Press release; European College of Neuropsychopharmacology (ECNP) congress, Copenhagen

The fast and the curious: fitter adults have fitter brains

Large database links fitness to better cognitive performance and healthy white matter in brain

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Type of work; peer reviewed/cross sectional study/in people

In a large study, German scientists have shown that physical fitness is associated with better brain structure and brain functioning in young adults. This opens the possibility that increasing fitness levels may lead to improved cognitive ability, such as memory and problem solving, as well as improved structural changes in the brain. This work is presented for the first time at the ECNP Congress in Copenhagen, with simultaneous publication in the peer-reviewed journal *Scientific Reports**.

Scientists have previously shown that "exercise is good for the brain", but most studies have not controlled for underlying causes which might give distorted results, such as body weight, blood glucose levels, education status, age and other factors, making it difficult to take an overall view of the benefits. In addition, studies have rarely looked at fitness in relations to both brain structure and mental functioning.

The scientists used a publicly available database of 1206 MRI brain scans from the Human Connectome Project**, which had been contributed by volunteers who wanted to contribute to scientific research. The volunteers (average age 30 years old) underwent some additional testing. The first test was a "two-minute walking test", where each person was asked to walk as fast as possible for 2 minutes and the distance was then measured. The volunteers then underwent a series of cognitive tests***, to measure such things as memory, sharpness, judgement, and reasoning.

As team leader, Dr Jonathan Repple (*University Hospital Muenster, Germany)* said "*The great strength of this work is the size of the database. Normally when you are dealing with MRI work, a sample of 30 is pretty good, but the existence of this large MRI database allowed us to eliminate possibly misleading factors, and strengthened the analysis considerably".*

The tests were able to show two main points: better performance on a 2-minute walking test in young healthy adults is associated with better cognitive performance, and with structural integrity of the white matter in the brain: healthy white matter is known to improve the speed and quality of nerve connections in the brain.

Repple continued, "*It surprised us to see that even in a young population cognitive performance decreases as fitness levels drops. We knew how this might be important in an elderly population which does not necessarily have good health, but to see this happening in 30 year olds is surprising. This leads us to believe that a basic level of fitness seems to be a preventable risk factor for brain health.*

This type of study raises an important question. We see that fitter people have better brain health, so we now need to ask whether actually making people fitter will improve their brain health. Finding this out is our next step. There are some trials which point in that direction, but if we can prove this using such a large database, this would be very significant".

Commenting, Professor Peter Falkai (University Clinic, Munich, Germany) said

"This is an important cross-sectional study demonstrating a robust correlation between physical health and cognitive functioning in a large cohort of healthy young adults. This correlation was backed by changes in the white matter status of the brain supporting the notion that better macro-

connectivity is related to better brain functioning. It stresses the importance of physical activity at all stages of life and as preliminary recent evidence suggests one can start improving physical health even in later life even if one has never trained before (see reference). These findings however need to be replicated in longitudinal studies and translated for the use in mental illness".

Note. **Dr Falkai was not involved in this work, this is an independent comment.**

Dr Falkai refers to the following paper: Mok A, Khaw KT, Luben R, Wareham N, Brage S. Physical activity trajectories and mortality: population based cohort study. BMJ. 2019 Jun 26;365:l2323.

Notes:

***See Opel et at, *White matter microstructure mediates the association between physical fitness and cognition in healthy, young adults*, released at the same time as the ECNP Presentation, https://nature.com/articles/s41598-019-49301-y (doi 10.1038/s41598-019-49301-y). A copy of the paper is available from the ECNP Press Officer on request (or the Nature press office)

**http://www.humanconnectomeproject.org/

***The team used a standard set of cognitive tests called the NIH Cognition Toolbox, developed by the National Institute of Mental Health in the USA. See http://www.healthmeasures.net/images/nihtoolbox/NIH_Toolbox_brochure_June_2017.pdf

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Notes for Editors

European College of Neuropsychopharmacology (ECNP)

The ECNP is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe. Website: www.ecnp.eu

The 31st annual ECNP Congress takes place from 7th to 10th September in Copenhagen. It is Europe's premier scientific meeting for disease-oriented brain research, annually attracting up to 6,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world. Congress website: https://2019.ecnp.eu/

Conference abstract P.552

The fast and the curious – higher walking endurance is associated with better cognitive performance and white matter microstructure J. Repple[1], N. Opel[1], U. Dannlowski[1] *; 1: Institute of Translational Psychiatry, Department of Psychiatry and Psychotherapy- University Hospital Muenster, Muenster, Germany*

Introduction: Physical fitness has repeatedly been associated with brain structural integrity[1] as well as with cognitive performance [2]. The majority of previous studies have investigated single cognitive subdomains, while studies simultaneously investigating associations between physical fitness, white matter integrity and multiple differential cognitive subdomains are rare which makes it difficult to delineate and to compare domain specific contributions of physical fitness. Here we aimed to extend our knowledge on the relationship between physical fitness and both brain structure and cognition through simultaneous investigation of various cognitive subdomains and by accounting for potentially relevant nuisance covariates in a well-powered sample.

Methods: To this end, associations between endurance as measured using the 2-min walking test, diffusion tensor imaging (DTI) based measures of fractional anisotropy (FA) and cognitive measures included in the NIH Toolbox Cognition Battery were investigated in a sample of n=1206 healthy, young adults (mean age= 28.8; 45.5 % male) as part of the human connectome project. Tract based spatial statistics (TBSS) was applied to investigate the association of endurance and FA in a white matter skeleton using threshold-Free Cluster Enhancement (TFCE). P-values (Family wise error (FWE) corrected) of < .05 are reported.

Results: Higher levels of endurance were associated with widespread increases in FA (pFWE < .05) as well as with increased global cognitive function (p< .001, R2= .115). Significant positive relationships between endurance and cognitive performance were found for almost all cognitive subdomains. Most pronounced associations between endurance and cognitive performance emerged for executive function (ß= .155, p< .001), Penn Progressive fluid intelligence (ß= .171, p< .001) and processing speed (ß= .155,p< .001). Higher FA was significantly associated with increased global cognitive function (p< .001, R2= .017). Inclusion of potentially relevant nuisance covariates including gender, age, BMI, HBA1c, and arterial blood pressure did not change the overall pattern of results.

Conclusion: Our results point to a stable relationship between higher levels of physical fitness and increased cognitive performance in a wide range of cognitive domains that significantly covaries with preserved brain structural integrity irrespective of sociodemographic characteristics or further risk factors. Taken together, while we fully acknowledge the cross-sectional character of the present study, the observed pattern of results appears to support the notion of a beneficial effect of physical fitness on cognitive function, possibly mediated by its effect on white matter integrity. These findings support the notion of a beneficial and potentially protective effect of physical fitness on brain structure and function [3]. The present findings were based on analyses in a relatively young sample of healthy adults and thus demonstrate that associations between physical fitness and cognitive performance are already present during early adulthood. However, we must acknowledge that physical fitness was measured using a single variable while the amount, intensity and type of physical activity as well as the extent of regular physical activity or previous physical exercise of the participants was not assessed in the present study.

References[1] Sexton, C.E., Betts, J.F., Demnitz, N., Dawes, H., Ebmeier, K.P., Johansen-Berg, H., 2016. A systematic review of MRIstudies examining the relationship between physical fitness and activity and the white matter of the ageing brain. Neuroimage131, 81-90.[2] Smith, P.J., Blumenthal, J.A., Hoffman, B.M., Cooper, H., Strauman, T.A., Welsh-Bohmer, K., Browndyke, J.N., Sherwood, A.,2010. Aerobic exercise and neurocognitive performance: A meta-analytic review of randomized controlled trials. Psychosom. Med.[3] Voss, M.W., Heo, S., Prakash, R.S., Erickson, K.I., Alves, H., Chaddock, L., Szabo, A.N., Mailey, E.L., Wójcicki, T.R., White,S.M., et al. The influence of aerobic fitness on cerebral white matter integrity and cognitive function in older adults: Results of a one-year exercise intervention. Hum. Brain Mapp. 2013, 34, 2972–2985.

For funding information, please see the published paper.