This is the podcast for the journal Neuropsychopharmacology, I’m Cynthia Graber.

Antisocial personality disorder, or ASPD, is a difficult disorder to study. There have been studies on psychopathic individuals, and on youth with psychopathic traits, but most studies on ASPD to date have been on incarcerated adults. A team of researchers at Heidelberg University wanted to study individuals who are not incarcerated and see what these findings could elucidate about the brains, in particular the amygdalas, of individuals with ASPD.

HJM: The amygdala has been the focus of many psychiatric disorders and has been named also threat detector. And patient with antisocial personal disorder, they are very aggressive patients, so you would expect that the amygdala is involved in those patients.

And there are some studies which say that it's actually under-activated, so like in psychopathic individuals. But also studies from other personality disorders, such as borderline personality disorder, they indicate that the amygdala might be hyperactivated. So we were curious, is it hypoactivated or hyperactivated. And oxytocin because it is known to modulate the amygdala, and because there's also sex difference between oxytocin levels and also reactions to oxytocin. And because we were also interested in sex differences in this population, oxytocin is of course a very promising agent.

Haang Jeung-Maarse is a medical doctor at Bielfeld University in Germany and is one of the authors of the paper in the journal Neuropsychopharmacology, on the effects of oxytocin on amygdala reactivity to angry faces in males and females with antisocial personality disorder. Dr. Yeung-Maarse, before we get into the study, was it difficult to recruit participants?

HJM: Yeah, these are antisocial people and usually it's really difficult to get hold of them and that they had to come at three points, they had to conduct a diagnostic interview, come in a second day to get the first scan, four weeks later a second scan. And the definition of this disorder is that the patients are unreliable.

I understand one place you recruited participants was EBay marketplace. If this population is unreliable, how did you convince them to show up?

HJM: I had a team and the members are really incredible. They phoned them all the time. They tried to get them into a good mood. My team was really very fantastic and creative in finding those individuals. They asked at football clubs or soccer clubs you would say, in in the US for fans who, who were known to be violent. So I think it was a good team behind it. And it also actually helped that they got money for the study, so it was of course very time consuming for them.

So you ended up with 20 men and 18 women with ASPD, and 20 men and 20 women as controls. Before we get to the results of the study, couldn’t oxytocin have an effect that might not be straightforward, isn’t the impact of oxytocin kind of complicated?

HJM: Yeah. That's the thing about oxytocin. So there are some studies which indicate that it might be beneficial to patients who are aggressive. And some studies say that it's actually not really helpful for patients, so they react more aggressively when they get oxytocin. And so this is also something we wanted to find out, because we would expect the amygdala is somehow altered, so hypoactivated or hyperactivated, and that oxytocin could modulate it also either way. Yeah, that was like a perfect target.

In the study, each person participated twice, once with oxytocin and once without. They were shown angry, fearful, or happy faces, and they had to classify them. What differences did you see between healthy subjects and those with ASPD?

HJM: The main difference was not in a classification. So they were, both groups were good at classifying fearful, angry, and happy faces. But the ASPD individuals, they were faster in recognizing angry faces.

And what did you see in their amygdalas?

HJM: In the amygdala, we saw hyperactivity in the ASPD patients, particularly in response to angry faces.

And so what happened when the subjects received oxytocin?

HJM: So that was very interesting because after they received oxytocin, actually the reaction in the amygdala towards angry faces was lowered in the ASPD group and was higher in the healthy group. So it was a reverse pattern, you could say.

What did that tell you?

HJM: It shows that it's really dependent on the context how oxytocin works. So you cannot generally say if you present an angry face and you administrate oxytocin, then generally the response to angry faces is lowering the amygdala activity. But it's also dependent on the context. So this might be true for ASPD individuals, but it might be not true for healthy individuals.

If the issue with ASPD is the aggression with which they react to faces, was there any way to correlate the activity in the amygdala, and the dampened activity, to a clinical outcome?

HJM: Yeah, we correlated the reaction of the reaction times to angry faces and amygdala activity. And we saw only differences in the female ASPD group, but not in the males ASPD group. And clinically it is described that patients with ASPD differ in their phenotype depending on the sex.

And so based on the reaction times and your description, it seems like the oxytocin dampened activity also in the male patients’ amygdalas, but they didn't show a similar clinical difference.

HJM: Yeah, because aggression actually is of course more complex. And there's a complimentary model of aggression that there's reactive aggression, and there's also instrumental aggression. And I think maybe we should detangle these types of aggressions better and see also whether there's a difference between male and female antisocial patients.

What might be the mechanisms behind the sex differences you saw?

HJM: There are some studies which show that oxytocin reactivity is also related to the sex hormones. So obviously there's a difference between men and female. And also brain development. We don't know how the receptors, for instance, are distributed, it might also contribute to the sex differences.

Did anything in these results surprise you?

HJM: Yeah, I was really surprised about it, because there are so many findings in psychopathic individuals, and these findings were pointing to hyporeactivity of the amygdala to angry faces. So I was expecting rather hyperreactivity of the amygdala. So that was surprising. And that shows again, maybe, that there's a difference between imprisoned patients and non-imprisoned patients.

Obviously this was a fairly small study, even if it is to date the largest study on ASPD individuals in a scanner, so that’s a limitation of the study. But even so, what are the implications for clinical care?

HJM: This is a very difficult question to answer, because I cannot really imagine that patients go into treatment regularly and that they take oxytocin, wait 45 minutes patiently, and then go and see the psychotherapist.

But it shows that oxytocin and therefore also the oxytocin receptor plays a role, and you can probably also address this hormone not only by administration, but by other strategies in psychotherapy. And there's also a trend that females react different from males and maybe benefit even better than males. So yeah, that, that is very promising, I think.

Why focus on oxytocin before therapy?

HJM: Yeah. I mean, in psychotherapy you learn how to adapt to situations which are difficult for you, for example, anti-aggression training, you would try to do it first in a kind of environment which is safe for you, so these are the psychotherapy sessions. That's why I thought you would first take it into therapy to see whether it has got a beneficial effect on the psychotherapy in terms of reacting to the therapist.

That makes sense. So what research does this point to for you? What needs to happen next?

HJM: There's a move now in personal disorders from personality disorder as a category to personality disorders at the end of a dimension. So I think now we need to look also at the gray colors, not only at black and white, and to see whether individuals who have got antisocial traits also could benefit from oxytocin or from therapies aiming at empathy.

This is the podcast for the journal Neuropsychopharmacology. To read the paper discussed in this podcast, go to www.nature.com/npp. I’m Cynthia Graber.