Study identifies two biomarkers for lack of sleep

February 13 2015, by Heather Zeiger

Credit: xiaphias/Wikipedia

(Phys.org)—Ideally, we would get the appropriate amount of sleep to keep our bodies healthy, but in our modern society things like jet lag, extended work hours, or using electronic devices cause disruptions in our sleep/wake cycle often leading to fewer hours of quality sleep. Most people suffer from chronic sleep restriction rather than complete deprivation, but there are very few studies that explore the effects of

sleep restriction. Amita Sahgal and Aalim Weljie from the University of Pennsylvania and Peter Meerlo, from the University of Groningen in The Netherlands, investigated at how chronic sleep restriction affects the body's metabolic processes. Their work is published in the *Proceedings of the National Academy of Sciences*.

Recent studies have shown that lack of sleep may be a culprit for increased risks of several health issues including obesity, heart disease, and diabetes. One theory is that sleep deprivation causes metabolic changes including changes in the brain's metabolic pathway. Sehgal, et al found two metabolites common in both rats and humans that change after chronic sleep restriction, oxalic acid and diacylglycerol 36:3. Both are byproducts of two different metabolic processes, but behave similarly when rats or humans lack sleep.

For the human subjects and the rat models, a baseline reading of blood metabolite content was taken after a 12-hour fast and eight to 10 hours of sleep. Then, both groups were subjected to five days of sleep that was restricted to four hours per night. Blood was taken after one night to test acute sleep restriction and taken after five nights to test chronic sleep restriction. Finally, blood was taken after a "recovery" night of eight to 10 hours of sleep to see if the metabolic profile returned to baseline levels.

While there was variation in metabolite composition between humans and rats, both showed an increase in phospholipids after acute and chronic sleep restriction. The particular phospholipids varied between the two, but indicated that under restricted sleep, the metabolic processes are operating in an oxidative environment. Both rats and humans showed a distinct decrease in oxalic acid and diacylglycerol 36:3 levels. Additionally, both showed a return to baseline levels for most, but not all, metabolites after a recovery night.

The reasons for reduced oxalic acid levels are likely from reduced synthesis or increased gut microbiota processing, and not from dietary intake. It is unclear why diacylglycerol levels are reduced in both humans and rats. Even though more studies are needed to determine why these levels decrease in both humans and rats, because oxalic acid and diacylglycerol 36:3 responded similarly in both species, they can serve as biomarkers for sleep loss.

Other results were species specific. After chronic sleep restriction, the rats had indicators of oxidative stress, which is due to the buildup of oxidants that are typically removed after sleeping, but humans did not show oxidative stress after four hours of sleep per night. Prior studies had shown that completely sleep deprived, humans showed signs of oxidative stress. This suggests that humans may be able to counteract the effects of oxidative stress with less sleep more easily than rats. The human subjects did show elevated levels of the amino acids, tryptophan and phenylalanine, both of which are precursors for neurotransmitter production, suggesting that amino acid metabolism is affected by sleep restriction.

This study elucidates some of the effects sleep restriction has on metabolic processes. Sleep restriction affects several different processes in the body and chronic sleep restriction likely induces an oxidative environment. Additionally, two biomarkers were found that can aid in further studies.

More information: "Oxalic acid and diacylglycerol 36:3 are cross-species markers of sleep debt." *PNAS* 2015 ; published ahead of print February 9, 2015
www.pnas.org/content/early/2015/02/03/1417432112

Abstract
Sleep is an essential biological process that is thought to have a critical

role in metabolic regulation. In humans, reduced sleep duration has been associated with risk for metabolic disorders, including weight gain, diabetes, obesity, and cardiovascular disease. However, our understanding of the molecular mechanisms underlying effects of sleep loss is only in its nascent stages. In this study we used rat and human models to simulate modern-day conditions of restricted sleep and addressed cross-species consequences via comprehensive metabolite profiling. Serum from sleep-restricted rats was analyzed using polar and nonpolar methods in two independent datasets (n = 10 per study, 3,380 measured features, 407 identified). A total of 38 features were changed across independent experiments, with the majority classified as lipids (18 from 28 identified). In a parallel human study, 92 metabolites were identified as potentially significant, with the majority also classified as lipids (32 of 37 identified). Intriguingly, two metabolites, oxalic acid and diacylglycerol 36:3, were robustly and quantitatively reduced in both species following sleep restriction, and recovered to near baseline levels after sleep restriction (P