The dynamics of auditory working memory impairment in logopenic and nonfluent variant primary progressive aphasia and Alzheimer's disease

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INTRODUCTION

Impaired auditory verbal working memory is a diagnostic hallmark of logopenic variant primary progressive aphasia (lvPPA) and nonfluent variant primary progressive aphasia (nfvPPA) and an integral driver of the clinical phenotypes [1, 2]. However, the pathophysiology of the auditory working memory buffer in these syndromes is poorly characterised [3, 4].

Here we addressed the temporal dynamics of auditory verbal working memory in patients with lvPPA, nfvPPA and typical Alzheimer's disease (tAD).

METHODS

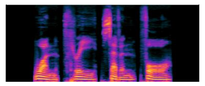
In a cohort of patients with lvPPA (n = 9), nfvPPA (n = 7) and tAD (n = 16) and in healthy age matched controls (n = 23), we assessed how temporal manipulations of standard auditory verbal working memory tasks (forward digit span and phrasal repetition) affected performance. All patient groups met diagnostic consensus criteria [5, 6].

INTRA-TRIAL: FORWARD DIGIT SPAN

3x Forward Digit Span:

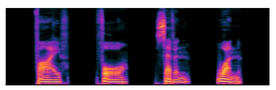
1. 0.1 second intra-trial gap

1 → 5 → 7 → 9
0.1s 0.1s 0.1s



2. 0.5 second intra-trial gap

2 → 8 → 6 → 1
0.5s 0.5s 0.5s



3. 2.5 second intra-trial gap

6 → 8 → …
2.5s 2.5s

5 seconds

Administered through headphones [Order counterbalanced]

INTER-TRIAL: PHRASAL REPETITION

First, a threshold was found using an extended version of the Graded Difficulty Sentence Repetition task.

Participants repeated 10 sentences of their threshold length consecutively in both the following conditions:

Short Next sentence given 1 second after participant response

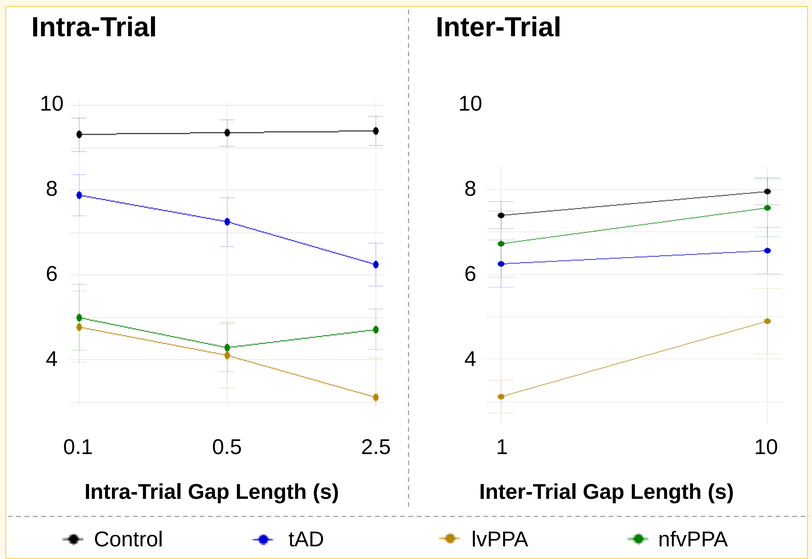
Sentence 1 → Sentence 2 …
1s

Long Next sentence given 10 seconds after participant response

Sentence 1 → Sentence 2 …
10s

Administered verbally [Order counterbalanced]

RESULTS



CONCLUSION

Initial results indicate that both AD and lvPPA groups perform better with shorter intra-trial gaps. In the inter-trial sentence repetition tasks, the lvPPA group demonstrated better performance at the 10s inter-trial gap length, suggesting that this longer gap benefitted the working memory phonological loop. Taken together, these results are consistent with a 2-phase model of working memory buffer dynamics, differentially affected in particular neurodegenerative syndromes: an initial 'buffer filling' phase, during which information must be kept online, affected in nfvPPA, lvPPA and typical AD; and a subsequent 'buffer emptying' phase, during which information must be cleared from the buffer, particularly sensitive to lvPPA.

Further work is warranted to assess how this dynamic deficit impacts communication in patients' daily lives, how it can best inform management interventions and its potential as a novel, rapid read-out of neural function in the era of disease-modifying therapies.

REFERENCES

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