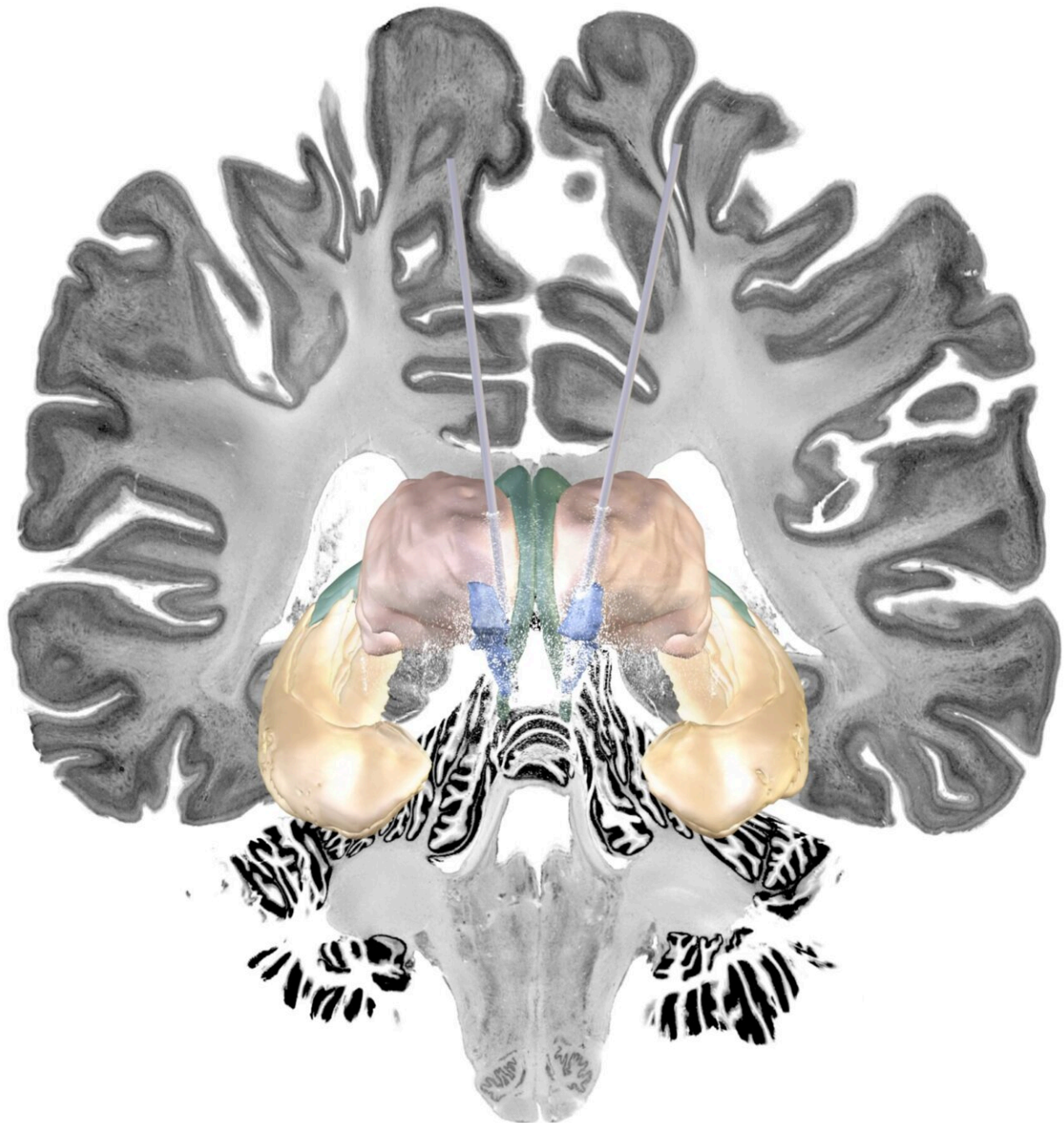# Deep brain stimulation could help treat Alzheimer's disease

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In persons with Alzheimer's disease, the largest positive effect has been observed when stimulating the region between the fornix (green) and the bed nucleus of the stria terminalis (blue). Also shown are two brain structures—the thalamus (pink) and the hippocampus (yellow)—as well as the stimulation electrodes. Credit: Charité | Ana Sofía Ríos

Alzheimer's disease is the most common cause of dementia, but it is not easily treatable. One potential therapy is deep brain stimulation delivered by a kind of pacemaker. A team of researchers at Charité—Universitätsmedizin Berlin has found that stimulating a specific network in the brain of Alzheimer's patients reduces their symptoms. The researchers hope the findings, which appear in *Nature Communications*, will pave the way for further studies.

Deep brain stimulation (DBS) is a form of therapy that is already approved in Germany for treating neurological movement disorders such as Parkinson's disease and dystonia, and neuropsychiatric diseases such as obsessive-compulsive disorder.

Very thin electrodes are implanted in the patient's brain and constantly deliver mild electrical pulses to a specific region. The electrodes remain in the brain permanently and are connected via wires that run under the skin to a pacemaker-like device implanted in the chest area. The device is used to adjust the strength and frequency of the electrical stimulation.

"Although DBS has been an established treatment for Parkinson's disease for a good 20 years now, and the costs are covered by health insurance providers, it's still not a very well-known therapy," says Prof. Andreas Horn, head of a lab that explores network-based brain

stimulation at the Department of Neurology and Experimental Neurology at Campus Charité Mitte, and at Brigham and Women's Hospital and Massachusetts General Hospital, both affiliates of Harvard Medical School.

"DBS works very well in patients with Parkinson's," he says. "It improves their quality of life significantly." Since Alzheimer's is also a neurodegenerative disease, it seems likely that DBS could be used to treat this condition, too. But safe, effective treatment is only possible if the precise brain regions that require stimulation are known."

The starting point for the current study, which the researchers carried out in close cooperation with multiple partners including the University of Toronto in Canada, was a random observation made within a Canadian study.

"In one patient, who was being treated for obesity, deep brain stimulation caused flashbacks—sudden memories of their childhood and adolescence," says Dr. Ana Sofía Ríos from the Department of Neurology and Experimental Neurology at Campus Charité Mitte, and the study's lead author. "This led the Canadian researchers to suspect that stimulating this brain region, which was located in the fornix, might also be suitable for treating Alzheimer's."
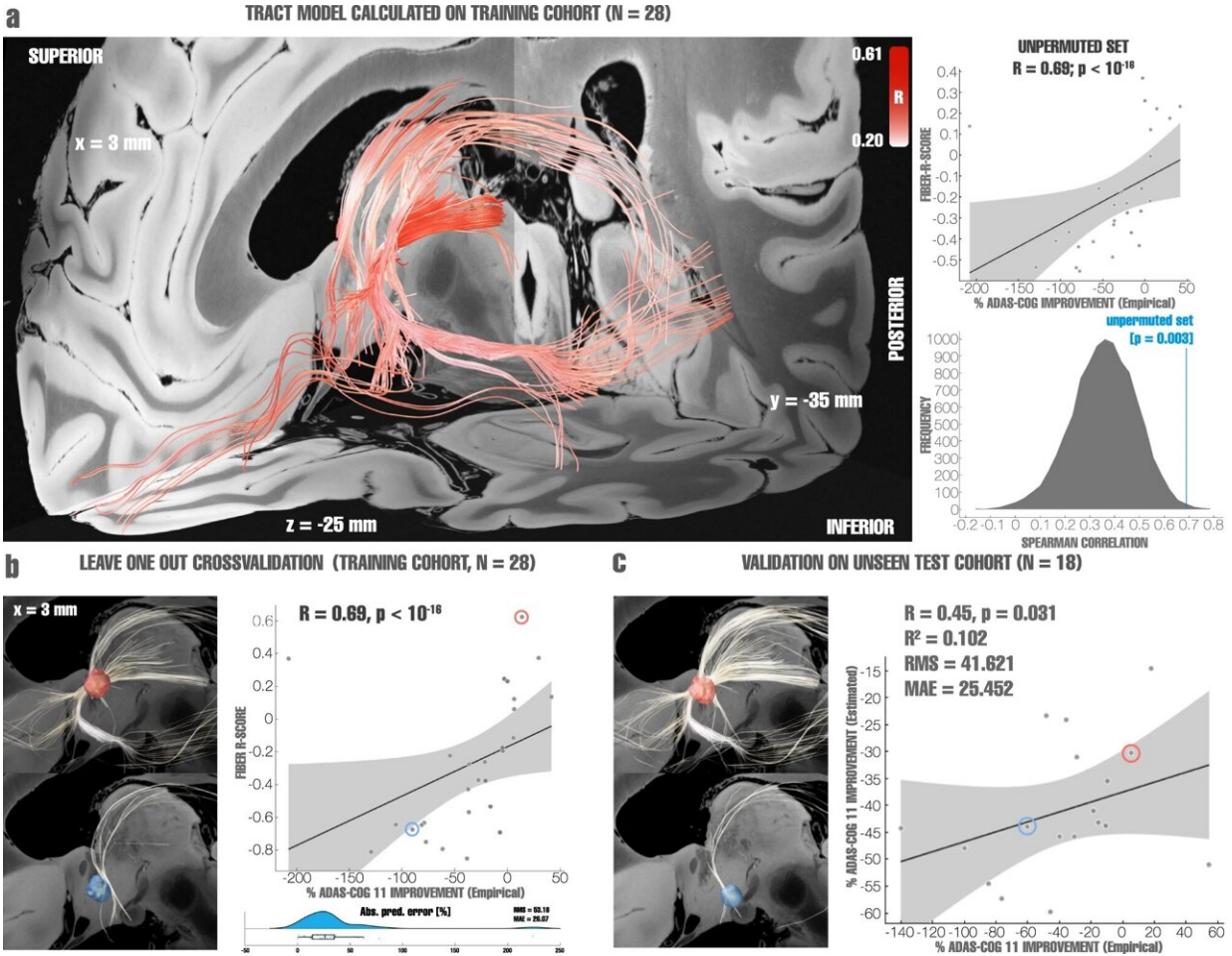
Validation of tract models predictive of clinical improvements as evaluated using ADAS-cog 11. **a** Left: Optimal set of tracts to be modulated as calculated from the entire training cohort ($N = 28$ subjects), red intensity codes for R-values ranging from 0.2 to 0.6, with darker colors indicating higher R-values. Right: permutation analysis calculated on the entire training cohort ($R = 0.69$ at $p = 0.003$). **b** Top left: stimulation volume of a patient with top clinical improvement overlapping the tracts associated with optimal clinical improvements (calculated leaving out the subject, $N = 28\text{-}1 = 27$ subjects). Fibers displayed in white correspond to the portion of optimal fibers intersecting with the patient's stimulation volume. Bottom left: Same analysis carried out with a poor-responding example patient. Right: Cross-validation within the training cohort ($N = 28$) using a leave-one-out design (top, $R = 0.69$ at p