I'm going to talk to you about a specific part of our candidacy determination which is neuropsychological assessment. And whenever I talk about what I do to people who aren't psychologists or neuropsychologists it's always important to first answer the question what is neuropsychology because many medical providers don't have a good idea about what it is that we do. And basically what we are are PhD trained psychologists who have been sub-specialized in assessment of the brain behavior relationship. So we are trained to understand how psychology and neurology interact to produce difficulty with thinking, behavior and so forth.

And in my opinion we are best utilized in a team setting. So you know the Movement Disorders Group is an excellent example of how people of various expertises can get together and really work in the best interests of the patient because we communicate regularly and we communicate often. So we are independent providers, meaning that we are licensed independently in addition to earning the PhDs and we do postdoctoral training which is typically 2 years after you receive your degree.

What happens during a neuropsychological evaluation which is a particularly important thing to understand when you tell a patient that that's what they are going to go do because it again sounds like a very mysterious thing. There are essentially four main parts that constitute what we do. First is obtaining a history both from the records, the other providers and the patient. And this history is often different and in addition to what's collected during a typical medical history. We want to know about a lot of premorbid factors so what was their education like, did they have any developmental problems growing up? Did they have any history of learning or attention disorders that might affect the testing at this point in a different way than how the disease or injury might affect the testing?

We certainly want to know about past psychological history and then of course as we interact with people then we accumulate behavioral observations. So how do people respond to success and failure on testing? Are they particularly guarded or defensive or are they so anxious that testing is difficult to complete? So all of those things are important in interpreting the other information which you get from the assessment.

Our assessment tends to come from a wide variety of tests that are typically commercially available to people who are deemed qualified to give them. They most often in traditional neuropsychology occur in a pencil and paper format, meaning you and I sit across the table from each other and I administer a memory list to you. So I read you a list of words and you say them back and see how many you can come up with. Then I do it again. We do this several times to get a learning curve. Then we do a bunch of other stuff, and then we come back later and I say hey remember that list of words that I read to you? So it's a very interactive process where we assess not just memory which is an example but multiple domains of cognitive function which I'll talk about a little bit later.

And then of course this all gets assimilated - assembled into a report and having worked with medical doctors and particularly surgeons now the constant that we hear about our reports as psychologists is this is really long and it seems like so you know we are trained in graduate school for some reason to write 10 to 12 pages of a report, which is very useless in the real world setting. So hopefully what you get as a physician from a psychologist or a neuropsychologist who is trying to answer this specific question for you is a 2 to 3 page report. And then if you just read the summary you can kind of know what we are trying to convey. That makes it more useful for the

patient and the physician and any other rehab providers if that becomes the case moving forward. So if you work with a neuropsychologist and you don't get that then it's always useful to say hey, you know this is what I - this is what else I would like to see in the report or you know can you make sure that the summary makes sense to you, both the patient if they pick it up and answers the questions that I've asked of you even in that concluding paragraph.

And then we do a follow-up consultation and of course the patient's physicians will - you know I'm just a small part of the process so they'll follow-up with their other medical providers but I do get feedback about to the patient and their family if the patient chooses to have the family present about their test results as well because you know one important questions is you know are you cognitive, are you cognitively okay to undergo surgery but also it's very important for you as the person who just went through 2 to 5 hours of testing what does that mean to me? And what are my testing patterns like and if there is an area of difficulty is there a way that I can improve that or are there things I can do in my life to work around that or compensate for any deficits. So the follow-up consultation is very important with the patient and it's also very important with the medical providers because working together as a group to figure out what may improve quality of life over and above surgery you know those are important components as well.

So in order to assess cognitive function what we really want to do is look at a wide array of cognitive function, and that's because even if this thing that you are concerned about is memory there are a lot of different things that can affect memory. If you cannot pay attention it's going to be very difficult for you to even encode the information to begin with. So there are people who have difficulty with

memory because they have an attention deficit. There are also people who seem to learn information just fine in the initial phases but then 20 minutes later may not remember that we've even gone over a list together. So there is different ways that these cognitive functions can kind of come forth if you do good detailed testing.

Language we test in a variety of ways as well. There is kind of the language that sticks with you almost despite any sort of illness or injury like reading and vocabulary which gives you a good idea of what along with someone's education and occupation gives you a good idea of what their pre-injury, pre-illness, premorbid function is like. And then there are other language measures such as naming that can be a little more fluid if someone develops some sort of cognitive disorder.

Executive function as Dr. Richardson has already referred to are one of the functions that are vulnerable in Parkinson's so we try to do a good detailed assessment of the those to track over time and those are your higher level cognitive functions, and they really incorporate a wide variety like decision making, judgment, planning, there are so many executive functions, inhibition, impulses, impulsivity.

Attention is our basic attentional functions. We look at kind of simple attention, so hearing something briefly and being able to say it back immediately. We look at complex attention for the ability to hold information in your head, manipulate it and then present it back.

Visuospatial function, so ow people process visual information. So can they integrate separate things into a unit and get a gestalt of a picture based upon its parts? Can they see something and perceive it well enough to draw it or copy it well?

Motor functions, we look at fine motor speed as well as gross motor activity.

And then of course we look at mood and mood in general you know we tend to see most for anxiety and depression because they are the most common, but certainly if there are other mood disorders present or a suggestion of other mood disorders then we certainly screen for those as well. And in the corner you can see what it might look like to sit across from a psychologist and do some of these tests.

Like I said there are a lot of tests and this is certainly just a sampling of what is sitting in the bookshelves waiting for the next patient in my office, but I just wanted to show this to you to illustrate that you know some tests are talking, some tests involve manipulation or stimuli, some tests involve both of those things. So we really do have a wide variety of ways to assess different cognitive abilities, so if there is something that is a specific concern it may deviate from our standard battery in terms of what we do for DBS screening but we always can incorporate that in if a physician or a patient has a specific concern.

And now as many of the physicians have already alluded to in their talks there certainly are cognitive effects that can be directly attributed to the progression of Parkinson's. And a lot of those that are

seen early on typically are the executive or frontal functions are the most well known and similar to that you can see difficulties with working memory or complex attention. Verbal fluency deficits can emerge relatively early and then some studies have shown less consistently difficulties with visual perception or memory. And you know we've mentioned this circuit over and over again but although the exact mechanism are unknown it's believed to be related to changes in that circuit.

There are many ways to perform a neuropsychological assessment as a screening tool for DBS candidacy and so when we thought about you know what are the best tests to choose for this one of the things to be mindful of is that you know neuropsych assessment in the traditional setting can be 6 to 8 hours, which is unreasonable for a patient who has a lot of fatigue, a lot of movement problems, who is going to be on and off throughout the day. So we wanted to try to capture a breadth of information that was number 1, able to assist us in understanding the patient's memory difficulties and cognitive problems and also able to give us a good idea about where patients are across multiple domains so that we then can track progress over time.

So this is the battery that I settled on which so far I think has worked pretty well for us. We do the mini-mental just as a basic screening mostly for orientation and just to kind of get a good idea upfront about where people are in a very basic sense. Same thing for the clock drawing which gives you a very basic understanding of planning and organization potential for detecting more significant problems as we move down the battery.

So Wechsler Test of Adult Reading provides in just a sample where you read and pronounce words, and that's one of those tests again that's relatively static that can give you a good idea of someone's premorbid functioning. So where would we expect them to fall prior to the development of disease or injury.

Trailmaking Test provides - the simplest version provides a good idea of psychomotor speed, attention, a little visual scanning. 'the second part adds in an executive function, so set switching, and this is where they move from basically connecting the dots from 1A. 2B, 3C, 4D. So not only do you have to have speed, attention, monitoring of responses you also have to understand where you are in the set so that you can continue to execute that switching correctly.

And then I use a screening measure called the R Band, which is used in - if you've read neuropsych research it's a screening test that's used relatively often. Number 1 because it's not - it doesn't take a really long time to administer and you get to capture a lot of basic information about cognitive function, you get memory, visual perception, fluency, 4 digit spans, so simple attention, a little bit of naming and some processing speeds all within about 45 minutes and the other thing is that it's a battery that has really good, it has really established norms for a dementia population and so one of the things that you've already heard a lot of providers mention so far is that dementia is a risk factor for having poor outcomes following DBS surgery. So not only can we look at the pattern of people's responses but we can also look at whether or not the norms are more similar to a dementia population or more similar to the general population. So it just gives us a little more objective information as we talk about cognitive functioning of patients.

I do the FAS test which is another fluency test, it gives us (inaudible) unique verbal fluency. We do a digits backwards, digits sequencing so I say a string of numbers, you say them in backward order. I say a string of numbers, you say them in sequential order. They start really short and they get longer and longer and longer. The more you can do the longer we can go. And that gives us a good idea of working memory, complex attention.

The color word test is pretty much the same as the Stroop Test for anyone who has read any sort of psychology literature from way back. You get basically two speed baseline tests and then you get key word executive test and this is even available in popular literature in the sense that you've seen the word red printed in yellow and blue printed in red and green printed in orange and you have to ignore what the word says and instead name the color of the test. And that provides an ability called inhibition. So what is your brain's ability to inhibit the dominant response and instead follow the given rules, which is an executive function.

And then the DKEFS, this one that we give also has a cognitive switching task where in addition - where on the final part of this sometimes we have to inhibit and say the color, but sometimes yo have to read the word. So you have to hold onto that rule and be able to effectively switch.

The Boston Naming Test is a classic well known and well normed, reasonably well normed naming test. So again naming, decline in naming is something that we see in dementias like Alzheimer's which the really low naming can give us a good cue about basic cognitive functions.

Picture Completion gives us visual attention, visual processing and then these three tests here number 1 can give us - vocabulary can give us a premorbid estimate or a pre-injury estimate whereas these two are abstract verbal and nonverbal reasoning, so that' sone of those executive type tasks that we can follow over time. And then we do screening for depression and anxiety as well, because depression and anxiety can also have effects on cognitive function. So there are people who go to their physician or bring their loved one to their physician with concerns for dementia and what we may learn sometimes is they don't have dementia, they are really depressed because the patterns of the testing can look very different. So assessing mood and talking about mood is always important.

What we do here at UPMC is typically a presurgical assessment so as well as a 6 month postsurgical assessment. In the literature scant as it is you at least see follow-ups that range from 3 to 6 to 12., one with a 1 year follow-up. We chose 6 because 5, 6 months we should see programing in general should be kind of on its way. And then we can also do it as needed. So if there are any major changes that are noted at any point postsurgery then we can go back and do some testing and really objectively document whether or not any changes have occurred and why those changes might have occurred.

So you know not everyone does presurgical neuropsychological evaluations at every site. We do them for everyone, but that's not - you know that's not 100% what happens across the country. the two main reasons to do it have been alluded to, particularly number one which is patient selection and/or exclusion. So we want to make sure that if there are risk factors for poorer outcomes that

both the physicians and the patients are aware of that and can have a better discussion about how and if to proceed. And then it's also good to have a baseline for neurocognitive status so again later down the road we can get more information about how they responded cognitively and certainly as the disease progresses that also gives us a way to measure change over time.

So in addition to risk we can also more objectively explore any subjective - any subjectively reported difficulties by patients or by their families. So if there are memory complaints what are they like, are they amenable to treatment? And with all surgical procedure you may get a good surgical outcome but there still might be subtle changes that the patient notices and they want to have that quantified and they want to understand it and explore it. And maybe you can still go back to work and do your job and do your daily activities and interact with your family but you know if you were high average before and now you feel like you are only functioning at an average level that's still a great outcome but for you the person that can cause some distress and that's something that a lot of people like to explore. And the other thing that testing can provide is to help make some other postsurgical decisions and we'll talk about those in a little bit.

Now some of these exclusion criteria or potential exclusion criteria have already been eluded to. If you look across the literature these are kind of the main ones that emerge and these are things that we consider: advanced age again, there is no - as has been said before there is no cutoff, most of the literature has looked at 70 and above versus below 70; advanced disease stage, dementia, severe other cognitive dysfunction or severe mood disorder. The problem with listing all of those potential exclusion criteria is that the research isn't great. There are case reports, there are very small end

studies, 5, 9, 13 patients. There are very strange ways that have been used to classify improvement or decline, which you know 1 for improvement, 0 for decline and it is really a wide range of how this has been classified and a few times you read it and like how did this get published? But what exists out there are very few controlled studies and very limited empirical data.

Now in terms of the second reason to do neurocognitive testing is to establish that baseline for a later comparison and you know the one thing you can say by reviewing the literature is that some people observe cognitive changes following surgery and the best way to monitor that change is to have something objective that happened prior to surgery so that you can compare it. Our subjective report of our experience can often be very different than what the actual numbers say. And that can occur for a variety of reasons. So when we do these comparisons you know it gives information to surgeons, to the neurologists, to the patient, to the family and it really helps with planning a little bit more because a lot of these problems could be amenable to some sort of therapy. So the sooner we know what the problem is and he more we know about what the problem is the better and more refined recommendation we can make, which hopefully will lead to improved quality of life. And then at some point we need to have data from multiple people that have collected in a systematic and objective way with good long term follow-up that we actually can understand better what specific inclusion, exclusion, red flag types of characteristics are because again it's not very clear just yet by reviewing the literature.

I made this one slide to summarize the literature because again with the neuropsych testing it's not fantastic. The literature has been divided into kind of location of placement of the stimulator and

what we'll - what we talk about is obviously GPi and SPN and overall there seem to be - there is evidence of improvement in some tasks and certainly subjectively I see improvements in motor speed and those kinds of things. Some studies have shown improvement in attention, many studies have shown some improvement in subjective rating of mood. Typically it's subjective rating of anxiety, subjective rating of depression has been a little more kind of marginally significant. What you see throughout the literature most consistently as Dr. Berman alluded to is - are changes in verbal fluency but that certainly doesn't happen in everyone and one study actually looked at the relation of cognitive changes to the relation of quality of life. And even though this group of patients experienced a decline in verbal fluency they still had improved quality of life that was comparable to those patients who did not have that decline.

So these subtle losses when we talked, when Dr. Richardson and Dr. Susky and Berman and Homayoun talk to patients about the risks and benefits of surgery you know one of the big things is quality of life. You have to think about you know with a loss of verbal fluency what's the tradeoff for you know having better movement and those kinds of things. So in some ways these things kind of muddy the waters but the big, I think the big take home point across all of these studies is they are never - in these studies there has never been an observed decline in overall cognitive function. So if you look from pre to postsurgery and you look at those big measures of cognitive function there has never been a statistically significant observed decline. So we see these subtle, this one has attention memory, most have verbal fluency but nothing that's this kind of huge, meaningful cognitive decline.

In terms of the psychological effect if you look across studies of mood changes there is an incidence of 1% to 25% in terms of experiencing transient mood changes that are often depressive after a DBS. That doesn't mean a major depressive episode, it just means an increase in depressive symptoms. These are often transient and the thought is that that may be due to the withdrawal of some of the dosage of the dopaminergic medications. And as I said before on the one study we saw that quality of life stayed up even if some subtle declines in cognition occurred and that we do see some reduction in mood symptoms in group data following surgery.

And that's not to say that you know Dr. Berman referred to and Dr. Susky severe mood disorder, and that's a separate thing. If someone is so depressed that they cannot followthrough with appointments or the decision making process is unclear as to whether or not they are able to make a good informed decision because of mood, or the mood is severe enough that we actually think that they are more at risk for having worsening mood following surgery then that is a separate issue. But the typical types of mood problems you most often see don't tend to change pre to postsurgery in a more than transient way.

The other thing that the report and assessment can be useful for is to make other types of recommendations. So sometimes it is helpful to know above and beyond what the physical symptoms are and what the patients think they are capable of in terms of are you ready to go back to work, are you ready to go back to driving? Is there any - and this is less so with DBS but with other surgical conditions is there any supervision that's required following surgery, and when people are

returning to school those kinds of things and objective neurocognitive evaluation can help you as a physician make that decision.

And then other recommendations we can provide, the two most common postsurgical recommendations that I tend to provide along with the physician based on neuropsych testing is number one cognitive rehabilitation. So if for any reason a patient has a persisting presurgical or a postsurgical difficulty with memory, attention, executive function you can go to a speech therapist who is trained in cognitive rehabilitation to learn compensatory strategies for that difficulty. And certainly if psychotherapy is necessary you know at times as Dr. Susky mentioned if someone has some mood complaints we want to make sure that if they are eligible for surgery we also don't ignore the fact that mood complaints are there. So we want to make sure that they have a good social support system, maybe get involved with psychotherapy or someone to monitor them, or psychiatry, someone to monitor them over time. Surgery is a big deal so if you already have some vulnerabilities with mood changes it may be useful to have someone else to kind of help you process those changes. There is such as thing as you stress, so even when good things happen to us that can cause a change in our mental health function, I mean retirement, marriage and childbirth are all good things but they also can cause big life changes that can cause the changes in psychological functioning. So just because you know it's something positive it still doesn't mean that you don't need to monitor mood. And then these are other evaluations that may or may not be necessary. The top two being underlined just because they are the most common.

So in summary what the literature tells us is that if a patient has borderline cognitive psychological or both functions that we believe that they are at risk at least at in somewhat increased risk for difficulty, increased difficulty postoperatively so having an objective measure is one extra piece of data that the team can use to really make a good determination about someone's candidacy and to give the patient all of the information that they need to make an informed decision. Research does suggest again the research that exists does suggest that older patients are at greater risk for postoperative decline, there is some suggestion but again it's controversial and still up in the air that GPi might be a safer target in that situation. And then again I think that you know this is one part of a big team decision that really helps us understand what's going on with a patient before and after surgery; but certainly in reviewing all of the neuropsychological literature the one thing we do understand is that we need a lot more objective research with larger numbers of people to really understand more precisely these risk factors. Thank you very much.