Conclusions

INFRONT-3 is designed to provide confirmatory evidence of efficacy and safety for latozinemab, a first-in-class neuro-immunological approach for treating FTD-*GRN*. Global enrollment is ongoing.

doi:10.1016/j.jns.2023.121461

121462

Structure-function association patterns of the brain in individuals with different level of cognitive impairment

Yauhen Statsenko[a], Sarah Meribout[a], Tetiana Habuza[b], Darya Smetanina[a], Gillian Simiyu[a], Fatima Ismail[c], Klaus Gorkom[a], Taleb Almansoori[a], Juri Gelovani[a], Milos Ljubisavljevic[d], *[a]College of Medicine and Health Sciences, UAE University, Radiology, Al Ain, United Arab Emirates, [b]College of IT, UAE University, Software Engineering, Al Ain, United Arab Emirates, [c]College of Medicine and Health Sciences, UAE University, Pediatrics, Al Ain, United Arab Emirates, [d]College of Medicine and Health Sciences, UAE University, Physiology, Al Ain, United Arab Emirates*

Background and aims

Age-related changes in brain structure and function differ between individuals with and without neurodegeneration. Hypothetically, distinct structure-function associations indicate different levels of cognitive impairment We intend to build models of brain structure-function associations (SFA) specific to cognitively normal individuals, patients with mild cognitive impairment (MCI) or Alzheimer's dementia.

Methods

We gathered T1-weighted MRI scans and cognitive test results of 1302 patients from the Alzheimer's Disease Neuroimaging Initiative Database. Next, we programmed regression models forecasting functional performance in cognitive tests from brain radiomics. The models were trained separately in each study cohort. Impurity-based variable importance was utilised to rank the characteristics according to their predictive performance. The mean absolute error with adjustment to the range of values (MAE/range) served as a measure of the model's performance.

Results

The test results in MMSE can be predicted much more accurately than in other tests (MAE/range = 4.5 ± 0.23 in the CN group). The error of the RAVLT, and DSST score prediction was significantly higher (10.62 ± 0.5 and 10.81 ± 0.51). Structural determinants of cognitive performance are specific to the test and to the level of decline in functioning. Unlike TMT, the top valuable predictors of MMSE score are the volumes of the total brain, cerebral cortex, accumbens, cerebral white matter, inferior lateral ventricles, and hippocampus.

Conclusions

In pathological ageing, the neuronal loss differs among distinct cell groups and brain regions. Logically, the SFA may have features specific to the pathology thus indicate the disease.

doi:10.1016/j.jns.2023.121462

121463

Protective effects of Urolithins A and B on learning and memory and anxiety-like behaviors in streptozotocin-induced Alzheimer's rat model

Kianoush Gholami[a], Mona Taghizade Salari[a], Leila Khani[a], Hananeh Ahmadnia[a], Maede Hasanpour[b], Milad Iranshahy[c], Morteza Behnam-Rassouli[a], *[a]Ferdowsi University of Mashhad, Department of Biology, Mashhad, Iran, [b]Mashhad University of Medical Science, Mashhad, Iran, 2. Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad, Iran, [c]Mashhad University of Medical Sciences, Mashhad, Iran, Department of Pharmacognosy, School of Pharmacy, Mashhad, Iran*

Background and aims

Alzheimer's disease (AD) is the most common dementia characterized by progressive cognitive decline, such as memory dysfunction. Urolithins are the products of the hydrolysis of ellagitannins, synthesized by intestinal microbiota in the distal segment of the gastrointestinal tract. They show antioxidant, anti-inflammatory, and mitophagy-inducing properties, making them potentially effective on neurodegenerative diseases. This research aims to explore the protective effects of Urolithin A and B on learning and memory, as well as anxiety-like behaviors, in male rats with the Alzheimer's disease model induced by streptozotocin.

Methods

In the present study, ten groups were investigated through Passive Avoidance and Elevated Plus Maze (EPM) behavioral tests after a two-week period following stereotaxic surgery.

Results

The results indicate that intracerebroventricular injection of streptozotocin caused a decrease in the delay in entering and an increase in the time spent in the dark compartment (Fig. 1). However, treatment with Urolithin A and B resulted in a significant increase and decrease of these two parameters, respectively, indicating an improvement in memory function. Furthermore, the negative control group exhibited a significant reduction in the percentage of open arm time (%OAT) and open arm entries (%OAE), suggesting raised anxiety (Fig. 2). While treatment with Urolithin A and B notably increased the %OAT and %OAE.

Conclusions

Treatments with Urolithin A and B, probably due to the above-mentioned properties, improve learning and memory function as well as anxiety-like behaviors which suggest the therapeutic potential of Urolithins in Alzheimer's disease.

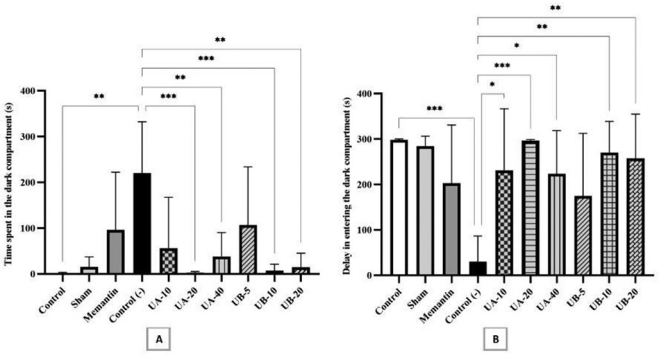


Figure 1) Passive Avoidance (Shuttle Box) Behavioral Test.

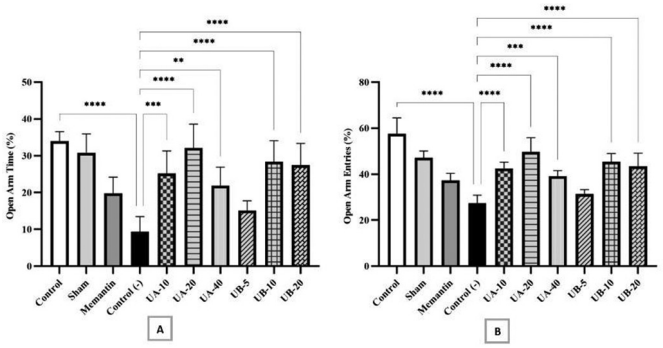


Figure 2) Elevated Plus Maze (EPM) Behavioral Test.

doi:10.1016/j.jns.2023.121463

121464

Total healthcare costs across the Alzheimer's disease continuum in the United States (US)

Amir Tahami Monfared[a], Noemi Hummel[b], Raymond Zhang[a], Quanwu Zhang[a], *[a]Eisai Inc., USA, Value and Access, Nutley, United States of America, [b]Certara, Evidence and Access, Lörrach, Germany*

Background and aims

This study describes the total healthcare costs integrating direct, indirect, and intangible or emotional cost components across the severity stages of Alzheimer's disease (AD) in the US.

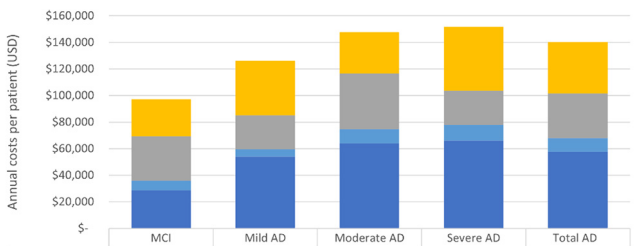
Methods

Data from the Health and Retirement Study (HRS), a bi-annual national survey of older adults in the US, were analyzed (1994–2018) to assess out-of-pocket and indirect costs including unpaid caregiving services, missed workdays, and cost of early retirement. Costs were adjusted to 2022 US price index. HRS was analyzed with sampling weights. Mild cognitive impairment (MCI) and AD severity were ascertained using the modified telephone interview of cognitive status (TICS-m). Patient-caregiver pairs were surveyed on quality of life (QoL) to derive utility scores. Intangible costs were calculated based on the loss of QoL. Cost conversion was calculated using the willingness-to-pay threshold of $150,000 per quality-adjusted life year. Direct costs were estimated using current literature.

Results

HRS patient sample (N = 18,786) with MCI (n = 17,885) and AD (n = 901) were aged 67.8 ± 10.7 and 80.9 ± 9.3 years, 55.7% and 63.3% female, and 28.3% and 0.9% employed, respectively. A total of 100 patient-caregiver pairs with MCI (n = 27) and AD (n = 73) were surveyed, with 21% and 47% > 75 years, 59% and 48% female, and 59% and 70% married, respectively. Fig. 1 shows the mean annual costs per patient across AD severity levels. Total annual healthcare costs increased from $97,232 for MCI to $151,579 for severe AD.

Figure 1: Yearly costs per patient



	MCI	Mild AD	Moderate AD	Severe AD	Total AD
Intangible costs	$27,880	$40,926	$31,157	$47,883	$38,860
Indirect costs	$33,362	$25,552	$41,968	$25,828	$33,583
OOP	$7,245	$5,433	$10,584	$11,834	$10,105
Direct costs	$28,746	$54,147	$63,996	$66,035	$57,798
TOTAL	$97,232	$126,058	$147,706	$151,579	$140,346

Conclusions

This study provides a comprehensive assessment of healthcare costs and shows increased annual costs per patient with more severe AD.

doi:10.1016/j.jns.2023.121464

121465

Need for cross-culturally responsive guidelines in remote cognitive stimulation interventions for patients with Alzheimer's disease and their caregivers: A literature review

Mohamed Taiebine, *University of Mohammed V, Faculty of Medicine and Pharmacy, Rabat, Morocco*

Background and aims

The World Report on Alzheimer's Disease (2022) states that non-pharmacological interventions should be routinely administered to people with dementia at an early stage. Clinicians of patients with Alzheimer's disease (PWAD) encounter an increase in clinical, cultural and socio-linguistic diversity in their caseloads during COVID 19 pandemic. Therefore, they have shifted from face-to-face to remote services delivered through telehealth. Given these changes, there is a need to implement cross-culturally and linguistically responsive guidelines in remote cognitive stimulation interventions for patients with Alzheimer's disease and their caregivers.

Methods

A literature review was conducted in April 2023 following guidelines by Tricco et al. (2018). The search strategy included articles published in English that addressed telehealth services in cogntive stimulation for PWAD and their caregivers in PubMed, Google Scholar, and Scopus.

Results

Out of 406 studies have been found, 80 full-text articles were screened for eligibility. 23 articles were included in this review based on the inclusion and exclusion criteria. This review has shown interest in establishing remote cognitive stimulation interventions for the benefit of PWAD and psycho-educational sessions for their caregivers. The focus on caregivers was reported in 9 studies, while 14 studies included randomized control trials of PWAD.

Conclusions

This review aimed to map the current extent of existing literature on remote cognitive stimulation interventions for PWAD and their caregivers. During the pandemic, clinical interventions have evolved drastically for PWAD leading to adapt and respond cross-culturally and linguistically. Thus, technological advances should be made accessible worldwide through equity and digital inclusion.

doi:10.1016/j.jns.2023.121465