In pharmacology and biochemistry, allosteric modulators are a group of substances that bind to a receptor to change that receptor's response to stimulus. Some of them, like benzodiazepines, are drugs.

The positive allosteric modulators of GABAARs allopregnanolone and DS2 also induced larger current shifts in the rosehip and layer 2-3 innervating cells, consistent with higher expression of the δ subunit of the GABAAR in these neurons. We have also examined how patient parameters, such as age, seizures, type of cancer and anticonvulsant treatment may alter tonic inhibitory currents in human neurons. The cell-type-specific differences in tonic inhibitory currents could potentially be used to selectively modulate cortical circuitry.

Tonic currents through GABAA receptors (GABAARs) are a potential therapeutic target for a number of neurologic and psychiatric conditions. Here, we show that these currents in human cerebral cortical GABAergic neurons display cell type-specific differences in their amplitudes which implies differential modulation of their excitability. Additionally, we examine whether the amplitudes of the tonic currents measured in our study show any differences between patient populations, finding some evidence that age, seizures, type of cancer, and anticonvulsant treatment may alter tonic inhibition in human tissue. These results advance our understanding of how pathology affects neuronal excitability and could potentially be used to selectively modulate cortical circuitry [1)].

1)
Field M, Lukacs IP, Hunter E, Stacey R, Plaha P, Livermore L, Ansorge O, Somogyi P. Tonic GABAA Receptor-Mediated Currents of Human Cortical GABAergic Interneurons Vary Amongst Cell Types. J Neurosci. 2021 Nov 24;41(47):9702-9719. doi: 10.1523/JNEUROSCI.0175-21.2021. Epub 2021 Oct 19. PMID: 34667071; PMCID: PMC8612645.