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INNOVATORS & IDEAS: RISING STAR

Alex Tsompanidis: Understanding the role of the placenta in human neurodiversity

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Dr Alex Tsompanidis emerges as a rising star in autism research at the University of Cambridge, where his pioneering work on the placenta-brain axis may revolutionize our understanding of neurodevelopment and human brain evolution. Named among the world's top 40 under 40 autism researchers by *Spectrum* magazine and recipient of the International Society for Autism Research (INSAR) Best Dissertation Award, Dr Tsompanidis has established himself as an influential figure in developmental neuroscience. His research, now supported by a collaborative multi-million-pound grant from the Simons Foundation, explores how prenatal steroid hormones and placental function influence brain development and predict the likelihood of autism. In this exclusive Genomic Press Interview, Dr Tsompanidis reveals his journey from discovering his passion through childhood microscopy experiments to coordinating international research consortia spanning three continents. His recent evolutionary hypothesis, published in journal *Evolutionary Anthropology*, proposes that the placenta and its hormonal production may have played a crucial role in human brain evolution, positioning pregnancy at the heart of our species' cognitive development. As Assistant Research Professor at Cambridge's Department of Psychiatry and Honorary Research Associate at Peterhouse College, Dr Tsompanidis continues to bridge disciplines from genetics to evolutionary anthropology, advancing translational approaches that could enable early autism screening after birth through placental biomarkers. His commitment to inclusivity in science and dedication to mentoring the next generation of researchers exemplify the collaborative spirit driving modern neuroscience forward.

Part 1: Alex Tsompanidis – Life and Career

Where were you born, and where do you live now?

I was born in Athens, Greece, and currently live in Cambridge, England, where I have been conducting research and teaching students for the past 8 years.

Could you give us a glimpse into your personal history, emphasizing the pivotal moments that first kindled your passion for science?

I have been fascinated by science from a very young age, always asking questions about natural phenomena and pondering the fundamental building blocks of life. When I was about 10, I managed to find an old microscope and proceeded to study everything I could fit under its lenses, from different textiles to small insects. I was also fascinated by the lives of famous scientists, reading about the journeys and adventures of people such as Charles Darwin, Jane Goodall, and Stephen Hawking. These stories truly inspired me to continue exploring the natural world and pursue a career in scientific research. I was fortunate to have a family and school environment that encouraged this curiosity and supported me throughout this journey.

Figure 1. Alex Tsompanidis, MD, PhD, University of Cambridge, UK.

Please share with us what initially piqued your interest in your favourite research or professional focus area.

I first met an autistic child during my sixth year of Medical School, while on a rotation in a neurodevelopmental clinic at a large hospital in Athens, Greece. The child, at the time, was about 7 years old, had not yet spoken a single word, and appeared unresponsive to any attempts at communication. However, he was also inquisitive about the world around him, exploring the room and carefully observing the various medical devices and tools. Still, the doctor had very little to say to the child's mother, who was distressed at the lack of meaningful information on the causes of autism or on the child's prognosis. I thought then that we ought to do better, to understand this enigmatic condition and help autistic people and their families.

We would like to know more about your career trajectory leading up to your current role. What defining moments channelled you toward this opportunity?

As an undergraduate, I sought out research opportunities wherever I could. I applied for internships and joined exchange programs that took me as far as the US, Germany, and Taiwan, where I assisted cancer researchers in testing therapeutics on rodent models. Back in my home

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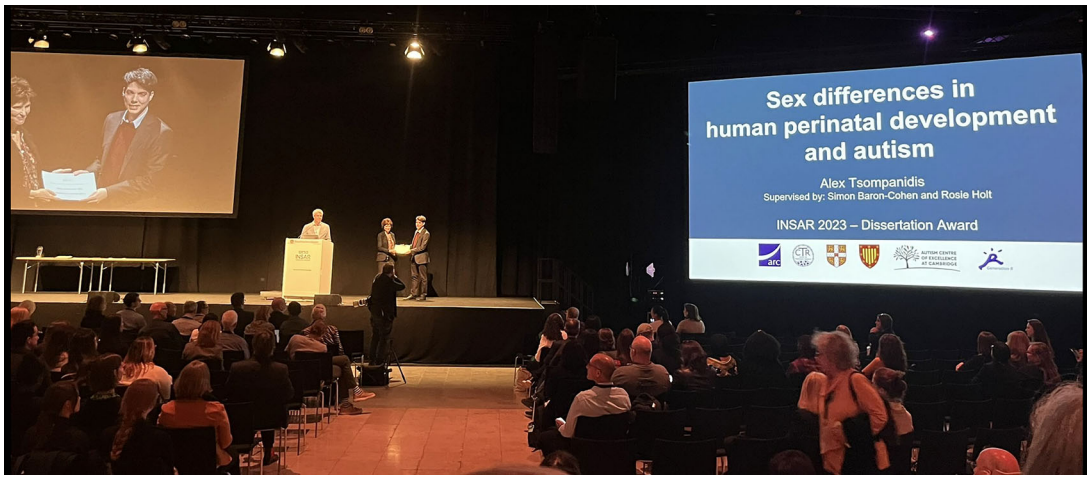

Figure 2. Alex Tsompanidis receiving the "best dissertation" award at the meeting of the International Society for Autism Research in Stockholm, Sweden, May 2023.

country of Greece, I was fortunate to join the newly established laboratory of Pharmacogenomics, led by Prof. Despina Sanoudou, who entrusted me with my own project, even though I had not yet completed a university degree. For two years, I attempted to decipher gene expression data derived from a weight-loss experiment in mice, examining every molecule affected by the administration of a novel therapeutic. This project opened my eyes to the complexity of the molecular world, as well as the uncertainties that are inherent in biomedical research. However, it also led to my first publication and enabled me to learn from my mistakes and develop critical thinking. In turn, this prior experience enabled me to pursue further opportunities and secure funding when I first came to Cambridge. That is why I always encourage students to reach out to academics and ask for opportunities, because it is often that first email that could very well set in motion a lifelong journey of discovery.

What is a decision or choice that seemed like a mistake at the time but ended up being valuable or transformative for your career or life?

As every academic, I have received a fair number of rejections in my career. I learned something from each one and built up my resolve, rather than getting discouraged. When I was applying to the PhD programme of the University of Cambridge, my first two research proposals were rejected. They were either not feasible enough or pertinent enough to advance the field at that time. However, I kept trying, and my third draft was accepted, leading to an offer for a funded PhD position at the University. The opportunity I was given to re-think my hypothesis and go back to the drawing board really led to some of the best ideas, which have shaped me ever since. It was then that I first thought to study the role of the placenta on brain development and neurodiversity.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?

I strongly believe in hypothesis-driven science, and I encourage the students I supervise to formulate interesting questions before they obtain any data or seek answers. While we need to be aware of our own biases and limited understanding of any system, it is important to have the courage to be proven wrong. In addition, we should strive for multi-disciplinary approaches and read as widely as possible. Approaching a problem from different angles not only increases insight but also enables us to "zoom out" and see the bigger picture. For example, to advance the field of Developmental Neuroscience, I realised that there was considerable insight that could be found in Obstetrics. After all, both pregnancy complications and neurodevelopmental conditions appear to have a sex bias; they are more frequent, on average, in males than in females. So this slight sex difference may hold insight about the way the brain develops in the womb, which may, in turn, help us understand conditions like autism.

Please tell us more about your current scholarly focal points within your chosen field of science.

The study of human neurodiversity is a fast-evolving and fascinating field. It is now clear that to understand conditions such as autism, we need to transcend the "medical model" that divides the world into "health" and "pathology". While many autistic people may have disabilities or need clinical support, this does not mean that the condition itself is always linked to these outcomes. Instead, autism and other similar neurodevelopmental conditions can be better understood as less frequent but contiguous aspects of the diversity inherent in our brains and human behaviour. This conceptual evolution means that we may need to redefine what autism is and which aspects of autism we should focus on studying. To do this effectively, we need to work together with the autistic community and their families to integrate data from lived experience, as well as from clinics and basic research.

My own aim is to contribute to these efforts by conducting clinical research that focuses on early development, from prenatal life to infancy and toddlerhood, when some of the first 'autistic traits' become apparent. During this period of rapid development, I study biological factors across all levels, from the genetic to the molecular and from brain structure to behaviour. Finally, I look to Evolution and the way these systems may have adapted in humans to enable the development of our large and interconnected brains.

What impact do you hope to achieve in your field by focusing on specific research topics?

More recently, I have taken an interest in the placenta and the way this, often overlooked, tissue can shape and "condition" many aspects of the developing brain, with long-lasting effects throughout life. For years, clinicians viewed the placenta as a passive barrier between the mother and foetus, but we now know that it plays an active role, producing growth factors, steroid hormones, and even neurotransmitter regulators that can guide the way the brain develops and functions. There is still much that we do not know about the 'placenta-brain' axis in humans, which makes this a very exciting scientific frontier. At the same time, the placenta holds translational potential, as it is readily available at birth. Once we understand more about its impact on the brain, it may be feasible to trial screening tests at birth, which could help accelerate diagnosis for children with special needs.

What do you most enjoy in your capacity as an academic or research rising star?

It is an honour for my research to be featured in this way. However, science is always collaborative, and I would not be here without the trust that was afforded to me by my mentors throughout the years.

At Genomic Press, we prioritize fostering research endeavours based solely on their inherent merit, uninfluenced by geography or the researchers' personal or demographic traits. Are there particular cultural facets within the scientific community that warrant transformative scrutiny, or is there a cause within science that you feel strongly devoted to?
When it comes to inclusion in scientific research, there is undoubtedly room for improvement. International students often face additional hurdles to being heard and accepted when they first arrive in a new country. Nevertheless, scientific progress requires international collaborations, and we should always strive for the free exchange of ideas and the mobility of people who can contribute to this team effort. Another cause that is close to my heart and particularly relevant to my research concerns women's health. Clinical understanding is still lacking for many endocrine conditions that are specific to women and people assigned female at birth, including endometriosis, polycystic ovary syndrome, and aspects of menstruation and pregnancy that have to do with pain and well-being. So we need a concerted effort to improve our understanding, raise awareness, and empower young women to pursue research in these areas.

Outside professional confines, how do you prefer to allocate your leisure moments, or conversely, in what manner would you envision spending these moments given a choice?
I am always mindful of the Ancient Greeks' belief that exercise is as important as philosophy for human well-being. I am not able to run a marathon, but I do go on long walks when I can. Humans evolved to think on their feet after all.

Part 2: Alex Tsompanidis – Selected questions from the Proust Questionnaire[1]

Among your talents, which one(s) give(s) you a competitive edge?
Persistence.

If you could change one thing about yourself, what would it be?
To be more patient with the pace of research.

What is your current state of mind?
Excited for future research opportunities and anxious about the ever-growing need for multitasking.

What is your idea of perfect happiness?
Reading a book by the beach.

When and where were you happiest? And why were so happy then?
Every time I get to travel to a new country and learn something new about the world.

What is your greatest fear?
Missed opportunities.

What is your greatest regret?
Not speaking up more when I should have.

What are you most proud of?
When my students get to experience the joy of scientific discovery.

What is your greatest extravagance?
Chocolate desserts.

What is your most treasured possession?
A signed autograph of Maria Callas.

What is the quality you most admire in people?
The ability to remain calm and composed in tense situations.

What do you consider the most overrated virtue?
Orderliness. There is insight to be found in the absence of structure.

What do you most value in your friends?
Empathy and a sense of humour.

Which living person do you most admire?
I am going to go with Jane Goodall, and I recommend that anyone working in science watch the National Geographic documentary about her life and work.

If you could have dinner with any historical figure, who would it be and why?
Sir Isaac Newton. He could teach me alchemy.

What aphorism or motto best encapsulates your life philosophy?
Two ancient Greek phrases. Μέτρον ἄριστον, meaning 'moderation is excellence'. And ἕν οἶδα ὅτι οὐδὲν οἶδα, meaning 'I only know one thing. That I know nothing'.

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[1] In the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35-question Proust Questionnaire became famous after Marcel Proust's answers to these questions were found and published posthumously. Proust answered the questions twice, at ages 14 and 20. In 2003 Proust's handwritten answers were auctioned off for $130,000. Multiple other historical and contemporary figures have answered the Proust Questionnaire, including among others Karl Marx, Oscar Wilde, Arthur Conan Doyle, Fernando Pessoa, Stéphane Mallarmé, Paul Cézanne, Vladimir Nabokov, Kazuo Ishiguro, Catherine Deneuve, Sophia Loren, Gina Lollobrigida, Gloria Steinem, Pelé, Valentino, Yoko Ono, Elton John, Martin Scorsese, Pedro Almodóvar, Richard Branson, Jimmy Carter, David Chang, Spike Lee, Hugh Jackman, and Zendaya. The Proust Questionnaire is often used to interview celebrities: the idea is that by answering these questions, an individual will reveal his or her true nature. We have condensed the Proust Questionnaire by reducing the number of questions and slightly rewording some. These curated questions provide insights into the individual's inner world, ranging from notions of happiness and fear to aspirations and inspirations.