A novel use of Angiotensin II AT1 receptor antagonists for the treatment of insomnia

ID 2562

Background
Insomnia is the most prevalent sleep disorder in the normal population and it is also a cardinal feature of several psychiatric disorders. Insomnia is associated with daytime sleepiness, fatigue, impaired performance and memory, cognitive and psychomotor deficits, and increased anxiety and irritability.

Insomnia can be triggered by stressful life events in predisposed individuals and, in general, insomniacs show increased neuroendocrine and sympathoadrenal activity. Current treatments for insomnia target the symptoms instead of the pathophysiologic alterations that underlie those symptoms, and these treatments are associated with undesirable side effects as well as high risk for abuse and dependence. In addition, current treatments decrease REM sleep substantially and do not restore normal sleep. Therefore, the development of more specific pharmacotherapy for the treatment of insomnia is a top priority.

Technology Description
Angiotensin II (AngII) is a signaling molecule found both peripherally and centrally. Peripheral AngII is well known for its role in cardiovascular regulation, and drugs that block AngII signaling are frequently used to treat cardiovascular disease. Recent work suggests that brain AngII is involved in the regulation of stress responses.

Pitt researchers have shown that AngII AT1 receptor antagonist seems to restore normal sleep (including REM sleep) in a rat model of stress-induced insomnia. This effect appears to be mediated by inhibition of the cortex and arousal system, which receive inputs from limbic neuronal groups that are activated during insomnia and have AngII AT1 receptors. Thus, brain AngII system constitutes a novel and more specific target for the treatment of insomnia.

Applications
• Therapeutic use for the treatment of insomnia

Advantages
• Angiotensin II antagonists are safe and well tolerated in humans
• Angiotensin II antagonists target specific brain areas that become activated during insomnia and, therefore, are more specific and will cause less side-effects and are non-addictive
• Decreases the time to fall asleep
• Increases non REM sleep
• Does not suppress REM sleep

Stage of Development
• In vivo data available
• Pilot clinical study will be conducted soon (next months)

Provisional Patent Application filed

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Pending Grants

2012-2014 R-03 Grant (NIH/NIMH MH097037): Effects of an Angiotensin II antagonist in a

2012-2017 R-01 Grant (NIH/NHLBI): Hypothalamic inflammatory and neurotransmitter
mechanisms involved in obesity-related hypertension (PI: D. Cai, Co-I: G. Cano). Albert Einstein
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Selected Publications

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7. Tupone D., Madden C.J., Cano G., Morrison
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