UKE HAMBURG

Department of Neurology

ESOC 2021

Neuroregeneration Enhanced by TDCS in Stroke (NETS)

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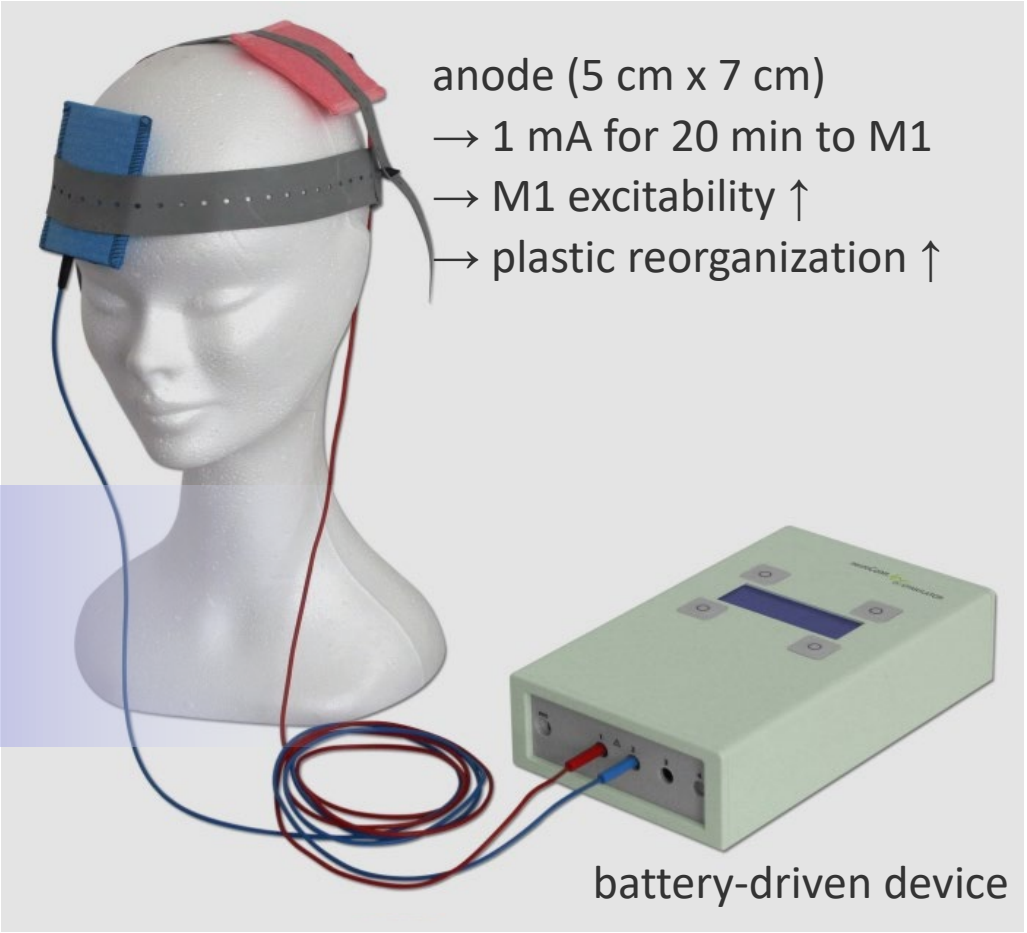
Trial Overview

- Investigator-initiated clinical trial (**IIT**), funded by the German Research Council (DFG Ge 844/4-1)
- Goal: Improving recovery of upper extremity function after stroke by transcranial DC stimulation (**tDCS**)
- Rationale: Plastic reorganization of the motor cortex (**M1**) contributes to recovery of motor function[1]; tDCS can enhance cortical excitability and plasticity[2,3]

Urgent need to improve recovery

extremity function is a key problem preventing patients to return to activities of daily living

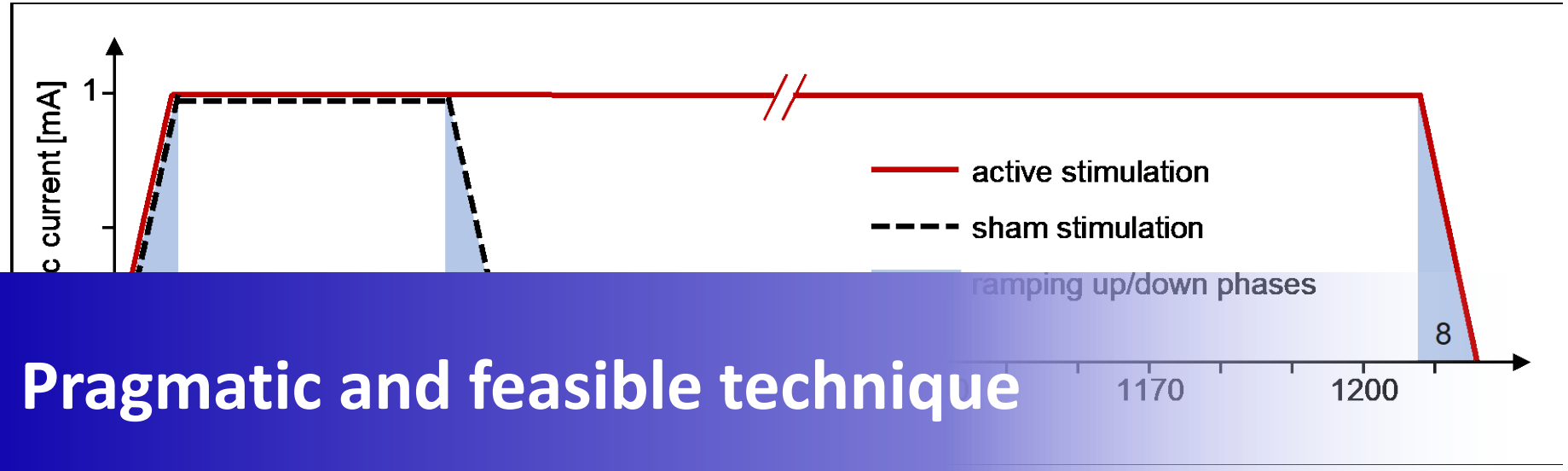
- **123** patients were randomized between 2009 and 2019 in 11 centers in 3 European countries (GER, ITA, AUT)

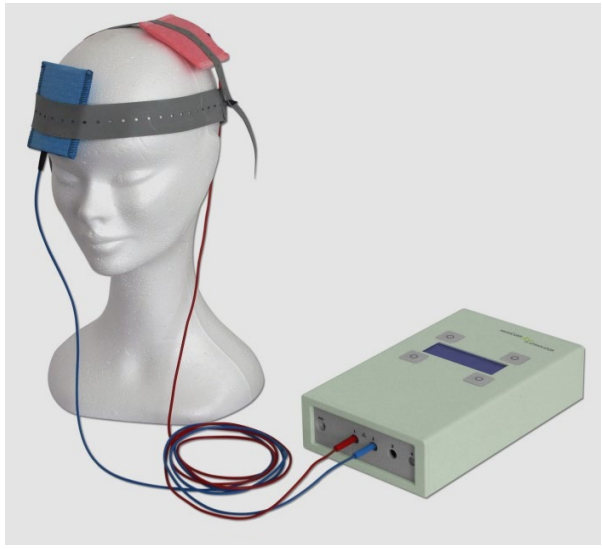


[1]Nudo Phys Med Rehabil Clin N Am 2003; [2]Buch et al. Clin Neurophysiol 2017; [3]Hummel et al. Brain 2005

Method of intervention

- **Anodal** tDCS over the primary **motor cortex** of the stroke hemisphere for **20 min** at **1 mA**





Pragmatic and feasible technique

- Repeated applications **(10 x)** over **2 weeks**
- **Standardized rehabilitation protocol** in both groups
- **Primary Endpoint**: Upper Extremity Fugl-Meyer-Assessment (**UEFMA**) **1-7 days** after the end of the intervention (Intention-to-Treat analysis)

Patients were

Baseline variables well balanced

(subacute phase)

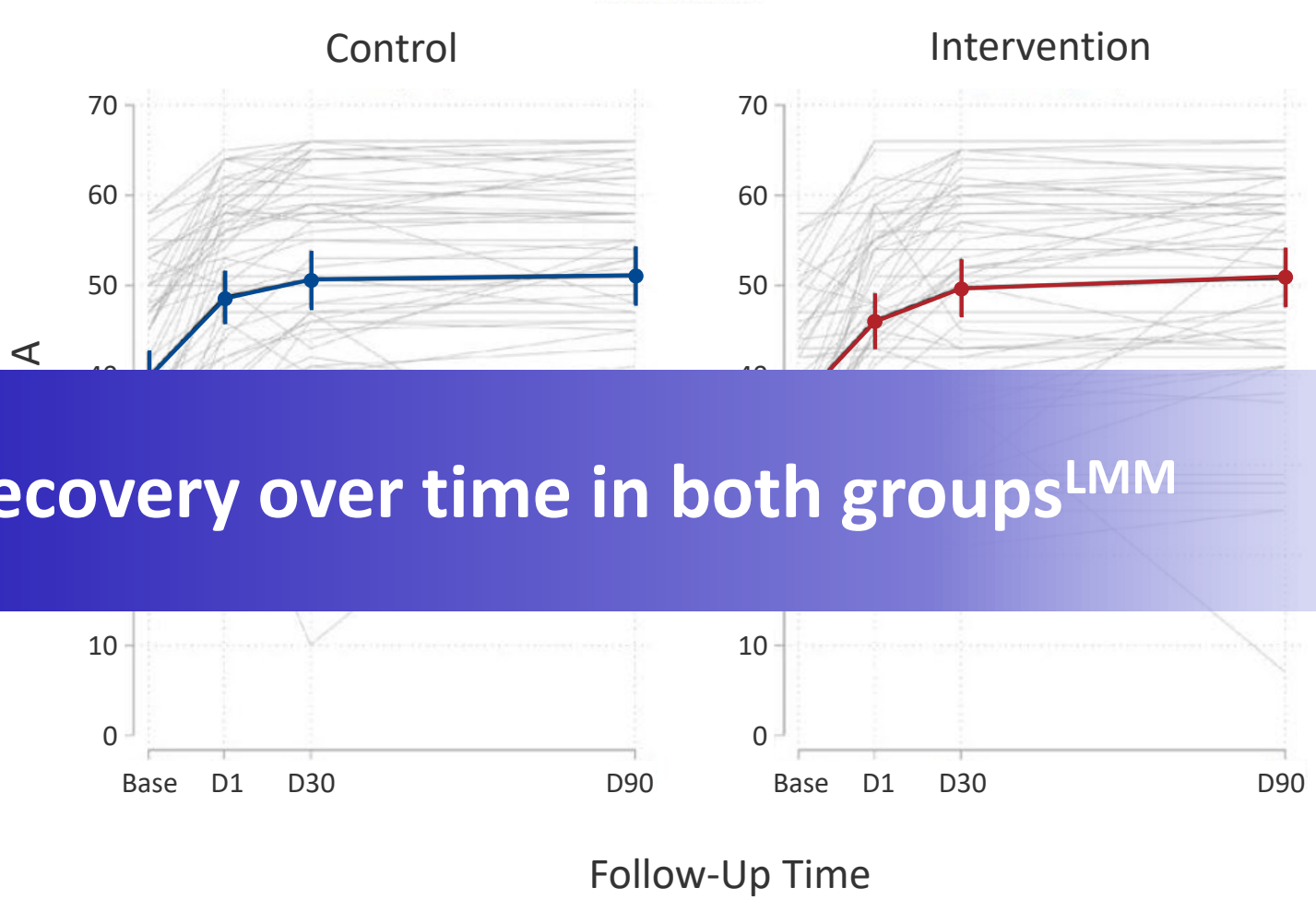
- **mild to moderate** stroke severity (NIHSS 3.8±2.0)

Safety profile

y safety endpoint)

Favorable safety profile

Results | Time-Trend Analysis of Primary Endpoint (ITT)



Significant recovery over time in both groups[LMM]

[LMM]Linear mixed model analysis: interaction between treatment group and time not significant (p=0.177)

- Primary efficacy endpoint: **no significant difference**

  Intention-To-Treat analysis of 119 patients (mean age±SD, 66±12 years; 63% male; NIHSS 3.8±2.0)

	N		Mean change (unadj.)		Mean change (adj.)[1]		Int.-Ctrl.			p-value
	Ctrl.	Int.	Ctrl.	Int.	Ctrl.	Int.	Diff.	95%-CI		
UEFMA	61	56	8.85	9.00	9.07	8.76	-0.31	-2.97	2.35	0.820

- Secondary efficacy endpoints: **no significant differences**

	Ctrl.	Int.	OR (Int. vs. Ctrl.)	95%-CI		p-value
Clinically relevant response [a]	40/51 (78.43%)	29/41 (70.73%)	0.65	0.22	1.95	0.445
Compound score response [b]	42/50 (84.00%)	31/40 (77.50%)	0.52	0.16	1.72	0.284

[a] number of patients with an UEFMA improvement ≥5

[b] number of patients with at least one of the following improvements in the affected upper extremity: UEFMA ≥5; NHPT time ≤-32 sec; grip strength ≥5.7 kg

No differences between treatment groups g upper-extremity function but also cant differences between active

[1]adjusted for baseline UEFMA, type of stroke (cortical, subcortical), age, time between stroke and baseline examination

Conclusion

- Anodal tDCS over the primary motor cortex of the stroke hemisphere in the subacute phase after ischemia **did not improve** functional outcome (Upper Extremity Fugl-Meyer Assessment [UEFMA])
- These results pertain to a population of **mild to moderate** stroke (NIHSS 3.8 ± 2.0) included on average **20.0** (± 11.7) days after the ischemic index event
- Potential reasons for failure include stimulation intensity (too low?), time point of study inclusion (too late or too early after stroke?), degree of neurological deficit (too mild? ceiling effect for tDCS?), intensity of standardized rehabilitative training in both study arms (too intense? ceiling effect for tDCS?)
- The results of the NETS trial give us a **solid basis** for planning future randomized clinical studies on the enhancement of upper-extremity recovery after stroke by neurostimulation