Defense and Veterans Brain Injury Center
"Clinical Updates in Brain Injury Science Today [CUBIST]" Podcast
"Lasting consequences of concussion on the aging brain: Findings from the Baltimore Longitudinal Study of Aging"
Total Running Time: 11:02
Host: Dr. Donald Marion

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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. Ms. Gano is a subject matter expert on TBI at DVBIC. Amanda and I will discuss a study entitled "Lasting consequences of concussion on the aging brain: Findings from the Baltimore Longitudinal Study of Aging," a study that was authored by Danielle June and colleagues and published in *Neuroimage* in July of 2020.

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

Gano: Hi Don, sure. So this was a really interesting article that came from the Baltimore Longitudinal Study of Aging cohort. And so for those who aren't familiar, the Baltimore Longitudinal Study of Aging is one of the world's longest running studies of aging. It started back in 1958, and they enroll healthy volunteers ages 20 and older and follow them longitudinally—for life—and even perform autopsies on those who have consented to that. So, it's a really valuable data resource. So, for this study, the researchers sought to find out whether a history of concussion had an impact on future neurodegeneration using both imaging modalities and cognitive testing.

The study examined various imaging and cognitive testing results from 51 older patients, so a mean age of 65 with a self-reported history of concussion and compared it to 150 matched case controls without concussion to determine the difference in structure, functionality, and clinical cognitive deficits over time. The imaging modalities they used were Magnetic Resonance Imaging, or MRI, Diffusion Tensor Imaging, or DTI, and 15 O-water PET scans. MRI was used to assess changes in total brain and ventricular volume in 21 different regions of interest. DTI was used to assess micro-structural damage in the white matter of the frontal and temporal regions of the brain. And PET scans were used to assess regional cerebral blood flow, or rCBF, as an indirect measure of localized neuronal activity. Cognitive tests were done using standardized neuropsychological assessments that tested the domains of memory, attention, executive function, and visuospatial ability.

Marion: Very interesting topic to me Amanda because the concern in the military are the long-term effects, or potential effects of blast exposure, and even low-level exposure, that's not sever enough to cause a concussion. And the question is, what effects, if any, are those blasts going to have on the aging brain. The only way we're really going to be able to answer that question and really figure this out is through these kinds of longitudinal studies like the Baltimore

Longitudinal Study on Aging. So, I'm glad they're doing it. I think that's important. So, exactly how was this study done Amanda?

Gano: Sure, so, of the 51 participants who reported a concussion, all 51 had at least one MRI and 37 of them had two or more brain MRIs. 40 had DTI, and 28 of those had longitudinal data, and 15 participants had PET scans with 12 of them that had longitudinal data. And then all 51 participants underwent the neuropsychological assessments with 46 of them that had longitudinal cognitive data with two or more visits. So I say this to emphasize this was a relatively small sample size. The researchers then compared the data in the concussed subgroup to matched case control data and performed statistical analyses to determine whether there was a difference.

Marion: Amanda, when you say longitudinal data, you mean they had more than one study correct?

Gano: Yes, correct. For MRI the second scan was done at a mean of about five years. For DTI, the second scan was done at three years. For PET studies, it was done at 5.3 years. And for cognitive studies, the follow up studies were done over 11.6 years.

Marion: Ok, great. Prior to getting their first study, how long had it been since they had their concussion?

Gano: Yeah, that's a really good question Don. So the average age of concussion was 23 years prior to the initial imaging. So a while ago. And the average age of concussion in this group was about 33 years old.

Marion: So typically, they were 33 when they had the concussion; then there was a lag of more than two decades before they had their first imaging study. Ok, I understand. So, exactly what did they find?

Gano: So, for MRI, in comparison to controls, the concussion group had smaller volumes of the temporal white matter and hippocampus at first imaging visit as well as larger ventricular volume. These differences remained stable over the follow-up visits. There were no significant differences in the rate of change between groups during longitudinal follow-up. For DTI, in comparison to controls, the concussion group showed significantly greater micro-structural damage in sub-frontal and temporal regions of the brain, particularly in the limbic system structures. And this was manifested by higher radial diffusivity at first DTI visit. These differences remained stable over the follow-up years and there was no significant difference in the rate of change between groups during longitudinal follow-up.

Changes in regional cerebral blood flow in those with a history of concussion, as measured by PET scanning were not as consistent. So that showed that both increases and decreases in regional cerebral blood flow, most predominately in limbic system structures like the hippocampus, insular cortex, and prefrontal cortex. And then finally cognitively, and this is interesting Don, there were no differences in memory, attention, executive function, language, or visual spatial abilities between the concussion and control groups. And this was true at first imaging visit and also during longitudinal follow-up.

Marion: That is interesting Amanda, I'm surprised and to me that raises an important question about the clinical significance of the structural and physiologic changes you described. You know this is not the first study that has shown micro-structural injuries six months or a year or more after a concussion. And I know it's the tendency for a lot of clinicians to say, "Oh look there's an abnormality on an MRI or an abnormality on DTI imaging that that must be the cause for your headache or your memory problems or whatever. And what this study shows is, not necessarily, that they're not related. So, what were the specific cognitive tests that they used Amanda?

Gano: Yeah, so memory, executive function, attention, verbal fluency, and visuospatial perceptual motor abilities were assessed using 11 different cognitive measures. And those included the California Verbal Learning Test, the trail making test, category and letter fluency, the card rotations test, and the clock drawing test, with 11:10 and 3:25 as times drawn on a clock.

Marion: I'm glad you tell us that because, again, they didn't find a cognitive deficit associated with these structural abnormalities. And it wasn't for lack of trying. They really did test these people cognitively in a number of domains. So that's interesting. So what were the limitations of this study Amanda?

Gano: So this study did have several limitations, and the biggest one was the small sample size, which, as you know Don, limits the statistical power of the results. Another limitation is that the history of concussion 20-to-30 years ago was based on subject self-report. And so, as you alluded to earlier, using independent medical record reports of concussion would have strengthened the study. And you know lastly, the demographics in this cohort were not necessarily generalizable to the population. So the study described 80-to-90 percent of the cohort as Caucasian and a more diverse group participants certainty would have better represented the population. Additionally, the majority of the members of this cohort were college educated, and I wonder if this had an effect on the results on the cognitive testing. Or you know, whether a higher level of education may have allowed for more active cognitive engagement as the participants age, which as you know can decrease the incidence of cognitive decline over time.

Marion: Interesting, so you're suggesting that there might have been a ceiling effect of the cognitive test that they used and that these people were kind of over educated if you will and may have had cognitive difficulties that just weren't picked up on these cognitive tests that they used.

Gano: Potentially, or that the higher educated cohort of patients were maybe more likely to remain cognitively engaged as they aged.

Marion: So finally Amanda, what are the key take-a-ways? What do you want the provider to walk away from this with?

Gano: You know, well I think this study really speaks to the compensatory mechanisms of the brain following a concussion. And clinicians should really be cautious about attributing abnormalities observed on MRI or other imaging reports to any particular behavioral, cognitive, or psychological symptom or sign. I thought that these preliminary results were really fascinating, and I look forward to reading more about, you know, how this might be replicated with a larger, more diverse cohort of patients and I wonder if the outcome would be different.

Marion: Well, thanks Amanda. I'm afraid 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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