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# DIFFERENCE IN CEREBELLAR NOREPINEPHRINE METABOLISM IN JUMPING AND NON-JUMPING MICE

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SUMMARY

The CBA gray and NMRI albino mouse strains differ in one aspect of motor behavior, i.e. the CBA gray mice exhibit a jumping response which is seldom seen in the NMRI albino. Concentrations of the monoamine metabolites HVA, MOPEG and 5-HIAA were compared in brain regions of these two strains. A 70% difference in MOPEG and a 30% difference in 5-HIAA was found in the cerebellum, both metabolites being higher in the jumping strain. In no other region did the two strains differ in metabolite concentration. The results indicate a role for cerebellar noradrenaline in jumping behavior.

The monoamines dopamine (DA), norepinephrine (NE) and serotonin (5-HT) function as neurotransmitters in specific pathways in the central nervous system (1). Much experimental work supports the view that the brain amines are related to specific behaviors. However, the relative roles of the particular amines in different types of behavior is still far from clear. Comparative studies on different strains of mice showing contrasting patterns of spontaneous behavior may be of value for further elucidation of the neurochemical correlates of behavior.

Over the last decade considerable effort was made to use this approach to find the neurochemical correlates to exploratory activity, various emotional responses, learning and seizure proneness in mice (2, 3, 4, 5, 6, 7, 8). In these studies neurochemistry was assessed predominantly as baseline concentrations of the transmitter amines, a method which does not adequately reflect dynamic changes in transmitter turnover. Some of the studies also estimated rates of amine metabolism by methods requiring pharmacological tools which may have affected the behavior of the animals.

The concentrations of the transmitter metabolites have been shown to be directly related to transmitter release in several monoaminergic systems (9, 10). Homovanillic acid (HVA), 4-hydroxy-3-methoxyphenylethylene glycol (MOPEG) and 5-hydroxyindoleacetic acid (5-HIAA) are the major metabolites of DA, NE and 5-HT respectively. The recent development of highly sensitive mass fragmentographic methods allows the determination of the

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concentrations of the monoamine metabolites in milligram amounts of brain tissue (11, 12). This new methodology makes it possible to follow biochemical events in the monoaminergic systems in the brain without the disturbance of pharmacological manipulations.

In our laboratory we are using mass fragmentography in the investigation of biochemical correlates of behavior in different strains of mice. Two of the mouse strains used show a peculiar and characteristic difference in behavior. The CBA gray mice are jumpers while the other strain, NMRI albino, do not show spontaneous high jumps.

In this study we were interested in finding out if this marked difference in one aspect of motor behavior was related to any specific alteration of central monoamine metabolism in brain regions known to participate in motor control.

## MATERIAL AND METHODS

### Subjects

NMRI albino and CBA gray mouse strains were used. These two strains exhibit a striking difference in motor behavior. The NMRI albino runs when chased by another mouse or by a human hand. In contrast the CBA gray tends to jump high and wide to avoid capture. When put into a 15 cm deep container the latter strain easily jumps out of it. All CBA gray mice in our laboratory showed this behavior while none of the NMRI albino was seen to clear this 15 cm barrier in one jump.

In the present experiment seven male mice from each strain were used. The animals were about 100 days old, their average weight was 31.3 g for the NMRI and 30.3 for CBA (difference not significant). The two groups were housed in plexiglass cages (15 x 46 x 33 cm) with woodshavings for bedding. Food and water was provided ad lib. The animals were maintained on a 12 h light/12 h dark reversed schedule for at least 10 days and were killed between 9-12 a.m., this time period corresponding to the 3-6th hour of their dark cycle.

The animals were killed by cervical dislocation and immediately decapitated. The brain was rapidly removed, weighed and placed on ice. It was dissected into six regions: 1) Cerebellum, 2) Brain stem, 3) Midbrain, 4) Hypothalamus, 5) Amygdala and 6) Striatum as described by Grimm and Sedvall (1978) (13). The regions were weighed and homogenized in 2 ml of 0.1 M HCl containing ascorbic acid (5 µM). The homogenates were centrifuged (25000 g, 40 min, +4°C) and the supernatants were decanted and stored at -80°C pending biochemical analysis. The pellet was dissolved in 1 ml of 1 M NaOH for protein determination. Concentrations of HVA, MOPEG and 5-HIAA in the supernatant were measured by mass fragmentography (11). For hydrolysis of conjugated metabolites an enzyme preparation containing arylsulphatase (29000 U/g) and β-glucuronidase (300000 U/g) was used.

The protein concentrations in the supernatant and the pellet were measured according to Lowry et al. (14). Concentrations