

# 48| Neuropsychology of Human Immunodeficiency Virus (HIV) – With Dr. April Thames

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**Speakers:** April Thams, John Bellone, Ryan Van Patten



**Intro Music** 00:00



**John Bellone** 00:17

Welcome, everyone, to Navigating Neuropsychology: A voyage into the depths of the brain and behavior, now brought to you by INS. I'm John Bellone...

**Ryan Van Patten 00:26**



...and I'm Ryan Van Patten. In light of recent events around racism in America, we want to say that although NavNeuro is not a current events or political podcast we strongly support cultural diversity, cultural responsiveness, and cultural neuropsychology. We've discussed these topics in the past and we are working on future episodes on cultural neuropsychology as well. For now, we will say that we support the AACN Relevance 2050 Initiative, as well as the Society for Black Neuropsychology, the Asian Neuropsychological Association, and the Hispanic Neuropsychological Society. And we are continuing to work on scheduling guests to talk about important issues in cultural neuropsychology.

**John Bellone 01:12**



Today we're covering the cognitive and emotional effects of HIV and AIDS. To help us we brought on Dr. April Thames, who is an associate professor at the University of Southern California, USC. She's done great work in this area and is very knowledgeable and articulate about it.

**Ryan Van Patten 01:27**



Human immunodeficiency virus, or HIV, as the name suggests, is a virus that infects the human body and interferes with the immune system, which puts the body at a high risk for opportunistic infections that are uncommon in unaffected people. The damage to the immune system caused by the virus is what leads to Acquired Immune Deficiency Syndrome or AIDS. The earliest documented case of HIV in the United States occurred in 1968 and the epidemic took off in the 1980s. People who receive blood transfusions, who have unprotected sex, especially men who have sex with men, or who are intravenous drug users are all at high risk for acquiring HIV. In the 90s, HIV became a leading cause of death in young and middle aged adults, and it disproportionately affected African Americans and gay men. In 1997, fortunately, highly active antiretroviral therapy, or HAART, became the gold standard intervention. Since then, mortality has decreased greatly and health outcomes have improved drastically. These days, the treatment standard is called combination antiretroviral therapy or CART. CART works by stopping HIV from replicating, which promotes immune reconstitution.

**John Bellone 02:54**



Although rates of infections and adverse outcomes have gotten much better, it is still a large problem. According to the 2018 CDC report, the US has the largest annual number of people with new HIV diagnoses of any high income nation in the world. In 2017, there were about 38,000 people with new HIV diagnoses and over a million people living with HIV. About 15% didn't even know they were infected. Unfortunately, the number of new HIV diagnoses remains stable from 2012 to 2016. Effective prevention tools are available but not widely implemented. This topic is relevant to us neuropsychologists because HIV can affect our brain and cause

cognitive impairment. Plus, as the population ages, people with HIV are aging as well, obviously, and age-related cognitive decline, as well as the conditions that are most common in older adults, all interact with HIV on neurocognitive functioning. We're going to get into all this with April. So now we give you our conversation with Dr. April Thames.



**Transition Music** 04:03



**John Bellone** 04:11

Okay, well, we're here with April. Thanks so much for joining us on NavNeuro.



**April Thames** 04:14

Thank you for having me.



**John Bellone** 04:16

This area of HIV is a pretty niche area. We're curious what got you involved or interested in studying it in the first place.



**April Thames** 04:24

I've always been interested in neuropsychology, but in particular how medical illnesses can affect the brain. I actually didn't know that HIV had an impact on the brain prior to my postdoctoral fellowship. I started learning about this on internship just because HIV was very comorbid with the population I was looking at, and people started talking about HIV effects on the brain. So I had the opportunity for postdoc to participate in a T32 program looking at the neuropsychology of HIV/AIDS.



**Ryan Van Patten** 05:09

HIV targets the central nervous system via the tight junctions of a blood brain barrier and allows neurotoxins to infiltrate the brain thereby promoting neuroinflammation. Are there other primary mechanisms through which HIV impacts the CNS? Or is that it?



**April Thames** 05:25

Most people relate it to HIV infecting monocytes and lymphocytes that are able to then cross through the blood brain barrier. So, yes, definitely affecting tight junctions. Allowing it to be a leaky blood brain barrier is one way that the virus itself can travel. However, also infecting cells that are able to easily get in and out of the blood brain barrier is another way. Whether it's an infected monocyte or

macrophage cell, or whether it's the virus itself, what happens at that point is it doesn't directly affect neurons, but there are viral proteins such as the GP-120 as well as transactivator of transcription protein that are really thought to have the most pronounced effects on neuronal integrity.



**Ryan Van Patten** 06:25

Got it. A leaky blood brain barrier, never a good thing. [laughs]



**John Bellone** 06:30

[laughs]



**April Thames** 06:30

No, it is not. [laughs]



**Ryan Van Patten** 06:31

Then next step in the path - thinking about what neural networks and brain regions are impacted - the frontal subcortical loops, the white matter connections between the basal ganglia and prefrontal cortex are especially vulnerable. As I understand it, dysregulation of the frontal subcortical loops impacts frontoparietal and frontotemporal areas as well. Do we know why this anatomy is more susceptible to HIV?



**April Thames** 06:57

In the beginning, it really used to be thought that the basal ganglia was the region most impacted. And that's because a lot of the early studies would detect the virus within the brain, particularly in the basal ganglia. Obviously, basal ganglia has connections with other frontal structures. It really is more, I think, recent in the literature that people have been looking at these white matter tracts in HIV. Or, at least I'll say in the last 10 years, it really has become important to look more at the networks because, as opposed to earlier on when there was HIV dementia and we will see a lot of subcortical involvement, now it's more diffuse.



**John Bellone** 07:45

Do we know if there are other common localized neuropathological effects that we missed here?



**April Thames** 07:51

The virus itself - it's tricky because although the cognitive deficits now with treatment are less pronounced, we don't see this classic HIV associated dementia that we used to see. Now there's actually studies that have seen more cortical

involvement. So looking at mesial temporal structure involvement, particularly with the hippocampus. But in terms of the virus, and when we think about viruses more generally, they just have a predilection for basal ganglia. I think that if we look at HIV, we could still say that it's more pronounced in subcortical areas, although the cognitive impairments seen are more widespread because of all the networks.

**Ryan Van Patten** 08:43



Interesting. To clarify that and make sure I understand it well. In the past, our treatments weren't as good and there was more HIV dementia, more pronounced cognitive impairment. Back then there was a more specific neurocognitive profile, which sounds like a subcortical frontal sort of vascular type profile. But now, we have better treatments, less severe cognitive impairment overall, and the profile is more diffuse. Is that accurate?



**April Thames** 09:11

Yes.



**Ryan Van Patten** 09:12

Okay. That's helpful.



**John Bellone** 09:13

Yeah.

**Ryan Van Patten** 09:14



So talking about treatments that have improved over time, CART has certainly greatly enhanced quality and duration of life for people with HIV. But as we're saying, there's milder forms of so-called HIV Associated Neurocognitive Disorders, or HAND, that are still common in affected people. I believe that about half of people with HIV have some degree of neurocognitive deficits. Can you tell us about HAND, this construct?

**April Thames** 09:42



Sure. It's an umbrella term, essentially, to represent various classifications of HIV-associated neurocognitive problems that are on a spectrum from those that are relatively mild - Asymptomatic Neurocognitive Impairment is how we refer to it, where you do not see functional impairments. Then we have a classification of Mild Neurocognitive Disorder. In terms of neuropsychological testing ANI and MND are very similar in that you will see two domains of which performance is one standard deviation below average. However, the functional impairments are definitely more pronounced in mild neurocognitive disorder as opposed to ANI. And then we look at HIV-associated dementia that has even greater functional limitations. So the

variations between ANI, MND, and HAD, which is HIV associated dementia, all fall under this umbrella of HAND, but the degree of functional impairment is really what distinguishes between the ANI and MND category.



**Ryan Van Patten** 11:03

Gotcha.



**John Bellone** 11:04

That's really helpful. The asymptomatic neurocognitive impairment almost sounds like an oxymoron...



**Ryan Van Patten** 11:09

[laughs]



**John Bellone** 11:09

But my understanding is that the classification is intended to assist in secondary prevention. So we identify subtle cognitive inefficiencies as early as we can so that we can intervene to prevent those steeper cognitive declines in the future. Is that accurate?



**April Thames** 11:27

Yes.



**John Bellone** 11:28

Okay.



**April Thames** 11:28

Yes. That's the idea. And also to see - I mean, unlike other types of neurodegenerative disorders, there's not a progression. HIV can wax and wane in terms of its severity. Often, you'll see in the beginning, before people are put on antiretroviral therapy, there might be more cognitive slowing, then once they've had a chance to be on therapy, some of those cognitive impacts can improve.



**John Bellone** 12:03

You just mentioned the kind of cognitive slowing. It seems like bradykinesia or bradyphrenia, the slowness of movement and thinking. It's pretty common in HAND overall, right? That's pretty central?



**April Thames** 12:17

It's a very common complaint in HAND. Yes.



**Ryan Van Patten** 12:23

Then to follow up on the course of the illness, just to reiterate what you said, it's very important that this is not a neurodegenerative illness in a way Alzheimer's disease or Parkinson's disease is, right? It's not invariably progressive.



**April Thames** 12:36

Right.



**Ryan Van Patten** 12:37

Can we predict if someone will get better or plateau or get worse? Do we have a sense as to the prevalence rates of improvement versus decline? Can we predict the future in any way?



**April Thames** 12:49

That's a good question. There are a few factors that have been extensively studied that are more likely to predict poor outcomes down the road. One is somebody's what we call "nadir", or lowest CD4 counts. This is how low their CD4 count ever got in the course of the illness. That actually seems to be a strong predictor of who is likely to decline cognitively. There are other factors such as medication adherence and how soon somebody was put on antiretroviral therapy after infection. So, obviously, the longer that someone has gone without being diagnosed or put on antiretroviral treatment, the more opportunity they've had for their immune system to be suppressed and the development of what we call central nervous system opportunistic infections. And those come with immune suppression. So, usually, the presence of those are an indicator that someone might not have a good prognosis. On the other hand, people who tend to do better in the course of HAND are people who have factors going for them that we would see in almost any other condition. So higher levels of cognitive reserve, if you will, better access to treatment, and they're put on less neurotoxic antiretroviral therapies. These are also indicators of better prognosis over time.



**Ryan Van Patten** 14:31

And for those people, can their cognition improve?



**April Thames** 14:35

They can. I mean, it depends on where they started. So with someone who has HIV associated dementia, will they improve? Probably not. But it's more that we've seen people go from a mild neurocognitive disorder category to an ANI, depending upon

- again, a lot of it is medication treatment and adherence to that medication. But in terms of prevalence rates of how many people go from MND to ANI? I don't know that number.

**John Bellone** 15:14



Yeah. We're going to talk more about all those things you mentioned - cognitive reserve and opportunistic infections throughout the course of our discussion. But to get back to a higher level, just HAND, what are the emotional and psychiatric sequela? Because there are some, right?

**April Thames** 15:30



Yes, definitely. Apathy is one of the psychiatric sequelae of HIV, at least that my lab has studied as well as others. It is a syndrome that is thought to arise from disruptions of these frontal circuits, particularly frontal subcortical. Often apathy is thought to be depression, or it's misclassified as depression, but it's not exactly the same thing. We also do see higher depression rates in the HIV positive population. Depression is often tied to social factors that are understandable as a result of the illness and various life changes and changes in functional capacity. So this is most likely why we see higher levels of depression, but apathy is another psychiatric sequelae that is thought to be more tied to the neurological implications of HIV.

**Ryan Van Patten** 16:35



Another term that I've run into is NeuroAIDS.

**April Thames** 16:39



Yes.

**Ryan Van Patten** 16:40



Can you talk about that? How does it differ from HAND?

**April Thames** 16:43



Sure. NeuroAIDS is a term that came out mostly in the pre-HAART era because [they were] really looking at neurological complications as a function of actual AIDS, you know, acquiring AIDS. And now, less people are going on to develop full blown AIDS. They are HIV positive, but that is much different from being diagnosed with AIDS. Once somebody is diagnosed with AIDS, we know that their immune systems have been really compromised and now we don't see that as much, at least in the United States I will say.



**John Bellone** 17:22

I'm curious how the aging process interacts with HIV to impact neurocognitive functioning, especially given that many people with HIV are now aging. Nowadays, they tend to have a normal lifespan. I've heard you talk about HIV infection as a model of accelerated aging and how some data even suggests that it accelerates brain aging by 15 to 20 years or so. I'm curious if you can elaborate on that.



**April Thames** 17:47

Sure. So there were a number of studies that came out around 2009. One of the studies by Beau Ances that looked at baseline cerebral blood flow in patients with HIV infection as well as those without and really saw this gap in terms of what you would expect from a healthy or non-HIV infected individual. In terms of their level of baseline cerebral blood flow, it really ended up matching. Someone who was around 20 years of age who was HIV positive would have a baseline cerebral blood flow that looked very similar to an uninfected person around age 40. That's where that 15 to 20 year gap came from. Keep in mind, though, that a lot of the individuals that participated in the study, they had been part of that pre-HAART era, for the most part, there was a mix of people in a lot of these studies even in the early 2000s. So the accelerated aging brain gap appeared to be much larger. We actually did a similar study a few years ago, it was led by a postdoctoral fellow at the time working in my lab, Taylor Kuhn, looking at white matter and could we use principles of machine learning to predict what is the person's age or using DTI metrics how well did that map onto chronological age. And when we use people who are virally suppressed, who had been infected for about 10 years on average, these people showed about on average a 5 year brain age gap relative to an older - sort of predicted age versus their chronological age - whereas with controls we did not see that. Other studies in HIV have looked at post mortem brain tissue looking to see, using methods of DNA methylation, how is the organ system aging? All studies have been consistent in that there seems to be a faster aging process. But keep in mind, also, these are individuals that have a lot of other things going on besides just HIV. So I think we're still, I would say at least for me, I'm still not entirely convinced that we don't have other social factors that might be accounting for that.



**John Bellone** 20:39

Sure. Yeah. That's a very good point. That paper by Ances was published in 2009. I think that's what you're referring to.



**April Thames** 20:45

Yes.



**John Bellone** 20:45

So it sounds like quite a bit of progress has been made just in treatment since then.



**Ryan Van Patten** 20:50

So the gap, where there was 15 to 20 years of accelerated aging in the past with worse treatment, now, with better treatment, they're still potentially aging more quickly but the gap is smaller.



**John Bellone** 21:02

Yeah.



**April Thames** 21:02

Right, exactly.



**John Bellone** 21:04

I kind of want to ask you more about machine learning, but that's going to derail the conversation. [laughs]



**Ryan Van Patten** 21:09

[laughs]



**April Thames** 21:09

[laughs]



**John Bellone** 21:09

Let's stick to HIV for today. [laughs]



**Ryan Van Patten** 21:12

On the topic of aging, we are aware of comorbidities that are common in aging, supravascular disease, for example. So, in other words, older adults who have HIV, just because they're older adults, and in addition, potentially because of lifestyle factors, are likely to have cerebrovascular disease, AD, falls and traumatic brain injuries, etc. Will you talk about the literature on HIV plus other brain diseases and the synergistic impact on cognition?



**April Thames** 21:46

Sure. Well, we do know that younger folks with HIV are showing these medical comorbidities that are commonly seen in older age among those who are uninfected. So there does seem to be this pattern in the population that these comorbidities are coming up a lot sooner. So we know that factors like diabetes, hypertension affect cognition, and even antiretroviral therapies are thought to contribute to comorbidities such as hyperlipidemia. So the population sort of has

two double hits, one with the medication effects that could be also contributing to these conditions, as well as the accelerated aging process that we think might be happening. So in terms of how they interact, it's actually more of a newer field, the way I see it. We're still looking at how HIV interacts with these other medical conditions that we know to affect cognition. The way I've interpreted the literature is that it's still in its infancy and some studies have seen interactive effects while others have not. I think it's because in large part it's hard to tease apart these lifestyle factors. Thinking about something, for example, like diabetes. It is often a disease of socioeconomic status. So people who go on to develop more severe forms of diabetes complications largely have to do with access to care, diet, nutrition - all of these factors that are really tied into socioeconomic status. And the HIV population, depending on where you're studying HIV, but for the most part, it also tends to be a lower socioeconomic status population. So that's what makes it complicated to really look at the interactions between the two on cognition.

**Ryan Van Patten** 23:52



Got it. You may have the same answer for this question, but could you focus in on substance use and opportunistic infections like Hep C that would be much more likely in a population who's potentially having unprotected sex or IV drug use?

**April Thames** 24:09



Right. Absolutely. So, back when I was on postdoc, we were actually looking at hepatitis C. And back then they didn't have the treatments for hep C that they do now. So we were looking at pre-post changes in brain integrity after pegylated interferon and ribavirin treatment. It's interesting because the population were mostly injecting drug users, and that's how they contracted hepatitis C. And whenever [you're] working with the HIV positive population, you have to consider the substance abuse comorbidity. There's been a ton of studies that have looked at methamphetamine or cocaine use. It tends to be more prevalent in the population. But with hep C in particular, it's harder to study now just because of the treatments - they can essentially clear the virus with hepatitis C. We've had a lot of participants come through our study, and they are essentially cleared of the virus with the newer forms of treatment. But thinking about the synergy between substance abuse and HIV, they do share very similar cognitive profiles. I know that there are some newer studies, and I wish I could do it justice by explaining, but there's actually a study that came out looking to separate brain regions involved in substance use disorders versus that of HIV and how they overlap, but also how they may differ. I think that direction is probably more important of a direction for us to go. But as you mentioned earlier in this podcast, you know, one of the ways that HIV gets into the brain is through this leaky blood brain barrier and there are substances like methamphetamine use, chronic use, that can also result in a leaky blood brain barrier. So we have to consider all these together when looking at the disease.



**Ryan Van Patten** 26:13

Yep.



**John Bellone** 26:14

We've been talking a lot about HIV and aging, but I'm curious about the other end of the age spectrum. Do you know if or how HIV affects kids and adolescents who are maybe affected at birth or early on?



**April Thames** 26:26

From the studies that I've seen, it really has this more diffuse white matter pathology among kids who were infected with HIV at birth. Also with more sensory motor impairments. There's some more occipital parietal involvement, which in theory makes sense if we think about neurodevelopment and how it's a lot different in kids. So the impairments tend to be much more severe, particularly in adolescents who have acquired the disease and if it wasn't treated appropriately.



**John Bellone** 27:11

That makes sense.



**Ryan Van Patten** 27:12

Cognitive deficits frequently lead to impairments in instrumental activities of daily living in multiple clinical populations. In HIV, a particularly critical IADL would be medication adherence given the importance of the treatment regimen to patient health outcomes including cognition. I'm curious, what are the findings from the literature on cognition and medication adherence in HIV?



**April Thames** 27:38

The findings in terms of its effects on cognition? We know that medication adherence is a good thing. It was more difficult in the past, because there were so many medications that patients had to take and they had to maintain this 95% adherence rate in order for it to work. Now with certain medications - the 95% rule of adherence is still reported in studies to be effective, but I've seen as low as 70% that can also be effective in terms of adherence. So I think it really depends on the regimen. We know that for people who are cognitively impaired, it is harder for them to maintain their adherence to medications. So that's also an issue to consider - that it's almost bi-directional. If you're not adhering, that leads to more cognitive impairment, and if you are cognitively impaired, you might not be as adherent. So it's very bi-directional. But that's where the literature is, at least right now.



**John Bellone** 28:51

It's like a cycle, unfortunately.



**April Thames** 28:53

Yes.



**John Bellone** 28:54

Is there a way that we can improve medication adherence in these individuals? Do you have any ideas?



**April Thames** 29:00

There's a number of studies now that have been looking at mobile supportive techniques like text messaging, reminders, things like that. I know a colleague, David Moore at UC San Diego, their group has been working on medication adherence technologies and they have been finding promising results.



**John Bellone** 29:22

I'm curious about the literature on the impact of HAND on other important functional outcomes, driving, finance management. Do you have an idea about those as well?



**April Thames** 29:32

Oh, yes. There's a number of studies that have shown that HAND impacts driving and Tom Marcotte at UCSD has done a number of these studies with a driving simulator. The driving simulator is actually pretty good at predicting people's actual driving, it's been compared to driving records. So there's a lot of ecological validity for using that type of task in the laboratory, and we definitely see the effects of HAND on that. Also, with medication management, there are laboratory-based tasks that we give. My lab gives it, it's called a medication management task. You ask participants questions based upon the fake pill bottles that they have set in front of them. The idea is to see, can they use judgments that you need to use in managing your medication routine? There are a number of other in-lab activities that have been used but correlate very well with real world outcomes, such as shopping and setting up fake kitchens and seeing if people can follow instructions with cooking. And HAND tends to affect all of these things.



**John Bellone** 30:50

Going back to something you said earlier about medication effects, I wanted to focus there a little bit more. So there could be some low grade and neurotoxic effects from CART. But obviously, the negative primary impact of the HIV virus is much worse than the small hit that CART potentially delivers. So it seems like a very easy decision to recommend full adherence to the medication regimen. But I don't know if you have anything else to add there or any anything about the medication effects that we should know more specifically?

**April Thames** 31:23



I think an important concept that sometimes is ignored in the literature is this idea about resistance. It's really a consequence of these different mutations that emerge in viral proteins that become targeted by these antiretroviral agents. So if we think about the number of patients that have HIV, or who are HIV positive, as many as 50% are infected with viruses that express some type of resistance to an antiretroviral med regimen. So not only are there these existing resistant strains that are within the viral type, but when people are not adherent, or they're infrequently adherent, to their medications, they can also develop a resistance to that particular regimen. So it can become really complicated if somebody is not adherent and that's why it's important. It's because for one, if they start on a medication regimen and then they stop, depending on their HIV viral type, they may actually develop more of a resistance toward that particular regimen. And if that keeps happening, you can see that it'd be really difficult to control the virus.

**John Bellone** 32:48



In terms of the cognitive profile, can we pick out how much might be due to the CART versus the other problems? I know that's a very difficult question to answer.

**April Thames** 32:58



Yeah, I haven't seen any investigation. Not saying that they're not out there, I just maybe haven't come across it. But it would be very difficult to do that. Now what people have done - Some work by Scott Letendre at UC San Diego looked at the CNS penetrating effectiveness of certain antiretroviral medications and actually graded them on how effectively they're able to cross the blood brain barrier. So we do know that certain antiretroviral medications are more neurotoxic than others, and therefore you see more neurocognitive impairment among those who have it. But in terms of looking at a cognitive profile and being able to say, this is HIV versus a neurotoxic effect of CART, I think that's very difficult to do.

**Ryan Van Patten** 33:53



Right. This is not an entirely novel idea. I'm thinking about someone with severe epilepsy, which can have significant effects on the brain and cognition, but also AEDs, some more than others, have negative effects on cognition. If someone has severe epilepsy and AEDs work, it's a pretty easy decision to medicate. It's just good to know that the treatment has subtle effects.

**April Thames** 34:20



Right.



**Ryan Van Patten** 34:22

I'd like to briefly talk about opportunistic infections that frequently occur in someone who's immunocompromised. Although CART has reduced the chances of additional infections, they can still occur sometimes, especially if someone is not taking the medication fully as prescribed. What are some of the most common opportunistic infections and might they have independent impacts on cognition?



**April Thames** 34:48

Yes, there's various types of opportunistic infections anytime the immune system becomes severely suppressed. Someone would have to completely stop their CART regimen and become so immune compromised in order to develop these types of opportunistic infections. In fact, we rarely see them anymore. They were much more prevalent back in the pre-HAART era. We would see, for example, a central nervous system lymphoma, toxoplasmosis, cytomegalovirus - those were some of the common central nervous system opportunistic infections. And yes, some of these would lead to psychiatric manifestations such as mania, even some features of psychosis. So they're pretty severe. When you see the manifestations, you're going to see this behavioral psychiatric component as well as the severe cognitive impairment. But once treated, it reverses. So that's how, you know, in terms of the severity.



**Ryan Van Patten** 36:05

Would you consider that a delirium or is it different?



**April Thames** 36:08

Right.



**Ryan Van Patten** 36:08

Okay.



**April Thames** 36:08

Yeah, that would be a symptom that there is an infection going on.



**Ryan Van Patten** 36:15

Got it.



**John Bellone** 36:16

So maybe we'll switch gears a little bit and talk about the clinical neuropsych eval of a patient with HIV. To start off, how often and under what circumstances does a patient with HIV usually get referred to a neuropsych clinic?

**April Thames** 36:32



It's rare, I think - more rare than it should be. Usually the doctors who refer are infectious disease doctors with a solid training in NeuroAIDS complications, and that's a very specialized field. So in academic institutions, which is where I trained, I would see patients with HIV. But in the community setting, in terms of doctors that are treating HIV patients, they are rarely sending them on for neuropsych evaluations. Typically, what I've seen happen in the community, is that the patient is seeing their doctor, having some complaints of cognitive slowing, it's thought to be depression, they then go see a psychiatrist, put on antidepressants, and then as the problems continue, eventually, they might be referred for neuropsychological evaluation. But it's not that common unless you're in an academic medical center with people who have knowledge of that. I don't know the percentages, but I would say they're not as common as some other areas within neuropsychology.



**John Bellone** 37:46

Yeah, that's been my experience. I haven't seen a patient with HIV for years.



**Ryan Van Patten** 37:51

Yeah, very few for me. So when we do see them, how can we be most useful and helpful to them?

**April Thames** 37:59



I think what's really helpful is to get an understanding of their medical history. I mean, even a neuropsychologist should definitely do that. Patients are not always consistent with their self report of how low their CD4 count ever was, or their viral load, the highest peak of that. So having access to any sort of medical records to look at the trajectory of their illness is going to give you a good prognostic indicator of potential severity of cognitive problems and whether or not this is going to have an impact on their day to day functioning. So I would say the most helpful thing is to get a really good medical history and asking about things like when they were put on antiretroviral medication, if they know when they were infected. I mean, some people just don't know. Usually, the first sign is when they felt like they had the flu and then they go to the doctor, and lo and behold, they are diagnosed with HIV. So it's hard to say how long they had the virus. But nevertheless, having that information, I think, is really important. It's much different than the patient that knows when they were infected and immediately was put on antiretroviral medication. That is much different clinical information that you'll use in a neuropsych evaluation. So I would say that's really important.



**John Bellone** 39:27

Okay, so potentially when they were infected, if that's known, when they started treatments, their nadir CD4 count, like you mentioned, viral load, T-cell counts. Anything else that I'm missing? That is really important?

**April Thames 39:42**



Yeah, just looking at - so often I'll ask people, "What was the first anti-retroviral medication that you were put on and was it successful at viral suppression?" because some patients, regardless of their adherence, are going to have those potential resistant strains, as I mentioned, and it may be harder for them to achieve viral suppression. If they've been adherent to their medications, yet, they're having a hard time achieving that viral suppression, that's important to know. Also, obviously, drug use history is a major factor that needs to be asked about and explored because it does tend to be very prevalent in the population. So I would say that those are questions that are often missed when I receive patient information that I would like to know more about and I end up having to ask them and dig for it.

**John Bellone 40:44**



Also their adherence to medications, right? If you can get a sense from them really how faithfully they're taking these meds, that's really important, too. Okay.

**April Thames 40:54**



Yes. And sometimes people won't be as forthcoming or they'll think that they're adherent. The best indicator is the viral load. If they went from being suppressed, then all of a sudden have - I mean, there are going to be viral blips, and we know about how many copies per milliliter of blood that number should be for us not to really be concerned. But if it shoots all the way up to the 100,000s or millions, and then they were at some point suppressed, you can probably get a sense that they had stopped their medication regimen at some point.

**Ryan Van Patten 41:30**



Right. If I have a patient who, to my knowledge, doesn't have an HIV history, or that's just not commented on, should I be asking about this routinely? Or maybe if I have a patient with a substance use history, or who has externalizing symptoms, and is impulsive - is there a threshold under which you would see a patient, you have no idea if they've had HIV or not, and you would routinely ask about it in the clinical interview?

**April Thames 41:56**



When I was training, we would ask about it in a questionnaire sort of checklist fashion before they came to the clinic, about whether or not they had been diagnosed with any of these conditions. Some people might be reluctant to disclose

their status so you'll never necessarily know for sure if they might have something. Sometimes I will tell patients the reasons why we're asking about certain conditions, and that might then prompt them to say, most of the time with me, it's been, "Oh, I do have herpes type 2". They didn't report it because a lot of people don't want to report it. But that's an example of a virus that's stigmatized and people often don't report because they don't really see the need to. But it's important to know, in a clinical evaluation, the presence of any of these viruses.



**Ryan Van Patten** 42:54

Right.



**John Bellone** 42:55

Yeah, that's a good analogy. In terms of the test battery, is there anything different that we need to be thinking about with these patients?



**April Thames** 43:03

I think in terms of the test battery, I guess the tests that will give you the most bang for your buck are those that are really looking at processing speed, motor, executive functioning. Obviously, being able to give tasks of learning and memory and really look at that single trial learning and also the learning curve relative to delayed recall and recognition. So I think a standard battery that you would mostly use, but if you are limited on what you could give, I would say make sure to throw in the processing speed and fine motor measures with the executive.



**John Bellone** 43:44

Right, because of bradykinesia and bradyphrenia. And just to clarify the learning aspects. So we would potentially, if it's a subcortical type of presentation, expect maybe fewer words learned on trial 1, and then with repetition, an improvement, right? But any specifics that you're looking for other than that?



**April Thames** 44:06

Exactly that, what you're saying. We don't have this very clean profile with HIV, so I don't want to say that you'll see this frontal contribution to memory profile that you would expect in a frontal subcortical disease, because sometimes they don't learn after repetitions. So it's possible. But in terms of classic, what we would expect in an HIV profile, it would look more like what you would see in a frontal subcortical.



**Ryan Van Patten** 44:43

Moving forward in terms of the evaluation, what HIV specific recommendations are common in reports? What do we look for in the assessment process of someone with HIV that would inform our recommendations for them?

**April Thames 44:58**



Most of the recommendations are going to center around factors that we would give anybody, which is “what's good for the heart is good for the brain”. But also focusing on their illness, managing their illness, and any of the potential comorbidities are better attended to that disease process. At least I'll say, at least from our research studies, the patients that tend to do the best are those that are in some type of HIV support group, or they're part of some HIV community, because they tend to be more on top of managing their illness. If they have friends that are also [HIV] positive, that has a beneficial effect. I'm always telling patients to join one of these groups because I think it tends to be really helpful in particular for this. This is not like epilepsy, where it's not really stigmatized to the degree that HIV is. I think that more so it's important to have that social network.

**John Bellone 46:12**



Regarding ethical and legal considerations, maybe we should talk briefly about what we can or should do if we know that an HIV positive patient is potentially exposing others. This is a kind of dicey area.

**April Thames 46:27**



Yes, it is a dicey area. I wish I could comment on [it], it's definitely not been my area that I've been worried about. But I know that, in my experience, most of the patients that have disclosed, they've already been tested. When you're tested positive, your results are sent to - I'm blanking on the name right now. But it's basically like a registry of people who are tested positive in various clinics. In terms of whether or not they are infecting other people, there is a degree of confidentiality that we have to maintain. So it is a dicey area. I don't know what the current state of affairs is on that. But I haven't been mandated to report someone who's HIV positive and who says they have a partner. I haven't been mandated to report that. So I'm assuming that it's not required at this time.

**Ryan Van Patten 47:34**



Right. That's how I would approach it based on the APA ethics code and confidentiality. As you said, the limits of confidentiality - think about Tarasoff, if someone has intent to harm a specific person, this is not that. So we're not calling their sexual partner to let them know. I think what we could do is have a discussion with the patient themselves.

**April Thames 47:56**



Right.



**John Bellone** 47:57

Listeners should look at the laws and ethical guidelines for their states and provinces and countries that they are listening to this in.



**April Thames** 48:05

There are these partner notification services that are available that I've read about - but it's almost that the patient has to agree to participate in it. So once they do, they can help them navigate. Either the health worker will inform the partner anonymously without the patient being known, or they can help the patient navigate how to have a conversation with the partner. So those are available, but it's really up to the patient to use them.



**Ryan Van Patten** 48:43

This is a really interesting and important topic, for sure. I'd like to move on as we get close to wrapping up our conversation.



**April Thames** 48:51

Yeah.



**Ryan Van Patten** 48:52

Given the rapid innovation in treatment for HIV, in addition to the pre-exposure prophylaxis, the PrEP, which reduces HIV transmission by over 95%, I'm curious what you think the HIV healthcare landscape will look like in 20 years, or in 50 years from now?



**April Thames** 49:10

Well, I'm hoping that this is not going to be an issue and that I'm essentially out of business.



**Ryan Van Patten** 49:18

[laughs]



**April Thames** 49:18

Best case scenario. No, but it would be really nice to see. I think that for the US where we have so much access to resources, it will become a point where the cognitive deficits, if any, are very mild because the treatments will be more effective. I mean, hopefully, we can eradicate the virus. I think in developing countries, we're still going to have issues and it's still going to be slower. In lower socioeconomic communities, unless there are some really aggressive community based actions, I think it's still going to be a problem in those areas. So, my hope is that whatever we do, however the treatments are improving, that the lower SES

communities as well as developing countries, they're not left behind. I would like to see that it's been aggressively handled across these situations so that we could get rid of this HIV associated neurocognitive disorder and people can live very normal and healthy lives. But I don't know. I don't know if that's going to happen. There's a lot of cool research on the horizon, and some promising findings, but I guess we'll see.



**John Bellone** 50:41

Along these lines, I know you're very interested in cross cultural issues in general, not just specific to HIV. Would you tell us a little bit about how HIV interacts with culture or anything else you want to say about cross cultural issues in general?



**April Thames** 50:55

Sure. So first of all, there's certain cultures where HIV is highly stigmatized. We know that certain groups, for example, Black men who have sex with men, there's a down-low phenomenon about that and they still have heterosexual partners. This is something that has been talked about in the Black community as being problematic. I'm speaking to African American communities, because that's what I've studied, I know more about it.



**John Bellone** 51:32

Sorry, by "down-low", you mean that they just don't talk about it?



**April Thames** 51:35

They're not talking about it. That they're having these sexual encounters, but they also have heterosexual partners. So the transmissions are happening because of these "down-low" relationships. That's one way. And then another way that's also affecting some of these communities are when men are coming out of prisons, and they have been engaged in sexual encounters with those who are infected, and then coming home to their wives or they're hiring prostitutes, whatever the case may be, the infection rates are spreading.

What we see among older women - we recently did a study not with HIV, but looking at sexually transmitted diseases more generally - is that some of the older women who are recently widowed or divorced and they're over 50, and they're out on the dating scene again, they're not using contraceptives because they don't think that they have a risk of becoming pregnant. There's a lack of knowledge about sexually transmitted diseases. So we tend to see in terms of culture there's this layer of stigma of which people just aren't talking about it, then there's also knowledge and educational gaps in terms of what is being talked about in health literacy and prevention. That's how HIV continues and is rampant in these communities because people are not talking about it for various reasons.

Even if you put up a testing clinic right in the middle of a community that is low SES, for example, or even high SES, people might not want to go in and be seen getting tested. So there's a lot of barriers to it. I would say that that's how culture interacts on a number of different levels. Not just race and ethnicity, but I think socioeconomic status and beliefs about health and disease in general play into who is going to take medications. If you think the disease can be prayed away or it can be resolved by some sort of herbal medicinal therapy, then you're less likely to take your antiretroviral medication.



**John Bellone** 53:33

It's a good point.



**Ryan Van Patten** 54:11

This is a public health issue, right? Education, resources. It's always so sad when we have good treatments for something like malaria or TB in Africa - we know how to treat it, and people are still losing their lives over it.



**April Thames** 54:29

Yeah. Now with the pre-exposure prophylaxis, that's great. We know it works. But the PrEP uptake rates are really low. And it's because most people don't like taking medications. A lot of people don't want to take a pill every day for the rest of their life and not know what it's doing and what the side effects are. Then the thought is that "Well, I'll only take this when I'm about to have a risky sexual encounter." And that's not the way it's supposed to be used. So these are all the issues that we're dealing with right now in HIV.



**John Bellone** 55:09

Yeah. So on that positive note... [laughs]



**April Thames** 55:13

[laughs]



**Ryan Van Patten** 55:13

Thank you for bringing this to light.



**John Bellone** 55:14

This is really important to talk about.



**Ryan Van Patten** 55:17

Hopefully, if we can make even a small difference for this conversation, that'll be a good thing.



**John Bellone** 55:23

Yeah.



**April Thames** 55:24

That'd be great.



**Ryan Van Patten** 55:25

With that said, this wraps up the portion of our conversation talking about HIV. Thank you very much for all the knowledge.



**April Thames** 55:32

Oh, yes.



**Ryan Van Patten** 55:33

Before we end the interview, just a few more minutes, we have bonus questions... [laughs]



**April Thames** 55:37

Sure.



**Ryan Van Patten** 55:38

...that we ask all of our guests.



**April Thames** 55:40

Bonus round! Okay.



**Ryan Van Patten** 55:40

Bonus round. Yeah, hot seat, as if you haven't already been on the hot seat. [laughs] So these are a couple of questions that are not specific to HIV. They're meant for the field of neuropsychology broadly, and we're very interested in your thoughts. First, if you can improve one thing about the field of neuropsychology, what would it be?

**April Thames 55:59**



I think if I could improve one thing it would be the access to neuropsychological services. I think it's a huge issue. It's shocking how many people either don't know what a neuropsych evaluation is, doctors aren't recommending it, and some physicians don't always see the value of it. We're in this bubble, at least I will say for myself, when I was being trained at an academic medical center, I thought everybody thought neuropsychology was important. It wasn't until I was out in the real world and interacting with people and the numbers are so shockingly low about how our services are accessed. So if I could improve one thing about the area it would be that, because I think we do provide a really important service, but we haven't been the best at marketing it.



**John Bellone 56:53**

We've talked about this a lot. Any ideas about how to do that?

**April Thames 56:57**



Well, I don't know anything that's probably beyond what people have tried to do. I think aligning with other healthcare professionals to demonstrate the importance. I think in terms of - we have funding issues, obviously, with insurance and reimbursement rates. If we can make evaluations quicker and more efficient, and reports not being 15, 20 pages long, I think that would be a huge improvement. I think people are going in that direction. I've always said, you know, in every other profession in medicine, the doctor can write a two liner about what's going on and nobody ever questions how they arrived at that. But, as psychologists, we feel the need to justify every single thought and every single opinion that we have. I think that that's essentially the biggest problem. We have not been efficient as a field.



**Ryan Van Patten 57:57**

Really well said.



**John Bellone 57:57**

You're preaching to the choir.



**April Thames 58:00**

[laughs]



**John Bellone 58:01**

For the second bonus question, what's one bit of advice that you wish someone had told you when you were training or that someone did tell you that really made a

difference? Just an actionable step that trainees can take that would really make a difference.

**April Thames 58:12**



I think that I was really shy as a trainee and afraid to speak up and get to know people. I wish someone would have told me to be better at networking because even to this day, I'm pretty horrible at it. I think that if I had someone take me under their wing and show me, like, this is how you get to know the people that are in the field and the people who are really making a difference out there. I wish I would have had that. I see how important it is in terms of making sure you're getting the optimal training, being able to bounce ideas back and forth. It's really helpful to know the people in the field that are actually doing the top notch work. That's the advice I try to give my grad students. I tell them, "You need to go to these conferences and go up and walk up to somebody and bug them. It's okay, nobody's going to turn you away." But I know how I was when I was a student. I was so afraid to talk to some of these big people. I didn't know what was gonna happen, so I just shied away in the corner and that did not help.

**John Bellone 59:21**



Yeah, I love that. So with NavNeuro, we thought, "Oh my gosh, we're not going to get anyone to talk to us. It's going to be really hard to get people. People are so busy...", but we've found overwhelming support for people who are interested in talking to us. Even not formally in a podcast but even at a conference or when you approach somebody. I think the neuropsych community is a really kind and compassionate community. I mean, that's why I went into this field to begin with, so.

**Ryan Van Patten 59:49**



Yeah, with a few notable exceptions. [laughs]

**John Bellone 59:52**



Ryan over here. [laughs]

**April Thames 59:55**



Well, I think this is a great thing that you guys are doing because this is really an education tool and a way of getting information about what we're doing out to the masses. I think more people need to be doing that. We always talk amongst our little silos of other neuropsychologists, but that's not going to get the information out to the public and that's who really needs it. So the fact you're doing a podcast is really cool.



**Ryan Van Patten** 1:00:23

Yeah. Thanks.



**John Bellone** 1:00:23

Thank you. That's nice of you. Just one last question. So we've covered advice for trainees, we want to ask about advice for early career professionals. Would it be different than your networking advice? The healthcare landscape is changing pretty rapidly, we want neuropsych to remain relevant and useful for decades to come. Any thoughts for how to continue to be relevant and provide kind of cutting edge scientific and clinical services?



**April Thames** 1:00:47

I think we have to be more involved in policy. As early career [neuropsychologists] you have more of an advantage than you do as a student to have a voice at the table where people are actually making decisions. There are obviously great people in our field. Tony Puente has been on the policy advocacy side for neuropsychology. We need more people to step up and do that. Whether it be at the national organizational levels, like NAN or INS, or one of the major neuropsych organizations, shaping the way we present ourselves as a field but also getting to people who are actually making decisions about neuropsychology services. I think that's huge. I would encourage early career people to start talking about how to do that process because obviously it's not something that happens overnight.



**Ryan Van Patten** 1:01:41

Yeah, I love it.



**John Bellone** 1:01:43

Well, April, thanks so much. This has been really great. People are going to love this conversation.



**April Thames** 1:01:47

Oh, good, I hope so. I hope the noises were not awful.



**Ryan Van Patten** 1:01:50

Oh, no.



**John Bellone** 1:01:51

Your dog wanted to contribute, it sounds like. [laughs]



**Ryan Van Patten** 1:01:54

We're dog lovers here at NavNeuro, so very welcome.



**April Thames** 1:01:57

[laughs] Thank you. Thank you so much, you guys. And thank you for putting up with my crazy schedule.



**Ryan Van Patten** 1:02:03

Not a problem.



**John Bellone** 1:02:04

My pleasure.



**Ryan Van Patten** 1:02:05

Yeah, have a safe flight.



**April Thames** 1:02:06

All right, thank you. Have a good one. Bye.



**John Bellone** 1:02:08

Take care.



**Transition Music** 1:02:08



**John Bellone** 1:02:13

Well, that's it for our conversation with April. If you've been enjoying these podcasts episodes, please just take one minute to leave a rating on Apple podcast or wherever you might be listening to this on. It really helps us out. And, as always, join us next time as we continue to navigate the brain and behavior.



**Exit Music** 1:02:29



**John Bellone** 1:02:52

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**Ryan Van Patten** 1:03:04

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**End of Audio** 1:03:22