

Transcript

Neuropsychology of Mild TBI: What Do We Know?

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Thank you very much for that introduction and thanks for inviting me here. I'm very impressed with your facility in particular we don't have flat screen TVs in our auditorium so I have "TV envy".

going to be talking about the psychology of mild TBI. There's my disclaimer slide. just briefly going to talk about diagnosis because that's already been covered. I am and mostly just focus on the neuropsychological outcomes and particularly long term outcomes because that's where the controversy is. This is the outline of the talk. I will talk about what we know, what we think we know and what we don't know.

OK so this has already been shown before so I won't go into detail so these are the ACRM criteria for mild TBI just to quickly review - basically the loss of consciousness or alteration of consciousness not to exceed thirty minutes PTA can't be longer than twenty four hours. Mild TBI is a huge problem eighty to ninety percent of all TBI's are mild so meet those criteria in other words but again there's controversy about the long term effects of this.

This is another summary to show you the different criteria for mild, moderate, or severe TBI I want to highlight that what I'll be talking about today these are studies in which if there was a clinical scan meaning an MRI or a CT, it was normal. if it's not normal than it's something that's often referred to as "complicated mild TBI" and there have been studies showing that those folks often ending up having a long term outcome that's more in line with moderate TBI.

OK so others have already talked about the VA clinical reminders so not going to go into too much detail on this except that I wanted to point out a few things. So this is the screen that was instituted in April of 2007 in the VA and it's meant to identify those OEF/OIF veterans who may have had mild TBI or a concussion. and this is what it looks like. You've probably all seen it. Its important to note that if the veteran says that they've already been diagnosed or treated for TBI then that's a a negative screen. They're still offered services if they want them but that's a a negative screen. Then the screen goes on and has four sections and the veteran would need to to answer all of these affirmatively to be considered a positive screen. so there would need to be some event that caused the injury, some disturbance of consciousness associated with that mechanism, and symptoms as a result and continuing symptoms so only if they say yes to all four of the sections is that considered a positive screen. And the reason I bring that up it is it's important to realize that it's not really a screen for concussion or mild TBI I because if someone did have a concussion or mild TBI and are not

still having problems they will screen negative and that's important to realize in research because if we want to know about mild TBI we really need to include the whole population of mild TBI and not just people who are still having problems.

so in other words there will be some false negatives. And there's a similar problem of course the private sector and this was demonstrated by recent study by Powell, et al. They looked at the charts in the emergency department and then they did they have research assistance that conducted a structured interview with patients and looked at the records as well to make a diagnosis of mild TBI. And not surprisingly they found that the emergency department personnel did not document the mild TBI in fifty six percent of cases. so there are some false negatives in the private sector as well. and again this is important for research purposes in terms of trying to figure out what is the long term consequence of a concussion or mild TBI again we need to study the whole population of mild TBI.

So again within the VA, after the screen, if they screened positive they go onto a second level evaluation, this is often when neuropsychology is called in to decide if cognitive testing should be done and also we are often asked to help in clarifying the diagnosis and its important to realize of course that symptoms can support a diagnosis of mild TBI but they do not constitute a diagnosis of mild TBI. Mild TBI diagnosis is a historical diagnosis - its an event that caused an injury and an alteration of consciousness.

Often as you all know we often don't have very good records of what happened and so we have to rely on self report and the best way to try to figure out if somebody did have a mild TBI, if there is not good documentation, is to ask them open ended questions about what happened and try to figure out if there was any kind of the memory Gaps or alterations in consciousness. but of course that's not fool proof.

I'm not really going to talk much about post-concussive symptoms. Dr. Abrams called this the swamp and I agree, so going to avoid the swamp - but can't avoid the swamp entirely when you talk about mild TBI. These symptoms are normally broken down into physical, cognitive, and emotional symptoms. The point I'd like to make which has already been made is that they're not specific or unique to mild TBI and um I think a lot of people get confused when people are complaining of these symptoms. It's important to realize that this is not the diagnosis. If somebody has these symptoms that's not the same as the diagnosis. Its not how you diagnose mild TBI. it's also important to realize that people who complain of cognitive problems may not do poorly on cognitive tests. There's actually no correlation between the two. Saying you have cognitive problems is not the same as having the cognitive problems. so I just wanted to point that out. The symptoms correlate better with emotional distress than with performance on cognitive tests.

OK, so let's talk about cognition and what we have learned over the years. there's no doubt that a mild TBI causes acute disruption of brain function. at best a person who sustains a concussion is dazed, confused,

temporarily disoriented, with memory gaps possibly - up to hours - at worst they're unconscious for up to thirty minutes. so there's no question about that and I'll also show you in a minute that there's no question that as a group of these folks do poorly on cognitive tests initially, in the acute and post-acute stage. But what remains a question mark in many peoples minds I think is if there is a long-term cognitive effect.

so let's look at the evidence. There have been five meta-analytic studies of this issue. A meta-analysis for those of you who don't know is basically a summary of all the studies that have been done. It is a statistical combining and you calculate an average effect size of all the studies that have been done on mild TBI. the first one was done by Bender and colleagues on and this meta-analysis included eight studies and all of the studies were prospective studies, in other words they recruited the subjects acutely from the ER and they weren't tested until at least three month post injury. And they found in those eight studies an average effect size of .1 to .2 which is not significant, so no effect basically, in the long run. In contrast, long term effect of financial incentives they found to be quite significant, .5.

The second meta-analysis was a summary of thirty nine studies and they found Schretlen and Shapiro found an overall effect size on neuro-psychological measures of mild TBI to be .24. They catagorized the studies into time since the injury when people were tested and as you can see, by three months post injury there's basically no effect. but clearly there is an effect acutely and post-acutely. OK?

The next meta-analysis to come along is by Frencham and colleagues found the overall effect size to be moderate, .32, but again it tended toward zero with increasing time since injury. So there's a theme emerging here. And then we jumped on the bandwagon in Tampa, everyone else was doing it so we thought we'd do a meta-analysis also. But we wanted to look at some moderators, we wanted to know if the effect size varied by cognitive domain and some other variables that I'll highlight in a moment. These were the inclusion criteria, there had to be a control group, etc, etc. I won't read this to you. so we looked at studies published between nineteen seventy and two thousand four; there were thirty nine and met her inclusion criteria. These are the moderators that we've looked at: cognitive domain as I already mentioned, time since injury since we already know from the other studies that this was important, and then we wanted to look at context, and I'll mention this word a couple of times today.

We divided the studies up into those that had what we called litigation sample, symptomatic Clinic-based samples and unselected samples so litigationsamples, these were studies in which the authors mentioned that some or all of the participants were involved either in litigation or some kind of compensation seeking. Symptomatic or clinic-based samples were studies in which the subjects were recruited because they were having difficulties they were presenting at a long term rehab facility for instance. Unselected samples are basically prospective studies. These are people who are followed after the diagnosis and onward. so these are the cognitive domains that we examined. Global cognitive

ability, these would be tests for the neuro-psychologists in the room, tests like the WAIS, the NART, anything that has an overall score. Attention, tests like the PASAT, Trails A, Digit Span, Executive functioning, tests like Wisconsin card sorting, Trails B, etc.

We found the overall effect size to be .54 which is significant and there were significant deficits in all domains except motor functions although there were only two studies that included motor functions. Most effect sizes were moderate to large and with fluency, you can see the numbers here, delayed memory having the largest overall effect size. The smallest effects were found on motor and executive measures but again there were fewer studies.

so this kind of sums it up with regard to context or sample selection. here I have this highlighted because this kind of tells the story. Prospective samples by a three month post injury, no effect. Same thing that the other studies found, OK? but again acutely, or less than ninety days, or some would say post injury I guess, there is a significant effect and this was true in the litigation based samples as well however unlike the prospective studies you can see litigation tends to make people get worse. there were no studies at less than ninety days for the clinic-based samples - here at the three months post injury there they look similar to the litigation-based studies.

When we did this we of course found a lot of sports studies, people studying concussion in athletes, and we really thought that was a different population and also the testing is quite different with this population so we had to separate out those and we did a different meta-analysis with these studies. they tend to be tested more acutely, right away and more frequently after their injury so we did a separate analysis and found twenty one studies that met our same inclusion criteria. Found the overall all effect size to be quite similar to what we found in the general population, .49, here you can see the acute effects are larger, but again these are people are tested right away, on the field, and so here we see delayed memory, memory acquisition, and global cognitive functioning having the largest effect sizes, however beyond seven days post injury no residual effects, so same story, its just a little faster. so this is for those like pictures, I often draw this for patients, if you're a member of the general population and you've had a mild TBI on average you'll be doing fine on these test by three months post injury. so is that the end of the story? Hopefully not, because then my talk would be over.

Those are 5 meta-analytic studies - pretty convincing, consistent, are you convinced? probably not. Well yes but isn't our population somehow different? All of those studies presumably most of them were conducted with civilians and all single concussions. And our population is different. so maybe there will be different outcomes. so before we get to the data, I want to make a couple of points about our context or our population. One is illustrated nicely by Julie Suhr and John Gustaad who talk about this thing called diagnostic threat and this is a brilliant study, and most brilliant studies are really simple and what they did was they took college students who had a history of a concussion, single concussion, and they divided them in half. Half the group They told them Your being evaluated, you're having this neuro-psych

eval, because you had a concussion. and the other half they didn't tell them that they save them some kind of neutral explanation like we're just studying college students. As you remember from psych 101, the importance of expectations and context and people respond to expectation and to labels and the people who are givin the mild TBI explanation for why they're being evaluated did more poorly than the neutral explanation group. Not only did they do more poorly but they produce more scores in the clinically impaired range. so that's a pretty powerful message there and I think it's important to keep in mind in the world that we work in because we know that TBI is such a focus, that's why we're all here it's the signature injury with the TBI clinical reminder, context is really important. another thing to keep in mind with our patients of course, is that many of them have PTSD and Jennifer Vasterling and others have shown that PTSD adversely affects performance on neuro-psychological tests, OK, us so its really impossible at this point to tease those things apart.

another study by Jennifer Vasterling also is relevant here and something to keep in mind, this was published in JAMA and they took a look at over six hundred soldiers and they tested them before and after deployment to Iraq and they found people who were deployed did more poorly on tests of sustained attention, verbal learning and visual spatial memory than people who were not deployed. now If you read the article they qualify this all over the place - by saying it was a really small effect, not really clinically significant, however it was still significant even after controlling for mood related symptoms and so forth. So its interesting. While this was not a focus of their study they did find that history of mild TBI had no impact on the scores on the tests. which is consistent with all the meta-analysis.

here's another study conducted with OEF/OIF service members this was presented recently at NAM, and they looked at a hundred and twenty three patients who were admitted to a burn unit due to blasts - explosions - and found no differences on cognitive measures between those who had had a concussion and those who did not. However, the mild TBI group was more likely to have a psychiatric diagnosis.

this is a study that's going to be coming out soon in a special issue of JHTR by some folks from DVBIC and they looked at 956 soldiers who were administered the ANam and 122 of them had had a concussion. They found that history of deployment-related mild TBI, up to two years prior to the cognitive testing was not associated with poor ANAM performance. also there was no association between ANAM performance and the number of concussions that they'd had, or the number of post-concussive symptoms that they endorsed this is actually false - injury severity was correlated to performance so people who were moderately to severely injured did do more poorly.

seeing here that there is the same story it seems, at least so far, in OEF/OIF veterans, as it were in the civilians studies so no effect of mild TBI, in the long run, on cognitive performance.

well you still might not be a believer what about different mechanisms of injury. We hear a lot about blast injury - this is really difficult

to study in human beings for reasons that have already been discussed, but there are 2 studies that I were published recently that speak to this issue. one was by Nina Sayer and colleagues and they reviewed Charts of a 188 OEF/OIF patients admitted to polytrauma centers during the first four years of the wars. And they wanted to find out if being injured by blasts would result in a different functional outcome than being injured by other mechanisms, OK? and they did that I by looking at FIM scores and also by the length of stay. these are symptoms that were the focus - one of the foci of rehabilitation. so for instance, cognition. in the blast injured group that was one of the foci of treatment eighty-eight percent of the blast injured patients, and that was also the focus of treatment in ninety-three percent of the non-blast injured so no difference and I've listed some of the other symptoms there but there are more. Not surprisingly, there was more hearing loss and tinnitus in the blast injured patients but no differences on these other symptoms that are listed here's one that I've highlighted and there were more PTSD symptoms reported in the blast injured group than in the non-blast injured group. With regard to their primary question, that is change in FIM score or functional gain, there was no difference between blast injured and non-blast injured patients. instead baseline functioning was the best predictor of gain which is not surprising right?, basically injury severity predicts the amount of gain their patient makes and that was the same for length of stay.

Here is a study that my colleague Tracy Kretzmer and I at the Tampa VA along with individuals from the Salisbury, Richmond, and Durham Va, go VA, we got together because we wanted to look at this question, even though its a messy question. we looked at 102 consecutively assessed post-TBI individuals, who are primarily returning active duty or veterans. we excluded people who - that stands for symptom validity task basically a measure of effort to see if the person was engaged in the evaluation, so if they weren't engaged in the evaluation, we excluded them, Or if they had other disorders that were not mild TBI basically. here are the demographics nothing too surprising. there were no differences in the demographics between the blast of and non-blast group. I need to correct something I just said this is not just a study of mild TBI, all severity levels were included here. and and this is kind of the punch line. the green bars represent blast injured patients, the light blue bars represent non-blast patient and you can see the bars are very far apart and in fact there were no differences between the groups on these different cognitive tests. Digit symbol, the reason that the way down here is because these are scaled scores the rest are T scores, OK?, and there was a funky interaction on this measure BVMT is a visual memory task and that I won't go into but the bottom line was the scores on these tests were predicted by injury severity, not by mechanism of injury. We did find a trend now for more PTSD symptoms reported by the blast injured group that was the value of .06 and more PTSD symptoms reported over time. so those tended to get worse over time. so in summary so far no evidence that mild TBI due to blast or experience in OEF/OIF is any different in terms of cognitive sequelae. there is evidence that PTSD impacts cognitive functioning and also that maybe there's more PTSD symptoms associated with being injured in an explosion at least that was hinted at in a couple of studies that we went over.

There is also evidence that deployment itself may have a small adverse impact on cognitive performance.

So, we can't stop there, we need to be obsessive and try to look at this problem from a different angle. I mentioned the importance of context before, and the importance of sample selection and my colleague Rod Vanderplog and Glen Curtis, have access to this large Vietnam experience data set and so we thought we would look at this question in a really big sample of the people who represent the population quite well, at least the male population. so this is the study that was described in detail back in the 80's in JAMA. there were four thousand, over four thousand randomly selected male US ARMY vets who descended upon, I think it was Arizona, for a three day evaluation. They were evaluated in every way that you can imagine. This is some of their demographic variables again this is back when people were drafted into the military so it represents the US population quite well at least the male US population at that time. and they underwent a three day evaluation, including extensive medical, psychological, and neuro psychological examination, and included in that were questions - but they were basically asked anything you can think of - and one of the questions had to do with whether they had had a concussion. these evaluations took place approximately sixteen years post military discharge. so this is definitely, for anyone studying mild TBI, this is definitely long term sequelae, because they would be an average of eight years post injury.

so these are the groups that we created. there are people who had a head injury with alteration or loss of consciousness, we excluded anybody who was hospitalized because we couldn't be sure that that was mild TBI and then we had 2 control groups, people who'd been in a motor vehicle accident but did not have a head injury and then people who did not have had injury or a motor vehicle accident. these individuals were given a number of neuro- psychological test and I won't go into all of them but they are names that you would recognize if your are a neuro- psychologist- things like the WAIS, trails, and wisconsin card sorting, and so forth. OK so we did a MANOVA, with all of those measures and looked at whether or not there was an effect of those 3 groups and the MANOVA was not significant. so again same old story, no long term effect of mild TBI on these cognitive scores. An eta squared of .005 indicates that across the group's the variation in neuro-psychological performance accounted for .5% of variation in level of performance , that is virtually no difference between groups. and these are some representative scores just to give you a flavor. you can see that there's really not much difference between the groups on some of these tests that I'm showing you.

But, we wondered, another presenter talked about within subjects designs, we know from statistics right if you are taking stats course that within subjects design is more statistically powerful than that between subjects design. so we thought well lets look at some tests using a more powered test to see if we can find anything - and those would be tests where there are multiple measures given. one such test is something called the PASAT. I'm going to show you what the PASAT is. basically the subject hears a series of numbers and they have to add them and it's not as easy as it sounds. So I'll show you, The subject would hear 2 and

then they would hear 3 so they would have to say 5 - because they add those two numbers. Now as soon as they say 5 they have to forget it because they're hearing another number right away - 4 - so then they'd say 7, and then they'd hear 8 and they've got to say 12, I can assure you that this is difficult. it is really difficult and what happens is that these numbers, there are 4 lists of numbers given, and each time you move to a new list, the rate of reading the numbers gets a little faster so it gets a little harder. So you start out with a little over two second interval between numbers and by the end its about a second between numbers so that's that's quite difficult.

all the neuropsychologists know that if you chose to give the PASAT, you're going to give it when? You give it last, thank you. Because it is really hard and it kind of ticks people off. because its addition and it should be easy but it's not, and you can damage your repore with a patient sometimes, not always so you tend to give it last if you're going to give it. so the evaluators knew this. they had these people working for three days so they gave them an option of dropping out of tests if they wanted to and they kept track of that, of course. As I told you before, there were no differences across the group on the PASAT. there are no differences on the scores that we typically use. But, we decided to look at dropout on the PASAT. Could there be differences between groups, if we use a within subjects design and indeed that's what we found. there were no differences between the groups on trial one or trial two, those are the ones where I told you there was about a two second interval between numbers, but once they get to the third trial that's when it moves down to a second between numbers there was a difference between - in that the mild TBI group tended to drop out more readily than the other two groups and that was an odds ratio 1.32 for people who like odds ratios. Thats a small effect. so on this difficult measure of sustained attention or working memory, subjects with mild TBI dropped out at a higher rate, once the test got difficult.

There is another test where we can look within subjects the California Verbal Learning Test, and specifically what we looked at was proactive interference. Let me tell you a little bit about the test so you can understand what I'm talking about. CVLT is a 5 learning trial test so you give sixteen words to the patient 5 times. they hear the list the first time, they have to give it back to you. They hear it a second time they give it back to you, 5 times they hear. Then they get the distractor list, or list B. totally different sixteen words, some of which are semantically related to the first list. And then they give you list B, as much as they can remember, and then you say OK, forget about list B, I want you to tell me that first list, the one I read to you five times and then they try to give you as many asthey can once again so the way this test is set up allows us to look at something called proactive interference. which is when previously learned material interferes with learning new material so in other words it's when the first five trials interfere with learning the list B, the new list. so what you do to calculate this is you compare how many words they learn from list B to how many words they learned that first trial, the first list. OK? So when we look at this across groups ew can see a significant difference in that the mild TBI group shows more proactive interference from the other two groups on this test. The mild TBI group had a larger proactive

interference effect than the normal control group with the MVA control group falling in between. OK, so you fished like heck and you found something here. it's a huge sample so is that clinically meaningful, I don't know, probably not but what we did in the next phase of the study is something I haven't told you about yet which is that as part of the medical examination they got a neurological exam. and as part of the neurological exam they got a number of tests that neurologists typically do and they quantify those and the mild TBI group was abnormal on two portions of the neurologic exam. and those 2 portions were tandem gait, tandem gait is when you walk toe to heel. And then, also on a test of visual perception which is basically kind of visual field testing so maybe you've seen a neuropsychologist or a neurologist at bedside and they go like this, look at my nose which finger am I wiggling left or right and sometimes they do it at the same time and they're looking for inattention to one side of his face or the other. so this was done in this study using a machine, so it was more accurate than what I'm doing with this. and the mild TBI group was - a portion of them were abnormal on that measure and on the tandem gait. But but these were separate groups of mild TBI patients or subjects there was only a 2% overlap between the two. OK, so we know that in the back of our minds so we decided to see if that's related to the neuropsych findings. so what we found is that those with excessive of PI and we define this statistically and excessive PI was defined as trial one minus trial B different score that was greater than 1.5 standard deviations larger than the overall proactive interference difference for the entire sample. So basically excessive PI here is a drop of more than three words. You can see from this graph that those with excessive PIs tended to be in this group and tended to have a greater percentage of impaired tandem gait.

Similarly when we look at the PASAT findings, there's a higher percentage of those who drop out who have the left sided visual imperception, the abnormality that I told you about earlier. so this makes it a little more interesting that these neuropsych findings had an external correlate, they were related to findings on the neurologic exam. so excessive problems on the PASAT were associated with subtle visual and attention problems on a formal visual exam. Excessive proactive interference was associated with greater rates of impaired tandem gait during the evaluation. so in conclusion, both cognitive sequelae associated with mild TBI resolves by three months post injury. If we look hard we can find evidence for subtle long-term problems with complex attention and these seem to have an external neurologic correlate. but of course we need to prospectively examine and replicate that.

so let's talk about what we don't know.

and there's a poem because I like poetry: we have many miles to go before we sleep so there is a lot we don't know, probably more than what we do know. one of them as you mentioned are ready and that is multiple concussions. What is the effect? We know the effect in general on average of one concussion but what about multiple, and most of our patients have had multiple concussions. Single concussions should resolve within three months but do multiple concussions resolve? certainly if you've been blown up more than once, you also have more, in theory, exposure to trauma, psychological trauma and maybe other

bodily injuries and so it's a difficult issue to study. those studies that have been conducted looking at multiple concussions have been conducted exclusively in the sport's literature and they also haven't looked at psychological variables at all. so you know you can find studies that do find adverse long term effects and you can find studies that don't. and so it sort of an open question and again needs to be studied in our population which is probably different. Treatment is another difficult issue. Mittenburg just published a number of studies that have shown that if you educate people who've had a concussion if you educate people who've had a concussion soon after they are injured, they do a lot better down the line than people who are not educated and so that's that's an important finding. But the problem is, all of those studies were conducted with people who were educated soon after they were injured and when when do we see patients generally, following their concussion, we see them months or years post injury so does that still work? Probably not. We also still don't know much about how to differentiate among overlapping conditions so other presenters have talked about this problem so you know you have a patient with mild TBI and PTSD, how do you tease those apart? I don't know. also an open question is the risk versus the benefits the population screening for mild TBI. some of the issues I talked about earlier about context and expectations you know are we, in some cases, we're helping people, maybe in some cases we're hurting people by putting the focus on this issue. Thank you.

you asked if there are any studies that have been done with mild TBI where they reward them for doing the cognitive task to see if that makes a difference. Not that I know of. certainly in some ways some of them, you could argue, get rewarded for not doing well, in our compensation and pension system. I don't know how that whole thing it works but not that I know of but certainly in your first point was related to that and that motivation clearly impacts cognitive performance and that really is the point I was trying to make with some of my context slides - that you know, what we expect of people, how we treat them, all of that undoubtedly impacts how people perform, not just on cognitive tests but on any tests. yes. I don't know that we looked at false positive errors in particular. I would look to see if they are semantically related - that is kind of a frontal lobe issue. but if they are unrelated, that is fishy.

Thank you.