Week 6

Friday, 3-3:50pm
2/13/15

Lecture 2/10/15 – Basal Ganglia and Cerebellum

Q: What does the neuromodulatory neurotransmitter (NT) dopamine (DA) do?

A: It depends on whether the NT binds to the D1 or D2 receptor, which create opposite effects.

The direct pathway is favored by high DA levels and is modulated by DA attaching to D1 receptors. This pathway increases the excitatory effect on the cortex.

1. Neurons from the cortex EXCITE the striatum with Glu, and neurons from the substantia nigra pars compacta (SNpc) EXCITE the striatum with DA, which synapse to D1.
2. Neurons from the striatum are excited, so they INHIBIT the globus pallidus internal segment (GPI) with GABA.
3. Neurons from the GPI are inhibited, so they REDUCE INHIBITION to the thalamus with GABA.
4. Neurons from the thalamus are less inhibited, so thalamic activity is INCREASED and MORE neurons excite the cortex with Glu.

The indirect pathway is favored by low DA levels and is modulated by DA attaching to D2 receptors. This pathway decreases the excitatory effect on the cortex.

1. Neurons from the cortex EXCITE the striatum with Glu, and neurons from the substantia nigra pars compacta (SNpc) EXCITE the striatum with DA, which synapse to D2.
2. Neurons from the striatum are excited, so they INHIBIT the globus pallidus external segment (GPe) with GABA.
3. Neurons from the GPe are inhibited, so they REDUCE INHIBITION of the subthalamic nucleus (STN) with GABA.
4. Neurons from the STN are less inhibited, so they EXCITE the globus pallidus internal segment (GPI) with Glu.
5. Neurons from the GPI are excited, so they ENHANCE INHIBITION to the thalamus with GABA.
6. Neurons from the thalamus are more inhibited, so thalamic activity is DECREASED and LESS neurons excite the cortex with Glu.
**Q:** What are the specific roles of the different cells in the cerebellum (CB)?

**A:** The dendrites of the purkinje cells are spanned in 2D space and are stacked on top of one another. They synapse perpendicularly with the parallel fibers, which are the axons of the granule cells. The granule cells are very small and make up about 70% of the brain.

The inferior olive from the medulla fires whenever it detects an error in the world, such as tripping. This causes a massive depolarization due to the climbing fibers from the inferior olive making contact the purkinje cells by wrapping around its dendrites.

**Lecture 2/12/15 – Sleep and its Function**

**Q:** Does sleep have a function?

**A:** Sleep may not have a function, besides making you less sleepy. It is a behavior in which your brain “jumps” into sleep (not “fall” into sleep) because it is an active process and not a default state of the brain. However, homeostasis is applied to sleep for maintaining internal stability, such as hormones.

**Q:** What causes narcolepsy?

**A:** The main cause is due to the lack of orexin neurons in the hypothalamus.

**Q:** What is electroencephalography (EEG) recording?

**A:** Local field potential (LFP) patterns are the same as EEG, which record temporal coherence of synaptic activity at the scalp.

**Q:** What happens when we take away REM sleep from a rat? How do you take away NREM sleep?

**A:** If you repeatedly wake up the animal so that it is sleep deprived and does not get any REM sleep, then it will die within 3-4 weeks. The peri-locus coeruleus alpha (peri-LCα), a nucleus in the pons where the REM-on neurons are located, activates REM sleep and paralyzes the muscles to prevent you from “acting out” your dreams. If you lesion this part of the brain, then you also take away REM sleep forever. However, damaging the peri-LCα and preventing it from having REM sleep will not kill the animal.
The ventrolateral preoptic (VLPO) nucleus in the hypothalamus is highly active during NREM sleep. If this area of the brain is lesioned, then you will have less or no NREM sleep because you have damaged the VLPO NREM-on neurons.

**Q:** Why is there a burst-pause pattern of waves during the NREM sleep stage?

**A:** Sleeping involves a progression of changes which includes firing rates of certain neuromodulatory neurons. In the waking stage, the normal resting potential for the cortical and thalamic neurons is at around -55 mV. High levels of ACh, NE, and 5-HT cause K+ leaky channels to become closed/inactivated. When K+ channels are closed, the cortical and thalamic neurons are depolarized. Also, the I_h and I_t are Ca++ voltage-gated channels that cannot be activated because the membrane potential is not hyperpolarized enough.

As you transition to Stage 2 sleep, the membrane potential changes to around -72 mV. Low levels of ACh, NE, and 5-HT cause K+ leaky channels to become a little more opened/deinactivated and allow some K+ to rush out, slightly hyperpolarizing the cortical and thalamic neurons. The membrane potential drops further to around -89 mV at Stage 3/4 of sleep, which is the final stage of NREM sleep. Now the K+ leaky channels are fully opened and cause I_h and I_t Ca++ channels to become opened/deinactivated, so Ca++ rushes in and cause a burst of action potentials known as the “spindle oscillations.”

Ca++ is depolarizing the cell and increasing the membrane potential, which causes the K+ leaky channels to close (hence the name Ca++ dependent-K+ channels, because the K+ leaky channels depend on Ca++). So the K+ channels close once more, inactivating the I_h and I_t Ca++ channels and hyperpolarizing the cortical and thalamic neurons. This repeats in a cycle, which is why there is a burst-pause pattern.

Image edited from Dr. Nitz’s lecture slide (2/12/15 – Control and Function of Sleep-Wake States)