Brain pills

New study shows that an Alzheimer's disease drug may also improve the memory of people with Down syndrome.

What did you eat yesterday? How was your last birthday party? What's your telephone number? These may sound like silly questions to you – probably because you know the answer to all of them. But what seems to be trivial is a daily problem to people with Down syndrome, a genetic disturb caused by an extra copy of the chromosome 21 which results, among others things, in memory deficits and cognitive disabilities.

The Brazilian physician and neuroscientist Alberto Costa, who has a daughter with Down syndrome, knows it better than anyone. After 16 years living in the USA and studying the syndrome at the Colorado Medicine School, he carried out the first study in which patients with this congenital disorder showed improvement on cognition by taking a drug. The substance used was the memantine. It is usually prescribed for Alzheimer and acts on the hippocampus, a brain region linked to memory that is also compromised in patients with Down syndrome.

Costa and memantine have a long story together. In 2007, he and his team showed that memantine was capable to reverse learning and memory deficits in mice with the trisomy 21. In his new study, 38 adults with Down syndrome were separated in two groups: half of them received a placebo and the others took memantine pills for 16 weeks. At the end of this period the patients underwent a battery of tests of their intellectual abilities and memory. In one of them the participants had to memorize long lists of words. In general, results were positive. People who received the memantine pills performed 30% better than the others who took placebo. The improvements were more significant in a specific area: episodic memory, a kind of mental diary of recent and autobiographic events.

"Our study was short and we didn't expect a significant effect on the ability of the patients to execute daily tasks", says Costa. "It was a small benefit in just one aspect, but it was a great improvement in this research field." The neuroscientist points out that the patients themselves noticed the difference in their thinking and felt motivated to participate in the trial. "Some of them started to call the drug of *brain pills* or *smart pills* and very often it was them who remembered theirs parents it was the time to take the

medicine. Moreover, almost all of them told me that they would like to participate in others trials in the future".

Costa tells that the patient with the best response to the drug, a 25 year old man, performed ten times better than achieved in former tests he did. "This was the most striking case without any doubt. This man almost didn't talk and didn't look into others people's eyes. The improvement in his behavior was very clear after eight weeks e even more evident after ten weeks of treatment. Of course, it wasn't a typical result but it was a remarkable experience to me and to the members of my team because it has shown the potential of this kind of pharmacological intervention for a better quality of life."

Ideas to the future

Zan Mustacchi, a physician specialized in Down syndrome at Center of Clinical Research and Studies of São Paulo (Cepec, in portuguese), points out that, statistically, the results of the experiment conducted by Costa weren't too impressive. Nevertheless, he believes that the study is an important step. "The study is a significant development if you think that it uses a drug that is already approved to treat another disease, that it does not cause any negative or collateral effect to the patient and that it has been shown to be effective in mice", says Mustacchi.

Costa says that in case the memantine is approved to treat Down syndrome, it should be taken daily during all life, as we do with medicine for chronic diseases as hypertension. But, he highlights that more clinical trials are still necessary to investigate if the drug really has an effect when used in a daily basis and if it will benefit the learning process of people with Down syndrome. For now, the researcher tells that he is already looking for financial support to keep his study. It is possible that more trials can be conducted in Brazil. "I am going to São Paulo soon to negotiate a deal with Brazilian medical centers and authorities", says Costa. "We hope to conduct more trials with a larger group and we also want to see if memantine can help younger children, since their brains are still developing."

Imminent threat

The research with the memantine is still at the beginning, but it may be a great solution to serious problems associated with Down syndrome. According to Mustacchi, 60% of the patients with Down syndrome develop a kind of dementia that has the same characteristics of Alzheimer's in their late 40s or early 50s. "It is an inevitable process",

he says. “We have observed lesions typical of Alzheimer in the brains of people with Down syndrome with 12 and 14 years old. These same lesions only appear in common people after 40s.”

Costa is concerned about it and believes that the use of memantine since childhood could stop or delay the development of the dementia in people with Down syndrome. “The life expectancy of people with Down syndrome is arising in developed countries and it is quickly approaching 60 years”, inform Costa. “The association between Down and Alzheimer is becoming visible and we can’t deny that it will reach epidemic proportions in the next few decades. Parents and doctors need to know that the cognitive ability of people with Down syndrome can be improved with medication.”

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