A Systematic Review on Transcranial Direct Current Stimulation in Primary Progressive Aphasia: Methodological Considerations

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1. Introduction

Primary Progressive Aphasia (PPA)
Syndrome of language deterioration, caused by neurodegenerative disease[1]

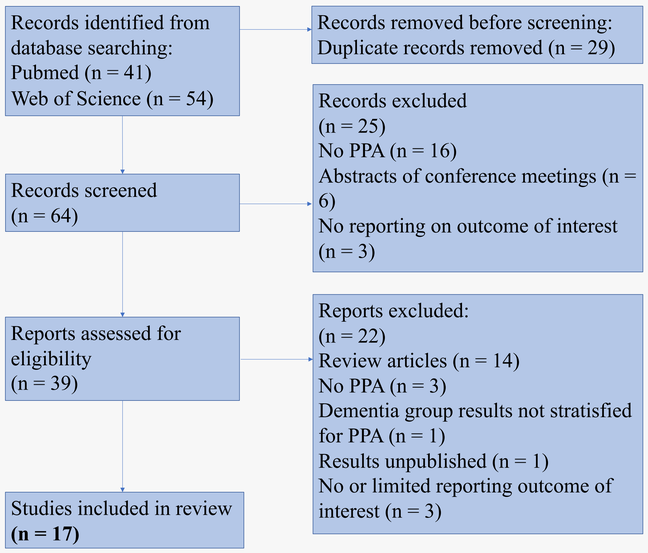
Three clinical variants of PPA[2]
- defined by core language symptoms
- associated with different patterns of brain atrophy

	Semantic variant PPA (SvPPA)	Logopenic variant PPA (LvPPA)	Nonfluent variant PPA (NFvPPA)
Core symptoms	Speech comprehension: lose the meaning of words and objects.	Word-finding and sentence repetition difficulties, slow speech.	Speech production: lack of grammar, effortful, halting speech, apraxia of speech
Atrophy epicenter	Bilateral anterior temporal lobes	Temporoparietal lobe	Left inferior frontal gyrus, premotor cortex, anterior insular region

Treatment
- Dependent on speech-and language therapy: slow down language decline, help develop alternative communication strategies[3,4]
- tDCS to augment effects of speech-and language therapy
- Studies tDCS in PPA have used a variety of methodological approaches

Aim of our systematic review
- Provide overview and compare methodological approaches
- Discuss linguistic outcomes in light of methodological and patient characteristics

2. Methods - PRISMA



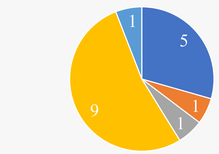
Keywords
(primary progressive aphasia or semantic dementia or logopenic variant PPA or non- fluent variant PPA or semantic variant PPA) and (transcranial direct current stimulation).

3. Results Systematic Review

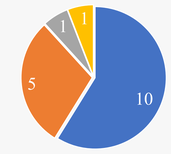
Methodological similarities	Patient characteristics similarities
20-30 minutes of stimulation	Mean age: 66 (SD: 8.3) to 68.7 (SD: 7.0)
Stimulation intensity of 1-2 mA	Average disease duration: 4.9 (SD 0.9)
Electrode surface of 5x5 or 5x7 cm	Mild to moderate disease severity
Most (13/17) studies chose the area of stimulation based on the combined language therapy	

Comparison Patient Characteristics

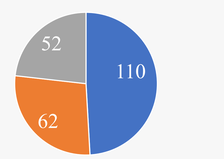
Language spoken by patient



Composition of the study population

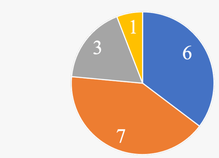


Total *n* per PPA variant

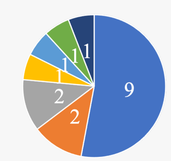


Comparison Methodological Approaches

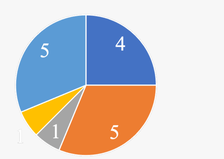
Neuroimaging studies



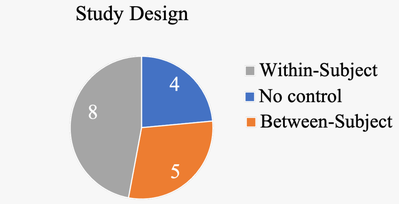
Stimulation location



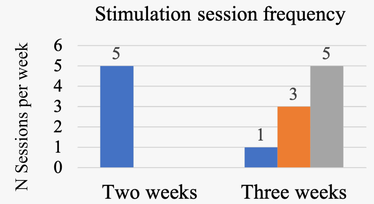
Language therapy in combination with tDCS



Study Design



Stimulation session frequency



Summary language and neuroimaging outcome measure results reviewed studies
- Despite protocol heterogeneity, 16/17 positive language outcomes
- These outcomes are variable regarding size, duration, generalization
- Gray and white matter volumes are negatively correlated with language outcomes
- tDCS effects are negatively correlated with functional connectivity between stimulated and connected regions.

4. Discussion and Conclusion

1. Patient characteristics as moderators of tDCS effects

Clinical variant PPA
Group results: tDCS-related improvements language outcomes.
- Different picture when
  - Looking at individual patient results of mixed group patient populations: NFvPPA patients often seem to benefit the most.
  - One study stratified results per variant: NFvPPA > SvPPA

-> Different effect sizes of language outcomes of different studies might be driven by composition of study population.

Language background
- Relevance native language in language processing and activation of language areas in brain.[5]
- Bilingualism? -> mediated by structural and functional changes, leading to neural differences between bi-and monolinguals.[6]

Post-onset timeframe of stimulation
- Higher atrophy -> more loss of function and poorer baseline language scores -> correlated with greater potential for functional improvement.

2. tDCS montage and language therapy as moderators of tDCS effects
- Left IFG often stimulated -> main site of atrophy NFvPPA
- While studies stimulating left IFG found less positive results for SvPPA, one study focussed on SvPPA and stimulated their main site of atrophy: did find positive results.
- Studies comparing electrode montages: positive results in both montages, but difference in duration and size of effects -> may reflect different functions of areas.

-> Suggests that stimulating different nodes in one particular network can lead to different results and location of stimulation might be a variable critical to success.
-> Search for other candidates for site of stimulation? e.g. **cerebellum**

3. Neuroimaging
Structural and functional imaging evidence can help understand underlying mechanisms of tDCS and can be used as predictors of success.

5. References and Funding

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