Pharmacology Biochemistry & Behavior, Vol. 18, pp. 673–675, 1983.

Failure of Dorsal Bundle Lesions in Rats to Increase Distractibility to a Low Intensity Tone

M. DRAGUNOW AND R. LAVERTY[1]

Department of Pharmacology, University of Otago Medical School, Dunedin, New Zealand

Received 21 May 1982

DRAGUNOW, M. AND R. LAVERTY. *Failure of dorsal bundle lesions in rats to increase distractibility to a low intensity tone.* PHARMACOL BIOCHEM BEHAV **18**(5) 673–675, 1983.—Bilateral lesions of the dorsal noradrenergic bundle in rat brains with 6-hydroxydopamine produced a depletion of cortical noradrenaline to 19% of control values. Rats so treated showed resistance to extinction of a lever press task but no increased distractibility from licking behaviour by a low intensity tone. These results cast doubt on the hypothesis that dorsal noradrenergic bundle lesions cause hyperdistractibility in rats.

Brain noradrenaline Selective attention Dorsal bundle lesions Distractibility

EVIDENCE has accumulated to suggest that the ascending noradrenergic pathways in the dorsal bundle originating in the locus ceruleus may mediate attentional processes. Direct tests of the dorsal bundle attentional theory (see [4] for a review of the literature) have involved selectively depleting ascending noradrenergic pathways from the locus ceruleus with 6-hydroxydopamine (6-OHDA).

The most widely documented functional deficit, induced by such a lesion, is a resistance to extinction (the dorsal bundle extinction effect-DBEE) [6, 7, 8]. Mason [4] suggests that the DBEE is best explained as a deficit in selective attention: animals with dorsal bundle lesions, being unable to filter out irrelevant stimuli, sample more stimuli in the environment than controls, and during acquisition, form more stimulus-response connections. During extinction more stimulus-response connections must be broken down before responding ceases.

The attentional theory for dorsal bundle function predicts that animals with dorsal bundle lesions should show a failure to ignore irrelevant stimuli. Mason and Fibiger [5] found that lesioned rats took longer to come to ignore an irrelevant flashing light placed above their heads introduced on a continuously reinforced lever pressing task. However in the same experiment the researchers found that these same animals did not take longer to ignore an irrelevant flashing light placed at eye level or a tone (7 kHz, 85 dB). Crow *et al.* [1] also found that dorsal bundle lesioned rats did not take longer than controls to ignore an irrelevant tone (7 kHz, 85 dB) introduced on a continuously reinforced licking baseline. In fact these authors found the dorsal bundle lesioned rats were less distracted than controls on the first tone presentation. Crow *et al.* [1] also measured the distraction ratio in dorsal-bundle lesioned and control rats to a lower-intensity tone of 7 kHz, 75 dB, and found no difference between groups. It should be noted, however, that in this experiment the rats were habituated previously to the higher-intensity tone making the interpretation of this result difficult.

Consequently Mason [4] refined the attentional theory of dorsal bundle function by suggesting that noradrenaline-depleted rats sample more environmental stimuli only in situations where control rats have come to ignore some stimuli (i.e., only when stimuli are of low salience). To test this "saliency" hypothesis we measured distractibility in dorsal bundle lesioned rats to a low intensity (i.e., low saliency) tone (7 kHz, 75 dB) introduced on a continuously-reinforced licking baseline.

METHOD

Subjects

Twenty-three male Wistar rats, mean weight 182 grams and aged approximately 8 weeks at the time of surgery, were anaesthetised with ketamine (80 mg/kg, SC), and pentobarbitone (10 mg/kg, IP). Stereotactic injections of 8 μg 6-hydroxydopamine (in 2 μl of 0.9% saline with 0.5 mg/ml ascorbic acid antioxidant), at a rate of 1 μl/min, were made bilaterally into the dorsal noradrenergic bundles in 11 rats (coordinates A/P =2.8 mm, L 1.4 mm, V 1.7 mm) [2]. Two μl of the ascorbic acid vehicle were injected into the dorsal bundles of the remaining 12 rats. Behavioural testing began two weeks after the injection.

Animals were housed singly with ad lib food and water, except where otherwise stated, in a room with a reverse 12 hour light/dark cycle.

[1]Requests for reprints should be addressed to Professor R. Laverty, Department of Pharmacology, University of Otago Medical School, P.O. Box 913, Dunedin, New Zealand.

Apparatus

Lever press task. Animals were trained in a rodent one-lever test chamber (Grason-Stadler) on a continuously reinforced schedule. The test chamber was enclosed in an acoustically insulated box. Experimental events were automatically programmed.

Distraction task. A drinking tube protruded from a slit in the wall giving access to a constant water supply and a photo-electric cell served to record each lick. Tones were delivered via a loudspeaker placed in the end wall of the chamber. The tone used was 7 kHz, 75 dB of 9 sec duration.

Behavioural Testing

Lever press task. Prior to training rats were maintained at 90% of free-feeding body weight. On 2 successive days rats received 10 min magazine training sessions in the test chamber. Following this each rat was placed separately in the test chamber and left to autoshape. The apparatus was programmed to deliver one noyes pellet per lever press. Acquisition criterion was set at 200 reinforced bar presses. Once this had been achieved reinforcement was automatically withdrawn and extinction testing commenced. Extinction parameters were defined as no lever press for a period of 7 min after reinforcement was withheld. For each rat the time required to learn the task and the time to reach extinction criterion was recorded.

Distraction task. Rats were placed on a 23.5 hour water deprivation schedule for 3 consecutive days prior to testing. On day 1 following the water deprivation rats were left in the test chamber until they had made 500 licks. Immediately following this rats were returned to their home cages and given 1/2 hour free access to water.

On day 2 rats were again placed in the test chamber. The rat's 50th lick switched on a control period of 9 sec during which the number of licks made (X) was counted. Following this the rat's next 50th lick switched on a 9 sec period in which the tone was delivered. The number of licks made during this period (Y) was counted. Control and tone periods alternated, each rat receiving 7 control-tone pairings. A ratio of X−Y/X was used as an index of distraction. Complete habituation to the tone gives a ratio of zero and complete distraction a ratio of 1. Three successive distraction ratios of ≤ 0.10 was adopted as the habituation criterion. For each rat the number of trials (defined as one control-tone pairing) needed to reach criterion and the distraction ratio to the first tone presentation were recorded and subsequently analysed.

Biochemical Testing.

After completion of behavioural testing animals were decapitated, the brains removed and dissected into cerebral cortex and hippocampus, brainstem (caudate, thalamus, midbrain, and pons-medulla) and cerebellum. Tissue regions were frozen on dry ice and stored in a freezer at −20°C until assay. The brain regions were assayed for catecholamines by the fluorometric method of Laverty and Taylor [3].

RESULTS

Biochemical

The results of the catecholamine assay confirm that 6-OHDA lesioned animals had a severe depletion of cortex-hippocampal noradrenaline (control mean=282.5 ±13.1 ng/g tissue, n=11; lesioned mean=54.6±7.2 ng/g, n=12), less severe brainstem noradrenaline depletion (control mean=576.2±18.3 ng/g, lesioned mean=391.2±14.4 ng/g), no cerebellar noradrenaline depletion (control mean=242.7±9.4 ng/g, lesioned mean=234.3±15.9 ng/g), with slight brain stem dopamine depletions (81% of control levels).

Behavioural

Lever press task. No difference was found between control (n=12) and lesioned (n=11) rats in the time to acquire the task (control mean=480±104 min, lesioned mean=516±194 min, $t=0.183$, $p<0.05$). However, lesioned rats took significantly longer than controls to reach extinction criterion (control mean=17±3 min, lesioned mean=27.6±5.0 min, $t=-2.12$, $p<0.025$).

Distraction task. No difference was found between control and lesioned rats in the number of trials needed to reach criterion for tone habituation (control mean=9.8±1.3 trials, lesioned mean=9.8±1.1 trials, $t(20)=0.03$, NS). Control rats had a mean distraction ratio of 0.41±0.11 to the first tone presentation. Lesioned rats showed similar distraction to the first tone presentation with a mean of 0.42±0.11, $F(1,20)=0.0013$, $p<0.97$.

DISCUSSION

Dorsal bundle lesioned rats (with severe cortical-hippocampal noradrenaline depletion) showed a resistance to extinction, but normal acquisition, in the continuously reinforced lever press task (i.e., the DBEE). However these lesioned rats were not more distracted than controls by the low intensity tone, and habituated to the tone at the same rate as controls. Our results are consistent with those of Crow *et al.* [1] and Mason and Fibiger [5] in that we found no difference between lesioned and control rats in the rate of tone habituation. Since we used a less intense tone than these other authors, it would appear that Masons' proposal [4] that only low salience stimuli (in this case a low intensity tone) produce hyperdistractibility in dorsal bundle lesioned rats is not supported by our results.

Consistent with previous reports we did find that lesioned animals took longer to extinguish a normally acquired task. Since dorsal bundle lesioned rats do not seem to be more distracted by an irrelevant tone than controls, this delayed extinction may not be due to heightened distractibility in these rats.

REFERENCES

1. Crow, T. J., J. F. W. Deakin, S. E. File, A. Longden and S. Wendlandt. The locus coeruleus noradrenergic system—evidence against a role in attention, habituation, anxiety and motor activity. *Brain Res* **155**: 249–261, 1978.

2. König, J. F. R. and R. A. Klippel. *The Rat Brain: A Stereotaxic Atlas of the Forebrain and Lower Parts of the Brain Stem.* Baltimore: Williams and Wilkins, 1963.

3. Laverty, R. and K. M. Taylor. The fluorometric assay of catecholamines and related compounds: improvements and extensions to the hydroxyindole technique. *Anal Biochem* **22:** 269–279, 1978.
4. Mason, S. T. Noradrenaline and selective attention: a review of the model and the evidence. *Life Sci* **27:** 617–631, 1980.
5. Mason, S. T. and H. C. Fibiger. Evidence for a role of brain noradrenaline in attention and stimulus sampling. *Brain Res* **159:** 421–426, 1978.
6. Mason, S. T. and H. C. Fibiger. Anxiety: the locus coeruleus disconnection. *Life Sci* **25:** 2141–2147, 1979.
7. Mason, S. T. and S. D. Iversen. Learning in the absence of forebrain noradrenaline. *Nature* **258:** 422–424, 1975.
8. Mason, S. T. and S. D. Iversen. Effects of selective forebrain noradrenaline loss on behavioural inhibition in the rat. *J Comp Physiol Psychol* **91:** 165–173, 1977.