Why has your career path followed a neurological route?

My passion for neuroscience has led me to devote my studies to forging a better understanding of the links between neuroscience and behaviour – a field that has extremely important societal implications and promotes the care of individuals with brain-based behavioural disturbances. Our research in the Neuropsychiatry and Brain Imaging research group at the University of Basel, Switzerland, draws on a wide range of research methods, including advanced neuroimaging techniques such as structural and functional magnetic resonance imaging (MRI), dynamic causal modelling (DCM), multimodal imaging, pharmacological imaging and imaging genetics. We also actively conduct psychopathological and cognitive assessments in both clinical populations and healthy volunteers. I appreciate the combination of knowledge and skills that are beyond the scope of those required for the practice of general neurology or general psychiatry, either alone or in combination.

What excites you most about your work on brain-gut interactions?

One of the most fascinating things about this kind of research has to be its inherent multidisciplinary nature. I thrive on working closely with researchers from completely different backgrounds and with diverse areas of expertise. For instance, my colleagues include medical doctors, psychologists, physicists and pharmacists, as well as researchers and clinicians from a variety of medical departments and specialisms such as psychiatry, gastroenterology and medical physics. It is inspiring to work together and see how our individual areas of expertise can influence our research and contribute to the bigger picture.

Your current project is focusing on the role of carbohydrate in the nutrient-induced human brain activation matrix. Can you briefly outline the issues being addressed?

The global obesity problem supports the urgent need for research that aims to understand the basic mechanisms that regulate food intake, appetite and body weight. In our project, we are exploring the role of ingested nutrients in triggering adaptive processes in the brain. We are aiming to uncover the temporal relations between gut and brain signals that control eating behaviour and find out how this information triggers regulatory circuits. Additionally, we will investigate how this links to feeding behaviour and energy consumption.

How do you investigate the complex neural responses to eating?

We started this research by addressing the question of how different behavioural and physiological responses to glucose and fructose are mirrored in the neural system; we used resting state functional MRI to examine neural changes after the acute ingestion of fructose in comparison with glucose. Resting state functional connectivity is based on the analysis of low-frequency fluctuations present in the blood-oxygenation-level-dependent signal. Previous research has highlighted that resting state functional connectivity analysis is particularly suitable for examining brain functions including sensory, cognitive and reward processes. Moreover, it is well established that many brain regions are strongly implicated in reward processes and dopamine function. We are therefore exploring whether there are any differences between glucose and fructose administration in respect to resting state functional connectivity within the basal ganglia/limbic network. In the future, we will also address these questions in clinical populations of patients with eating disorders.

Where do you hope to see your current project progressing over the coming year? What are your plans upon completion?

We hope that this study will clarify our understanding of the mechanisms that underlie the basic physiological circuits controlling energy homeostasis, with important implications for public health with respect to weight control and obesity-related morbidity. More information on these fuel-sensing mechanisms could even lead to novel therapeutic targets for obesity. In 2015, we will extend our study to clinical populations – and we are planning to include patients with both eating disorders and depression in order to address clinically relevant conditions.
As a growing problem that is particularly prevalent in Western countries, obesity has more than doubled worldwide since 1980. Characterised by the excessive accumulation of fat, this condition represents an urgent public health issue. Indeed, in addition to causing discomfort for afflicted individuals it also dramatically increases the likelihood of multiple chronic conditions such as diabetes, cardiovascular diseases and some cancers. While longevity in the overall population is rising, in the obese population the mean age of death is falling. Revealingly, the majority of the world’s population live in countries where obesity and overweight are more likely to cause mortality than malnutrition.

It is against this backdrop that Professors Stefan Borgwardt and Christoph Beglinger’s research into the biochemical processes that underpin hunger and satiety has emerged. Knowledge about these complex processes is highly limited at present – and so, at the beginning of 2012, Borgwardt and his team in the Neuropsychiatry and Brain Imaging group, and Beglinger in the Department of Gastroenterology, in the University Hospital Basel launched a project to address this knowledge gap. Focused on defining the role of carbohydrates in the nutrient-induced human brain activation matrix, the study is nearing its completion. "Our multidisciplinary team is comprised of academics with expertise in the application of psychopathology, neuroimaging, imaging genetics, cognition and psychopharmacology in mental illness," Borgwardt outlines. "Our research also benefits from extensive collaborative links with scientists and institutions worldwide."

**FOCUS ON FRUCTOSE**

As a monosaccharide sugar found in fruits and honey, fructose is frequently added to foods and drinks for taste enhancement. For instance, high-fructose corn syrup – a mixture of fructose and glucose – is an increasingly common ingredient found in soft drinks and has been implicated in the global rise of fructose consumption. Worryingly, research has linked the excessive consumption of fructose to higher food intake and the down-regulation of dopamine receptors in reward-sensitive pathways, thus leading to a number of health issues including insulin resistance and obesity. It is also possible that these glucose- and fructose-induced behavioural responses are mirrored in the neural system, hence the term ‘diabetes of the brain’ in reference to Alzheimer’s disease. Borgwardt’s research in this area is attempting to elucidate the complex mechanisms that culminate in the behavioural and physiological effects of glucose and fructose.

**A weighty worry**

Researchers based in the Neuropsychiatry and Brain Imaging group at the Department of Psychiatry and the Department of Gastroenterology of the University Hospital Basel, Switzerland, are conducting fascinating and needful research into the basic mechanisms that regulate appetite, food intake and body weight.
systems in the brain and gut that regulate food intake and satiety. With specific nutrients connected to the activation of different pathways, such labyrinthine processes are difficult to track. “The challenge of studying these signals is to map where and when the brain will respond to specific nutrients that are delivered to the gut,” Borgwardt points out. “Essentially, the picture that emerges is that numerous peripheral fuel sensors communicate with the central nervous system (CNS) via a combination of neural and hormonal routes.”

Borgwardt, Beglinger and their colleagues are drawing on previous research that demonstrates the balance between calorie consumption and expenditure and how it depends on interactions between multiple organ systems. Interestingly, recent studies suggest that fuel sensing takes place in a number of peripheral cell types, including the taste receptors in the gut. It is thought that some of these peripheral cells have the capacity to send neural or humoural signals to the brain, subsequently affecting energy balance in the entire body. Moreover, it is known that specialised neurons in the CNS have the ability to sense fuel status, with a significant body of research linking glucose levels to specific nerves that appear to have a role in modulating appetite and energy balance. Indeed, with recent data suggesting that fuel sensors are linked to important signals of stored energy in adipose tissue, Borgwardt’s team is eager to provide definitive evidence of the mechanisms that integrate all the body’s fuel signals.

The study incorporates three different groups of participants – obese, diabetic and healthy individuals – who are given identical and predefined nutrients via oral and gastric administration. The effects of these nutrients on the brain-gut interaction are analysed via neuroimaging techniques and measurements are taken of the metabolic parameters associated with fuel intake and energy homeostasis. Finally, an assessment of appetite perception is also conducted. “For the pharmacological imaging studies of cannabinoids and glucose, we used a wide range of advanced multimodal neuroimaging techniques,” Borgwardt discloses. “These structural and functional techniques generate or imitate psychopathological and cognitive symptoms in both clinical populations and healthy volunteers.”

FUTURE IMPLICATIONS
Looking ahead, the hope is that Borgwardt’s innovative and illuminating study will shed new light on the basic mechanisms and pathways that control energy homeostasis in the human body. It is probable that the findings from this multidisciplinary project will provide a solid basis for informing the development of weight control strategies and aid in the discovery of novel therapeutic targets for obesity. Ultimately, this will have important ramifications for public health, potentially leading to a reduction in obesity-related morbidity.