# PLOS Science Wednesday: Hi Reddit, we're Ben and Liz and we found age substantially impacts cognitive processing, indicating our method is useful for examining individual age-related differences in brain function – Ask Us Anything!

PLOSScienceWednesday [1] and r/Science AMAs[1]

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**Abstract**

Hey Reddit, I'm Liz Davison, a graduate student at Princeton University in the Mechanical and Aerospace Engineering Department. My research centers on development and application of analytical and computational methods from network science and engineering to study complex dynamical systems, including the human brain. And I'm Ben Turner, and I'm a postdoctoral researcher in cognitive neuroscience at the University of California, Santa Barbara. My research focuses on using functional magnetic resonance imaging to better understand human memory. We recently published a paper titled "Individual Differences in Dynamic Functional Brain Connectivity Structure Across the Lifespan" in PLOS Computational Biology. This paper applied a method for characterizing how connections between brain regions change together over time (see our earlier article published in PLOS Computational Biology to a group of people including young and older adults. Using different methods, other researchers have shown that the neural activity in parts of the brain that belong to the same "network" in young adults tends to become less similar by older adulthood. Our results extend this previous result by showing that when brain regions are put in groups based on how their connections change together over time, older adults have a larger number of groups relative to young adults, indicating less-cohesive changes in connectivity. We'll be here at 1pm to answer your questions – Ask Us Anything! And feel free to follow Ben on Twitter @neurobot01.

the WINNOWER

REDDIT

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PLOSSCIENCEWEDNESDAY R/SCIENCE

Hey Reddit,
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How do you know it's age related instead of atrophy caused by the grind of jobs that are not intellectually stimulating? Children are constantly stimulated through school, while most adults have fairly dull jobs relative to school.

HappyJaguar

Unfortunately, the individual data we acquired didn't have any information about differences in careers, so we can't make any inferences about career vs. school. The only significant correspondence we found was with age, which could mean age causes the differences, or there are life changes related to age that are the actual causes.

Hello, thank you for joining us!

I'm interested to know what you controlled for in this - were similar results found amongst subjects from

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different socioeconomic groups, for example?

StonedPhysicist

Really interesting question. In this case, we included dozens of variables as covariates, including some that tend to correlate with socioeconomic status (SES) like education level, although we did not include any questions about SES explicitly. However, our participants were sampled from the Santa Barbara community, so it is possible that there are systematic differences in SES or other factors relative to the US or global population, so it is an open question to what degree our results generalize to the wider population. In particular, SES has been shown to have profound effects on brain development and function (for instance, see http://www.pnas.org/content/112/51/15530.full.pdf or http://www.attn.com/stories/2442/effects-poverty-brain-mental-health) so we certainly might expect SES to impact hypergraphs.

As a person who watched his mother transform from a talkative, talented, intelligent person into someone who had the reasoning skills of a four year old and had difficulty forming a sentence, I am wondering if your research has led you to know what things one can do to help avoid dementia. I don't intend to cheat death, but I wouldn't mind staying intellectually fit as long as possible. Thank you for doing an AMA.

canadianpastafarian

We are truly sorry to hear about your mother. A major goal of work in related fields is to understand how healthy aging progresses. There were no significant differences in memory performances between the age groups in our study, so the differences in hyperedge structure could be related to cognitive mechanisms developed by older adults to compensate for memory changes related to age. We hope future work can clarify how structural hypergraph changes are related to age, which may give insight into strategies for maintaining memory.

Note also that, because we were primarily interested in studying memory-related processes, we specifically selected older adults who didn't exhibit memory impairments. Given the large differences in hypergraph structure between age groups, but the lack of any behavioral differences, one of the most interesting future extensions of our work will be to apply the same methodology in populations exhibiting cognitive decline, or in patients with a genetic predisposition toward early-onset dementia (for instance, see this recent NPR article: http://www.npr.org/sections/health-shots/2016/12/27/506720771/early-alzheimer-s-gene-spells-tragedy-for-patients-opportunity-for-science). It is also unclear from our work whether changes in hypergraph structure with age are inevitable, or if there are measures individuals can take (for example, exercise, diet, or so on) that might affect hypergraph structure.

Hypergraphs seem like a really interesting way to study the brain. Especially hypergraph cardinality since using that you found that while they vary greatly between groups, they don't vary much between tasks for a single person. Do you see this as a way to map individual "personalities"? What is the potential application of this kind of research?

firedrops

Great question! The finding that hypergraph cardinality doesn't vary much across tasks for an individual but varies enormously across individuals is one of the most exciting findings from our paper. This trait-like quality was what motivated us to look for possible relationships with the data on individual differences between subjects. We investigated a diverse set of possible factors (including scores from personality tests such as the Big 5) and found that age was the only significantly related measure. It

would be very interesting to investigate this further and determine whether the differences in hypergraph structure arise as a result of age, or whether they are indicative of a mechanism that works to mitigate age-related changes in memory function (there were no significant differences in memory performance between the age groups). Applications of this type of research are varied, but one of the most critical is an understanding of how healthy aging takes place!

Marijuana is being studied for the treatment of Alzheimers / Dementia and it's my understanding that preliminary results show improved brain connectivity and new neural connections / pathways? (I'm no scientist) throughout the brain. From what I recall, they've isolated it to the benefits of CBD not THC, but are trying to understand the mechanism of action.

Has your research accounted for the possibility that some of the results among young adults may be influenced by this factor?

I've also wondered how the cognitive load is normalized between groups.

Younger adults often have very few responsibilities and it's largely to themselves while older adults have very large cognitive loads - work with greater responsibilities, parenting, children's schedules, dental, medical, extracurricular activities, social relationships, caring for elderly parents, complex financial arrangements, etc.

Taking just one variable (social relationships), it's easy to see why younger adults have better memory - their relationship considerations are in the context of how it relates to them and solely them. So they can have a large social network because they only manage it for themselves.

An older adult is responsible not just for managing their own social relationships, but that of their children, etc. so they're using their cognitive capacity at least in part for others.

How is this accounted for in your study?

A simple example is watching an older adult who runs a small business and has many financial arrangements - pass away - and see their younger adult next of kin quickly (cognitively) overwhelmed by the responsibilities when they step into the role of the older adult.

How is this normalized in order to study the groups for cognitive function?

Cloud9

These are some great examples of different cognitive demands that can be placed on us throughout our lifespans. A main takeaway message from our paper is that older adults appear to have developed different methods for performing our memory tasks than the younger cohort uses on average. We actually do not see significant differences in performance between these two groups - potentially indicating that the adaptations are effective! In this study, we controlled for alcohol, caffeine, exercise, and cigarette use in the past 24 hours, but the data on other drug use was limited to one out of the two data sets we used. Although there are complications in doing studies that involve the use of controlled substances in humans (in the US), it is certainly possible that future research will apply our techniques to examine the impact of the use of various substances (including, for example, tobacco, alcohol, pharmaceuticals, or cannabis).

Would you mind giving a brief layman-friendly explanation of what a hypergraph is, and why it's useful for this kind of analysis?

rslake

In our work, we use hypergraphs to represent changes in brain networks over short time intervals. Traditional brain network analyses use the strength of correlations in activity between each pair of brain regions as edges. Hypergraphs extend this to another dimension by using the strength of correlations in activity between each pair of edges as hyperedges. In short, hypergraphs represent how regions are linked in a way that factors not only the correlations in activity, but how these correlations change over time. In the future, more complex analyses of brain dynamics could be done using this framework - for example, community detection and other graph theoretic measures could be applied to the hypergraph.

To give an analogy, imagine that you have the GPS coordinates for a set of people. Whenever two (or more) people are moving together, we'll say they're "connected". In traditional approaches to functional brain connectivity, the connectedness of each person to each other person would be determined over the course of an entire measurement (say, a single day, in our analogy). However, the hypergraph approach extends this in two ways. First, it determines connectedness dynamically (for instance, hourly). Then, for each pair of people, you compare the timecourses of their connectedness, and group together pairs where those timecourses are similar.

To make the analogy more concrete, imagine a set of four people: a parent and their child, and another parent with their child. Each parent separately takes their child to different schools at 9am and picks their child up from those schools at 3pm. Each parent's location tracks closely with their child's when the child is not at school, and is unrelated while the child is at school. The traditional approach would conclude that each child/parent pair is weakly connected, and that the two pairs have no relationship. However, the hypergraph method would observe the pattern that each pair is "connected" before 9am and after 3pm, and "unconnected" between 9am and 3pm. (Like the traditional approach, it would also note that the two children and the two parents aren't connected at all.) Because that pattern of connectedness over the course of the day is similar for both pairs, they would be grouped together into a hypergraph!

In our analogy, people are brain areas and GPS coordinates are brain activity, but otherwise everything is the same.

Hi There,

So I am interested in knowing how diet affects this as well as age. Have you done anything with different diets? For instance, I tend to do a high fat / low carb diet. When I started this diet, I noticed that my cognitive abilities started getting sharper. Like a lot sharper.

ThatKetoTreesGuy

In our study, we didn't examine diet in any detail; we did control for some variables very loosely related to diet (namely, caffeine and alcohol use), neither of which was related to hypergraph structure. However, there is a wide literature relating diet to brain function, cognitive performance, and age. This article by a colleague might be a good place for you to start if you want to read more: http://journal.frontiersin.org/article/10.3389/fnagi.2016.00297/full. Although age tends to have some of the most pronounced impacts on brain organization, we look forward to future work specifically examining the role diet plays in hypergraph structure.

What might some of the real-world effects of these changes be? Are there specific cognitive impairments that you think might be linked to these changes? And would the changes you observe be more likely related to typical age-related memory/cognitive impairments, or the more severe changes like dementia?

fsmpastafarian

This is the most interesting seeming paradox in our study: we are looking at organization in a memory task, yet despite these changes in brain organization, we don't see any behavioral changes across age groups. As we hinted at in other replies, one intriguing possibility (given that we intentionally studied only participants who were unimpaired on the memory task) is that the changes we see in hypergraph structure actually reflect adaptive changes that protect these individuals from age-related memory decline. Another possibility is simply that the hypergraph properties we are focusing on, which reflect very high-level, whole-brain properties of brain organization, simply aren't specified on a level where the differences we can measure would have any reliable impact on memory. Either way, it is certainly a question we hope to see answered soon!

Hello from a senior in mechanical & aerospace at NC State, repping the east coast.

Could you summarize how you observe and record the neural networks?

Is there a continuum for cognitive decline, or are there discrete, sudden changes based on your data?

rosin_exudate

In this study, we used fMRI to measure brain activity while participants performed the memory task. We then applied a mathematical technique (described more thoroughly in some of the other answers) to quantify how cohesive the brain activity in different brain areas was. Our results showed that the functional organization of connectivity between brain areas is less cohesive in older adults, and although there are some gaps in our age scale, this change seems to be fairly continuous and gradual with age, rather than being discrete or sudden.

In our sample, there was no significant age-related cognitive decline, which was at least partially due to our intentionally selecting older adults who were able to perform the task. However, other work on cognition and aging suggests that, absent any sudden change like illness or injury, cognitive performance also tends to change gradually with age, although it does tend to be nonlinear, such that the changes accelerate with increased age.

Hello! Very interesting study. I wonder, though, how to disentangle age from cohort. They are both just proxies for something else of course, but it seems to me that you'd really need a longitudinal design to properly compare older and younger individuals. Have you considered applying this method to other datasets?

PoofOfConcept

That's an excellent point. Indeed, it's entirely possible that changes in society (for instance, food production, the chemical composition of daily products, and technology have all changed radically in the past several decades) are responsible for the differences in hypergraph structure we observed, rather than age per se. Unfortunately, fMRI has existed for under three decades, and there are (to our knowledge) no longitudinal studies that cover even a majority of this span. Nonetheless, we certainly hope that going forward, this technique will be applied to other datasets. In the last five years or so, there have been more concerted efforts to collect longitudinal fMRI data (particularly so-called resting state data), so it may soon be possible to more directly address the question of what exact role age plays.

I hear all over that learning a second language helps all kinds of mental stuff. For the late life cognitive

benefits and dementia delay, do you have to keep using or learning the language? Or am I still protected from the French I learned in elementary and highschool (immersion)?

twat69

Our research didn't examine the impacts of multilingualism on cognitive decline. However, this is an area of active research (see, for instance, https://doi.org/10.1075/lab.14028.gol). Speaking from personal experience, we would expect that continuing to use and learn the language would be the most likely to provide benefit!

Hi Ben and Liz, how do you expect current and future advances in MRI to affect your work? Recently there was an MRI breakthrough that included more sensitive monitoring without chemical or radioactive labels. What future advances do you look forward to in MRI. Will future tech advances be implemented in a reasonable time frame?

Thanks for taking the time to do the AMA!

blodbender

Excellent question! This is indeed an exciting time for the field of fMRI. For the most part, our method won't change as the technology improves, because those improvements most involve increases in spatial and temporal resolution (and our method, roughly speaking, works at an effective resolution well below the current state-of-the-art, because it considers brain regions hundreds of cubic millimeters in size on a timescale of roughly a minute). However, some advances, such as multi-echo imaging (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3350785/), may improve our method if they help us do a better job removing unwanted sources of noise (such as head motion or physiological noise) from the signal of interest (that is, blood oxygen level dependent signal).

Hello. I'm a 23 year old. Do I have a decrease in cognitive function & learning ability in comparison to my childhood/teenage years? If so, by how much? Any tips on increasing cognitive function & learning ability? Thank you.

holywowwhataguy

The good news is that we found no significant differences in cognitive function or brain dynamical structure between the 18 year old subjects and the group in their mid 20s! You can see this nicely in Figure 11 of our paper. There are, however, major developmental changes in brain structure and function throughout childhood and teenage years - Dani Bassett at the University of Pennsylvania and her colleagues have some particularly interesting results using network methods. So it's not surprising if you feel that your cognitive function and learning ability is different from when you were younger, but it is not necessarily worse!

There is research suggesting that early childhood is associated with a sort of special capacity for learning, especially in domains like language, although there is some debate in the field on this so-called "critical period" theory. If such a critical period exists, it is unlikely that there is anything one can do later in life to recapture this critical period—nor is it clear that it would be a good thing if one could. Regarding the goal of increasing cognitive function, this is a topic of a considerable amount of active debate. We will note only that the evidence for the effectiveness of, for example, "cognitive training" regimens is mixed at best. Existing research suggests that simple practices like getting enough sleep, exercising regularly, eating healthily, and engaging in cognitively demanding practices like learning a foreign language are probably the best place to start in the quest to stay mentally fit!

Did you examine subgroups other than age cohorts, such as bilingual vs monolingual? If so, what differences, if any, did you observe?

aethauia

We had data on hundreds of individual differences such as gender, years of education, personality, and preferred cognitive strategy (as measured by well known tests). Unfortunately, we did not record whether the subjects were monolingual. Despite all of the data we had access to, the only significant correspondence with the hypergraph cardinality trait was age. However, hypergraph cardinality is only one way to simplify the hypergraph. There could be other features that we did not investigate that may exhibit differences between subgroups. There is an interesting literature suggesting that multilingualism may confer various cognitive benefits, and may be associated with changes in brain function or organization.

As I age, I find it more difficult to have paradigm shifts. What causes this, and what can I do to stay flexible/critical?

Zerotan

This is definitely an interesting area of research, which unfortunately our study does little to address! As we noted in other replies, it's unclear whether the properties of brain organization that we focused on can be changed; it's also unclear what specific role these properties play in cognitive performance, if any. Generally speaking, current research favors tried-and-true methods for maintaining cognitive function—eating and sleeping well, exercising, and staying cognitively active—over less proven approaches like "brain training" or neurostimulation (the latter of which can actually be dangerous).

Hey there! Maybe I'm misunderstanding what you do, but is it possible to measure a difference between physical age and mental age?

LolerCoaster

In terms of the data we have, physical age is easily measurable in years, but the concept of "mental age" is harder to quantify. We saw changes in dynamics that can be related to physical age, but are unable to obtain a variable as concrete as mental age from these results. However, there is a range of hypergraph cardinality for any given age, which could indicate that some older individuals are able to effectively use a typically "younger" hypergraph structure to achieve roughly the same performance as others in their age group.

In the broader field, there is a lot of recent interest in trying to predict various aspects of individuals on the basis of properties about their brain (for example, see this month's special issue of NeuroImage, which is devoted to individual subject prediction: http://www.sciencedirect.com/science/journal/10538119/145/part/PB). In this vein, hypergraph cardinality may in fact be one component of an individual's mental age.