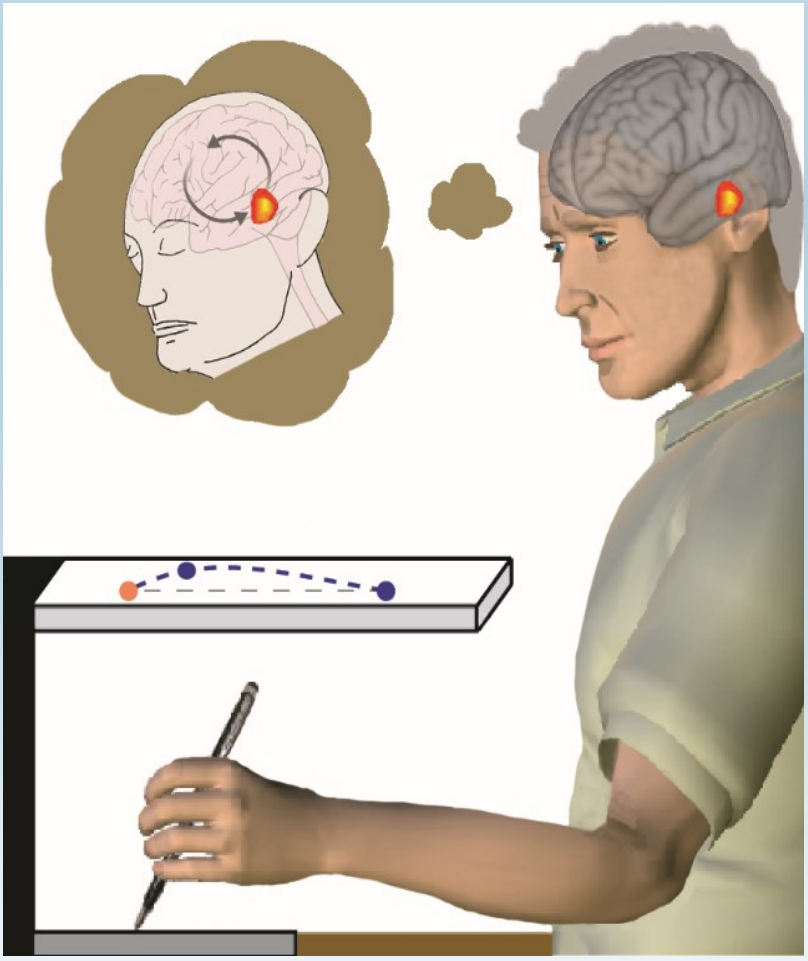
Cam-CAN Newsletter 2020

Learning new tricks *Noham Wolpe*

As we grow older, it becomes more difficult to learn new skills. This holds true for skills that are purely "mental", like learning a new language, but also for motor skills that involve movement, like learning how to ride a bike. Neuroscience research has classically separated these two types of learning into: 1) 'explicit' learning, which is considered a conscious and deliberate process of attaining new information, and which relies on a brain structure called the hippocampus. 2) 'implicit' learning, which happens automatically without conscious awareness, and which depends on a brain structure called the cerebellum. Research has shown that as we grow older, our explicit learning is not as good as it used to be when we were younger. By contrast, implicit learning remains largely unaffected by our age. However, these observations could not explain why in old age it is similarly difficult to learn both mental and motor skills. A new Cam-CAN study shows that as we get older, motor skill learning shifts to rely more on explicit learning and its brain structure. Changes in the hippocampus, but not in the cerebellum, explain why for many people, this type of learning gets more difficult as they get older. While the reason for this shift is unclear, it might help us design new learning methods for older people that will encourage them to use their intact implicit learning, so that they can easily continue to learn new tricks.



Wolpe N, Ingram JN, Tsvetanov KA, Henson RN, Wolpert DM; Cam-CAN, Rowe JB. Neurobiology of Aging. 2020; 90:13-23. doi: 10.1016/j.neurobiolaging.2020.02.016.

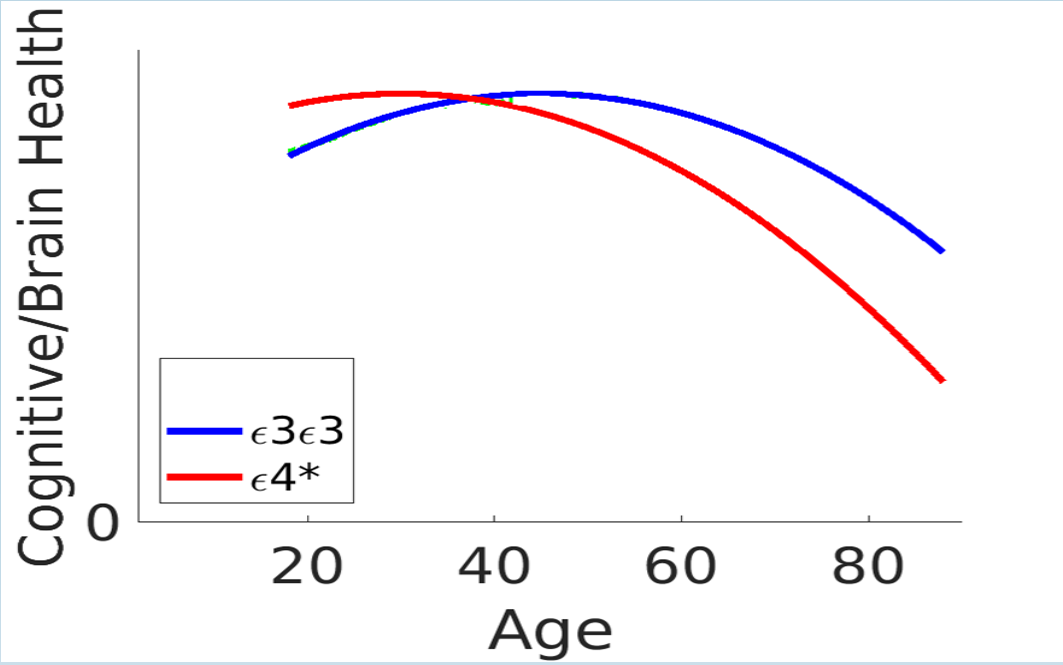
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7181181/

Supported by: BBSRC bioscience for the future; University of Cambridge; MRC Cognition and Brain Sciences Unit

A gene associated with dementia doesn't help earlier in life

Rik Henson

APOE is a protein that has been implicated in brain function and modulation of neurodegenerative processes in Alzheimer's Disease. The gene coding for APOE varies in the general population, with possession of the "ε4" variant allele (compared to the more common "ε3" variant) being associated with a 3-4 fold increase in the risk of Alzheimer's Disease in old age. However, there are also reports that the ε4 allele confers benefits earlier in life (see schematic figure below). Cognitive and neural benefits while still fertile might contribute to the persistence of ε4 in the population. For example, there are reports that brain activity during certain tasks in young, healthy people is higher in those possessing the ε4 allele. This hypothesis that some traits associated with a gene are beneficial while others are detrimental is called "antagonistic pleiotropy".



While several lines of evidence support antagonistic pleiotropy of APOE, these have tended to come from small samples, particularly those using brain imaging such as structural and functional magnetic resonance imaging, given the expense of these methods. CamCAN is rare in this respect – i.e, to have cognitive and brain data from nearly 700 people across the adult lifespan. In our analyses, we found no evidence to support the antagonistic pleiotropy hypothesis: though the measures of cognition and brain varied with age, there was no evidence that this variation depended on APOE variant. While CamCAN is still smaller than many other genetic studies, it should have been able to detect the effect sizes reported in previous studies. Further work is therefore needed to understand the possible impact of the APOE "ε4" variant earlier in life.

Henson, R.N., Suri, S., Knights, E., Rowe, J.B., Kievit, R.A., Lyall, D.M., Chan, D., Eising, E. & Fisher, S.E. (2020). Effect of APOE polymorphism on cognition and brain in the CamCAN cohort. Brain and Neuroscience Advances, 4, 1-12.

https://journals.sagepub.com/doi/full/10.1177/2398212820961704

Having healthy heart-brain link may be a key to cognitive resilience in old age

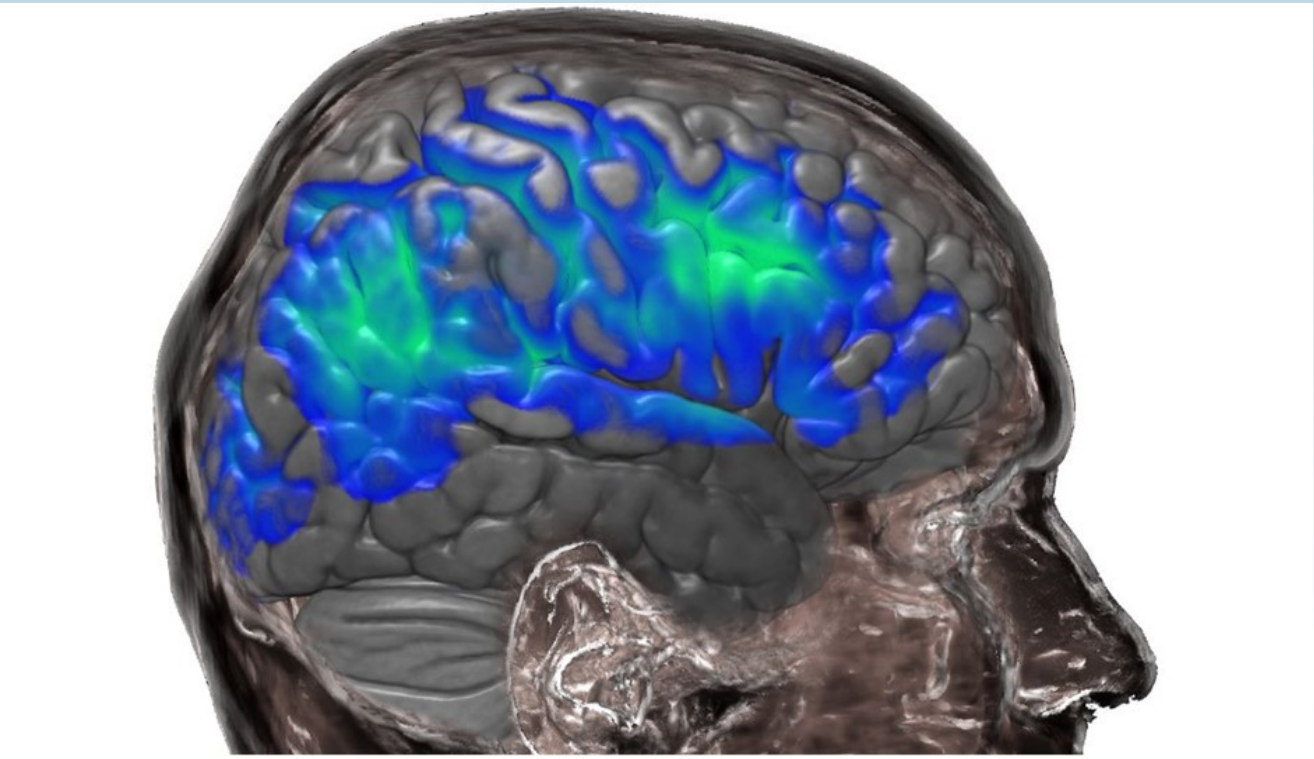
Kamen A. Tsvetanov

The brain and the heart influence one another, and these influences can go awry with age, leading to poorer brain health later in life, according to a new CamCAN study. The findings, published in the special issue of Psychophysiology, call for a new way to study how brain-heart changes affect mental processes as we get older.

The brain signals the heart to either increase or reduce its contraction rate through what is called the autonomic nervous system. In return, the heart controls the *delivery* of nutrients and removal of waste from the brain through the blood vessels. As we get older, this reciprocal relationship falls apart leading to poor brain health. Further discussion of these changes with age appears in an article by CamCAN authors, published in the world's oldest journal Philosophical Transactions of the Royal Society.

However, it remains unclear how this two-way link between heart and brain changes with age and how these changes affect brain health. For example, could an older person with deficits in brain-heart *communication* have an intact *delivery* of nutrients to the brain? Are all brain parts influenced in the same way, or are different brain parts more vulnerable to changes in brain-heart communication than delivery with ageing?

Answers to these questions are important, because they could help us understand how the link between heart and brain can influence cognitive health in old age. It can also tell us whether changes in the ageing brain previously observed using functional magnetic resonance imaging (fMRI) – one of the standard ways of measuring brain activity – may be due to changes in the link between brain and heart, rather than changes in activity of our brain cells.



To address these questions, CamCAN researchers have validated a novel technique enabling them to assess brain vascular signals that measure how brain-heart communication and transportation change with age. The unique combination of a large dataset across 250 healthy volunteers over the lifespan, as part of the CamCAN project, allowed the scientists to measure age-related differences in brain vascular signals in conjunction with measurements of brain-heart communication and delivery.

Their results reveal that some people can maintain high levels of brain-heart communication despite poor heart-brain delivery, and vice versa. Importantly, there were regional differences in the vulnerability of brain vascular health based on whether deficits were detected in either communication or delivery processes.

These findings establish a novel brain marker of vascular health that can be used to separate vascular signals from neuronal signals in neuroimaging studies and call for a new way to study how brain changes affect mental processes as people grow older.

We are just beginning to understand how the links between brain and heart are ageing, and their roles in keeping our brain and cognitive health as we get older. The ability to integrate brain vascular health measures in the research of ageing paves the way to the development of better models of ageing and age-related disorders.

The effects of age on resting-state BOLD signal variability is explained by cardiovascular and cerebrovascular factors by Tsvetanov et al is published in Psychophysiology.
https://onlinelibrary.wiley.com/doi/full/10.1111/psyp.13714

Separating vascular and neuronal effects of age on fMRI BOLD signals by Tsvetanov et al is published in Philosophical Transactions of the Royal Society B: Biological Sciences.
https://royalsocietypublishing.org/doi/full/10.1098/rstb.2019.0631

Thank you for taking part and please do keep in touch...

We are very grateful for your participation in the Cam-CAN project and for the time you have generously given us. Your contribution to our research is invaluable - we really couldn't do it without you!

We will be in contact again so please let us know if you have recently changed your contact details or if you have any questions about the research. You can contact us on:

Thank you!

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