Psychopharmacology and PTSD 4
Written Video Transcript

Wait for the mike folks. Whoever's asking a question?

Well, actually I'll just repeat it because I don't want to take too much time doing this. Come on, come on. We treat these people all of the time, what do you think is going on?

[00:16]

Okay and how, how could that have [00:00.20.00] (affect it) do you think?

Well, I mean I hope that's not but that's what comes to my mind working in the VA. If I get better, if there's—I may lose my financial compensation. On some level there may be some dynamic on that.

Yeah, it's a pretty strong force wouldn't it be. If we were, [00:00.40.00] you know, couldn't work any more and we were getting a check for being ill it's going to probably influence our treatment—you know, whether we say we're getting better or not. Any other ideas as to what could be going on? I mean normally people are very reluctant to say [00:01.00.00] that answer. They often come up with all these other things before they say compensation. But these are ones that I've come with and some other people in the literature have mentioned. I mean gender was the first one that came up because what I didn't tell you then at the (Certraline) trial if you looked at the men only, they didn't seem to be responding as well. But even within the (Certraline) trial it didn't really hold up [00:01.20.00] and they had a really small number. Most of those men were combat veterans. In the next study that I'm going to show you with Paxil the men responded just as well, in fact a little bit better than the women. So, it doesn't seem to be the case, gender doesn't seem to be the case. Certainly PTSD severity, duration. I mean there's difference, co-morbid disorders. One that I think [00:01.40.00] the data is actually there for but I haven't seen, it must be buried in these studies, would be the history of the previous treatment. You know, a lot of our veterans have already been on tricylids and MAOs and they're still in the system because (they all) and so they've already failed pharmacological treatment. And that could be one of the explanations. Other co-morbid disorders. [00:02.00.00] And it has been mentioned financial compensation, disability compensation. I would take that a step further and suggest there's also social compensation effect that I see that occurs in a lot of patients too. Again, particularly with our older Vietnam veteran population now you've been—had a very bad life, you've been ill, you've done a lot of things you're not very proud of. Now [00:02.20.00] you've been given a diagnosis with PTSD, you're getting support, you know, for your behavior, given an explanation for it. That's probably also going to influence your treatment

response as well as the financial compensation. Any other questions in that? We can actually come back to this at the end of the talk too. [00:02.40.00] Because I think =

If there was any possibility of getting at the data in those. For instance, that large study probably had people with different levels of combat exposure, different durations of illness and different levels of compensation or need for compensation. [00:03.00.00]

Right. I think that, yeah, that's a good question. I think there are people within the VA that have seen that data. But I'm not sure at what level they've been allowed to dig into it. Because the drug companies, they're always very protective of [3:12], first thing they didn't want to screw up their chance of getting FDA approval to start with. They may be a little bit more open to do it now that they have it.

Have any of the [00:03.20.00] drug studies used measures of change that would be less reactive, for example information processing tasks or psychophysiological responses that might be able to sort out some of these things?

No, not a lot. And in fact I don't know as well for even social function tasks in these studies whether or not. [00:03.40.00] When you do a drug study like this and go before the FDA they have to prove—they present a primary efficacy measure. You said a priori this is what you're going to do, you're going to look at CAPS, that's what you're stuck with. That's kind of how they present [3:54] and again that data would be there if they've collected it. I know with the Paxil study there was lots [00:04.00.00] of studies on social functioning, both at work and at home. So, that data would be there. Okay, well, because of this last concern with the compensation though for the next—for the Proxitene study they were concerned about this enough that they actually excluded anyone that was on [00:04.20.00] disability as part of this study. We were part of this multicenter study so I have a little bit—I was somewhat familiar with how this was done. There were this data—I say two published studies, there were two studies actually, one of which has only been published so far but the second one is on its way. And it as of a couple of months ago I heard they were just [00:04.40.00] about there with the FDA approval but I haven't heard anything since then. So, but it's close that you'll see Paxil for an indication for PTSD as well. This (Randall Marshall) and colleagues wrote up the results. It was a large study, 563 patients entered, 355 completed. [00:05.00.00] A few more males in this study than in the (Certraline) study, 68% were female. And what I'm showing here, I know this is a little hard to make out, there were two doses in this study, a 20 milligram dose and a 40 milligram dose and then placebos, so three groups. And this shows the patients who dropped out—there were 66, 61 and 69 patients [00:05.20.00] that dropped out of the three different groups—and the reasons that they dropped out. And the point being that if you look at the higher dose of Paxil more people dropped out, 28 for an adverse event, than the 18 for the placebo. But if you look at efficacy, 12 people dropped out because of lack of efficacy in a placebo whereas only two dropped out [00:05.40.00] at the higher dose of Paxil. So, again, kind of the pattern you'd like to see if you think this medication is actually working different than placebo. This was one piece of the data, the total CAP scores. Now this isn't a change of scores, this is actually

the total scores. They were starting out at about 75. The green line being [00:06.00.00] the placebo, the purple and red line being the 20 and 40 milligrams of Paxil, going out to 12 weeks. So, in addition to seeing that you had a nice effect of the medication, significant improvement with the medication, the two doses were more or less the same. Not more or less, it's pretty amazing that they lie right on top of one another [00:06.20.00] so they were actually exactly the same. And given that the higher dose actually had more, much more in the way—had more in the way of side effects, you know, this would say for most patients you probably want to stay at this lower dose of 20 milligrams. Okay. And these were—[00:06.40.00] is a sub scale of the CAP scores. In other words, you can using the CAPS you can divide them into the reexperiencing, avoidance and hyperarousal symptoms. And this shows that all three of these clusters got significantly more better with the drug than with the placebo. So, (there had been) some earlier literature to [00:07.00.00] suggest that drugs may affect one cluster but not another. But they seem to affect PTSD in general. If you just look at clinical improvement overall, (human) response, again, a significant affect at both the 20 and 40 milligram dose of Paxil. You know, between this, pretty strong evidence here that these drugs do [00:07.20.00] seem to be helping in PTSD. Now, the next study actually went on asked a slightly different question. They took advantage of this very large study, in fact that took advantage of the (Certraline) trial that you had these large trials going on. [00:07.40.00] And they looked at patients in a continuation phase to ask the questions whether symptoms returned, if they get better, if they're taken off the antidepressant. So, what I'm saying here is that they had patients who had responded. After the double blind phase they were put into an open labeled phase, [00:08.00.00] so they were all given Certraline. The ones that got better then were given a chance to go back into a double blind phase. They were on Certraline now they're back on either Certraline or placebo. Now, you probably can't see this but that's kind of shown here. The red was the first phase that we already saw, the acute double blind phase, orange was the continuation phase, the green one [00:08.20.00] was a 28 double blind placebo controlled study. If you—the numbers start dropping of course as you move through here. But you still had 46 patients in the (Certraline) group and 50 in the placebo. So, it was pretty large for a continuation study. And the results [00:08.40.00] are right here. Again, one of these probability plots, this time looking at the reverse. You're looking at the probability of getting worse. Actually here this was the probability of being discontinued from the study, being pulled out. they had a certain criteria that they pulled people out. Basically, there's about a six times greater chance [00:09.00.00] of being pulled out of the study if you are on placebo than if you were on (Certraline). Another way of looking at that was just looking at exacerbation of PTSD symptoms, similar profile. So, it seemed to make a difference. Even if you had gotten better, you know, if you come off the drug you have a six time greater chance of getting better than [00:09.20.00] if you were—getting worse if you were on placebo than if you were on the drug. An interesting piece of data that the authors pointed out here possibly is that most of that worsening seems to occur in that first four to eight weeks. So, they made the suggestion that this is probably you know a critical period [00:09.40.00] that if a patient wants to come off a medication you should follow them pretty closely for that first couple of months. They make it past that couple of months, according to this data, you know they have a pretty good chance of

maintaining their improvement. So, you probably want to see whether you would want to intervene in that first couple of months. Something we, you know—[00:10.00.00] I normally would have done anyway. But some people do tend, you know—you don't want to say, okay you're going to come off the antidepressant, come back in three months. It would not be clinical practice—good clinical practice to do that based on this data. Okay, so that's the data with [00:10.20.00] (Certraline). Now, as far as the other antidepressants, lots of open labeled data. There's a lot—there's a number of double blind trials that are going on but—and one that had been with (nathazadone)—now (nathazadone) is a little bit different than these other antidepressants. It actually acts at a [00:10.40.00] receptor to influence serotonin neurotransmission at what's called the 5HT2A receptor. And there was one published—unpublished multicenter study done I know at least in part at VAs. And I've never seen that data but I've certainly heard references to it that it didn't work. [00:11.00.00] Again, this is kind of a problem we don't get the data of the studies that don't work. There was a small study from a colleague of ours, (Lori Davis), at Tuscaloosa VA, who did a study in veterans, 41 veterans, in which she looked at 27 were (on nathazadone), 15 in placebo, 12 retrialed, double blind trial. [00:11.20.00] She presented this at a meeting in December. This is from her poster. And she showed us [11:26] (nathazadone) in veterans with PTSD greater than placebo. Just in talking with her I know she said this population in general was a little bit different. A lot of her patients are new to treatment. So that could part of the difference here [00:11.40.00] than the other studies. And I think there's (a nathazadone) study that's underway as well, so. But in general there is strong evidence then that SSRIs are very effective in treating all the symptoms of PTSD, that this response does not seem to be related to just being an antidepressant, that [00:12.00.00] it seems to influence PTSD symptoms in and of themselves. And then although there's no conclusive data I'd suggest that disability status probably is a factor in reporting. And we can get back to that point at the end of the lecture if we have time.

[end of audio]