



**Defense and Veterans Brain Injury Center  
“Clinical Updates in Brain Injury Science Today [CUBIST]” Podcast  
“Neuroendocrine function and associated mental health outcomes following  
mild traumatic brain injury in OEF-deployed service members”**

**Total Run Time: 9:38  
Host: Dr. Donald Marion**

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**Marion:** The views, opinions, and findings contained in this podcast are those of the host and subject matter experts. They should not be construed as official Department of Defense positions, policies, or decisions unless designated by other official documentation.

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**Marion:** Hi. Welcome to Clinical Updates in Brain Injury Science Today, or “CUBIST,” a podcast for health care providers about current research on traumatic brain injury, also known as TBI. This program is produced by the Defense and Veterans Brain Injury Center, otherwise known as DVBIC. I'm your host today, Don Marion.

Today I'll be speaking with Amanda Gano about a recently published article on traumatic brain injury. Amanda and I will discuss a study entitled: “Neuroendocrine function and associated mental health outcomes following mild traumatic brain injury in OEF-deployed service members” by Stephanie Ciarlone and colleagues, published in the *Journal of Neuroscience Research* in March 2020.

**Marion:** Hi Amanda, and thanks for bringing this article to our attention today. Can you tell me a little bit about this study?

**Gano:** Hi Don. Sure, I'd be happy to. So, this study examined 131 patients that were seen during deployment at the Concussion Restoration Care Center, or CRCC, at Camp Leatherneck, in Afghanistan from 2010-2012. So, all of the patients were active duty service members deployed in support of Operation Enduring Freedom. Of those service members, 59 had been diagnosed with concussion, and 72 were considered to be concussion negative. So, medical records and blood samples were collected before injury and for up to three years after injury for the majority of patients. The serum levels of anterior pituitary hormones were then correlated with mental health outcomes. So, compared with the non-concussed group, serum levels of LH, or luteinizing hormone, and testosterone were significantly decreased at three years after injury, and cortisol was significantly decreased at one year after injury. The study found that 47.6 percent of head injured service members had “hypofunction,” defined as a decrease in hormone levels from baseline, in at least one of the five anterior pituitary hormones post-injury. Mental health disorders in general, and specifically anxiety disorders, were seen more often in concussed service members with deficiencies of one or more of the anterior pituitary hormones. So, Don, it's really important to note here that the researchers did not describe clinically relevant hormone levels, or actual diagnosed neuroendocrine disorders, so they only compared pre-deployment levels to post-deployment levels. In other words, they didn't find that service members with deficient testosterone levels had impotence or other endocrinopathies specifically related to that hormone, but just that there levels were decreased from baseline.

**Marion:** Amanda, did they tell you what the baselines were or what the threshold was below which they were calling these hormones deficient?

**Gano:** You know they did not define a specific baseline threshold. And so they just defined the deficiency as anything lower than their baseline.

**Marion:** I see. So I guess it's important to note that while this study is examining a change in hormone levels pre and post-concussion, there are a lot of other things that can impact those hormone levels. Amanda, I know that most previous studies, including a DVBC study by Therese West and Steve Sharp published in 2014, found that growth hormone is the most common anterior pituitary hormone effected by TBI. Yet this study found no significant differences in growth hormone between the control and concussed patients over the three year period. How do you explain that?

**Gano:** Yeah, so I think that this could probably be explained by how the samples were tested, and I'll get into that a little bit more when we discuss limitation section of this study.

**Marion:** That's a great segue into how was this study done Amanda?

**Gano:** Sure, so this study was a retrospective case control study that examined 59 positive concussion patients and 79 concussion negative controls who were seen at the CRCC in Afghanistan from 2010-2012. This study then examined the difference in five different hormones: testosterone, luteinizing hormone, or LH, human growth hormone, cortisol, and prolactin, from samples obtained before deployment, and then for up to three years after deployment. The study team used serum samples obtained from the Department of Defense Serum Repository, along with demographic and concussion data obtained from service members medical records in the CRCC database.

**Marion:** Alright Amanda, just so I get this straight, all of these service members were referred to Camp Leatherneck, or the CRCC. But once they got there, only 59 of those service members were determined to have a concussion. The other 79 were determined not to have had a concussion, even though they were referred there. Is that correct?

**Gano:** Correct. So those service members were likely just referred for a concussion evaluation for being exposed to a potentially concussive event, or something like that. And then once they were evaluated, they were determined to be concussion negative.

**Marion:** Great. It's my understanding that they used the Department of Defense definition for concussion in diagnosing concussion, correct?

**Gano:** That's correct. So alteration of consciousness, loss of consciousness, or post-traumatic amnesia, so a memory gap would be the DoD definition of concussion

**Marion:** What exactly is the DoD Serum Repository?

**Gano:** That's a good question, Don. The DoD Serum Repository stores serum samples from active duty service members who are required to provide samples pre and post deployment, as well as every two years, for HIV tests. So, those samples are frozen and stored and are made available to researchers within the DoD for military relevant research.

**Marion:** That sounds like a great resource for this kind of research. Finally, what were the limitations of this study?

**Gano:** Well, Don there were several things that limit the clinical applicability of these study findings. One of the biggest ones is that the blood samples used to test these hormones was taken from the DoD Serum Repository, and in order to get an accurate clinical result for lots of these levels, those tests need to be drawn at a specific time of the day. So the study could not control for that. Additionally, to further test for disorders like adrenal insufficiency, provocative or stimulation tests would need to be completed to get an accurate result. Provocative tests like ACTH Stem tests, and Insulin Tolerance Test or a Glucagon Stimulation Test are in fact the recommended methods for obtaining accurate results for a lot of these deficiencies, and those tests were not done. And that could be one reasons the investigators did not detect low growth hormone levels, to get back to your early question from earlier.

So, the rationale for this study also was to look at the effect of blast as a mechanism of TBI and cause for neuroendocrine dysfunction, but the study listed that nearly 40 percent of their TBI group did not have a blast as the known mechanism of injury. So we thought that was a limitation as well. And then finally, the study also did not take into account other factors that may influence these hormone levels, specifically in the military community, altered sleep schedules, and chronic high stress situations which can contribute to an altered hypopituitary axis functions. So, those were some limitations.

**Marion:** That makes a lot of sense Amanda. Finally, what would you consider the key takeaways? And by that I mean, what do you want providers to take away from this podcast?

**Gano:** Yea, so, the findings from the study are a little soft. But it does appear that blast-induced concussion may be associated with a mild, though significant reduction in serum, LH, and testosterone levels. And there is some evidence that that reduction may be associated with increased anxiety levels in active-duty service members. But, you know the most important thing that I took from this study, Don, was that further research really is needed before we can truly determine the impact of head injury on neuroendocrine dysfunction. So I hope that future studies need to determine if hormone replacement therapy is effective in treating mental health or behavioral problems that may be attributed to the hormone deficiency. And this study was not designed in that fashion, so.

**Marion:** Thanks Amanda. Sounds like there are important limitations to the study, so I really appreciate you bringing that to our attention. That's all we have time for today. You can stay up-to-date on future episodes by subscribing to "CUBIST" on iTunes, Sound Cloud, Stitcher, or wherever you listen to podcasts, where you can also find links to the articles we discuss and other relevant resources.

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"CUBIST" is produced and edited by Vinnie White and was hosted today by me, Don Marion. It is a product of the Defense and Veterans Brain Injury Center, led by Division Chief Captain Scott Pyne, Medical Corps, United States Navy.

Thank you for listening to this episode. Next time, we will discuss TBI research getting attention in the mainstream press.

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