DOI: 10.1002/alz70860_105004

PUBLIC HEALTH

POSTER PRESENTATION

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

PREVENTION (NONPHARMACOLOGICAL)

Hippocampal vascularization is associated with greater efficiency during a remote real world wayfinding training in older adults

Jonas Marquardt[1] | Niklas Vockert[1] | Niklas Behrenbruch[1,2] | Beate Schumann-Werner[1,2] | Anne Hochkeppler[1,3] | Anna-Therese Büchel[1] | Eóin N. Molloy[1,4] | Svenja Schwarck[1,2] | Larissa Fischer[1] | Enise I. Incesoy[1] | Berta Garcia-Garcia[1] | Hendrik Mattern[1,5,6] | Barbara Morgado[7] | Hermann Esselmann[7] | Andrew W. Stephens[8] | Andreas Schildan[9] | Henryk Barthel[9] | Osama Sabri[9] | Jens Wiltfang[10,11] | Michael C. Kreissl[1,4] | Emrah Düzel[1,12] | Esther Kuehn[2,13,14] | Stefanie Schreiber[1,6,15] | Anne Maass[1,6,16] | Nadine Diersch[1]

[1]German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany

[2]Institute of Cognitive Neurology and Dementia Research (IKND), Otto-von-Guericke University, Magdeburg, Germany

[3]University Clinic for Psychosomatic Medicine and Psychotherapy, Otto-von-Guericke University Magdeburg, Magdeburg, Germany

[4]Division of Nuclear Medicine, Department of Radiology & Nuclear Medicine, Faculty of Medicine, Otto von Guericke University, Magdeburg, Germany

[5]Department of Biomedical Magnetic Resonance, Otto-von-Guericke University, Magdeburg, Germany

[6]Center for Behavioural Brain Sciences (CBBS), Magdeburg, Sachsen-Anhalt, Germany

[7]Department of Psychiatry and Psychotherapy, University Medical Center Göttingen (UMG), Göttingen, Germany

[8]Piramal Imaging GmbH, Berlin, Germany

[9]Department of Nuclear Medicine, University of Leipzig, Leipzig, Germany

[10]Department of Psychiatry and Psychotherapy, University of Göttingen, Göttingen, Germany

Abstract

Background: Alzheimer's Disease (AD) pathology accumulates early in the medial temporal lobe (MTL), crucial for spatial navigation. As spatial navigation is among the first cognitive functions affected by AD, it may benefit from targeted behavioral interventions. We investigated the potential of a novel smartphone-assisted real-world wayfinding training, tailored for healthy older adults, to improve their spatial abilities and explored associations with hippocampal vascularization and AD biomarkers.

Method: 38 cognitively healthy older adults (62–84 years; 18 females) participated in a 3-week navigation training, using our smartphone application "Explore" (Figure 1). Training involved finding several locations displayed on a map in the medical campus area of Magdeburg, Germany, while GPS data were recorded. Pre- and post-training, participants underwent fMRI, performed a pointing task in a virtual campus version, and completed the VWLT. At pre-assessment, AD pathology was characterized by plasma sampling (Abeta1-42/1-40, Ptau217) and [18F]PI-2620 PET in a subsample. Hippocampal vascularization was assessed by 7T angiography. Performance in the virtual pointing task and a map drawing test was compared to a control group ($n = 20$) who performed a walking task of equal length without a navigational component. Additionally, changes in different mobile wayfinding performance indicators and their

[11]German Center for Neurodegenerative Diseases (DZNE), Goettingen, Germany

[12]Institute of Cognitive Neurology and Dementia Research (IKND), Otto-von-Guericke University, Magdeburg, Sachsen Anhalt, Germany

[13]Hertie Institute for Clinical Brain Research, Tübingen, Germany

[14]German Center for Neurodegenerative Diseases (DZNE), Tübingen, Germany

[15]Department of Neurology, Otto-von-Guericke University, Magdeburg, Germany

[16]Institute for Biology, Otto von Guericke University, Magdeburg, Germany

Correspondence
Jonas Marquardt, German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany.
Email: jonas.marquardt@dzne.de

associations with AD biomarkers and hippocampal vascularization (i.e., mean distance of hippocampus to surrounding vessels) were examined.

Result: Performance in the pointing task and map drawing, but not in the VWLT ($p = .321$), significantly improved due to the training (all $p < .001$; Figure 2A C). The control group showed no improvements in navigation. Training benefits were also evident in the mobile data (all $p \leq .017$; Figure 3A-E). Better wayfinding efficiency was associated with less vessel distance to hippocampus, r=.44, $p = .012$, and the number of orientation stops was negatively related to pTau217, r=-.38, $p = .019$ (Figure 3F).

Conclusion: We provide evidence that a remotely administered real-world wayfinding training enhances wayfinding abilities and improves spatial memory in older adults. Importantly, hippocampal vascularization may benefit wayfinding efficiency. Higher pTau217 was related to fewer orientation stops during navigation. As a next step, potential mediating effects between vascularization and AD pathology on wayfinding performance will be investigated.

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

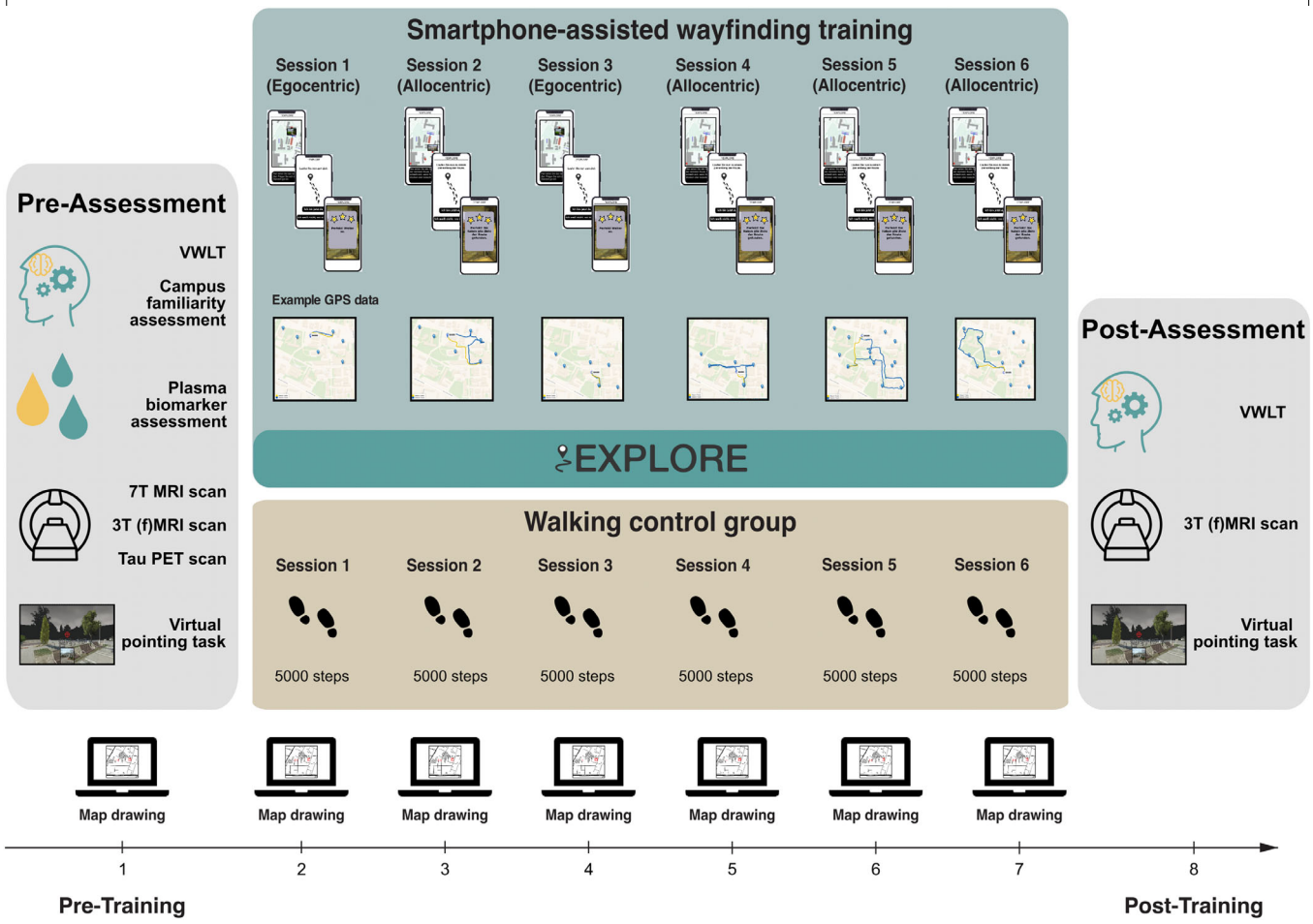

Figure 1: Study design and procedure overview. Before the training, all participants performed a virtual pointing task using a 3D model of the medical campus Magdeburg during a fMRI session, and completed the VWLT (Visual Way Learning Test). Plasma samples were collected to measure amyloid-β1-42/1-40 ratios and pTau217 levels (using Lumipulse G Fujirebio). A subsample underwent a 7T MRI scanning session, in which a high-resolution time-of-flight angiography was acquired to assess hippocampal vascularization (n = 54). A subset of participants underwent positron emission tomography (PET) using the [18F]PI-2620 tau tracer (n = 44). Afterwards, participants were randomly allocated to either the smartphone-assisted real-world wayfinding training (green box) or a walking control group (brown box). The training consisted of six sessions, alternating between egocentric (sessions 1 and 3) and allocentric tasks (sessions 2, 4, 5, and 6). In egocentric sessions, participants navigated in several trials from a starting location to a target landmark, displayed on a map in the app, and back. In allocentric sessions, participants saw three locations on the map and were asked to navigate to each of them on the shortest-possible route, before returning. Each allocentric session included four route repetitions. GPS data and number of map view were recorded for each session. Example movement trajectories of one participant are provided and show search paths to landmarks (blue) as well as return paths to the start (yellow). After each session, participants completed a map drawing test, assigning 12 landmarks on a map of the campus. The walking control group completed 5000 steps per session on the university campus but were not asked to perform a navigation task. Participants walked on average 3880 meters per session in the training (~5094 steps, assuming 0.76 m per step). After the training, participants completed neuropsychological tests and a second 3T (f)MRI scan during which the pointing task was repeated (n = 58).

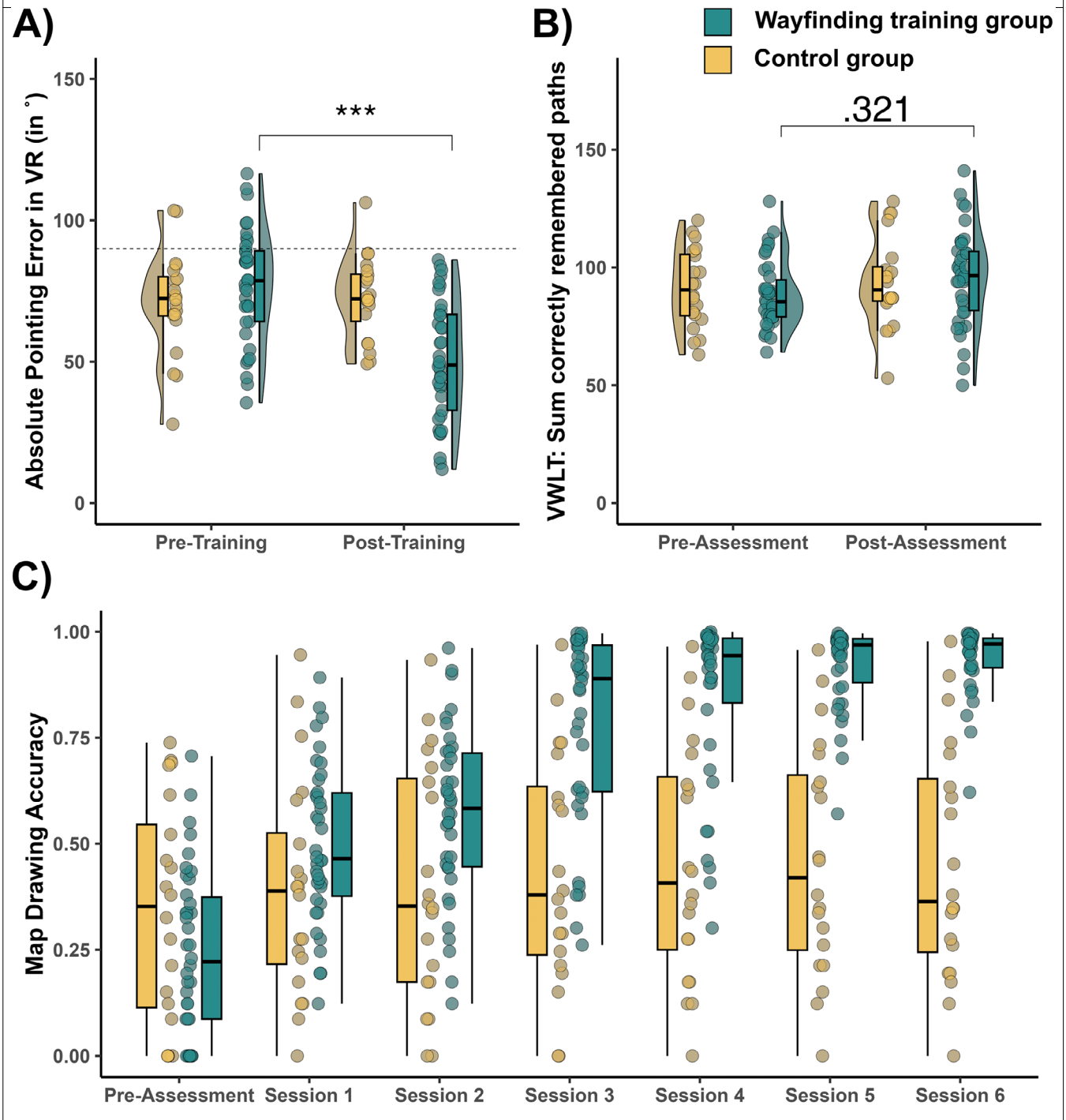

Figure 2: Effect of smartphone-assisted real-world wayfinding training on spatial memory performance. A) Virtual pointing task: Pre- and post-training assessment showed significant decrease of the pointing error, i.e., deviation angle from the target building by the participant, in the navigation training group compared to the control group, $p < .001$.The dashed line denotes chance level (90°). B) VWLT: Participants were required to learn and recall a sequence of interconnected dots forming a line. Number of correct connections between dots were used to assess performance. No significant interaction effect of group-by-time was found, $p = .321$. C) Map drawing test: Participants assigned an array of twelve landmarks to their corresponding positions on a 2D campus map. Map drawing accuracy was calculated using the Gardony map drawing analyzer, which measures configuration and completeness of the spatial representation. A significant group-by-time interaction was found on map drawing accuracy, $p < .001$. Boxplots display the lower and upper quartile of the measure; center line the median; whiskers the 1.5x interquartile range; dots the individual data points. All analysis (A-C) controlled for age, sex, and years of education. Additionally, analysis in A and C controlled for environmental familiarity.

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

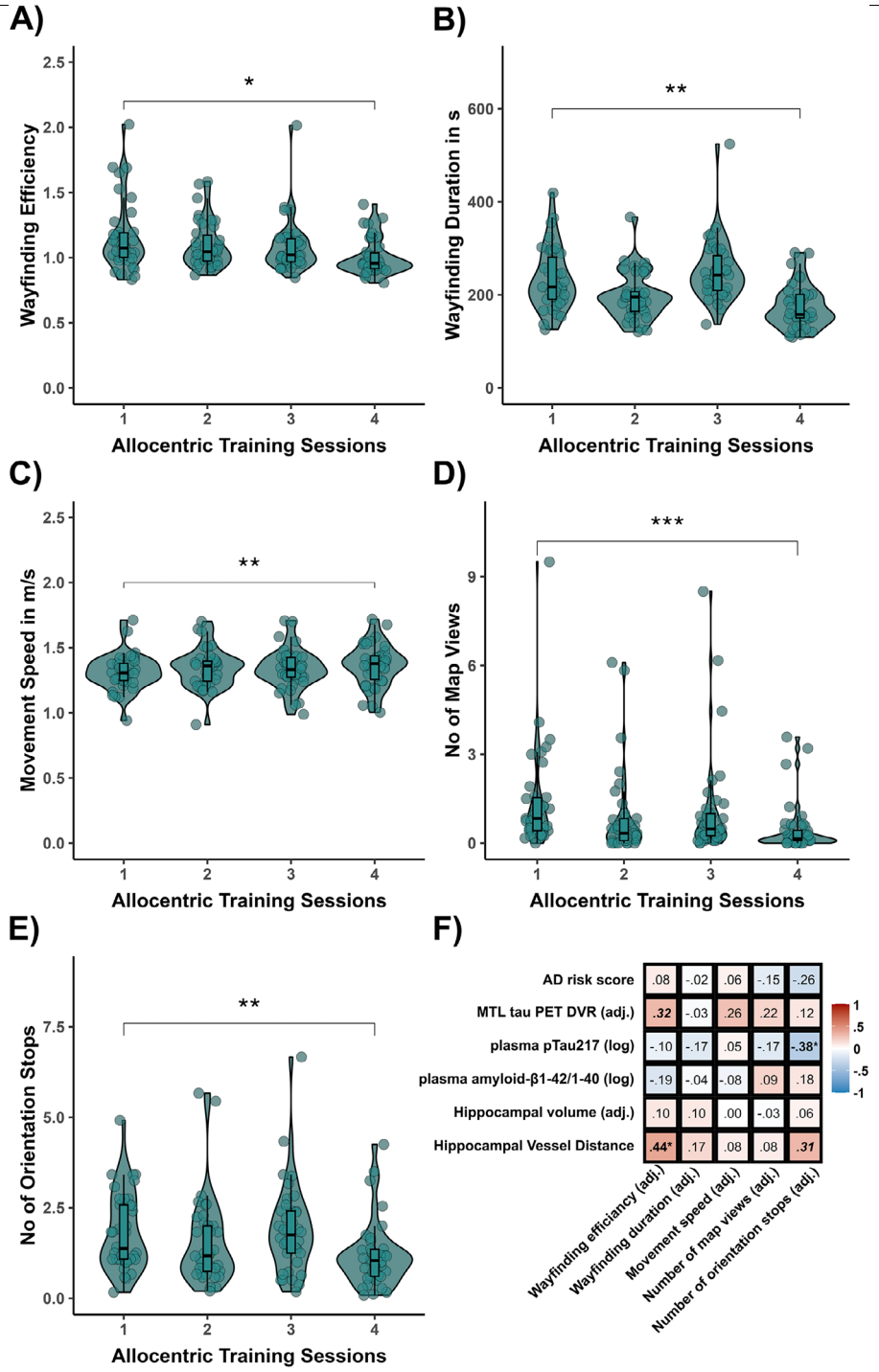

Figure 3: Training-related improvements in performance measures of navigation and their association with Alzheimer's disease risk and protective factors (n = 38). Linear (A–C) and generalized (D–E) mixed-effect models assessed training-related behavioral improvement: A) wayfinding efficiency (traveled/optimal distance) decreased, p=.017; (B) wayfinding duration decreased, p=.005; (C) movement speed increased, p=.006; (D) number of map views decreased, p<.001; (E) number of orientation decreased, p=.002. Models controlled for age, sex, education, and environmental familiarity, with random intercepts for tracks and both random intercepts and slopes per participant. F) Correlation matrix of AD-related markers, vascularization, and navigation performance from allocentric training sessions. The AD risk score was derived from z-transformed, age- and total intracranial volume-adjusted hippocampal volume, log-transformed plasma amyloid-β1-42/1-40, and plasma pTau217. MTL tau DVR was age-adjusted and log-transformed. Hippocampal volume was obtained via FreeSurfer. Hippocampal vessel distance was estimated via automatic vessel segmentation of the angiography and coregistration to ASHS-derived hippocampal masks. Distance of each hippocampal voxel to its nearest vessel was calculated and averaged. Navigation performance measures were adjusted for age, sex, education, environmental familiarity, and track. Greater hippocampal vessel distance correlated with less direct navigation paths, r = .44, p = .012 (n = 32). Higher plasma pTau217 was linked to fewer orientation stops, r = -.38, p = .019 (n = 38). Trends suggested that higher MTL tau was related to less direct paths (r = .32, p = .095, n = 29), and greater vessel distance linked to more orientation stops (r = .31, p = .079, n = 32). Other correlations were nonsignificant (p ≥ .01).