Mind-Brain-Body interactions in stress-related disorders
Could you begin with an overview of the work you do at the University of California Los Angeles (UCLA)?

As a practicing gastroenterologist I see patients with complex, chronic gastrointestinal problems. The majority of patients are referred from across the country or seek a second, third or fourth opinion. They all fall in the category of disorders of mind-brain-gut interactions. As a clinical investigator, I pursue research in mind-brain-body interactions with a primary focus on the interface of pain, stress and emotions in the human brain. Also, I am Director of the UCLA Centre for Neurobiology of Stress (CNS).

How has technological progress advanced your work?

It has primarily influenced research into mechanisms underlying mind-body interactions, and mind-body therapies. The advent and rapid progress in neuroimaging of the brain has been the main driving force in this: structural and functional magnetic resonance imaging (MRI) and positron emission tomography have rapidly advanced our knowledge of how the brain responds to stimuli from the body (interoception), how it responds to stress and expectation of pain, and how pain, stress and emotions are processed and modulated by the brain.

Functional disorders like Irritable Bowel Syndrome (IBS) have been considered psychosomatic; what success has there been in countering this prevalent opinion among clinicians?

One could argue that mind-body interactions are just another expression for psychosomatic interactions. At a clinical level, both refer to the same phenomenon of close interactions between psychological processes (or activities of the mind) and bodily symptoms. However, a major change has occurred in viewing the brain as the main mediator between these processes. Rather than speculating about the influence of unconscious processes on the expression of distinct patterns of disease, now we can directly study neurobiological processes, including interactions between early traumatic life experiences and genetic factors, which often play a role in symptom generation. We now need to reframe the old erroneous and biased viewpoint of many clinicians that symptoms are ‘all in the head’ to a neurobiological based concept, that the brain is a key mediator in mind-body-body interactions.

Could you outline the potential therapeutic benefits your work could produce for Inflammatory Bowel Diseases (IBD) and Irritable Bowel Syndrome (IBS) sufferers?

Our work will have major implications for the development and evaluation of more effective treatments for both disorders. We have a longstanding interest in changes in the brain-gut axis in IBD and recently began investigating the effect of gut inflammation on the expression of an important signalling system in the brain. We are also studying how gut inflammation changes the brain’s response to emotional stimuli. I strongly believe that mind-brain-gut interactions play a major role in severity and exacerbation of IBD and therefore therapies targeted at the mind/brain may become an important complementary component to IBD treatment.

The role of psychosocial factors and stress are well established for IBS and other functional bowel disorders. In the absence of any reliable symptom-related biomarkers, brain imaging has become an essential approach to identify the neurobiological underpinnings of this disorder. A better understanding of these mechanisms will legitimise IBS and related disorders as a real disease, identify treatment targets within the central nervous system, and enable the objective evaluation of new interventions.

To what degree do ‘gut instincts’ relate to physical wellbeing?

Our gut is by far the largest interface we have with the outside world – the size of a football field. It is packed with trillions of microorganisms which communicate with the gut and it has its own immune, endocrine and nervous systems. In terms of complexity this system is therefore only comparable to the brain. There is no doubt that the impact of signals reaching the brain from this complex organ must have major influences on homeostasis, wellbeing and mental function.

What areas of research is the UCLA-CNS going to be pursuing in the future?

Under the umbrella of mind-brain-body interactions, brain-gut interactions will continue to be a main area of research. Specifically: developing a fully integrated model of bidirectional brain-gut interactions; understanding interoceptive, cognitive and emotional factors influencing food intake in health and disease; explaining symptoms in functional bowel disorders such as IBS, and bidirectional interactions between brain and gut in chronic gut inflammation. We will develop understanding of the neurobiological and genetic basis of persistent pain disorders (such as fibromyalgia or interstitial cystitis) and evaluate and develop new treatment options for these disorders; pharmacologically by identifying symptom generating brain signalling systems for drug targeting and non-pharmacologically by identifying the neurobiological mechanisms of mind-body treatments including yoga, meditation, cognitive behavioural therapy and hypnosis.
In 1994 Dr Emeran Mayer, alongside Drs Bruce Naliboff, Yvette Tache and Lin Chang, founded the Center for Neurobiology of Stress (CNS) at the University of California Los Angeles (UCLA). Initially a small programme concentrating on common gastrointestinal disorders (such as IBS or functional dyspepsia), over the last 15 years UCLA-CNS has grown into a federally funded centre focusing programmes on the basic premise that bidirectional brain-body interactions are crucial in both health and disease, and their greater scrutiny will further our understanding of chronic diseases. Still a Director of the CNS, Mayer has garnered a reputation across the U.S. as a considerable mind in gastroenterology: “I see patients with complex, chronic GI problems,” he explains. “The majority of patients are referred from across the country or seek a second, third or fourth opinion.” Mayer is also an administrator at UCLA-CNS, running the neuroimaging research core of the Center, and a clinical investigator within the Centre for Neurovisceral Sciences and Women’s Health, a CNS translational research programme.

GROUP EFFORT

The work being performed at UCLA-CNS is inherently collaborative. Dr Mayer is conscious of the benefits of cooperation: “The success of our centre has been a collective effort,” he states, “and has only been possible with the invaluable input and expertise of several similarly minded individuals, such as the co-directors of the centre who play a key role in running the mind-body programme, Drs Tache, Naliboff, Chang and Dr Tillisch.”

The bidirectional signalling between the mind-brain-body holds new therapeutic possibilities – the concurrent treatment of both mind and body.

The CNS is based in the Division of Digestive Diseases at the UCLA Medical School and has very close intramural ties with departments across the University. Collaborations with the Department of Psychology are aimed at evaluating the effectiveness and underlying neurobiological mechanisms of cognitive behavioural approaches to chronic pain conditions including IBS, and anxiety disorders, in understanding the neurobiology underlying ‘wellness’, and in basic mechanisms of learning and memory. Research collaborations with investigators at the Semel Institute of Behavioural Neuroscience include studies into the role of the brain’s dopamine system in chronic pain and the placebo response, and into mindfulness meditation. Within the Department of Pediatrics, UCLA-CNS are engaged primarily with evaluating the effectiveness and underlying mechanisms for yoga therapy in children with chronic pain conditions. Beyond UCLA, the Center works with international academic institutions including the University of Linköping, Sweden, conducting a large study evaluating the effect of hypnosis on symptoms, and brain structure and function in patients with IBS. Collaborators at the University of Leuven in Belgium are working with CNS investigators on brain responses in patients with functional dyspepsia. Domestically, investigators at the Department of Psychiatry at the University of California in San Diego are collaborating with the UCLA-CNS on the neurobiology of interoception – how the brain responds to stimuli from the body – in pain and anxiety. This degree of intra and extramural interaction is testament to the growth of understanding and appreciation of what investigators like those at UCLA-CNS are trying to achieve. Mayer asserts: “The way the field has unfolded over the last decade is nothing less than revolutionary”.

THE ADVANCE OF TECHNOLOGY

The advances in neuroimaging technology have afforded the considerable progress in the neurobiology of stress, as Mayer is keen to point
INTELLIGENCE

MIND-BRAIN-BODY INTERACTIONS IN STRESS-RELATED DISORDERS

OBJECTIVES

The UCLA Center for the Neurobiology of Stress is comprised of an interdisciplinary group of investigators (from the fields of neuroscience, psychology, genetics, psychiatry, medicine and pediatrics) studying biological processes the interface between pain, stress and emotions. Areas of particular interest are sex-related differences, brain-gut interactions in health and disease (chronic abdominal pain syndromes, functional and inflammatory bowel diseases, eating disorders), and persistent pain disorders (including irritable bowel syndrome [IBS]), and pharmacologic and non-pharmacologic therapies.

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EMERAN A MAYER, MD, has been a member of the faculty at UCLA in the Division of Gastroenterology since completing his Gastroenterology fellowship at UCLA in 1982. There, over the past 26 years, Dr. Mayer has had a major role in the development of one of the world’s preeminent clinical and research programmes in digestive diseases, previously serving as the Founding Chair of UCLA Collaborative Centers for Integrative Medicine, and more recently functioning as the Executive Director of UCLA Center for Neurobiology of Stress, and the Co-Director of the CURE: Digestive Diseases Research Center. He has joint appointments in the Departments of Medicine, Physiology and Psychiatry.

He has authored over 160 original, peer-reviewed publications in leading journals, including Nature and the New England Journal of Medicine and has written seminal book chapters in the leading textbooks on Pain, Gastroenterology and Medicine. He has published 90 reviews and chapters, edited three books, and has been invited to give more than 250 scientific presentations all around the world.

out: “At the outset of my career, it would have been impossible to foresee the power of brain imaging techniques to eventually probe directly into the living human brain,” he states. The definition of the biological mechanism of stress stems from the ability to undertake comparative studies of the brain in response to stimuli, during certain tasks, and at rest. Neuroimaging techniques, such as structural and functional magnetic resonance imaging and positron emission tomography, have enabled the characterisation of brain structure, function, and of neurotransmitter systems involved in brain function.

The ability to visualise the brain’s function as well as structure has highlighted mechanisms of signalling from the gut to the brain; the impacts of this link on disease are slowly being identified. The enteric nervous system (ENS) or ‘second brain’ is a neuronal network sandwiched within the layers of the gut. It is the GI portion of the autonomic nervous system; it runs most gut functions autonomously from the brain. The central nervous system is linked to the ENS by multiple pathways, including the autonomic nervous system, and various chemical and immune signalling systems. These connections communicate the condition of the GI to the brain and send brain signals back to the gut — this is a physical manifestation of the bidirectional mind-body axis.

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UNCONVENTIONAL THERAPIES

Mind-brain-body interactions are a long standing interest of Mayer; the concept was responsible for him going into medical school at the Ludwig Maximilians University in Munich. From his time at University until now, the Cartesian view that the human being is divided into the mind and the body has dominated thinking on this subject. “A good example for this is the prevalent attitudes about inflammatory bowel disease (IBD),” he declares. “There has been a long tradition in IBD research to deny any involvement of the nervous system, the brain or the mind in disease.” However, recent studies are upsetting this traditional dogma — compelling results indicate a relationship between an individual’s mood and IBD activity and symptoms. It is as yet unclear if the mood changes are a result of the inflammation or vice versa. This exemplifies the integrative view of medicine held by those at the CNS. The bidirectional signalling between the mind-brain-body holds new therapeutic possibilities — the concurrent treatment of both mind and body.

Mayer believes hypnosis and non-Western treatments, such as acupuncture, as well as cognitive behaviour therapy, could be legitimate and cost-effective complements to pharmacological treatments for many chronic diseases. Efforts to understand chronic diseases not as mechanical problems limited to the body, but as complex interactions between mind, brain and body, reflects the growing pursuit of personalised medicine. It emphasises common vulnerability factors in the development of chronic disease (such as stress, emotional imbalances, unhealthy lifestyles, old age, etc.) which can be targeted with mind-body approaches long before permanent damage manifests in bodily symptoms. Individualised treatment approaches have to take into account the uniqueness of these interactions in each patient. Many of these treatment approaches empower and engage the patient as an active player in the therapeutic process, rather than viewing him/her simply as a passive consumer of medications and other treatments. As the understanding of mind-brain-body connections increases, the potential for personalised, holistic and cost effective therapy for a wide range of conditions comes closer to being realised.