

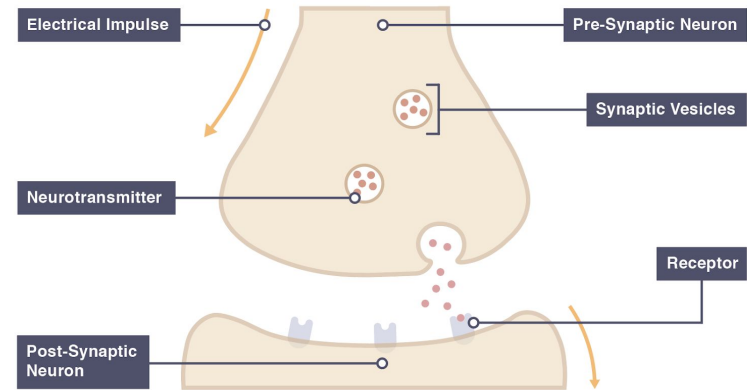
Neuromodulation

Week 18



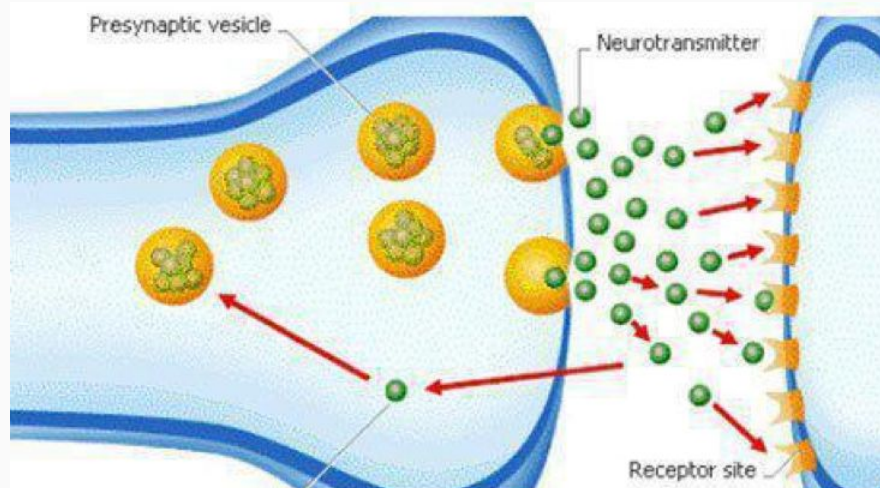
What is Neuromodulation?

- Targeted release of a substance from a neuron that can do one of the following:
 - Alter efficacy of synaptic transmission
 - Alter synaptic properties of pre-synaptic neuron
 - Alter synaptic properties of post-synaptic neuron
- The physiological process by which a neuron uses one or more of its neurotransmitters to regulate diverse populations of neurons



Neurotransmitters

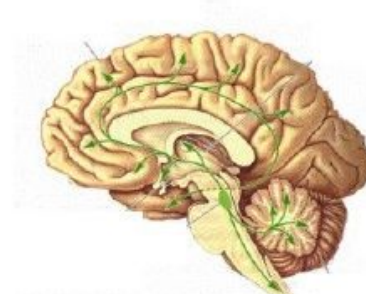
- A substance that gets released by a neuron at a synapse to affect another cell (e.g., another neuron)



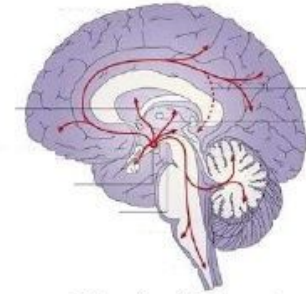
Neuromodulators

- Neuromodulators are neurotransmitters that have spatially distributed effects on recipient neurons and neural circuits
- Neuromodulators secreted by a **small group of neurons** can diffuse through large areas of the nervous system and affect **multiple neurons**
- Major neuromodulators in the CNS:
 - Norepinephrine
 - Histamine
 - Acetylcholine
 - Dopamine
 - Serotonin

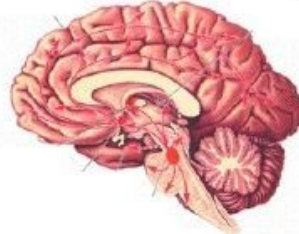
projection patterns of the five major neuromodulatory systems of the brain



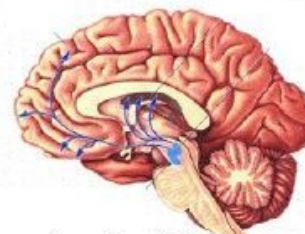
norepinephrine (NE)
system: main nucleus is
the 'locus coeruleus' in
the pons



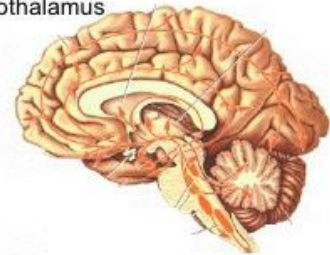
histamine (HA) system:
the 'forgotten one' –
neurons localized to
posterior hypothalamus



cholinergic (ACh) system:
pontine and basal
forebrain groups



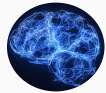
dopamine (DA) system:
ventral tegmental area
and substantia nigra area
(both in midbrain) – note
more localized projections



serotonin (5-HT) system:
several 'raphe' nuclei
distributed in brainstem

Neuromodulatory Systems

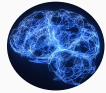
- Ascending Systems (projections from brainstem and basal forebrain to broad areas of CNS)



Cholinergic



Dopaminergic



Serotonergic

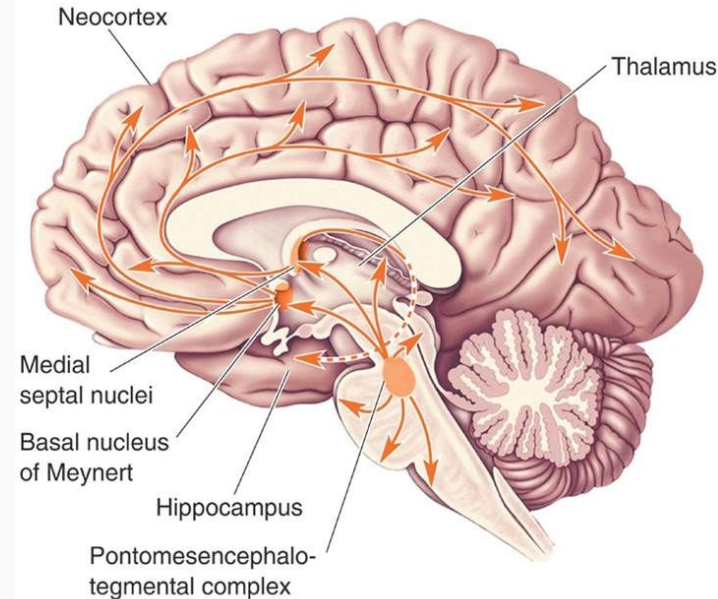


Adrenergic

Acetylcholine (Cholinergic System)

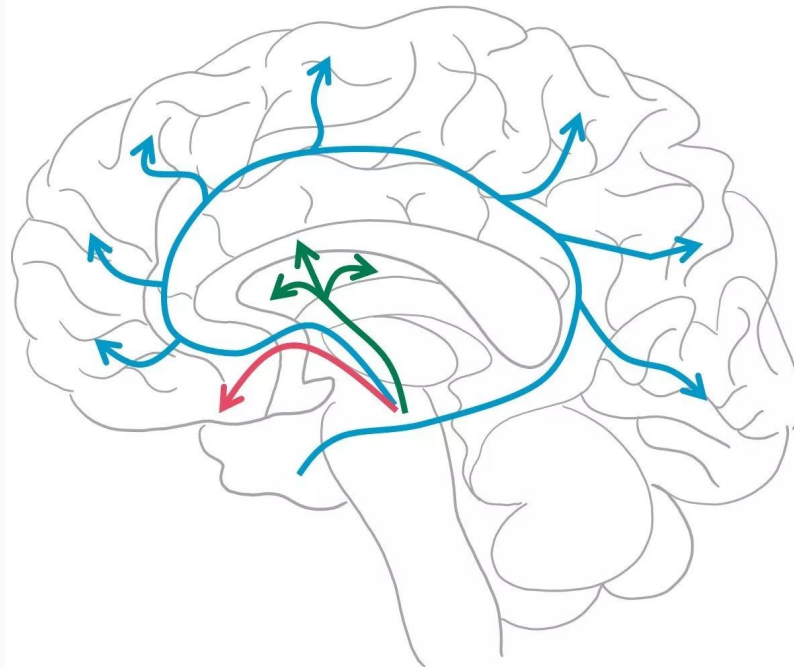
- Can influence thermoregulation, sleep patterns, food intake, endocrine functions (i.e. insulin/glucagon release)
- ACh signalling might be important in stress response → stress increases its release in a brain

Acetylcholine system



Dopamine (Dopaminergic System)

- Centrally involved in reward, exploration, behaviour, approach, and various aspects of cognition
- Variations in this neuromodulator appear to be associated with variations in personality



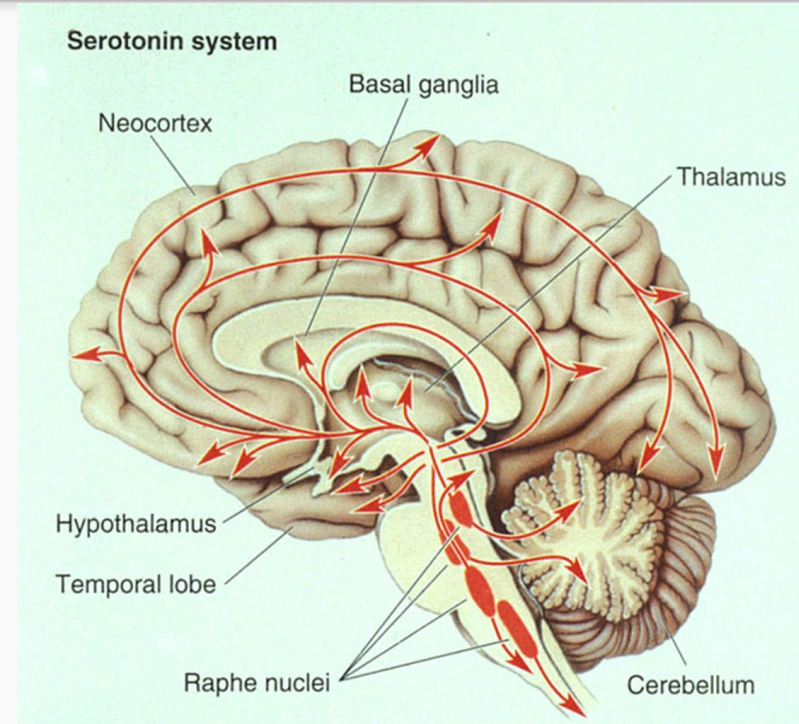
MESOCORTICAL
Cognition, Memory,
Attention, Emotional
Behavior, & Learning

NIGROSTRIATAL
Movement & Sensory
Stimuli

MESOLIMBIC
Pleasure & Reward
Seeking Behaviors;
Addiction, Emotion,
Perception

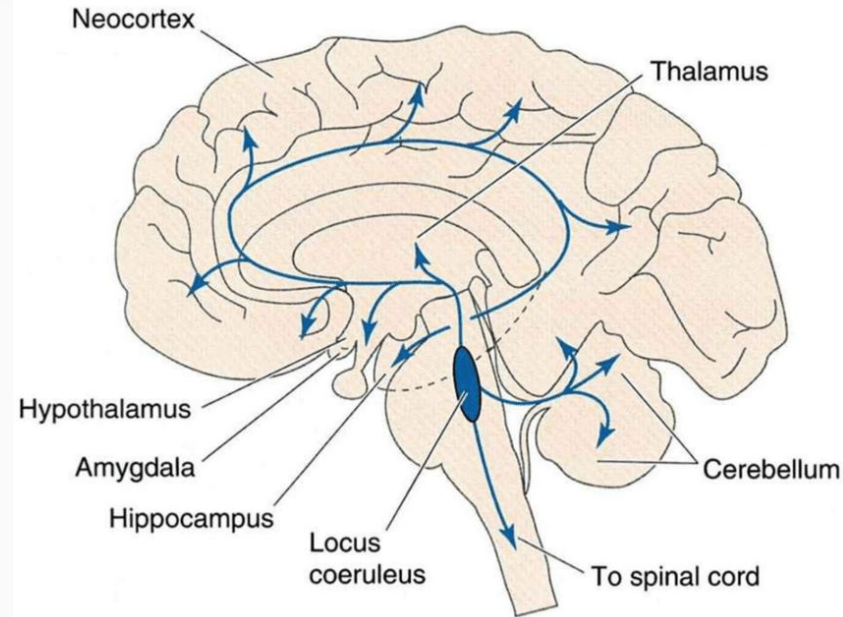
Serotonin (Serotonergic System)

- Serotonin plays a major role in regulating mood and anxiety
- 90% of the body's serotonin is found in the gastrointestinal tract where it has a role in regulating bowel function and movements
- Also is responsible for satiety (reducing appetite while consuming a meal)



Noradrenaline (Adrenergic System)

- Regulates activity of neuronal and non-neuronal cells
- Participates in modulation of cortical circuits and cellular energy metabolism (rapid) and inflammation and neuroplasticity (slow)
- Noradrenaline is found in many regions of the brain, but the **locus coeruleus** plays a major role in noradrenergic signalling
- Noradrenaline plays a critical role in modulating plasticity, learning, and memory via the **hippocampus** in the brain



How does it work?

- Neuromodulation works by either actively **stimulating nerves** to produce a natural biological response or by applying targeted **pharmaceutical agents** in tiny doses directly to the site of action
- Neurostimulation devices involve the application of **electrodes** to the brain, the spinal cord or peripheral nerves
 - A low-voltage electrical current passes from a pulse generator - that is connected to the electrode - to the nerve, and can either inhibit pain signals or stimulate neural impulses where they were previously absent



Applications of Neuromodulation Technology

Modulation of nerve activity by delivering electrical or pharmaceutical agents directly to a target area

- Deep brain stimulation (DBS) treatment for Parkinson's disease
- Sacral nerve stimulation for pelvic disorders and incontinence
- Spinal cord stimulation for ischemic disorders
- Cochlear implant to restore hearing for deafness

Tech Feature

- **BrainGate Neural Interface System** - can analyze brain signals and translate them into cursor movements
- Grants severely motor-impaired individuals an alternate “pathway” to control a computer with their thoughts
- Offers potential for restoring some degree of limb movement



Cortical Control of a Tablet Computer by People with Paralysis

Nuyujukian*, Albites Sanabria*, Saab*, Pandarinath, Jarosiewicz, Blabe,
Franco, Mernoff, Eskandar, Simeral, Hochberg**, Shenoy**, Henderson**

PLOS ONE, Nov. 21, 2018

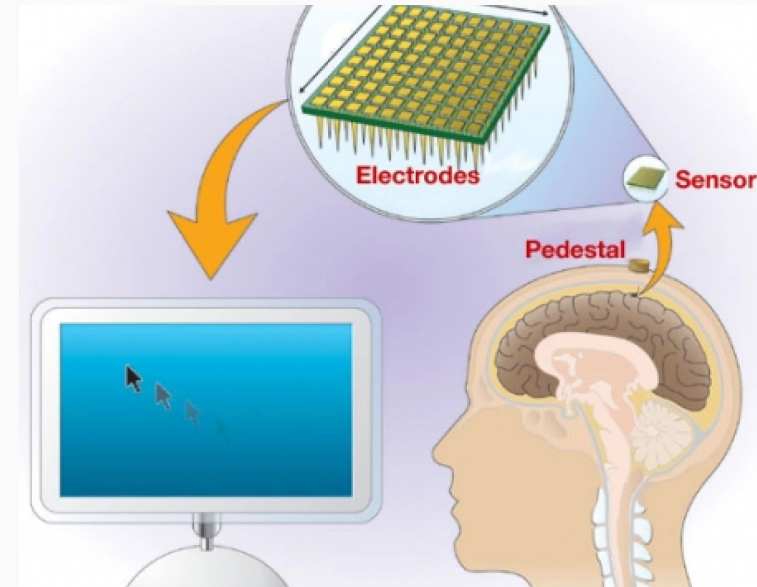


BrainGate2 Pilot Clinical Trial
Caution: Investigational Device. Limited
by Federal Law to Investigational Use.



How is this Possible?

- Device Components:
 - Internal neural signal sensor
 - Consists of a tiny chip with 100 electrode sensors that can detect brain cell electrical activity
 - Implanted into the motor cortex area (controls movement)
 - External processors
 - These computers convert neural signals (controlled by the user) into output signals (communication) using custom decoding software



Future Directions

Paralysis Treatment

- Implant **stimulators that connect to both brain signals and muscles**, using electrical impulses created by the system's hardware to **allow people with paralysis to move their arms**

Epilepsy Monitoring

- Implant **brain sensors to measure minute changes in brain activity** which may be used to **detect warning signs** like the onset of an epileptic seizure



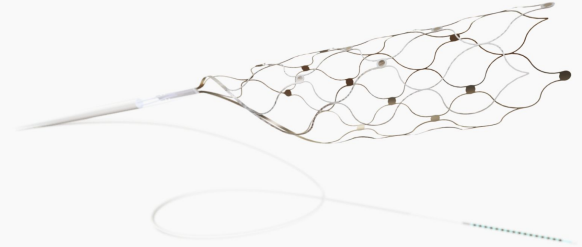
Stentrode: A Breakthrough Device

- FDA designated Stentrode as a “breakthrough device” in 2020
- What is Stentrode?
 - A fully-implantable device that **can translate brain activity or stimulate the nervous system from the inside of a blood vessel**—no need for open brain surgery
- **Safer** than BrainGate and Elon Musk’s Neuralink, which both require drilling into the skull for device insertion

From Neuromodulation to Neuroprosthesis

How Synchron's tech works with paralysis

- **Stentrode** is inserted into a blood vessel to capture brain signals related to intended movement and stimulate the nervous system
- **BrainPort** is implanted in the chest (similar to a pacemaker) and wirelessly receives brain data from the Stentrode to wirelessly transmit to BrainOS



From Neuromodulation to Neuroprosthesis

How Synchron's tech works with paralysis

- **Stentrode**
- **BrainPort**
- **BrainOS** is an app platform that transforms the brain data into a standardized digital language, controlling apps and potentially other digital devices, or telling BrainPort to stimulate the nervous system through Stentrode



Deep Brain Stimulation (DBS)

- FDA has approved the investigation of DBS use in:
 - Depression
 - Alzheimer's disorder
 - Addiction
 - Headache
- **DBS traditionally requires open brain surgery**—Synchron's Stentrode overcomes this safety risk

