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Uncovering Unknowns in TBI: An Exploration of Manifestations in Women

Dr. Wilner:
You're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner, and joining me today to talk about traumatic brain injury and just how little we actually know about its manifestations in female patients, particularly those in the military, is Dr. Maheen Mausoof Adamson. Dr. Adamson is a Clinical Associate Professor of Neurosurgery at Stanford School of Medicine and the Clinical Research Director for Rehabilitation Services at VA Palo Alto. She's also a leader in identifying gender differences in brain injury, particularly in the veteran population. Dr. Adamson, thanks so much for being here today.

Dr. Adamson:
Thank you very much for having me.

Dr. Wilner:
To start us off, Dr. Adamson, can you explain why there is a skew in our evidence-based data towards men versus women who have traumatic brain injury, or TBI for short?

Dr. Adamson:
Sure. I think one of the most important things we have to look at is the history of males and females and their enrollment in the military. In military conflicts, since about 2000, more than 383,000 military personnel have sustained traumatic brain injury. The majority of these non-penetrating TBIs that were sustained were classified as mild TBI. There's been an incredible amount of publications that have come out of mild TBI in this population, however, 95% of this military data is male.

What's really surprising, also, is that since that time, there's been a growing number of females in the military; there were about 15% cases in 2010 and now I think recently it's gone up to 17%. But that still seems to be like the cohort for females is either reported as part of the overall cohort or it's not looked at separately.

In a recent TBI Model System Study, which is national, women veterans tended to have fewer support, meaning financial, social, and romantic than men. They also sought less help through the VA. In this national dataset of 1,554 patients, only 91 were women. This is more important for us to do more research in women because now, women make about 17% of the military and veteran population. We just don't know whether they are actually suffering less from TBI post-concussive symptoms or they're seeking less help.

There's also less known; because of this, less is known about natural history and pathophysiology and outcomes of TBI in females. And we already know that they suffer from very unique physical, mental, and social challenges, triggers, and stressors.

Dr. Wilner:
Well let me be devil's advocate for a moment. I think the fact that there is fewer females is not due to any discrimination is simply because there have been less women who have put themselves in harm's way to get TBI. So I don't think that the medical community can be accused of any discrimination in terms of data collection. But my question is why would you assume that females need to be studied separately? Apart from being slightly smaller overall and having smaller brains, are there differences in anatomy or physiology that would suggest that they would respond to TBI differently?

Dr. Adamson:
So very loaded question, I will go ahead and try to break this apart. You're absolutely right that the number of women have been less and that is not because of any discrimination or anything, it's just what it is. However, as we have looked at in the past few decades, women are now getting into fields that have more risk. So I'll give you an example that's not military. Women are enrolling more in high-

risk activities, so an NCAA surveillance program from 2004-2009, females reported 1.4 times higher concussion rates than males playing the same sport. And so they actually returned to play guidelines in NCAA actually take into account the sex of the athlete.

Now why are those differences there? That's the second part of your question. There's two ways to look at it. One is symptom reporting; what kind of symptoms are actually different in males and females? So to give you a breakdown of that, 30% of women in the military are more likely than males to experience PTSD. That's 30%. They're 4 times more likely to have substance abuse. They're 2.7 times more likely to be unemployed. There's also a huge incidence of intimate partner violence and intimate partner violence is obviously reported very highly in the civilian population, but it's actually higher in female veterans. One-fifth actually are female veterans screened for intimate partner violence. They're 7 times higher rate of homelessness among injured female veterans. And I can tell you more about within our own datasets what we have found in terms of symptom reporting. And I'll get to that in a minute but I want to get more into the physiological aspects of things.

Now overall, the amount of blood we have in our bodies, as well as the size of our brain, is historically considered to be smaller; obviously it's dependent on your BMI and your diet and things like that. What's also important is that we have hormones, well women have the hormonal, and we also have a different way of dissolving and digesting medicine. So this is one example. The reason why women get addicted more is because the medication we take it gets digested faster because our stomach has a different setup. Now in terms of that would allow us to take in more medication; that takes into addiction. However, men do not digest the medicine faster, so they take more of it so that there's higher rates of what's called 'overdose.' That's just one example of the physical body.

Now in terms of the brain, we have different anatomical locations of certain functions, and there's been some areas that have been shown to be either bigger or smaller and data presents they represent different types of connectivity in terms of whether you are male or female.

So within our datasets, we have what's called the polytrauma network in the VA. We have several reports of sex differences that we have actually written and we also collaborate with people and other people have reported. I'm presenting female VA polytrauma TBI patients, and it's leading to major gaps in the understanding of the role of sex in military polytrauma TBI. Those gaps exist not just in the diagnosis of what is happening in the brain and in the symptoms but also in the treatment and also in the outcomes. And what we did was we wanted to get at it from both sides. We wanted to look at the symptoms as well as we wanted to look at what's happening in the brain. So we matched our sample based on age, the time of injury as well as the mechanism of injury, meaning whether it was a sports concussion during the military time, whether it was a motor vehicle accident, a blast or intimate partner violence, or a fall. So we matched the males and females on those three major things, and we looked at their symptoms and what we found was that there was a moderate effect on the symptoms of TBI in the difference between male and female. But the most important difference was that females reported more cognitive problems. Females were also living alone more than men. They were also more unemployed females not seeking employment. And these are basically results that kind of mirrored other studies that we have seen and read about.

Then we went and looked at brain differences. So we ended up looking at their brains after injury. Now this is a problem with TBI because you get to look at brains after injury; you don't have what's called 'pre-morbid data', so you don't know what the brain looked like before they had injury. But that's when you go into literature and you look at healthy adults and you also have a. control population. So what we did was we looked at male and female with TBI and their brains and then we looked at male and female controls. What we did was we looked at something called cortical thickness, how thick your cortex is. Usually women have thicker cortex. And it has been reported to be thin after TBI in some studies, but in our study, what we found, that after TBI, compared to males, females had thinner cortex. This is years after TBI 'cause remember we're looking at veterans. So the time to injury is quite high, it could be anywhere from five to ten years. And these are chronic symptoms that we're looking at. So women actually had thinner cortex after brain injury than men. So, whatever it is, it's happening after brain injury. Men seem to be gaining the cortex, viability back but women the cortex remains thin.

Dr. Wilner:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner and I'm speaking with Dr. Maheen Muasoof Adamson about gender differences in traumatic brain injury, or TBI for short.

So Dr. Adamson, there's a natural experiment that compares male and female brains after injury, and it's been going on for a long time and that's neurosurgery. So have you been able to glean any data on post-op, recovery times, or neurologic deficits by comparing men and women?

Dr. Adamson:
So my answer to that is we wrote a review paper about neurosurgery in males and females in veterans. Now there's one thing we have been able to look at is just the incidence of and the symptoms reported and they're very similar to what I've, just recently just spoke about. What's important in looking at this is that I study mostly mild and moderate TBI and people who've had TBI and still suffer from

post-concussive symptoms years after the injury. When you have severe TBI and you actually go through surgery, I see that as a separate thing because that is more severe TBI and it's complicated by other factors, such as recovery from surgery and so I don't have specific data on pre- and post-op but I do know that women have longer recovery time, longer return to duty or return to work, return to education, and one of the reasons why that happens is and I, this is my opinion as well, is that women have several different stressors than men. And the reporting of psychiatric issues in women, including anxiety and depression is higher. Women disproportionately represent the caregiver population in the world, and it actually increases as you get older. That's one of the reasons why it's difficult to get women to be enrolled in research studies, it's difficult to get access to them, ask them to access the VA healthcare because they're usually at home taking care of someone. They're higher, so they represent the caregiver burden more. Caregiver burden includes having 40 to 60% higher depression than non-caregivers. They have a higher rate of psychiatric issues, including depression, including anxiety, and all of these psychiatric issues affect cognition.

Dr. Wilner:
Now, before we wrap up, Dr. Adamson, I want to address the potential mental health impacts of traumatic brain injury. Did you find any association with PTSD in female patients with TBI?

Dr. Adamson:
So there's a lot to say about that. I'd mentioned earlier that females, more than males in the military, are 30% more likely to experience PTSD, and, as I mentioned earlier, a recent national study reported women with TBI to have more PTSD. They also reported that women veterans tend to have fewer support mechanisms, and by support, I mean financial, social, and romantic support than men. They also seek less help through the VA, even if they're suffering from these mental issues. And I think that is a very important factor to consider because they may be suffering from this, but they are not reaching out for help.

Dr. Wilner:
Well, this has certainly been an eye-opening look at our knowledge gap regarding TBI in female patients and more specifically among female service members. And I want to thank you, Dr. Adamson, for joining me to discuss this research. It was great having you on the program.

Dr. Adamson:
Thank you very much. It was wonderful.

Dr. Wilner:
I'm Dr. Andrew Wilner. To access this and other episodes in our series, visit ReachMD.com/NeuroFrontiers, where you can Be Part of the Knowledge. Thanks for listening.