

A Multimodal Investigation of Perceptual Awareness in Alzheimer's Disease

How consciousness science can help make sense of what it is like to have severe dementia.

Jonathan Huntley^{1,2}, Benjy Barnett^{3,4}, Daniel Bor^{5,6,7}, Marco Mancuso⁸, Pedro A. M. Mediano⁹, Lorina Naci¹⁰, Stephen Fleming^{3,15,16}, Giacomo Bertazzoli¹¹, Linda Clare¹, Adrian M. Owen^{12,13,15}, Lorenzo Rocchi¹⁴ and Robert Howard²

1. University of Exeter, UK; 2. Division of Psychiatry, UCL, UK; 3. Dept Experimental Psychology, UCL, UK; 4. School of Psychological Sciences, Birkbeck, University of London; 5. Department of Psychology, University of Cambridge, UK; 6. Department of Psychology, QMUL, UK; 7. Centre for Brain and Behaviour, QMUL; 8. Human Neuroscience Department, Sapienza University of Rome, Italy; 9. Department of Computing, Imperial College London, UK; 10. School of Psychology, Trinity College Dublin, Ireland; 11. Berenson-Allen Center for Noninvasive Brain Stimulation, Boston, USA; 12. Department of Physiology and Pharmacology, UWO, Canada; 13. Department of Psychology, UWO, Canada; 14. Institute of Neurology, UCL, UK; 15. CIFAR Program in Brain, Mind and Consciousness, Canada; 16 Institute of Cognitive Neuroscience, UCL, UK. **Contact: j.d.huntley@exeter.ac.uk**

INTRODUCTION

- Understanding how awareness changes with the progression of AD is essential for person-centred care.
- Assessment of awareness is especially challenging in severe AD due to impairments in communication.
- EEG and fMRI markers established in healthy older adults may reveal preserved awareness in Alzheimer's disease (AD)

AIMS

To determine whether established neural signatures of visual awareness remain detectable across mild-moderate and severe Alzheimer's disease.

METHODS

- We used a no-report masked visual perception paradigm with healthy older adults (n= 27, GDS 1), patients with mild-moderate AD (n = 17, GDS 4) and severe AD (n = 7, GDS 7).

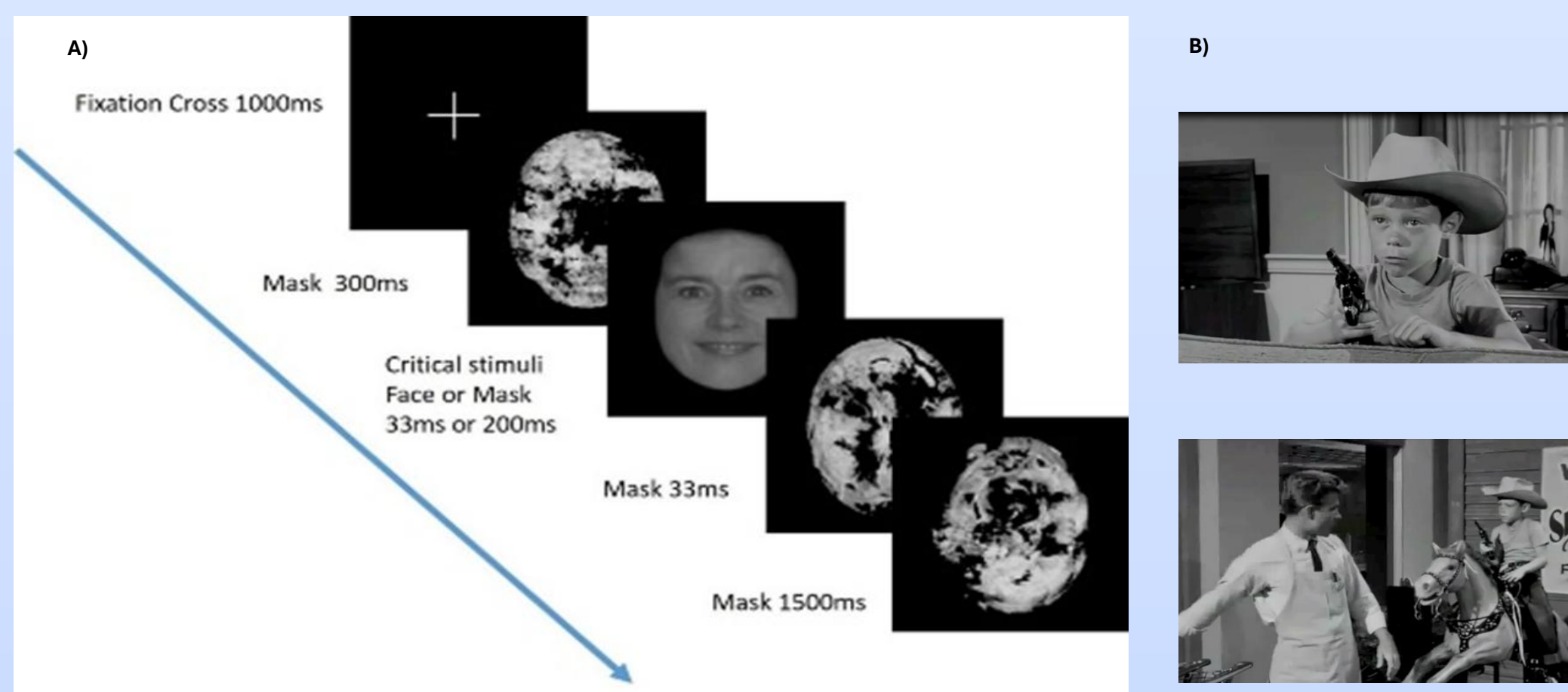


Fig 1. A: Schematic of visual masking task, B: Stills from the 'Bang! You're Dead' movie task

- We contrasted neural response to pictures presented for 200ms vs 33ms, associated with conscious vs unconscious perception (Fig 1 A).
- In the ERP study we examined visual awareness negativity (VAN) and P400 electrophysiological responses.
- In the fMRI study we examined activation in visual cortex and fronto-parietal regions associated with awareness.
- In a second fMRI study we showed an 8 - minute film (Fig 1B) and conducted synchrony analyses by correlating each participant's BOLD time course with the mean time-course of other participants.
- Fronto-parietal synchrony was used as a marker of awareness of the movie.

RESULTS

Fig 2: Reduced VAN and P400 in AD.

- Controls (red):** demonstrate VAN and P400 components associated with visual awareness.
- Mild-moderate AD (blue):** patients show significantly reduced VAN and P400.
- Severe AD (green):** limited evidence of VAN or P400
- Both markers are significantly reduced in AD vs controls (C), and correlate with disease severity (B).

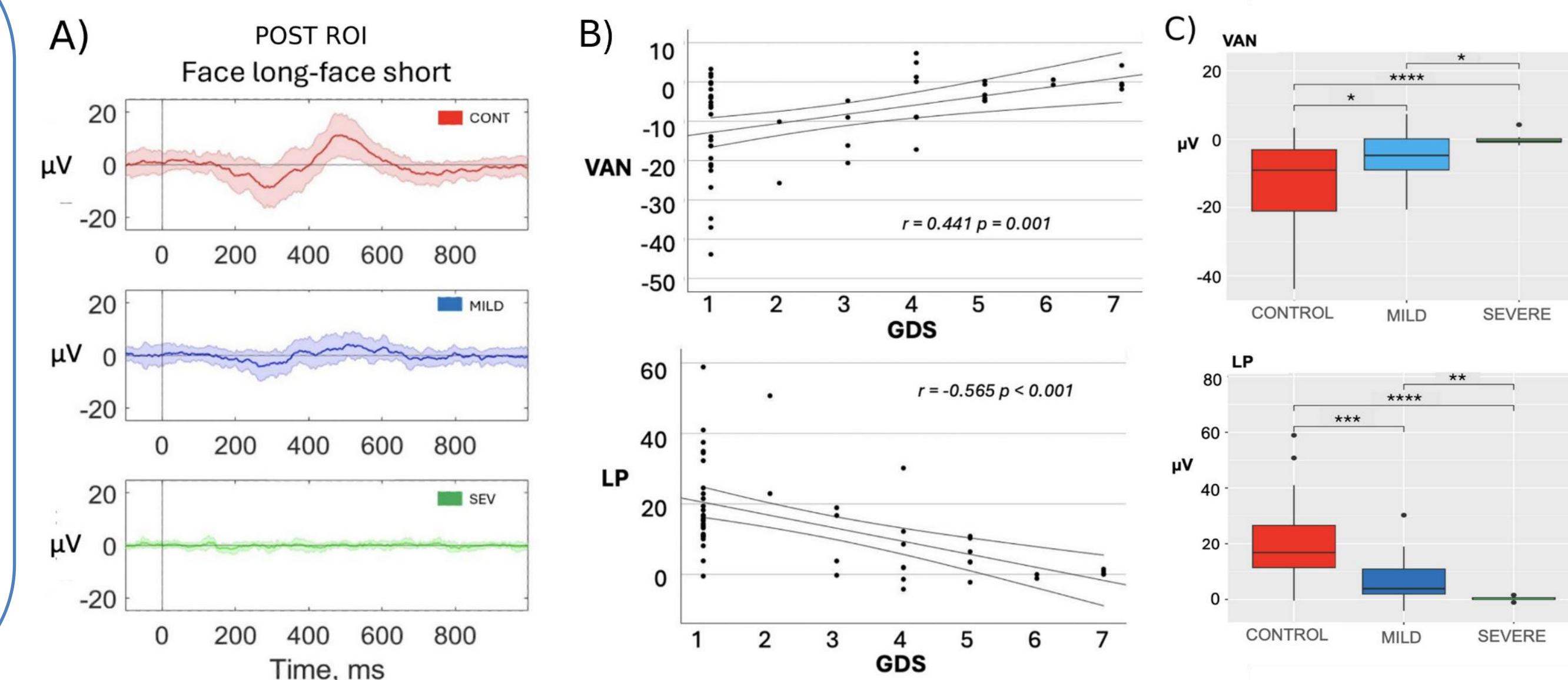


Fig 3. Decoding analyses reveal reduced awareness-related activity in AD.

- Controls:** Showed widespread awareness-related activity in visual, parietal, and frontal regions (left top).
- Mild-mod AD:** patients showed reduced awareness-related activity (left middle), compared to controls (left bottom).
- Severe AD:** One patient with severe AD (#1) retained some awareness-related activity across posterior and frontal regions (right top).
- The remaining severe AD patients demonstrated no awareness-related activity.

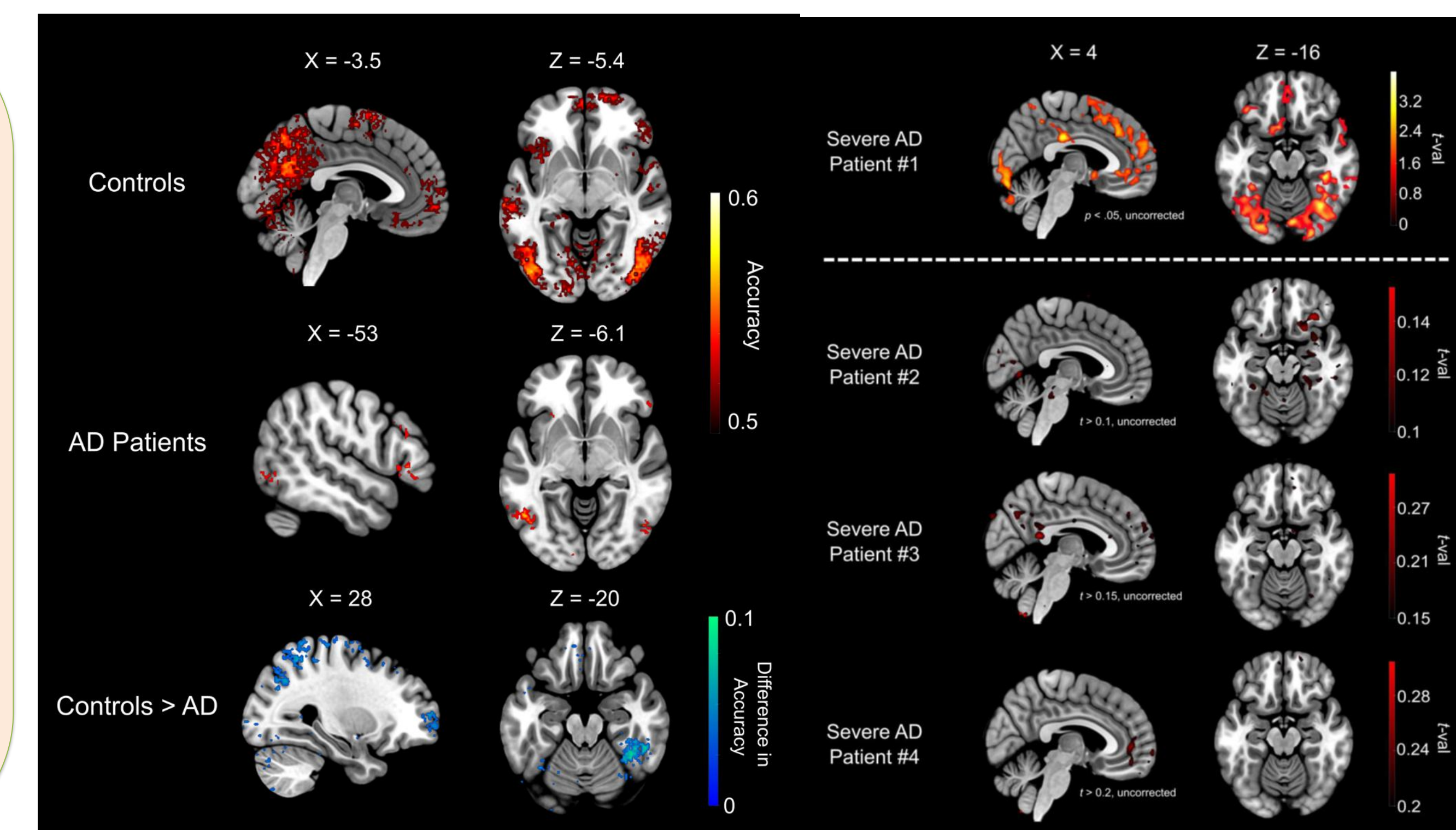
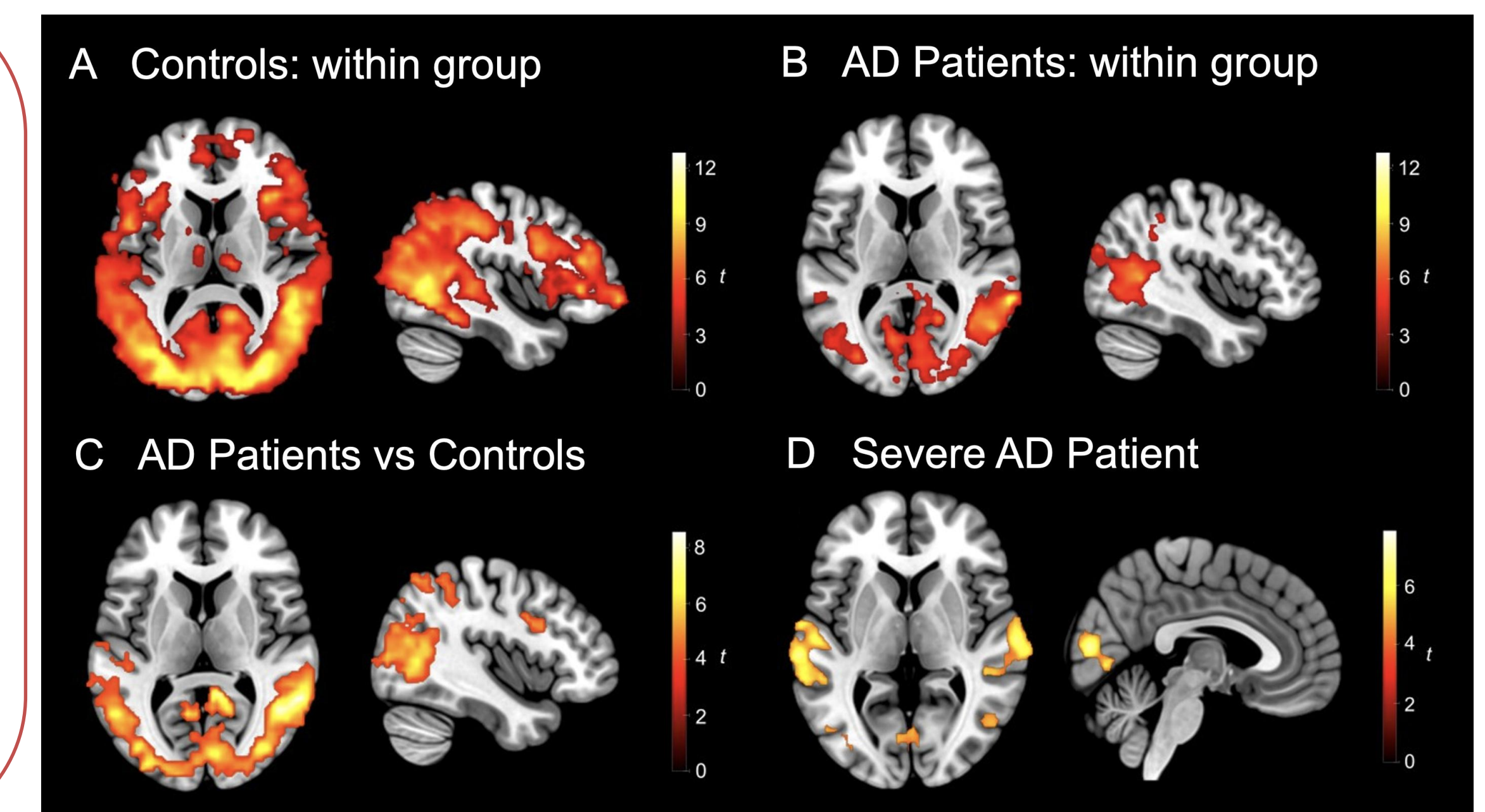


Fig 4: Reduced fronto-parietal synchrony during movie watching in AD.

- Controls:** Fronto-parietal, auditory and visual synchrony was present in controls (A).
- Mild-mod AD:** Mainly auditory and visual synchrony was found within the AD group (B).
- Mild-mod AD patients showed synchrony with controls in auditory and visual regions, with limited fronto-parietal synchrony (C).
- Severe AD:** Only one patient showed synchrony with controls in sensory regions, with no frontoparietal synchrony (D).



CONCLUSIONS

- Consciousness science provides objective tools to study awareness in advanced dementia
- Classical EEG and fMRI markers of visual awareness were reduced in AD.
- In people with severe AD, there was minimal evidence for any markers of conscious perception.
- The role of impaired attention and general task insensitivity in severe AD requires further research.
- This study provides evidence that consciousness-related neural processes are disrupted in Alzheimer's disease