Mitragynine (Kratom) impairs spatial learning and hippocampal synaptic transmission in rats

ABSTRACT

Background: Mitragynine is the major alkaloid of Mitragyna speciosa (Korth.) or Kratom, a psychoactive plant widely abused in Southeast Asia. While addictive effects of the substance are emerging, adverse cognitive effects of this drug and neuropharmacological actions are insufficiently understood.

Aims: In the present study, we investigated the effects of mitragynine on spatial learning and synaptic transmission in the CA1 region of the hippocampus.

Methods: Male Sprague Dawley rats received daily (for 12 days) training sessions in the Morris water maze, with each session followed by treatment either with mitragynine (1, 5, or 10 mg/kg; intraperitoneally), morphine (5 mg/kg; intraperitoneally) or a vehicle. In the second experiment, we recorded field excitatory postsynaptic potentials in the hippocampal CA1 area in anesthetized rats and assessed the effects of mitragynine on baseline synaptic transmission, paired-pulse facilitation, and long-term potentiation. Gene expression of major memory- and addiction-related genes was investigated and the effects of mitragynine on Ca2+ influx was also examined in cultured primary neurons from E16-E18 rats.

Results/outcomes: Escape latency results indicate that animals treated with mitragynine displayed a slower rate of acquisition as compared to their control counterparts. Further, mitragynine treatment significantly reduced the amplitude of baseline (i.e. non-potentiated) field excitatory postsynaptic potentials and resulted in a minor suppression of long-term potentiation in CA1. Bdnf and αCaMKII mRNA expressions in the brain were not affected and Ca2+ influx elicited by glutamate application was inhibited in neurons pre-treated with mitragynine.

Conclusions/interpretation: These data suggest that high doses of mitragynine (5 and 10 mg/kg) cause memory deficits, possibly via inhibition of Ca2+ influx and disruption of hippocampal synaptic transmission and long-term potentiation induction.

Keyword: Kratom; Mitragynine; Morris water maze; Field excitatory postsynaptic potentials; Long-term potentiation