### Voiceover:

As neuroscientists, our research is at the heart of our everyday lives, from designing experiments to analyzing data, to writing grants and journal articles. This work brings us closer and closer to understanding the most fascinating and mysterious part of our bodies, the brain and nervous system. But for neuroscience to have the greatest possible impact on our world, it must be rooted in a strong foundation of rigorous principles.

#### Voiceover:

You're listening to Pathways to Enhance Rigor: A Collection of Conversations, where neuroscientists come together to discuss how to embed rigor into every part of the scientific process. This podcast is a part of the Society for Neuroscience's Foundations of Rigorous Neuroscience Research program, or FRN. Supported by the National Institute for Neurological Disorders and Stroke, FRN is designed to inform and empower neuroscientists at all career levels to enhance the rigor in their research and the scientific culture. At large. In this episode, we hear from Drs. Christie Fowler, Olavo Amaral and Kip Ludwig. They discuss sources of bias that can affect experimentation or interpretation of results and the considerations neuroscientists must face to conduct research while minimizing bias and maximizing objectivity. Without further ado, let's hear about Battling Bias in the Pursuit of Objectivity.

#### Kip Ludwig:

My name is Kip Ludwig. I am an associate professor in the departments of biomedical engineering and neurosurgery at the University of Wisconsin-Madison. And my research focuses on small implantable devices to hijack the nervous system for diagnostic and therapeutic use, the translation of those devices and the basic neuroscience understanding to make them better.

#### Olavo Amaral:

My name is Olavo Amaral. I'm an associate professor at the Federal University of Rio de Janeiro, Brazil. I used to be a neuroscientist full time, studying the neurobiology of memory in rodents, but these days we mostly do meta research applied to research reproducibility. We currently coordinate the Brazilian Reproducibility Initiative, which is a large systematic multicenter replication of published experiments in Brazilian biomedical research.

#### **Christie Fowler:**

Hello, my name is Christie Fowler. I'm an associate professor in the Department of Neurobiology and Behavior at the University of California Irvine. My laboratory research focuses on animal models to determine the circuit and molecular genetic epigenetic underpinnings of drug addiction. And we really focus on animal behavioral models. I also serve on the editorial boards for J Neuro, eNeuro in Neuropsychopharmacology.

#### Olavo Amaral:

The exploratory/confirmatory distinction comes from whether you have a very clearly outlined hypothesis to test. From the point of view of statistics and science, actually, you can not form a hypothesis and test it with the same data. So if you were looking for a research to be truly confirmatory, you should have everything outlined from the start. Not only a general hypothesis, but a very precise way of measuring things, of analyzing things. That said, obviously you're not always going to be sure when you start what's the best way to look at data. Frequently, you have to learn as you go. You collect

data and then figure out how to best analyze or normalize something to get an answer. But of course, if you have infinite ways of analyzing data differently, you can always find what you want.

### Olavo Amaral:

It's hard to talk about statistics as we tend to use them being valid when you can tinker with the data in a lot of different ways. So we probably did both. You do need to learn from your data and to help your data generate your hypothesis, your analysis methods. So that is what I'd call exploratory research. But at some point, you want to get to a more confirmatory mode in which you have a very, a predefined way to measure and to analyze something. And then you have to have a severe test of your hypothesis that it can really be more confirmatory in nature.

## Kip Ludwig:

I think that was a great general explanation. I come from a clinical trial background. And so the standards are a little bit different than basic science animal or benchtop research. And so typically for a confirmatory studies, we are typically looking for studies that have been pre-registered with specific primary outcomes and the analysis methods also pre-specified as part of that. But the distinction blurs when you get into nonclinical studies or for clinical studies that aren't for regulatory approval.

## Christie Fowler:

So I think it's important to derive some pilot data that you're going to be able to have a clear plan to go forward with the confirmatory study. At that point, it's important to then take a step back and really start to think about and preplan what you're going to do for the confirmatory study, thinking about the experimental design, doing power calculations, inclusion/exclusion parameters is really important blinding conditions, we're going to talk about that later. But all these different factors to ensure rigor and reproducibility are really important to plan from the outset. And so when you get to the end of that study, you can have high confidence in your findings, and it's going to be something that's going to be able to be published in a high tier journal.

# Olavo Amaral:

Yeah. For the sake of transparency, I guess the ideal way to make it clear when you go into this mode is actually to preregister your confirmatory experiment. There's various ways to do this. You could just preregister it and leave it at a repository. It could be public, it could be timestamped, just to make sure this was written out in advance. There are other forms. Journals have been experimenting with the registry reports system in which you submit your methods, your analysis plan for peer review. I think that would be an extra step towards pre-registering and making things more confirmatory. You don't have to always do it. And you certainly cannot do it for everything. There are going to be exploratory experiments, maybe your whole paper will not be confirmatory in nature, but once you get into this mode, I think it's important to be transparent that you're switching gears from one thing to the other.

# Christie Fowler:

I would just say, I agree, that's a really kind of interesting concept to pre-register. At eNeuro, I have reviewed papers in which they have done that. And so it's really nice because they lay out all the studies and they preplan it. And regardless of the findings, it's going to get published with that format that they have set up there for that pipeline. So just by taking that extra step upfront, you don't have that pressure to find one way or the other because whatever comes out is going to be publishable.

### Olavo Amaral:

Even if you have preregistered something, nothing limits you from doing exploratory analysis, which you had not thought about before. And then it's fine because then you have made clear that this is exploratory in nature, if I thought of this afterwards. But I mean you're not bound and tied to your preanalysis plan. You can always change your mind. And as long as you make it clear, then this is exploratory in nature.

# Kip Ludwig:

I think all of us can speak to times when we had laid out a confirmatory study, but then due to situations beyond our control, we primarily wound up not being comfortable that the confirmatory study was as well controlled as we hoped, and that it became an exploratory study where there is still very good data to help generate hypotheses that should be tested in the future with confirmatory studies. We definitely do a trial by fire. For us, before we do a confirmatory study, we typically do pilot runs of the majority of the experiment. And one of the most difficult things when laying out your hypothesis and testing it, is really being comfortable that you're addressing all possible confounds, alternative mechanisms, physiological mechanisms you may not have been considering as well as all the possible sources of artifacts and statistical analysis that can be misleading.

## Kip Ludwig:

And so that's why with these retrospective studies, it's very difficult to do a confirmative retrospective study, and it typically winds up being exploratory. And that's because you haven't built it from the ground up to debug it. And that's an important part of our process. We definitely feel that having outside people come in, because you get a little groupthink and you get a little bit of blinders on, to come in and talk about your experimental design at an early stage to say what they would be concerned as a confound, either from a mechanistic standpoint or from a technique standpoint, that really helps you address and debug before you're comfortable doing a confirmatory study.

### Olavo Amaral:

I think one thing we have to realize is that variability is actually good in a lot of senses. In basic science, people tend to look at variability in a very negative way, like it's noise. Sometimes it is noise, it could be just measurement error. But it's like if it's one mouse being different from another or conditions in one lab being different from another, you actually want to include this. Of course, it's hard and it requires work and maybe you don't want to include a lot of variability in your early stages when we're building a hypothesis. It's probably the time to start with a more controlled design with the isogenic mice or with very controlled conditions. But at some point, you want to grow your hypothesis and test it for robustness in slightly different conditions with different methods, perhaps in different environments. And I think this is something positive, which you should be looking forward to as you're trying to get more confirmatory again, in your scale of evidence.

### **Christie Fowler:**

Yeah. I would just really agree with what Olavo said. And to add on that, I think it's really important to consider the representation of the sample. So gender or sex, looking at both males and females. And then when you're getting to human studies, consideration for ethnicity, race, those types of things. I think that within our society right now, we're really seeing that there's this differential being identified in how a lot of the prior research has analyzed and built foundations based on subjects that are primarily of Caucasian descent. And so being able to look across different races really provides information. That's

really essential for us to really be able to have concrete findings that will be applicable to all these different populations that we're really want to enhance the health of everybody. Right?

### **Christie Fowler:**

And so taking that into consideration, we can then limit some of this systemic bias, improve the generalized ability of our research and of our findings. I think that's really important. And then just going back to mouse studies, I primarily work with a certain wild type mouse lines, but I think it's really important to confirm those findings across species. So once we get a really solid finding in mice, we'll then go and confirm it in rats. And once you get confirmation across multiple species, that really enhances the likelihood that that data is then going to be translatable to humans. And so on the preclinical end, I think that's a really important consideration as well.

# Kip Ludwig:

I do love the idea of progressively moving to and showing demonstrations in multiple animal models. One of the things that really formulated how I think about this subject was the spinal cord injury replication contracts at the NIH, which were led by Naomi Kleitman and Shai Silberberg, and I had the pleasure of shepherding it for several years. In which case we replicated 10 major studies in animal models that went to human trials, which subsequently failed. And when we tried to have those replicated to find out whether or not the animal data was not being predicted or predictive of the human situation or whether or not there were some sort of issue at a fundamental level, only about one and a half of those actually replicated when in the hands of another investigator. And the one that I referred to as a half is the most illustrative to me where the separate investigator tried to do the same experiment and couldn't replicate. And then we had them communicate with the original investigator and then they had to redo the experiment to get the exact same genetic line from the same provider.

# Kip Ludwig:

And then they wound up seeing very similar results. And that just went to show you that the therapy that was being forwarded wasn't very robust under a lot of situations. The thing that I keep in the back of my head is always, and this is actually very pointed in terms of COVID and a lot of the early studies we've seen that got a lot of media attention, but didn't turn out to be viable clinically. A lot of early stage studies look promising, but roughly, depending on the numbers that you look at, between 10 to 16% of IND enabled studies for phase one go on to successful FDA approvals through phase two and phase three. And a lot of the reasons is our animal models don't capitulate the long-term pathology, all the drugs that these subjects have been manipulated with to treat over many, many years, and safety concerns. We tend to ignore things that would limit deployment in the clinic in animal models that aren't acceptable in humans. And that jump at the phase one and phase two level kills a lot of studies. So it gets to that general robustness.

# Christie Fowler:

Yeah, I would also add, within manuscripts, to kind of mitigate some of this, I think it's important to add a discussion of the limitations of the findings with regards to the study, how it was conducted or generalized ability, those types of things. I think as researchers and scientists, we want to present this really beautiful piece of work that's without flaw. And we all know that with everything that we do, there's some considerations or confounding variables that we cannot control for. So just having an open discussion of that within the manuscript, when it's being submitted, whether it's, "Oh, this was done in one line of mouse and we haven't looked at other mice," or whatnot, I think that can really provide guidance for future people when they're looking at those findings. But also when they're going on to conduct their own studies. And along those lines, giving some indication of future studies that will be really essential to further extend or confirm the findings is I think really nice to add within the manuscripts.

## Olavo Amaral:

Yes. I completely agree with Christie. I think an extra thing is like limitations should not be limited to the limitations section. People usually do like a title and an abstract, which can be very overgeneralizing. And then at the end, stick this in, just a limitation section, just maybe hoping that nobody will read it. This goes from the start. You should be clear up front. Your statement, like your opening statement or your title, should actually, I mean, of course sometimes it's hard to reflect all the limitations. They don't want to have a title that's like, "In my lab, this happens." But you should keep this in mind for the whole writing of the paper and not only the limitations section, I guess.

## Christie Fowler:

Yeah. And I would just echo that with the several journals are now requiring a significance statement and you do see a lot of overgeneralization of findings within the significance statements. So again, just taking an assessment and is this really an honest statement that really represents the work that's being presented? I think that's really important.

## Christie Fowler:

So yeah, so I think minimizing bias in your work is really essential and important. There's a lot of ways that we can do this in the research environment. For example, blinding, it's really important that certain researchers don't have information as to the expectations of the outcome of the study or even what the groups are. So having group ID numbers or subject ID numbers that are very vague and don't explain what the group is. And so sometimes that's not always possible with the experiments that we're doing.

### **Christie Fowler:**

And so having multiple levels of individuals that have information can then come in to be really important with that. And so one person might know those, the unblinded conditions, and one person might not. And so now you have cross-check. The other way we can do it is through automation. So there's a lot of different application software out there that'll allow for automation of behavioral assessments and that kind of thing. And so just having it being automated really kind of takes away some of those implicit biases. And I think it's really important to recognize that we all have these implicit biases. We like to think that we don't, we like to think that we're like really hardcore scientists and we would never have implicit bias. But we have motivation to find really important things because that's where our funding comes from and how we publish papers and that kind of thing. So just recognizing that you have the bias and then doing things to limit the likelihood that that's going to get into the study, I think is important.

### Christie Fowler:

Another way that we can do this is through inter-rater analysis. So having multiple people do the same assessment and then comparing their differences. So we do this a lot with our behavioral studies in which we do not use automation, two experimenters will do that, will compare it. If the same findings are found with both assessments, then we'll go forward with the data. And then also training raters is really important. Being able to have people be trained by experts. I always thought that was something

that was interesting in science is that we spend our whole career getting to this point where we're so good at so many things, we have all this expertise. Then we hire people to come into our labs that don't have that expertise and we sit in our offices. So just, as a PI, I really like to take the time to actually train a lot of the people on the really essential tasks that I know can be really difficult to score. And I think Kip had some thoughts about this as well.

### Kip Ludwig:

First of all, I absolutely love that answer, both in terms of observer bias is underappreciated. And ways to automate, ways to cross-check and ways to get people who have no vested interest looking at that data as many ways as they can do that, that's a really, really important part of the process.

## Olavo Amaral:

Yeah. I also agree that implicit bias is huge for scientists, we're humans. So we should be aware of it. And some things should be the default. Blinding should be something you do by default, unless there's a very, very serious reason not to do it. That said, it is not the case. People who have looked at the prevalence of studies in basic science, in preclinical research that do describe that people assessing outcomes are blinded are actually, these studies are actually the minority in the vast majority of views. So this is something that is simple, but we have not yet made standard, and I think that is a major problem. I think bias comes in acquiring data, I think bias comes in selecting data.

## Olavo Amaral:

And a huge problem in bench research, it's like a lot of stuff goes wrong and it's very easy to throw an experiment because, "Oh, this didn't work. This is methodologically flawed." And that opens up a huge avenue for bias as well because whenever something doesn't really look like what you were expecting, you can just say, "Oh, there's something wrong. Yeah, the controls look funny. Yeah, it was too hot in the lab or whatever." And people throw away experiments very easily. So I think these things should be thought of at the start of the experiment, like what are your criteria for keeping data, for throwing data away and trying to stick with this. If you can preregister, that is ideal. Bias in analysis is also huge. But again, I think pre-registering analysis helps. I think having outsiders blind analysis from someone external to the lab is also important.

### Olavo Amaral:

And I'll just add bias is not the only problem. Noise is huge, especially if you can select experiments or select what you're going to include in the paper. So I think we do underestimate the effects of low statistical power and just random variation across experiments and sample size calculations, and knowing what effects you actually expect to find with your pre-planned sample size, I think is important. And a lot of the non-reproducibility between results is really just random statistical fluctuation which goes above or below significant threshold. So I think you should be aware that besides minimizing bias, you also have to be aware of your limitations in terms of like how far will your sample size and your variability get you in terms of being able to generate strong conclusions.

# Kip Ludwig:

There's a push towards new tools, the NIH Brain Initiative, next generation, calcium indicators, different brands of genetics and different options. But we're learning that new tools typically aren't as well characterized, especially for all the uses they might be done. There've been some really interesting studies in the cochlea showing that when they use channel rhodopsin that natural physiological signal, actually it changes the natural behavior in chronic situations. There's some slow channel leakage. And we're learning more about these tools as we use them. So I think in terms of sources of bias, often people want to use a new tool because it's cool and they're excited, but they're not really doing a hazard analysis of all the possible ways it could create a bias and a confound and then doing the fundamental characterization. And so I think in many cases tried but true tools that are well characterized for a specific situation trump the latest and greatest in terms of scientific rigor.

### **Christie Fowler:**

Yeah, I would completely agree with that, given my experience with transgenic mouse models. So these models are created, these mutant mice, transgenic mice are amazing, amazing tools. But often, when they're being produced, they're produced and then they're let loose on the scientific community without really rigorous characterization. If those modifications have resulted in a change in the endogenous state of the animal, for example, with Cre-driver lines. And so, yeah, and I think as a new PI, I was really excited to use all these new tools and techniques. And for me personally, that actually put a big bump, negative bump I guess, in my progression during the early years, because I had to take a step back and do a lot of characterization in mouse models to be able to then use them and have faith and reliability in the data.

### Kip Ludwig:

Yeah. Let me respond to that quickly because I completely agree. And you shouldn't use multiple methods just for using multiple methods. There should be logic and structure to your reasoning, and you should only use it if it's well vetted. Two wrongs don't make a right here for scientific rigor.

### **Christie Fowler:**

Yeah. I think in an ideal world, if we're really trying to get to optimal experimental design, looking at the experiment from the start and really taking the time to preplan is really essential. But I think there's a different component here in that we spend perhaps five, six, sometimes seven years a project, and we have to distill that down into a manuscript that's a couple of pages in a paper. And it's really difficult for us to really highlight all of that, the intricacies of the experiments and the conditions that were done. And so I think in the future, it'd be really amazing if we got to a point with publications in which we could have supplementary online material in which we can go into more of the conditions and we can talk about things that may or may not have affected the study and just to put it in the context of the research.

### Christie Fowler:

And for example, with circadian rhythms, we see differences in hormonal fluctuations throughout the day, throughout the year even. And so the time of testing during the day is really important. In our studies, we use a reverse light cycle, so we test the animals during their dark phase when they're most active. However, other labs don't do that. And if we're trying to compare data across labs, we might not even recognize that that could be a confounding factor. And so I think being able to really more fully discuss these things. And now this is up to debate if that's something that a reviewer would evaluate with publication. I would say that maybe keep the reviewers evaluating the research, but have these additional considerations here so that people can dissect them out.

### Christie Fowler:

In that respect, I think that J Neuro has taken a step in having a bio protocols. And so if you submit a manuscript, it's accepted, there's a new protocol that you've designed to do that research. Then you can publish in bio protocols. I'm not sure how that pipeline quite works, but we did it for one of our studies in which we developed a new protocol for choroid plexus cell culture. And so having that, now you have the second outlet to really go into more of the methodological details of the research and how that protocol was developed in the more specifics of it. So I think that's really great. And I think that there's some steps that are being taken. So for example, having the RRIDs, which is a resource identification initiative, in which we have these numbers that we can cite and identify key resources, whether it's a model organism, a tool like a software or technology, antibodies. And just encouraging everybody to use these RRIDs so that we can then cross reference and really have a better understanding of what was actually done, what was actually used in that study.

## Christie Fowler:

And so if we're trying to replicate that study so we can build off those findings, we have a really solid foundation from which we can start.

## Olavo Amaral:

I think there's a big question of incentives here in terms of... a lot of our incentives are geared at novel, high impact revolutionary research. I'm not sure we're very good at assessing basic rigor, even though we know what basic rigor looks like for a long time, I don't think we have the right metrics for it. Maybe we do have metrics, but we don't really use them. And I think the whole way the scientific rat race is structured as this, is very detrimental in the sense that peer review, as it occurs in high-impact journals, really conflates rigor and novelty impact importance. Right? And in the push for getting both, you can frequently sacrifice rigor for impact and cut corners.

### Olavo Amaral:

And really, it does bug me a lot that you're required to have very impactful research to be considered a good researcher, because most results will eventually not be revolutionary, and will not change the world. And most science is normal and not super disruptive in a sense. If everybody wants to have a very, very novel, very revolutionary...that's important...

### Olavo Amaral:

Impact is important. I'm not saying that this is not a dimension, but it's not the same dimension as rigor. And I think one comes before the other. Impact is nothing if your result is wrong. It's actually bad because it disseminates more quickly. So I think we have to assess rigor in a more systematic way, and that should come from the start. I think we have to put this in the culture of training that before anything, there's basic scientific rigor, objectivity criteria that you should meet to really be a good scientist. And if that is fulfilled, then we can talk about how novel or how impactful your research is. But I think there's a major change of incentives to be made and that should be made since the early days of a scientific career.

# Kip Ludwig:

Yeah. First of all, these are fantastic suggestions. I do agree that the incentive structure is important and really there's a culture issue, to some extent, that is really important to establish in your lab and to establish as a community. I hear too many people trying to, "I want to prove this." The hypothesis needs to be in equipoise and the students need to be empowered to do hazard analysis. They need to be

brainstorming every single way they could be misled or what can go wrong. And that actually happens too infrequently. And that it's completely okay to get down a path and have missed a possible confound and then corrected. There's a fear of failure, a fear that we have to prove something. You want to solve some of those perverse incentives, double pay line that would help a lot. But I think individual researchers need to understand that the people who are really the stewards of rigor is the culture of your lab.

# Kip Ludwig:

It's the undergrads and grad students from the moment they come and have to feel empowered to say, "I'm concerned that this might be wrong," and then you have a conversation with them because several times for me, outside parties and new people help bring in different perspectives that help debug the experiments and identify confounds. And it's okay to miss things. You just have to be aware that you are going to miss things and constantly try to improve, and that's kind of a culture you need to create in your lab for rigor.

### Christie Fowler:

Yeah, I would completely agree with Kip. I think that the culture of the lab is really essential. I think that all students need to feel like they have an equal voice in stating their opinions and being able to discuss research and that they don't have a fear of quote unquote saying something stupid and being ridiculed. Right? I think that having a diverse lab environment, whether that's just diversity with the representation, the backgrounds of the individuals, the ethnic backgrounds of the individuals, where people are coming from, different universities, I think that's really amazing as well, because it gives you more voices and more things and recognizing that we all have something to learn and we're all learning at the same time, I think even the PIs. I think that's really important because it's the team, right? We're part of a team and we're not a dictatorship, but we're really a lab team that we need to push our research forward with.

### Olavo Amaral:

Yeah. I completely agree with that as well. If I can get back to a point that Christie made before, not everything fits in a paper that you wrote after five or six or seven years of project. I agree. But since we aren't in an ideal world, maybe not everything has to be lumped up, like seven years of work shouldn't be in a single manuscript. I think there's a point to be made and I think Christie started to make that about, I'll say atomizing research output. The paper can still exist as a narrative summary of what you did, but your data should probably be somewhere else in a much larger, complete analyzable dataset. Your code should be available and your protocols should be available. This might not all come in at the same time. Maybe you should put this up and publish this in different venues as you go.

### Olavo Amaral:

Maybe one of the problems is the idea that you have to have the one big paper with everything in it. And the idea that peer reviewers should somehow look at all of this at the same time. Maybe breaking this scientific output in smaller pieces would allow a more effective peer review in terms of data. I think peer review as it stands, works okay for conceptual discussion of implications and limitations and general views of the hypothesis. You do not expect reviewers to be able to adequately check data for 40 or 50 experiments in a paper, or to check the code of analysis. It's impossible.

#### Olavo Amaral:

So I think breaking this up into smaller pieces would also help quality control in terms of you can have it in different steps as you go along the way. And of course this costs time, money, everything. So I think in an ideal world, we would be devoting more resources to doing institutional, organized quality control, to have actually people who professionally check, code check data. I don't think the current peer review system actually works for ensuring data integrity. I think it was designed to do something else. And I think we do need a better quality control, and of course we have to eventually pay for it, right?

## Christie Fowler:

Rigor starts with you, but it also starts with the community. And we need to be looking for ways to incentivize rigor, to reward rigor. I don't trust any study until it's been replicated by outside people under different conditions. But we need to be moving towards situations where that's rewarded to do for tenure committees and things like that. And that we see the value for it, as opposed to the innovative new proof of concept.

## Olavo Amaral:

There's a lot to be done and I think it happens in multiple scales. It happens in scales of communities. So there's stuff that you can do by yourself. There's stuff that maybe your lab or your university can do. There's stuff that depends on funders. But multiple actors actually can make this better. And I think we do have simple solutions in a lot of levels. I do think it starts with you as well. And I think a lot of people blame the system, but we are the system, and we have to find ways to fix it. And I think there are incremental solutions, right? I mean, not have to fix the whole problem at once, like doing small steps. "I'll blind my study," is a small step.

### Olavo Amaral:

And like the sum of small steps goes a long way. We can all think about the little steps. And my second thought is I think things have been changing and we're much more aware of those reproducibility issues than we were, five or 10 years ago. I think we're discussing those much more openly and I think this will eventually have an impact in terms of how scientific careers go. I think if you start off being more rigorous now, you will be rewarded in the future, I think. The whole incentive structure will eventually, it is changing already. I think it will eventually change. There's also very selfish reasons for being a more rigorous scientist, but of course those are not the ones that really matter. You really want to produce science studies that is true, applicable and that it can actually change the world in a positive sense.

# Christie Fowler:

So as a final note, I would encourage everybody to really think more critically about experimental design prior to starting a study. A few hours of pre-planning can really save a lot of time in the long run because you don't want to have to reproduce the whole study and waste several months, years perhaps, of time later on. And so really take that time to sit down, preplan, discuss it with others, get other perspectives and then start to execute it. And I think with the pre-planning step, it'll also enhance the likelihood of being able to publish in a really highly respectable journal because they're going to want some evidence of that rigor within the experimental design and you'll be ready to really discuss it fully.

### Voiceover:

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