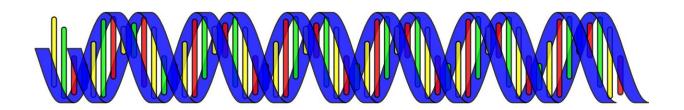


Research sheds light on body clock and links to mental health and disease

January 29 2019



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A large-scale genomic analysis has revealed some of the inner workings of the body clock, shedding new light on how it links to mental health and disease.

The study, published in *Nature Communications*, suggests that being genetically programmed to rise early may lead to greater well-being and a lower risk of schizophrenia and depression. However, despite much



previous speculation, the results did not reveal any strong links to diseases such as diabetes or obesity.

The study was conducted by an international collaboration, led by the University of Exeter and Massachusetts General Hospital and funded by the Medical Research Council. It highlights the key role of the retina in the eye in helping the body to keep time. It also increases the number of areas of the genome known to influence whether someone is an early riser from 24 to 351.

Professor Mike Weedon, of the University of Exeter Medical School, who led the research, said: "This study highlights a large number of genes which can be studied in more detail to work out how different people can have different body clocks. The large number of people in our study means we have provided the strongest evidence to date that 'night owls' are at higher risk of mental health problems, such as schizophrenia and lower mental well-being, although further studies are needed to fully understand this link."

The work was conducted in 250,000 US-based research participants from 23andMe, a company that provides private genomic analyses, and 450,000 people in the UK Biobank study. All participants were asked if they were a "morning person" or an "evening person", and their genomes were analysed to look at which genes they had in common which may influence their sleep patterns.

The researchers confirmed their results using information from wrist-worn activity trackers worn by more than 85,000 individuals in the UK Biobank. This information showed that the genetic variants the researchers identified could shift a person's natural waking time by up to 25 mins—changing some people's waking time from 8am to 8.25am, for example. The researchers found that the genetic areas influence sleep timing, but not the quality or duration of sleep.



The genomic regions identified include those central to our body clocks, also referred to as circadian rhythms, as well as genes expressed in the brain and in retinal tissue in the eye. The body clock cycle is slightly longer than the 24-hour daily cycle. The eye tissue connection may help explain how the brain detects light to "reset" the body clock each day and to align with the 24-hour cycle.

Our body clocks are influenced by genes and lifestyle factors including diet, exposure to artificial light and our jobs and activities. Our body clock affects a wide range of molecular processes, including hormone levels and core body temperature, as well as our waking and sleeping patterns.

Lead author Dr. Samuel E. Jones, of the University of Exeter Medical School, said: "The discovery of this fundamental body clock mechanism in the brain recently won the Nobel prize for medicine in 2017. However, we still know very little about whether or not your body clock influences your risk of disease

"Our work indicates that part of the reason why some people are up with the lark while others are night owls is because of differences in both the way our brains react to external light signals and the normal functioning of our internal clocks. These small differences may have potentially significant effects on the ability of our body clocks to keep time effectively, potentially altering risk of both disease and mental health disorders."

Co-lead author Dr. Jacqueline M Lane, of the Massachusetts General Hospital Department of Anesthesia, added "By understanding the genetics of sleep and activity timing in the general population, we also gain insights into potential avenues of therapy for individuals with more extreme conditions, such as those with advanced or delayed circadian rhythm disorders."



Dr. Rachael Panizzo, Programme Manager for Mental Health and Addiction at the Medical Research Council, said: "We know that there are links between how the body clock functions and our health and wellbeing but, to date, we have understood little about the part genetics plays. Now, with the help of publicly funded datasets like UK Biobank, researchers are able to study on an unprecedented scale, the interplay between the genetics of the body clock and the risk of mental health conditions such as schizophrenia and depression. This study provides valuable new insights which we hope will lead to more effective interventions for those most at risk."

Dr. Dave Hinds, Principal Scientist, Statistical Genetics at 23andMe said: "Data shared by 23andMe research participants made this work possible—and we now have a report in our product that shares with our customers whether they are predisposed to be a morning or evening person. This work will enable better estimates of the genetic contribution to this trait, as well as helping us to understand how one aspect of sleep behavior relates to other health conditions,"

The full paper is entitled 'Genome-wide association analyses of chronotype in 697,828 individuals provides insights into circadian rhythms'.

More information: Genome-wide association analyses of chronotype in 697,828 individuals provides insights into circadian rhythms, *Nature Communications* (2019). DOI: 10.1038/s41467-018-08259-7, www.nature.com/articles/s41467-018-08259-7

Provided by University of Exeter

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January 29) retrieved 26 April 2024 from https://medicalxpress.com/news/2019-01-body-clock-links-mental-health.html

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