

Mind & Life Podcast Transcript Brian Dias – Epigenetics and Intergenerational Trauma

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Opening Quote – Brian Dias (<u>00:04</u>): The journey that I'm on right now is in many ways trying to understand how I don't bequeath my own legacies of stress and trauma to my own children, but also one that seeks to give voice to people who might have their own legacies of stress and trauma that they're dealing with—to tell them that those are not only voices in their head, that biology has registered that stress and trauma, but also provide silver linings to say that legacies of stress and trauma can be muted, they can be halted, they can be dampened, and to provide that healing perspective as well.

Intro – **Wendy Hasenkamp** (00:45): Welcome to Mind & Life. I'm Wendy Hasenkamp. Today, I'm speaking with neuroscientist and trauma researcher Brian Dias. Brian has been one of the pioneers in understanding how trauma can be transferred between generations. Research in this space has helped fuel a major revolution in biology, because it means that not just our genes, but some aspects of our experiences can be inherited. As you'll hear, there are multiple pathways for this, involving the classic roles of both nature and nurture. Brian has been instrumental in our understanding of the biological side. I've been increasingly fascinated with this phenomenon. It really opens a new window on how we're shaped, how we become the people that we are, and it has significant implications for well-being on individual and societal levels. In today's conversation, Brian takes us through what we know about intergenerational transmission of trauma, strategies and interventions to help, and what this might mean for building what he calls legacies of flourishing.

(01:59) I've been following Brian's work for more than a decade, so it was a real pleasure to get to speak with him last fall. I think this episode and everything we're learning about how experience and sensitivities are inherited really highlights the importance of how we live our lives and how we build our societies. We're seeing more and more that the things that happen to us and the things we choose to do in our lives don't just affect us. So I love how this is yet another lens on interconnection, helping us see a little more of the complex tapestry that we're all weaving together. I hope you enjoy it—as always, there's lots more in the show notes. I'm so happy to share with you Brian Dias.

Wendy Hasenkamp (<u>02:46</u>): It is my great pleasure to welcome Brian Dias to the show today. Thank you so much for being here, Brian.

Brian Dias (02:52): Pleasure to be here. Thanks for having me.

Wendy Hasenkamp (02:54): Well, I'm really excited to chat with you about your work. I've long been a fan. You've done so much groundbreaking work in the area of trauma and intergenerational trauma.

Before we get into that though, I would love to hear a little bit, just personally, how you got interested in neuroscience and studying the kinds of things that you do.

Brian Dias (03:13): I grew up in India, in Bombay specifically, and I would classify my career as one of just meandering and doing things that interested me. In fact, science was never on the radar. I was coaching volleyball professionally in India when someone said, "You know, you're moderately good at academics. Someone's starting a lab in India. You should think about joining their lab and pursuing a scientific career." And therein started my scientific career. So I only half joke when I say I'm still a beach volleyball player trapped in the body of a scientist.

Wendy Hasenkamp (03:51): [laughter] That's great.

Brian Dias (<u>03:52</u>): But I do think that it honors some of my childhood ambitions. I wanted to be a detective for the longest time. I wanted to be a Catholic priest for the longest time; I was raised Catholic in Bombay. And I feel like I do aspects of both of those professions as a scientist. I am a detective solving mysteries of nature, and I do sermonize and evangelize science around the world. And so I feel like those childhood ambitions are being honored and... we're working towards being that beach volleyball player that I so want to be. *[laughter]*

(04:26) But in terms of the work that I'm currently doing, I've arrived at it after a lot of meandering in different fields. I started off studying stress and antidepressant treatments. I then looked at pro-social and antisocial behavior. Then I looked at genetics of behavior, and now we are currently studying intergenerational legacies of stress.

(04:51) And the story for me right now is a personal one because I was abused as a child, and the journey that I'm on right now is in many ways trying to understand how I don't bequeath my own legacies of stress and trauma to my own children, but also one that seeks to give voice to people who might have their own legacies of stress and trauma that they're dealing with—to tell them that those are not only voices in their head, that biology has registered that stress and trauma, but also provide silver linings to say that legacies of stress and trauma can be muted, they can be halted, they can be dampened, and to provide that healing perspective as well.

Wendy Hasenkamp (<u>05:43</u>): Thank you for sharing that. Well, let's jump into it. I first came to know your work about 10 years ago from a groundbreaking study you did using mice. Can you share how you came to develop that project and what you found?

Brian Dias (<u>06:00</u>): We know from data that has been gathered in the aftermath of the Holocaust, 9/11 terrorist attacks, famines that have occurred across history, that ancestral environments profoundly influence descendant generations, even if those descendants did not experience the atrocities or environmental experiences themselves. What we are trying to do is to try and understand how that happens. And as you can imagine, that's challenging to do in humans because of that really important interplay between nature and nurture, between genes and the environment. And so we'd like to control both of those. We'd like to control the environments, and we'd like to control the genes that we're looking at. And to do both of those, we seek to do so in more reductionistic systems that are animal studies. We do so, of course, with the approval of institutional ethics committees, and what we're trying there is to control our experiments such that we can, as I mentioned, distinguish between the impact of nature and nurture, and the interplay between those two.

(07:14) What we did was we took mice, we made them fearful of a particular smell, an odor, and what we found is that future generations are more sensitive to that odor that their male father had been made fearful to, their brain devotes more real estate towards processing that odor, and the sperm of those male fathers registered information about being fearful of that particular odor. Now, this has been characterized in the media as mice "inheriting the fears of their fathers," when really it's conferring a behavioral sensitivity to the next generation, which makes the next generation more attuned to their own environment, such that when they smell that odor, they register it in a better way.

(08:12) Why this is important is because, as I mentioned across history, we know that ancestral environments affect descendant generations, and studies in a multitude of species have emphasized the importance of nutritional stressors or insults, stressors in general, on the next generation. But what we wanted to do was we wanted to follow a stressor across generations. And for that to happen, we would need to look for a needle in a haystack. And so what we wanted to do is we wanted to make that haystack smaller and that needle much bigger. And so essentially, what we did was we used smell to make that haystack smaller and that needle bigger, because there are odorant receptors that we know are activated by particular smells. And so then, we have not only a behavior that we can look at in the next generation, but we can also look at the impact of an ancestral experience—like becoming fearful of a particular smell—in the next generation, at the level of genes.

Wendy Hasenkamp (<u>09:26</u>): Yes, it's so fascinating. I remember when this study came out and I read it, it kind of blew my mind because I think... Correct me if I'm wrong. Was it the first time showing that these kinds of things were transferred between generations?

Brian Dias (09:39): Previous studies had shown that ancestral environments influence future generations using broader stressors like manipulating diet in mice or exposing mice to stressors, but this was one of the first studies to show that an experience, like becoming fearful of a particular smell, confers a particular set of properties to that next generation, where the next generation is more sensitive to that smell, their brain, as I said, devotes more real estate to processing that smell. And now, we've also gone on to show that relay of information, that baton of stress being handed from one generation to the next, occurs via RNA in sperm. So this was one of the first studies to show that an experience could be inherited across generations.

Wendy Hasenkamp (<u>10:31</u>): So this work raises so many interesting questions, and there's a lot of different directions that I would love to go with you today. But one... and I know you've done a lot of work with Tibetan Monastics and the Emory Tibet Science Initiative program, and so I know you've probably had a lot of conversations overlapping with Buddhist theory as well. So that makes me think about ideas from that perspective about karma, and things that are transmitted through generations— or in that tradition, the idea of past lives and things like that. So have you thought about those kinds of intersections, and if this might be speaking to that a little bit in a biological way?

Brian Dias (<u>11:13</u>): I love this train of conversation because it's something that has really captivated my interests since, as you noted, my time teaching Tibetan Monastics neuroscience as part of the Emory Tibet Science Initiative. And as I understand it, the concept of karma is, in one dimension, how parental substances (sperm and egg), in some ways come to bear imprints of past lives, and how that then can have repercussions for the future generations. And I find that synergy with what we are now understanding about how intergenerational legacies of stress and trauma echo across generations to be remarkable. What we now know is that sperm and egg, cells in a fetus as a fetus is developing, cells in you and I, can register information about the environments that we are being exposed to.

(12:12) The way that happens is through a process called epigenetics. And I like to encourage people to think about epigenetics as a book needing to be read. That book is our DNA, which resides in all of us. It's how that book is read that will change the meaning of that book. So within you and I are an army of editors—called readers, writers, and erasers—that put the equivalent of full stops and commas and white-outs and highlights on our book of life. And depending on that punctuation, maybe in your book of life, page number two is read, whereas in my book of life, page number two is completely redacted, but page number three is read. And that's how we get differences in gene expression, and that's how sperm and egg, cells in a fetus, cells in you and I come to register information about the environments that we experience.

(<u>13:17</u>) So now when we are thinking about how sperm and egg come to bear imprints of a particular experience, you can see how exposure to a particular environmental insult, be that nutritional, or an environmental stressor, be that economic strife, how that might put these different punctuations on the book of life so that now, the book of life in a sperm or an egg is differently edited, such that when they meet and their union gives us the multicellular you and I, how that embryonic development can be affected to actually bear imprints of that environment that the "past life" had seen.

(14:07) – musical interlude –

Wendy Hasenkamp (<u>14:30</u>): This is an amazing mechanism that we've really only just started to understand in the last couple of decades in biology and in science, neuroscience, which kind of... I just want to take a moment and note how this completely turns our previous understanding of evolution on its head. And I remember when we first started learning about this, historically, there were the theories of evolution (at least when I went to school), we learned about Darwin's ideas and Lamarck's ideas. So just briefly, Darwin's idea is that information is transmitted between generations solely through the DNA, and everything that makes us "us" and the ways that we change are just due to kind of random mutations that may or may not be adaptive. And those that are adaptive are then transmitted to the next generation. And Lamarck's ideas originally were much more in line with what we're talking about now, where experiences in the life of an individual can somehow change what is inherited and what is passed on. And so it's almost now like we're understanding that both of those are true. So that, I just think is a fascinating explosion in biology, and I love when theories are overturned like that. Just wondering if you have any reflections on that.

Brian Dias (<u>15:53</u>): So as biologists, as scientists in general, we always want to keep an open mind to revise our theories. And you're exactly right, I think we're revising and revisiting our ideas of inheritance. The saying goes right now that Lamarck was not wrong, just born at the wrong time. Which is why it was so important for me to correct the record with all the media surrounding the work that we've done over the years. So we started this in 2014. We've published another paper in 2019, and another in 2020 about this phenomenon where you take these male mice, you make them fearful of a particular smell, and the future generations are more sensitive to that smell. Because what Lamarck would've said is that the next generation of mice would be fearful to that smell.

(16:41) So that would be, the first generation being fearful, the second generation being fearful. When actually what we are saying is that the next generation is more sensitive, and that sensitivity confers an advantage to the next generation when they smell that odor themselves. And so there are subtle differences in what Lamarck was saying versus what the data are showing, not only our data, but other people's data as well. But I think it does suggest to us that we need to revise and revisit our idea of inheritance and incorporate elements of Lamarckian views into our existing worldview of inheritance. And people have started talking about how this might result in how instincts evolved way back when.

And so there are all of these now new ideas that are churning about, and it's really exciting times in this field.

Wendy Hasenkamp (<u>17:35</u>): Yes. Thank you. I love the way, as we learn more, things get overturned and that's such an essential part of science. And thank you for clarifying that about, it's not the fear per se that is transmitted; it's a sensitivity. I think that's really important.

Brian Dias (<u>17:52</u>): I will also say in the spirit of revising and revisiting our ideas of inheritance, it also, I think, behooves us to just marvel at scientists from way back when, who were so prescient about certain things that we are now discovering. There's beautiful prose from Darwin and other scientists talking about actually how experiences might be inherited by future generations. And Darwin suggested this idea that there are little gemmules, little gems that are circulating through all of us and that find themselves with sperm an egg, and that gives that information to the next generation about an experience.

(18:38) Well, fast forward to all these years now, we now know that Darwin's gemmules take the form of these tiny little vesicles, tiny little balls coursing through all of us called extracellular vesicles, which leave one cell in our brain and maybe get into circulation, and then go and dump their contents into— I'm making this up—the liver for example, or the lung. And how that intercellular communication actually does serve as a way by which information about experiences in one generation can be transmitted or inherited by sperm and egg in the next generation. And beautiful work has shown this using nutritional stressors in the mouse, using psychosocial stressors in the mouse, where you have these extracellular vesicles coursing through us, which we think are handing the batons of stress to that sperm and egg to allow for the parental substances to, again, bear imprints for what the body is seeing.

Wendy Hasenkamp (<u>19:43</u>): Just amazing. That is fascinating. I was going to ask if we knew anything about how it actually gets from our nervous system or brain or perceptual experience into the sperm or egg. So it sounds like we're starting to understand that process.

Brian Dias (<u>19:59</u>): We have an appreciation for how information can be relayed to the germ cells in organisms like worms through extracellular vesicles. So there are beautiful data to suggest that the nervous system can relay information to the germ line. However, we don't know how that might occur in mammals. But we're knocking on that door right now, us and other labs, and it's going to be interesting times to see how... Again, coming back to that idea that parental substances bear imprints of ancestral experiences, we are knocking on the door to try and figure out how that occurs. And then how those parental substances, when they meet to give us the zygote and the embryo, and that embryo develops, how that embryo can roll down one side of the hill and you can have serenity, versus if it rolls down the other side of the hill because of the marks that it had accrued because of the ancestral experiences, how you could have strife.

Wendy Hasenkamp (21:03): Right. And it's really just highlighting the incredible elegance of life and biology, and how we're just learning the littlest bit, it seems like. But I appreciated you noting also that this is all understood to be adaptive for the offspring, to be able to transmit information about the experience that the parents have had over the course of their lives to set up offspring to hopefully be more effective or successful, able to thrive in the environments that I guess ostensibly would be a similar environment to the parents. So is there more to say about that, because I feel like there is other research too about... maybe it's more about the nutritional situation of the parents, and then transmitting into children who are set up different in a metabolic way?

Brian Dias (22:01): Our understanding of the fidelity of information that is inherited or transmitted to the next generation as being either beneficial or detrimental to the next generation is one that we are still trying to figure out what the logic is. The prevailing understanding is that parents, ancestral generations, are transmitting information to allow for the future generation to navigate their own environments in the most optimum manner possible. But that understanding, that premise is based on the supposition that the environment that the future generation is going to see is going to be the exact same environment that the ancestral generation saw.

(22:51) We know that environments change very rapidly, as a result of which you have these matches, ancestral-descendant environment, or you have a mismatch. And therein now, we don't know whether the influences of ancestral environments is actually beneficial or detrimental. Because you could have a situation wherein you have information that's passed to the descendant generation. But now, that descendant generation doesn't see less food. It actually sees a lot of food. But the system, the information that was passed on, might biologically have primed the next generation to seek as much food as they could. But now, because there's a mismatch between those, that's detrimental, because now you have high-fat, high-sugar food being consumed in copious amounts that results in health consequences. So that could be a mismatch. But then when there might be a match, that's when it may be actually beneficial.

Wendy Hasenkamp (23:52): Okay, that's very helpful. Thank you. And that makes me think about... all of us, I feel like have inherited, or at least I've heard this theory, from a nutritional perspective this craving for sugar and fats because long, long, long ago of kind of a scarcity environment that we evolved in. And how for many people now, that's not the case. So it's interesting to think about that in individual cases and for all of us as a species, that mismatch potential.

Brian Dias (24:23): This idea that there is a mismatch between the ancestral environment and the descendant environment is causing us to revisit what the consequences of legacies of stress and trauma might be. However, in our entire conversation we need to appreciate that we've talked a lot about nature and the environment, when genes play as much (depending on what trait one is looking at) a role in one's responsiveness to one's environment. And so to be able... Therein lies the complexity of the human condition. When people say, "Why is everyone not affected equally by a stressor or trauma?" it's because of that interplay—the genes brought to the table and the environment, that interplay is so complex that you can't really predict who will or will not respond in A or B way to that particular environmental insult.

Wendy Hasenkamp (25:25): Right, okay. So coming back to your work, it sounds like the impacts of information that's transmitted between generations that you all have studied has mostly been detrimental impacts. Is that right?

Brian Dias (25:40): So most of our studies right now do suggest and have focused on the detrimental consequences of ancestral environments on future generations—be that in the metabolic space, nutritional insults setting the future generation up possibly for higher incidence of diabetes and obesity, psychosocial stressors in one generation setting the future generation up for higher incidences of depression and anxiety. But I think what we're also coming to appreciate that there are some silver linings.

(26:16) And again, it's the work in more reductionistic systems that is suggesting to us that there are silver linings. We just need to look for them, and we need to understand what the logic of those silver linings are. Why do they come about in certain instances? Why don't we see them all the time? Because

in being able to understand that logic comes our best hope to engineer what I'm calling legacies of flourishing. And we want to be able to engineer those legacies of flourishing because there is a lot of trauma and stress in this world, and the idea is, how do you reverse that?

(26:55) The data first are showing that you can reverse that, and then the second set of data are showing that, can you preemptively "lay a red carpet" in some ways, by creating ecosystems that allow for legacies of flourishing to occur, independent of anything else happening in people's lives? And we have to hold onto that hope because in those legacies of flourishing lies our best chance to dampen and halt these legacies of trauma.

Wendy Hasenkamp (27:30): Yeah, I'm really excited to talk about, as you say, the legacies of flourishing. It makes me think, if sensitivities, threats, traumas, those kinds of things can be transmitted, can the opposite be transmitted? Like experiences of deep safety or compassionate tendencies? And people who train—as you and I both know many people who've trained so deeply in things like compassion and other virtues—and so can those be transmitted equally to the next generation? So can you talk a little bit about what we know about positive things that can be transmitted as well?

Brian Dias (<u>28:11</u>): Our understanding of how we dampen these legacies of trauma comes to us from more interventional studies. To address this dimension, I'd like to take us into a new frontier of epigenetics, which we're now appreciating, which is called the epigenetic clock. And when we think about a clock, we think about aging in some ways, and we think about a chronological age, the age that is our age based on our year of birth. But we are also appreciating that now, every cell in our body has a clock based on, again, the marks that a particular editor has put down. These marks are called DNA methylation marks. And so you have an epigenetic clock that is different from the chronological or biological clock.

(29:04) And what we're finding is that insults—like nutritional insults, like structural racism, like discrimination—all of those alter the DNA methylation marks in cells, that can be used as a readout then to say that the epigenetic clock is a little off kilter. Now whether that epigenetic clock is the cause of some of the detrimental consequences of structural racism or nutritional insults is up for debate, and I'm not prepared to say one way or the other. But to use epigenetic clocks to emphasize that biology registers information about all of these atrocities and insults is well established at this point.

Wendy Hasenkamp (29:53): When you talk about the epigenetic clocks, is it like certain cells are "older" or...? I'm having trouble kind of thinking about that.

Brian Dias (<u>30:03</u>): Right. When we think about epigenetic clocks, we want to think about most of these clocks come from cells that are found in one's blood. And so you can think of a clock in "a control condition" versus an experimental condition. What you might find there is that the clock in the experimental condition might be sped up, or it might be slowed down because of the insult that has been experienced. That doesn't necessarily say that they're "older" or "younger" as much as it says they're different—and use them as, again, a register, a witness of the environmental insult.

Wendy Hasenkamp (<u>30:51</u>): Interesting. I don't know if this is related at all, but it's making me think of research that I've heard about children who are exposed to adverse events or trauma in childhood have a faster developing prefrontal cortex, which is normally a later developing part of the brain. So my understanding was that the thought is that this helps them adapt to the stressful environment that they're in. I'm just thinking of developmental trajectories that are sped up or that are different than normal because of trauma. Do you think that has any relation to what you're talking about?

Brian Dias (<u>31:28</u>): So there's a well-established literature that adverse childhood exposures do actually either accelerate, or in some cases decelerate, the development of circuits in the brain and the development of other organ systems. What we know is that that acceleration and deceleration can be measured in the laboratory based on a bunch of metrics like the thickness of cortices, immune responses to particular challenges, and a whole host of other measures.

(32:05) What we are trying to play catch up on is, are the DNA methylation changes which are seen in the aftermath of adverse childhood exposures, which are robust findings, are they causal to that, or are they a consequence of that? I don't think the data are there as yet to make those kinds of definitive claims about causality versus correlation at this point. Until a point where one can go in and manipulate DNA methylation and show that it changes the arc of development—that's where one can say that the epigenetic clock no longer is just a measure of, or readout of the adverse childhood exposure, but it's actually causing, has a consequence on the accelerated development or the decelerated development that we are seeing.

(32:56) – musical interlude –

Wendy Hasenkamp (<u>33:22</u>): I've heard you talk about some examples that we know from human work and experiences of tragedies where these sensitivities are passed through multiple generations. Not just one, but like grandchildren. So that might be interesting to talk about that too. And it just... I'm thinking about how cycles of trauma and violence in the world that we see so much of, again and again, are part of this biological system too.

Brian Dias (<u>33:50</u>): So as we think about these legacies of trauma perpetuating across generations, I think it's important to view these through the lens of three real avenues by which this happens. Yes, sperm and egg could be affected by stress or trauma. Fetal development could be affected if the stress or trauma is experienced while in utero, but then you could also have adolescents, you could have adults, their behavior and the development of brain circuits in those individuals be affected by the experiences that they experience. All of those, it's a cycle. Because you could envision a scenario wherein sperm and egg are affected, that goes on to result in brain development being affected, which in turn results in that same individual bestowing a different level of parental care or caregiving on the next generation. And that's how the next generation might bear the imprints of a particular stress or trauma—without their sperm neck being affected. Or fetal development being affected, for example, in that fetus as it grows up. But then that fetus goes on as a consequence to bestow different caregiving on their wards, and that's how legacies of stress get perpetuated.

(35:22) So it's not always going to be the same vehicle that allows for the legacy of stress to be perpetuated across generations. The thinking in the field is that social behavior is the most robust vehicle that allows for intergenerational legacies of stress and trauma to perpetuate.

Wendy Hasenkamp (<u>35:44</u>): Like an experience of a family telling stories, developing behaviors and biases or sensitivities, and then just transmitting those kind of socially, culturally through the family. Is that what you mean?

Brian Dias (<u>35:55</u>): Absolutely. So there's social transmission of information. You're sitting around the table at family dinner, you're hearing about stories about X, Y and Z. That gives you a physiological response. That physiological response is going to affect how you behave, potentially, towards someone.

And if that's someone is the next generation, then that might perpetuate that legacy of anxiety or violence in that next generation. And so there's that idea that you could have social transmission of information.

(36:28) But then there's also the idea that whatever experiences that we are talking about actually affect the cells, as we talked about, actually affect the development of circuits, that are involved in parental behavior, that are involved in the manifestation of violence and aggression. As a result of which, then one may be, if one sees certain instances in one's own life, more likely to exhibit violence and aggression as a result of that legacy. And that cycle gets perpetuated. And so it can come at us from various different ways—from stories, but also very organically from regions of the brain that we know to manifest behaviors that would perpetuate legacies.

Wendy Hasenkamp (<u>37:13</u>): Great. So this then speaks to the need for a multi-pronged approach also for interventions, or ways to, as you say, reduce this trauma or maybe even perpetuate different kinds of legacies. I forgot to ask you too, what is your own personal trajectory within the contemplative space? How did you come to be exposed to those practices? And it seems like they integrate in various ways now into your work and thinking.

Brian Dias (<u>37:45</u>): I don't know if this is me growing up in India or not. As you well know, religion is a big component of Indian life. I was raised Catholic. But having taught neuroscience to these Tibetan monastics now as part of the Emory-Tibet Science Initiative, I always say that I learn more than I teach. And so not only have I learned how to meditate from them and be mindful—some days are better than others, as we well know—but I've also learned how to have productive and respectful conversations in taking lessons from the Tibetan style of Buddhist debate, right? And so the education that I've received from the Tibetan monastics has been life-changing for me.

(38:34) To be fair, I bring up the fact that I grew up in India a lot because in neuroscience, in psychiatry, there's the idea that you can have pharmacotherapies that are going to be the panacea to all our ills. But having grown up in India with a more holistic bent of mind, the answer always has been, it's going to community-based. It's going to be more holistic. It takes a village. And so from that perspective, I'm deeply moved by being able to learn to be mindful from the monastics who've been so generous with educating me about that.

(39:17) And then also just having an open mind to whatever it is that the data show. And that is exemplified by the Tibetan style of debate, where one person is the challenger on one day and I'm the defender of that position on one day, and then I become the challenger the next day and the other person becomes the defender. So I'm not holding on to my opinions in any way. As the mantra goes, starting off that debate, let's just move closer to the truth. And sometimes I think we forget that—we're moving closer to the truth. It's not me be right, you be wrong. And I take that into my practice of science as well. I try and not hold on to theories, because theories are meant to be tested and proven or disproven, and we want to always be questioning whatever we are doing to move closer to the truth. And so I will just say that those are the two facets of my life that have been deeply enriched by my interaction with the monastics as part of the Emory-Tibet science initiative.

Wendy Hasenkamp (40:21): I appreciate too, you just mentioned in the West and this emphasis on pharmacological solutions and, "We're going to find a pill that's going to magically erase your trauma," or something like that. And from what we've been talking about, you've mentioned how the social avenue is considered to be the strongest. And it strikes me that there's an alignment there because that is again leveraging experience, rather than any sort of just purely biological or molecular action. We

change through experience, it seems, in the most kind of holistic way, as you were saying. So I think there's a lot of encouragement there in the possibility for change. And I just wonder, is there anything to say about biological or medical-based approaches around ameliorating trauma, or is the emphasis really primarily on social-based interventions?

Brian Dias (41:19): I think it's important to realize that pharmacotherapy is extremely important and does work, because it does affect systems that have been altered in several ways by whatever insults that we may be talking about. So to not diminish their efficacy, and that's not what I intended to do. But what I intended to say is that to think, and you alluded to this, to think that pharmacotherapies are the be-all and end-all of our journey, I think is myopic. I think what we are finding right now is that the best strategy in several instances is a combinatorial regimen where you have a behavioral intervention in addition to pharmacotherapy. And that might be our best line of defense in terms of not only halting legacies of trauma, but also changing behavioral states.

(42:18) Now, when we think about halting legacies of trauma, most of the solutions that seem to be working are in the space of policy and practice. So let's just take the reductionistic approach right now. Even in studies in animals, including our own, what we find is, A, we find we can reverse all the effects that we have found—ourselves, as well as others—by exposing animals to the equivalent of cognitive behavioral therapy in humans and giving them really enriched environments. Those are the two biggest factors that have allowed us to reverse all the effects that we've talked about before. So that behavioral sensitivity in the next generation, the enhanced neuroanatomy, the more real estate being devoted to that particular smell in the next generation, the effects on sperm of the male mice who'd been made fearful to that odor—all of those go away if we expose the male mice fathers to the equivalent of cognitive behavioral therapy in mice, called extinction training.

Wendy Hasenkamp (43:30): Extinction training, okay. Can you say a little bit about how that works?

Brian Dias (<u>43:33</u>): So what extinction training is, is we've made mice fearful of a particular smell, and then we diminish the fear towards that smell in that same generation. And now, what we find is that those male mice, their sperm no longer have the imprints of the fear association with that particular smell. As a consequence, the next generation doesn't bear that sensitivity to that smell and doesn't devote more real estate towards processing it.

Wendy Hasenkamp (<u>44:05</u>): Okay, cool. So you can, after making the male mice afraid of a certain smell (ostensibly associating with shock or some negative outcome), then you can repeatedly expose them to that smell in a safe environment and kind of make a new memory or a new association?

Brian Dias (44:24): Exactly.

Wendy Hasenkamp (44:25): And then that erases all of the molecular changes that you see transmitted?

Brian Dias (<u>44:29</u>): Right. Absolutely. So we can now reverse and halt that legacy of paternal olfactory experience by just exposing the male mice who had been previously made fearful of this particular smell, diminishing their fear towards that particular smell. And so that's at the reductionistic level with respect to the animals.

(44:52) Then we talk about how you do this in humans, by providing strategies that allow for individuals to have supportive, nurturing environments around them. By giving parents the tools to be the best parents that they can be. By providing, and this is a new frontier in this particular area, which is

providing resources to mothers, for example, soon after giving birth that allows them to feel supported and nurtured such that they can bring their best caregiving to their child.

(45:30) And also now one of the frontiers in this field is cash transfers being talked about a lot. The idea, which has taken the form of universal basic income, on a microcosm, that takes the form of conditional or unconditional cash transfers—where you give individuals a certain amount of money, and that's reaping benefits for future generations for various reasons because it affords the generation that's given that money the flexibility to be able to do a lot of things that would not be able to be pursued prior to that.

Wendy Hasenkamp (<u>46:05</u>): Oh, wow. What kinds of outcomes have they seen then on the next generation from those kinds of cash infusions? That's fascinating.

Brian Dias (<u>46:14</u>): So these data are still in their infancy, and there's a lot of debate about whether there should be a conditional cash transfer versus an unconditional cash transfer. So an unconditional cash transfer is, you just give the money, and then the individual is free to do whatever it is they need to do with it. A conditional cash transfer is, give you a certain amount of money, but then you have to meet certain metrics. You have to show up to parental coaching, for example, or you might have to show up to some social support groups that give you that nurturing environment within which you can structure how you care for your child, for example. And so there's debate about the conditionality versus the unconditionality, but what the data are showing is that the attachment ties are better, the outcomes in terms of temperamentality of the children is better at a particular age. And so we're now appreciating that there are all these nuances to be able to give the support at periods of time which are really important for development, that bonding between caregivers and their wards, and that is reaping benefits.

(47:23) I think it's also important to emphasize that what these interventions tell us or reemphasize to us, and we've known this for a while, is that there are epochs of development where the intervention is most efficacious. Those epochs are during infancy and during adolescence. And so if we can capitalize on those two epochs of development to intervene, we have our best chances of being able to halt these legacies of trauma because those are the epochs at which there's a lot of development that is happening. And so to be able to intervene at those times lies our best chance of halting these legacies of trauma, increasing that bonding, increasing that attachment, decreasing the behavioral challenges that sometimes manifest.

(48:11) – musical interlude –

Wendy Hasenkamp (<u>48:37</u>): Oh, I love that this is really weaving into ideas around attachment and resourcing and safety. I feel like these are issues that are coming up a lot on the podcast from different angles. And it really makes me think what you were just saying, the studies around the cash infusions, there's so many different kinds of resources that we can have in our lives—at any age, but thinking about child development. So yeah, money is an obvious resource. Social support and connection is another resource. Nutrition, literally biological resources. So it's just fascinating how all of these things, it's almost... In my mind, I sometimes just kind of reduce it to this level of energetic resources somehow that our body... That's how our body sees these things. I don't know, do you have reflections on that?

Brian Dias (<u>49:40</u>): What you said is absolutely right. There are all these levers that we can pull, be they financial, nutritional. There's safety that's involved too in terms of being raised in safe environments. There's wanting to be raised or needing to be raised in environments where there's not a lot of chemical

pollutants in one's environment. Again, all of this comes to become embedded under the skin. And it's interesting that you use the word energetics because another couple of levers, biological levers that I think our environments are pulling to allow for legacies of stress to be perpetuated, but also would then allow for legacies of flourishing to be engineered, are these energetic demands on our biology. So we now know, for example, that mitochondria, which our listeners might've heard about is the powerhouses of the cell. They're providing all the energy for our cells to either run a sprint or to run a marathon, one of those two. And what we are now finding is that mitochondrial stress is a big readout of what's happening in one's environment.

(50:48) And then the second biological lever that environments seem to be pulling is the microbiome. And the microbiome is really affected, of course, by food that one gets or does not get. We're now appreciating that the microbiome changes in response to stressors that one has experienced. And that results in, of course, now this idea of, mind versus body? No, it's mind and body. Nature versus nurture? No, it's nature and nurture. So we are realizing these dichotomies are now breaking down, and it's always an interaction between the two. We now know, of course, that what's happening in our gut affects our brain, what's happening in our brain affects our gut, and this communication is really one of those things, which is again, a new exciting frontier that allows for us to think about how we might use, for example, nutrition to be able to buffer communities that might actually bear these imprints of trauma, how we might buffer them from that trauma by intervening at these particular levels.

Wendy Hasenkamp (<u>51:53</u>): I love this. Yeah, the more you look, the more integrated and interconnected the whole system becomes. And I also love how you're extending your interests and work into thinking about policy-level shifts and societal-level changes. So all the way from the very small molecular up to systems-level changes. And so I wonder how you think about that dynamic, working at the scientific level, basic science, molecular level, and then thinking about policy changes. How do you hold all that together in your mind?

Brian Dias (52:31): A hashtag that I often use, which is a little clunky, but I think emphasizes to people the point is "human first, scientist second." We often think of scientists as being removed from being humans in some ways, and that science and their profession is all that there is. But eventually, a scientist operates within particular spaces. I have kids, I have a family, I do laundry, I do dishes. I do all of the mundane things that all of us do and should do and need to do. And so to think that I operate in a different, and scientists operate removed from that, I think is utopia. And so one can't help but obviously emphasize that we are contributors to society and we use, in my case, the puzzles that I solve in the lab to hopefully inform and inspire what happens at a policy level. And working across that spectrum is how I am seeking to make my contribution to society. I don't view those as mutually exclusive. It does require me to learn a completely different trade, a completely different vernacular or vocabulary. But at the same time, that's the joy in the contribution that I want to make to society.

(53:56) But I think it also behooves us to talk about the fact that sometimes, we think that science does not hold any utility other than utopia, and other than what we see in the laboratory. And I think work like what we've talked about—we've talked about three ways by which legacies of stress and trauma can perpetuate across generations—we know a lot of that comes from basic science work. We know that the epigenetic clock, epigenetics, mitochondria, the microbiome, all of those are levers that environmental experiences pull to allow for our biology to register them. We know that from basic science. And so it really behooves us as a community to appreciate how important basic science is, as we build these legacies of flourishing at a community level, at a policy level to be able to dampen these legacies of trauma. **Wendy Hasenkamp** (<u>55:01</u>): Thank you for sharing that. I really appreciate what you were saying about human first, scientist second (or whatever else second), and I'm thinking back to the beginning of our conversation and how you shared your own experience of trauma and abuse and how that's been a motivator for you in doing all this work. So I'm just wondering kind of stepping back, for you personally, how this work and these experiences have affected you, and maybe lessons learned or things that you think about at a very high level that may be useful to share for the audience as a kind of take home.

Brian Dias (55:41): Like I stated at the start, this is a very personal journey for me, and it takes on special significance right now because I have a ten-year-old and a five-year-old. And I see myself trying to dampen the legacies of my own stress and trauma so that they're not bequeathed to these beautiful, amazing individuals who are ten and five at this point. And so every day for me is a journey of selfdiscovery where I'm trying to be mindful of my parenting, knowledgeable about what parenting does to them and potentially how they will parent in the future, and relying on our understanding of the malleability of being able to break legacies of trauma—to know that one harsh word today doesn't mean that I don't have the ability to remedy that harshness tomorrow.

(56:43) Those are the three pillars that I take from my work every single day, and from my time teaching and learning from the Tibetan monastics through the Emory-Tibet Science Initiative. Because I'm understanding, from all of those experiences, that the die is never cast, that the ability to change lies within me, with help from the village that I want to surround myself with, and that I will have bad days, but those bad days don't define who I am. And that community is so, so important.

Wendy Hasenkamp (<u>57:28</u>): Thank you, Brian. This has really been such a wonderful conversation. I really appreciate all the work that you're doing. I think it is so essential in today's world, and I appreciate you taking the time today to chat with us. So, thank you.

Brian Dias (57:43): Thanks for having me, Wendy. This was a pleasure.

Wendy Hasenkamp (<u>57:49</u>): This episode was edited and produced by me and Phil Walker, and music on the show is from Blue Dot Sessions and Universal. Show notes and resources for this and other episodes can be found at podcast.mindandlife.org. If you enjoyed this episode, please rate and review us on Apple Podcasts, and share it with a friend. And if something in this conversation sparked insight for you, let us know. You can send an email or voice memo to podcast@mindandlife.org.

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