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# Gene predicts how brain responds to fatigue, human study shows

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New imaging research in the June 24 issue of *The Journal of Neuroscience* helps explain why sleep deprivation affects some people more than others. After staying awake all night, those who are genetically vulnerable to sleep loss showed reduced brain activity, while those who are genetically resilient showed expanded brain activity, the study found. The findings help explain individual differences in the ability to compensate for lack of sleep.

"The extent to which individuals are affected by sleep deprivation varies, with some crashing out and others holding up well after a night without sleep," said Michael Chee, MBBS, at the Duke-National University of Singapore Graduate Medical School, an expert on sleep deprivation who was not affiliated with the study. However, studying how the brain produces these behavioral differences is difficult: researchers usually do not know whether their study participants will be vulnerable to sleep deprivation until *after* a study is complete. Previous studies have shown conflicting results, perhaps because the study subjects differed widely in vulnerability to sleep deprivation.

In the current study, the researchers, led by Pierre Maquet, MD, at the University of Lěege in Belgium and Derk-Jan Dijk, PhD, at the University of Surrey in the United Kingdom, avoided this problem by selecting study participants based on their genes. Previous research showed that the *PERIOD3* (*PER3*) gene predicts how people will respond to sleep deprivation. People carry either long or short variants of the gene. Those with the short *PER3* variant are resilient to sleep loss —

they perform well on cognitive tasks after sleep deprivation. However, those with the long *PER3* variant are vulnerable — they show deficits in cognitive performance after sleep deprivation. Now the new study explains why.

The authors imaged study participants while they did a working memory task that requires attention and cognitive control — also called executive function. The researchers imaged each participant four times: the night before and the morning after a good night's sleep, and the night before and morning after a sleepless night.

They found that the resilient, short gene variant group compensated for sleep loss by "recruiting" extra brain structures. In addition to brain structures normally activated by the cognitive task, these participants showed increased activity in other frontal, temporal, and subcortical brain structures after a sleepless night.

In contrast, after a sleepless night, vulnerable participants, the long *PER3* group, showed reduced activity in brain structures normally activated by the task. These participants also showed reduced brain activity in one brain structure — the right posterior inferior frontal gyrus — after a normal waking day. These data are consistent with previous research suggesting that people with the long gene variant perform better on executive tasks earlier, but not later, in the day.

"Our study uncovers some of the networks underlying individual differences in sleep loss vulnerability and shows for the first time how genetic differences in brain activity associate with cognitive performance and fatigue," said study author Maquet. "The data also provide a basis for the development of measures to counteract individual cognitive deficits associated with sleep loss," he said.

"This study and others like it could help in identifying those who may be

at risk for performance decline in jobs where sleep deprivation is an integral feature, for example- all-night health care staff, senior decision makers, commercial aircraft pilots, and truck drivers. Such knowledge might also guide the development of more effective, possibly personalized countermeasures for at-risk people," said Chee, the expert unaffiliated with the study.

More information: www.jneurosci.org/

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