

8^ο Συνέδριο

Ελληνική
γλώσσα και
διαταραχές

LDG8

30 Σεπτ. - 01 Οκτ. 2022

Αριστοτέλειο Πανεπιστήμιο

Θεσσαλονίκη



“Constraint Induced Language Therapy (CILT) combined with Transcranial Magnetic Stimulation (TMS) as a treatment option for recovery of language deficits in chronic aphasia post-stroke”

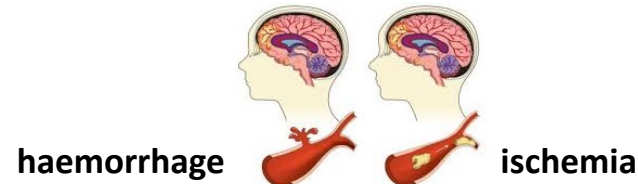
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Cyprus

Aphasia



- acquired language disorder
 - injury to the brain – most typically **stroke** in the left hemisphere

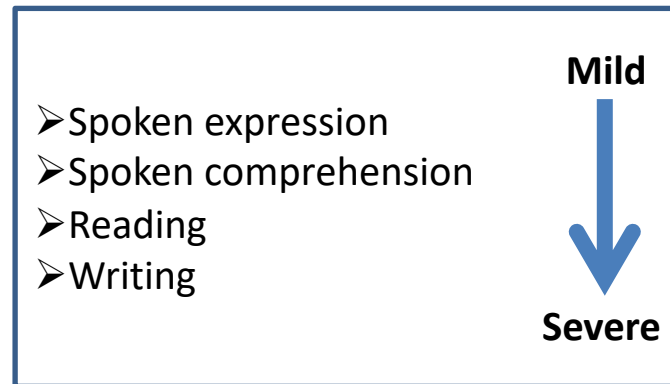


Overall, more than 1/3 of post stroke patients

1/3: improvement within the first 4 weeks

1/2: improvement within the first **6 months**

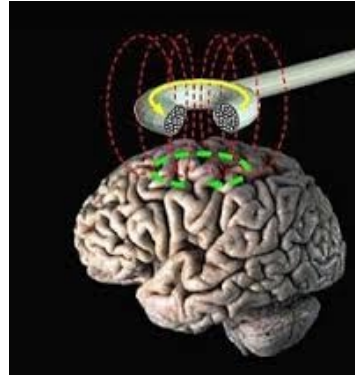
(Heiss & Thiel, 2016)



non-fluent:
reduced speech output

fluent:
speech output is not reduced, but speech is incoherent

Evidence so far



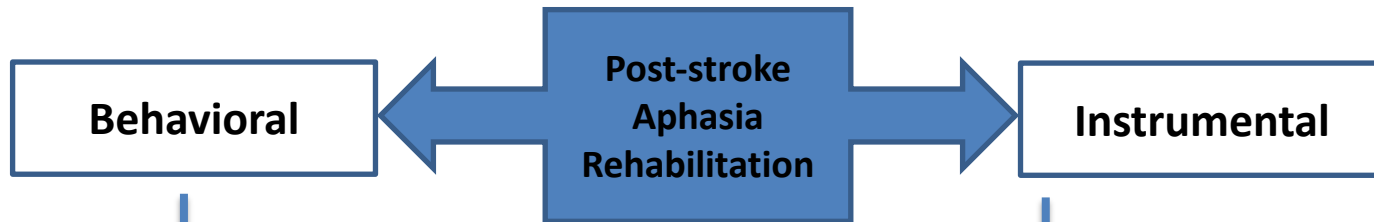
language gains
in post stroke
aphasia

- ✓ **Naming** (e.g., Hu et al., 2018; Rubi-Fessen et al., 2015)
- ✓ **Naming reaction time** (e.g., Waldowski et al., 2012)
- ✓ **Repetition** (e.g., Barwood et al., 2013; Seniow et al., 2013)
- ✓ **Comprehension** (e.g., Hu et al., 2018)
- ✓ **Spontaneous speech** (e.g., Hu et al., 2018)
- ✓ **Aphasia profile** (Rubi-Fessen et al., 2015; Heiss et al., 2013)

- **30-minute** SLT, **post-TMS**, focusing on **naming** (Hu et al., 2018)
- **45-minute** SLT, **post-TMS**, focusing on **word retrieval** (Rubi-Fessen et al., 2015)
- **60-minute** SLT, **post-TMS**, **twice a week** focusing on **expressive skills** (Wang et al., 2014)

significant inconsistencies
between studies regarding
intensity & type of SLT

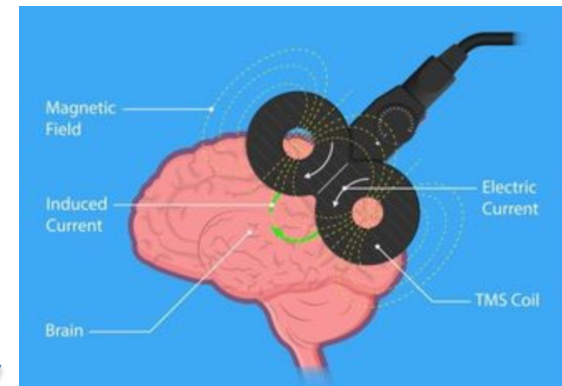
Aim of the study



- Constraint Induced Language Therapy (CILT)



+ | -

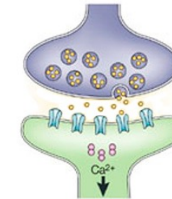
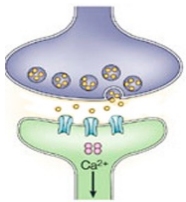
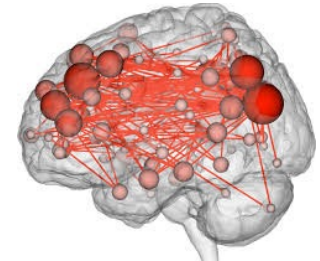


- Transcranial Magnetic Stimulation (TMS)

Transcranial Magnetic Stimulation (TMS)



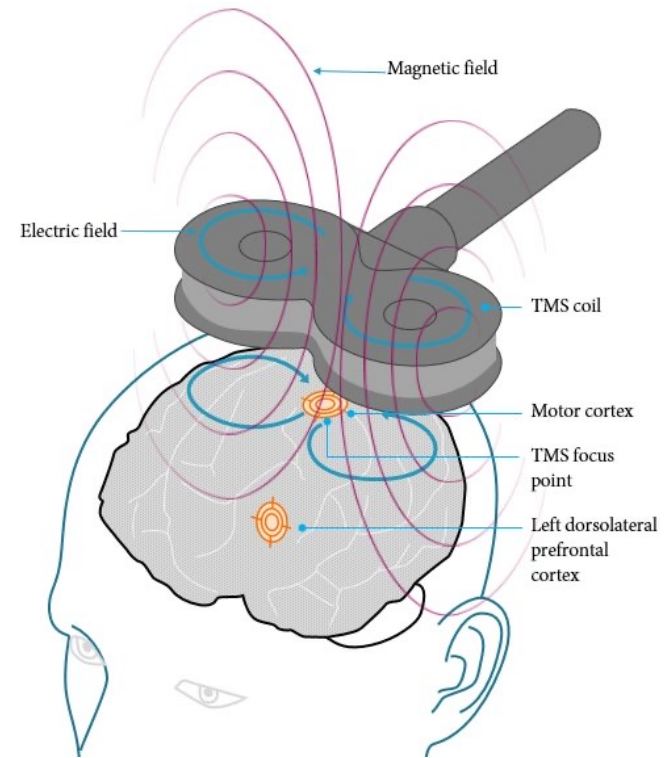
- ✓ non-invasive brain stimulation technique
- ✓ safe (Lefaucheur et al., 2020; Rossi et al., 2009)
- ✓ investigation of brain areas responsible for specific functions (e.g., language)
- ✓ stimulation of areas of interest for treatment



- ✓ enhancement of neuroplasticity (i.e., the ability of the brain to change in response to environmental stimuli (e.g., trauma, treatment))
- ✓ TMS after-effects represent changes in synaptic efficacy (long term potentiation (LTP)/ long term depression (LTD))

TMS: Basic Principles

electromagnetic induction (1831)



- time-varying current (value/direction) → magnetic field → electric field and hence a secondary current within nearby conductors
 - there is always electric current flowing through neurons
 - TMS stimulates neurons that act as conductors
- the more current in the coil, the stronger the magnetic field

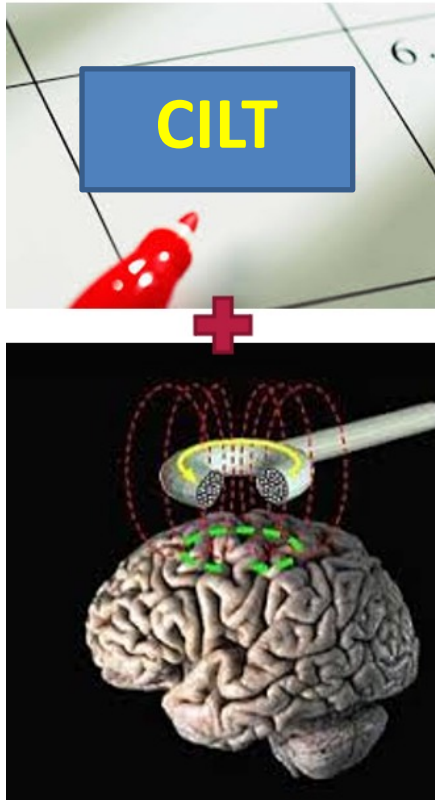
Constraint Induced Language Therapy (CILT)

- **patients are prompted to use only speech for communication purposes** - intensive delivery (short time period) with massed practice (intense) (Maher et al., 2006; Pulvermuller et al., 2001)
 - alternative forms of communication, such as gestures, are **restricted**
- designed to enhance speech production → CILT is associated with benefits across a wide **range** of language faculties (Meinzer et al., 2012; Carter et al., 2010; Berthier et al., 2009; Cherney et al., 2008)



- *the participant interacts verbally with a conversational partner (here, the SLP), in turn requesting a card of given description and complying with the partner's request → the treatment targets both production and comprehension*
- *verbal targets increase in linguistic complexity across the protocol ("a ball", "throw a ball"; "Do you have a ball?") → a variety of lexical and phrasal structures are targeted*

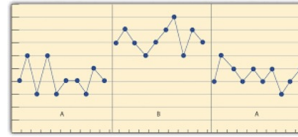
WHY CILT in particular ?



The decision to combine **CILT** with **TMS** is motivated by **4** considerations:

1. hypothesis that the combination of TMS with behavioral therapies is **better** than TMS alone
 - TMS alters the brain's circuitry → the brain is more receptive to behavioral therapies
2. CILT: **structured** (predetermined measurable ingredients of therapy)
3. evidence that CILT **combined** with TMS **benefits** people with aphasia (Martin et al., 2014)
 - **not replicated** by one study (Heikkinen et al., 2019)
4. providing CILT ensures that all patients receive **therapy**

Methodology: Single Subject Experimental Design (SSED)



- small sample sizes + heterogeneous participants → particularly relevant to **post-stroke aphasia in Cyprus**



- no control group → each participant provides their **own control** for purposes of comparison

- **individual detailed assessments**

- **2 - 3 pre-treatment (baseline) assessments** on language and cognition →
 - level of performance prior to treatment
 - rate of change
 - rule out spontaneous recovery

(Howard, Best & Nickels, 2015)

Overall, more than 1/3 of post stroke patients have aphasia
→ 1/2: improvement within the first **6 months** (Heiss & Thiel, 2016)

Incidence: **564** strokes per year

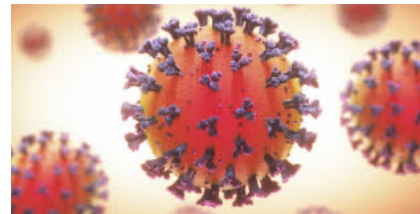
45.9 strokes per **100,000** inhabitants annually

S·A·F·E
Stroke Alliance For Europe

THE STROKE PATIENT
VOICE IN EUROPE



≈ **100 per year**



remote and rural areas
immobile
severely disabled
not motivated to participate in experimental treatments
pass away

1. Background Measures

Speech & Language History Form

- several types of information (e.g. medical, educational)

Face Sheet

- specific information about the stroke and rehabilitation processes (e.g. chronicity of stroke, duration of Speech & Language Therapy)

Screening for TMS eligibility Form

Hemispatial Neglect Test (Albert, 1973)

- deficits in attention to and awareness of one visual field

Handedness Inventory (Short Form) (Veale, 2014)

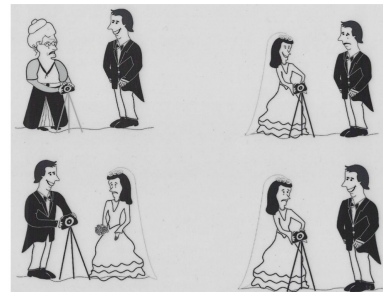
- to assess the dominance of a person's right or left hand in everyday activities

2. Language Measures

- **Boston Diagnostic Aphasia Examination-Short Form (BDAE-SF) (Messinis et al., 2013)**
 - ✓ Language skills in adults suspected of having aphasia
 - comprehension – expression – naming – reading

- **Peabody Picture Vocabulary Test-Revised (PPVT-R) (Simos et al., 2011)**
 - ✓ receptive vocabulary at the word level

- **Relative clauses task**
 - ✓ comprehension at the sentence level

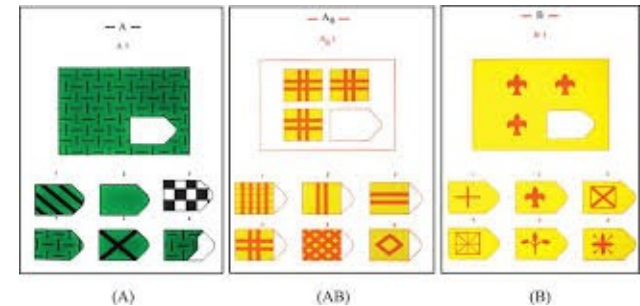


Relative Clauses Task – sentence 14: The bride photographs the groom who is sad.

- **Pseudoword repetition task (Kambanaros & Grohman, 2013)**
 - ✓ phonological analysis, memory, retrieval, programming & production

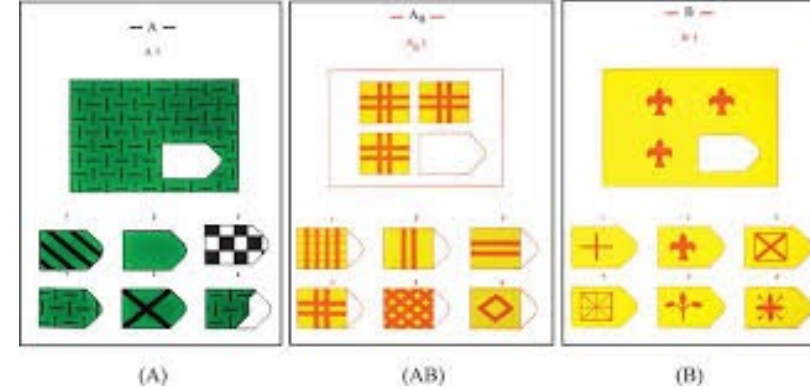
3. Cognitive Assessment & Quality of Life Measurement

- Raven's Coloured Progressive Matrices (RCPM) (Raven, Raven & Court, 1998) → cognition (problem solving skills)



- Stroke and Aphasia Quality of Life scale-39 item (SAQOL-39g) for Greek → quality of life
 - comprehension problems in 2 participants
 - common policy adopted for all → proxies' reports

Cognitive testing (control variable)



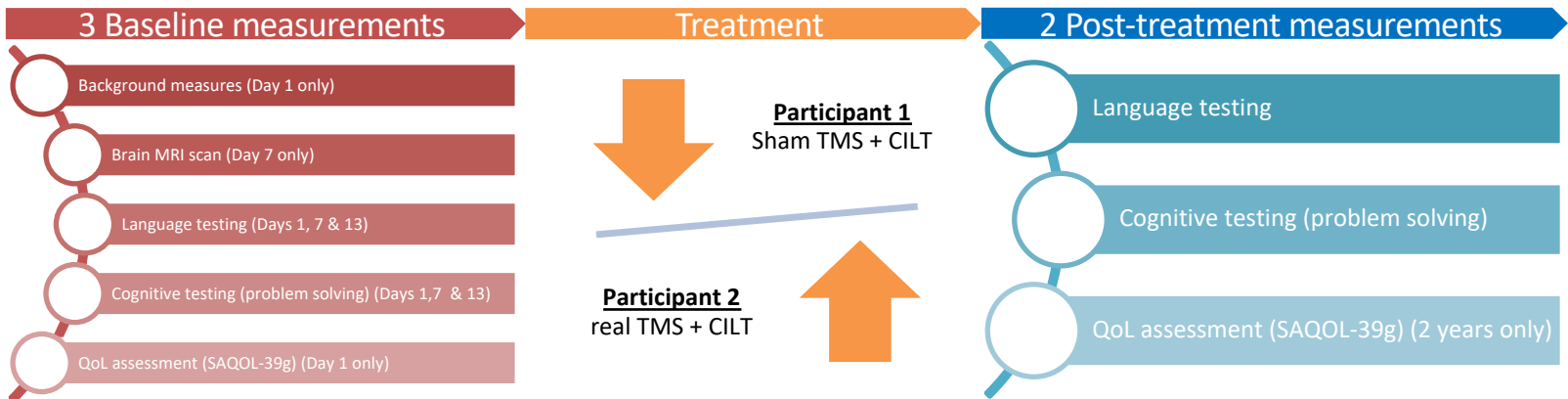
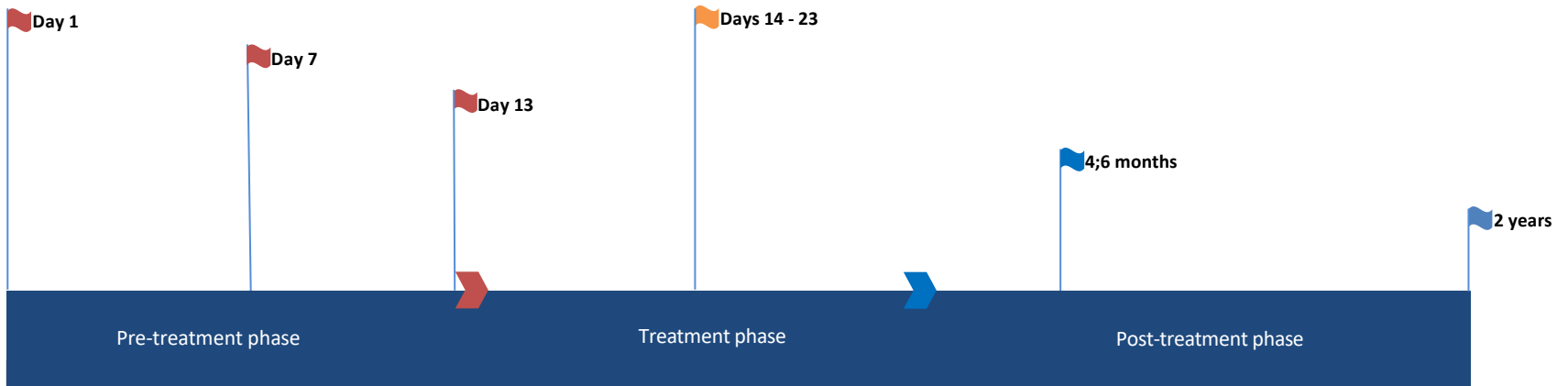
if a change in language skills is noticed but the control variable
(i.e. **problem solving**) remains stable →

- ✓ the chances that TMS leads to language specific gains are increased
- ✓ the possibilities for the placebo and training effects are reduced

Demographic and clinical characteristics of the 2 participants

Participant	Sex	Age (years)	Handedness	Education (years)	Type of stroke	Months post stroke	Lesion site (left hemisphere)	Type of Aphasia	Severity of Aphasia	SLT prior to enrolment	Termination of SLT
1	M	57	right	18	ischemic	108	<ul style="list-style-type: none"> Brain parenchymal loss involving the left frontoparietal lobe extending inferiorly at the anterior left temporal lobe. Mild perifocal brain gliosis. Mild ex vacuo dilatation mainly of the frontal horn and body of the left lateral ventricle. Asymmetry of the cerebral peduncles noted, with the left side significantly smaller than the right, also involving the pons. - This is compatible with a left-sided Wallerian degeneration. 	anomic	mild to moderate	12 months – 3 times per week for the upcoming 24 months - 2 times per week	6 years before enrolment
2	M	58	right	12	ischemic	48	<ul style="list-style-type: none"> Brain parenchymal loss involving the left parietal lobe with mild perifocal gliosis. 	anomic	mild	3 months – 2 times per week	3 years before enrolment

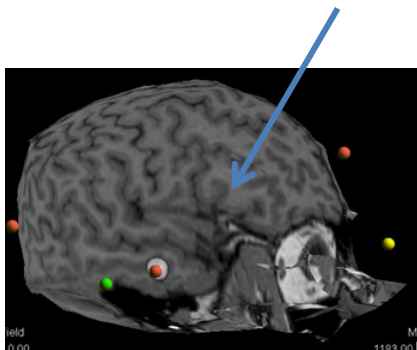
Experimental timeline of the study



Neuronavigated Continuous Theta Burst Stimulation (cTBS)

Participant 2 underwent cTBS at 80% of their individual resting motor threshold (rMT) to the pars triangularis (Tr) of the right inferior frontal gyrus (homologous BA45) with a Magstim Rapid2® stimulator (Magstim Co., Wales, UK) linked to a 70 mm Double Air Film Coil. The stimulation parameters were set according to Wassermann's recommendations (1998).

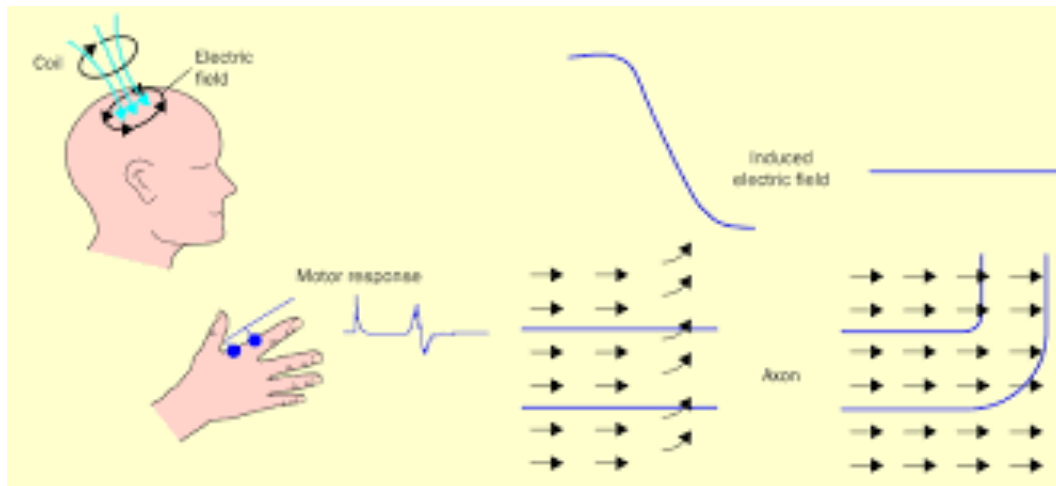
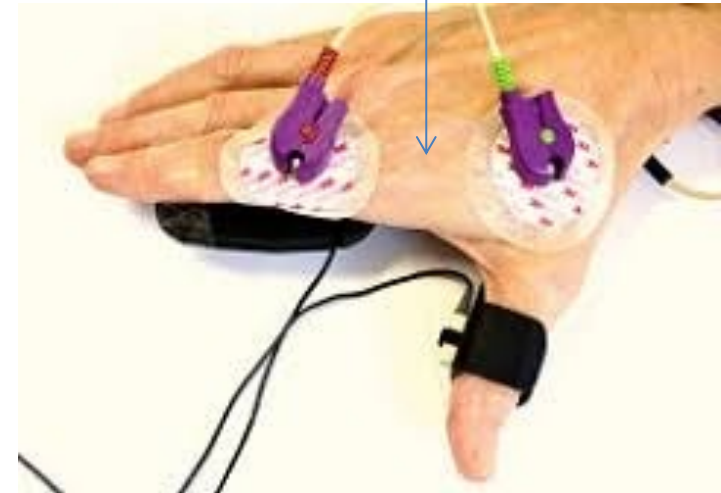
Patterned rTMS



Exploration of rMT

- EMG of the FDI
- Brain area controlling the FDI identified through neuronavigated TMS → 80% of the minimum TMS intensity output resulting in FDI contraction of a **specific value** (50 μ V) defined as the intensity value (rMT) used in **all subsequent TMS sessions**

First dorsal interosseus





Modified Constraint Induced Language Therapy (M-CILT) (1)

- 10 consecutive days treatment – each session lasted 90 minutes
- 1 speech-language therapist (**conversational partner**) sitting opposite the patient and 1 speech-language therapist (**therapist coach**) sitting next to the participant to help them
- treatment stimuli created by Prof. Maria Kambanaros and Dr. Anastasios Georgiou for each level of treatment, using the Snodgrass & Vanderwart (1980) picture set, measured on psychometric properties (name agreement, visual complexity, age of acquisition) by Dimitropoulou et al., (2009) – the Ktori et al. (2008) GreekLex database provided data on word frequency
- 96 black and white cards which were separated as follows:
 - 48 duplicates of 24 different high frequency nouns with associated verbs
 - 48 duplicates of 24 different low frequency nouns with associated verbs



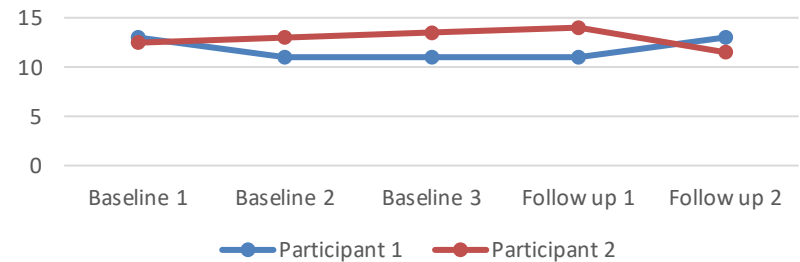
Modified Constraint Induced Language Therapy (M-CILT) (2)

- 30cm wooden barrier
- **Goal** of the game: making pairs of same cards & getting rid of them– **only speech is allowed**
- "Go fish" game → verbal description of cards according to their level (e.g., for agent noun level - Please give me the/ I want the/ Do you have the "book"?) – no match ?
Then Go fish !
- increasing level of talking demands – from 1 word level to sentences

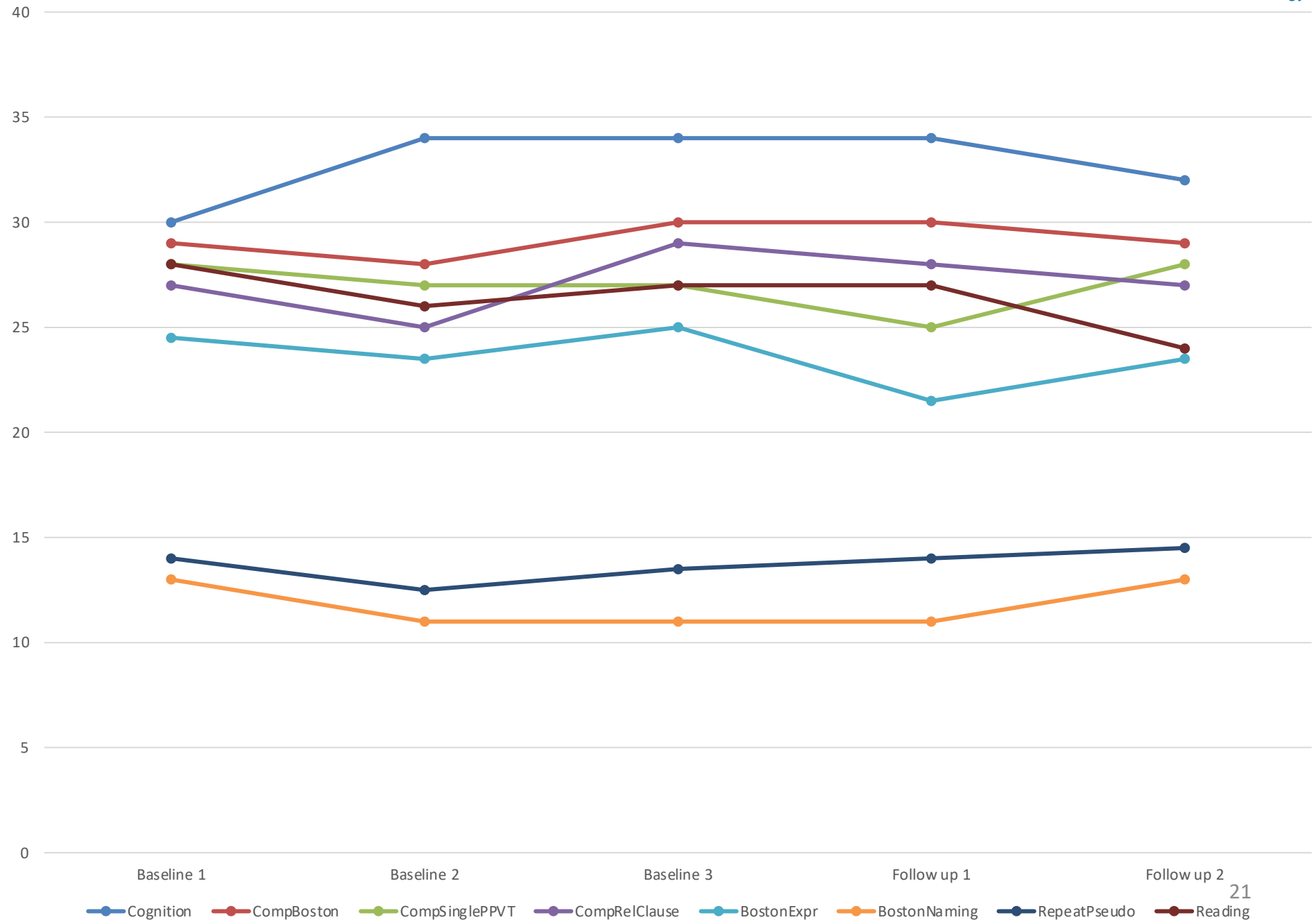
Data analysis

- **Weighted Statistics (WEST)** (Howard, Best & Nickels, 2015)
 - WEST-Trend → is there is an upward linear trend for improvement?
 - WEST-ROC → analyses the amount of change in
 - treated vs the untreated period
 - long - vs short-term
 - studies with small sample sizes, heterogeneous participants
 - does not exclude any participant from receiving treatment
 - **novelty in small-scale TMS aphasia research**

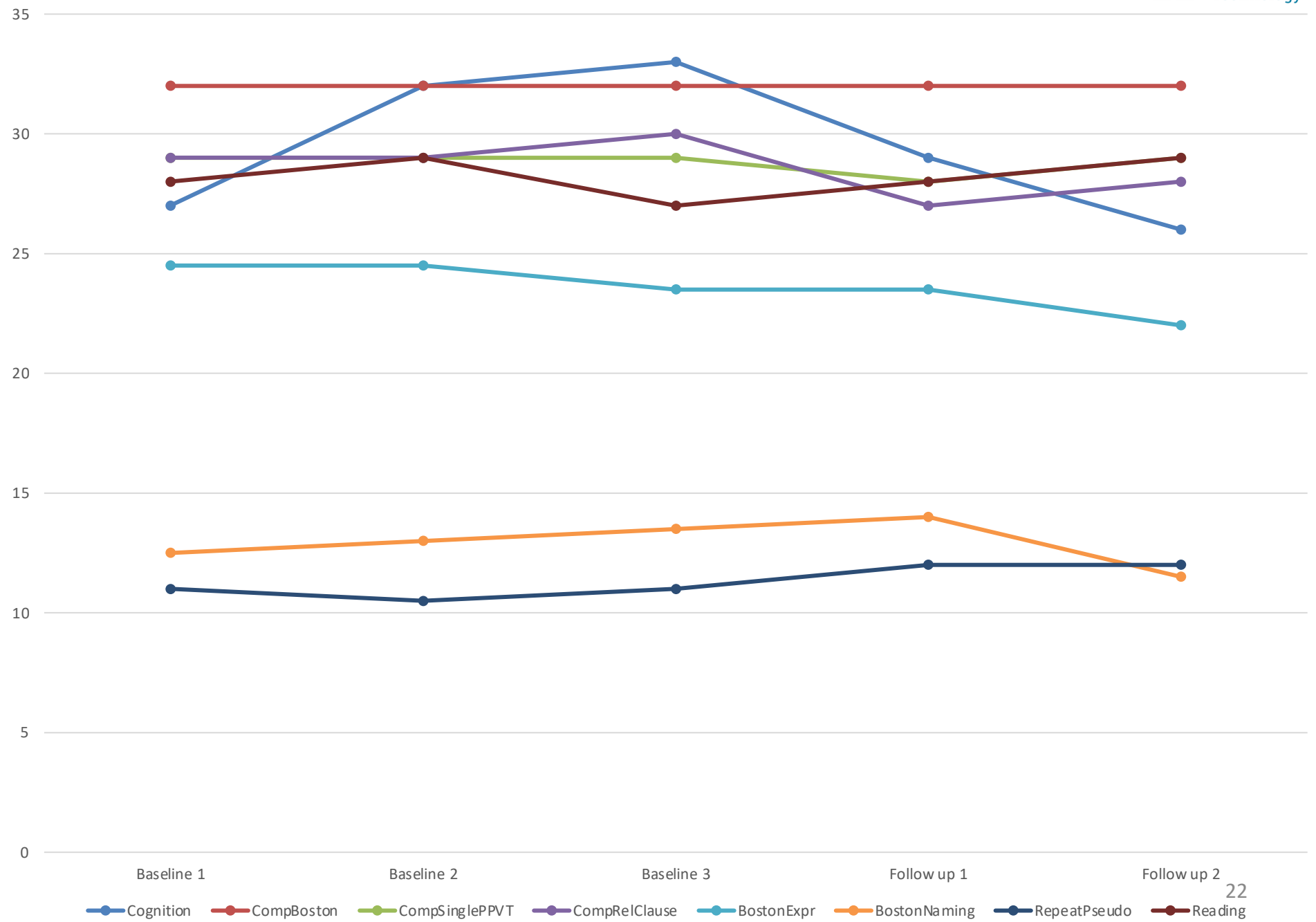
Boston Diagnostic Aphasia Examination - Short Form (naming)



Participant 1: CILT + sham TMS



Participant 2: CILT + TMS




QoL Results

Quality of Life	Participant 1		Participant 2	
	Pre TMS	Follow up 2	Pre TMS	Follow up 2
SAQOL- 39g Mean score	3.23	-	2.85	4.02
Physical score	3.38	-	2.69	3.5
Communication score	2.86	-	2.29	4
Psychosocial score	3.25	-	3.25	4.56

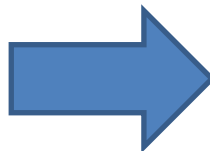
- No data for P1
- Significant improvement in all QoL scales for P2

Conclusions

- 1st of its kind conducted in Cyprus on aphasia and TMS 
- COVID19 → **only** 2 participants + **no** assessment of immediate & short-term effects of treatment
- standardized language measures to assess language skills → no improvement in any assessed language skill (i.e., comprehension, expressive language, naming, reading, repetition) nor cognition
- QoL measure → no data for P1 – significant improvement in all scales → **as no language improvement was noticed post-treatment, it could be hypothesized that treatment offered a psychological boost to P2**
- based on the present preliminary data, it seems that lesion location & extent, type & severity of aphasia do not predict CILT +/- TMS efficacy as patients with similar aphasia types and severities & lesions show improvement post-treatment
 - chronicity may play an important role in treatment response **in some patients** – recent studies show that behavioral therapy improves language skills in chronic aphasia (e.g., Johnson et al., 2019; Fridriksson et al., 2018; Mozeiko et al., 2018)
- **disappointing findings need to be reported / published → exploration of factors (intrinsic & extrinsic) affecting response to treatment**

Implications

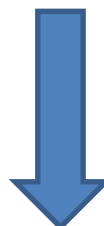
- even though CILT was not proved to be beneficial for P1 & P2
- ✓ several studies support CILT related language gains in PWA (e.g., Johnson et al., 2014; Sickert et al., 2013; Pulvermüller et al., 2001)
- ✓ more recently it was found that CILT delivered in **both intensive and distributed dosages** had beneficial effects on both standardized and discourse measures (Mozeiko et al., 2015)



variability (failure/success) in response to TMS may be attributed to:

- aphasia type
- aphasia chronicity
- site of stimulation
- TMS stimulation parameters
- SLT ingredients
- age
- gender
- genetics & epigenetics
- ...

(Coslett, 2016; Lefaucheur, 2014)



Need for:
➤ biomarkers of good responders and non-responders



importance of identifying **patient-specific factors** that may account for **variability** in recovery of lost function **with or without treatment**

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