

PEDIAPOD AUGUST 2023 TRANSCRIPT

Geoff Marsh

Hello and welcome to PEDIPOD for August 2023. This month we look at novel metrics to characterize the temporal lobe size of very preterm infants.

The temporal lobe may be particularly vulnerable to the impacts of very preterm birth. This region of the brain facilitates many complex neurological processes. Alterations to these processes are known to correlate with specific functional deficits commonly found in preterm-born children at and beyond school age. As such, an improved understanding of the nature and timing of temporal lobe disturbance will help in identifying risk factors and in developing strategies to improve outcomes. However, as yet there is not an objective, validated method to assess the temporal lobe structure or size in very preterm infants. In this episode of PEDIPOD, I speak to neonatologist and this month's highlighted Early Career Investigator, Katherine Bell from the Brigham and Women's Hospital Boston. She and her team developed a new method for quantifying temporal lobe size in very preterm infants at term equivalent age, using simple metrics performed on brain MRI.

Katherine Bell

I attended medical school at the University of California, San Diego, and I happened to come across the summer research programme that was in pediatrics and I worked on a project at Stanford University where we were looking at monitoring strategies to look at oxygenation of the brain during heart catheterization procedures for children. And as a pediatric resident I got interested in neonatology because you have a real chance to impact the trajectory of their health. I attended my neonatology fellowship at the Harvard Neonatal-Perinatal Medicine Programme in Boston. And I met my primary research mentor there, Dr. Mandy Belfort who's an expert in neonatal nutrition and the impact of nutrition and growth on later outcomes. And that's where I first got exposed to the idea of what we call the developmental origins of health and disease. So a lot of my previous work had actually looked at how growth and nutrition in the first few months of life in the NICU impacted brain development. And so as I was looking at brain development, we had these brain MRI images that we're taking of preterm infants and we needed to find a way to analyze them to tell us how is the baby's brain development doing and we realized that there were some gaps in the current strategies for measuring brain size and brain development in preterm infants. And one of those was that a particular part of the brain, which is the temporal lobe, the area that's kind of behind the ears on each side of the brain, was something that wasn't captured in previous MRI scoring strategies. And that's an area that is vulnerable to abnormal development in preterm infants. And so we wanted to set out to develop an extension of some of the previous methods for measuring brain size by adding this component of being able to measure the temporal lobe.

Geoff Marsh

So before we get onto some of these new metrics that you explore in this paper, can we just hone in on the long-term impacts the structure and development of the temporal lobe has on very preterm infants.

Katherine Bell

The first few months after a preterm infant is born is a really critical period for brain development and a number of the sort of processes underlying later connections that the brain needs to learn are being developed during that time. And there are critical windows in which if you miss that window, you may not be able to catch up or develop those connections or that growth later on in life. And so it's a really important period for brain development overall. And a number of studies now have shown that the size of the brain or the development of the brain at the time that infants leave the NICU, even after just those first few months of life, does predict later cognitive outcomes and neurodevelopment even years down the line at school age. The temporal lobe in particular is one area that has been shown to be altered in terms of its development in infants who are born preterm when you compare them to infants who are born on time. And there are a number of important structures within the temporal lobe like the hippocampus, which is involved in memory and learning. There's also speech and language pathways. So there are a number of important cognitive processes that rely on the temporal lobe. And so its development during the preterm period is really important.

Geoff Marsh

MRI has been used as a really good, non-invasive way of imaging brain development for a long time, but you're not really talking about any new technology here. You're talking about using the same images that come out from conventional MRI, but basically trying to validate a new method specifically for assessing this temporal lobe structure?

Katherine Bell

Yeah, that's exactly right and I think that was one of the key goals of our project, to create something that was relatively simple, both to understand and to use, that used images that most people would have access to from just a clinical database of MRI, and that a person who didn't have a lot of specialized knowledge about neuroanatomy, and the brain could understand and could learn.

Geoff Marsh

And I don't want to dumb down to the point of getting it wrong, but without getting bogged down in neuroanatomical jargon, is it fair to say that you basically picked up on three different crude dimensions of the structure?

Katherine Bell

That's exactly right. We just wanted to look at can we draw a line from one side to the other of the brain that tells us, you know how long is the temporal lobe? How wide is the temporal lobe? How big are the fluid spaces inside it? And can we use a simple strategy to do that so that it's relatively straightforward to implement.

Geoff Marsh

So tell me a little bit about how you set this study up. Because you had a few different goals, comparing very preterm infants with term-born infants, but also validating your metrics. Just talk us through the design.

Katherine Bell

We actually started out with six or seven different metrics, different lines in different areas of the temporal lobe that we could draw. And we tested them both within ourselves, so we would measure the same baby more than once to see if we would get the same result, and then we also did inter-rater reliability testing, meaning we had four people on our study team, and we would each measure the same image and then compare it to each other and say which of these metrics were ones that were reliable enough that we could get the same result each time. And we started out with probably six or seven different metrics that we were investigating and only three made the cut. So those are the length of the temporal lobe, the amount of fluid space kind of around the temporal lobe and the amount of fluid space within the temporal lobe. And those fluid spaces are essentially spaces where there isn't brain. So if you have more fluid, it represents that the brain could have grown bigger, but it didn't.

Geoff Marsh

And then you were also interested in comparing the temporal lobe structure between the very preterm infants at term-equivalent age and some term born infants.

Katherine Bell

That's exactly right. So we were fairly sure that preterm infants might have smaller brain size than term infants. That's been shown in other areas of the brain and we suspected it would apply to the temporal lobe as well. And another component that we wanted to look at was what are some other factors besides just being born preterm that might impact the size of the temporal lobe. And so we looked at things like what size was the baby when they were born, their birth weight, or their gestational age, and found unsurprisingly, as many other studies have that babies who are older when they're born, so born less early, or babies who are born with larger birth weight, larger size at birth, tend to have larger brains. And that's consistent with other studies looking at other parts of the brain. One thing that I found interesting was that we found that infants who had a longer duration of IV nutrition, parenteral nutrition, had smaller brains. And that generally represents that they've been building up a nutrition deficit during the time that they're in the hospital. So we did see some signs that some of the modifiable things that we can do in the hospital like providing nutrition to infants could have an impact on brain size as well.

Geoff Marsh

What was the comparison between very preterm and term-born infants in terms of that temporal lobe structure?

Katherine Bell

So we saw that the temporal lobe length, which was kind of the primary indicator of the size of the temporal lobe, was smaller in preterm infants. One important thing to do when looking at brain images is correct for how old the baby is at the time of the MRI. And when we apply that correction, we saw that there wasn't a statistical difference anymore between the two means, probably because our sample size is somewhat small, but that the temporal lobe length was still smaller on average in the preterm infants. We also found larger fluid spaces in the preterm infants compared to the full term infants. And as I said, that generally represents that the brain had space to grow bigger, it could have grown bigger, but it didn't for some reason. And so usually, that also represents that there was some limitation in growth of that structure.

Geoff Marsh

So it does suggest that some of those neurodevelopmental outcomes associated with temporal lobe structure changes could be traced right back to those very few days and weeks of life?

Katherine Bell

That's exactly right. And that's been shown in other studies as well, looking at other parts of the brain and longer term outcomes, that there really is this critical period early on in the first few months of life. And absolutely, there's a lot of learning and growing that the brain and the baby does after leaving the hospital but we have a real window of opportunity during the first few months of life in the neonatal intensive care unit to maximize or optimize development as much as possible and I think one of our hopes for this work is that other people and ourselves will be able to employ these metrics in order to study factors that impact on the temporal lobe's development, so that we can optimize what we're doing during those critical months.

Geoff Marsh

But I suppose the usefulness of it is going to increase when more and more people use the same validated method, right? So I guess one challenge is to convince people that this is a good way of doing it and get lots of people on board.

Katherine Bell

And the same thing has happened with other scoring strategies for preterm brain MRIs. There are a number of scoring strategies out there and after their publication, when people start to be able to use them, you can start to see more of the impact or the benefit of using those strategies once we start to show for example that it's related to later outcomes or we can identify factors in the NICU like we did that are related to the temporal lobe that give us some idea of how we might use this information to alter or adjust our clinical care. So certainly, the value of it increases over time as more people use it and one of our goals in publishing it is to allow other people to use these same metrics so that we can learn more about how they might be useful in research and understanding the brain.