Could a better diet make your brain younger?

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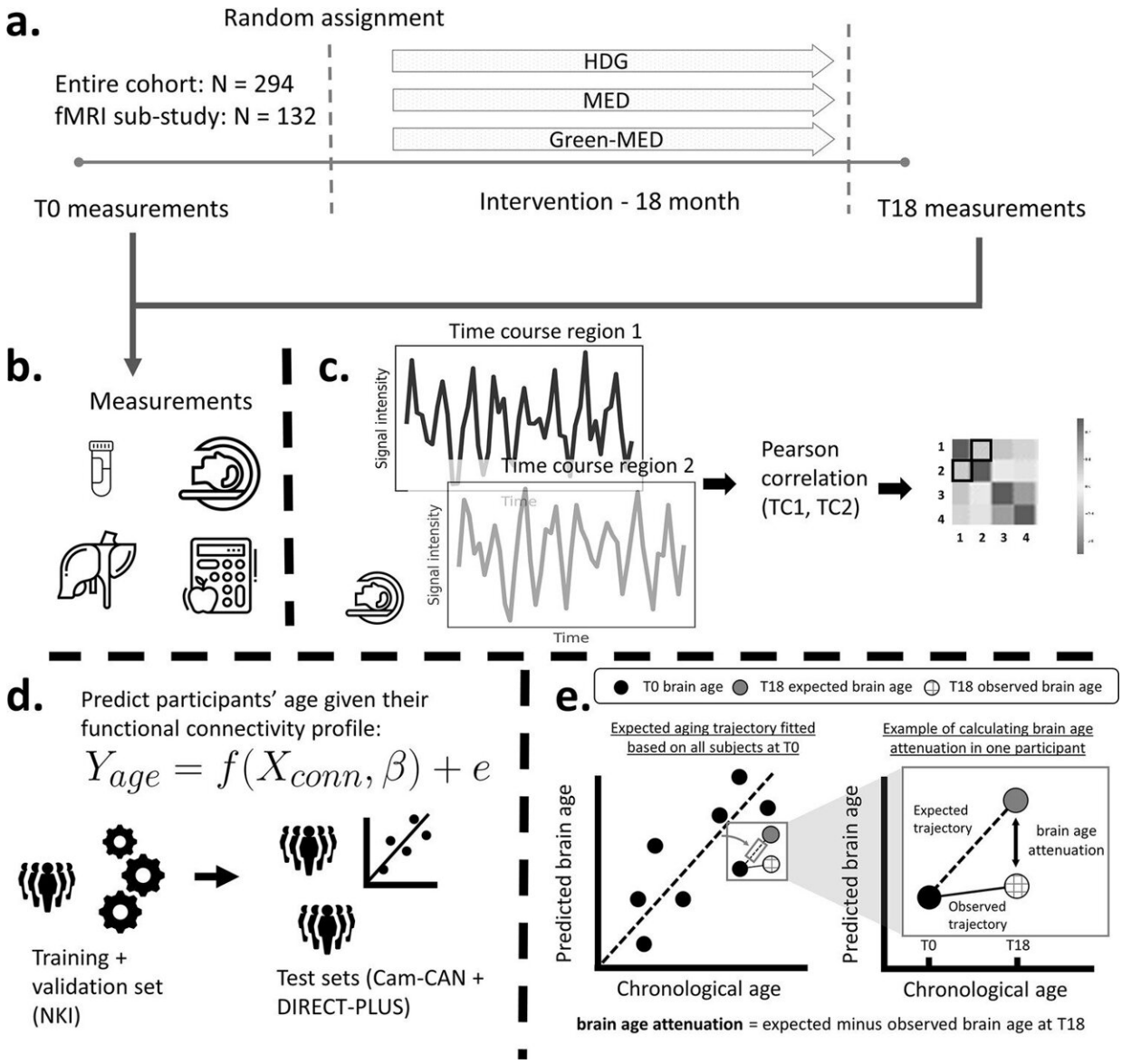

Study design and workflow. The Dietary Intervention Randomized Controlled

Trial Polyphenols Unprocessed Study (DIRECT-PLUS) trial examined the effect of successful weight loss following 18-month lifestyle intervention on adiposity, cardiometabolic, and brain health across intervention groups. (**a**) Participants in the functional connectivity sub-study (N=132) completed the baseline measurements at T0. They were randomly assigned to three intervention groups: healthy dietary guidelines (HDG), an active control group, Mediterranean diet (MED), and green-MED. All groups were combined with physical activity (PA). Eighteen months following intervention onset, all measurements were retaken (T18). (**b**) Measurements included anthropometric measurements, blood biomarkers, fat deposition, and structural and functional brain imaging. (**c**) Functional brain imaging was conducted while subjects were at rest and was used to estimate resting-state functional connectivity (RSFC). RSFC measures the correlation between the time series of pairs of brain regions. (**d**) We fitted a linear support vector regression to predict chronological age from all pairwise correlations. We fitted the model on the Nathan Kline Institute (NKI) dataset, then tested and applied it to the Cambridge Centre for Ageing and Neuroscience (Cam-CAN) and the DIRECT-PLUS data. (**e**, left scatter plot) Based on the T0 data, we first computed the expected aging trajectory as the linear relation between the chronological and predicted age of all subjects. The fitted line represents the increase in the predicted age in relation to chronological age in the absence of an intervention. (e, right scatter plot) The fitted line was used to estimate the expected brain age at T18, given each participant's T0 brain age and the time passed between the T0 and T18 magnetic resonance imaging (MRI) scans. We computed the observed brain age by applying the brain age model to the T18 scans. Brain age attenuation was calculated as the expected brain age minus the observed at T18. Credit: *eLife* (2023). DOI: 10.7554/eLife.83604

Switching to a Green Mediterranean Diet positively affects brain health, according to new research from Ben-Gurion University of the Negev. Weight loss attenuated brain aging in a sub-study of the DIRECT-PLUS trial.

DIRECT PLUS was a large-scale, long-term clinical trial over 18 months

among 300 participants. The sub-study was conducted by Prof. Galia Avidan of the Department of Psychology and Dr. Gidon Levakov, a former graduate student at the Department of Cognitive and Brain Sciences. Their findings were published recently in *eLife*.

The larger study was led by Prof. Iris Shai of Ben-Gurion University of the Negev, an adjunct Professor from the Harvard School of Public Health and an honorary professor at the University of Leipzig, Germany, along with her former graduate student Dr. Alon Kaplan, and colleagues from Harvard and Leipzig Universities.

Obesity is linked with the brain aging faster than would normally be expected. Researchers can capture this process by calculating a person's 'brain age'—how old their brain appears on detailed scans, regardless of chronological age. This approach also helps to check how certain factors, such as lifestyle, can influence brain aging over relatively short time scales.

Levakov, Kaplan, Shai and Avidan studied 102 individuals who met the criteria for obesity. The participants received a brain scan at the beginning and the end of the program; more tests and measurements were also conducted at these times to capture other biological processes affected by obesity, such as liver health.

They used the brain scans taken at the start and end of the study to examine the impact of the lifestyle intervention on the aging trajectory. The results revealed that a reduction in body weight of 1% led to the participants' brain age being almost 9 months younger than the expected brain age after 18 months.

This attenuated aging was associated with changes in other biological measures, such as decreased liver fat and liver enzymes. Increases in liver fat and production of specific liver enzymes were previously shown

to negatively affect brain health in Alzheimer's disease.

"Our study highlights the importance of a healthy lifestyle, including lower consumption of processed food, sweets, and beverages, in maintaining brain health," says Dr. Levakov.

"We were encouraged to find that even a weight loss of 1% was sufficient to affect brain health and lead to a 9-month reduction in brain age," says Prof. Avidan.

The findings show that lifestyle interventions which promote weight loss can have a beneficial impact on the aging trajectory of the brain seen with obesity. The next steps will include figuring out whether slowing down obesity-driven brain aging results in better clinical outcomes for patients. In addition, the study shows a potential strategy to evaluate the success of lifestyle changes on brain health.

With global rates of obesity rising, identifying interventions that have a positive impact on brain health could have important clinical, educational, and social impacts.

The DIRECT-PLUS trial research team was the first to introduce the concept of the green-Mediterranean, high polyphenols diet. This modified Mediterranean diet is distinct from the traditional Mediterranean diet because of its more abundant dietary polyphenols (phytochemicals, secondary metabolites of plant compounds that offer various health benefits) and lower red/processed meat.

On top of a daily intake of walnuts (28 grams), the green-Mediterranean dieters consumed 3-4 cups of green tea and 1 cup of Wolffia-globosa (Mankai) plant green shake of duckweed per day over 18 months. The aquatic green plant Mankai is high in bioavailable iron, B12, 200 kinds of polyphenols and protein, and is therefore a good substitute for meat.

More information: Gidon Levakov et al, The effect of weight loss following 18 months of lifestyle intervention on brain age assessed with resting-state functional connectivity, *eLife* (2023). DOI: 10.7554/eLife.83604