EFFECTS ON DL-5-HYDROXYTRYPTOPHAN ON DEPRIVATION-INDUCED ETHANOL CONSUMPTION IN RATS

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SUMMARY

While the specific aim of this research was to examine the effects of 5-HTP and other pharmacological treatments on ethanol consumption in rats, the long range goals of such experiments are to attempt to understand the complex human disease state of alcoholism. Through the use of animal models such as this, much useful information can be obtained. Once basic mechanisms using animal model are ascertained, efforts can be directed at developing adequate therapeutic procedures for treatment of alcoholism.

The fluid deprivation animal model used in these studies provided stable baselines of fluid intake which is necessary for pharmacological evaluation of ethanol consumption. While the effect of an injection of 5-HTP to decrease ethanol consumption is an interesting finding, the post-injection time course is of the utmost importance since these rats had no other source of fluid available to them. The fact that the effect of 5-HTP was shown to be a dose dependent phenomenon strengthens the evidence implicating the serotonergic system in the regulation of ethanol ingestion. Further evidence for the involvement of the serotonergic system came as a result of the acceptance of water by a rat following almost total rejection of ethanol following a dose of 5-HTP which had almost no effect on water consumption.

While at first the results of experiments with 5-HTP and PCPA seem to be in conflict with each other, analysis of these findings indicates this may not be the case. 5-HTP injections decreased ethanol consumption by rats and since this effect is presumed to be related to an increase in brain levels of serotonin, then a decrease in serotonin by

pretreatment with PCPA would have been expected to result in an increase in ethanol consumption. Not only did PCPA not cause an increase in ethanol consumption, but rather a significant decrease with a time course for return of consumption to baseline values which followed remarkably well the time course for return of brain serotonin levels to control values. While both these sets of data strongly support the implication of the serotonergic system in the regulation of ethanol consumption, two entirely different mechanisms may be operative. In the case of 5-HTP the marked decrease in ethanol consumption followed by almost total subsequent rejection may be due to a conditioned aversion phenomenon. Evidence in support of this hypothesis is the persistent rejection of ethanol long after the effect of a single dose has worn off. Secondly the acceptance of water by a rat which rejected ethanol and presumably would have died otherwise is further evidence. Finally the effect of 5-HTP was proportional to the concentration of ethanol consumed, but since equivalent pharmacologic doses were consumed regardless of concentration, the greater aversion to the higher concentration was presumably due to the more aversive taste. In the case of PCPA, the effect was presumably due to its effect on brain serotonin.

While these data provide considerable evidence for the involvement of the serotonergic system in the regulation of ethanol ingestion, there are still many questions to be answered. Further elucidation of the mechanism by which this action is mediated would certainly be a major contribution toward understanding alcoholism. Only through a thorough understanding of this complex problem can efforts be undertaken toward treating and hopefully controlling the excessive use of ethanol by man.