Researchers identify molecular mechanism associated with juvenile Parkinson's

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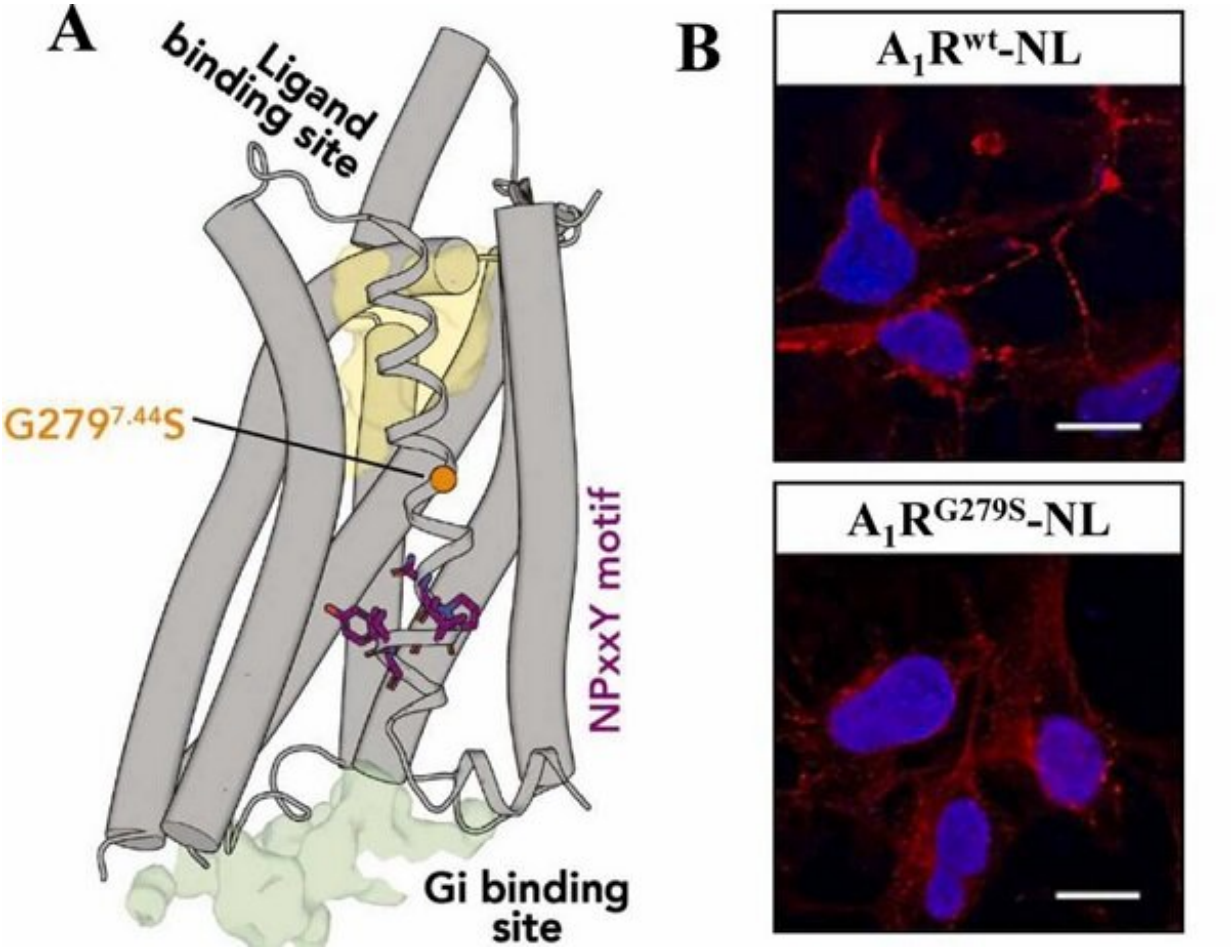


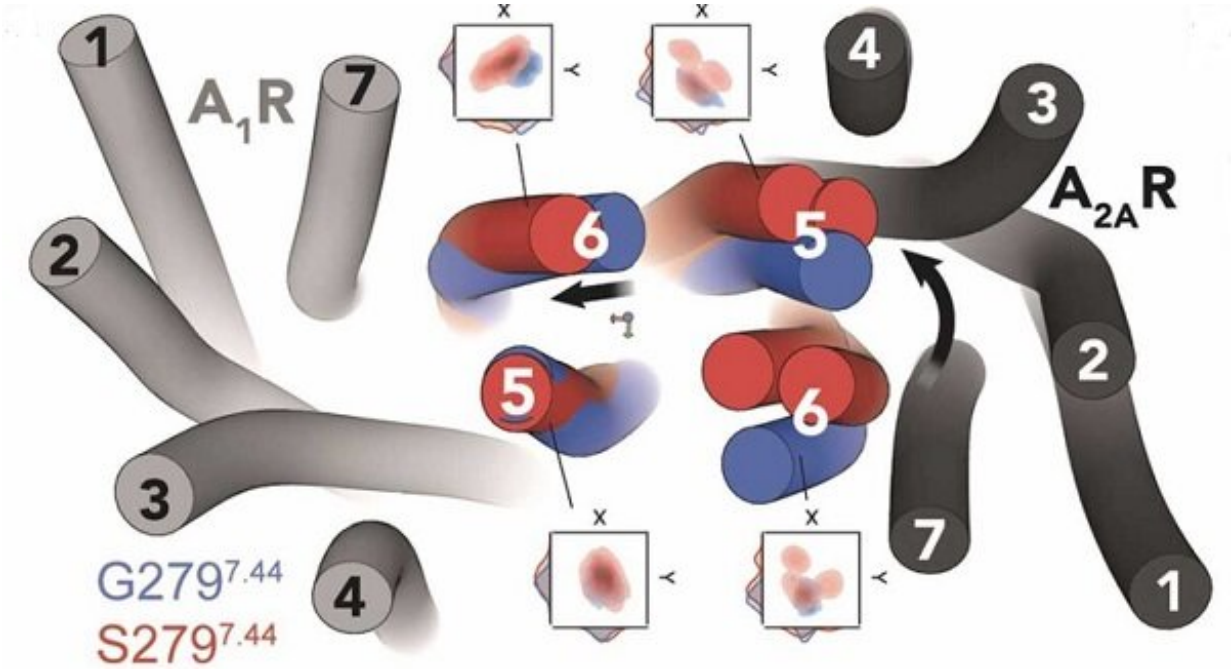
The paper states that the lack of interaction between two neuronal adenosine receptors may be responsible for the disruption of neuronal circuits in early or juvenile Parkinson's disease. Credit: *Biomedicine & Pharmacotherapy* (2022). DOI: 10.1016/j.biopha.2022.113896

Parkinson's disease affects 3% of population over 65 years old, and the average age of onset is 60. In juvenile Parkinson's, which accounts for 5–10% of Parkinson's cases, the disease begins before 40 years old.

Now, a group of researchers of the Faculty of Medicine and Health Sciences, the Institute of Neurosciences of the UB (UBNeuro) and the Bellvitge Biomedical Research Institute (IDIBELL), has deciphered, for the first time, the molecular mechanism by which a mutation of the adenosine type 1 receptor gene is associated with juvenile Parkinson's.

The team, led by Professor Francisco Ciruela (UB-IDIBELL-UBNeuro), focused on the study of the mechanistic field of the mutation of the brain receptor, previously defined as the potential cause for the early disease. The results, presented in the journal *Biomedicine and Pharmacotherapy*, reveal that the mutation reduced this receptor's ability to interact with other adenosine receptors—with the type 2 receptor—which would cause an increase in the neuronal circuits' excitability in the brain region called the striatum.

"We propose that the inability of both adenosine receptors to interact would generate glutamatergic hyperexcitability in the neuronal circuits of the striatum, a key mechanism in the pathogenesis of juvenile Parkinson's," notes Francisco Ciruela, professor of the Department of Pathology and Experimental Therapeutics of the UB and head of the IDIBELL Research Group on Neuropharmacology and Pain.



The article studies the impact of a genetic mutation of the adenosine type 1 receptor that has previously been associated with the early onset of the pathology in two Iranian brothers. Credit: *Biomedicine & Pharmacotherapy* (2022). DOI: 10.1016/j.biopha.2022.113896

An imbalance in the excitability of the neuronal circuit

The adenosine receptors are brain receptors assembled to G proteins and involved in motor functions. Previously, their involvement in neurodegenerative pathologies such as Parkinson's disease had already been suggested.

The studied mutation affects the type 1 adenosine receptor, which has an inhibitory effect on its counterpart—the type 2 adenosine receptor—through which it facilitates the glutamate release and the circuit's excitability. According to the conclusions, the mutation would prevent the molecular and functional interaction of both adenosine

receptors and, as a result, it would facilitate glutamate release, which would cause hyperexcitability in the striatum neuronal circuits.

More information: Laura I. Sarasola et al, The ADORA1 mutation linked to early-onset Parkinson's disease alters adenosine A1-A2A receptor heteromer formation and function, *Biomedicine & Pharmacotherapy* (2022). DOI: 10.1016/j.biopha.2022.113896

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