New method for treating stress

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(PhysOrg.com) -- A new analysis of the way the body responds to stress suggests that administering constant high levels of drugs is not the best way to treat this condition. A better way might be to design drugs that follow the body's own naturally-occurring rhythms.

Drug companies have traditionally sought to design new drugs that are as potent and as long-lasting in the body as possible.

However, a new analysis of the way the body responds to stress suggests that administering constant high levels of drugs is not the best way to treat this condition. A better way might be to design drugs that follow the body's own naturally-occurring rhythms.

Writing in the Proceedings of the Royal Society B, researchers from the University of Bristol report this week that the body has its own built-in processes which ensure the body regulates the way it responds to stress.

The team found that hormonal oscillations occur in the HPA axis (hypothalamo-pituitary-adrenal) which controls the body's reaction to stress, trauma and injury. The oscillating network of signals between these glands results in rapid rhythmic changes in hormone levels throughout the day.

Regulation of these rhythms is vital for protecting the individual from damage caused by stressful situations, so drugs designed to treat stress should take these rhythmic changes into account.

This finding - that rhythms can be generated by interactions between peripheral glands - is in stark contrast to the concept that all hormonal rhythms originate in the brain. The author's hope this work will stimulate pharmaceutical companies to consider not only the structure of new drugs but also their optimal patterns of release.

The researchers took a non-linear mathematical approach to examining data from the HPA axis. They found that delays inherent in regulating signals sent between the pituitary and adrenal glands is all that is necessary to ensure the body has oscillating levels of the potent hormone, cortisol. Oscillations of cortisol are necessary for the body to respond effectively to stress.

Dr John Terry, who did the mathematical modelling, explained: "Think about taking a shower - you turn the tap on to hot, but the water stays cold for a while. Then it gets too hot, so you turn it down. The temperature oscillates due to the delay between you adjusting the tap and the feedback you receive from the water temperature. It is the same principle at work in this complicated hormone system!"

Stafford Lightman, Professor of Medicine at Bristol University, added: "The oscillation of these hormones is very important as it maintains the body in a state of permanent flux and allows the unexpected - such as a lorry hurtling towards you - to result in a very rapid response, providing maximum opportunity for you to react and hopefully get out of the way".

Many of the systems in the body - from the central nervous system to intracellular control systems - depend on feed-forward and feed-back regulatory systems, such as those found in the HPA axis.

The new use of mathematical modelling to explain the rhythmic activities that have been described here could also be used to look at many other activities in the body - from brain rhythms to pulsatile

activity of individual genes.

More information: Origin of ultradian pulsatility in the hypothalamic-pituitary-adrenal axis by Jamie J. Walker, John R. Terry and Stafford L. Lightman. Proc. R. Soc. B (2010) . doi:10.1098/rspb.2009.2148

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