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INNOVATORS & IDEAS: RESEARCH LEADER

Peter Falkai: In order to understand the neurobiological origins of psychoses we need to understand the genetic underpinnings of brain plasticity and its modulation due to environmental risk factors

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Peter Falkai stands as one of the world's leading authorities in psychiatric research, particularly in understanding the neurobiology of schizophrenia. As a Scientific Member of the Max Planck Society and Director and Head of the Hospital at the Max Planck Institute of Psychiatry since October 2024, he continues to advance our understanding of mental health disorders. His distinguished career spans over three decades, during which he has held multiple prestigious leadership positions, including President of the European Psychiatric Association (2021-2023) and current President of the World Federation of Societies of Biological Psychiatry. A member of the German Academy of Sciences Leopoldina, where he served as Senator of the Neurosciences Section, Prof. Falkai has been instrumental in shaping modern psychiatric research and treatment approaches. His groundbreaking work on brain plasticity and innovative treatment combinations has opened new pathways for understanding and treating psychotic disorders. As site spokesperson for the German Centre for Mental Health and former President of the German Society for Psychiatry and Psychotherapy, Psychosomatics and Neurology, he continues to bridge the gap between basic research and clinical application. In this Genomic Press Interview, Prof. Falkai graciously shares insights into his remarkable professional journey and personal life, offering readers a glimpse into the mind of one of psychiatry's most influential figures.

Part 1: Peter Falkai - Life and Career

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

I was a first-year medical student when I listened to the lecture on human neuroanatomy and was immediately taken by the topic of "brain structure and functioning." After one of the subsequent lectures, I asked the professor to recommend a seminar to deepen my knowledge of this subject. I attended the suggested one and had to do a seminar work on Parkinsons' disease, on which topic I read many papers without – at least so it felt – understanding any of them. However, the paper I handed in was well received. I went back to the professor of neuroanatomy, who was also the director of the C. and O. Vogt Institute of Brain Research at that time, and asked whether I could join a research group. He introduced me to Bernhard Bogerts, who opened my passion for mental disorders, especially schizophrenia.

We would like to know more about your career trajectory leading up to your most relevant leadership role. What defining moments channeled you toward that leadership responsibility?

Bernhard Bogerts supervised my M.D thesis and enabled me to spend 4 months at Tim Crow's group at his CRC unit in London in 1987, which was



Figure 1. Peter Falkai, MD, PhD, Munich University Hospital, Germany.

and still is a model for how basic and clinical researchers can interact and achieve meaningful research. I then followed Bernhard to the Department of Psychiatry at the Heinrich-Heine University in Düsseldorf, where I assisted him build up a neurohistological laboratory besides doing my specialization in psychiatry. As a clinical psychiatrist, I was influenced by my first chair, Prof. Heinrich, and in terms of clinical leadership by his successor, Professor Gaebel. In 1996, I moved on to the Department of Psychiatry of the University of Bonn, headed by Prof. W. Maier, where I enjoyed learning much about the genetics of mental disorders and how to build international networks and collaborations. In 2002, I obtained my first chairperson position in Homburg/Saar and Göttingen. These stations prepared me to take up my current and most relevant leadership role as the head of the Department of Psychiatry at the Ludwig-Maximilians-University in Munich, formerly led by Emil Kraepelin (1902-1924). This year, I was appointed director of the Max-Planck Society and head of the Department of Psychiatry at the Max-Planck Institute of Psychiatry. Bridging these two institutions allows for bringing together excellent basic and clinical

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

I was stunned during my work with Bernhard Bogerts by how unremarkable the Nissl-stained sections of patients with schizophrenia looked under the microscope in comparison to sections of Patients with late-stage Alzheimer's or Parkinson's disease. This was in sharp contrast to the medical records of the patients with schizophrenia, who were ill for a long time

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and demonstrated a marked functional decline as the consequence of illness. Fostered by Jan Stevens, we performed a Holzer stain per case to see whether a significant degree of gliosis could be detected, which was not the case. We then quantified astroglia using GFAP, and neither found any differences, refuting the idea of schizophrenia being a degenerative disorder. Since then, I have been convinced that schizophrenia is a disorder of disturbed regeneration, which was supported when we found that aerobic exercise recovers the hippocampal volume loss, reduces negative symptoms, and improves cognitive dysfunction in this disorder.

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

20 years ago, I started to become interested in the question of what aerobic exercise induces in the brains of patients with schizophrenia. To our surprise, our research group could develop several lines of evidence from post-mortem, imaging genetics, and induced pluripotent stem cell (iPSC) studies, which point to myelin-based plasticity and the involvement of the synaptic machinery. We initiated an RCT where we combined aerobic exercise and the repurposed drug Clemastine to see whether this has a bigger and longer-lasting effect on myelin regeneration, leading to improved cognition. If this were true, it would open the door for more repurposed or new targets to improve neural plasticity in schizophrenia. leading to improved treatment options, especially in the early phases of the illness.

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

I do believe that only by understanding the mechanisms of mental disorders we will be able to conceptualize mechanistically informed new treatments, which will lead to progress in psychiatry. Therefore, I hope that with our current work on disturbed myelin plasticity in schizophrenia, we can find mechanistic understanding in this small area, which eventually should result in targeted treatments, at least in a subgroup of patients.

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

I enjoy getting up early, doing my routine jobs, and then start reading the research articles I had picked up the days before. I continue to do so late in the evening when most people rest, but when I enjoy thinking and dreaming about current and potential future research projects. I enjoy it when our young people talk about their science, and I regard it as a privilege to read their papers and watch how they develop. I love to listen to good talks and, therefore, attend some lectures every year on topics with which I am not very familiar.

At Genomic Press, we prioritize fostering research endeavors 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 deeply stirs your passions?

Following the 1956 Hungarian Revolution, my family and many relatives settled across Europe and beyond. Since then, English has been our common language at family gatherings because we have built lives in different countries. Therefore, I enjoy different views and ideas from different cultures. I can also understand the fears such multicultural communities can mean to some people, but based on my experiences, fostering research endeavors based solely on their inherent merit is a sound basis for excellent research.

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

To listen and interact with scientists in our department and beyond and exchange new research ideas and methods.



Figure 2. Peter Falkai (center) preparing for the Tegernsee-Lauf, a scenic halfmarathon around Lake Tegernsee in Bavaria, with his son (left) and Professor Jens Werner, Chair of Surgery at Ludwig-Maximilians-University Munich (right). The Tegernsee-Lauf is one of Germany's most picturesque running events, taking place in the Alpine foothills about 50 km south of Munich.

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?

Outside my professional confines, I most enjoy spending time with my family and friends. Since I love travelling very much, my biggest joy is traveling to unknown places with them. I also enjoy spending time on my own, reading, and running. Every weekend, I run approximately 20 kilometers with our dog, 10 km on Saturday and 10 on Sunday, always early in the morning.

Part 2: Peter Falkai - Selected questions from the Proust Questionnaire¹

What is your idea of perfect happiness? Spending time with my family and/or friends.

What is your greatest fear?

To lose a close family member.

Which living person do you most admire? Eric Kandel.

¹In the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35question 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.



What is your greatest extravagance?

To travel to amazing places.

What are you most proud of?

That I became a member of the German Academy of Science (Leopoldina).

What is your greatest regret?

That I did not spend more time abroad visiting top research groups as a junior person before entering the clinic.

What is the quality you most admire in people? Smartness.

What is the quality you most dislike in people? Not being able to listen to other people.

What do you consider the most overrated virtue? Being orderly.

What is your favorite occupation (or activity)? Reading, listening, and talking to people.

Where would you most like to live? Munich.

What is your most treasured possession? My wife and kids.

When and where were you happiest? And why were you so happy then? I am happy now, but I was even happier when the kids were still living with us, and we discussed future plans and ideas.

What is your current state of mind?

I am happy and content with my life as it is now.

What is your most marked characteristic? Being disciplined.

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

Ambition.

What do you consider your greatest achievement? To become a Department Chairperson in Munich.

If you could change one thing about yourself, what would it be? Be more patient.

What do you most value in your friends?

A sharp mind and a big heart.

Who are your favorite writers?

Thomas Mann, Svetlana Alexievich, and Ferdinand von Schirach.

Who are your heroes of fiction?

People who under difficult conditions find their way and are successful.

Who are your heroes in real life?

Parents with small kids who do their jobs (e.g., research) with much passion

What aphorism or motto best encapsulates your life philosophy? Do not dream your life, but live your dreams.

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