Hemicerebellectomy and motor behaviour in rats

II. Effects of cerebellar lesion performed at different developmental stages

M. Molinari¹, L. Petrosini², and T. Gremoli³

Institutes of ¹Neurology and ³Human Physiology, Catholic University of Rome Largo F. Vito 1, I-00168 Rome, Italy
²Department of Psychology, University of Rome “La Sapienza”, I 00185 Rome, Italy

Received August 29, 1989 / Accepted June 6, 1990

Summary. Rats with a right hemicerebellectomy (HCb) performed in adulthood or at weaning were compared behaviourally to rats with a similar lesion performed on the first postnatal day. The age at which animals received cerebellar lesions made a significant difference with respect to the behavioural outcome in adulthood. Posture, locomotion and motor behaviour were analysed by a battery of sensorimotor tests. Behavioural measurements showed a clear relationship between age at surgery and behavioural effects; rats with neonatal cerebellar lesions showed a slight extensor hypotonia contralateral to the lesion side and efficient locomotor activity, while the adult operated group exhibited a severe extensor hypotonia ipsilateral to the lesion side and hampered locomotion characterized by a wide base and ataxia. Weanling operated rats displayed a symptomatology similar to that observed in adult operates, although less severe. In the postural dynamic adjustments which the sensorimotor tests required, the youngest operated animals obtained higher scores in comparison to the other two experimental groups, except for the lack of hindlimb usage in the suspension on a wire test. These results, which show the importance of the age-at-lesion factor for the recovery of motor function after HCb in the rat, are discussed in the light of the widespread anatomical reorganization already demonstrated following neonatal HCb in rats.

Key words: Hemicerebellectomy – Recovery of function – Infant lesion effect – Rats

Introduction

Kennard’s (1936) experiments, demonstrating sparing of function following motor cortex ablation in infant monkeys, led to the general view that the infant brain, whose connections are still in formation, has a capacity to compensate for an injury greater than that of the adult brain (Teuber 1974; Bregman and Goldberger 1983; Robinson and Goldberger 1986; Villablanca et al. 1986). This view is at odds with another set of experimental data, which report both similarly affected motor patterns regardless of the age at which the lesion occurs and more impaired motor function when lesions are sustained neonatally than in adulthood (Isaacson 1976; Schneider 1979; Kolb and Whishaw 1985; Kolb et al. 1987).

Differences in the extent of recovery after lesions occurring at different developmental stages are particularly evident in the cerebellar system. On one hand, the clinical literature contains a number of case reports of asymptomatic, and very well compensated, cerebellar agenesis, which remained undetected throughout life (Macchi and Bentivoglio 1977). Experimental cerebellar ablations in monkeys are reported to result in less severe motor abnormalities in neonatal than adult operates (Eckmiller and Westheimer 1983). And yet, studies performed in rats report the presence of sustained deficits after early cerebellar lesions (Smith et al. 1974; Gramsbergen 1982). These reports indicate that cerebellar lesions at the 5th or 10th post-natal day lead to a more impaired locomotor behaviour than the same lesions at a later age.

This topic is further complicated by discrepancies among different reports about the post-lesion effect of hemicerebellectomy (HCb) in adult rats. In the first description of behavioural effects of a HCb in adult rats, Manni and Dow (1963) reported a symptomatology mainly ipsilateral to the side of cerebellar ablation. Conversely, more recently Gramsbergen (1982) described a contralateral symptomatology following HCb in adult rats.

The numerous behavioural tasks which can be used in the evaluation of neurological deficits may further confound the problem, since different functional aspects may respond differently to the same lesion (Hovda and Villablanca 1989).
Therefore, in this study we decided to investigate the effects of HCbed, made at different developmental stages (at birth, at weaning or in adulthood), on a variety of postural reflexes, locomotor movements and complex motor behaviours, in order to clarify the extent of functional recovery in neonatal and adult HCbed rats and to study whether different facets of motor functions were similarly affected. A preliminary report has been published elsewhere (Petrosini et al. 1988).

**Material and methods**

In this study useful data were collected from 36 rats. Of these, 12 were hemicerebectomized neonatally (the development of their motor function and their deficits has already been described in the companion paper), 5 at weaning and 11 in adulthood; the remaining 8 animals were normal littersmates of the neonatal operates and were tested as adults. Neonatal animals received a right HCB on the first postnatal day under hypothermic anaesthesia. Weaning (21 days of age) and adult (3 months of age) animals received the cerebellar lesion under sodium pentobarbital (Nembutal 40 mg/kg i.p.) anaesthesia. A craniotomy was performed and the dorsal surface of the right side of cerebellum was exposed. Suction was used to remove the right cerebellar hemisphere and the right portion of the vermis, with care being taken to not lesion extracerebellar structures. Following ablation, the wound edges were sutured and the animals were allowed to recover from anaesthesia for 24 h. Adult, mature weanling and neonatal operates, as well as normal adult rats, were tested for their postural and locomotor behaviour twice a week for 4 post-operative months. After 2 months, insignificant changes were seen in the test scores of all lesioned animals, indicating a stable neurological and behavioural state. The measurements used for the statistics reported here were taken only during the fourth postoperative month.

**Behavioural testing**

**Qualitative assessment.** Head and trunk posture, position of limbs in relation to the trunk, and spontaneous overground locomotion were examined by behavioural observation. Limb motility was also examined by suspending the animals with their forelimbs on a 3 mm thin wire. The attempt to pull up and to provide support with one or both hindlimbs, the presence of dysmetric movements and of tremor were recorded. The time of suspension was also measured.

To gauge balance and coordination capacities, the animals were tested for their ability to traverse a smooth 5 cm wide and 60 cm long elevated bridge.

Lastly, the animals were put in a glass tank filled with 37 °C warm water and allowed to swim freely. Swimming direction, water line, body tilt, and limb usage were analyzed.

**Quantitative assessment of spontaneous locomotion.** Prior to filming, the limbs were shaved and limb bone lengths were determined. The skin overlying the following bone prominences was inked: greater trochanter, femoral lateral condyle, lateral malleolus and metatarsophalangeal joint for hindlimbs; humeral head, olecranon process, radial epiphysis and metacarpophalangeal joint for forelimbs. The markers for the knee and the “elbow” joints were included in this study had a complete ablation of the right cerebellar hemisphere and deep nuclei, with variable extent of vermal lesions. In 2 out of 11 adult HCBbed rats sparing of the right flocculus and paraflocculus and the most lateral tip of the lateral deep nucleus of

---

**Statistical analysis**

Metric unit results of neonatal, weaning and adult operate animals were first tested for homoscedasticity of variance, and then compared using p x q analyses of variance (ANOVAs) with repeated measures, followed by multiple comparisons using Tukey's tests. When the cell frequency was unequal, Winer's (1962) model of p x q ANOVA with unequal cell frequency was used. For those tests where qualitative lesion effects were evaluated, statistical comparisons were made with non-parametric statistics, such as the χ² test.

**Histological controls**

After testing, various neuroanatomical techniques were used to histologically verify the cerebellar lesions and to analyze the consequent postlesional remodelling of the cerebellar projections and related structures (manuscript in preparation). The extent of cerebellar lesions was determined from Niss-stained 40 μm frozen sections. Minimal and maximal cerebellar damage in the experimental groups are represented in Fig. 1. All lesioned animals included in this study had a complete ablation of the right cerebellar hemisphere and deep nuclei, with variable extent of vermal lesions. In 2 out of 11 adult HCBbed rats sparing of the right flocculus and paraflocculus and the most lateral tip of the lateral deep nucleus of

---

![Fig. 1. Reconstructions of minimal (stripes) and maximal (empty circles) lesion damage in weanling (W) and adult (A) HCBed groups. The minimal and maximal extent of lesion damage in neonatal HCBed rats has been reported in the comparison paper (Petrosini et al., Fig. 1). L: lateral cerebellar nucleus; I: interpositus nucleus; F: fastigial nucleus; VL: lateral vestibular nucleus; VM: medial vestibular nucleus](image-url)