- Treatment was carried out at home by caregivers, after training;
- During the treatment no changes were made to the ongoing therapies;
- A 10 point VAS was administered to the caregivers to assess the most disturbing and disabling behavioral problems at baseline, after 1 month of treatment and every three months afterwards.

Results:

- One patient has been treated uninterruptedly for three years (Figure 1), two patients for one year, and one for three months.
- One patient stopped the treatment after 43 sessions due to lack of clinical improvement.
- The five patients who are continuing the treatment showed a significant improvement during the first few months, which has been maintained over time.
- The only patient who did not show any improvement suffers from a comorbid rare genetic syndrome.
- No adverse effects were reported, besides mild skin irritation.

Conclusion: Our findings suggest that fronto-cerebellar tDCS is feasible, safe and easy to administer to ASD patients even at home and for long periods of time, provided that the patients' caregivers are appropriately trained. Long-term therapy ensures the persistence of the previously obtained clinical improvement without additional side effects.

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A 20-YEAR JOURNEY IN TRANSCRANIAL ULTRASOUND STIMULATION – LESSONS LEARNED

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Introduction: Transcranial Ultrasound Stimulation (TUS) is an innovative technique allowing for the first time non-invasive deep brain neuromodulation with a millimetric precision. But since the proof of concept of ultrasonic neuromodulation with the skull bone removed, in 1958, many challenges remained to be overcome: (i) the development of technologies enabling to focus ultrasound beams through the human skull, (ii) the identification of stimulation parameters allowing sustained neuromodulation effects and (iii) the definition of safety limits for clinical application. Over the last 20 years our laboratory has gained an internationally recognized track record in addressing each of these three key issues. In this presentation, we review 20 years of research in our laboratory that paved the way to the translation of TUS in medicine.

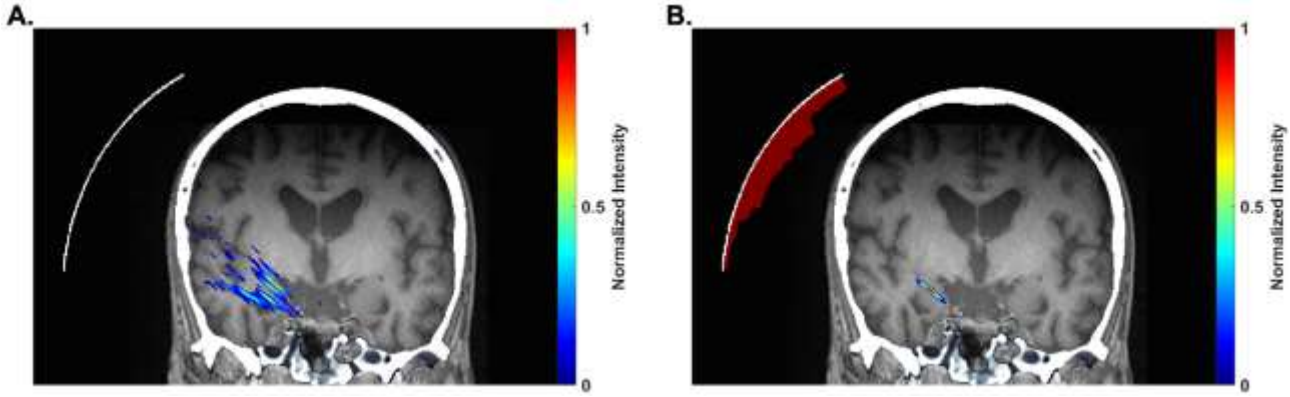

Figure 1. Acoustic intensity map when targeting the right amygdala without (A.) and with (B.) the use of a 3D printed acoustic lens (in dark red) covering a single-element ultrasonic transducer (in white). Sagittal planes are represented. The thickness of the lens was calculated based on a CT scan of the skull

Methods: Ultrasonic neuromodulation has been demonstrated in rodents, non-human primates and healthy volunteers. We will first review the pioneering studies on transcranial ultrasonic neuromodulation. Transient effects (lasting less than 1s) were initially induced. The acoustical stimulation parameters were further optimized to extend the duration of the neuromodulation to more than an hour (Verhagen et al. 2019), in line with potential clinical applications. Nevertheless, the first proofs of concept on healthy volunteers were limited to cortical stimulations because of the defocusing effect of the human skull. To counteract this, transcranial focusing was initially achieved by using multi-element arrays made of hundreds of ultrasound transducers. But a disruptive approach was introduced recently: it consists in the use of a single-element transducer covered with a 3D printed acoustic lens (Maimbourg et al. 2018) (Figure 1). The acoustic lens also enables non-invasive simultaneous multisite deep brain stimulation.

Conclusions: Altogether, the demonstration of sustained ultrasonic neuromodulation and the development of precise, low cost and mobile prototypes for noninvasive deep brain ultrasound focusing indicate that Transcranial Ultrasound Stimulation is now ready for clinical translation.

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COMBINING APP-BASED PSYCHOLOGICAL INTERVENTION WITH HOME-BASED TRANSCRANIAL DIRECT STIMULATION FOR THE TREATMENT OF DEPRESSIVE AND ANXIETY SYMPTOMS: A CASE SERIES

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Evidence indicates high heterogeneity in tDCS efficacy as a stand-alone treatment. Combining tDCS with psychological interventions may yield promising results to increase its therapeutic effects (Dedoncker et al. 2021). The current case series details the effects of 6 weeks of self-administered tDCS paired with behavioral therapy smartphone app (using Flow™), on depressive and anxiety symptoms, in seven patients (26-51y; 5 female) presenting distinctive neuropsychiatric disorders. The stimulation protocols consisted of 30min daily sessions, for 10 working days (two weeks from Monday-to-Friday; Protocol 1) or 15 consecutive workdays (three weeks from Monday-to-Friday; Protocol 2), followed by twice-weekly sessions for 2 or 3 weeks, respectively (18 or 21 sessions in total). Flow™ uses a current intensity of 2mA, targeting the bilateral dorsolateral prefrontal cortex. The app offers virtually guided sessions of behavioral therapy to be completed during stimulation which are not mandatory. At baseline and week 6 of treatment, we assessed depressive symptoms using MADRS-s and BDI-II, anxious symptoms using STAI-Trait, acceptability using ACCEPT-ETCC, and side effects using the Portuguese translation of the Thair et al. questionnaire (Thair et al. 2017). According to the Reliable Change Index (RCI), clinically reliable changes were found in symptoms of depression in 4 patients using MADRS-s (out of 7; RCI: -1.44 to -4.82; 90% CI) and in 3 patients using BDI-II (out of 4; RCI: -3.61 to -6.18; 90% CI). For anxiety symptoms, we found clinically reliable improvement in 4 patients (out of 5; RCI: -1.79 to -8.64; 90% CI). Stimulation was well tolerated and accepted (M=87.71, SD=4.92), with mild tingling sensation and scalp discomfort being the most common side effects. This case series highlights the applicability, acceptance, and promising results of combined home-based tDCS and app-based psychological interventions for the treatment of depression and anxiety symptoms.

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