Models reveal how a drug can "boost" our neurons

This project's models showed that a "booster-drug" increased neurons' firing rate and sensitivity to stimulation, by affecting a specific ion channel in the cell membrane.

An adult has almost 85 000 000 000 neurons inside their skull, and each of them connects and sends signals to up to tens of thousands of other neurons. That's a lot of traffic going on in a small lump! How does the brain control this traffic? It employs special "director-neurons" that tell the other neurons to stop, start, slow down or speed up their signaling. And in a fully functioning brain, they works nicely. But when they don't, problems arise. Scientists think that schizophrenia, autism and Alzheimers may be linked to these director-neurons working incorrectly. It is therefore important to see how these dysfunctions can be corrected. But first we need to know how to change how these director-neurons behave.

One way of doing this is to test how different drugs affect certain proteins in these director-neurons' fatty membranes. A protein that is necessary for these director-cells to work is a specific pore (an ion channel) that opens and closes to let sodium ions into the cell. By studying how certain drugs affect this ion channel, we can start finding ways to change different aspects of director-neuron behavior. If we can do that, we will be able to develop tools to treat some of these debilitating brain disorders.

Most of the time, drugs' effects are studied through experiments conducted on cells, brain tissue or on living animals. Animal testing can provide very specific and reliable results. However, this requires a large investment of time, money, effort and animal lives. One way of reducing these costs in drug development is to make models of the ion channels and neurons to then simulate experiments using these. We can, in advance, get a good idea of how a drug would affect neurons, by only looking at how it affects the ion channels.

To perform this modeling, cells with only the specific ion channel were used. These cells were stimulated and the flow of sodium ions through the membrane recorded. From the measurements on the sodium flows, we built an electrical model of the sodium flows through the membrane. When this model was combined with that of a neuron, we could start simulating neuron firing! By looking at how the drug affected the ion channels and the neurons, we saw what effects might be linked together.

What we could see from the models was that the drug made more sodium ion channels open in response to stimulation, made them close slower and stay closed a shorter time between stimulations. Overall, this means that the drug "boosts" the amount of sodium ions that goes into the cell during a stimulation. This not only leads to the neurons firing faster, but also makes them more sensitive to smaller levels of stimulation. This is just the beginning of what insights models can show us. In time, they may accelerate the development of sorely needed drugs.