

ECNP special news feature: interview Tom Insel

[Tom Insel](#) is the Director of the US National Institute for Mental Health. The ECNP invited Dr Insel to visit our annual Nice Workshop, where he spoke to a packed audience of young researchers. Afterwards he spoke to Tom Parkhill.

[Dr Insel, What brings you to Nice?](#)

The ECNP. It was really the opportunity to be part of this special ECNP session for young investigators. How impressive! I don't know of anything quite like this where we have brought this many of the best and brightest students and post-docs from across Europe to spend 3 days with some senior investigators. The young investigators have the chance not only to present a poster, but an oral presentation. It's a terrific environment, and I'm delighted to be a part of it. This is our future -- each one of us needs to think about how we can make sure that the people coming through this next generation have every chance to succeed.

[And as you say, this highlights one of the differences between what is happening in Europe, and what is happening in the 'States. Are there any other differences you can see?](#)

There are. In the States what we see now is that the best and brightest of the M.D. - Ph.D. students coming out of medical school with a degree in neuroscience all want to go into psychiatry. In the UK now, there's a real crisis to get people with deep scientific training into psychiatry. In the U.S., neuroscience is the hottest area for undergraduates who have any kind of interest in psychology or behavior. The result is that we have this whole new generation of people going to medical school, some of them fascinated by autism, some focused on mood or schizophrenia, but all excited about brain research. It's just remarkable when you see the quality of young people coming into the field. I don't think that has fully happened yet across all of Europe. But it's beginning to happen, so you do see people who have this interest in neuroscience or molecular biology who want to take on a very complex problem like autism. What about the physicists, the engineers, and the mathematicians who can also tackle these tough problems? We're just starting to see people from these fields attracted to solving the problem of brain disorders in the U.S., but I haven't seen that yet in the EU.

[You mentioned autism, and I've read that this is one of the areas you have put a lot of effort into?](#)

Well for us, autism is a sort of prototype. We think of mental disorders today as neurodevelopmental, and the most prototypic neurodevelopmental disorder really is autism. By definition, it begins before age 3. It also gives us a little more traction on trying to look at the relationship between brain development and the onset of a disorder. It's very difficult to do that in schizophrenia; if the formative event is prenatal, or early post-natal, you've got a 15- to 20-year window to work with; in autism it's more like 15 to 20 months. If you know who's at high risk, like the younger sibling of an autistic child, when a mother of an autistic child knows that she is pregnant, you can look with great precision across the pregnancy and the first 18 months of life to see whether this next child, who is at high risk for autism, moves off the typical developmental trajectory. And that's starting to pay dividends; we have some results from as early as the first 12 post-natal months. That's surprising, because we haven't been able to identify anything behavioral in the first 12 months—at least anything in terms of symptoms. But subtle changes in brain development and cognitive development, do seem to be predictive.

So that's a great model that we want to follow eventually for mood disorders, for psychotic disorders, and other mental illnesses. That's the promise of prevention.

[So how do you see the NIMH taking this forward, what are your challenges](#)

For us it is going to be moving towards an era when we have the biomarkers for very early detection. And then we have to figure out—and this is the tough part—when you have a way of predicting autism at 3 months, instead of 3 years, or you have a way of predicting who is at highest risk for schizophrenia at age 12, what do you do for them? What's the intervention? We know from the rest of medicine that interventions for prevention are very different from the interventions for 'post -vention', what you do after something occurs. Heart disease is a great example of that. We have to think through what these early preventive or pre-emptive interventions will look like. They may not be medicines; there may not be a statin for psychosis or schizophrenia, but instead, some kind of cognitive training, or some way of building plasticity, or building resilience in the brain. It could be something nutritional or some training app, it could be something that we're not even thinking about yet. It's a whole different world that I think offers great promise, and obviously if we take a page from other areas of medicine, it is prevention that ultimately has the highest public health impact. If we can figure out how to do this well, in this field, I think that we can start to save lives.

[Thinking internationally, I know that you have also been interested in the Global Alliance for Chronic diseases, and I wonder how you see that. Chronic diseases, people tend to see as diabetes, etc?](#)

Originally the GACD was a relatively small effort, but it has now extended to a much more serious enterprise. The reason I got involved is that the NIMH has had a deep interest in global mental health and in trying to put mental health on the world's global health agenda. We are so fortunate that our colleagues at the WHO, especially Shekhar Saxena, have created some valuable, very insightful strategies on how to improve global mental health. It's been heartening to see the World Economic Forum, the World Bank, and now some of the private foundations join the effort to address mental disorders as a global health issue. The GACD represents another collaborative opportunity, this time to create a network for research projects and potentially even clinical trials. I had high hopes that the GACD would engage on a mental health project, perhaps depression. The first year depression got edged out by hypertension, then by diabetes, and now I believe they have decided to focus on pulmonary disease. But I am hopeful – only in the last week – I have heard that depression will be addressed by the GACD, probably in 2016. So even on the way here I received an email about how we should sit down and plan what the GACD mental health issue would look like.

[It will be really interesting. I have been keeping abreast of what has been going on, but to try and get people... they just see it as another WHO initiative which is all about the third world and won't really affect them. It's been a struggle for me to say "you should be looking at this"](#).

This one's different. I think that's a lesson we've learned over the last five years, as we've started to make some serious commitments to global mental health. For us, it's been important for people to understand that mental disorders are not just a "first world problem". For us, global mental health is not necessarily only about the developing world, or even international – it truly is global. Meaning that we are trying to work out principles in low-resource environments, wherever they are, that can be easily translated to other settings. We have clinical trials in hubs around the world now, in

environments such as Sub-Saharan Africa, where we are learning lessons that can be imported back to low-resource environments in the developed world. We are going global with our research because of opportunity, not because we are trying to spread the wealth to as many places as possible (though that might be a good thing). What we have learned about task sharing, collaborative care, creating mobile health apps and technologies in South Africa or Nigeria or India or Chile turns out to be incredibly helpful back in Chicago or Los Angeles, or any part of the U.S. So it really is global – not necessarily foreign.

[That's good to know](#)

This is one other thing which is fascinating about global mental health. I used to joke that you could tell somebody's age by just saying the words "global mental health" and looking at their face. Five or six years ago when I would visit universities and departments of psychiatry around the United States, I would always ask "What are you interested in, what's next..." Then I would go through my checklist, and when I would say "global mental health," the only people who would raise their hands would be the students. Then I noticed about three or four years ago it was more the residents, and now it's the young faculty. So it's absolutely generational. There was almost no-one in this field, apart from a few very senior people prior to five years ago, and now it's the hottest thing. I give Vikram Patel a lot of credit for getting people excited about this. He's kind of our Paul Farmer person, the person who has really held the flag to make young people realise that this is a great area.

[I wanted to ask you about RDoC*. This is obviously something you put a lot of work into, and I was talking to Eduard Vieta, who was saying that the European Union – have put forward various proposals, contained within Horizon 2020, which have similarities to what you had put forward \(with RDoC\). And I was wondering if you have had any cooperation of contact with the EU?](#)

Yes, we have had some great meeting with the ROAMER team. They started in a different place, but they brought us in at various times to talk about RDoC. And now there's a call through IMI** for a project linking psychiatry to quantitative neurobiology, that sounds very much like RDoC. In Europe there certainly seems to be a growing interest in the problem that RDoC is struggling with, which is how to we get beyond diagnostic systems that are just based on symptoms. How do we bring in a broader phenotype, whether or not we call that 'precision medicine' or quantitative neurobiology? How do we develop biomarkers or cognitive tools to refine diagnosis? I am delighted that the European funders are thinking now about the same problem. I'm not sure that RDoC will be the final answer, but it's a process. What we really wanted to do with RDoC was to build a research framework, so that as we are funding research we are not constrained by diagnostic categories that we know don't really have biological underpinnings. The whole point of RDoC was really to liberate investigators from feeling that, if a person didn't have six of the following ten categories or criteria for the last two weeks, he or she couldn't be considered as having XYZ. You can have two people standing side by side with the same label who share one out of the ten symptoms—that's not precise, and you don't really want to start looking for biomarkers with people who probably have very different disorders.

[And of course you have been talking to Yossi \(Zohar\) about the nomenclature project](#)

Yes, what's behind all of these efforts is realising that words matter, that language really does constrain us and we have to get clear what we mean when we use terms like

‘depression’ or ‘anti-depressant’. Of course, the value in having a common language is that we can create a way to share concepts. At the same time the language constrains us by keeping us from thinking about the things that aren’t captured by those words. Is there a better way to carve Nature at the joints? Is there a way to find categories that might have more biological significance and more clinical values—so that you can tie diagnosis to which treatment someone should receive, or what the prognosis might be, or where the genetics might lead – any of that? I think we’ll get there. I don’t think this is an impossible problem, but it’s one for which we have to first begin to clean up our language. We’ll start to do that with RDoC, with the nomenclature project, and maybe with the Horizon 2020 or the IMI projects. What an exciting time to be in this field!

**The Research Domain Criteria (RDoC) project implements Strategy 1.4 of the 2008 NIMH Strategic Plan: “Develop, for research purposes, new ways of classifying mental disorders based on behavioral dimensions and neurobiological measures. See <http://www.nimh.nih.gov/research-priorities/rdoc/index.shtml>,*

***<http://www.imi.europa.eu/content/imi-2-call-3-1>*