BRAIN HEALTH FOR LIFE

PREVENTING BRAIN-RELATED DISABILITY

VIRTUAL EVENT

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BRAIN HEALTH FOR LIFE. PREVENTING BRAIN-RELATED DISABILITY

Brain diseases are the main cause of disability, with a greater impact than cancer or cardiovascular diseases. However, there are many factors that can be changed to considerably decrease the risk of getting them.

Research is providing information on the effects of each of these factors and the best way to use them in our favor. Because, in addition to treatments, **we urgently need to promote brain health, educating and encouraging people to adopt lifestyles that lower their risk of illness and disability.**

To discuss the importance of this problem and the latest advances, a group of top international experts met for a session of B·Debate, an initiative of Biocat and "la Caixa" Foundation to promote scientific debate, with the collaboration of Institut Guttmann in this case. The topics covered included the healthiest lifestyles, but also concepts like cognitive reserve and even the pandemic's repercussions on mental health.

CONCLUSIONS

- Three of the most important modifiable factors that affect brain health are nutrition, exercise, and sleep. Evidence shows the benefits of eating a complete Mediterranean diet over specific nutritional supplements, the need to encourage an active lifestyle and getting enough good-quality sleep.
- The effects of air pollution on the brain, the damage caused by social isolation and the influence of personality traits are other, less commonly discussed elements that also have a notable influence on our brains.
- 'Cognitive reserve' is an important concept that decreases the risk of disability. It acts as a type of neurological 'cushion' that can delay the onset of symptoms when damage builds up with age.
- The pandemic and lockdown have affected people's mental health in different ways depending on their age and situation. Paradoxically, feelings of isolation and loneliness have decreased in general, probably due to the effect of public shows of solidarity.

1. MODIFIABLE FACTORS THAT CAN IMPROVE BRAIN HEALTH

"There are many factors that we can change to improve our brain health," began Álvaro Pascual Leone, professor of Neurology at Harvard Medical School and leader of this B·Debate. "Some are quite well known, like nutrition, exercise and sleep, but there are others we don't talk about as much, like environmental, psychological and social factors."

Several studies have shown beneficial associations between eating certain foods and cognitive function. In general, the candidates are rich in omega-3 fatty acids and antioxidants like polyphenols. Some of these are fruit, legumes, fish, and nuts. However, "the evidence is weak," recognizes Emili Ros, researcher at Hospital Clinic Barcelona. Clinical trials have not always confirmed these associations, especially with nutritional supplements. One example is taking the typical capsules with omega-3 fatty acids from fish, which didn't show any overall cognitive benefits when information from 25 different trials was compiled.

Instead of isolated foods, evidence currently points to **the benefits of a well-rounded Mediterranean diet**. A review of 17 studies showed an improvement in older people, and data from the PREDIMED clinical trial coordinated by Emili Ros also pointed in that direction: a Mediterranean diet (enriched in this case with olive oil or nuts) delays onset or even stabilizes age-related cognitive decline.

"Even though there is a lot still to learn, **there are many mechanisms that indicate physical exercise is good for the brain**," noted Arthur Kramer, director of the Center for Cognitive and Brain Health and professor of psychology at Northeastern University in Boston. Studies show that exercise improves brain function, and that "the benefits are global, mainly related to executive functions."

"Walking regularly is enough to see the structural changes in the brain's gray and white matter," said Kramer. These changes, which appear in areas like the hippocampus, which is closely tied to memory, seem to favor connectivity, making older people's brains "look more like those of a young person."

Lack of sleep, in quantity or quality, has been associated with numerous illnesses, and poor memory, concentration and cognitive performance. According to Alex Iranzo, a neurologist at Hospital Clinic Barcelona, "we need to sleep

well and enough to be healthy, to be more productive (at work, socially and in the family) and, in short, to be happier."

Sleep alterations can also be a harbinger of some neurological diseases. Iranzo's group studies REM sleep behavior disorder, which can appear several years before a patient develops Parkinson and could help test the effects of neuroprotective drugs.

Other factors that seem to be important in brain health are environmental, specifically those related to air pollution. "Brain development in the early stages of life is also important to the later stages, and even to the risk of developing dementia, we believe," explained Jordi Sunyer, head of the ISGlobal Childhood Health Program in Barcelona. In recent years, his research group has been studying the relationship between particles that mainly come from traffic and the neurological development of children of various ages. Their studies show that brain development is slower in more polluted areas, and that pollution has both chronic and acute effects on working memory.

"One thing I've learned," noted Sunyer, "is that scientists can't focus solely on research and our labs, **we also have to work to transfer our results**. I'm proud that our research has led to urban planning measures around schools in several cities."

As Professor of Neurology at Harvard Medical School Amar Dhand noted, the definition of health isn't just the absence of disease, but also alludes to "full physical, mental and social wellbeing." This final pillar of health is also crucial, although many times completely overlooked. "Social isolation is detrimental to the brain, both directly and indirectly," said Dhand. In terms of mortality, the effects of loneliness are comparable to smoking three or four packs of cigarettes a day.

Another factor that impacts brain health and the risk of cognitive deterioration is personality, which can make a person more likely to suffer from depression or anxiety. According to Nathalie Marchant, a researcher at University College London, both have been associated with increased risk of dementia in the elderly. Although they could be an initial symptom of the disease, it also seems there is a causal relationship, as with anxiety the risk has been observed even ten years before dementia is diagnosed.

"**In general, it is personality traits with a certain degree of neuroticism that increase risk**," said Marchant. "And they all have something in common, which is that they lead to repetitive negative thoughts." They involve brooding and worrying that has more to do with the process than the content of the thoughts.

The studies carried out by Marchant's group show that people with these traits tend to show more build-up of the amyloid plaques typical of Alzheimer and greater age-related cognitive decline. This doesn't seem like good news because "personality traits are fairly stable," she explained. "The good thing is that **repetitive negative thoughts can be controlled. For example, using practices like mindfulness.** Our next studies will focus on finding out whether these psychological interventions decrease the risk of dementia," she concluded.

2. THE IMPORTANCE OF 'COGNITIVE RESERVE'

Many definitions of cognitive reserve have been proposed, but this is the one preferred by Yaakov Stern, professor of Neurology at Columbia University. "**Cognitive reserve is a property of the brain that allows it to continue functioning regardless of age-related changes and brain disease**. It acts like a safety cushion: the bigger the reserve, the more damage the brain can accumulate before its effects are seen.

"Studies show, in general, that the higher the level of education, the greater the cognitive reserve," explained Stern. This reduces the risk of serious cognitive deterioration and means that symptoms appear later even with the same level of neurodegeneration. "Once they appear in these people, however, they progress more quickly."

Another related concept is **brain maintenance**, the relative absence of age-related changes in the brain, which depends on genetic, environmental and lifestyle factors. Although these are two independent concepts, they are also complementary and can have common influences. For Stern, it is key to standardize how we define and refer to these concepts because it "would be a great help for research and increase the chances of successful intervention."

One way to quantify cognitive decline is using the "classic verbal episodic memory test," which has patients repeat a list of words at different intervals of time. It is harder, though, to quantify cognitive reserve. To do so, University of Sydney Professor Michael Valenzuela has developed a procedure that looks at the rhythm and how the words are spoken instead of their content, in a sort of "vocal fingerprint".

Although memory fails with cognitive decline, "not all types of memory suffer equally," explained Lars Nyberg, professor of Neuroscience at Umeå University, Sweden. The most sensitive is episodic memory (related to personal experiences), but in some people it is

preserved better than in others**. Some of the modifiable factors that help preserve it are those mentioned previously, like physical activity, sleep, and nutrition**. "There are three mechanisms involved," noted Nyberg, and they have to do with "the neurons themselves (although there is some debate as to whether the hippocampus can generate new neurons throughout life), synapse integrity and vascular factors that feed the brain."

Beyond the 'traditional' ways of caring for the brain, there may be more alternative options. One of them could be video games, but not "your typical video games; ones designed specifically for this purpose," explained Joaquín A. Anguera, professor at the University of California, San Francisco. According to this researcher, **video games can be a resource to boost cognitive control and be used with specific populations**, like to help improve attention in children with attention deficit and hyperactivity disorder.

Another way could be through **meditation**. The hypothesis presented by Gaël Chételat, director of research at Inserm in France, is that "it **can improve cognition in the elderly and even help reduce the risk of developing Alzheimer**." Her studies are looking into the effects of combining practices like mindfulness and compassion meditation, as they seem to act on different brain mechanisms.

3. MENTAL HEALTH DURING THE PANDEMIC

The session also discussed the impact of the pandemic on mental health. Maite Garolera, head of Clinical Neuropsychology at Consorci Sanitari de Terrassa, looked at the direct and indirect mechanisms through which SARS-CoV-2 can cause neurological damage. David Bartrés-Faz, professor of Psychology at the University of Barcelona and principal investigator in the Barcelona Brain Health Initiative (BBHI), presented the results on the **pandemic's mental health repercussions from the BBHI**, a research project at Institut Guttmann with over 5,000 participants that aims to discover and understand how to maintain brain health. Taking advantage of prior information and adding interviews carried out by a group of volunteers during the pandemic, the study's scientists have analyzed **how the social restrictions affected mental health**. "Our hypothesis was that the impact would depend on individual differences," explained Bartrés.

The results of the study show that, **during the lockdown in Spain that began in March, participants' anxiety rose moderately but returned to 'pre-pandemic' levels in the following months.** "It particularly affected young people," highlighted Bartrés, "probably because it had a greater effect on their daily lives."

The lockdown also increased ratings on depression scales, although clinically the effect wasn't very significant. Unlike anxiety, however, this increase held steady in the following months. And in this case, "it mainly affected the older segment in the study (between 60 and 70 years old), and particularly the lowest income bracket."

Plus, there was a **paradoxical effect: feelings of loneliness and isolation decreased during lockdown**, especially among those who suffered from depression before the pandemic. "There were a lot of public displays of solidarity those days, which could have increased their feeling of belonging and community," said Bartrés.