Brain stories Tamar

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**SPEAKERS**

Tamar Makin, Steve Flemming, Selina Wray

**Selina Wray** 00:02

Hi everyone and welcome to UCL brain stories. I'm Celina and I'm here with my co host Steve on brain

**Steve Flemming** 00:09

stories, we aim to provide a behind the scenes profile of the latest and greatest work in neuroscience, highlighting the stories and the scientists who are making this field tick.

**Selina Wray** 00:17

We don't just ask about the science, we ask how the scientists got to where they are today, and where they think their field is going in the future.

**Steve Flemming** 00:28

It's a real pleasure today to be joined by Professor Tamar makin, who is a professor in cognitive neuroscience at the ICN, the Institute of cognitive neuroscience at University College London, and she's the group leader of the plasticity group. So welcome, Tamar, thanks so much for joining us.

**Selina Wray** 00:48

Thanks for joining us,

**Steve Flemming** 00:49

we usually kick off these interviews by asking our guests to say a few words about who you are, and what do you focus on in your research?

**Tamar Makin** 01:00

Okay, so I'm tomorrow. And the question that has been inspiring most of my research, is the question of cortical reorganisation. So let's take a brain area that has been carefully crafted many millions of years of evolution, and maybe even in early development to perform a very specific function. And the function I care most about is hand function. Now let's take a person who doesn't need hand function, because they don't have a hand because they lost it, let's say computation. The question I'm interested in is, given this redundant brain resource, can we make this hand area carry out a function that is not the one that it was originally designed to carry out? So maybe instead, it can support feet in order to increase the dexterity of the feet? Or maybe it can do something completely different, like controlling an artificial limb? So if we could, as neuroscientists harness this process of urbanisation where we can mix and match brain powers based on demand, we could potentially offer a really incredible tool for society and for the clinic. But the more work on bringing your organisation, the more disenchanted I am with this notion. So maybe the question that has been more useful to ask in recent years is okay, given reorganisation is not a real promise? What can we do with these redundant resources in order to improve the clinical care and quality of life of people?

**Steve Flemming** 02:43

It'll be interesting, maybe at some stage to get into your disillusionment, maybe later on. But I just wanted to go back to something you said there about, just so for our listeners, they kind of understand where you're coming from, with this research. So you mentioned the hand area. So maybe you could just say a little bit about what area of brain you're focusing on there. And what do we know about its anatomy? What kind of questions are you currently asking about how that part of the brain works.

03:10

So hand function is straight up one of the most important, necessary functions that the body affords. And in order to achieve hand function, it's not enough to just be able to get tactile information from the hand, or just be able to control the fingers of the hand and the rest and so on. You really need the court is coordinated orchestrated synchronisation of inputs coming from all systems, including vision, which is also really important for a function, and all the way to water intent and what people are trying to do with their hands. So the input and output primary areas of the hand are primary somatosensory motor cortex. And right there, there's this great big cortical patch that is dedicated to input and output from the hand. And it really benefits from Prime cortical real estate, because it is connected to lots of premotor in association areas, cerebellum, subcortical, structures, lots of D synaptic pathways in order to direct and control them. So it's a really great area in terms of structure.

**Steve Flemming** 04:23

When you say, real estate, so the homunculus, I guess, is important here. So the idea that in the brain, there is more or less territory of cortex that's devoted to different areas of the body. And so for you, the hand is, I guess, one of the biggest areas of expanded cortex.

04:44

Yeah. So it is probably the biggest territory if we factor in how small the physical hands are. But it's not just the size of the cortex, it's also the connections. So you know, if if we had To sell brain areas based on where they are along the sensorimotor stream. And most of us would want to, we want to put some money on the hand area.

**Selina Wray** 05:10

It's the zone, one of the brain. And so what happens? You alluded to this in your introduction, but I, and it might be a part of your disillusionment. So I'm diving straight in there. But if somebody does lose a limb, if they lose their hand, how does that affect the the kind of function of that area of the brain is this why we have phantom limb syndrome picks, the brain still feels that like that hand is there.

05:41

So just to just to highlight sensory motor cortex is great, but as we said, it's not enough for him to function. So hand function is highlighted across multiple systems in the brain. Even the visual system has its own kind of territories where there seems to be strong selectivity for visual representation of the hands. So if you lose your hand to an amputation, you have a network of brain areas that are essentially unemployed. And intuitively, you might expect them to shrivel up and die. But that doesn't happen. And what if you read the textbook, what the promise, especially for the sensorimotor areas is that these areas would be taken over or conquered by other neighbouring territories. And it is this process that makes computation and sensory motor system unique and different from other situations, for example, blind individuals. So according to the textbook, and again, I think the textbook is inaccurate to wrong, but according to the textbook, if you lose your eyesight, late in life, you know, once once the once the system has been kind of set up, once the blueprint has been realised, correctly development, you can't you can't do much to change it and it becomes kind of redundant resources. But in the sensorimotor system, maybe and I'm just speculating, maybe because our trajectory for development model development is much more protracted and vision rotation, and other basic functions. The idea is that there's a lot more scope for learning plasticity and reorganisation within the sensory in the motor networks. And the idea is that the territory of the hand would be taken by neighbouring body parts. And there's been lots of theories and speculations about whether this process is adaptive, whether it would be helpful, you know, provide people with superpowers to cope with a disability because they have now increased computational resources in order to support by the function. Or, and unfortunately, that's the dominating theory today, that this amount of change at this amount of scales so late in life is going to be maladaptive. So the brain wouldn't know how to interpret these conflicting signals. And this has been speculated to be the trigger and cause of phantom limb pain. So the sensation of pain arising from the bony part that is amputated.

**Selina Wray** 08:22

I find it fascinating. So how does this then interact with the idea of prosthetics, I was sort of reading it in advance of his recording this a little bit about the third film project. So maybe I can ask you about, about in your own words, rather than me asking a silly question.

08:40

So the notion of organisation whether it's adaptive, or maladaptive, and working with amputees raises lots of questions not just about Phantom Pain, where there's heaps and heaps in literature about the relationship between organisation and pain, but also the notion of adaptive plasticity, that you could do something with the resources you have. And of course, artificial limbs is a big part of it. So if you go into the nature of prosthetics, there's a very strong interest and ambition from the biomedical engineering community to try and interface the technology, the artificial body part with the infrastructure that is already available in order to represent our hands and our body. And the notion is pretty simplistic. We tend with retirement embodiment, the idea is that we, if we could piggy bank or take advantage of the resources that are already there, in order to afford hand function, then this would potentially make it much more easy for the brain to learn to control the artificial body part. So there's been lots of interest in how to physically interface the artificial limbs with the body, through the periphery or through direct Brain machine interfaces. But just as important is cognitive neuroscience questions about how would it feel for the user to control the process? Would it feel intuitive? Would it feel like a part of them? Would it be? Would it be possible to generalise all this rich knowledge that we already have about what it's like to operate our own body in order to support motor control of an artificial body plant. And, again, you know, starting to think more critically about these ideas that are very intuitive and very appealing, by the practice, don't necessarily work. Because an artificial name is, by definition, not the body part, it is very different in the functionality that it affords and how it's being operated. And this could be a technological barrier, maybe one day in the future, we don't have sky look. Look Skywalker arms. But but maybe it's a conceptual problem. Either way, if you free yourself from this notion of embodiment, if you stop trying to be biomimetic, meaning mimic the way the body solves these problems, in how you design your technology. This opens up really cool opportunities, for example, about making an artificial arm to be more than just the biological arm, either know, allowing you to maybe have like super strength and tell it operate your house, or whatever you want to do, because it's technology, right? So we're no longer limited to financial plan. And then, you know, if you're drawn to this idea, then the road to saying, hang on, why do we have to chop off our limbs in order to get superpowers is really short. And then you're like, hang on. So can we create artificial body parts that can do things differently, or, or just, you know, just more then compared to our biological body parts. And this was the short road, we've taken to what we call Mater augmentation. So trying to achieve more or beyond what the biological body body affords. And this is a really, really fun, and very novel topic that introduces completely new research questions for cognitive neuroscience that I don't think anyone had to worry about before. Like, how do you control a body part that you've never had before? Or where it wasn't even designed to have through your blueprint for your genetic template? How do you provide feedback when you've controlled this new body part? How do you learn to use it? Can you? Can we take principles from the body? Or do we have to, you know, to come up with new models in order to represent these technologies?

**Steve Flemming** 12:58

With a third term project? What is it that you're actually asking people to control that is novel in your experiments recently,

13:05

so the third time is a prosthetic device designed by the wonderfully talented prosthesis designer, Danny Claude, who is part of our lab. And Danny designed an opposable thumb, which was a third time because it goes on top of your biological already functioning science. So the thumb would be attached just under your pinky. So it is it mirrors your biological exam. Currently, depending on the version, it is controlled by two or three degrees of freedom, which are operated through your toes. So we put sensor pressures underneath your big toes, which would allow which will allow you to flex extend, or adaptive duct, the thumb, the Fed down, is a surprisingly intuitive design. So within a couple of trials, so one or two trials, people can already achieve very basic, grasping within five minutes, they can already coordinate the movements of the third time with a biological hands, I should say, the family's proportional control, meaning you can pretty much afford any movement that you want with it. And this provides us with a very simple and beautifully designed model to ask, what would happen to the way people operate their own biologic content, when we give them the opportunity to achieve daily tasks in a completely new model?

**Steve Flemming** 14:39

And this might sound like to be questing, I'm just immediately thinking about the trade offs with the foot so can people learn to kind of walk and not activate their new theatre?

14:50

So this is actually a study that we're currently setting up trying to look at? Side effects for the toes at the moment Most of the tasks are being done while people are stationary. So we're we're not providing pure augmentation because we have to trade off one function which is walking, and maybe bands to an extent, to afford another function, which is this extra time. But other labs and other projects are trying to think about the opportunity to provide additional motor function without impairing another one. It's just a much more difficult and less intuitive endeavour.

**Selina Wray** 15:31

And how would this contrast with again, I was sort of reading a little bit of background just to get myself familiar with the work you do? And how does this contrast with the way the brain deals with those using tools, for example? So I think he had a recent study about litter pickers, is that right? I was reading about, and I've never, I've never thought about it in this way before that, when we use something that's hand operated, whether it's a screwdriver or something like lit picker, how does your brain kind of deal with that. So how is how the third thumb would, would would work different to how we'd use

16:12

a tool. I think the thumb and other augmentation devices have some shared attributes with tools and with prosthetics, but also their unique attributes. So where the attributes are shared is that both for a tool and for an augmentation device, you're trying to enhance your motor abilities. So with a tool, you would do something that you can't do with your hand because you don't have the strength, or you don't have that experience. And same goes for the for the exam, you can, you know, for example, grasp bigger objects or multiple objects or do several things at the same time. But this is where the analogy ends. Because when we use a tool, we manipulate the tool with our hands, at least traditionally. So similar to the discussion we had about the toes you to an extent give up your hand function in order to afford another function with the tool. So a litter picker is a good example. So you perform something with your hand at the tip of sorry, the grasper of the tool, in order to operate the tip of the tool. With the thumb, we actually invite you to operate your hand in a complimentary way to the exam. So you have you have your full ability from your hand, we don't take away in your feet, and you don't have to adapt it in order to operate. So themself or the augmentation device. Instead, the exercises to extend your motor repertoire, in order to figure out new ways to take advantage of this extra body part. And cognitively, I think it's much more complicated process because it's not just motor skill. And it's not just the creativity to be able to operate the scale. It's, you know, kind of coming to the prefrontal cortex and you know, Steve's expertise about thinking about, you know, thinking about more ambitious goals and how you'd like to achieve them. So you really need to kind of, in a sense, build new building blocks to your motor plan, which is quite complicated.

**Steve Flemming** 18:27

So I've got so many questions, but operators, we also want to have some time to talk about you as a scientist and how you got into this field. So I guess the short question is, have you always wanted to augment the human? longer, longer question is, what can you tell us a bit about your route into science? Like, where did you? Where did you get started,

18:52

um, I start to getting interested into the body or in my undergrad. So I guess compared to people in the UK, I started pretty late. So I started my undergrad when I was 23. Completely standard for Israelis, but very unusual here in the UK. And the advantage of starting at 23 is that you've had multiple years to kind of examine within yourself, where are your passions? And what are your interests and you know, you work at a few jobs and you do a few things. And you know, it comes with a level of I think, maturity and resilience. And I started working on body representation in my undergrad. The first thing that grabbed me back then was the rubber hand illusion, which I've grown to hate. So we want to talk about today but I have too many friends who will have a stake in Robert handy. Okay,

**Steve Flemming** 19:57

all right. We were just

20:00

When I was doing my PhD about hen centred body representational, or hand centred or presentation of external objects more accurately. So we know that in order to, you know, manipulate objects, we need to have a reference frame of the hand and how it moves in terms of, you know, the the muscle scheme and so on. But we also need a representation of the object in space, and we need to interface them. And I was working on and network of areas that seemed to have this inherent information of the objects relative to the hand stored online so that as you move the representation of the object changes, and that led me to ask out of curiosity, what would happen to people that don't have a hand? Right? I mean, would that mean that they represent visual information differently? And the hypothesis was yes, because because of my previous work. And as a side project, I just got into, you know, this this project, looking at visual presentation in people without a hand. And I got my answer mice, and it was yes. Like, it was a tiny, tiny, tiny effect. So you know, they're the visual distortion about one degree over 60 degrees, peripheral vision. But getting to, you know, meeting people with an upper name, amputation was a really extraordinary experience for me, because they are the most optimistic, you know, like level headed, lovely, inspiring people you can imagine. And I've noticed that whenever I was coming to the lab, you know, when to test a participant, I was kind of leaving the lab feeling like, the world has to be a better place than I think it is. Because these people are just, you know, they're such an incredibly positive and supportive attitude. I mean, they've already been through so much, and they have to cope with so much and yet they find time to come to my lab to take, you know, party mindset medical study. So by the end of my PhD, it was very clear to me that I want to continue and work with amputees, and that they provide a really interesting model to ask lots of questions about brain plasticity. But this experience also made me realise that I want to do work that has impact, I don't want to do work just for intellectual curiosity, there has to be a clear path towards impact. And this means I can't work on small effect sizes. So one degree out of 60 is just not something I can I can work on. So that really drove me to think about larger effects and methodologies that allow me to see effects in single subjects.

**Steve Flemming** 22:55

That's really, it's really interesting you say about effect sizes, because I feel like I mean, saline is more on the clinical side of things, then I feel like in psychology, in basic science, we often lose sight of the fact science, right. So there's so much focus on whether you've got a significant result that people kind of sometimes minimise whether it needs to be also a big effect to be interesting, right. And so I think that's a really useful corrective to have for everyone's research. But I'm just wondering, it's something else that struck me while you were talking, there was something you mentioned earlier was this, it sounded almost like you've had a, a bit of a fight to change the textbook way of viewing things, and actually that this could have an interesting intersection with how much optimism you could expect from say adopting a novel prosthesis and, and so on. So just wondering whether you could say something about, like, has that been a fight? Has that been difficult, politically within your field with how has that played out?

23:53

I had incredible timing. Because when, you know, when the textbook was being written back in the late 80s and early 90s, the concept of brain reorganisation was really dominating in clinical research, because the idea was that if you know, we can potentially guide our participant, sorry, our patients from neuro rehabilitation. To do more with what's left on the brain this this is until today very, very prominent in treatments for something like phantom limb pain or stroke rehab. So everyone wanted to find reorganisation. You know, the clinicians wanted it. The funders wanted it. The scientists wanted it the patients wanted it because that was the promise of neuroscience research. But when I started working on these old questions, this is when you know the renaissance of brain computer interfaces started. And to do a brain computer interface. The last thing you want is your organisation. Because imagine, you know, opening someone's brain and sticking electrodes just to find out that oops, it's been reorganised, it can no longer control an artificial limb, right? So suddenly there's a big sociological pool away from your organisation. Can you find this evidence that even if there's reorganisation, maybe it's incomplete. And I found a lot of attentive audience to kind of, you know, to hear my side of the story, which is, you know, previous evidence has been misleading. I think it has been misleading for political reasons, not not because of because of science. But actually, if we come with a new paradigm, then there's, you know, ample evidence against your organisation for stability of the brain. And the added bonus of brain stability is that when you're designing technologies, you don't want to, you know, you don't want to customise too much you want you want participants, you know, buying by to be pretty similar to each other. So it's, it's, it's a great advantage that you can count of something that is shared no matter what, how long it's been since you were amputated, or what were the circumstances by which you lost your hand function. So on that we all have the same shared infrastructure. So with that, I've had great success. Phantom Pain is a different story, trying to change, trying to change the paradigm for phantom pain has been a lot more difficult.

**Selina Wray** 26:31

And so then looking forward, maybe tomorrow to sort of next five years, what are your kind of big questions that are coming up in your lab and the areas that you're most excited about? It's not

26:45

fair, because augmentation is so much fun. That it makes me feel like I'm going to neglect in my answer mind my other very important questions. So

**Steve Flemming** 26:58

you don't want to have a favourite child.

27:02

But augmentation is fun, because like, everything is kind of for the first time, and there's just so much opportunities for cognitive neuroscience, that hasn't haven't been, you know, explored yet. So it is truly, you know, it feels like you know, we're pioneering a new field that has, you know, kind of my wish list, it has societal impact is going to change the way we're going to interact with the world, it affords so many exciting completing other solutions for clinical care and rehabilitation. But also, it gives us a new model to ask really basic questions about the brain in the body and what it means to be a body part. And how do you learn to control the body part. So it's just such a great research programme, but it's not the only one. So I do have other children. Were actually literally doing research in children that were born with hand malformations. This is such a difficult project, working with kids is so challenging, because they're not others. You can't just, you can't just tell them what you need from them, you know, but their families in the case has been incredible. And we are now scanning children of increasingly young ages. And I'm super excited about this, because all of the research pretty much, you know, all of the research on the sensorimotor plasticity is retrospective, because we're looking at adults, and we're trying to speculate what happened at the time where the brain was being shaped. And now we have the opportunity to actually track these changes as they unfold. And that's really, really exciting for us. And then lastly, my my nemesis, phantom limb pain. It's a terrible infection, that doesn't go away. incredibly common. We don't know why it happens, how it happens and how to treat it. And I think there isn't a big failing so much it's it's making a meaningful impact on treatment for Phantom Pain is that I haven't been able yet to come up with a successful treatment. So you know, I can I can shout through the rooftops that what I was doing is wrong. But until I provide an alternative, I don't think anyone would have a strong reason to listen. So we're trying to understand why why people have fun to play and how we can modulate it.

**Steve Flemming** 29:48

I was wondering about the augmentation, whether there's limits on this and because the reason I ask is because there's a lot of hype around the kind of neuro tech space I'm thinking about you Elon Musk and so on about kind of all we're going to need to do is plug you in and you can interface with language. So I'm just wondering whether there's, you know, can you can does your science that's like taking a very rigorous step by step approach on the motor system tell us anything about like the limits of that beyond motor control.

30:21

So just for the record, Elon Musk's is doing amazing, serious work. Yeah, they're not It's not high. So they might pitch some of it, as you know, is very kind of cool and funky, but during the legwork, ya know, a lot of serious work

**Steve Flemming** 30:41

was not okay, maybe my question was reading between the lines, maybe it's not that I didn't mean to say they weren't doing serious work now. But the promise is are big. Right. And so what I guess I'm asking you to do is speculate on whether those are over promises or reasonable ones.

30:57

Yeah, I mean, but we always over promise, we over promise done on reorganisation, I think, you know, this is the natural progression of every field, we over promise to get resources and to get interest and excitement. And then we do the hard work. And then we come up with the, you know, with the fine print, and we come up with a more mature realisation of what the field can promise. So there's a lot of promise right now, but I am not worried about it. Because we are committed in a logical perspective so far away from the labouring right now. But it's okay to you know, to get carried away with some over promises. But having said that, I you know, I sit on this forums about, you know, enhancement and augmentation. And, and people do get carried away, because I think it is on us alongside developing an appetite and excitement for the technology, also thinking about safety. And, you know, we mentioned kids, for example, there's hardly any research looking at how these technologies are accepted by kids, and whether they could have more serious side effects on them because of their critical period of development in terms of brain plasticity compared to adults. So this is something that, for me is, you know, it's the same question, because we asked him always, what are the opportunities, but also automating mutations for these technologies. So this is work that needs to be done.

**Selina Wray** 32:24

It's been an absolutely fascinating conversation. And I think what I've enjoyed most I mean, apart from the fascinating science, your enthusiasm for it really shines through, and also your desire to kind of do something, I really love that phrase to do something not just for the sake of being an intellectual, but to do something that really has, has impacts. So even though my field is completely different, I'm sort of leaving the recording, feeling quite inspired to go and make a difference in my own area as well. So thank you so much for sharing your insights with us. We asked you, Oh, absolutely. We always finish with the same question, which is, could you give us what your your favourite fact about the brain?

33:08

This fact I think, tends to be missed a lot by neuroscientists and cognitive neuroscientists. The brain is actually housed within our body and is designed to protect our body. Often times when I talk to cognitive neuroscientists and proper neuroscientists, they tend to talk and think and study the brain, as if we're brains in a vat. And I feel like you know, this fact is too often missed that you can only study the brain within the context of the body, and how using the brain is going to affect your day to day behaviours.

**Steve Flemming** 33:52

I think I'm often guilty of thinking in terms of, so I often need a reminder about this. Thank you so much to our making for tourney's On today's episode of prey stories, and thanks to all our listeners for listening, and we'll see you next time.