

AUTISM IN GIRLS AND WOMEN:
A PANEL DISCUSSION

WEDNESDAY, SEPTEMBER 19, 2017

The Seminar/Webcast: Autism in Girls and Women: A Panel Discussion convened in Rockville, Maryland, at the National Institute of Mental Health, (NIMH), 6001 Executive Boulevard, NSC, Conference Room 7102 at 12:49 p.m.

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PROCEEDINGS

Coordinator: Good afternoon and thank you all for holding. Your lines will remain on a listen only mode for the duration of today's conference. I would like to remind all parties the call is now being recorded. If you have any objections, please disconnect at this time. And thank you. You may begin.

Dr. Susan Daniels: Good afternoon. I'd like to welcome you today to our seminar, Autism in Girls and Women, that's hosted by my office, the Office of Autism Research Coordination here at NIMH, Institute of Mental Health. And also by our sister office which will be introduced as well. This topic has been of importance in the autism community as well as in the Interagency Autism Coordinating Committee, which is a committee managed by the Office of Autism Research Coordination. We felt it was a

timely topic to discuss in a broader context. And we look forward to hearing from our speakers today.

Ms. Tamara Lewis-Johnson: So welcome this afternoon to the Autism in Girls and Women NIMH Women's Health seminar. I want to thank Susan Daniels, Director of the Office of Autism Research Coordination. I want to thank the Office of Research on Disparities and Global Mental Health which is where I reside. And also the National Institute of Mental Health Women's Mental Health team, for their support of and assistance with this seminar on autism in women and girls, this afternoon. As the Chief of the Women's Mental Health program at NIMH, I serve with the women's health team, to nurture and support scientific advances to promote the mental health of women and girls.

This afternoon's seminar is illustrative of the importance of sharing NIMH-sponsored research findings with the research community, our federal partners and the public at large. The field of autism research is also important because it is indicative of the influences of sex and gender on the mental health of women and girls. Indeed, research findings suggest the influence of sex and gender operate on many levels that affect the health and disease burden of both men and women living with autism.

I'll now introduce our speakers. So I want to just - if you have a program you will see there is the brief bio of the speakers on the back and I'm just going to briefly introduce each of them. First is - the first speaker is Kevin Pelphrey. He is the

Director of the Autism and Neurodevelopmental Disorders Institute at George Washington University and Children's National Medical Center. He will be followed by Pamela Ventola - Dr. Pamela Ventola, Assistant Professor at the Yale Child Studies Center. She'll be followed by Ms. Zoe Gross, the Director of Operations at the Autistic Self Advocacy Network.

And then after all of the presentations, we will have a question and answer and final discussion. I welcome you this afternoon and we'll begin.

Dr. Kevin Pelphrey: Great, thanks. Okay. So I'm delighted to be here today and I thank you for hosting this event and having us. Thank you for your interest in this topic. I thought I would use my time to tell you about this project that we've been doing now going

onto the 6th year where we are conducting a major now longitudinal study of girls with autism and now we're going to be studying as they become women with autism. And so I wanted to give an update on that study and what we're doing and what we're finding. And put it in the context of what we're hoping to do with the discoveries that we're making.

So I'll tell you a little bit about our network - so we are a five data collection site network with a data coordinating center, so we have Yale and the Child Study Center with Pamela Ventola and Jim Duncan. And Harvard/Boston Children's Hospital with Chuck Nelson there. Now, a new site in Washington, DC with George Washington University and Children's National with Lauren Kenworthy; UCLA and with Susan Bookheimer, Mirella Dapretto, and Dan Geschwind handling our

genetics. And then within Los Angeles we also have the University of Southern California with Art Toga and Jack Van Horn's group with the LONI Center, our data coordinating center.

And then we're also involving colleagues at the University of California, San Francisco - Matt State in genetics and Somer Bishop as an expert on the ADOS. And then the University of Washington Seattle Children's Research Center as another data collection site with a lot of expertise on EEG. So what we did in designing this was to try to spread out our data collection so that we could find as many girls with autism as possible, knowing that, you know, up until the point of the study, really all of the studies that existed, were very small samples and couldn't really say much at all about

heterogeneity, about what's really different about girls with autism versus boys.

And we knew and suspected that there were a lot of very, very interesting differences in terms of the biology and phenotypic presentation of autism for boys and girls. So these are the aims. I'm not going to read them to you, but I want to focus today on the first one, identifying sex differences in autism brain development leading to gender specific biomarkers that we hope will inform treatment selection and response. So ultimately, I think this is our most important aim and we're addressing it now with, you know, what I think is a really beautiful longitudinal design, I'm biased, but we're starting with what I consider a national treasure. So we have about 250 girls with autism who are now moving into and

through adolescence. And they're about to become young adults. And then we have an equal number of boys with autism, as well as unaffected siblings, boys and girls, and then typically developing individuals boys and girls who don't have a first-degree relative with autism. And so we have this opportunity to follow longitudinally these individuals - woah sorry, that wasn't supposed to come up - follow these individuals as they transition to adulthood, as they transition into adulthood. So why is this important? Because in addition to sort of ignoring girls with autism, our field has also ignored that adult transition. And what we're learning from neuroscience and cognitive neuroscience is that the game isn't over at 9 weeks or 9 months old. Really there's incredible development that's happening and we can think

of adolescence as another period of plasticity where we could think of very creative interventions that we could utilize to help maximize life course outcomes.

And so we're not taking advantage of that plasticity and that opportunity, we're really ignoring cognitive neuroscience and everything the cognitive neuroscience of adolescence is telling us. And so we want to leverage that and study the individuals as they transition through - or transition into adulthood. We're very much taking a systems biology approach and applying it to the study - the longitudinal study of human brain development, so we have comprehensive imaging data and electrophysiology data on our individuals. The microphone is interfering. And we have that imaging data in the context of comprehensive genetic data, both in terms

of gene structure and gene expression from
(inaudible comment).

And we're putting that data together with very deep phenotypic data, where we have all of the gold standard clinical assessments as well as a lot of more experimental clinical assessments that we're using, so we get a real picture. And one of the things that I think is very unique is that we're actually collaborating with individuals with autism and the Autism Self Advocacy Network. And taking our imaging findings and using them in the context of the cognitive interviewing to check whether what we're finding kind of fits with the experience of individuals with autism. And then that feeds back into the systems biology approach in a way that I think is going to be very important. Putting all of that data together

in the same space allows us to come in and really get at modules of kind of latent underlying constructs that can follow their development over time. And those are what will serve as the biomarkers of interest for predicting treatment and for following treatment outcomes.

Okay. So I've used this term biomarker several times. And one of the things that we've been working on, there's a simple - you live and die by the movies - these simple biomarkers derive from people viewing people moving - in this case, playing patty-cake - versus scrambled versions of that. And so - oh, there we go. So what those look like. And so one very much evokes kind of a social gestalt and the other doesn't. And these quite beautifully - when you have people look at these and they're lying in the magnet and

we're recording their brain activity, we can reliably differentiate people with and without autism at the group level. And a lot of imaging studies have shown differences at the group level; very few have actually shown differences at the individual level, which is of course something we want a biomarker to do. So we've tried to do that. This is Malin's work - I'm highlighting several scientists who actually all happen to be young women doing very high end science and technology work. Malin is appointed at one of the most prestigious technical universities in Sweden. And she's doing this work that allows her to use machine learning to try to understand what are the brain systems that most reliably differentiate an individual with and without autism, again at the level of the individual.

And what she found was that she could replicate our prior findings - that this so-called social brain that we've all been very interested in, will reliably differentiate at the individual level very reliably a boy with autism from a typically developing boy. But what was stunning to us, those of you who are familiar with receiver operator characteristic curves - you don't get to say that very often at parties - it's washing out against the white background, but the little curve at the top - either I broke math, or we're worse than chance at differentiating people with and without autism. And you can't really break math. And so what that says is that using the social brain and social brain differences, you can't distinguish a girl with autism from a typically developing girl. And that gave us

great pause because what it suggested was that the story we were kind of evolving about autism being dysfunction in the social brain only applied to boys and that the neural differences we had been publishing on for, you know, a decade at that point. All - and all of the papers in the field had two or three girls in the sample but the samples were 15 or 16. Here we had, you know, a sample approaching equivalence and what we were finding was that our samples were drawing from two different populations. Even though they were carefully matched on every variable you can imagine and both had the diagnosis of autism with gold-standard criteria. And so that kind of blew us away.

So okay, how do we follow this up? This is Allison Jack. And so now we've been going along - and Allison is a brilliant cognitive

neuroscientist who's been following up this issue of is it that the girls with autism, actually have some sort of compensatory social brain activity that given the differences for example, on social demands, being a girl within the world, that their social brains aren't showing this dysfunction. Does this dysfunction have nothing to do with autism, it's just epiphenomenal? So what's going on? And what she's reliably finding is that boys of autism yes, the social brain dysfunction is very much there. In girls with autism, relative to typically developing girls, do have social brain dysfunction, but they're actually equivalent to typically developing boys. Right? So it very much matters who you're comparing them to. Because a typically developing girl has a very early

developing social brain system, it's very robust.

And a lot of, the other kind of dirty secret out there within cognitive neuroscience is a lot of the normative studies that we do, the kinds of studies on college kids - so many papers published in the 1990s and the early 2000s with 20 subjects in Science from imaging - were over half girls. And so a lot of the most robust social brain findings were coming from girls. They activate really well to the social stimuli. And so it's not just a stereotype. There's this very interesting developmental phenomenon on early social brain development that might well be the basis for female protective effect that helps to explain why girls are much less likely to be diagnosed

with autism. So that's what we're tending to see in our data.

Now a very smart person once said that, you know, if you have a hammer and you see a nail, and so I'm a social neuroscientist, I study the social brain. Now what if we take a step back - this is Archana, she has a PhD in electrical engineering from MIT and she just became an assistant professor in engineering at Hopkins. So she developed a technique to look at resting-state data, and so in a new and creative way, and is applying this to the study of autism and basically she's finding latent constructs in the imaging data. And if you don't know, resting-state data is exactly what it sounds like, you ask the person to lie in the magnet and be still while you record how the brain is sort of co-varying together. It gives you

a sense of how different brain parts are communicating.

So she's able to pull out networks that are dysfunctional, if you will, or communicating differently, that characterized autism from typical development. So what's nice about this is that it's not a hammer in the sense that the data can speak for themselves. So I'm not assuming social dysfunction, I'm not giving the person a task other than lying in the magnet and being still. But I'm letting the data kind of tell me what are the constructs of interest? So I get out these networks and then we took them and applied this technique called Neurosynth. It's sort of taking the finding and you kind of give it to the oracle and you say, this bit of brain is different in this group. Tell me what does the, you know, the hive think

that this part of the brain does? And it spits back some probabilities and it says, well most people say that's working memory; a few people say it's short term memory; a few people say executive function, you get the idea. So when we do that, and we make a Wordle, because everybody makes Wordles these days, the top one is the constructs that most reliably differentiate girls with autism from typically developing girls. When you ask the brain to speak for itself at rest and tell you what are the networks that are different. And so then I'm loading the value of that by font size so I'm saying if it's strongly different, make it a bigger font. And then for boys, I'm doing the same thing at the bottom. Okay?

So boys, person perception, social perception, comprehension, language, all

those are the things that define autism, right? The top one I think you would be hard pressed to pull out the DSM-5 criteria for autism, but the brain hasn't read the DSM-5. And so what that's saying is that even though these individuals have gone through DSM-5 diagnoses for autism spectrum disorder and received the ADOS and the ADI from some of the very best autism centers in the world, people with extensive clinical skill and credentials, so they couldn't be more alike because we forced them to fit a particular mold.

When we put them in the magnet and we asked, well what are the differences in brain networks, what we're getting is very different answers for boys and girls. And maybe you might want to come back to this and say well, could we define a different type of

autism in girls? And if this is accurate, might we want to focus on emotion regulation and anxiety, in terms of developing treatment for autism symptoms in girls, if these are the networks underlying autism symptoms.

Okay?

So the last point that I want to make, getting at this idea of biomarkers, this is the work of Pam Ventola who you'll hear from next. She's been doing this collaboratively with myself and Daniel Yang. Looking at how to use brain imaging to actually predict treatment response for evidence based interventions, in this case, Pivotal Response Training. So the question here is, you've got these therapies that we know work for some to a lot of kids is autism, but when you meet the kids you really can't say which kids will benefit and which ones won't, not in any

reliable way. And usually kind of they get the treatment that's available locally, but there isn't any real science to it. And this is important because we're talking about incredibly expensive treatments and depending on where they live, insurance may or may not cover it. This is a real issue. And frankly, with most of these treatments, this is a parent that - that really won't be able to work because they're having to take the kid to so many appointments, and so this is a true commitment. So, when Pam is using Pivotal Response Training to treat a group of kids, what you're seeing in this graph with the lines, the black and the red lines, the red line is symptoms as measured by the Social Responsiveness Scale, a behavioral outcome measure. And you're seeing that in this case you've got symptom reduction,

right? So on average, Pivotal Response Training works. We already knew that. The black lines are the individual variability, right. And that's pretty wild variability, so how do you account for that?

And what we found is that you could use these brain biomarkers, so what I'm showing you is the network of brain systems - one was involved in social perception, emotion regulation, perceiving the motivational significance of social stimuli, strongly predicts how active that is and how connected, strongly predicts whether or not a child will benefit from an evidence-based intervention. Right? So the clinicians in the room are thinking great, you know, you just used a 2-million-dollar magnet and a thousand-dollar scan to predict which kids will benefit. And what she found was that

the kids that kind of knew more about social stuff, could regulate and sit still, and paid attention to social stimuli, they were the ones that will benefit more.

Congratulations, right?

Yes, but nobody had a quantitative measure of those things that was reliable and, you know, if they did then let's see it. And then furthermore, we're saying that in addition to that, those bits of brain when they're active, kids do better with intervention. That's a mechanistic prediction. And so if I have a drug or a stimulus or a way to stimulate with a magnet or a current, those brain system, the strong prediction is that those kids will do better and I can take a non-responder and turn them into a responder.

And so that's what Pam is working on next with funding from the Simons Foundation, actually, most recently. And the very last thing that I want to show you is kind of where we're taking this even though I was saying we want to go older, we haven't given up on the little ones yet. So a lot of the things that we're doing, you know, I still want to understand very early sex and gender differences in social brain development; I haven't given up on the social brain either. And so to do that requires very different techniques - optical imaging is certainly one of them, EEG. Although, you know, frankly we find that up until about two years of age, fMRI works great as long as the babies are asleep. And everything I told you about today we can do, speech sounds are a form of biological motion and clapping is another.

And so we can do a lot of the same things and certainly resting-state data can be done while babies are asleep. So what's neat about this is that we and others, this is one example, have found measures of risk, right, and so we can differentiate kids who will go on to - kids who are at high risk versus those that are at low risk, by virtue of having a sibling with autism, by genetic risk. And we can find brain differences, we can find eye tracking differences. And that's very exciting I think, but it's not what we really want to do.

Because even if we had perfect measure of risk, with perfect sensitivity and specificity, for infant siblings, it would be about chance when it's applied to the population, because infant siblings have a 20% conversion rate and what we need is

something that works on the child where we don't really know anything about them, at a very, very early point in development. So I think where we are going with this next and one of the reasons why it's particularly attractive to moving to DC, so this is Ashley Darcy-Mahoney. And Ashley is a nurse practitioner. And if one wants to do work in the neonatal intensive care unit and in the maternity ward, one needs to have a nurse practitioner in the group.

And so she is able to bring these techniques, these near, near-infrared techniques and EEG systems, into the maternity ward because we already universally screen for hearing, and it's just a small leap then to bring in social and non-social stimuli and actually begin to do that population-based study. We're looking at the

process into those social versus non-social stimuli and see if we can begin to pull apart risk but in a much more universal, epidemiologically-based level. And so in doing that at the GW hospital which is one of the two to three where most of the babies are born in DC. And so that's been a great opportunity. So stop there and just thank the different funding sources that have made this possible.

Dr. Pamela Ventola: Good afternoon. Thank you so much for having me. I'm very excited to talk about girls and women on the autism spectrum. It's a topic that I've been working on with Kevin for a number of years now and I feel very passionately about through my clinical work. So I'm an assistant professor at Yale Child Study Center and I'm also a clinical psychologist.

So I'm going to speak about the behavioral presentation and clinical phenotypes of girls and women with ASD. So we have - I'm going to talk about two primary areas - one, to identify the clinical differences that we see between females and males with ASD.

So Kevin started talking about the brain differences and I'm going to tie that now to the behavioral differences. So we see these differences in the level of the neural systems and what does that look like - with the children and young adults and older adults in our office and in our communities? I'm also going to talk about some of the factors related to the misdiagnosis or delayed diagnosis of females with ASD. Again, as a clinician, this is a topic I get asked about quite a bit. You know, why are we missing girls with ASD or why are we

identifying them so much later? And it's a very - it's a complex issue. It's multifaceted and I'm going to describe some of the elements related to that this afternoon.

So there is a differential prevalence in ASD, the sex ratios estimated to be about 4 to 1. And very recent work though, in considering individuals that have IQs above 70, suggests in just this group of individuals is that ratio is estimated to be as high as 8 to 1 for boys versus girls. And girls with ASD are diagnosed later than boys. The average age of a boy being diagnosed with ASD is about three years and it's about four years for a girl.

Now you may not think a year is a big deal, but in the world of early intervention for autism it actually is a very big deal.

The earlier we can intervene the greater the outcome and particularly with relation to language and the window for language development. And I'll say qualitatively - I don't have research to support this, but qualitatively in my clinical practice, I see a lot of young women coming in, later school-age, teenage years who are struggling. A lot of internalizing symptoms - anxiety, depression, sort of struggling to fit in. And these are young women that have autism that has yet to be identified.

And we certainly see that in males as well, but at least in my practice, I can say I see that much more commonly in women. So, as we talk about how girls with autism differ than boys with autism, I think it's just - take a minute and think about typical development, in girls and boys are typically

developing, differ from each other. Some of this is biological, some of this is socially constructed, and probably a combination, there's a wide range of literature in the world of child development that says it is a combination. But what we're left with are girls and boys differ.

And this is very relevant to individuals on the autism spectrum, because as these children grow and develop, the social demands differ. What we think about as the social demands for a boy, differ than the social demands for a girl. And the social behaviors that individuals need to possess to fit in and make it work for boys on the playground, are different skills and behaviors than for girls on the playground. To put this concretely, boys tend to have large stable groups of friends, enjoy more rough and

tumble play and competitive team games. And I can say this goes even into young adults and adulthood where boys and men tend to socialize through activities.

Girls and women on the other hand, tend to have smaller groups of friends. They interact - it's more conversational and they develop intimacy and relationships through sharing - through sharing insights, through sharing experiences. So what we expect of boys and what we expect of girls is quite different.

And now shifting into the presentation, specifically girls on the spectrum. There's an idea of our - our classic female phenotype, and this is not all girls on the spectrum, but generally speaking, when we think about girls on the spectrum, they tend to have lower cognitive abilities compared to

boys, more severe social communication deficits, yet a more mild behavioral presentation. So fewer externalizing behaviors and fewer repetitive behaviors and restricted interests. And this description of a girl with autism has persisted for some time now. And I'd say in the last, even several months, maybe a couple of years, we see not all the girls on the spectrum fit this model, not - not even close to it. So it's sort of driven people to think about what about our more cognitively-able girls, because those are the ones in particular, so girls and women with IQs above 70, that really aren't fitting this profile.

So, in very recent work when we're comparing just females and males with IQs above 70, it's found that boys with autism tend to be more isolative, so more socially

sort of removed and less socially motivated. And had a strong level of unusual interests. So interests that are unusual in content. So rote content - schedules, calendars. I had this amazing guy that I worked with who's five years old and he had a very strong interest in portable toilets and could tell you all about the portable toilets in New Haven.

So very quickly, you talked to this little guy for a couple of minutes and trust me the topic will come up. And it strikes you as odd and usual so it's quick to alert you to there is something different about this child from others. The boys also tend to have more disruptive behaviors, which is important too as we progress in thinking about this, as this is often what captures

adults' attention, so teachers and parents, this level of disruptive behavior.

Now girls with autism are now less isolative and tend to be more socially motivated. And their strong interests are present, but the content of their interests tends not to be atypical. So I have many young patients who are interested in princesses or unicorns or My Little Pony. These are interests that lots of preschool and early school-aged girls have. The magnitude of their interest is what sets them apart from typically developing girls. So it's not the content. They're not going to suddenly talk to you about train schedules. They might to talk about unicorns, but they're going to talk to you a lot about unicorns. But it becomes tricky then in determining what is atypical there because

there are lots of young girls that are interested in these same topics. So their interests are consistent with their peers.

Also though, and this is very critical for us to think about, there's greater internalizing symptoms in girls on the spectrum, compared to boys on the spectrum. They have higher rates of anxiety and depression and these are comorbid mental health, mental illnesses that are quite impairing and can dramatically affect an individual's quality of life. So it's very important for us to think about these mental health elements when we're thinking about girls and women on the spectrum.

Now I want to illustrate some of the features of girls with autism, by presenting - I have two cases I'm going to present. This first one, I'm going to tell you about

her and then I'm going to show you a quick video. So this is a little girl and she was - she is four years old and she was diagnosed somewhat recently, at four years of age. And what's striking though is when I met her and did an evaluation of her, her nonverbal skills are about the 2-1/2 year level, so her cognition at the 2-1/2 year level. Her language skills are about the 2-year level. So she's quite delayed. She has very significant delays in her development but her family and her child care providers - lovely, wonderful people - they didn't detect the delays because her behavioral presentation was such that masked her difficulties. So she talked constantly. So she - and you're going to see in a moment, but she is beautiful and endearing and looks like this little princess and she just talks and talks

and talks. But she's not communicating, so she's just talking but she's not directing it to another person, she's not monitoring the other person's reaction. She will talk whether you're, you know, attending to her or not.

You know, I could leave the room, she'd still be talking. So she's not using her language for communicative purposes. But if you observed her like in the classroom, she looks highly verbal, so it didn't raise any flags. She also is quite active and loves to - what the family conceptualizes as dancing. I think about it as repetitive behavior but I, I could see where they're coming from. You know, this little preschool girl just sort of flitting about and it looks like, you know, she's dancing. And it was confounded by, she's hyper-focused on her own

reflection. So you can imagine, this beautiful preschool girl who dances about in front of a mirror, posing for herself, talking. I mean it looks truly - I mean it looks absolutely adorable.

But when you scratch the surface and think about what she's really doing, you can appreciate how it's quite isolative and nonsocial. And to the point I made before about the restricted interests - she was very, very - and still is - very interested in Disney princesses. Lots of four-year-old girls are interested in Disney princesses. She's interested in Disney princesses more than other four-year-old girls. But again, from the perspective of like a preschool teacher or a family, you could see all of these behaviors and not really think anything of it, where how do you draw the line as to

what's, you know, too into Disney princesses when you're four? I think that's a hard line to make.

So because of this, it - she didn't sort of rise to the level of concern until she reached four years of age. And the last part about her - she's very directive. So she liked things her way. But again, you know, amazing little girl is telling everyone what to do, and people just embraced it as part of her - her persona and fitting with her interest in princesses. So I'm going to show you now a video of her. And when you watch this video, she's in one - she's in our clinic room and one of our clinicians is with her. And I want you to notice how she's talking but there is no one - she's not talking to anyone.

And when our clinician talks to her, she actually - if you listen, she actually doesn't respond. So you might lose her because she's still talking and going on, but she's really not responding to posed questions. And the last thing you'll hear, she's repeating things she's heard previously. So she's scripting something from Angry Birds, so you'll hear that as well. So let me play this.

(Video shown)

Dr. Ventola: So I appreciate the volume was low there, but as you can see, she's really, you know, definitely presenting with this positive affect and so lovely, yet she's not engaging with the adult who's in her - in the room. And the adult I mean gets physically close to her, in her space and she's still, just again, presenting with

this, you know, a high level affect, so happy, but not socially engaging with the adult.

And I have one other case to present that will illustrate some of the features of ASD in girls as well. This is an older child. She's 10 and her cognitive ability, non-verbal, is a little below average, verbal ability is average. I think when you think about her and going through this, you generally think of a cognitively-typical ten-year-old. Now this girl is highly socially motivated. She's outgoing, she's talkative, I think when you see her you may think she's a little immature, but she can absolutely carry on a conversation and wants to talk with you. No disruptive behaviors, totally fine there. But she's hyper feminine. So her interests are related to style,

celebrities, boys. So this is really - she talks about these topics, that again, are not atypical for a child her age. It may be a little, you know, mature - some girls at 10 aren't quite there yet and she's there in a very big way. And has trouble shifting, so she starts getting you, you know, talking about the different, you know, styles or the different stores that sell girls' clothes. I mean she can go on and on and on without being able to shift to a new topic. But again, not as unusual as, you know, train schedules, but definitely unusual in terms of magnitude. And this girl also has a characteristic that we see fairly commonly in girls on the spectrum, where she's socially motivated but doesn't have the nuances and the skill to figure out how to get in with the other girls.

So what she does is becomes myopic on one or two particular peers, where she learns about these peers, follows these peers, wants to be close to these peers. And the peers experience this as overbearing and almost intrusive. And she's doing it in a way that's absolutely well-intentioned and as her way of connecting, but it just - as she's hyper focused on style and celebrities, she gets hyper focused on these peers. So this is just a manifestation of her social disability. And I presented these two cases because I wanted you to see a younger child and a school aged child and how in girls, the social deficits and communication vulnerabilities may present differently than perhaps what you'd expect or what we might see in boys.

Now I want to shift gears and talk about why we're missing or delaying our diagnosis of ASD in girls. And like I mentioned in the beginning, it's absolutely multifaceted. I think part of it is related to how we make the diagnosis. There's some argument that there might be a bias in our diagnostic measures and, honestly, in our diagnostic processes. So how we make the diagnosis, we use our, really our gold-standard instruments, ADOS and the ADI. The ADOS relies heavily on the presentation we see from the individual in our office. And the ADI relies on parent report.

We also though definitely lean on teachers quite a bit, to hear about how the child is doing in school setting. And girls, more than boys, report problems with their social relationships. So girls are

experiencing problems with their social relationships. But when we go and corroborate this or gain information from a different perspective we're hearing a different idea from the teachers. When you compare girls with boys, teachers are saying girls with ASD are actually having fewer symptoms, they're actually doing okay. So then you're left with a girl who's reporting problems but the teacher and those who are around the girl saying everything is okay. And in the clinical setting, boys are more active and atypical than girls. So like the ten-year-old girl presented, honestly in a clinical setting, she can hold it together quite well and has high level of conversation skills, can tell about her experiences. You wouldn't be struck by the magnitude of the social disabilities one-on-one with an adult. When

she's with her peers, you absolutely are. But in a clinical setting, girls with ASD aren't necessarily outwardly atypical.

And in order to meet diagnostic criteria in several of our measures that we use, we need to have these atypical interests. It's required to meet the threshold. And it's easier for clinicians to identify these repetitive behaviors, circumscribed interests, when the content is unusual. Even for me it's hard to say you're interested in My Little Pony - are you interested in My Little Pony to a threshold that's higher than other three-year-olds or four-year-olds that are interested in My Little Pony, versus when you're interested in calendars, absolutely. So that judgment involved that we see more in girls it, you know, we have to use our judgment more in girls, you know, sometimes I

think that may bias how girls these girls are presenting on our diagnostic measures.

There's also a recent idea that's come about that girls with ASD may be masking their difficulties and I think this is illustrated in the preschool-aged child that I presented and how she was so endearing and just happy that people didn't pick up on her difficulties. And in a recent study by Dean and colleagues, this is out of UCLA, they studied elementary school-aged children on the playground, so children with autism and typically developing children. And they found that the girls with ASD maintained their physical proximity to the group, just like typically developing girls, so they're right there. They're in the group. They're in the mix.

They may be flitting in and out of the group, they're not maintaining engagement, they're not maintaining a deeper relationship. But they're physically close and this is very important because if you think about us asking teachers, sometimes or asking paraprofessionals, how is this child doing on the playground - they're standing over by the building watching everyone play and they see the girl right in there with the group and they're going to tell me the girl's doing fine. It's not until you really get closer and follow that girl over time and really analyze that behavior that you're seeing that she's struggling to maintain the engagement, that the peers are detecting the differences between this girl and some of the other girls.

And this is in contrast to the boys who were on the playground more isolative, so these boys with ASD had trouble initiating and sustaining interactions. So again, when you asked the teacher, which we do in our diagnostic processes, the teachers report that the boys are excluded and alone, but in contrast they're reporting the girls are right there, they're right in the mix. And this idea of masking continues into adulthood. And adults with ASD may camouflage their symptoms, so use scripts, learn jokes, you know, mimic others' expressions and gestures. And I've talked with several patients of mine who have described how they adapt to social settings, by adapting a different persona. So they'll take a persona from a character in a book and sort of take that in as their own.

And these aren't necessarily maladaptive. Women use these strategies much more readily and often than men, there's a very recent study that came out showing that. And again, these aren't inherently poor strategies. I think we actually teach kids, you know, in terms of social skills, sometimes to look at, look at the social panorama and think about what other people are doing and do the same thing - but this idea of camouflaging takes it to the next level and my patients have described this as bringing increased stress, increased anxiety and I had one young woman tell me that it's exhausting to be someone you're not, which I can only imagine. So I think - thinking about this, it's an important idea and the implications this has on our young women.

And so when we take this all together, you know, why are we delaying our diagnosis, why are we, you know, potentially misdiagnosing ASD in females? It is, it's multifaceted, I think there's differing gender-based expectations - I think that's related, girls and boys on the spectrum present differently. I think you can make an argument that there is some bias in our diagnostic instruments and processes. And girls and women are using these compensatory strategies more often than boys and men are.

In my last couple of minutes, I'm just going to touch on some of the treatment work we've done in my lab particularly related to girls with ASD. As Kevin mentioned, much of my work focuses on behavioral treatment for individuals with ASD and particularly Pivotal Response Treatment, which is a naturalistic

behavioral intervention with a strong evidence base showing it works in supporting social communication development in individuals on the spectrum. It's based on behavioral principles from ABA combined with motivational strategies. And we focus on targeting areas that have a large impact, so reciprocity, social initiations, social responsiveness, where you'll get a big response if you improve these areas of function. And this is work I did with Kevin, where we had a pilot study where we wanted to look at sex-based differences in treatment response.

And we enrolled 28 children, roughly matched boys and girls. They all received PRT for four months. It's an intensive treatment, they received eight hours a week of behavioral intervention. The demographics

they were on average age five. DAS is an IQ measure, so mean of 100, standard deviation of 15, so they're average IQ. And the CELF is a measure of language, so again average language scores.

And what we found was that - using a measure of adaptive functioning, so how the individual is able to function at home and the community - at the start, the girls had significantly greater impairment than the boys. So they had more impairments in adaptive function, the girls did than the boys. But after our trial, they were equivalent. The girls made more progress in adaptive functioning than the boys did. And the children also completed an fMRI before and after treatments and these behavioral findings were mirrored in the brain-based findings.

So in the areas of the brain that are responsible for social processing, so thinking about social information, at the start the girls had less activation in social regions of the brain compared to the boys with autism. But after our trial, the girls had a greater change. So their brain activation changed more than the boys' did.

Then this is in contrast, so we also looked at core social communication skills, and there was actually, there was no sex difference at the start in social communication skills based on a parent report measure of social functioning and both groups, so both the girls and the boys, had a decrease in symptomatology as a function of our trials. So there was no sex difference at the start and no sex difference in relation to achievement response with relation to

social communication skills. Just really in this adaptive functioning that we did see mirrored in the brain findings.

So lastly, I would like to acknowledge our sources of funding. We are extremely grateful for the support and this work wouldn't be possible without these sources of funding. Thank you very much.

(inaudible comments)

Ms. Zoe Gross: Hello. Can everyone hear me? All right. That was a good start. Thank you for having me. I'm Zoe Gross, I'm the director of operations at Autism Self Advocacy Network. ASAN is a policy advocacy organization run by and for autistic people. We are for autistic people all across the spectrum. We have an autistic board of directors, an autistic staff and we focus on

policy and on advancing policies and research that will help autistic people.

I wanted to talk about research briefly at the moment because that's what we're doing right now. When we're talking about research on the topic of autistic women and girls, it's important to remember that we only have research on people who have been diagnosed, and as we've heard, there's an underdiagnosis of autistic girls and women. So more people are out there not being diagnosed than is the case for autistic boys and men. This gap is wider for people of color, there's also under diagnosis there. So these diagnostic disparities, they bleed back into our research. For example, current diagnostic traits, as we talked about, may miss girls so studies on autistic people skew very male or entirely male.

We might learn insights from the studies that may not apply to autistic women and girls but they are generalized to all autistic people and the traits demonstrated by a group are considered to be diagnostic. So we have a cycle where diagnostic disparities feed into research and it becomes self-reinforcing.

I think talking about how to better think about diagnosis when it comes to groups that are currently underdiagnosed is good for that and will help with that. The experience of diagnosis as we've talked about is often a bit different for autistic women and girls. We talked about people being diagnosed a bit later in early childhood. There are also a lot of autistic women who are never diagnosed until they bring their kid in for diagnosis, and then the clinician says, hey you might

want to take a look at this yourself, and they find out some things.

Often, girls or adolescents, even adults with autism who are women, are often diagnosed after several incorrect diagnoses. So an autistic girl might come in and be evaluated and be re-evaluated and told she has emotional difficulties or a learning disability or given a variety of diagnoses and once they've cycled through all of those, maybe someone will take a look at her paperwork and say, oh she's autistic and has been autistic this whole time. But way back here when she was three we wrote down, she can't be autistic, she's a girl, so we stopped looking in to that, that was a mistake.

There are - having a diagnosis or not affects your life, and there could be

involved in not having a diagnosis. There's less risk of losing your legal status of someone applying to put you under guardianship if you don't want it, or if your parent or someone is using it against you in discriminatory ways in a custody dispute, for example. But it can be a problem not to have access to supports and services that you need. Not to have access to get reasonable accommodations if you need them in school or in work. To long-term services and supports that will help you live in the community, and just to access a community. Having access to services and to a supportive community of people who understand you can be a life or death issue for autistic adults. There is a heightened mortality rate for autistic adults and one of the causes of that is suicide and something we hear from our members and people

who are talking to ASAN is that having access to a community of autistic adults who understand them and who they can talk about these issues with has been really helpful for their own mental health and how they feel about themselves.

But it's difficult to find your way to that community if you don't know that you're autistic or think that that could never apply to you. Being diagnosed can get you into that community, you can find supportive people, you can find services, you can have your reasonable accommodations in school or in employment, but there are risks as well especially for adults - we talked about the right to decision-making, custody of children, things like that. It affects many women's decision about whether to pursue a diagnosis. And this is such a damaging thing

if it does happen, and such a common thing that self-advocacy orgs will advise people to weigh this and to consider it when they're thinking about pursuing a formal diagnosis and we do that as well when people approach us about it. It isn't always the right option; it depends on the situation that they're in and whether there is a way that someone might use that in way that would hurt them.

I wanted to talk briefly about some myths about autism and how they affect our lives as autistic women. A lot of people talk about empathy in autism. There's a belief floating out there in popular culture and in the research community that autistic people lack empathy and people debate what that means. Some people will say that when they say empathy, they mean only that we

can't tell what people are feeling if they don't express it to us. But when people out in the world hear "empathy" and hear that autistic people lack it, what they think is, well those autistic people they don't care about anyone, and you do find some researchers who would be willing to say that as well.

In fact, a lot of autistic people say that they feel empathy in a way that can be overwhelming for them and this is very common to autistic women. A lot of people describe it as hyper-empathy, like a feeling that they are overwhelmed by caring about the people around them and wanting them to feel good and anxiety about if they might feel bad, but it may be expressed or felt in a way that others don't recognize.

I want to talk about extreme maleness. This is a fun concept that we hear in the field of autism research. There's an idea that because of brain structures or because of behaviors or those things that being autistic is a way of being extremely male. And people talk about this in a couple of different ways. You know, they say like, you know men, they like things like engineering and Legos and not talking about feelings, and that's how autistic people are. But women, they're very, very socially nuanced, and they're wily and cunning in the ways that they socialize, and that's not how autistic people are. And we've already talked about socialization how that can look different for autistic women because of the pressures that we come under at an early age.

But the perception that autism is a way of being extremely male, both in brain structures and in behaviors that our culture stereotyped as male, can be a real problem for autistic women, in that sometimes it comes down to us being perceived as not really autistic because of this stereotype or as not really women because of this stereotype. We're going to get into later some of the things that happen in health care. When autistic women need specific kinds of health care.

But there can be a perception that being autistic means that you don't need some of the same things that other women might need and need to access and this can be really damaging. I should also note here, while we're talking about this, that autistic people are more likely than average to be

transgender or gender non-conforming and the idea that autism is a way of being extremely male causes a lot of problems for these people as well. Especially if you get like a kid saying I think I'm transgender and I want to transition, and the response being, no you're autistic, you don't understand gender. You just think this because you have an extremely male brain, but it doesn't mean that you understand your own gender and what you want out of life. So these ideas that are out there about autism have a different impact on people based on gender.

There are some unique and some common struggles that autistic women and girls experience. A lot of these things are things a lot of autistic people experience but they can be different for autistic women. In terms of health care, there are common co-occurring

conditions for autism, and some of them are even more common in women. Anxiety and depression already mentioned. Finding disability-competent providers, people who view you as a whole person, want to talk to as a patient, won't run out of the room if you get out your communication device, aren't embarrassed to talk about whether you're sexually active because they view you as an eternal child - finding that kind of a provider can be difficult, and it can be even more difficult when you get out of primary care and look into specialization.

So whether that's for just general health or for treatment of those co-occurring conditions, that can be a real struggle for a lot of autistic people. For autistic women as I talked about earlier, there is perception out there that being autistic

trumps things related to being a woman and something that women commonly need are things like reproductive health care, or breast cancer screenings or things like that and autistic people may not be referred for those things if we need them. It's surprising but we've heard about this from a lot of people. Whether it's because of assumptions that we're not sexually active or just because we're being slotted into a different box in the minds of health care providers. This is something that a lot of autistic women really struggle with.

Autistic women and girls are at a higher risk of being victimized in violent crimes. This is true with all peoples with disabilities, higher risk of being victimized in violent crimes. Disabled children are at higher risk of being abused by family

members. There've been some studies that indicate that people with disabilities of all types are at a higher of risk of intimate partner violence. And people intellectual and developmental disabilities in particular face high risk of sexual assault, and for women with developmental disabilities, some studies have found that it may be as high as 80%. Which, I've talked to some people who dismiss that statistic out of hand but they aren't people who know a lot of women with developmental disabilities.

In terms of employment, this is an issue across the board for autistic people, both unemployment and underemployment is very common for autistic adults. For women, we might struggle with some additional expectations in the workplace that aren't placed on autistic men. Whether that's

something that we can't do for sensory or motor reasons, like wearing heels or makeup, or just demands that women in the workplace be more intuitive or subtle in the way that we communicate even if there are times when a man in the same situation could be blunt and not pick up on things and still be seen as a cultural fit.

And then access to community-based services - again an issue for a lot of autistic people and people with a lot of disabilities. We need access to whatever services we need to stay in the community and I talked before about the right to decision making and how important that is for adults with intellectual and developmental disabilities. A lot of people face issues with people in their lives trying to take control of lives where they live, what kind

of services they get and what kind of health care they receive and things like that.

That's another struggle that for all autistic people, but also for autistic women can be very personal and very challenging if it comes up in our life.

I was asked to come here and talk about challenges and needs and struggles but I also wanted to make sure I take a moment to talk about strength. Because we don't often hear about strengths of autistic people when we talk them in clinical or research contexts. So I'm just going to start with neurodiversity. And neurodiversity is the idea that all kinds of brains are okay brains to have and all have their own strengths. And in general a lot of autistic people find we have strengths that come from our autism, whether that's the ability to find great joy

in a specific topic or in movement, or in noticing details that others might not notice, or developing our own way of communication that works for us.

It's important when you talk about autism not to get lost in thinking of it as a series of deficits, because then we get lost in thinking of what we need to do for autistic people as being a series of deficit-reduction models and that's mostly not what we need in our lives.

Autistic women, as I've talked about, deal with a lot of stuff in our lives and I have found that we are a very resilient community. We've been through a lot of things and this may lead people to look at an autistic woman and say she does not need services because she clearly is doing fine but although we're resilient and we're at

dealing with stuff sometimes, someone dealing with a lot of things doesn't mean that she doesn't need support or services. So that's a strength that can lead to another challenge if it's not well understood.

I also want to talk about advocacy. I know that autistic people who've gotten involved in advocacy because they want to make sure that autistic kids have better experiences in life than they did. And for some autistic women that I know, they're talking about their own kids here. We want a better future for autistic children. We want to have a better future for autistic adults. That's why people who get involved in advocacy are doing that.

And finally, because this is a research-heavy audience, I wanted to make sure to talk about how to address the needs of autistic

girls and women. I recommend starting by asking us about them. I want to talk about community-based participatory research work real quick. Community-based participatory research or CBPR is a research model that brings in community members from a group that is being studied as equal partners at every step in research, starting with identifying the problem or issue to study, moving on the design of research, the IRB process, the study itself and then research dissemination - interpreting the data you get and communicating it to your field and to the broader world.

Often at ASAN or just as autistic people generally, we hear from researchers at the recruitment stage and they will say help us find people to be in our study, but what they're studying isn't actually that relevant

to our lives as autistic people and it isn't aligned with the community's research priorities so we have to say no. But when people approach us and say, I would like to do research that benefits autistic people. What kind of research might that be? Then you can have the conversation and I find that really helpful and useful to bring autistic people more into this research process.

I want to list some resources. ASAN, I've already talked about, you know who we are. You can read about our research agenda and our research priorities on our website. AWN - Autism Women's Network - I should mention here because they are a great resource specifically focusing on issues affecting autistic women. They have a lot of writing collected on their website. They do a lot of great work.

AASPIRE is - I didn't write down the acronym for AASPIRE but it ends in something, oh it's over there, fantastic. AASPIRE - the Academic Autism Spectrum Partnership in Research and Education. Everything they do is around bringing together autistic people and academic researchers to engage in community-based participatory research and begin, execute, and then disseminate research projects which are relevant to the needs of adults on the autism spectrum. So you can check out their projects. They have currently a study going on employment. They did a great study on health care and health care needs of autistic people that led a lot of the conclusions that I talked about earlier today. They're doing fantastic stuff. And in general we're starting to see more research efforts all the time that are based

in major universities but led by autistic researchers. So do your homework, find people in your own communities, start talking to them about how the needs and perspectives of the autistic community can inform your work.

That's all I got.

Dr. Daniels: Well thanks so much to all of our presenters for these outstanding presentations. We have some time for Q and A now so if the speakers would like to come up to the table, and Tamara also, we'll take some questions.

Man 1: Hi, this is Stuart Spielman from Autism Speaks. Very interesting presentations, thanks to all of you. I've got a question about low IQ boys and girls with autism. You've spoken about how boys and girls compare. But I'm wondering if IQ

is a factor in the difference in presentations.

Dr. Ventola: (inaudible comments) There we go. That's a great question, and I think in the short yes. I think when we get towards the very lower end of the IQ spectrum there's a host of other considerations and what might present as autism, you know, I think there's some genetic syndromes that might be involved. The genetics of it becomes more complex.

In terms of the differences we see behaviorally, I think the girls with autism that have the IQs below 70 versus the boys with autism with the IQs below 70 tend to have more, generally speaking more significant social communication and language deficits but fewer of the behavioral characteristics you see in boys.

Woman 1: So related to that I guess it used to be the opinion that girls with autism tended to be more severely impaired related to low IQ for sure. But it seems like the descriptions that were given today, make it sound like your view is that girls are actually less impaired because everything you talked about in terms of the girls with IQs above 70 made it sound like they were much less severely impaired than boys.

Dr. Ventola: I can speak from the behavioral standpoint. I think the message is more that they're differently impaired. So it might - they definitely have impairment, they definitely have challenges. We see the symptoms, they just manifest differently than they do in boys. So right - the one view is that girls with autism tend to be more affected than boys with autism. But as we're

parsing that apart and understanding that more, that seems to hold true for the individuals that have an IQ below 70. But when we think about individuals with IQs above 70, it's not that the girls have better outcomes or that the girls have less severe symptom presentation, it's that their symptoms differ more. And not necessarily in line with how the boys and girls differ whose IQs are below 70 where it is this greater language impairment, greater social impairment. It's that, you know - just to be concrete about it, the patient I described where she hones in on a couple of peers, I don't actually think that's better than being isolative. I mean it's highly impairing it's just different than it being more isolative in terms of social functioning.

Woman 2: I have two questions and the first question - if it's possible to get input from all three of you. So the first question in terms of kind of thinking about biomarkers or biobehavioral markers, there's the approach of, you know, neuroimaging - of course, I'm a neuroscientist - but I'm wondering about increasing the sensitivities, specificities, real world longitudinal abilities to measure behaviors in a fine-grained way.

We recently had a workshop about developing technologies to better analyze for example longitudinal videos or audio recordings and I'm wondering what Kevin and Pamela think about how that would integrate into your kind of research framework whether that would be useful? And then I'm wondering how Zoe thinks from a community-based

participatory research point of view how patients and families with autism might feel or want to be involved in the project that essentially involved instrumenting your home.

(Inaudible comments)

Ms. Gross: So the first thing I think like I would like to raise is that this sounds like a fairly intrusive study that you would want to get consent for from everyone involved including participants who are on the autism spectrum, regardless of their age or whether they are under guardianship just because it's a more than usually intimate look at someone's life.

And there are a lot of reasons that like a 16-year-old or a 21-year-old who has been denied legal capacity might still not want to do that and should have that respected. In terms of how people would feel about it I

think there's a variety of opinions. You know, it's like with all studies you could find people who are willing to do some things that others might not do because they find them weird or unpleasant, because it's for science. For a lot of people I think it would depend what was being measured and what the goal of the study was.

Dr. Ventola: I think from a research standpoint, understanding how we can measure, particularly as a treatment researcher, how we can know our treatments are working and how we can measure behavior change is really just a critical issue in our field. Because right now we don't have great measures to know that our treatment's working.

There's not a strong consensus in the field as to what measures we use as outcome measures in clinical trials. You talk to

different clinical trials researchers and they're using different measures, all justified and reasonable but in some fields there are some standards around you know how we know a treatment's working. And one of the reasons why we haven't got there yet, it's multifaceted, but thinking of social functioning it's such a complex construct that manifests itself so differently at different ages and at different functioning levels, and different IQ where we have - and sex differences too, and how you use one measure to assess such a broad and diverse construct is very challenging.

So what we're trying to do to feedback to that because that's an area of high need in our field, because not everyone can do an fMRI, nor should everyone do an fMRI - costs, burden, etc. But given that we've looked and

looked for outcome measures and ways to measure social functioning and we're a ways off, but can we tie what we have in terms of measures of behavior to biological markers, through fMRI and potentially through eye tracking, through objective measures, can we use that to better inform our behavioral outcomes. And one of the ways we are doing that is exactly the way I think how you described in looking at behavior in a very fine-grained way. The difficulty in that is that it's not scalable. So we can do that with a smaller sample and in a really intensive academic laboratory but to take that in the community or as a way for a larger scale clinical trial is not feasible. But if we can use to inform development of a measurement that is feasible or a way that

correlates heavily with a measure we have available to us, that's strong information.

Dr. Pelphrey: I think the potential use kind of non-intrusive, meaning doesn't require very much of a researcher - smart phones are always listed as an example. I think the other day I found out my iPhone counts my steps, whether I want it to or not, unfortunately. It's kind of embarrassing. But that type of data, that kind of passive data collection can be very valuable. It doesn't get around like John Anderson's classic structure-function problem of the multi-determined nature of the behavior, right? So I can get the same number of steps a lot of different ways and a lot of different brain processes more importantly for the case of a psychiatric considerations, going into that same number of steps.

So for me the question is, I want that type of data and I want rich behavioral data because I believe that the information for development for the information for both positive and maladaptive, unusual development is in the interaction between those levels of analysis and ultimately the best biomarkers are going to come from understanding the interactions between the levels of analysis. And it's almost like a meta data problem. Instead of trying to go to the level of the brain and record every connection and focus in, and if only we had more and more data, we could get it and let's do the same thing in genetics, let's do the same thing in behavior; but rather think of it as a metadata problem of the interactions across those levels of analysis and then that metadata gives us the biomarkers. That seems

to be a more tractable problem. So I want to see development within those domains but ultimately I want to look for patterns of behavior across levels of analysis. Whether it be behavior of the genes, the behavior of the brain, behavior of the individual, the organism and then the interactions across those levels. I think that's what's going to be valuable for informing mechanisms.

Woman 3: What about syndromic disorders - for example Tuberous Sclerosis Complex, Phelan McDearmid Syndrome - where there are bimodal distributions in cognitive function as well as maybe 50% or less than all of the subjects develop autism. Is much known about male/female biases in developing autism and differences between males and females in how autism is manifested? Does anybody know

about that? I've heard that for TSC there's not a male/female bias.

Dr. Ventola: That's exactly what I was just going to say and I can confirm that - that's my understanding as well. I think in the clinical presentation we are really just now focusing girls and boys with autism. I mean, it's been the past - literally within the past year where we said wait, our idea of girls with autism being more severe doesn't apply to all individuals with autism.

And I think the next step is to look at it in a more fine-grained way with more sub-groups involved. I don't - I can say with a fairly high level of confidence that it hasn't been studied widely yet.

Dr. Pelphrey: It's a brilliant question. I'm a little embarrassed because I spent the morning in the Rare Genetic

Disorders Symposium downstairs and it didn't occur to me to ask, and if it didn't occur to me then who's it going to occur to, given that I direct the Sex Differences Network in Autism? It's a great question. Other than - Mustapha's downstairs, that one we kind of know about, Rett Syndrome of course. But otherwise I don't know, and it's a great question.

Woman 3: So I asked Mustapha that question and he said there's not a male/female difference from TSC. But the question is whether there is trends with cognitive function. I don't know the answer to that.

Dr. Pelphrey: Yeah, I don't know.

Woman 4: Getting to Zoe's point of the diagnostic disparity leading into research. Often as researchers we screen people and

say, do you have an autism diagnosis, do you meet criteria on the ADOS or ADI? Given that ADOS or ADI is not great or is flawed in picking up autism in high-functioning girls, I wonder, I've heard of, for example GABS I think it's an abbreviation - some girl-specific metric of scoring the ADOS or what other - maybe or should we, could we be developing so that we are picking up these girls who might be missed with the standard evaluations?

Dr. Ventola: That's an absolutely fantastic question and I think we need to understand even better than we do now how girls and boys actually differ, both of at the level of behavior and at the level of the brain, to know what to go after. I do think, using the information we have now, there are things being studied and being put out there

about how to use the measures available to us with girls.

As a concrete example in thinking about the restricted interests and repetitive behaviors, I mean that is extremely clear that it looks different in girls and boys. And I think as we get further understanding around the topic we're going to be able to refine our measures even further.

Ms. Gross: I did want to mention that although diagnostic instruments, I think, do contain a bias, it is also worth pointing out that people apply this bias on top of the diagnostic instruments. So you were talking about the difference in special interest and how a girl who is interested in princesses might not be spotted by a clinician in the same way that a boy who is interested in sea shells was. But there's nothing in the DSM

that says the interest must be unusual among the person's peer group. It's just says that there's restricted interests, or whatever language specifically they use. People will apply that. The DSM-5 has a lot of items saying "currently or by history." And so if you see a 16-year old girl and you say, how are you doing socially? And she says I have a couple of friends now, but it took me a really long time to learn to make friends. We have some clinicians who would say, well people with autism don't have friends. So nope. But if you look at "currently or by history" you may see that she has had struggles that she currently has learned compensation techniques for or that she is currently having struggles that aren't revealed by that particular question.

Woman 5: So I just wanted to loop back for a moment to the genetics comment. I think Fragile X might be an example of one of these things where boys with the full mutation of Fragile X syndrome are very much impaired but it presents differently and so that case is interesting because - so the males have zero FMRP, the protein product, and then the female generally have a 50 percent of normal.

So the boys are very much affected but then it seems to be a possible dose response curve at the genetics level and that might result in some kind of categorically differences at the systems and behavioral levels. It's just an interesting kind of disconnect, it is something that is across the spectrum sort of at the genetic level

might result in different kinds of categories.

Ms. Lewis-Johnson: So I had a question. Oh, are there more questions?

Woman 6: First I want to thank you. I wish had taken place 5 years ago and I want to ask when the children, females, express highly skill, high skill but totally, totally dry socially. And you go to school and they say, there's nothing wrong with you and you know as a parent, it's a struggle. Like social skills group - I spent five years trying to find a social skills group for girls, and there's none, and I'm very disappointed because my daughter was diagnosed under Lauren Kenworthy and we have not gotten anywhere.

It's just so hard, and I wish there was someone on the panel who's a parent to tell

everybody what we go through and how hard it is. It just hurts. It's not until your kid tells you that they're going to hurt themselves and run into a car and you go, like, what do I do? My school says there's nothing wrong with her. I had to get her out of school and homeschool her. I call her the child left behind by everyone.

Not until we had to hire an attorney to have some help from the school system and said, oh I'm sorry she fell through the cracks. Yes she did. Since she was three or four, we struggled everywhere. (Inaudible comments) Everything, even insurance. We researched to do our own therapy and it's just so hard. I wish the parents in the organizations that are out there doing all the research, I wish they would reach out to parents and say "How can we help you?"

Because there's none, especially when you're Hispanic. There's nothing and then all we're left with is, just do the best you can and that's what we're doing. And thank you for doing this. I wish it had taken place five years-ago.

Woman 7: Hi, so I would just ask, in terms of research, given the last comment was made, as you're doing this wonderful research how are you translating that into practice and being able to share that information with schools and others so that they can then have a greater awareness of the latest research that's out here?

Dr. Pelphrey: I think all three of us in our own ways translate our work, whether it be through advocacy, policy and advocacy. I'm a parent of a daughter with autism and a son with autism so the reason why we pulled

together this network was because even given that I was in the field and had the resources I had, it took 4 1/2 years for my daughter to get a diagnosis and that's how I met Pam who diagnosed my daughter.

And so you know it's a different types of translation. Then the reason why Pam began the work she's doing is, so much of what we were doing was diagnosing and giving very, very long detailed reports to school systems that would then usually say thanks but no thanks. In Connecticut where we were, from town to town, schools were either pretty good at working with kids with autism - meaning they would all of the sudden have an outbreak of autism because parents would move there - or they were terrible at it. And then if they were terrible at it, they would

spend the money that they had for services on retaining a law firm to fight every case.

And so Pam has been to more than her share of IEPs to try to unpack these recommendations, but what we were doing and I think Pam's work was the first work done at the Child Study Center that was explicitly focused on intervention or even implicitly focused on intervention.

And it took 200 years to get there and so I think that that's now where all of our work is going because we can begin to do interventions and then see how we're affecting both the deficits and the strengths of the individuals with autism that we're measuring so that we can kind of get the right - we can leverage the strengths that can be revealed through brain imaging for example, that might - that they can't really

tell us about and then also address differences in brain function that are maladaptive.

And so we're translating directly there. We're doing, you know, drug trials. We're doing intervention trials, behaviorally and now we're combining the two. So still doing a lot of public speaking. I write - I try to write more publicly accessible things for Spectrum News and Atlantic Monthly and stuff like that. I still think I've mostly put people to sleep doing that, but we try.

Dr. Ventola: Absolutely, and Kevin's right. Kevin and I teamed up to do treatment work because we've heard the concerns from families that there's nowhere for us to go. So that's why we went there. And to your point - it's a great one you just raised - how do we take our small samples in our

clinical trials and you know, we're seeing great effects, but how do we take that to the world? And that's what we're hearing from our families now.

Five years ago when we first started our treatment work, it was, fine you give me a diagnosis of autism, but how can you help me? And now it's how can you help people that can't access your clinical trial or don't live in New Haven? So one of the things we're starting to do is lean more on telemedicine and video conferencing and software and app design to try to get our work to broader communities where you can't - you know I'm at Yale, but you can't drive to Yale every day for treatment.

And we are - that work is truly - I think our technology around it and the work - in autism, we really are leading some of it,

around telemedicine. The technology around is sort of in its infancy and it's a little bit clunky. But we're pushing through and doing some trials, some remote access trials where families around the world or in places in our country they just don't have any access because there's no providers.

Dr. Pelphrey: I think this notion of utilizing technology and apps to broaden access to interventions is going to be - it is currently very, very exciting. One area that we all kind of talked about was the need for interventions in older adolescents and adults who need things like cognitive behavioral therapy to address particular concerns that are, but the cognitive behavioral therapists need to be aware of the autism and some of the techniques need to be modified to better fit individuals with

autism. And now we're arguing women with autism and we have this kind of vision of utilizing technology so we can get a network of CBT - cognitive behavioral therapy - providers almost like an Uber for cognitive behavioral therapy. Whereas one CBT person can't necessarily handle the whole crowd, many that are signed on at any one moment can. So we can take advantage of these techniques to much more effectively in a large-scale way address the needs that are out there.

Woman 8: Hi, I'm a recent graduate and I'm currently working at NINDS, I'm a postbac there. And I'm really grateful that I was able to come to this meeting because I'm very interested in behavior and my background is electrical engineering. But I'm just wondering how can myself, a current graduate,

how can I learn more about career options about learning more about research done at NIH? Is there anyone I can talk to or any websites to learn more?

Dr. Daniels: You can contact either myself or Tamara about that afterward. We can help direct you.

Ms. Lewis-Johnson: I also wanted to say, to those who are parents, that the advocacy community is one way, and if that doesn't meet your need, creating your own advocacy group, your own support group. One way to be able to feed into research is that - I know that we have Rebecca del Carmen Wiggins here from the Office of Research on Women's Health, and they have just released a request for information about forthcoming women's health strategic plan so that's open to the public to be able to raise your voice there.

So if you want to know how to access it, get in contact with me. But I just thank everyone for coming and for all the presenters, I we could give them a round of applause.

Dr. Daniels: Thank you very much for joining us this afternoon. The webcast will be available through the IACC website. So if you visit iacc.hhs.gov, it should be up in a couple of a days along with the slides. And we greatly appreciate this really important discussion and hope to continue many more discussions on autism in girls and women in the future. Thank you.

Whereupon, at 2:31 p.m., the seminar adjourned.