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Evaluating the interplay between endocrine function and traumatic brain injuries

NEUROENDOCRINOLOGY MAY PROVIDE THE OBJECTIVE PROOF OF MILD TBI

Mild traumatic brain injuries are a serious health issue affecting millions of people worldwide every year. Sometimes referred to as an mTBI, this injury has been appropriately given more attention as its occurrence and prevalence among athletes and service members has been recognized.

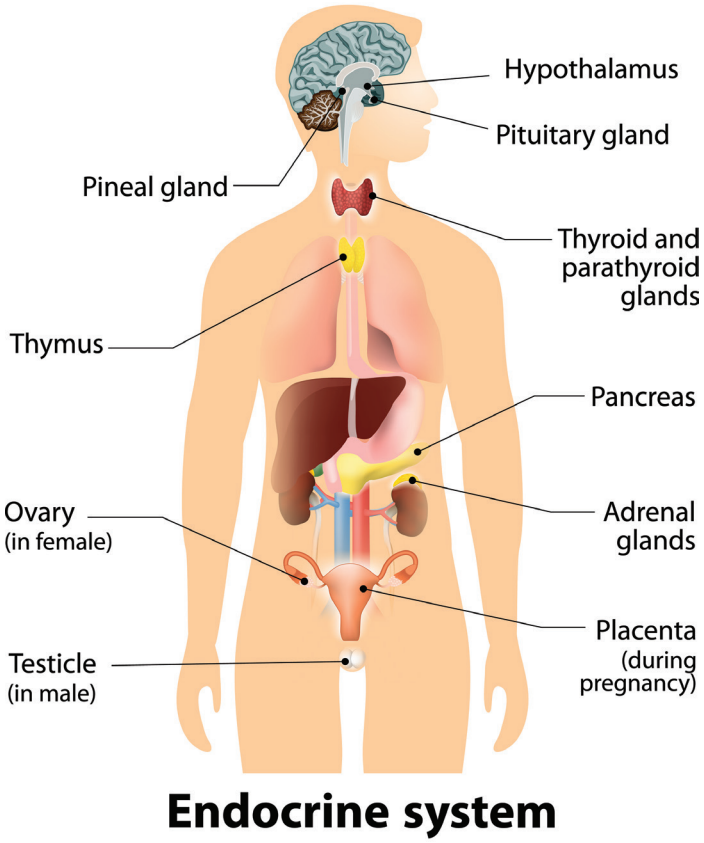
Attorneys are often presented with a client who has all the hallmarks of a traumatic brain injury – headaches, issues with vision, confusion, concentration and memory problems, changes in mood, behavior, or personality – but who wasn't diagnosed with one in the emergency room or whose initial imaging of their brain reveals no acute injury. That doesn't mean that the client hasn't sustained a TBI, and that doesn't mean there aren't ways to prove it. This article will focus on identifying and proving mTBI through evaluation of symptoms of neuroendocrine dysfunction.

Mild traumatic brain injury

A traumatic brain injury results from the transfer of energy to the brain from external forces, from things like the head being struck by an object or striking an object, the brain undergoing an acceleration/deceleration movement without direct contact with anything, or from forces generated from an explosion. The majority of brain injuries diagnosed in the United States have been classified as "mild." For years, medical providers would often define a TBI as mild, moderate, and severe. However, these categorizations have been described as problematic by the medical and research community as being too simplistic. While defining a brain injury as "mild" can help clinicians triage patients more effectively, describing it as such can be misleading – it can imply that the injury is insignificant or that the person will recover without any long-lasting effects. But for many people, the effects of a mild traumatic brain injury can be persistent, life-altering, and permanent.

Mild traumatic brain injuries can have serious consequences. The general consensus is that at least a quarter of patients who have sustained a mild traumatic brain injury have symptoms that do not resolve within three months. Some studies have found that over half of mTBI patients are still experiencing cognitive impairment one year after their injury. Recent studies of long-term data have recognized that traumatic brain injuries, even those that would be considered mild, are a dynamic and chronic condition that requires ongoing resources and care. They are also associated with an increased risk of dementia and Parkinson's disease.

It is not uncommon for someone who has suffered a mild traumatic brain injury to not be diagnosed with one in the emergency room – in fact, over 50% of mild traumatic brain injuries are not diagnosed by emergency room providers. This is due to a host of factors, including healthcare providers' and patients' own lack of awareness of the signs and symptoms of an mTBI as well as the fact that emergency room imaging like traditional CT scans and 1.5 Tesla MRIs do not detect the microscopic injuries that occur to neurons in the brain as a result of a mild traumatic brain injury. But a lack of positive imaging showing damage to the brain doesn't mean it didn't occur.



Endocrine system

There are a variety of ways to prove that your client has sustained a serious injury to their brain that's disrupted processes in their body and affected their mental and emotional health. Everything from advanced MRIs that measure and map brain activity associated with blood flow or that use diffusion tensor imaging to measure the diffusion of water molecules in the brain, to sleep studies to evaluate whether a brain injury has caused sleep disturbances, to neuro-optometric testing, and speech evaluations. Another lesser-known avenue to rule-in a brain injury is to determine whether the client is suffering from neuroendocrine dysfunction and whether that hormonal dysfunction was a result of the brain injury.

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Neuroendocrine dysfunction and mTBI

One of the ways a traumatic brain injury can reveal itself is through disruption of endocrine functions in the person's body. The endocrine system is a network of glands, which release hormones into the bloodstream. The main functions of the endocrine system are (1) to produce hormones that control things in the body; (2) to control how those hormones are produced; and (3) to actually send those hormones into the bloodstream so they can travel to other body parts and tissues. Hormones are chemical messengers that regulate various physiological processes in the body. They are released into the bloodstream and travel to specific parts of the body where they elicit responses. Hormones control mood, growth, metabolism, and reproduction.

The human body has eight main endocrine glands. The thyroid gland is located in the neck and controls metabolism. The thymus gland is located in the lungs and makes white blood cells, which are part of the immune system. The adrenal glands are located in the kidneys and regulate metabolism, immune system, blood pressure, and the body's response to stress. The pancreas is located in the stomach and makes enzymes that break down sugars, fats, and starches. The reproductive glands (ovaries and testes) are located in the pelvis and help with growth and reproduction. The remaining three are located within the brain – the pituitary gland, the hypothalamus, and the pineal gland.

The pituitary gland is considered the endocrine system's "master gland." It uses information it gets from the brain to tell the other glands in the body what to do. When there is a disruption in the communication between the nervous system (i.e., the brain) and the endocrine system – that's called neuroendocrine dysfunction (also known as NED).

The anatomic and physiologic complexity of the pituitary gland increases its likelihood of injury during the forces that cause a traumatic brain injury. Damage to the pituitary gland resulting from a traumatic brain injury can cause that interruption in communication and then disrupt the production and distribution of hormones in the body.

It's important to understand how damage to the pituitary gland is caused. The mechanism most likely to occur due to a mild traumatic brain injury is vascular damage to the pituitary gland. This happens due to the structure and location of the gland. The pituitary gland looks a lot like two boxing speed bags next to one another. It has two parts – the anterior pituitary gland and the posterior pituitary gland. The anterior portion is connected directly to the brain by blood vessels, and the posterior portion is part of the brain itself and secretes hormones directly into the bloodstream. Both portions are surrounded on the outside by blood vessels and nerves. The gland is found behind the bridge of the nose and hangs off the brain into a bony compartment at the base of the skull called the sella turcica.

During an event that causes rapid movement of the brain, the pituitary gland can stay in place as the brain moves backward and forward or side to side. This can cause stretching and micro-tearing of the blood vessels and nerves around the gland that connect it to the brain. This kind of damage to the gland can interfere with the production of hormones and can result in neuroendocrine dysfunction. It is well-settled that trauma can be a cause of neuroendocrine dysfunction – well-known sufferers of NED are service members who have been exposed to blasts or explosions during combat. One type of dysfunction a TBI can cause is hypopituitarism, where the damage to the pituitary results in other glands in the body failing to produce at all or not enough of certain hormones. Neuroendocrine dysfunction can be a contributing factor for people who have prolonged symptoms from their brain injury or have a difficult time rehabilitating after a TBI.

This damage to the pituitary gland will almost certainly not show up on imaging. But it will reveal itself in hormonal deficiencies that can occur immediately or develop over time. Pituitary deficiencies are seen at a high rate in persons who have sustained a traumatic brain injury – up to 60% of adult patients who have sustained traumatic brain injuries, and 42% in minor patients. It's such a significant consequence of a traumatic brain injury that the United States Department of Defense has developed a training for doctors to use to screen for and identify neuroendocrine dysfunction in active-duty and veteran military members.

The diagnosis of neuroendocrine dysfunction can be difficult and is not typically considered because the symptoms may overlap with issues that typically accompany a brain injury, like post-concussive syndrome, sleep disorders, depression, and post-traumatic stress disorder.

The Department of Defense recommends that healthcare providers screen patients for neuroendocrine dysfunction who have been diagnosed with a mild traumatic brain injury and are experiencing persistent symptoms suggestive of neuroendocrine dysfunction for more than three months or have a new onset of symptoms suggestive of NED within 36 months of the initial injury. Such symptoms include fatigue, insomnia, impaired cognition and memory loss, difficulty concentrating, and emotional and mood disturbances.

Types of hormonal deficiencies caused by neuroendocrine dysfunction

Damage to the pituitary gland can cause a variety of hormonal deficiencies throughout the body. Some of these deficiencies present themselves immediately (like adrenal insufficiency, which causes low blood pressure and low blood sugar that presents as severe weakness and abdominal pain, or hyponatremia, which causes the body to hold onto too much water and causes nausea and fatigue); others develop

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months or years later (like low growth hormone, which is discussed below).

The most common pituitary hormone deficiency that is seen in long-term survivors of mild traumatic brain injuries is in growth hormone. Human growth hormone is a single-chain polypeptide that is involved in a variety of biological functions including growth, development, and immunity. Symptoms of growth hormone deficiency include decreased muscle mass and strength, irritability, low bone density, reduced heart rate, low blood pressure, a loss of interest in socialization, memory issues, fatigue, weight gain (particularly around the waist), depression, anxiety, and problems concentrating.

Another common hormonal deficiency is in gonadotropin. Gonadotropins are essential for regulating reproductive function in both males and females. There are two main gonadotropins – luteinizing hormone (LH) and follicle- stimulating hormone (FSH). These facilitate important functions like triggering ovulation and the production of estrogen in women and the production of testosterone and development of sperm cells in men. Symptoms of gonadotropin deficiency include libido changes, infertility, anemia, hair loss, decreased muscle mass and strength, and mood disorders.

Other hormone deficiencies seen in patients who have sustained traumatic brain injuries include TSH deficiency (secondary hypothyroidism) and ACTH deficiency (adrenal insufficiency). ACTH deficiency causes hypotension, weight loss, malaise, and fatigue, and TSH deficiency causes weight gain, cold intolerance, impaired short-term memory, and dry skin.

Testing for and treating neuroendocrine dysfunction

It's important that mild traumatic brain injury sufferers be evaluated for neuroendocrine dysfunction because untreated NED is associated with increased mortality. It also goes without saying that getting to the bottom of a patient's symptoms and finding the cause so it can be treated results in overall improvements in prognosis and quality of life.

The Department of Defense recommends that a person who a healthcare provider suspects is suffering from neuroendocrine dysfunction caused by a traumatic brain injury have the following screening labs:
0800 Cortisol levels
TSH – Thyroid Stimulating Hormone
LH – Luteinizing Hormone
FSH – Follicle Stimulating Hormone
IGF – 1 Insulin-like Growth Factor
Ft4 – Free Thyroxine
Testosterone (males)/Estradiol (females)

These labs can be ordered by a client's primary care physician, or even better, by a treating endocrinologist (or even better, a neuroendocrinologist). They can also be ordered by a neurologist or other traumatic brain injury provider. The results will tell the clinician whether the client's hormone levels are too low, which would indicate that something has disrupted the pituitary gland's production of those hormones. Once low levels of a hormone are discovered, the client can have testing done to determine what exactly their deficiency is.

For neuroendocrine dysfunction-induced low growth hormone, their hormone levels can be tested via a stimulation test (because growth hormone is released in the body in pulses, a random blood measurement of growth hormone is not a reliable indicator of growth hormone status). There are a handful of different tests that can be used which take around two hours and are performed on an outpatient basis.

If a person's stimulation test reveals their mild traumatic brain injury has caused damage to their pituitary gland that has resulted in low growth hormone, they can be treated with recombinant human growth hormone (rhGH). This is a synthetic medication administered via daily subcutaneous injections. Growth hormone therapy has been shown to improve body mass, bone density, exercise tolerance, personal productivity, and quality of life. The research that has been done on the effect of hormone-replacement demonstrates that such treatment does improve some mild traumatic brain injury symptoms – meaning that while some symptoms may be permanent, others may be treatable. People who have used rhGH have found an improvement in their fatigue after three months, and an improvement in cognition after five months. It is a treatment that someone suffering from low growth hormone will have to endure for the rest of their life in order to minimize the treatable symptoms of their traumatic brain injury.

Similarly, persons suffering from low gonadotropin, secondary hypothyroidism, and adrenal insufficiency can have testing done that will determine what their level of deficiency is. There are also medications that will help address the hormonal insufficiency, which they will have to be on their entire lives to address the symptoms caused by these neuroendocrine dysfunction issues.

Having a person who has sustained a traumatic brain injury evaluated for neuroendocrine dysfunction is one of many ways to substantiate brain injury. More importantly, it can help guide them to the medical treatment they need to improve their quality of life and give them an opportunity to resume their life as close to the way it was before their injury.

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