Doctoral dissertation at Göteborg University, Göteborg, Sweden, 2001.

Abstract

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Research on alcoholism has identified a subgroup, i.e. type 2 alcoholism, in which the drinking problem is associated with high rates of violence, an impulsive disposition, reduced serotonin functioning and a temperamental constellation of low harm avoidance and high novelty seeking. The present doctoral dissertation, consisting on four research papers, suggests behavioral and neurochemical signs in basal forebrain lesioned (axon-sparing ibotenic acid) rats not unlike those seen in type 2 alcoholism. **Paper I** studied alcohol intake, defensive behavior, passive avoidance behavior, future-oriented behavior and neurochemical status in rats with ibotenic axon-sparing lesions (5μg/0.5μL) in the basal forebrain. Paper I also investigated the above mentioned behavioral parameters in serotonin depleted (5,7-DHT) rats. **Paper II** followed up on the results in Paper I and monitored alcohol intake and defensive- and passive avoidance behavior in rats with medium sized lesions (3.5μg/0.35μL) and small discrete lesions (1.5 μg/0.15 μL) to either the septal or the ventral striatal area. **Paper III** made further observations on defensive aggressive behavior and temperamental traits such as harm avoidance and novelty seeking in basal forebrain lesioned (5μg/0.5μL) rats. **Paper IV,** finally, examined alcohol ingestion, harm avoidance and novelty seeking in normal intact rats as well as in ventral striatal and amygdaloid lesioned rats, respectively.

The results in **Paper I** showed that, compared to controls, the basal forebrain lesioned rats exhibited excessive alcohol drinking and showed an augmentation of certain defensive behaviors, including defensive aggression and fleeing. The experimental animals also showed less disruption of ongoing behavior in the passive avoidance test and virtually no hoarding in the food hoarding test, indicating increased impulsivity. Basal forebrain lesioned rats also had lowered levels of serotonin in the cortex and lowered levels of norepinephrine in the cortex and the hippocampus. However, in a subsequent experiment, serotonin depleted animals displayed no differences in alcohol intake and no behavior alterations except for a modest increase in defensive aggression as compared to controls. In **Paper II** medium sized lesions to either the septal area or the ventral striatum elicited a qualitatively similar behavioral profile. Both lesion types enhanced 6% alcohol intake and elicited defensive aggression. A brief door bell signal elicited more fleeing and in the punished drinking test licking from an electrified water spout caused lesser suppression of locomotor activity. Both groups also showed significant deficits in food hoarding. Histological examination revealed that the two lesion types typically overlapped with one another and a subsequent experiment in Paper II hence examined rats bearing small lesions to either the nucleus accumbens or the dorsal septum. Lesions to the nucleus accumbens were associated with an increase in alcohol drinking, no defensive aggression, potentiation of fleeing and suppressed freezing in response to a sudden auditory signal and increased punished licks and reduced behavioral suppression in the punished drinking test. Rats bearing small septal lesions displayed a weak enhancement of defensive aggression, but no other behavioral alterations. Furthermore **Paper III** revealed that basal forebrain lesioned rats showed more exploration of a hole-board (indicating increased novelty seeking) and less risk assessment behavior in an unfamiliar arena (indicating reduced harm avoidance). The rats also showed signs of motor restlessness. Finally, the results in **Paper IV** suggest that intact animals high in novelty seeking drink more alcohol that rats low on this trait. Paper IV also reported that amygdaloid lesioned rats have lower levels of harm avoidance and ethanol intake as compared to before surgery, especially in animals showing above average levels of risk assessment preoperatively. The ventral ventral striatal lesioned animals on the other hand, had higher levels of novelty seeking and alcohol intake compared to before surgery, particularly rats which initially showed less novelty seeking than average.

Keywords: Aggression – Alcohol – Amygdala – Harm Avoidance - Ibotenic acid – Impulsivity – Novelty Seeking - Passive Avoidance – Septum – Ventral Striatum.

Åsa K. Johansson, Department of Psychology, Göteborg University, Box 500, SE-405 30 Göteborg, Sweden.
Fax: +46 31 773 4628, E-mail: asakjohansson@hotmail.com
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