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Experts in the Art & Science of Pharmaceutical Compounding

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Sedative Effects of Progesterone

Points/Quotes from Articles

1. Progesterone is known to exert multiple effects on brain functioning, including a rapid depression of neuronal excitability, as reflected by its anesthetic, anxiolytic, anticonvulsant, and antinociceptive properties.[2]
2. Progesterone induces changes in sleep comparable to those of agonistic $GABA_A$ receptor modulators.[3]
3. Research in rats and humans has shown that exogenous progesterone evokes a sleep profile similar to that induced by agonistic modulators of -aminobutyric $acid_A$ receptors, such as benzodiazepines.[2]
4. Intraperitoneal administration of progesterone in rat had a dose-dependent hypnotic effects; it shortened sleep latency, decreased the time spent in wakefulness and REMS and selectively promoted pre-REMS (intermediate-stage or transition-type sleep).[2]
5. Administration of progesterone in humans produced small, delayed increases in heart rate and feelings of fatigue, and it impaired smooth eye pursuit. These results suggest that progesterone and its metabolites can produce sedative-like effects in both men and women.[1]
6. Preclinical studies have demonstrated that certain metabolites of progesterone produce sedative-like effects and anesthesia, apparently through their actions on $GABA_A$ receptors.[1]
7. Oral progesterone is helpful for insomnia, in contrast, transdermal progesterone cream does not have the same effect as oral progesterone on sleep.[4]
8. The behavioral effects of progesterone and its metabolites have been examined in humans, most commonly in women. *Merryman et al. (1954)* reported that intravenous injections of progesterone (100-500mg) produced hypnotic effects in healthy women. Oral progesterone produces some subjective sedation and memory impairment in postmenopausal women but the effects have been subtle and highly variable. The variability after oral progesterone administration is largely due to pharmacokinetic variability.[1]
9. One study found that progesterone 100mg produced mild sedative-like effects in normally cycling women and post-menopausal women.[1]
10. 200mg progesterone induced moderate sedative like subjective effects and ocular motor inhibition in both men and women. The study concluded that 200mg IM progesterone increased POMS fatigue scores and has mild sedative-like effects.[1]
11. Progesterone dose dependently shortened non-rapid eye movement sleep (NREMS) latency, lengthened rapid eye movement sleep (REMS) latency, decreased the amount of wakefulness and REMS, and markedly increased pre-REMS, an intermediate state between NREMS and REMS.[3]
12. Progesterone administration elicited changes in the amount of time spend in the various sleep states and in the sleep state-specific EEG that are highly similar to those induced by $GABA_A$ agonists such as benzodiazepines in rats.[3]
13. The *Lancel et al. (1996)* study concluded that the study showed that exogenous progesterone has dose-dependent hypnotic properties with a short-onset latency, which may have biological relevance. The effects of progesterone on sleep architecture and on sleep EEG are strikingly similar to those of agonistic modulators of $GABA_A$ receptors. Progesterone also dose dependently elevates the concentrations of its potent $GABA_A$ receptor agonistic metabolites. These observations strongly suggest that progesterone influences sleep indirectly through the potentiating action of its neuroactive metabolites on $GABA_A$ receptor functioning.[3]

References

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2. Lancel M, *et al.* Allopregnanolone affects sleep in a benzodiazepine-like fashion. *The Journal of Pharmacology and Experimental Therapeutics.* 1997; 282(3): 1231-1218.
3. Lancel M, Faulhaber J, Holsboer F, Rupprecht R. Progesterone induces changes in sleep comparable to those of agonistic GABA(A) receptor modulators. *American Journal of Physiology. Endocrinology and Metabolism.* 1996; 34(4): E763-E722.
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