[Transcript] Daniel van den Hove - “We should not want to live forever”

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Katherine 0:02
Dr. Daniel van den Hove is an associate professor in behavioral epigenetics at the Department of Psychiatry and Neuropsychology at Maastrichy University, the chair of the translational neuro-psychiatry initiative, and coordinator of a collaborative European project EP-AD, which stands for epigenetics, Alzheimer's disease. And on another note, he believes that science is fun. Now, I Katherine Bassil your host, [00:00:30] am very pleased and honored to be interviewing him today about the neuroethics, specifically of biomarkers and aging and depression, and to touch upon the implications of psychiatric genomics and personalized medicine.

Katherine 0:42
Daniel, thank you for accepting this invitation. As you know through this podcast, I am trying to raise awareness on the importance of neuroethics and neuroscience research and practices. And with your help today, I am sure we can make this happen. Now, Dr. Daniel, can you begin by describing your [00:01:00] academic trajectory followed by your research area briefly.

Daniel 1:04
Yeah. But first of all, thank you for the invitation. Happy to join this initiative. Yeah, so I actually studied biomedical sciences by going on what's called medical biology at the University of Amsterdam. After which I ended up here in Maastricht doing a PhD. And part of the PhD I spent abroad was actually on development of stress exposure and how that affects the risk of developing psychopathology [00:01:30] later in life. After my PhD, I did a postdoc moving more in the direction of epigenetics at the University of Roseburg in Germany. I'm still partially employed over there, and I'm now at least mainly employed here at Maastricht University, as head of the neuro epigenetics group, and my research has expanded a bit more, from solemnly developmental stress exposure on epigenetics and [00:02:00] moved also in the direction of, of aging. So the other extreme end of life. And we actually in part of this work link the two so that when we look at how stress exposure throughout life may affect aging, and particularly the risk of developing Alzheimer's disease, and to what extent neuro- epigenetic mechanisms may play a role there. So that's it in a nutshell.

Katherine 2:19
And when you say epigenetics, what do you mean by that? Exactly?

Daniel 2:23
Well, you can define epigenetics in many ways, but in this case, we particularly we are particularly interested in to which extent [00:02:30] environmental variation so that could mean anything could be nutrition, could be stress exposure, exposure to neuro-toxic compounds, how that affects your DNA, in this case, not changing the DNA code, but the epigenetic code, so to say, which means, for example, methyl groups can be added or removed from the DNA and that eventually defines the degree of expression of a gene. So in this case, it's not [00:03:00] genetic variation that is doing so, which is of course, also important, but we particularly look at how environmental exposure, directly or indirectly impacts on brain function and associated behaviors by by means of epigenetic regulation.

Katherine 3:13
Okay. And if I may ask what was your drive in studying two of the most prevailing disorders of our of our time- one being Alzheimers disease, which is characterized by progressive cognitive abnormalities, and the other being stress and depression and mood disorder targeting really [00:03:30] millions worldwide?

Daniel 3:32
Yeah, my initial interest was particularly in the latter. So so in mood disorder and affective disorders...maybe not really from from personal experience or so, but but generally, like many neuroscientists, I'm fascinated about the brain and how this works, and how our thoughts are regulated, and of course, there's a huge gap between biology and psychology there. But that's a gap that I like to bridge. [00:04:00] And stress is, I think, an extremely interesting phenomenon in that respect and as such, of course also related disorders.

And actually accidentally or via my work here at Maastricht University, I moved into the direction of Alzheimer's disease as well. So let's say there was not not not an initial interest there or no personal link with with a family member or so initially, but then I moved into the direction sort of [00:04:30] automatically and in the meantime, I'm completely fascinated by that as well. Of course, in the meantime, also family members and so on, have aged a bit as well. And I can also look at my parents. And whereas initially as a young person, you think, okay, you're getting all this brilliant and fun, just like sides. You now see that there's lots of challenges still ahead of us. And aging and particularly dementia are incredible challenges there. [00:05:00] And with the aging The population in general and those particularly in this region of the Netherlands, yeah, it's it's everywhere. And by one means or another I can contribute to to a solution there. That that is a daily driver.

Katherine 5:13
Okay. And do you think there's a connection between the two disorders? Or do you really find them interesting independently,

Daniel 5:21
That's actually also the reason why I ended up studying Alzheimer's disease because they are linked disorders like depression and Alzheimer's disease. [00:05:30] Some people claim depression is an independent risk factor for Alzheimer's, I think it's more of a prodromal phase of the disease. Although it can also be a consequence of the disease as well at all times. And actually one of our projects that this EP-AD project is focusing on this link. So we particularly look at brain regions that are important for stress regulation. Coincidentally, they also seem to be affected earliest in the Alzheimer disease process. And well that's actually another[00:06:00] coincidence of my opinion, so that there's a clear link between stress related disorders like depression and Alzheimer's. And yes, for us to unravel how that link looks like and what are based on the knowledge you gain from from studying that link, whether you can develop new treatment strategies or anything in that direction.

Katherine 10:18
Okay, so now let's let's go back a bit to aging. So aging and in particular, Alzheimers disease is a disorder that you have studied extensively throughout your career. And this particular disease targets millions worldwide [00:10:30] and is expected to increase in the coming decades, especially the elderly and is really characterized by several debilitating

symptoms- including memory loss, changes in personality and many more. Now, research trying to understand and hopefully treat Alzheimer's disease is really much needed.

What is your opinion on last year's news when Pfizer, a world leading pharmaceutical company decided to abandon research on [00:11:00] neurodegenerative diseases, including Alzheimer's disease.

Daniel 11:05
Yeah, that's difficult one. I love the industry, of course. But this would not be a field where I would flourish. I think I understand these decisions. Don't get me wrong there. I understand the decision of companies, they eventually have to think about what makes them survive and what brings in profit and whatnot. [00:11:30] So these decisions, yeah, I can completely understand them. But at the other hand, is of course, a big pity in terms of scientific developments, but that doesn't mean [I'm] demotivated- the motivate on you or anything and I think it's primarily on us as academics to to move the field forward in this respect and if you find something promising then the industry will move in your direction again. [00:12:00] I'm not too worried there. It's not a nice development. But on the other hand, first of all, I understand that and secondly, this should just be a bigger motivator for for people in academia to to move forward.

Katherine 12:14
Now I can I cannot think of many unethical reasons that drove probably this decision and you kind of pointed it out nicely, which is like perhaps monetary gain or, yeah, a lack of monetary income. Now, even though Pfizer's reason was and I quote, [00:12:30] "to focus on those areas where our pipeline and our scientific expertise is strongest" end quote, do you agree?

Daniel 12:38
So the question then is?

Katherine 12:40
Like, do you agree with their change and allocation of resources?

Daniel 12:45
I completely understand it as said before but yeah, so it's not a matter of agreeing or not agreeing.As that, if we as people in academia... let's say compensate for the lack of development [00:13:00] in relation to this specific disease and disease area, then then they will be the first ones to say our pipeline is perfectly adapted to to look into Alzheimer's again. It's a setback but but not a setback that de- motivates me at least, it only motivates me more.

Katherine 13:21
Okay, so now moving a bit deeper looking into biomarkers of aging. So we discussed a bit research trying to better understand and [00:13:30] find treatments for aging disorders, but we haven't really discussed research trying to predict Alzheimers disease. Now, can you mention a few examples of similar research where scientists are really trying to predict or foresee who will and who will not develop Alzheimer's disease?

Daniel 13:47

Yeah, we ourselves are also looking into this. So we have also unpublished observations, but we for example, found epigenetic changes when comparing brain tissue of Alzheimer patients and controls. [00:14:00] Actually then we discovered similar patterns in the blood of people, elderly people that were still healthy when we started to follow them up. These people have been followed up for about 10 years now and some of them developed Alzheimer's, some of them did not. And we can see actually profiles and a lot epigenetic profiles, predicting who converts to the Alzheimers stage and who[00:14:30] doesn't. The bottom question of the of course, there's, what will that bring you if you can predict this because we don't even have a cure for Alzheimer's yet.

But actually, in that respect, I'm not interested to biomarker research per se. I use the same study designs to also get more insight into your pathophysiology. Because if you identify a potential biomarker that predicts who develops disease and not, it's not just giving you this prediction, but at the same time, it's pointing you at the disease mechanism, potential disease mechanism. So I particularly, let's say, [00:15:00] I particularly do that type of research to find out more about the pathophysiology and to eventually use that same biomarker as a potential therapeutic target. So, for me that that is more important in terms of the biomarker research that I've been involved in than the my biomarker principal per se.

Katherine 15:18
Okay. Now, do you think as a scientific community or as people working in this field, do you think they are ready? Or are we ready to predict Alzheimer's disease based [00:15:30] on the evidence of biomarkers? And by biomarkers, I mean, it's a molecule or a gene that can be free floating in the blood or even a certain signature in the brain, such as activity and connectivity that really correlates with the disorder.

Daniel 15:44
Well, technically, I think we will soon be ready. If you look at the possibilities to use multiomics modalities, and to even link that with, for example, as you pointed at imaging data, I think we will soon be [00:16:00] ready to give a reading...now let's see- Reasonable, accurate prediction. But again, then we're predicting something that we cannot cure. So, so predicting per se might not really be of help I think because we simply don't have the drugs yet to help patients no matter to which extent we can predict their future path

Katherine 16:25
Okay. Now, many worry that predicting Alzheimer's disease carries potential [00:16:30] ethical, legal and social consequences. For instance, living with AD is not only difficult emotionally, but it's also extremely expensive and to be accurate, $221 billion dollars expensive- and who's really concerned, so other than your family and close relatives, your insurance is concerned. If testing for AD risk becomes routine practice, two scenarios might occur. So none of them is good or at least desirable [00:17:00] for the moment, but for example, one scenario would be insurance companies might really increase their rates based on your results of having a risk gene for the developing Alzheimer's disease. That's a very bad situation. And two, insurance companies might not accept you as a client in the first place. And that's an even worse situation. So should we as scientists really care about that?

Daniel 17:24
Good question. As a scientist, you should for sure care. But I think it's [00:17:30] merely a thought for society to accept insurance companies to have a policy like this. I mean, for

example, you can also do some prenatal testing already. Currently, and also there I don't think consequences of the test implying risk of for example, having a child with Downs Syndrome are also effects insurance related policies. So when the whole system about health insurance changed in the Netherlands several years ago,[00:18:00] I think insurance companies were forced to accept everybody in- so I'm not sure how this situation is now, I'm not an expert on this matter. But I would assume that with the aging of the population and the costs associated, that we cannot simply then say, "Okay, wait a second, you're at an increased risk of developing AD we will not accepting you in, in our program or not". In terms of giving [00:18:30] you an insurance, so, yeah, I still hope that society will will be social there. But you never know. I mean, there's presidents all over the world that might think otherwise, but I hope the Netherlands would still be okay. In this respect.

Katherine 18:46
Okay. So now, staying within the, the topic of biomarkers, but now we're going to move on a bit into the biomarkers of depression and discuss a bit yeah, psychiatric genomics. So now that we are touched upon [00:19:00]the research underlying Alzheimer's disease, including biomarkers for the prediction of Alzheimer's disease risk-this is not really a unique practice for Alzheimer's disease per se, but as it's also being investigated for psychiatric disorders like depression, which is also an area of your expertise.

So let's imagine this scenario. You are a researcher who recruited participants for your research, you have screened their genome and discovered that one of the participants carries the risk gene to depression. [00:19:00] That is not an easy question, but I would ask it to you anyway. As a scientist, do you inform your participant about your findings and why?

Daniel 19:37
That's a good question. First of all, independent of the question itself, I think in this case, depression is a very interesting one in terms of biomarkers because in depression we know one of the issues is, heterogeneity among patients and they are we do have some cures or potential cures. And the likelihood of certain cure to be successful depends on the type of depression or the heterogeneity among patients. [00:20:00] So If you can use if, you can identify that heterogeneity and get to a sort of personalized profile, personalized medicine, I think that it's really promising eventually, of course, you also have to reach that for Alzheimers. But in terms of disorders like depression, I think the chance of having success there in a few years from now is much bigger. But anyway, your question concerned about informing a patient? Well, I think I'm not a clinician, because I think this is particularly relevant for the clinicians that that treat those those patients etc. [00:20:30] But I think this is an important that in advance of recruiting people for a study, you decide upon this, and actually, you actually put that decision with the people joining your cohort, joining your study. So they want to know, and that's possible ethically or whatsoever in terms of human ethics application whatsoever, whatever you are obliged to, and then then that's fine. If they don't want to know that's another thing. [00:21:00]

So I'm not sure about the rules and regulations there because I don't directly work with with patients in this respect. So I can only speak on behalf of how I see that. And I think you're not necessarily forced to it depends on what also the patient wants and how you design your study in the first place. And, and so it's about informed consent and what people that join your study one in this respect, because it needs for some disorders...Yeah. You might not want to know your risk, [00:21:30] particularly when there's no solution to the problem. Whereas if I would join a study myself as a healthy participant and then

getting sort of a risk profile for certain disease, I would want to know for the sake of curiosity. So I will not give you a reasonable answer to that, because I'm not directly involved in studies like this. But I think it depends on what what the individual wants

Katherine 21:53
So based on your answer, I would say you belong to the school of thought that says....the right to know and the right not to know where you leave this really [00:22:00] for the individual for the person that's going to be screened to kind of decide for themselves whether they want to know or not . But now there is another school of thought that argues for the right to know and the duty to tell where individuals whose genome was screened have the right to know and that the concerned scientist has an obligation to inform them of their results. What what are your comments on the other school of thought?

Daniel 22:26
Well, I would have to give that a thought. That [00:22:30] basically would be my answer in general and why because of course, as I said before ethics is part of daily work my daily life. But it doesn't mean I'm an expert on it, per se and so I might have an estimated guess or my own opinion at this moment, which I sort of shared before that I will let this depend and my initial thought would be to have this depends on what the participant [00:23:00] prefers, but I'm happy to hear that say representative of those two schools debating potentially with me being involved. And I'm also happy to change my opinion if needed, because that's why we think to bring ethicists and neurobiologists and psychiatrists and psychologists and patients and caregivers [together]. That's why we have to bring them together because I can see something based on my view, but but I can't look through [00:23:30] the eyes of other people's

Katherine 23:31
Okay, nicely said. Now these practices we have briefly discussed contribute to an emerging field in medicine known as personalized medicine, which is a move from generalizing treatments and diagnosis to a more individualized handling of patients. Because after all, we are all unique. But we have also seen that practices aimed at applying personalized medicine carry ethical and societal implications, which makes it more challenging to translate research findings into clinical practice. [00:24:00] At least for now. That being said, this necessitates necessary measures to prepare ourselves for the day where the technology is so far advanced that it will become our reality.

So, Dr. Daniel, you have also invested a lot of time throughout your career, studying stress, but particularly prenatal and maternal stress. With my fictional time machine, which does not exist, but I have transported us to the future- this is 2030, [00:24:30] and now all newborns are being genetically tested to identify their risk for heritable, but also non heritable diseases. Doctors are now able to identify risk genes for several diseases, including heart disease, cancer, Alzheimer's disease, but also psychiatric disorders like depression. Now from this scenario, can you identify some advantages but also some disadvantages of such a practice?

Daniel 24:55
Yeah, that's a tricky one. I think for part of this example, you don't have [00:25:00] to go to the future you can always go to the past. Because, for example, it's not really related to prenatal stress, per se, but in the Netherlands, one now screens fetuses for for potentially having Downs Syndrome. So if you talk about an ethic, ethical issue there, people then get

simply a number, a risk of their child having Downs Syndrome and then they are free to decide whether they want to end this life. Because you can, of course, argue [00:25:30] whether this.... whether this fetus has feelings yet, yes or no, but I mean, there's lots of ethical discussions ongoing on, on on this issue that we allow ending a life there. And that's actually based on the same examples that you know, give or the same suggestive time machine brings us to the future. Well, the same is already out there in terms of for example, Downs Syndrome

Katherine 25:56
I think this also kind of implies some judgment for those that are already have [00:26:00] Down syndrome also right? That are that are alive and that are diagnosed with down syndrome. I think also saying okay, we want to end the life is also precurring some kind of judgment...

Daniel 26:11
We sort of conclude that this life is, is less in terms of value. And of course, well I don't have anybody in my close surroundings that has Down syndrome. But I'm always very fascinated when I when I when I see [00:26:30] people with Down syndrome and I think they're an enchrichment to our society. And of course I also understand the other side and that may be particularly for caregivers. It can also be quite, quite heavy. Of course, I will not deny that but but, let's not call these people in one way or another less than others. It's interesting that... a lot of them develop dementia later on in life or relatively early in life but.... so back to your question.

[00:27:00] About time machine going to the future, then where you would really be able to identify risk profile for every individual before or around birth. Yeah, well, if we use that in the proper way, then then then I'm okay with it in a sense that of course, some of these diseases that might develop along the time could maybe be prevented. So if we, for example, would identify increased stress [00:27:30] sensitivity, and we know based on biological research that we can compensate for that... only the normalized development in this respect by providing extra care or whatsoever or by intervening with nutritional support or whatever possible solution you can think of then then I think this is for the better. If we start moving in the direction of creating design babies or whatever, and of course, then I'm not up to this. So it all depends. So I assume that we, as a society will will generally go for the good. And, of course, technically, there's also a lot of pitfalls or or technically this there's also provides the possibility of to abuse this knowledge and abuse as information but

Katherine 28:22
What about also creating some unnecessary anxiety? Because I mean, this tool will really let you know if [00:28:30]you are at risk, it does not necessarily imply that you will develop a certain disease or disorder. So, I think, do you agree that one of the disadvantages would be that it could in some way...

Daniel 28:43
I mean, I have three children myself and then every time you have a test like this during pregnancy, or actually every time you go for an ultrasound, there's anxiety there and all these moments of assessment that we introduce no matter whether they are very lightly technically advanced, like the ones you are [00:29:00] suggesting now or the simple ones where you just want to hear the heart beating of a fetus. They all increase anxiety. But that's another thing. I mean, I did my PhD on prenatal stress. So I would strongly advise

that during pregnancy, you don't just go to the midwives or to counseling, and that they check whether the heart is beating and how fast the baby's growing or whether everything is alright. But they also take more care of or spend more [00:30:00] time and attention to the mental well being of the parents, and particularly the mother with a pregnant woman.

Because now you're in and out of an office like that, within 10 -15-20 minutes and only dealt with this is the physical well being of mother and child, but nobody cares about mental well being or at least, that really gets less attention than needed. And there have already been studies that show that if you [00:30:00] spend more time on on mental well being of the mother during pregnancy that this also benefits not just a mother but also the offspring. So generally any diagnosis or any test or whatever you would introduce during pregnancy or on birth of course, would involve anxiety. At the same time we have all the tools ready to to lower levels of anxiety there. Yes.

Katherine 30:28
[00:30:00] Okay. So coming back to this room, this moment, we are still 2019 yeah, how can we better prepare ourselves for this kind of tool? So how can we better prepare ourselves as a society to kind of not worry or become anxious whenever we go to the to the GP for a test for ourselves, but also for our unborn child?

Daniel 30:53
Yeah, that's a good question. I wouldn't really know the answer to that. Straight away, but I think[00:31:00] bringing this under people's attention that these developments are ongoing, and that it might potentially lead to a situation like you just described. I think that's the first step. And we've seen a few weeks ago that genetic editing is already being applied, although in this case, if I understood it correctly without ethical approval from an ethics committee. But even independent from this, technically, the future is now. [00:31:30] So how can we prepare ourselves better? Well, if we you have already seen that in reaction to this event, lot of debates opened up a lot of discussions about what is ethically correct yes or no...emerged from from from the genetic editing and this is I think, crucially important, so we should raise attention and awareness of issues like this. And and that's what I think is a very nice development about as you call it neuroethics.

And you being representative of the Neuroethics Police [00:32:00] is that this used to be disciplines that were quite distant from each other, you had the signs on one hand and then you had to ask permission to an ethics committee, whether you could do either your animal work or or your human experiments... and and then your proposal got granted yes or no and I think that was a huge gap. And now, this gap is closing and and scientists on a daily basis becomes more aware of ethical constraints and concerns. [00:32:30] And not as being the enemy of one's research line, but but being on board and on the same side there... so yeah. One has to create awareness and then society can also judge or form their opinion about certain matters. And that can be implemented into forming rules and regulations, instead of having this go on silently [00:33:00] and then all of a sudden,you might end up in a scenario where there's no way back.

Katherine 33:07
So my last question for our conversation, it's, it's bringing us back a bit to aging. So wrinkles are signs of aging and particularly the aging of the skin, with the skin being humans largest organ. Now to fight off those aging signs we have discovered Botox, which is mostly known for its cosmetic uses. Now Botox can [00:33:30] be easily administered at your local doctor or clinic- but it is also very affordable, making it a valuable product. Aging

signs are not specific and unique to the skin alone. They also surface on all other organs and especially the brain, of course. Do you think we would one day creates a procedure for the aging brain that will become common practice like a Botox for the brain.

Daniel 33:53
Didn't see that one coming! Well, Botox for the brain [00:34:00] and being affordable. Well, let me think of a nutritional intervention or just nutritional support that would help you age more healthy or whatsoever. If that is at your disposal, then why not take. But if you, let's see, in an artificial manner that would maybe be on the expense of something else, be able to increase your lifespan...and that's another issue. So if it's [00:34:30] something that doesn't harm anybody and doesn't harm yourself, then I would say why not? Although we should not want to live forever.

Katherine 34:44
That's a nice concluding remark. So Dr. Daniel, it has been a pleasure to discuss with you some of the most interesting, but also pressing questions of our times. Thank you for joining me and thank you for all for tuning in. We hope you have enjoyed this conversation. [00:35:00] We may have answered some of your questions or maybe even raised many more. You can always send your comments and suggestions to me, but also to Dr. Daniel for a chance to be featured on the next episode of the Neurothics Police. Stay curious, stay critical until next time. Thank you very much, Dr. Daniel.

Daniel 35:17
Thank you for increasing awareness.

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