Serotonin and dreaming

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Abstract

Many clinical anecdotes and an experimental study have reported intensification of dreaming by the selective serotonin-reuptake inhibitors (SSRIs). However, no published neurochemical dream model invokes serotonin as a dream-promoting neuromodulator or accounts for serotonergic dream enhancement. An experimental study of normal volunteers showed that, although SSRI treatment decreased dream recall frequency, several subject-rated dream-intensity measures were greater during steady-state drug administration compared with pre-drug baseline and early drug treatment. Additionally, such subject-rated dream intensity as well as dream report length and judge-rated bizarreness were greater during acute discontinuation than during pre-drug baseline and drug administration periods. Nightcap ambulatory monitor data showed increased REM latency during treatment and increased REM density during acute discontinuation, indicative of SSRI-induced REM suppression and REM rebound following drug discontinuation, respectively. The bulk of pharmacological evidence suggests that drugs that enhance serotonergic neurotransmission lighten sleep. Sleep-disruptive effects of SSRIs are accompanied by electroencephalographic and electromyographic signs of brain activation, abnormally prominent eye movements in NREM sleep, and REM rebound following drug discontinuation. Explanations of SSRI-induced dream intensification suggested by these findings include, respectively, generalized brain activation during sleep, enhanced NREM dreaming, and within-night REM rebound. Additional clues as to potential causes of serotonergic dream enhancement are provided by: (i) the cellular pharmacology of hallucinogens that act on 5-HT2A receptors, (ii) the phenomenological and functional neuroimaging effects of serotonergic hallucinogens, and (iii) putative neurophysiological mechanisms of lesion-related complex hallucinosis.
Introduction

Reports of direct effects on dreaming by endogenous serotonin (5-HT) or by pharmaceutical agents impacting serotonergic neurotransmission are rare as, indeed, is direct evidence for dream effects of any other endogenous neurochemical or its exogenous modulators (i.e., agonists, antagonists, reuptake inhibitors, degradatory enzyme inhibitors, presynaptic releasers). This is, of course, because the experiments with animals that have been so usefully employed to describe the neurochemical modulation of sleep are uninformative with regard to a behavior that depends upon verbal report of a subjective experience. Nonetheless, biopsychological models of dreaming have been proposed that invoke roles for endogenous neuromodulators based upon animal studies of behavioral state control, clinical anecdotes and the few extant human experimental pharmacology reports (see [1–3] for reviews). Several recent reviews on the pharmacology of nightmares [4–6] have also provided valuable data for speculation on neurochemical factors in dreaming.

Interestingly, although clinical anecdotes [7, 8] and an experimental study [9] have reported intensification of dreaming by the selective serotonin reuptake inhibitors (SSRIs), none of the three major neurochemical dream models invoke serotonin as a dream promoting neuromodulator (see [3, 10, 11]). Moreover, two of these models specifically cite diminished serotonergic modulation in REM as a contributing factor in dreaming. Specifically, the activation synthesis/AIM model of Hobson and McCarley [3] suggests that the nadir of serotonergic (and noradrenergic) tone in REM sleep enhances the relative forebrain-activational importance of acetylcholine (ACh) in determining the formal characteristics of dreaming. This is because the ascending cholinergic system becomes the major neuromodulatory system activating the diencephalon and cortex during REM [3]. Likewise, the psychotomimetic theory of Gottesmann [10, 12] suggests that the relative importance of dopaminergic neurotransmission during dreaming is enhanced by the absence of serotonergic inhibitory influence on the forebrain in REM.

Although the complex neurochemistry underlying dreaming (as well as any other behavioral state) is unlikely to be reducible to a simple interaction of a few neuromodulatory systems [2, 6, 13], the question remains as to why exogenously enhanced serotonergic neurotransmission appears to enhance dreaming in at least some individuals.

Effects of serotonergic drugs on dreaming

Enhancement of dreaming has been noted during treatment of mood and anxiety disorders with the SSRIs fluoxetine [7, 9, 14, 15] and citalopram [16]. Our preliminary unpublished interview data suggest that, in patients treated for