Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/neurofrontiers/figuring-out-frontotemporal-dementia-a-look-at-social-emotional-impacts/12277/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Figuring Out Frontotemporal Dementia: A Look at Social & Emotional Impacts

Dr. Weisman:
Frontotemporal dementia primarily affects the brain's frontal and temporal lobes. But that's far from the only effect that this disorder can have on patients. Patients with FTD develop striking shortfalls in their fundamental social and emotional behavior, causing them present a lack of empathy for even closest family members. But new research could point us in the right direction for treating this disorder.

Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. David Weisman. And joining me to discuss her latest research on FTD is Dr. Elizabeth Finger, a clinical neurologist and an Associate Professor of Neurology at Western University in Canada. Dr. Finger, welcome to the program.

Dr. Finger:
Thanks so much for having me.

Dr. Weisman:
Just to start off, Dr. Finger, can you explain what's going on with frontotemporal dementia in just broad strokes?

Dr. Finger:
Yep, so we consider frontotemporal dementia a midlife neurodegenerative dementia. And it starts younger than we'll usually think of in somebody developing dementia, typically in one's 50s, or early 60s. But patients can present as early as in their 40s. And rarely in their 30s. The frontotemporal dementias are a group of disorders that share degeneration of the frontal and temporal lobes. And this seems to happen because different molecules start to aggregate in the neurons in those regions. And those aggregations most likely are toxic to the neurons, so eventually they cause them to stop working and die off. And when enough have died off, of course, then we can see symptoms that relate to those regions of the frontal and temporal lobes and their normal functions.

Dr. Weisman:
It's a slow and steady frontal problem. And just remind us what the frontotemporal regions do for us?

Dr. Finger:
Typically our right frontal lobes are important for guiding our attention, keeping us focused, for regulating our impulses, for helping with our decision making, and our emotion regulation. And in the left frontal lobe, of course, for expressive speech. When it starts in the temporal lobes or affects the temporal lobe strongly on the right temporal lobe, we see trouble with processing of facial expressions and emotions. And if it's in the left temporal lobe, we typically see the loss of word meaning. So comprehension difficulties.

Dr. Weisman:
Yeah, then I guess a lot of that has to do with picking up on attention of other people.

Dr. Finger:
That's right, exactly. Part of the networks of the frontal lobes, in particular, are what we call salience networks now, and those are regions that direct our attention to things in our environment that are most relevant to the situation and to our behavior. And so with the degradation of those networks, we see an internal focusing on really only one's self interest and motivation and a loss of attention to other social cues and other people's perspectives that most humans have automatically or do automatically.

Dr. Weisman:
Now, that's interesting. Is it like a neglect for other people? Is that what this is?

Dr. Finger:
Well, that's, I think, an interesting way to conceptualize it. In some ways, yes. Part of it is the attention was not directed to the cues. But that doesn't seem to be the whole picture. So as an example, we know that patients with frontotemporal dementia have trouble processing others' facial expressions. And if we ask them to indicate what emotion someone is displaying on their face, they're often wrong. We and others looked at well, is that because they're not paying enough attention to the critical parts of the face. And so for many expressions, the eyes are critical to seeing that someone is afraid or angry or upset. When we designed the tasks so that we knew patients with frontotemporal dementia were paying attention to the eyes, interestingly, it did not improve their ability to recognize or label those facial expressions. So probably, it has a few different causes there, and both trouble with attention, but trouble with some of the fundamental aspects of processing social cues and emotions as well.

Dr. Weisman:
And regardless of the cause, it renders these people with no empathy.

Dr. Finger:
That's right. For the most part, you know, as the disease progresses, empathy continues to erode. You know, some extreme examples of that, patients not only no longer kind of ask their spouse how they're doing or offer to give them, you know, coffee as they're pouring in for themselves, but even lose empathy for their grandchildren, which is quite striking, because usually that's such a social joy at that stage of life, lose empathy for their pets, their children, and others as well.

Dr. Weisman:
How did you get involved with this? How did you get interested in this area of the brain and this disease?

Dr. Finger:
So after neurology residency, I was quite interested in learning more how the frontal lobes do regulate our decision making and our emotions and was particularly interested in why some people have rather violent or aggressive or anti-social behaviors. So I had gone to the National Institutes of Health to study with James Blair, who is a cognitive neuroscientist, looking at psychopathy and emotion processing and decision making in psychopaths who have very low trait empathy lifelong. After that, I did go back a bit closer to my neurology roots. And while I still maintained an interest in empathy and decision making, I have, you know, applied that to frontotemporal dementia, which is quite different in the sense that although you can see some overlap in terms of decreased empathy and decreased processing, it's in individuals who did develop normally, and who were very caring, empathic, productive, you know, parents, grandparents, siblings. And then when they hit this third or fourth or fifth decade, for the first time, we really see an emergence of these problematic traits and changes in personality because of the neurodegeneration.

Dr. Weisman:
So what's the approach to try to make this better?

Dr. Finger:
Yeah, so I became very interested in this hormone, oxytocin, that as you know in medicine, we know or have known for a while is involved in making the uterus contract during pregnancy and delivery. But beginning in the 1990s or so, it was discovered and then increasingly appreciated that oxytocin can function as a neurotransmitter in the brain, that it is normally produced in the brains of men and women. It's highly conserved across species and across species, including humans. When you increase oxytocin, it seems to promote a group of behaviors that might be considered pro social or nurturing, such as, you know, more peer bonding or affiliative behaviors, grooming, nest building in non-human animals. And in humans, studies tend to aggregate around showing that it does perhaps induce a positivity bias, reduces our processing of threat cues, and may promote more empathic or positive affiliative behaviors towards others.

Dr. Weisman:
How did you go about studying it? What was that process like? You must have had a collection of FTD patients?

Dr. Finger:
Yep. So I have a behavioral neurology clinic here in London, where we do specialize in frontotemporal dementias and related conditions. And in one of our first studies looking at oxytocin, we had patients who had FTD one day receive oxytocin via nasal spray, another day received placebo. It was double blinded and randomized, so we didn't know which day they got which treatment, nor did they. And we found that it reduced their recognition of anger and fear expressions a little bit, which at the time was an unexpected finding, but later has been seen in several studies involving healthy adults. And that might be a part of this role in a positivity bias or reduce threat processing. But more interesting to us at that time was that caregivers, who were also blinded to the treatment, rated patients' behaviors as better the day they got oxytocin compared to the placebo.

So from there, we did a dose-finding study to make sure we knew sort of what we thought the most effective or the highest dose that would be tolerated was. And then our most recent study looked at the effects of oxytocin on brain activation during fMRI imaging in patients with FTD.

Dr. Weisman:
A biomarker study.

Dr. Finger:
That's right. So in a similar crossover design, where all of the patients on one occasion got oxytocin and another got placebo, we looked at their brain activity patterns using fMRI, while they were viewing videos of actors making different facial expressions, and we both measured the change in brain activation during viewing of those facial expressions, as well as outside of the scanner, whether it changed their ability to recognize the faces at all or to process other kinds of social pictures.

Dr. Weisman:
And so what were the behavioral effects of the treatment group?

Dr. Finger:
The behavioral effects were not very impressive. We did not see any statistically significant differences for the patients in their labeling of the facial expressions or the social pictures on the day they got oxytocin or placebo. So that, you know, is, as of yet, not something that's been established at all.

However, when we looked at the brain activation patterns from the functional imaging, there they were pretty striking and quite robust findings that their activity in limbic regions of the brain, so that frontal insular junction where FTD often starts, the amygdala, lateral regions of frontal lobe, were showing increased activity on the week the patients got oxytocin compared to the same week when patients received placebo. And there haven't been many fMRI studies in FTD nor drug studies with fMRI and FTD, and so we were quite intrigued to see that increase in activity and the fact that it could be modulated at all, in the context of this neurodegenerative disease.

Dr. Weisman:
What are the limits with oxytocin? It's a nasal, it must be of a short half-life?

Dr. Finger:
In the blood, it does have a short half-life, really on the order of 10,15 minutes or so. But in the central nervous system, as far as we can understand from said studies, measuring cerebral spinal fluid levels of oxytocin after it's been given intranasally, it probably is there in elevated levels for about five to eight hours after the intranasal dose.

Dr. Weisman:
Wow. And then are there oxytocin analogs that pharma could be interested in developing?

Dr. Finger:
Yes, certainly. I've seen some from the literature, carbetocin I think is an analog that's been developed mainly in the obstetrics field. But certainly, if we see some promise of oxytocin or possibly even, you know, independently, it may be worth taking a look at for these symptoms as well.

Dr. Weisman:
So Dr. Finger, we talked about the study design, let's talk about the results. And I guess that is the question. Well, we sort of have to go back to that. But where is this field going?

Dr. Finger:
Yeah. So I think with our Phase 2 clinical trial, we will have the evidence we need to decide whether this should be pursued as a treatment for empathy and social apathy in frontotemporal dementia. We are also measuring spinal fluid levels in that trial. So we will have a sense if the study is negative and doesn't show a benefit, is it because insufficient levels of oxytocin are getting into the central nervous system? Or is it truly negative that the levels were elevated but there was no effect? I think in the field of FTD, we're seeing more and more creative approaches to both measuring and trying to approach these kinds of social cognitive deficits. Some pharmacologically, but others with different kinds of brain stimulation, and other behavioral techniques as well. We know when we're viewing someone else's facial expression, we automatically and subconsciously do micro facial expressions that mimic it. And that's probably a way that our brains help to represent what that other person is feeling. So we are also looking at instructed mimicry in patients as to whether that may similarly kind of boost that activity in the limbic brain regions that would normally happen when they're looking at someone else's face. So I think, you know, no smoking-gun leads yet, but I think a lot of creative approaches out there.

Dr. Weisman:

Well, this has been a fascinating look at frontotemporal dementia and what oxytocin might hold for the future as a treatment option. And I want to thank my guest, Dr. Elizabeth Finger, for joining me to share her research on the topic. Dr. Finger, it was great having you on the program.

Dr. Finger:
Thank you so much for having me today.

Dr. Weisman:
I'm Dr. David Weisman. To access this and other episodes in our series, visit ReachMD.com/NeuroFrontiers, where you can Be Part of the Knowledge. Thanks for listening.