

Longitudinal Hippocampal-Amygdala Subfield And Functional Connectivity Changes In Alzheimer’s Disease Following Physical Activity

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A 6-month multimodal physical activity intervention reshaped hippocampus–amygdala functional connectivity and strengthened brain–behaviour coupling, supporting compensatory network plasticity and highlighting functional MRI as a sensitive marker of early intervention response in Alzheimer's disease (AD).

INTRODUCTION

Why this matters

- Early Alzheimer’s disease affects medial temporal networks that support memory and emotion.
- Physical activity may promote brain plasticity, even when structural atrophy continues.
- Hippocampal–amygdala subfield connectivity remains underexplored as a marker of intervention response.
- Linking brain changes with fitness, activity, sleep, and cognition may help explain who benefits from exercise.
- Functional connectivity may capture early intervention-related brain changes that are not yet visible at the structural level.

Research Focus

- Does 6 months of multimodal physical activity reshape hippocampal–amygdala structure and functional connectivity, and are these brain changes linked to fitness, activity, sleep, and cognition in early AD?

METHODS

- **Dementia-MOVE randomized controlled trial**
- **Participants:** 46 individuals with early AD
- **Groups:** Intervention, n = 25; Psychoeducation control, n = 21
- **Intervention:** 6-month multimodal physical activity program vs psychoeducation control
- **Imaging:** 3T structural MRI + resting-state fMRI at baseline (T1) and 6 months (T3)
- **Segmentation:** FreeSurfer hippocampal and amygdala subfield atlas
- **Connectivity:** ROI-to-ROI hippocampal–amygdala functional connectivity
- **Statistics:** Linear mixed-effects models adjusted for age and sex
- **Associations:** Spearman correlations between brain changes, fitness, activity, sleep, and cognition

RESULTS

Physical activity strengthened hippocampal–amygdala functional connectivity

Brain–behaviour coupling

CONCLUSIONS

- Physical activity altered functional brain trajectories in early AD.
- Hippocampal–amygdala connectivity strengthened despite structural atrophy.
- Brain changes tracked fitness, activity, sleep, and cognition.
- Functional connectivity may be an early marker of intervention response.

Key findings

- Hippocampal–amygdala connectivity increased after 6 months of physical activity.
- Strongest effect: left lateral amygdala ↔ right presubiculum ($t = 4.80, p < 0.001$).
- Similar structural decline in both groups suggests a primarily functional intervention effect.

Clinical relevance

- Longitudinal brain changes were linked to changes in fitness, physical activity, sleep, and cognition.
- Associations were observed for both structural subfields and functional connectivity.
- Stronger functional associations support compensatory limbic network plasticity in early AD.

REFERENCES

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