Adverse Effects of Psychotropic Medications on Sleep

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KEYWORDS

• Antidepressant • Antipsychotic • Insomnia • Sedation • Adverse effects • Sleep • Somnolence

KEY POINTS

- Psychotropic medications have a broad range of mechanisms of action, which are presumed to be involved in their sleep-related adverse effects.
- Insomnia and daytime somnolence are common adverse effects of these medications.
- These effects can be beneficial or detrimental depending on the particular symptoms of the patient's psychiatric disorder.
- Being aware of an agent's most likely adverse effects on sleep can aid the prescriber in choosing an agent that is more likely to improve the sleep component of a patient's psychiatric disorder.

ANTIDEPRESSANTS

People suffering from depressive disorders typically complain of difficulty falling asleep, frequent awakenings, early morning wakening, and non-refreshing sleep. Polysomnographic studies of depressed persons have confirmed these findings and show reduced rapid eye movement (REM) latency, increased REMs, increased total time in REM sleep, reduced slow wave sleep (SWS), and frequent awakenings throughout the night.[1] Antidepressants are widely prescribed for mood and anxiety disorders. According to the National Health and Nutrition Examination Survey, 11% of Americans over the age of 12 are taking an antidepressant medication.[2] Most of

Dr K. Doghramji owns stock in Merck and is a consultant for Merck, Inspire, Jazz, Xenoport, Teva, Pfizer, and Pernix. Dr W. C. Jangro has nothing to disclose.

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Psychiatr Clin N Am 39 (2016) 487–502
http://dx.doi.org/10.1016/j.psc.2016.04.009 **psych.theclinics.com**
0193-953X/16/$ – see front matter

Abbreviations	
5-HT	5-Hydroxytryptamine
ADHD	Attention-deficit/hyperactivity disorder
H1	Histamine 1 receptor
MAOI	Monoamine oxidase inhibitor
MDD	Major depressive disorder
NNTH	Numbers needed to treat to harm
PLM	Periodic limb movement
PSG	Polysomnogram
PSQI	Pittsburgh Sleep Quality Index
REM	Rapid eye movement
RLS	Restless legs syndrome
SNRI	Serotonin-norepinephrine reuptake inhibitor
SOL	Sleep onset latency
SRED	Sleep-related eating disorders
SSRI	Selective serotonin reuptake inhibitor
SWS	Slow wave sleep
TCA	Tricyclic antidepressant
TST	Total sleep time
VLPO	Ventrolateral preoptic nucleus
WASO	Wakefulness after sleep onset

these antidepressant medications are thought to exert their effects through modulation of various monoamines as well as interactions with receptors such as histamine and muscarinic cholinergic receptors. Through these interactions, antidepressants can have a significant impact on sleep physiology. The central processes governing sleep and wakefulness are dependent on the complex interaction of these various neurotransmitter systems.[3,4] The ascending arousal system, which traverses from the brainstem regions to the cerebral cortex, consists of noradrenergic neurons of the ventrolateral medulla and locus coeruleus, cholinergic neurons in the pedunculopontine and laterodorsal tegmental nuclei, serotonergic neurons in the dorsal raphe nucleus, dopaminergic neurons of the ventral periaqueductal gray matter, and histaminergic neurons of the tuberomammillary nucleus. Orexin (hypocretin) neurons of the lateral hypothalamic area contribute as well and are thought to have a modulatory influence on the transition between sleep and wakefulness. On the other hand, the sleep system is thought to be controlled by activation of sleep-active cells in the ventrolateral preoptic nucleus (VLPO), which contain the inhibitory neurotransmitters γ-aminobutyric acid and galanin. These cells project to the essential components of the ascending arousal system. Inhibition of the arousal system by the VLPO during sleep is critical for the maintenance and consolidation of sleep.

Antidepressant classes and their receptor profiles are listed in **Table 1**. For definitions of polysomnographic terms, readers are referred to standard scoring manuals.[5]

SELECTIVE SEROTONIN REUPTAKE INHIBITORS

Subjective Effects

Subjective complaints of insomnia and daytime somnolence are common in people with depression being treated with selective serotonin reuptake inhibitors (SSRIs). Of the SSRIs currently indicated for the treatment of depression, fluoxetine's effects on sleep have been the most thoroughly studied. These effects may represent a class effect. Fluoxetine has been found to cause both significant activation and sedation compared with placebo.[6] Rates of activation tend to be stable at dosages between 5 and 40 mg per day, but increase at dosages greater than 40 mg per day. On the other