PRESS RELEASE
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COULD SLEEP PROBLEMS PREDICT DEPRESSION?

Troubled sleep is a well-known hallmark of depression — including difficulty falling or staying asleep, poor sleep quality, and other altered sleep patterns. In the quest to understand the molecular mechanisms of mood disorders including depression, scientists at the Max Planck Institute of Psychiatry in Munich are finding strong links between sleep disturbance, anxiety, and stress hormones. **Dr Mayumi Kimura**, head of the Institute's Sleep & Telemetry research core unit, today (Monday 7 July) described research examining these connections.

The associations are multi-fold. Most patients of stress-related disorders, including mood disorders, also have a sleep disorder, noted Dr Kimura. Sleep disturbance in depression is linked to increased levels of a stage called REM sleep — related to less deep sleep and early awakenings. Impaired sleep, in turn, is also linked to anxiety; and to increased production of CRH, a stress hormone. Anxiety and CRH overproduction are also associated with mood disorders. In fact, many anti-depressants suppress REM sleep, she mentioned.

Dr Kimura wanted to understand whether causes of mood disorders are equivalent to those of sleep disorders, or separate. "If we examine sleep, can we predict some potential mood disorder patients?" she asked. "We queried whether sleep changes might be a predictor or biomarker for potential mood disorders."

The team led by Dr Kimura examined how changes in REM sleep might be linked to these stress and anxiety factors. They observed, analysed, and measured sleep and behavioural patterns in specially-generated mice expressing several relevant gene variants. Some mice overproduced the stress hormone CRH in various brain areas. Other mice exhibited high anxiety-related behaviour. Dr Kimura's team examined which type of animal model would exhibit hallmarks of sleep disorders, and might be suitable to further understand molecular mechanisms of sleep and mood disorders.

Dr Kimura's team was interested in the role of CRH, a key hormone produced in different brain areas, regulating stress response and linked to wakefulness. As CRH overproduction is associated with various psychiatric disorders including depression, they examined whether overproduction of CRH might be directly linked to the REM sleep changes seen in mood disorders. They were also interested in the role of anxiety, as sleep disturbance is known to be affected by high anxiety.

Most CRH-overproducing mice showed elevated REM sleep (shallower sleep) resembling that seen in depressed patients. These findings were the first to suggest that overproduction of CRH in specific brain areas generates increased REM sleep and wakefulness. The high anxiety mice also showed increased REM sleep. But they also showed increased non-REM sleep (sleepiness) during times they normally should be awake. "This indicates that anxiety might be the mechanism keeping them awake. Since they can't stay asleep for a longer period, their sleep debt accumulates, so they must sleep during normal waking hours." Dr Kimura's team is investigating these mechanisms further.

The research so far demonstrates that altered REM sleep is very much connected to mood disorders, said Dr Kimura. The findings also clarify that CRH and anxiety — already linked separately to depression and to sleep disturbance — directly influence REM sleep patterns.

"So how does it all connect, and how does it relate to humans?" asked Dr Kimura. People with chronically impaired sleep might be more predisposed to depression, she noted. If changes in sleep habits occur before patients start depression symptoms, knowing more about these associations might eventually improve prediction. These results could therefore be important for ongoing research on REM sleep in humans, enabling enhanced assessment of vulnerability, or therapy outcomes.

Dr Kimura intends to further investigate the molecular mechanisms of mood disorders. She hopes to validate how altered REM sleep might directly relate, help, or even predict mood disorders. "If patients can be helped to sleep better, perhaps might it improve their mood disorder."

END

Abstract Reference R10076: *Studying REM sleep in animal models to understand depression in humans.*
Symposia S20: *Neurobiological and neurogenetic bases of the link between sleep, stress and depression*

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NOTES TO EDITORS
The 9th FENS Forum of Neuroscience, the largest basic neuroscience meeting in Europe, organised by FENS and hosted by the The Società Italiana di Neuroscienze (SINS) (Italian Society for Neuroscience) will attract an estimated 5,500 international delegates. The Federation of European Neuroscience Societies (FENS), founded in 1998, aims to advance research and education in neuroscience, representing neuroscience research in the European Commission and other granting bodies. FENS represents 42 national and mono-disciplinary neuroscience societies with close to 23,000 member scientists from 32 European countries. http://fens2014.neurosciences.asso.fr/

Further Reading (Kimura)
Conditional corticotropin-releasing hormone overexpression in the mouse forebrain enhances rapid eye movement sleep. M Kimura, P Müller-Preuss, A Lu, E Wiesner, C Flachskamm, W Wurst, F Holsboer, JM Deussing. *Molecular Psychiatry*. February 2010; Vol. 15, No. 2: 154-165. DOI:10.1038/mp.2009.46

Sleep Phenotyping in a Mouse Model of Extreme Trait Anxiety. V Jakubcakova, C Flachskamm, R Landgraf, M Kimura. *PLoS One*. July 2012; 7(7): e40625.
DOI: 10.1371/journal.pone.0040625