Migraines
an
interactive
lecture

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• I am not here for me. I am here for you.

  Questions are a compliment.

• The information will be presented in 2 segments of 20 minutes each with a summary and Q and A after each session.

• Then there will be an enactment of a migraine. The audience will participate.

• Identify partner or partners.
Outline of the lecture

Clinical Symptoms of Migraine and Anatomy of a Migraine
Neurochemistry of a Migraine
Physiology of a Migraine

THE BRAIN BECOMES REAL--ACTION
There are 3 phases of a migraine. The phases are:

Aura

Pain

Postdrome
THE FIRST PHASE OF A MIGRAINE

Consists of complex neurological symptoms that typically occur 20-60 minutes before the migraine pain starts.

The neurological symptoms resolve completely and simultaneously as the headache begins.
TYPICAL AURAS INVOLVE

Visual disturbances (most common)
Sensory symptoms - tingling, numbness
Motor weakness
Speech disturbances
The pain classically begins over the eyes or behind the eyes.

May be unilateral or bilateral, can always be one-sided, can switch sides during the migraine or from one migraine to the next. It can be anywhere on the head.

Pain can be throbbing or sharp stabbing. It is always constant.
ASSOCIATED SYMPTOMS

1. Nausea
2. Vomiting
3. Photophobia (dislike of light)
4. Phonophobia (dislike of sound)
After the pain has dissipated these symptoms arise and can last for hours to days.

Common symptoms include confusion, feeling hungover, somewhat disorientated or just “not right”
What's next?

ANATOMY of a MIGRAINE
What's next?

1. The cerebral vessels and the dura mater
2. The trigeminal nerve (aka the V cranial nerve) and its 3 divisions, V1, V2 and V3
3. The trigeminal ganglion
4. The trigeminal nucleus.
5. The VPM nucleus of the thalamus
6. The sensory cortex
7. The limbic system
8. The hypothalamus
9. The autonomic nervous system - sympathetic division
| The cerebral vessels are the arteries and veins that supply the cranium. | The blood vessels that supply the brain are highly innervated by the trigeminal nerve and the first three cervical nerves. | This blood vessel-nerve connection is key to the physiology of a migraine. It is referred to as the trigeminovascular system. |
Meninges

The meninges are the membranes covering the brain and spinal cord.

- **Dura mater (2 layers)**
  - Arachnoid
  - Pia mater

- **Brain**

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The Dura

The dura is innervated by the trigeminal nerve and by the first three cervical nerves.

The dura above the tentorium is innervated by the trigeminal nerve and pain is referred to the forehead and the face.

The dura below the tentorium is innervated by the first three cervical nerves and the headache is referred to the back of the head.
The Brain in insensate

It does not feel pain.

You can open ones brain and touch it.

It does not hurt.

ALL PAIN COMES FROM THE DURA
Where is the dura?

Can I have an artery please??
Sensory Division

V1 is also called the ophthalmic division
V2 is the maxillary division
V3 is the mandible division
These provide sensory innervation to the face.

Motor Division

Provides motor innervation to the muscles of mastication. These are located in temporal area.
Trigeminal Dermatomes

Dermatomes are areas on the skin supplied by sensory fibers of the spinal nerves.
TRI-GEM-inal Nerve
V1, V2, and V3 all connect at the trigeminal ganglion. The trigeminal ganglion is also called the gasserion ganglion.
Trigeminal Ganglion
Where is the GANGlion??

How do we know it is a GANG-Lion??
The trigeminal nucleus is located in the brainstem. There is a tract—a group of nerve fibers—that travels from the ganglion to the trigeminal nucleus.

The trigeminal nucleus connects to the ventral Posterior medial nucleus (VPM) of the thalamus.
Neuroanatomy

Where oh where is the trigeminal new-clean us?
VPM

Ventral posterior medial nucleus of the thalamus

Sensory Cortex

Trigeminal nucleus

Pain Pathway
Where is the Ventral Posterior Medial nucleus Of the Foul-on US?? (Thalamus)
• WHERE IS THE SENSORY CORTEX ???
• AND HOW IS IT FEELING???
The Autonomic Nervous System

- **Sympathetic**
  - Fight or flight

- **Parasympathetic**
  - Rest and digest
DO WE HAVE A REPRESENTATIVE FROM THE SYMPATHETIC NERVOUS SYSTEM?

GEE I THINK SO.....
Is where our emotions live.

Includes the hypothalamus which has a direct neural connection to the sympathetic nervous system

Connects our emotional state to our biological state

Thus, when we feel pain, we change our heart rate, blood pressure, respiratory rate, sweating and digestion automatically.
LIMBIC SYSTEM
WHERE CAN I FIND A GROUP FEELING LIMBER ENOUGH TO BE AN EMOTIONAL SYSTEM??
WHAT'S NEW

WHAT DID YOU LEARN?
There are 3 phases of a migraine.

- aura
- pain
- postdrome

The phases are defined by clinical symptoms.
The dura contains the cerebral vessels. The trigeminal nerve and the dorsal roots of the first 3 cervical nerves innervate the dura. All head pain comes from the dura because it is the only membrane that is innervated.

The trigeminal nerve has 3 divisions, V1, V2, and V3. AKA ophthalmic, maxillary and mandibular. They innervate the dura in the face and forehead.

The trigeminal nerve connect to the trigeminal nucleus which is located in the brainstem.
The trigeminal nucleus connects to the ventral posterior medial nucleus of the thalamus (VPM).

The VPM nucleus of the thalamus connects to the sensory cortex.

This is where the pain signal is interpreted: OUCH!!

One does not feel pain until the signal gets to the sensory cortex.
Pain has an emotional component.

Emotions live in our limbic system.

Our limbic system contains the hypothalamus.

The hypothalamus connects to the ANS.

The sympathetic nervous system is referred to as flight or fight.
When one is in pain, the sympathetic nervous system is activated.

When they sympathetic system is activated there is an increase in blood pressure, pulse, sweating, and the GI system shuts down (nausea and vomiting).
What’s next

NEUROCHEMISTRY

Of a

MIGRAINE
Nerve cells use chemicals to send messages from one neuron to the next.

The neurochemicals are released by the neuron into the synapse and float across to connect to a dendritic receptor on the next nerve cell.
A receptor is usually named for the neurochemical that binds to it.
Receptors are grouped into families and further identified by numbers.
Additionally, a receptor may be characterized by a subgroup designated by a letter.
Serotonin, scientific name 5-hydroxy-tryptophan (5HT), has 7 families of receptors.

There are at least 4 subgroups in most families. Receptors are named 5HT1a, 5HT1b, 5HT1c, 5HT1d, 5HT1f, 5HT2a, 5HT2b,… Serotonin has 26 receptors!

A change in serotonin level will potentially affect 26 receptors and may have 26 different physical consequences!
Clinically important serotonin receptors for migraines are 5HT1b and 5HT1d.

5HT1b is inhibitory. These receptors are located on cerebral blood vessels and the trigeminal ganglion. Stimulation causes constriction of cerebral blood vessels.

5HT1d is inhibitory. These receptors are located in nerve terminals. Stimulation causes inhibition of release of norepinephrine, Substance P and 5HT (serotonin).
Triptans act as agonists at 5HT1b and 5HT1d receptor sites. Examples are shown here.
WHAT DID YOU LEARN?

WHAT'S NEW???
What you learned

Neurons communicate by neurotransmitters. Serotonin (5HT) has 26 receptors which are grouped into families and subfamilies.

The 5HT1b and 5HT1d are important receptors in migraines.

5HT1b and 5HT1d are both inhibitory. When stimulated they inhibit the trigeminal ganglion and the cerebral vessels.
What you learned

When 5HT1B and 5HT 1D receptors are stimulated by serotonin the cerebral vessels constrict.

The trigeminal nerve no longer fires and the pain decreases.

Triptans are 5HT1B and 5HT1D agonists.
What's next ??

PHYSIOLOGY
of a
Migraine
The single consistent physiological event of a migraine is neuronal dysfunction.

The dysfunction is an imbalance between stimulation and inhibition at various levels of the nervous system.

This leads to a dysfunction at the vascular level that leads to pain.
These neuropeptides cause dural blood vessel dilation, increased vascular permeability, platelet injury and plasma extravasation.
It releases these neurochemicals for a variety of reasons and for NO REASON.
The trigeminal nucleus is activated.

The trigeminal nucleus activates the VPM nucleus of the thalamus.

The VPM nucleus of the thalamus activates the somatosensory cortex and pain is present.
Neurophysiology

The VPM of thalamus activates the limbic system.

The hypothalamus is part of the limbic system and activates the sympathetic nervous system.

The sympathetic nervous system increases the heart rate, blood pressure and shuts down the GI system.
How does one stop this process?

Stop the outpouring of the CGRP, Substance P, histamine?

Stop the Trigeminal Ganglion sending the message to the Trigeminal Nucleus?

Stop the VPM nucleus of the thalamus?
Neurophysiology

- **Acute treatment involves focus on artery**
  - Make the artery constrict!
  - Muscle in artery constricts
    - DHEA (dihydroergotamine)
    - Caffeine
  - Nerve telling artery to dilate is blocked
  - Triptans
Prophylaxis treatment

- Magnesium 400mg-2,000mg
- Prevent the artery from dilating

- Calcium channel blockers (Calan SR)
- Beta blockers (inderal)
Prophylaxis treatment

Prevent the nerve from responding

- Depakote 125mg TID to 375mg TID
- Topamax 50-100mg BID
Audience Participation

Dura-white gloves
Artery-red gloves and cellophane
Red blood cells-red hats
Inflammatory cells—white hats

Trigeminal Nerve—hats, boas
Trigeminal ganglion—chain gang with water spray
Trigeminal nucleus---aprons, smocks and bubble and wands

VPM Thalamus—baseball caps, water spray and colored balls

Somatosensory cortex—noisemakers

Limbic system---jester hats and balloon hats

Sympathetic nervous system---
Heart rate—drum
Blood pressure—RED balloon
GI tract—green shirts with squish