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A Comprehensive Model of the G-protein in the Context of Pain

Abstract

Neurons elicit action potentials through either ionotropic or metabotropic receptors. Pain occurs when damaged cells release neurotransmitters like Bradykinin, which activates the G-protein metabotropic receptors. By using a Rube Goldberg diagram, several toys and a video created in macromedia flash, we were able to demonstrate to a group of fourth graders that some kinds of pain worked through the slower metabotropic mediation which relied on a cascade of events. After being judged by kids, we averaged 1st place by a vote by hands and 2nd place in evaluations over the average of four categories: understanding, fun, friendly and learn more.

Introduction

The human brain has long been an interest for human beings. The realization that the brain contributed to bodily function was first initiated during ancient Egyptian times when manuscripts for brain surgery were discovered during excavations (Curt, 1997). Also, during the Roman Imperial times, when a physician known as Galen dissected deceased gladiators he would observe the presence of ventricles, or large fluid filled cavities within the brain, and hypothesized that they controlled muscle function (Clark and Dewhurst, 1972). Even philosophers such as Plato, during the ancient times before Christ, philosophized about an organ within the body that directed other organs (Dent, 1937). Most human beings have an interest in cognition, emotion and bodily function. Today, many medications and preventative health practices are implemented from neurological research. Young children in elementary school might find it interesting to know a little bit about the brain. One of the fundamental responsibilities of the brain is for it to communicate with the body and for the body to communicate back to the brain. For this reason, we believed that it was important for children to learn how this communication worked.

The brain communicates through neurons, and neurons communicate to one another via electric signals known as action potentials. Action potentials are generated when an influx and efflux of ions pass through the semi permeable membrane of a neuron. Resting on the membrane are many different kinds of proteins that act as receptors for certain molecules. There are two main types of receptors that are used when neurons communicate. The first receptor is called an ionotropic receptor. The idea is that a ligand, or a molecule that activates the receptor, lands on the receptor at the same time as a change of voltage occurs, and the pore on a receptor opens up and ions flow through it. The flowing of the ions causes an action potential. The second type of receptor is a metabotropic receptor. A ligand binds on to this receptor as well, except that the ligand will change the actual arrangement of the receptor, and this in turn will activate metabolic activity within the cell. The metabolic activity in some cases actually makes an ionotropic receptor more sensitive to voltage changes and causes the neuron to communicate more often (Hall, 1992).

When a ligand binds to a metabotropic receptor, this receptor experiences a change in one of its intracellular loops. This change causes an attached G-protein to become phosphorylated. The G-protein then breaks down into its sub-units and then activates a cyclase, the cyclase then activates either cAMP or cGMP. These enzymes then activate other enzymes that can lead to the phosphorylation of ionotropic receptors (Velazquez-Prado et al., 2003).

We believed that it was important to place the g-protein into context. If we were to just show the whole cascade of events occur and label each protein, enzyme and sub-unit, we believed that the children would be bored quickly. And so we decided to link pain with the activation of a g-protein, which we called our “action protein”. By associating something which was totally unfamiliar to them, such as the action protein, with something that they all knew and

experienced them selves, like pain, we felt we could competently teach a group of higher elementary level children some general concepts about the g-protein. There are many different kinds of pain, yet this explanation will focus on kinins affecting tyrosine kinase receptors which send signals to the brain when ruptures in erythrocytes occur (Couture et al. 2001).

The g-protein cascade, also called the 2nd messenger system, is very complex. Because of this there were three main concepts that we wanted the kids to understand. We wanted the kids to know that pain transmits via the 2nd messenger system which is slow (Velazquez-Prado et al., 2003). We also wanted the kids to know that the g-protein transmission occurs as a cascade of events, in other words, one part of the sequence needed to occur before another and that this cascade would give us an end result. The final concept we wanted them to learn was that the brain perceives pain, and not that the pain occurs in that area, and that sometimes, pain that can be perceived is relatively slow because the mode of transmission is slow.

Methods

The model was presented at a Neuroscience fair in Washington State University. A group of 60 or so fourth graders were given a crash course on neuroscience and were then sent to different stations where Undergraduate students from WSU presented various models to them to understand certain neuroscience concepts. Each kid was given a score sheet where he scored a model based on four categories from one to five; understand, friendly, fun, learn more. The average of these scores was then recorded. A comment section was then provided to the kid where he/she would mention what his/her favorite part of the exhibit and what did he/she learn

from the exhibit. After every kid filled out an evaluation form, they voted for their favorite presentations in order of first place to last.

Our model was divided up into four sections. In our first section, we had a Rube-Goldberg model that depicted a cartoon with a complicated device that would drop a pillow should he happen to slip on a banana peel. The device had a lever which his foot would hit as he flew upwards; the lever would push a hand close to a snapping turtles head; the snapping turtle would bite the finger, pulling a rope attached to its neck; the rope would then pull a pair of prongs which would release a pillow and land on the pavement before the man hit the ground.

My partner and I would introduce our selves to the group of kids and we briefly told them that we would explain how the action protein would work. After showing the kids the Rube-Goldberg model, we asked them what they saw. After the kids successfully identified how the mechanism worked, we would ask them what would happen should the turtle be removed from the device. We would then expect them to say that the pillow would not drop, and that the man would hit his head on the pavement. This model was presented first to the kids to set the tone of both, a cascade of events and pain.

During the second stage of the model, we showed a short animation created in Multimedia Flash. The animation began with a teenager riding a bicycle in the middle of the road. A family in a car the runs over the poor teenager and the video zooms into the teenager. At this point we explain to the kids that after being hit by the car, we want to see what is going on in this guy's body. A red blood cell is then seen floating around and is ruptured. Some transmitters (bradykinin) are released and they are seen floating directly towards a neuron. The membrane bilayer on the neuron is then depicted with the metabotropic receptor. As soon as the receptor is activated by the neurotransmitter, the sequence of events begin to occur and finally

the kids are shown the production of cAMP molecules that look like little triangles floating around in the intracellular space of the membrane. In the final scene of the video, the teenager tearfully cries as his hand bleeds. There are a series of neurons that connect from the injured area to his brain and red flares are used to indicate that signals are being sent up to the teenagers brain so that he knows that he is in pain.

The third part of the model was designed to be interactive. We gathered various toys to act as the various parts of the cascade of events that occurred through out the movie during the 2nd messenger system. We had a ball, a pair of 10 sided dice, a toy car, a spin top, a stick-copter and pick-up-sticks. The idea was that the ball, acting as the neurotransmitter, would be tossed to the kid with the dice, as soon as that occurred, then the kid with the “probability” dice would roll until he achieved over 75% after combining the two 10 sided dice together. After 75% was achieved, the kid with the car would roll the car (G-protein) until it hit the spin top. When the spin top (Adenyl cyclase) was activated the stick-copter (cAMP) would be flown up into the air and the kids with the pickup sticks would pick-up-sticks (signal transmission) until the spin top stopped. The idea was to reinforce the idea of a cascade of events occurring intracellularly while having the kids actively participate in the learning process.

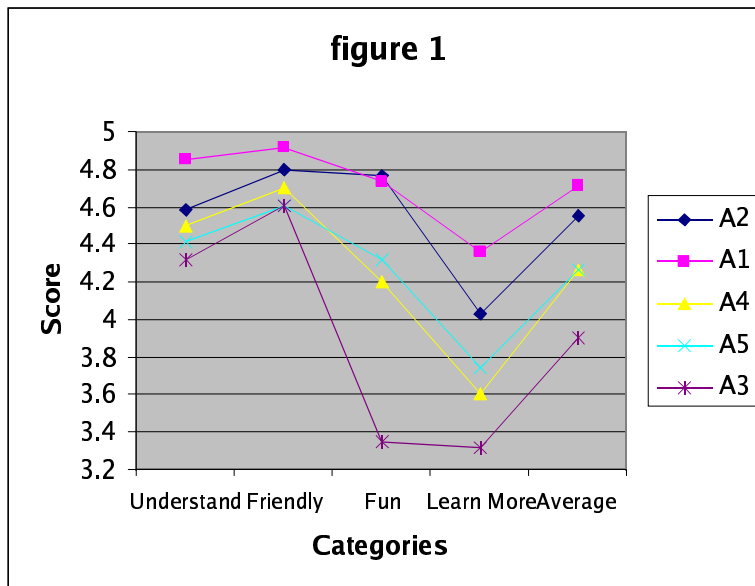
The final part of the model was to show the video one more time so that the kids could reinforce the interactive part of the model with the intracellular events once again. At the end of the model, we explained that since the sequence of events is a slow way of communication when dealing with some kinds of pain, people actually perceive pain after the incident occurs. We then asked the kids for a show of hands if they have ever hit their thumb with a hammer and if it took a while for them to perceive the pain.

Results

By comparing four other groups to our model, we were able to determine the score each kid ranked us and other groups for each category. With 5 being the highest score possible, we got an average score of 4.58 for how well the kids were able to understand our model, a score of 4.8 for friendly, 4.77 for fun, 4.03 for learn more, and an average score of 4.55. We were also voted as 1st place by the kids over all.

| | | Underst and | Friend ly | Fun | Learn More | Avera ge | Place Vote |
|-------------------------|----|----------------|--------------|------|---------------|-------------|-----------------|
| Action Protein | A2 | 4.58 | 4.8 | 4.77 | 4.03 | 4.55 | 1 |
| Blood Brain barrier | A1 | 4.85 | 4.91 | 4.73 | 4.36 | 4.71 | 2 |
| SNAP | A4 | 4.5 | 4.7 | 4.2 | 3.61 | 4.27 | 3 |
| Don't Bang Your Head | A5 | 4.41 | 4.61 | 4.32 | 3.74 | 4.27 | 4 |
| Brain Parts | A3 | 4.32 | 4.61 | 3.35 | 3.32 | 3.9 | 5 |
| | | -0.75 | -0.83 | -0.9 | -0.82 | -0.88 | Correlat ion |

Figure 1 demonstrates a graphical representation of the scores.



Discussion

Interestingly enough, we were voted 1st place by the kids even though they gave group A1 the highest average score. Our over all average score ranked 2nd place above all other scores, except for A1 at 4.55. We scored the highest in Fun at 4.77, just above group A1 who scored a 7.73, and we scored 2nd relative to other groups in all other subject matters. If the placement was based on the average of the combined scores for each category, then we would have been placed as 2nd.

In the evaluation form, the kids were asked to mention a part of the exhibit which they liked the most. Most kids answered the movie. When asked what they remembered, most kids seemed to remember mentioning either that “cascade of events” occurring and that “pain traveled slowly”. We believe that the actual scoring and judging of the exhibitions did not actually

represent entirely the quality of the material presented. An interesting experiment would be to hold several other fairs with subjects other than neuroscience that involve a wide variety of presentations and use the same categories. Another interesting experiment would be to use visual media, like the flash animation on another exhibition that scored relatively lower, keep every other exhibition relatively the same, and see how if the video has any impact on the scoring. The same could be said with friendliness. If we were to be complete jerks, how would that affect our scoring?

Given the current results which may or may not be affected by other categories, we can say that our model was a success and that with improvements we can successfully teach forth graders how signaling is generated via the G-protein 2nd messenger system.

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