Stress with disrupted body clock increases risk of metabolic disease

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Everyday stress coupled with disruptions to the body's internal clock may increase the risks of developing metabolic disorders including obesity and type 2 diabetes, according to a study presented at the Society for Endocrinology annual conference in Brighton. These mouse data indicate that environmental stress coupled with alterations in normal body clock function can affect food intake, promote weight gain and have long-lasting effects on stress responses. This may help explain why shift-work, jet lag and chronic stress in people can lead to metabolic disorders, as well as highlight therapeutic targets to investigate for future treatment.

In modern society the prevalence of everyday stress has been linked to the development of metabolic diseases, including diabetes and obesity. These diseases are also more common in people suffering from disruption to their normal body clock, such as shift workers. The internal body clock, or circadian rhythm, is a natural 24 hour cycle that regulates processes related to hormones, sleep and feeding that are essential for good health and can be affected by external factors. External stress induces release of the stress hormone, cortisol, to adapt energy metabolism to a perceived fight-or-flight situation. Levels of cortisol throughout the day are also regulated by our body clock. The connection between the circadian system and the stress response is very well characterised in rodents but the interaction between stress, our body clock and metabolism is not yet fully understood.

In order to investigate this interaction, Professor Henrik Oster and

colleagues at the University of Lübeck in Germany performed experiments using mice with genetic alterations in different parts of their body clock machinery. Mice exposed to social stress, in which male animals were repeatedly exposed to an unknown, dominant male, had increased stress responses that were dependent on the time of day of the stress exposure. Further experiments indicated that these stress responses were dependent on the body clock system, and that food intake and body weight were more likely to be negatively affected when stress occurs during their inactive phase (daytime for a mouse, night-time in humans). Repeated exposure to stress also led to long-lasting adaptations to responsiveness of the stress system that negatively affect metabolism.

Professor Oster states, "We have shown that stress responses depend on the time of day, are affected by the internal body clock and can interact to negatively affect food intake and body weight to predispose to metabolic disorders. These data suggest that body clock rhythm may be an underestimated factor in assessing the impact of chronic stress on general health and well-being."

Prof Oster now plans to further analyse the molecular targets of the body clock-stress interaction with the aim of identifying the mechanisms that affect metabolism and how these adverse health effects may be counteracted. Whilst rodent studies provide a useful and effective model for investigating this system, clinical studies would be required to confirm these effects in people.

Professor Oster comments, "Although in rodents, these data provide some mechanistic explanations for the negative effects of shift work and chronic stress on people, suggesting that both the timing and levels of stress are important factors for development of metabolic disease."

Prof Oster continues, "Further investigation of this system could lead to recommendations for better timing of working hours, stressful meetings

and rest that may increase productivity and enhance quality of life, reducing the financial burden of care for work-related stress."

More information: The study "The interplay between stress, biological clocks and metabolic function" will be presented by Professor Henrik Oster on Wednesday 13 November 2019, at the Society for Endocrinology BES 2019 Conference in Brighton, UK.

Provided by Society for Endocrinology