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The metabotropic glutamate receptor, mGluR5, is a G protein-coupled receptor (GPCR) widely expressed in the brain where it is linked to various developmental pathways involved in intellectual disabilities such as autism spectrum disorders. Most GPCRs are located on the surface of the cell where they receive signals from the environment which they convert into signals inside the cell. What makes mGluR5 unique is that most of it is inside the cell where it can also be activated and hence trigger signaling from its position inside the cell. Because cell surface mGluR5 activates different responses than the intracellular receptor, we hypothesized that compounds that inhibit mGluR5 might do so in a differential fashion. Specifically that some mGluR5 inhibitors might only block the cell surface receptor whereas others might block intracellular mGluR5. To test this hypothesis, I used primary cultures of spinal cord dorsal horn neurons which we have previously shown to express high levels of this receptor. When activated mGluR5 leads to increased intracellular calcium which can be conveniently measured in dishes of cells using fluorescent calcium-sensitive dyes. By measuring a range of concentrations of 5 different inhibitors, I was able to deduce that certain drugs were more effective at inhibiting the cell surface vs. the intracellular receptor. This information will be useful in developing new therapies for disorders linked to mGluR5 signaling such as autism spectrum disorder.