

Research suggests multiple 'body clocks'

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Research conducted at Oregon Health & Science University suggests that contrary to popular belief, the body has more than one "body clock." The previously known master body clock resides in a part of the brain called the suprachiasmatic nucleus (SCN). Researchers at OHSU's Oregon National Primate Research Center (ONPRC) have now revealed the existence of a secondary clock-like mechanism associated with the adrenal gland. The research also suggests a high likelihood that additional clocks exist in the body.

The study results are printed in the current edition of the journal *Molecular Endocrinology*.

"We're all familiar with the idea that the body has a master clock that controls sleep-wake cycles. In fact, most of us have witnessed the impacts of this clock in the form of jet lag where it takes the body a number of days to adjust to a new time schedule following a long flight," explained Henryk Urbanski, Ph.D., senior author of the study and a senior scientist at ONPRC. "Our latest research suggests that a separate but likely related clock resides in the adrenal gland. The adrenal gland is involved in several important body functions, such as body temperature regulation, metabolism, mood, stress response and reproduction. The research also suggests that other peripheral clocks reside throughout the body and that these clocks are perhaps interconnected."

To conduct the research, scientists studied adrenal gland function in rhesus macaque monkeys which is very similar to human adrenal gland function. Specifically, researchers measured gene expression in the

adrenal gland of monkeys during a 24-hour period (six times a day, four-hour intervals). In analyzing this information, researchers identified 322 genes in the adrenal gland with functions that varied rhythmically over a 24-hour period, meaning that each gene's function peaked and diminished at the same time each day. Interestingly, the scientists also noted that a subgroup of these 322 genes also exist in the SCN – the home of the body's master body clock. This suggests that the adrenal gland has its own timing mechanism that is related to, but separate from, the SCN body clock.

"Of course, different genes peaked in function at different times of the day," explained Dario Lemos, an OHSU graduate student in the Urbanski lab and first author of the study. "For instance, genes controlling catecholamine secretion were more active in the day with function greatly decreasing at night. Catecholamines are involved in many important body functions, such as stress and mood."

This research provides important new information regarding the complex, rhythmic, 24-hour functions of the body. The research may also impact current therapies for a variety of diseases. For instance, data gathered in this study and future studies may suggest that certain therapies be delivered at certain times to synchronize with normal body functions controlled by body clocks.

"One example is testosterone replacement, a common treatment for certain disorders in males such as sexual dysfunction and depression," explained Urbanski. "Patients receiving testosterone late in the day often complain of sleep loss. This is likely due to the fact that in healthy people, testosterone levels are lower in the afternoon and evening. As more data is gathered about body clock functions in our lab and others, we will likely learn of a specific window of time during the day where testosterone therapy is effective, but less disruptive for patients."

Source: Oregon Health & Science University

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