



Brain-Immune Link and the Suicidal Brain

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Brain References
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www.LLM.life

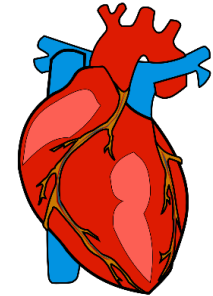


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Circulatory Systems - Vascular

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The heart pumps blood throughout the brain and body through blood vessels:



- Arteries and Veins, along with tiny Capillaries



Depending on the size and weight of the individual, there may be 60,000 – 100,000 miles of blood vessels

Blood pressure measures the pressure of blood in mm of mercury against these muscle-lined vessels

Circulatory Systems - Lymphatic

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Lymphatic vessels are thin-walled valved structures—slightly larger than their capillary counterparts in the vascular system—that carry lymph fluid throughout the body



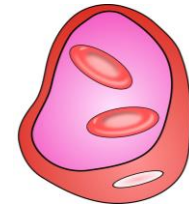
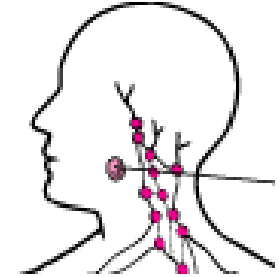
Walls of lymphatic vessels are not muscular and depend on action of large muscle groups in the body to move the fluid along

Based on a person's size and weight there may be 200,000 to 250,000 miles of lymphatic vessels

Previous Beliefs

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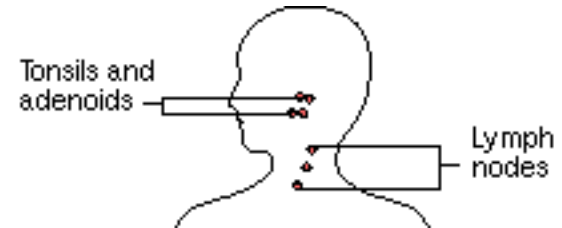
- **The human brain has no lymphatic system**
- **There's no direct physical connection between the brain and the immune system**
- **The brain is connects with the immune system via immune messengers that are carried in the blood stream (e.g., white blood cells, natural killer cells, enkephalins...)**



Puzzling Observations

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Researchers observed that strategies to strengthen brain function also tend to strengthen immune function—a puzzle



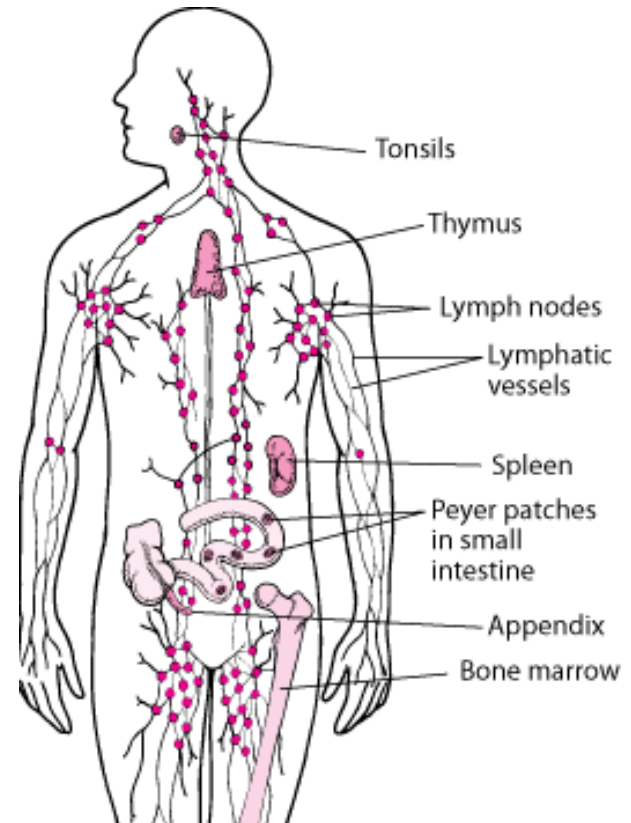
One editor quipped that the brain and immune system have their hands shoved so deeply in each other's pockets that it's hard to tell who is who and which is which—but there was no evidence of any physical connection

Example of Drawings

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Textbook drawings of the brain and immune system showed no physical connection between the two systems

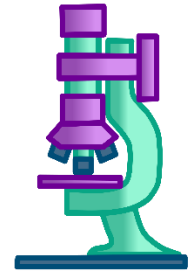
Drawings showed lymph vessels throughout the body and passing through lymph nodes but nothing in the brain





Late 2015 ...

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University of Virginia School of Medicine researchers led by Jonathan Kipnis MD, a professor in Department of Neuroscience and Director of the University's Center for Brain Immunology and Glia, were 'dissecting brains'

Antoine Louveau, a postdoctoral fellow in Kipnis' lab, saw something he had never seen before

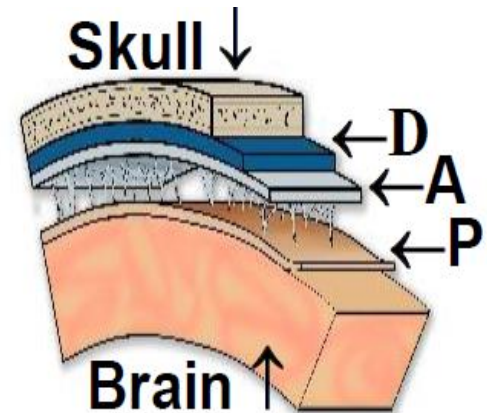
Antoine asked Dr. Kipnis to take a look at what he was seeing

Dr. Kipnis Looked

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He saw lymph vessels going throughout the meninges, the three membranes that cover the brain and spinal cord: Dura mater, Arachnoid mater, and Pia mater

Dr. Antoine Louveau's stunning discovery overturns decades of textbook teaching—the brain is directly connected to the immune system by lymphatic vessels *previously thought not to exist*



New Discovery!

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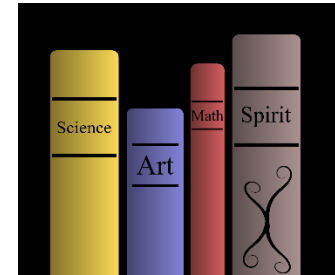
Dr. Kipnis said: “I really did not believe there were structures in the body that we were not aware of. I thought the body was mapped... This changes entirely the way we perceive the neuro-immune interaction . . . We believe that for every neurological disease that has an immune component, these vessels may play a major role.”

There always had been a lymphatic system for the brain and central nervous system—just no one had discovered it

Kevin Lee

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Kevin Lee, chair of the Department of Neuroscience, recalled his reaction when researchers told him about the new discovery:



“I just said one sentence: ‘They’ll have to rewrite the textbooks.’

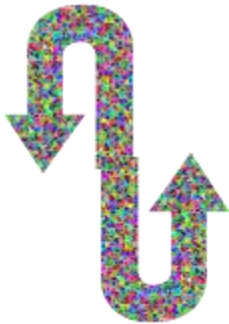
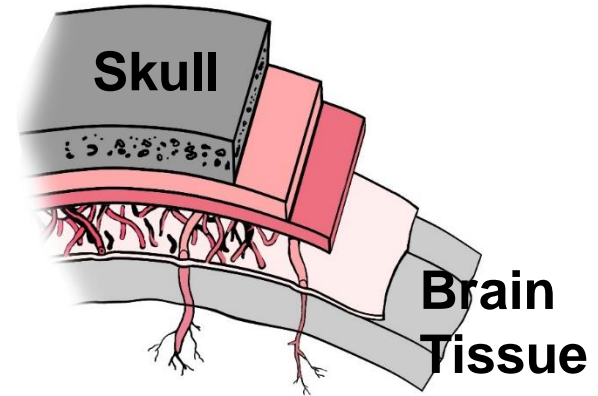
“It is very clear that this will fundamentally change the way people look at the central nervous system’s relationship with the immune system.”

Scrambling to Re-write

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Due to this new discovery:

- **Authors are scrambling to re-write textbooks, articles, and Internet resources**
- **Clinicians are taking a closer look at diseases that are believed to have auto-immune components and asking questions regarding bi-directional linkages between the brain and the immune system**



More Questions to Answer

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There is an array of neurological diseases, from autism and multiple sclerosis to dementia and Alzheimer's that need to be reconsidered in light of the presence of something science did not know about or even believe existed

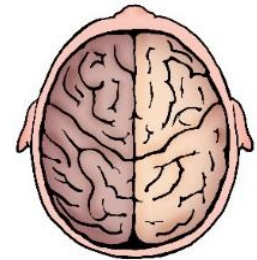
According to Dr. Kipnis, in Alzheimer's, there are accumulations of big protein chunks in the brain... that may be accumulating because they're not being efficiently removed by these lymph vessels

More Discoveries – July 2016

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According to Jonathan Kipnis MD, additional study results are showing not only that the brain and immune system are connected but also that some behavior traits may be developed and exhibited because of immune response to pathogens

Part of your personality may actually be dictated by your immune system linking your brain with pathogenic organisms

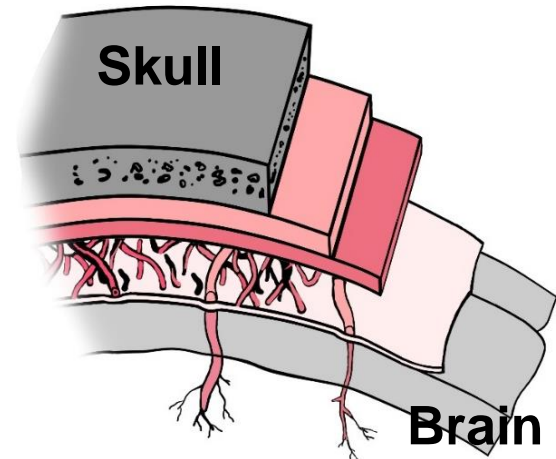


Brain-Immune Examples

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Protective immune microglia cells have direct involvement in creating the cellular networks at the core of brain behavior

Stress is known to suppress the immune system function—ongoing chronic stress may impact immune cells in the brain, leading to mental disorders



Brain-Suicide Connection?

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Some wonder if suicide is a mental disorder that may be connected with a mal-functioning immune system



Candace B. Pert PhD was clear that when in the grip of a strong emotion (especially the protective emotions of anger, fear, and sadness), the brain is in an *altered state*

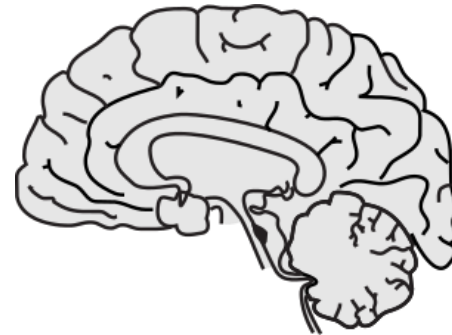
Suicide likely occurs only in a brain that is in an altered state because the brain's first goal is believed to be that of staying alive . . .

Suicide—A Unique Entity

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Studies by Cornelius van Heeringen MD PhD of The Netherlands have pointed out that suicide may be a unique entity, reflecting the culmination of several complex processes including:

- ✓ **Depression**
- ✓ **Impulsivity**
- ✓ **Disinhibition**
- ✓ **Anxiety**
- ✓ **Executive function dysregulation**

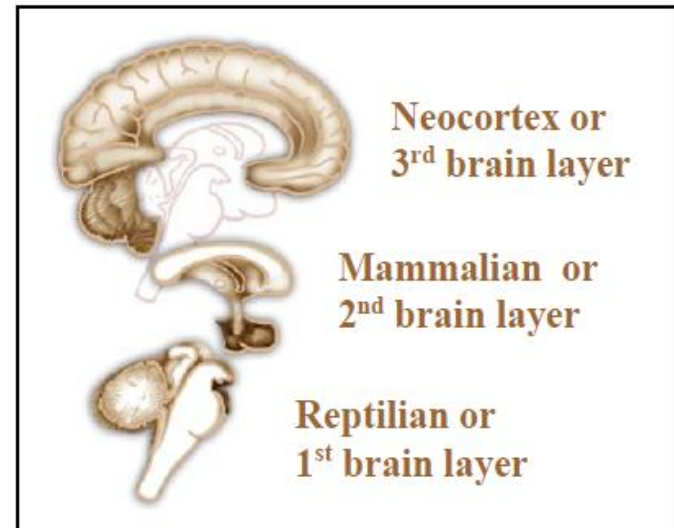


CRF Alters the Brain

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Corticotropin Releasing Factor (CRF) is both a hormone and neurotransmitter

In response to a stressor, the hypothalamus (in the mammalian layer) releases CRF that binds to receptors on cells in the locus ceruleus (an alarm center deep in the reptilian layer)—which in turn impacts emotional impulses in the mammalian layer and critical thinking in the neocortex



CRF is Immensely Powerful!

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- **Can suppress appetite**
- **Can increase subjective anxiety**
- **Is linked with euphoric feelings that accompany alcoholism**
- **Triggers inflammation (a process being investigated in Multiple Sclerosis research)**
- **High levels have been found in the cerebrospinal fluid of individuals who are very depressed and in those who committed suicide**



Cortisol Alters the Brain

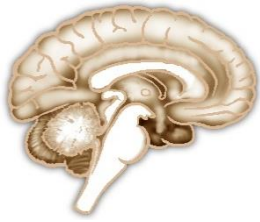
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Cortisol is a powerful steroid hormone produced by the adrenal cortex



Cortisol has many important functions including working with the thyroid gland and assisting with the fight-flight reaction to stress

Elevated 24-hour urinary cortisol production was found in patients who recently attempted suicide compared with patients who did not have a history of suicidal behavior



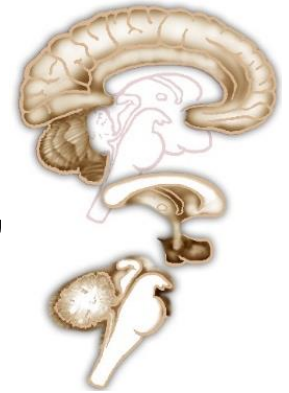
Serotonin Alters the Brain

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Serotonin is a neurotransmitter that regulates mood, sleep, a sense of wellbeing, intestinal movements (90% is in gut), etc.

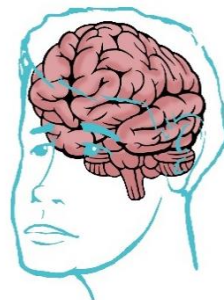
Neurons in the reptilian layer produce serotonin from amino acids—abnormal levels (up or down) are associated with depression, anxiety, OCD, alcoholism, and suicidal tendency

In suicide, neurons appear to send less than normal amounts of serotonin from the reptilian layer to the to the prefrontal cortex



Cholesterol Alters the Brain

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Low levels of cholesterol—precursor for the synthesis of cortisol, progesterone, testosterone, estrogen, and vitamin D—impacts memory functions

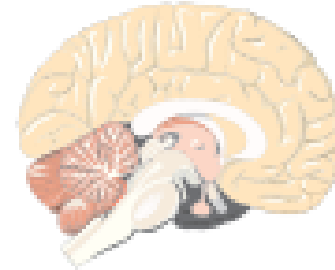
This waxy, fat-like substance found in all cells of the body is made by cells in the liver and also can be ingested in foods from animals

Lowered levels of cholesterol have been linked with increased suicide risk—whether the decrease occurred spontaneously or from drugs or diet

Norepinephrine Alters the Brain

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**Norepinephrine is both a
Neurotransmitter and a hormone**



**It mobilizes the body for action (e.g., fight-flight)
and increases restlessness and anxiety**

**Elevated levels of norepinephrine inhibit activity in
the prefrontal cortex—the part of the brain that
helps regulate conscience, willpower, decision-
making, emotions, and behavior—and have been
linked with increased risks for suicidal behavior**

Grief and Depression

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Cytokines are proteins released by immune cells that regulate immune responses—proinflammatory cytokines coordinate inflammation processes

Increased levels of proinflammatory cytokines have been linked with symptoms including dysphoria (opposite of euphoria), anhedonia, fatigue, apathy, a sense of helplessness, and depression

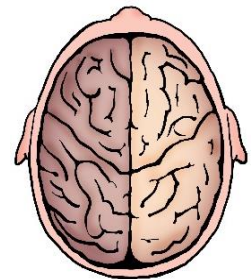
Prolonged grief and depression with high levels of proinflammatory cytokines may contribute to suicidality ...

Vitamin B

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B vitamins, especially B12, are believed to help keep the brain and body functioning in balance and minimize triggering stress chemicals such as CRF, norepinephrine, adrenalin, cortisol, and proinflammatory cytokines

Some believe that adequate levels of B vitamins, especially B12, may help survivors as they deal with the aftermath of loss—regardless of the type of loss or how it occurred—and may also be preventive against brain shrinkage and memory problems



Grief Recovery

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**Grief is the appropriate response to a loss—
every brain is unique
and so is its loss-grief
recovery experiences**

- **Article:**

***Grief Recovery
Pyramid***

- **Mini-monograph**

***Loss, Grief,
and Recovery***

