

WHEN THE CHEMISTRY IS NOT RIGHT FOR SLEEP

THOMAS LANGE
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JUNIOR FELLOWS
INTERDISCIPLINARY
RESEARCH GROUPS



Sleeping well is priceless. In fact, in our hectic modern world, peaceful sleep is becoming an increasing luxury and it has long been the case that waking up refreshed following a relaxing night's sleep cannot be taken for granted. Around 10% of those living in Western societies suffer from chronic difficulties initiating and maintaining sleep, and there is a lack of fundamental research to develop effective treatment that is successful in the long term. Once people have fallen into the vicious circle of a sleep disorder, it often takes decades for them to regain a better quality of life. As pointed out by the Austrian philosopher, communication scientist and psychotherapist Paul Watzlawick, deliberately choosing to sleep more deeply is just as impossible as doing something spontaneous on command. To date, just as little research has been undertaken into why people sleep badly as has been carried out to explore the reasons behind which we need sleep at all. Sleep research is still in its infancy, a fact which makes the interdisciplinary research project being conducted at FRIAS by Junior Fellows Thomas Lange and Kai Spiegelhalter be-

tween October 2012 and July 2013 so exciting.

In the joint project, entitled "When the chemistry is not right for sleep: investigating the biochemistry of primary insomnia using magnetic resonance spectroscopy", the physicist and psychologist are using magnetic resonance spectroscopy to examine the behaviour of the neurotransmitter gamma-aminobutyric acid (GABA) in the brain. GABA is the brain's most important inhibitory neurotransmitter and one of its functions is to "switch off" the brain, allowing people to fall asleep. "A total of 88 sleep disorders have been discovered, ranging from sleep apnoea to restless legs syndrome. However, we are focusing specifically on individuals whose sleep disorders are not linked to other physical or mental diseases," states Spiegelhalter, who works as a research assistant in the area of sleep medicine at the Freiburg University Medical Centre. The researcher adds that whilst sleep disorders are predominantly caused by short-term psychological or biological triggers, such as a traumatic life event or, in women, the menopause, insomnia subsequently takes root in

the majority of cases. On average, the early-stage researchers' test subjects have been suffering from difficulties initiating and maintaining sleep for ten years, and it is these cases of primary insomnia which concern the interdisciplinary research group. This means that as opposed to suffering from sleep disorders in the short term, caused for instance by depression or back pain, their test subjects are enduring, as termed by Spiegelhalter, "pure sleep disorders".

The two researchers are therefore predominantly interested in paving the way for the development of treatments that are successful in the long term and their research is focusing on far more than the mere causes of sleep disorders. The customary medication-based treatment currently prescribed can only be taken for between six and eight weeks, and whilst its chief aim is to regulate the neurotransmitter GABA, the risk of addiction is very high.

Kai Spiegelhalter and Thomas Lange are also concentrating on this neurotransmitter. Their research method consists of a special process, the kind of which has never been used in this way before. The experiment involves 40 people aged between 18 and 65, half of whom belong to a control group of test subjects who do not suffer from sleep disorders. The fact that primary insomnia naturally affects more women than men means that the experiment has a higher number of female participants than male. The test subjects are first examined in a sleep lab to rule out the possibility that their existing sleep disorders are caused by other

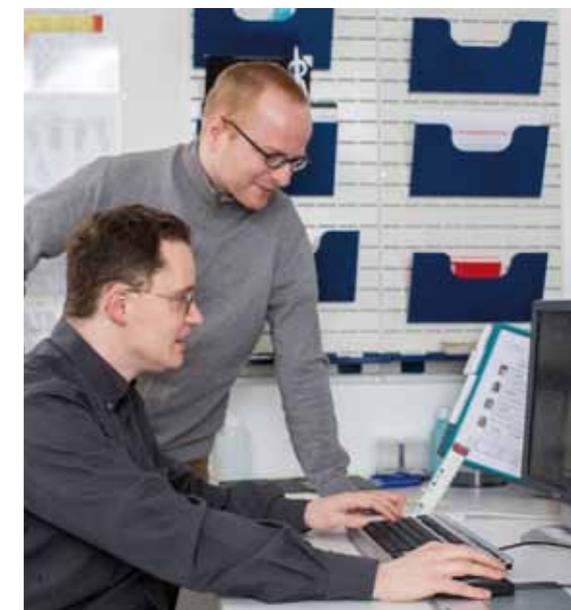
diseases. The second stage involves using magnetic resonance spectroscopy to measure the proportion of various neurotransmitters in the test subjects' brains, the focus being on the neurotransmitter GABA.

Thomas Lange, who is carrying out research in the area of magnetic resonance imaging and spectroscopy as a project manager in the working group Advanced Brain Imaging at the Freiburg University Medical Centre, explains the process: "The special sequence we are using to trace the neurotransmitter is not routinely put to use in this way and is therefore not provided as standard with clinical scanners. The manufacturer has, however, added this feature especially for research purposes. To detect the neurotransmitters' presence, we are measuring the characteristic frequency of the electromagnetic waves emitted by the atomic nuclei following stimulation with radio frequency impulses." The data obtained by the magnetic resonance spectroscopy allows both researchers to determine the concentrations of various neurotransmitters within the brain and to visualise these on a screen. They are working on the assumption that overstimulation of the central nervous system is responsible for the severe disruption to sleep suffered by insomniacs, and that this in turn is caused by altered brain metabolism.

The levels of various neurotransmitters in the test subjects' brains are measured in the magnetic resonance scanner twice a day, once in the early morning and once late at night. The main aim is to prove that the patients' concentration of GABA, the

brain's most important inhibitory neurotransmitter, is significantly reduced in the evening, resulting in it being unable to stop the stimulation of the nervous system on a neurobiological level. "Insomniacs are also typically more anxious during the day, meaning it could be the case that their concentration of this neurotransmitter is lower in general," adds Spiegelhalter.

The interdisciplinary research group will spend ten months at FRIAS researching the biochemical basis of primary insomnia. They have one aim above all others: to acquire knowledge of a disease which is well known but has long been shrouded in mystery. (ab)



Thomas Lange and Kai Spiegelhalter