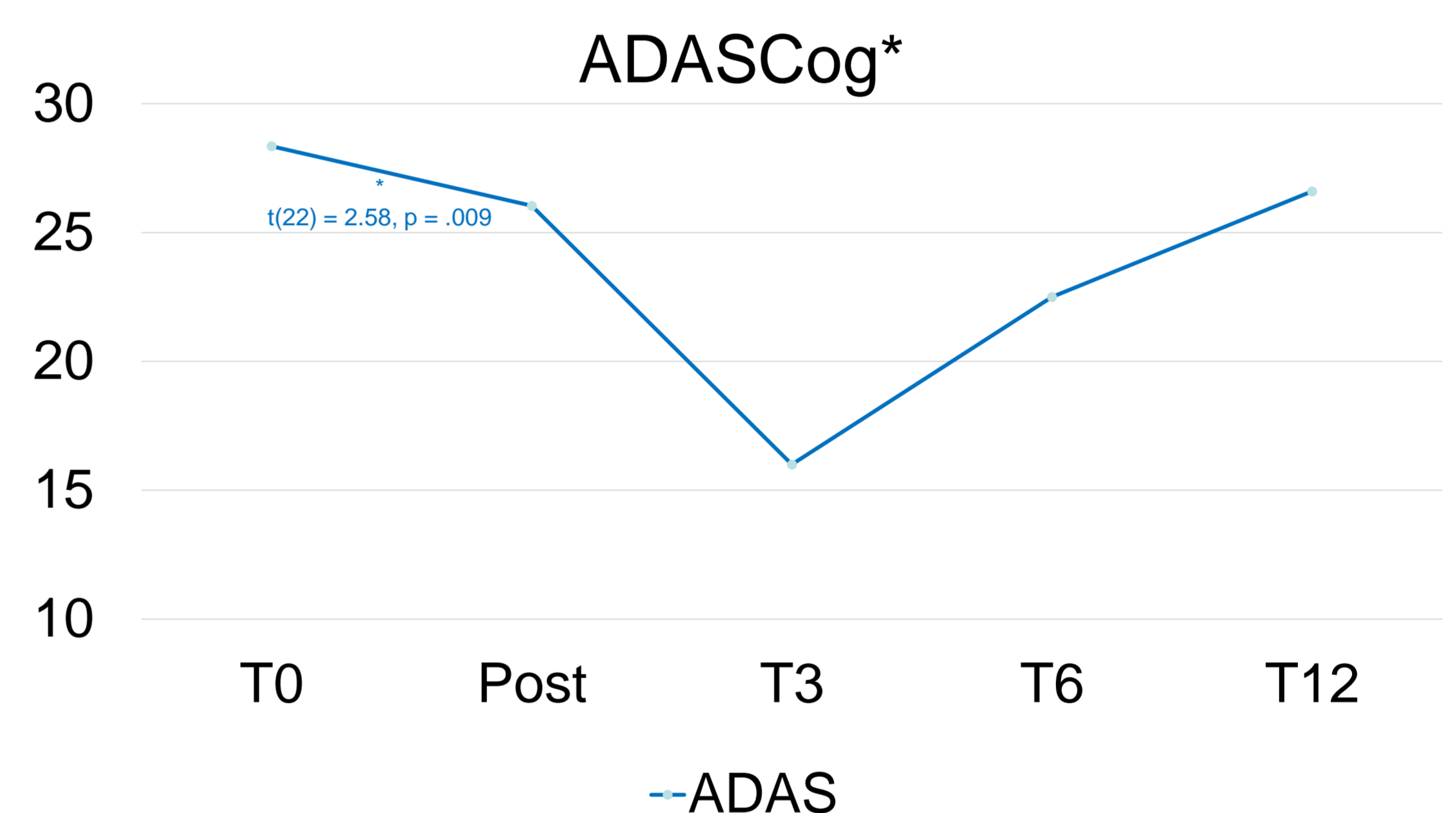
	n	M	SD	df	t	p	Cohens d
MMST- T0	24	16.17	8.042	23	-2.58	.009*	.53
MMST-Post	24	17.29	7.123				
MoCA - T0	24	11.29	6.517	23	-2.24	.018*	.46
MoCA - Post	24	12.33	6.611				
ADAS - T0	23	28.35	13.217	22	2.58	.009*	.54
ADAS - Post	23	26.04	13.227				

## Long-Term Results

Long-term data of the mean scores of the group show improvement in cognition after the first treatment cycle (see short term results), and after 3, 6, and 12 months in every test.



**Figure 2.** Overall improvement in mean scores over time.



**Figure 3.** \*A lower scores indicates improvement. Mean scores improve after the first treatment cycle and 3 months and then transition back to baseline at 6 and 12 months.

Whereas the t-tests comparing T0 and post stimulation show a significant improvement, a Pearson correlation with MMST for the whole time span (T0, Post, T3, T6, T12) revealed no significant change, thus patients show stable performance ( $p = 3.21$  with  $r = .057$ ).

## Conclusion

These pilot results confirm the recently published results with respect to low ADE and extent of cognitive improvement as a short-term effect. Long term data show an overall improvement in mean scores and a stable score after one year, which could indicate a slowing down of symptom progression of the disease measured by behavioral scores. Yet, a placebo controlled study is needed. More data and subgroups need to be analyzed. Prospective controlled trials would be the next step to prove the efficacy of this new technique.

## References

Cont, C., Stute, N., Galli, A., Schulte, C., Logmin, K., Trenado, C., & Wojtecki, L. (2022). Retrospective real-world pilot data on transcranial pulse stimulation in mild to severe Alzheimer's patients. *Frontiers in neurology*, 13, 948204. <https://doi.org/10.3389/fneur.2022.948204>

## Disclosure

LW received consultancy honoraria, and CC and LW received travel payments from Storz Medical.