reports of hallucinations are very rare. Perhaps, patients attending a psychiatric clinic are more susceptible to psychiatric side effects of these medications. In the above FDA study, approximately 10% cases had a previous history of a similar psychiatric condition, and <3% of patients suffered from drug abuse. Younger children were affected more often than adolescents, almost half of the cases occurring at <10 years of age. A review of the data also appears to show that the frequency of psychiatric adverse events is correlated with the duration of exposure. A dose effect was not studied, but this may be a factor. The number of person years of exposure is greater with drugs (methylphenidate patch and atomoxetine) that account for the higher number of hallucinatory reports.

An FDA warning was added to package inserts for ADHD drugs regarding psychiatric and cardiovascular adverse effects in 2006. Patients and physicians should be aware of the possible psychiatric adverse events, especially hallucinations, when prescribing stimulants or the nonstimulant, atomoxetine, for the treatment of ADHD in children. An incidence of 1 in 400 cases is estimated in one report. (Ross RG. Am J Psychiatry 2006;163:1149-1152). Physicians should be especially vigilant when treating younger children with the newer agents. The relative freedom from psychosis/mania events during double-blind treatment with Adderall XR is of interest, although isolated reports occur with open-label trials.

MODAFINIL-INDUCED INCREASES IN BRAIN DOPAMINE LEVELS

The acute effects of modafinil on extracellular dopamine and on dopamine transporters in the male human brain were measured by PET study in 10 healthy subjects at Brookhaven National Laboratory and National Institute on Drug Abuse, Bethesda, MD. Modafinil decreased mean [11C]raclopride binding potential in caudate, putamen, and nucleus accumbens, reflecting increases in extracellular dopamine. Modafinil also decreased [11C]cocaine binding potential in these sites, reflecting blocked dopamine transporters. The changes in dopamine brain levels with modafinil were similar to those reported with methylphenidate. Modafinil in the therapeutic doses (200mg and 400mg) used in this study significantly increased heart rate and systolic blood pressure. Drugs that increase dopamine in the nucleus accumbens have the potential for abuse. The results of this study indicate the need for a heightened awareness for potential abuse and dependency on modafinil in patients who may be vulnerable. (Volkow ND, Foiwler JS, Logan J, et al. Effects of modafinil on dopamine and dopamine transporters in the male human brain. **JAMA** March 18, 2009;301:1148-1154).

COMMENT. The mechanism of action of modafinil as a wake-promoting agent and cognitive enhancer in patients with narcolepsy and ADHD was believed to differ from that of the stimulants, methylphenidate and amphetamine. Whereas the stimulants are known to increase dopamine and norepinephrine in brain, modafinil was theorized to affect epinephrine, g-aminobutyric acid, and glutamate. The above study is evidence of a dopamine mechanism of modafinil, similar to that of CNS stimulants. The authors advise caution in the use of modafinil in patients with a history of drug abuse or other vulnerable populations. In the treatment of ADHD during childhood and adolescence, researchers find little evidence of abuse or overuse of stimulant medication (Goldman LS et al. **JAMA** 1998;279:1100-1107).