Study may help explain 'awakenings' that occur with popular sleep-aid Ambien

June 29 2009

Some people who take the fast-acting sleep-aid zolpidem (Ambien) have been observed walking, eating, talking on the phone and even driving while not fully awake. Many often don't remember doing any of these activities the next morning. Similarly, this drug has been shown to awaken the minimally conscious into a conscious state. A new study by Georgetown University Medical Center (GUMC) researchers may help explain why these "awakenings" occur.

The study, published online in the Proceedings of the National Academy of Sciences Monday, suggests that while some powerful brain circuits are shut down with zolpidem, the powerful sedative activates other circuits when deprived of activity.

"Brain cells or neurons are highly reactive to incoming activity throughout life," explains Molly M. Huntsman, an assistant professor in the department of pharmacology at Georgetown University Medical Center and corresponding author for the study. "When brain activity is silenced, many neurons automatically react to this change. We see this in our study which suggests that inhibitory neurons responsible for stopping neural activity are themselves shut down by zolpidem. The excitatory neurons, responsible for transmitting activity, are then allowed to re-awaken and become active again, without monitoring because the inhibitory neurons are 'asleep'."

Rodents are especially dependent upon their whiskers to explore their environment; for the study, researchers trimmed the whiskers of mice

(while under anesthesia). They then studied the region of the brain responsive to whisker movements to examine activity-dependent brain circuits. After removing the whiskers and depriving neural activity, the inhibitory neurons that normally don't respond to sedation by zolpidem underwent a change, becoming more sensitive. The researchers posited that these neurons are shut down and, in turn, not able to monitor other brain circuits.

"This was really unexpected. It appears the receptors on some inhibitory neurons were changed and were able to be inhibited by zolpidem, preventing them from performing their normal functions. We merely wanted to use zolpidem as a tool to examine which type of functional inhibitory receptor is expressed in certain neurons. Yet it turns out that sensory deprivation in the form of whisker trimming is enough to alter the receptor composition expressed in these cells." Huntsman says.

Researchers say that while the study suggests that zolpidem shuts down active neural pathways and perhaps then triggers others, the activation of this trigger is unknown.

"Nevertheless, the paradoxical activation of brain circuits by a powerful sedative definitely needs more attention in additional studies both human and in animal models," Huntsman concludes.

Source: Georgetown University Medical Center (news : web)