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Depression linked to altered activity of circadian rhythm gene

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(PhysOrg.com) -- Depression appears to be associated with a molecular-level disturbance in the body's 24-hour clock, new research suggests.

Scientists examined genes that regulate circadian rhythm in people with and without a history of depression. As a group, those with a history of depression had a higher level of activity of the so-called Clock gene, which has a role in regulating circadian rhythm, than did people with no mood disorders.

Higher expression levels of this gene suggest something is amiss in the body's 24-hour biological and behavioral cycle, which could affect sleep patterns and other physiological functions governed by circadian rhythm. Sleep disturbance is a common symptom of depression.

But the researchers noted that the association between the gene activity and depression is just that – a link, with no demonstrated causal effect in either direction. At this point in what is known about the relationship, this genetic profile could lead to depression or depression could alter this particular gene function, or some other biological or environmental influences could combine to disrupt the circadian clock.

Though this study offers just a snapshot in time of circadian activity in people with and without depression, the finding could have important clinical implications if it is supported by additional research. People with depression who share this genetic profile might benefit most from sleep-related treatments, such as light therapy or a class of antidepressants that

act on melatonin, a hormone that regulates sleep.

“We know that there are a lot of insomnia symptoms in depression, especially early morning awakening,” said Jean-Philippe Gouin, a graduate student in psychology at Ohio State University and lead author of the study. “We can’t say with this study that there is a direct relationship between this altered gene function and behavior, but the research suggests that over-expression of circadian genes might serve as a biomarker of vulnerability to depression.”

The research is published in a recent issue of the *Journal of Affective Disorders*.

Gouin is currently serving a predoctoral clinical psychology internship at Rush University Medical Center. As a graduate student at Ohio State, he has worked for years on studies led by the Institute for Behavioral Medicine Research that examine the health effects of chronic stress in people who take care of loved ones with dementia. Some of the people who participated in this study were from that population.

“There was some evidence that chronic stress led to changes in circadian gene expression in animals,” Gouin said. “We wanted to see if that would be the case in humans, and one of the models of chronic stress in humans is dementia caregiving stress. We found that caregiving was not related to circadian genes, but instead it was really the history of depression that distinguishes between regulation of these genes.”

The researchers collected blood samples from, and conducted interviews with, 60 people: 25 who were providing at least five hours of care per week for a family member with dementia and 35 non-caregiving controls with similar demographic characteristics. Thirty participants had a lifetime history of depression, while the other 30 had never been clinically depressed.

All blood samples were drawn between 9 a.m. and 11 a.m. to control for variations in circadian clock gene activity that occur throughout the day.

The researchers analyzed the blood to determine the messenger RNA levels for four circadian genes, including Clock. Messenger RNA (mRNA) contains the set of instructions for building proteins, so its level in genes dictates how much protein each gene is making.

As a group, the participants with a history of depression had a significantly higher level of Clock mRNA expression than did participants who had never been depressed. The researchers didn't find statistically significant results for the other three genes.

The association between depression and elevated Clock mRNA levels held up even when figures were adjusted for differences in age, sex, body mass index, alcohol and tobacco use, exercise, other medical conditions and caregiving status, Gouin noted.

He said that to further define the relationship between this genetic profile and depression, researchers ideally would monitor research participants over time to measure the changes in mRNA expression in circadian genes through a 24-hour cycle.

"If we look at people who have depression, they can have very different groups of symptoms. So if some of them have a biological profile that shows circadian dysfunction, there is a chance that a circadian type of treatment might be more helpful for them than for others," Gouin said.

He conducted the study with co-authors James Connors, Janice Kiecolt-Glaser, Ronald Glaser, William Malarkey, Cathie Atkinson and Ning Quan of Ohio State's Institute for Behavioral Medicine Research, and David Beversdorf of the University of Missouri.