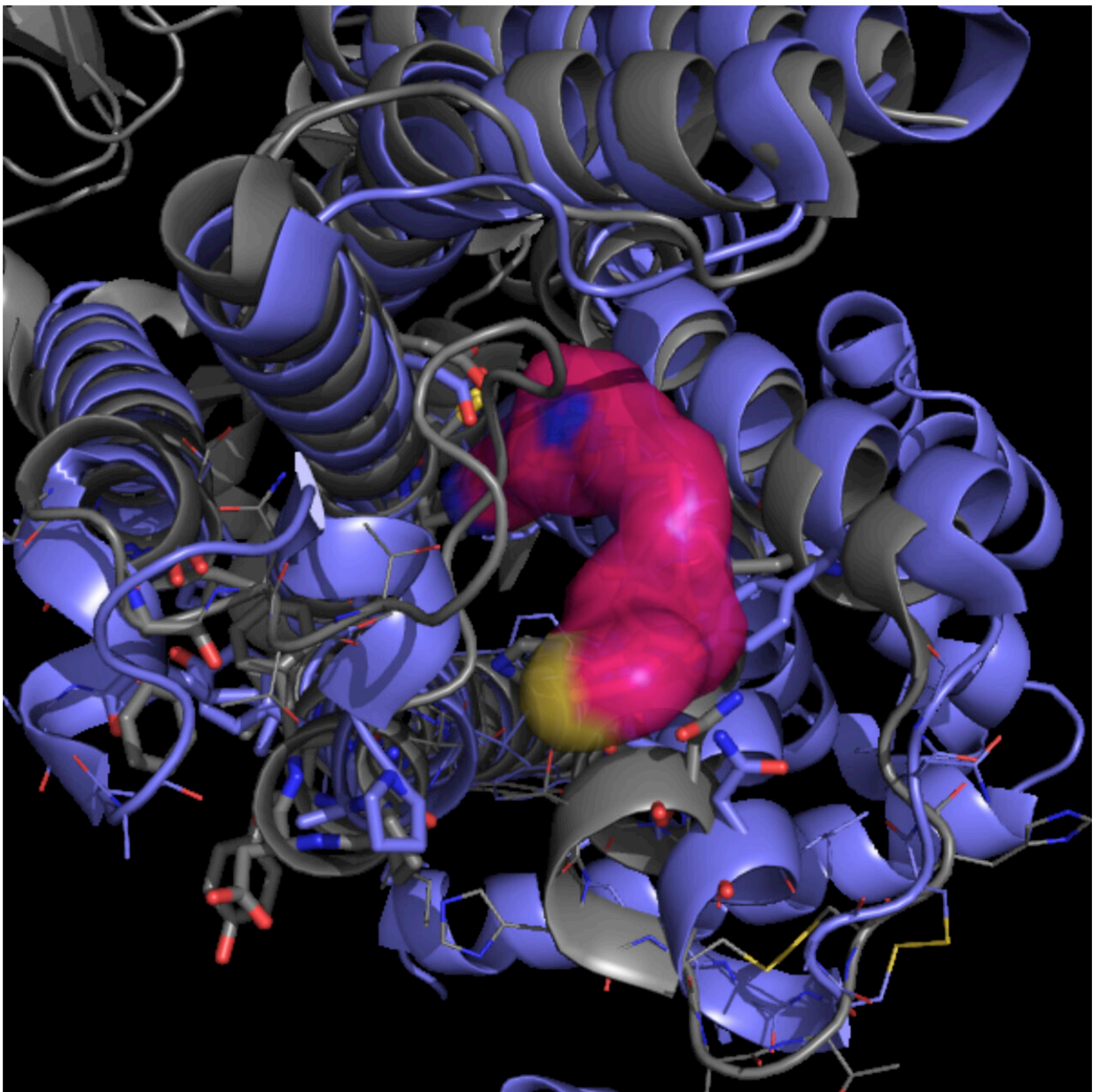


Compound shows promise for minimizing erratic movements in Parkinson's patients

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The small molecule PD13R (magenta) interacting with the dopamine D3 (grey) and D2 (purple) receptors cryo-EM structures, as predicted by RhodiumTM.
Credit: SwRI

A new study from Texas Biomedical Research Institute (Texas Biomed) and collaborators has identified a promising drug candidate to minimize uncontrolled, erratic muscle movements, called dyskinesia, associated with Parkinson's disease.

The small molecule, called PD13R, reduced dyskinesia by more than 85% in the marmoset animal model of Parkinson's disease. Additionally, the animals got much better sleep taking this compound compared to another drug often prescribed for dyskinesia. The results were published in the journal *Experimental Neurology*.

Dyskinesia is a common side effect in patients with Parkinson's disease. It is not a symptom of the disease itself, but typically emerges about five years into taking levodopa, the leading medication used to restore balance, reduce shaking and manage other motor control issues patients experience.

"Levodopa is amazing, it works like magic, but it has side effects. If we can eliminate these side effects, it could change the life of patients with Parkinson's," says Marcel Daadi, Ph.D., an associate professor at Texas Biomed and lead paper author.

Designing drugs for Parkinson's and its side effects is notoriously difficult. This is in part due to the progressive nature of the disease as neurons deteriorate, and because it involves the [neurotransmitter dopamine](#). There are five types of dopamine receptors, all with different functions, yet very similar structures. Finding a compound that only

interacts with the desired receptor is a major challenge.

To try to identify a compound that only binds to dopamine receptor #3 (D3), Daadi teamed up with Southwest Research Institute. SwRI's drug discovery software Rhodium™ identified PD13R as a likely candidate and predicted how it would bind to D3. Daadi reached out to medicinal chemists at Temple University, who are currently working on this class of compounds for their antipsychotic properties, to synthesize the compound.

Daadi and his team at Texas Biomed explored how well the compound targeted the D3 receptor compared to the other dopamine receptors in cell culture tests. They found it had a 1,486-times higher selectivity for D3 than for D2, which is the most similar in structure.

The team then administered PD13R to the [marmoset](#) animal model of Parkinson's. Like human patients, the [nonhuman primates](#) developed dyskinesia after receiving [levodopa](#). When treated with PD13R, dyskinesia dropped dramatically.

"We were very excited to see the robust antidyskinetic effect of the drug," Daadi explains.

The animals wore activity monitors, and with PD13R, their activity was low at night, when they normally sleep. In contrast, when given a different drug currently on the market for [dyskinesia](#), their nighttime activity was significantly high, suggesting that PD13R may be a good treatment option without this side effect.

Daadi and his team plan to continue with safety and efficacy studies required by the U.S. Food and Drug Administration (FDA) before [human clinical trials](#) can begin. "I am very hopeful we can move this into Phase 1 clinical trials within two years," Daadi says.

More information: Thomas Oh et al, Dopamine D3 receptor ligand suppresses the expression of levodopa-induced dyskinesia in nonhuman primate model of parkinson's disease, *Experimental Neurology* (2021). DOI: [10.1016/j.expneurol.2021.113920](https://doi.org/10.1016/j.expneurol.2021.113920)

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