



DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury

Mild Traumatic Brain Injury: Neuroendocrine Dysfunction

Indications and Conditions for Neuroendocrine Dysfunction Screening Post Mild Traumatic Brain Injury



Objectives

Upon completion of this educational module, the learner will be able to:

- Describe the basic pathophysiology of neuroendocrine dysfunction (NED) as it relates to mild traumatic brain injury (TBI), including the two primary endocrine glands that are affected during a blast injury
- Identify at least five symptoms that differentiate NED from persistent mild TBI symptoms
- Identify at least five laboratory tests used for NED screening post mild TBI
- Identify the major criteria for Endocrinology referral among patients with strong suspicion of NED

Scope of DCoE NED Recommendation

What it is:

The DCoE clinical recommendation described in this educational module is specifically intended for use in the mild TBI patient population, including:

- Individuals diagnosed with mild TBI with persistent symptoms at least three months post injury (post-concussion syndrome)
- Individuals who develop symptoms suggestive of neuroendocrine dysfunction up to 36 months post injury

This educational module is relevant to all health care professionals conducting screening for patients with mild TBI in any Defense Department (DoD) health care setting, including both primary and specialty care.

Scope of DCoE NED Recommendation

What it is not:

The DCoE clinical recommendation described in this educational module is not intended for use for the moderate to severe TBI patient population, and patients with acute endocrine disorders, including adrenal crisis and hypoglycemic coma.

This educational module is not relevant to patients seen in an acute inpatient setting, and should not be used for screening other symptoms or disorders of the endocrine system.

Introduction

The information that follows on the definition, classification, and overall symptom profile of NED is provided:

- As introductory materials for those who are new to the subject of NED
- With an assumption that the reader has principal knowledge of TBI, including assessment, treatment and differentiation between mild, moderate and severe TBI





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Neuroendocrine Dysfunction (NED)



Background

Approximately **233,425** mild TBIs have occurred from year 2000 through Dec 2011 among service members

- 77 percent are classified as mild TBI
- The majority of mild TBI patients have symptoms that last only a short period of time, recovering within minutes to several weeks

Approximately 15 percent of patients (among civilian cohorts) with mild TBI experience persistent symptoms

- Of the approximate 15 percent who experience a mild TBI and remain symptomatic, an estimated **15-30 percent develop NED**

Definition of NED

The term “neuroendocrine dysfunction” refers to a variety of conditions caused by imbalances in the body's hormone production directly related to the brain.

There are two areas of the brain responsible for regulating the production of hormones, the **hypothalamus** and the **pituitary gland**.

Damage to the hypothalamus or pituitary gland caused by TBI (including vascular damage, rupture, brain swelling, vasospasm, pituitary swelling or inflammation), may impact the production of pituitary hormones and other neuroendocrine functions of the brain.

TBI-Related NED

NED following TBI is the result of direct trauma (e.g., coup-contrecoup injury), or biochemical response to a blast exposure, that interferes with the normal production and regulation of hormones produced by the pituitary gland and the hypothalamus

Pathophysiology

The most common **hormonal deficiencies** associated with TBI include:

- Pituitary deficiencies (TSH/FSH/GH/IGF-1)
- Gonadotropin deficiencies (LH/FSH/testosterone/estradiol)

Adrenocorticotrophic hormone, thyroid deficiency and prolactin deficiencies are also seen among patients with neuroendocrine involvement following TBI

List of Hormones

FSH	Follicle-Stimulating hormone
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GH	Growth hormone
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IGF 1	Insulin-like growth factor 1
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LH	Luteinizing hormone
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TSH	Thyroid-stimulating hormone
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Hormone Deficiencies Symptoms

Growth hormone: Increased abdominal fat mass, fatigue, decreased vigor and concentration, decreased lean body mass, dyslipidemia, anxiety, depression, impaired judgment

Gonadotropin: Males — infertility, decreased libido, erectile dysfunction, decreased muscle mass, decreased exercise tolerance, anemia and testicular atrophy.
Females — amenorrhea, sexual dysfunction, breast atrophy

Corticosteroid: Adrenal crisis, hypoglycemia, hyponatremia, myopathy, anemia, depression, fatigue, anxiety, apathy, weight loss, loss of libido

Hormone Deficiencies Symptoms

Thyroid hormone: Decreased energy, depression, cold intolerance, weight gain, fatigue, poor memory, muscle cramps, constipation, myopathy, hypotension, bradycardia, neuropathy, skin, hair and voice changes

Prolactin: Males — decreased libido, impotence.
Females — amenorrhea, oligomenorrhea, galactorrhea, infertility, hot flashes, vaginal dryness, hirsutism (in post menopausal women).

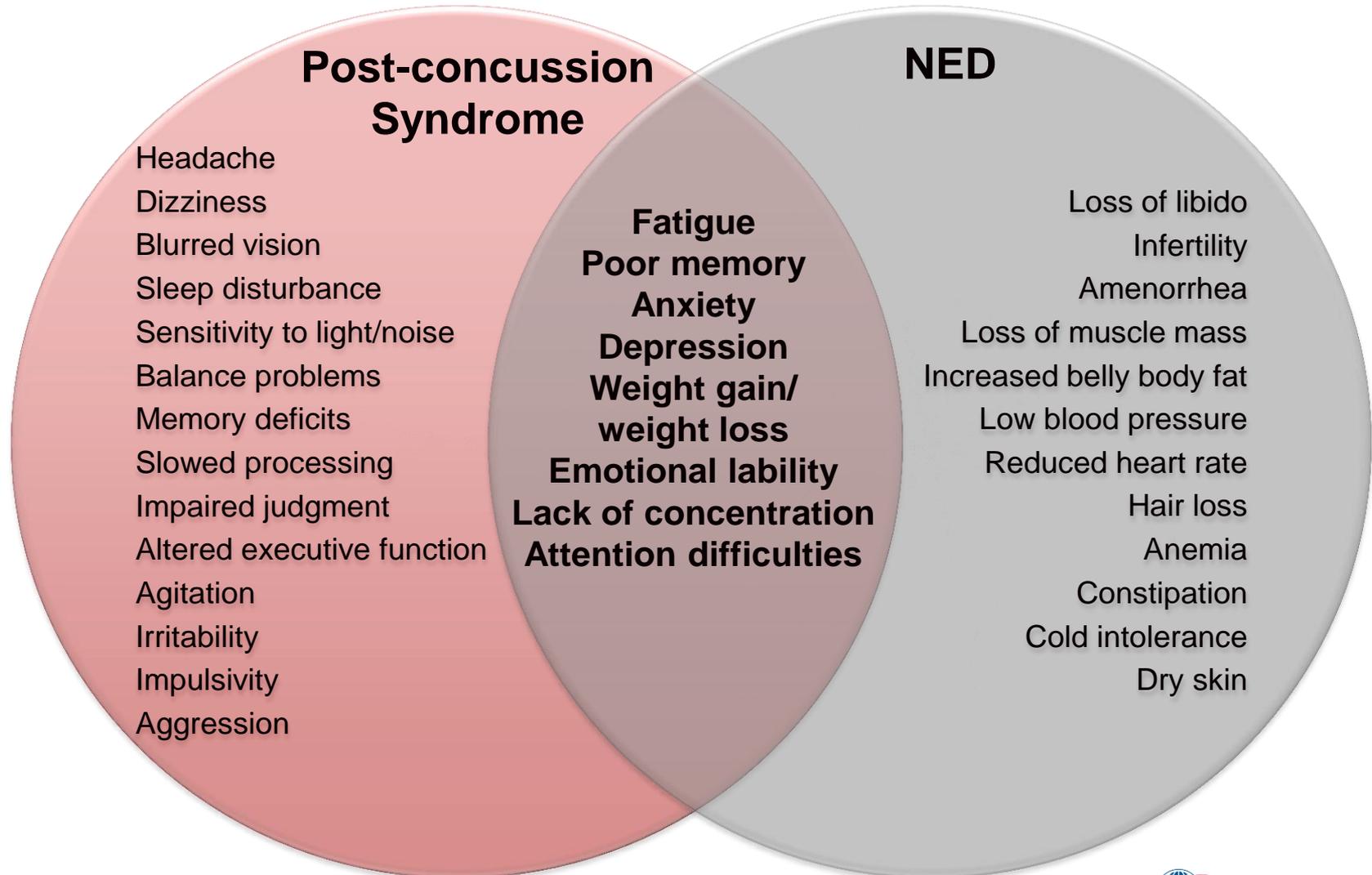
Both — sudden onset of depression

Antidiuretic hormone: Excessive urination, dehydration, excessive thirst, hypernatremia (potentially leading to weakness, altered mental status, coma, seizures)

Hormone Deficiencies Symptoms

	Males & Females	Males	Females
Growth Hormone (GH)	Increased abdominal fat mass, fatigue, decreased vigor and concentration, decreased lean body mass, dyslipidemia, anxiety, depression, impaired judgment		
Gonadotropin (LH/FSH)		Infertility, decreased libido, erectile dysfunction, decreased muscle mass, decreased exercise tolerance, anemia, testicular atrophy	Amenorrhea, sexual dysfunction, breast atrophy
Corticosteroid (ACTH)	Adrenal crisis, hypoglycemia, hyponatremia, myopathy, anemia, depression, fatigue, anxiety, apathy, weight loss, loss of libido		
Thyroid-stimulating Hormone (TSH)	Decreased energy, depression, cold intolerance, weight gain, fatigue, poor memory, muscle cramps, constipation, myopathy, hypotension, bradycardia, neuropathy, skin, hair, and voice changes		
Prolactin (PRL)	Sudden onset of depression	Decreased libido, impotence	Amenorrhea, oligomenorrhea, galactorrhea, infertility, hot flashes, vaginal dryness, hirsutism (in post menopausal women)
Antidiuretic Hormone (ADH)	Excessive urination, dehydration, excessive thirst, hypernatremia (potentially leading to weakness, altered mental status, coma, seizures)		

Overlap of Symptoms



Symptoms Suggestive of NED

Behavioral, Emotional and Sleep Related Symptoms

- Depression
- Emotional lability
- Anxiety
- Fatigue
- Poor memory
- Lack of concentration

Symptoms Related to Reproductive Function

- Loss of libido
- Infertility
- Amenorrhea

Symptoms Suggestive of NED

Somatic Symptoms

- Loss of muscle mass
- Increased body fat around the waist
- Weight gain/weight loss
- Low blood pressure
- Reduced heart rate
- Hair loss
- Anemia
- Constipation
- Cold intolerance
- Dry skin

Screening for NED

NED should be considered in the differential diagnosis during screening for the following:

- Patients with persistent mild TBI symptoms suggestive of NED that do not resolve after **three months** from initial injury
- Patients with onset of **new** symptoms, suggestive of NED, up to **36 months** after the initial injury
- Patients with co-occurring conditions:
 - Review overlapping symptoms for NED and mild TBI, as well as other psychiatric disorders including sleep disorders, depression and posttraumatic stress disorder (PTSD). Symptoms include fatigue, poor memory, anxiety, depression, weight gain/weight loss, emotional lability, lack of concentration, attention difficulties

Delay in diagnosis and treatment of NED may impair overall recovery and rehabilitation of the mild TBI patient

NED Screening Recommendation

For patients with persistent symptoms suggestive of NED that do not resolve in **3 months** following mild TBI, OR patients with onset of new symptoms suggestive of NED up to **36 months** following mild TBI.

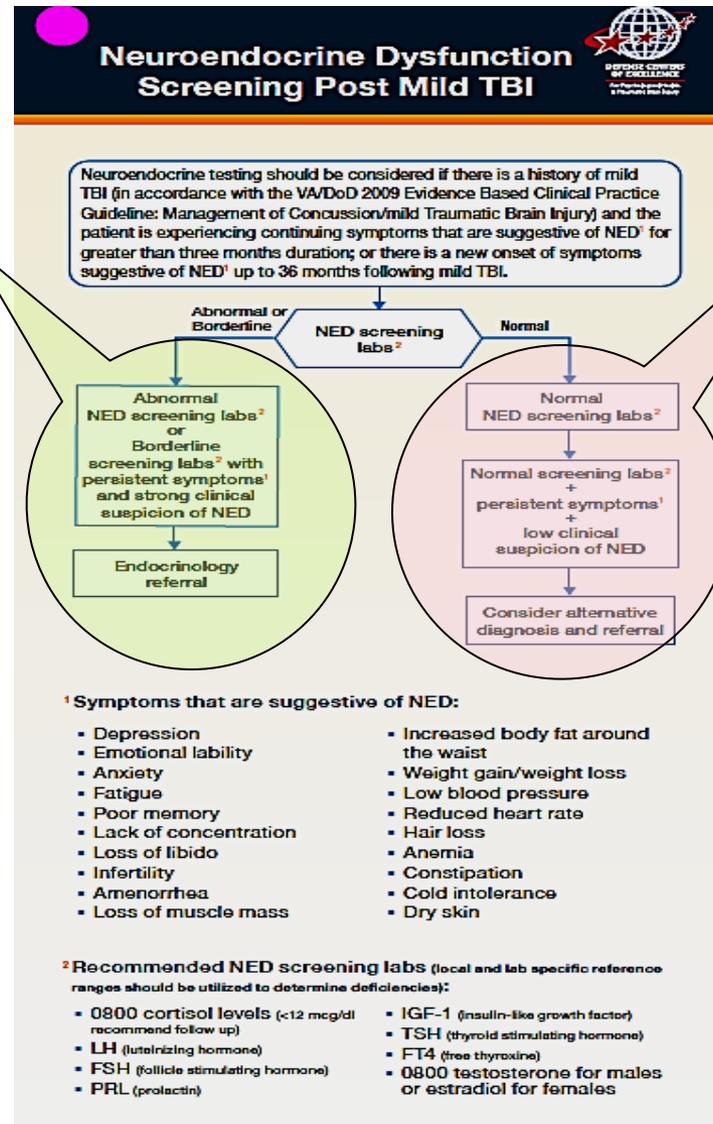
Recommended NED laboratory screening includes:

- 0800 Cortisol levels: <12 mcg/dl, recommend follow up
- Thyroid Stimulating Hormone
- Luteinizing Hormone
- Follicle Stimulating Hormone
- Prolactin
- Insulin-like Growth Factor
- Free Thyroxine
- Testosterone (males only)
- Estradiol (females only)

Clinical Recommendation

Consider referral to Endocrinology for:

- **Abnormal NED screening lab results**
- **Borderline NED screening lab results among individuals with persistent symptoms and a strong clinical suspicion of NED**



If the patient continues to have **normal NED** screening labs and persistent symptoms, consider alternative diagnosis and referral



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Case Study



NED Case Study

Air Force Staff Sgt. Cardenas is a medic who deployed twice to Afghanistan. He was involved in a mortar attack during his second tour. One of the mortars landed 10 feet from him. Cardenas does not remember losing consciousness, however complained of the following symptoms during his in-theater medical evaluation:

- Headache
- Sensitivity to light
- Dizziness
- Ringing of ears

NED Case Study *cont.*

Cardenas was evaluated, diagnosed and treated for mild TBI in-theater. His symptoms (sensitivity to light, dizziness and ringing of ears) resolved within 48 hours, except for a mild persistent headache.

Three weeks post injury, while still deployed, Cardenas developed the following symptoms:

- Anxiety
- Difficulty sleeping
- Lack of concentration
- Continues to have mild but transient headaches

He chooses not to seek medical attention assuming that symptoms are a result of deployment related stress.

NED Case Study *cont.*

Three months after his initial injury, Cardenas returns home from his deployment.

He continues to have difficulty concentrating at work and home. While his headaches have completely resolved, he continues to have difficulty sleeping, and increased anxiety. His symptoms are now weighing heavily on his personal life. He has a poor appetite but has gained 10 pounds since return from his deployment. He has also lost interest in sexual activity.

NED Case Study *cont.*

The primary care manager (PCM) at Cardenas' home base conducts further medical evaluation while considering the differential diagnosis including post-concussive syndrome, PTSD, depression and NED.

The PCM informs Cardenas that, although uncommon, mild TBI patients may experience neuroendocrine dysfunction three to 36 months after their initial injury, he orders the following labs:

- 0800 Cortisol levels: <12 mcg/dl, recommend follow up
- Thyroid Stimulating Hormone (TSH)
- Luteinizing Hormone (LH)
- Follicle Stimulating Hormone
- Prolactin
- Insulin-like Growth Factor
- Free Thyroxine
- Testosterone (males only)

NED Case Study *cont.*

Cardenas' results showed marginally low TSH, borderline testosterone deficiency and borderline low level of LH. However, all of the other lab results are normal.

Cardenas continues to experience persistent symptoms including:

- Low libido
- Loss of lean muscle mass
- Weight gain
- Anxiety
- Attention difficulties
- Mood disturbances

Cardenas' PCM recognizes a strong suspicion of NED based on unresolved symptoms and borderline lab results.

NED Case Study *cont.*

Test Question 1:

Identify possible symptom(s) that may overlap between NED and mild TBI.

- a) Ringing in ears
- b) Weight loss or weight gain
- c) Lack of concentration
- d) Answers b & c
- e) All of the above

NED Case Study *cont.*

Test Question 2:

Due to possible delayed onset of NED, when should laboratory screening be considered for patients with persistent symptoms suggestive of NED?

- a) 1-10 days from initial injury
- b) 2-3 week from initial injury
- c) 50 month from initial injury
- d) 3-36 months from initial injury

NED Case Study *cont.*

Test Question 3:

Understanding the pathophysiology of NED, what glands are most likely affected in a patient presenting with symptoms of NED with history of TBI?

- a) Hypothalamus
- b) Adrenal glands
- c) Pituitary gland
- d) Answers a and c
- e) All of the above

NED Case Study *cont.*

Test Question 4:

Based on Cardenas' symptoms, which of the following endocrine labs might be abnormal in an individual with mild TBI-related NED?

- a) 0800 Cortisol
- b) Luteinizing hormone
- c) Prolactin
- d) Testosterone
- e) All of the above

NED Case Study *cont.*

Test Question 5:

Based on information presented in the case study, what should the PCM do next?

- a) Endocrinology consultation
- b) Consider alternative diagnoses and referral
- c) Cognitive processing therapy
- d) Prescribe selective serotonin reuptake inhibitor
- e) All of the above

Resources

Defense Centers of Excellence for Psychological Health & Traumatic Brain Injury (DCCoE)

dcoe.health.mil

Phone: 800-510-7897

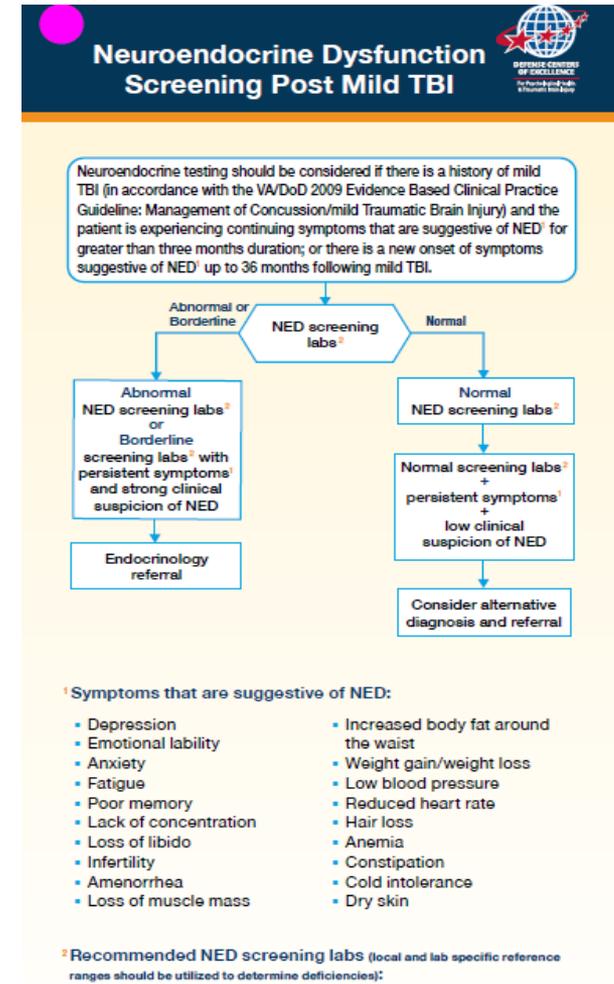
Email: Resources@DCCoEOutreach.org

Defense and Veterans Brain Injury Center (DVBIC)

www.dvbic.org

Phone: 866-966-1020

Email: info@dvbic.org



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