

This Week's Citation Classic

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Takahashi Y, Kipnis D M & Daughaday W H. Growth hormone secretion during sleep.

J. Clin. Invest. 47:2079-90, 1968.

[Washington Univ. Sch. Med., Dept. Med., Metabolism Div., St. Louis, MO]

In young adults a remarkable peak of GH secretion occurs about one hour after the onset of deep sleep. This GH secretion is clearly entrained with the onset of deeper levels of sleep and not with discernible metabolic stimuli. [The *SCJ*[®] indicates that this paper has been cited over 285 times since 1968.]

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"In September 1966, Yasuro Takahashi came to the metabolism division of the department of medicine of Washington University as a research fellow for only one year to learn immunoassay procedures and endocrine physiology. He arrived with a sound background in neurophysiology, particularly in the area of sleep physiology, which he had obtained at the Neuropsychiatric Research Institute in Tokyo. He was intrigued with earlier preliminary reports suggesting increased GH secretion during the night and wished to correlate GH secretion with the stages of sleep. Our division provided radioimmunoassay resources, an excellent Clinical Research Center equipped with a small but adequate sleep study room, and an active research program of study of growth hormone and insulin secretion. Within a very short period Takahashi initiated this study by

recruiting the subjects, personally monitoring their sleep by EEG and EMG, and conducting many of the assays.

Truly this was a remarkable performance of varied technical skills and Japanese industry.

"The results of this study were clear. The early period of deep sleep in young adults is associated with a major peak of growth hormone secretion unassociated with detectable changes in plasma glucose, fatty acid, insulin, or cortisol concentrations. GH secretion was clearly entrained with sleep as shown by sleep delay and sleep interruption studies. Administration of five CNS active drugs did not inhibit GH secretion with the possible exception of imipramine which did block GH secretion in two of the four subjects.

"We concluded that the GH secretion of early sleep was regulated by primary hypothalamic mechanisms unrelated to metabolic clues.

"As in many clinical investigations, this study brought together ideas and techniques from a number of disciplines which characterized an important human neuroendocrine function. The results of our study were rapidly confirmed and extended in other laboratories. The findings still have important implications in the study of human growth because for most subjects the sleep related GH peak represents the most active period of GH secretion for the entire 24 hours.

"This paper attracted much reader interest and stimulated others to undertake physiologic, neuropharmacologic, and clinical projects because of the direct linkage of growth hormone secretion with a specific neural mechanism—the sleep process. This, I think, accounts for the frequent citation of this paper."