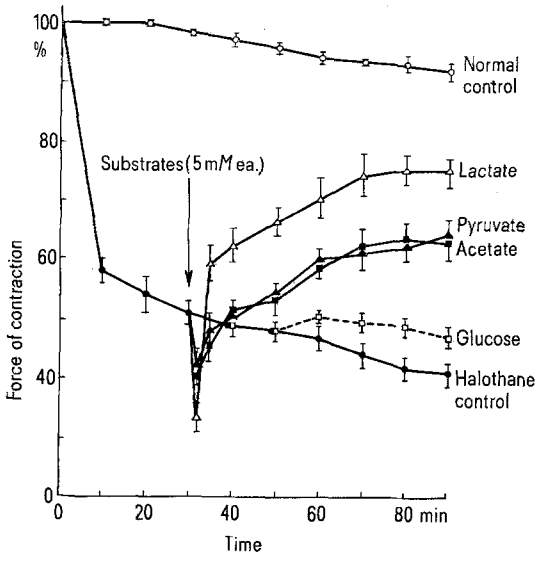

Fig. 3. Comparative effects of substrates (5 mM) on halothane-depressed rat atria.

pyruvate. The results obtained with these experiments are consistent with the considerable data in the literature that lactate, acetate and pyruvate were effective in increasing the substrate-depleted rat ventricle strips[5] and those in bicarbonate-free medium[15] in which glucose metabolism on the heart was impaired[16]. In Figure 2, it was shown that glucose at any concentration tested was ineffective in increasing the declined contractility of rat atria by halothane. The data obtained from these experiments are similar to those in the previous reports that glucose was ineffective in restoring the force of contraction of rat atria depressed by 2-desoxyglucose[6] or by bicarbonate-free medium[14]. Glucose was also ineffective in restoring the amplitude of contractility of rat ventricle strips depressed by iodoacetate[5].

Thus, our results are consistent with the hypothesis that halothane exerts at least a part of its negative inotropic effect on rat atria by inhibiting either the uptake or utilization of glucose via the glycolytic pathway. The site of blockade must be prior to the conversion of pyruvate to acetyl CoA.

Zusammenfassung. Nachweis, dass die nach Halothan eingetretene Verminderung der Kontraktilität des Myokards durch Lactat oder Acetat verhindert werden kann. Das Ergebnis stützt die Hypothese, Halothan hemme die Aufnahme von Glykose oder beeinträchtige deren Verwertung.

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Brain Abnormalities in the Lurcher (*Lc*) Mutant Mouse

Lurcher (symbol *Lc*) is a mouse mutant first discovered and described by PHILLIPS[1]. The mutation arose spontaneously in a White (Mi^{wh}) homozygote and is expressed as a semidominant in heterozygotes (*Lc*/+). The *Lc* gene is on chromosome 6 (linkage group XI). Homozygotes (*Lc*/*Lc*) are believed to die during the early neonatal period. Heterozygotes are fertile, although the litter size of *Lc*/+ females is reduced. Lurcher body weights of both sexes are less than those of normal counterparts.

Lurcher heterozygotes show abnormal behavioral characteristics consisting of ataxia with a tendency to fall to either side[1,2]. These animals also tend to walk backward when placed outside of the cage on a smooth surface[1]. Although lurcher has been classified as a neuromuscular mutant, little is known about the morphology of the nervous system in these animals. However, lurcher manifests many of the behavioral characteristics which have been described in the mutant reeler (*rl*) in which the cerebellum has been shown to be defective[3–6]. Since several other cerebellar mutants such as staggerer (*sg*), weaver (*wv*), and nervous (*nr*) also exhibit ataxic behavior[2,6–11], the present study was undertaken to obtain information on the gross structure of the brain, particularly the cerebellum, in the lurcher mutant mouse.

Materials and methods. The lurcher mutant colony used in this study was originally derived from a male lurcher heterozygote (*Lc*/+) carrying the translocation T(2:6) 7Ca who was mated to C57BL/6J females. *Lc*/+ progeny were subsequently backcrossed to C57BL/6J individuals for several generations. Lurcher (*Lc*/+) and normal (+/+) littermates of both sexes were sacrificed at ages ranging from birth to approximately 10 months of age. The brains were quickly removed and wet weights were determined. The brains were then fixed for 4 to 5 days in Bouin's solution, transferred to 70% ethanol, and examined at magnifications up to 60×. The nomenclature of SIDMAN et al.[12] was used to describe gross features of the mouse brain.

Results. Lurcher (*Lc*/+) mice in our colony show a hesitant, lurching gait as well as a tendency toward tonic-clonic seizures, particularly when suddenly disturbed. This behavior is clearly manifested on approximately the 12th day after birth. Prior to this time the pale coat, light

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ears, and pink snouts produced by the Mi^{wh} gene serve as characteristic markers for $Lc/+$ heterozygotes, since Mi^{wh} is linked on the same chromosome with *Lc*.

The overall size of the adult lurcher ($Lc/+$) brain appears to be similar to that of an adult normal ($+/+$) brain from the same strain. However, there is a noticeable reduction in the size of the lurcher cerebellum, which is approximately one-half the size of the normal cerebellum (Figures 1 and 2). In addition to the reduced size, the lurcher cerebellum shows lobular defects. All of the lobules are usually present, but most are narrower and flatter than their normal counterparts. The uvula vermis, in particular, is quite narrow and extends further laterally than is the case in the normal cerebellum.

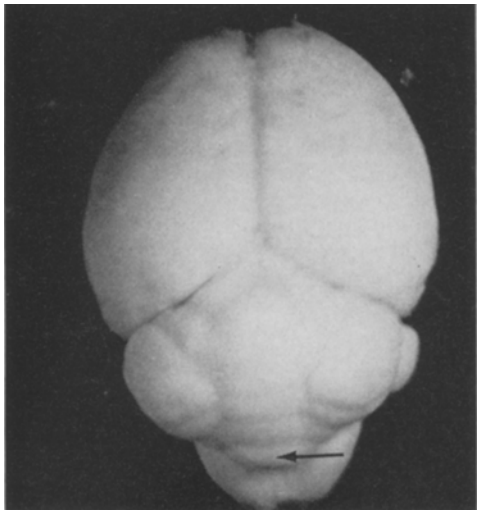

Fig. 1. Dorsal view of normal ($+/+$) adult brain. Arrow indicates uvula vermis. ×6.

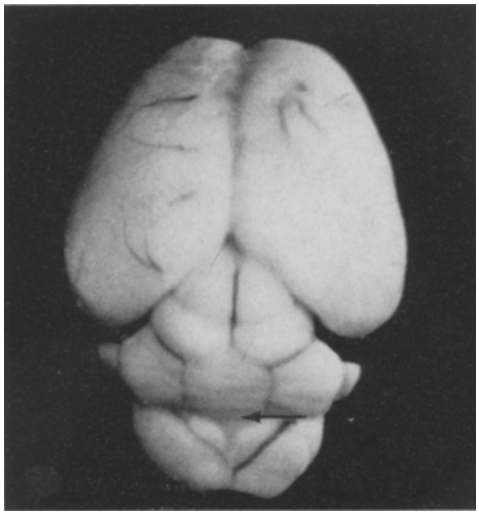

Fig. 2. Dorsal view of lurcher ($Lc/+$) adult brain. Arrow indicates slender uvula vermis. Note also the small size of the cerebellum, the exposed roof of the 4th ventricle, and the prominent collicles. ×6.

The reduced cerebellar hemispheres do not adequately cover the anterior portion of the medulla; as a result, the roof of the 4th ventricle is usually exposed in a dorsal view of the lurcher brain. The collicles appear to be more prominent in lurcher than in normal mice, possibly because of the less acute angle formed by the cerebral hemispheres. The ventral surface of the brain does not show any obvious defects.

Gross defects in the lurcher brain, particularly the cerebellum, are exhibited as early as 3 days after birth. At this time the uvula vermis is prominent and oval in shape in the normal brain, but narrow and elongated in the lurcher. The overall reduction in the size of the cerebellum becomes obvious at approximately 5 days after birth.

Discussion. The cerebellar hypoplasia in lurcher adult mice is similar to that described in the reeler (*rl*) mutant[2,3]. As in reeler, this reduction in size is constant from animal to animal, although a thorough study of lurcher cerebellar histogenesis is warranted before comparisons can be made with other cerebellar mutants. Since the lurcher individuals in our colony are descendants of a translocation stock, it is also necessary to determine whether or not this genetic background exerts any effect on the phenotypic expression of the lurcher gene. However, preliminary observations on the brain of a lurcher individual believed not to be carrying the translocation show no gross morphological differences from those carrying the translocation.

It is probable that the defects observed in the collicles and medulla result from the failure of the cerebellum to grow properly, although primary malformations may also occur in these regions. Since defects in the shape of certain $Lc/+$ cerebellar lobules become apparent by the third day postnatally, well before any behavioral characteristics are manifested, the early stages of cerebellar histogenesis are accessible for study in this mutant. Moreover, $Lc/+$ neonates are distinguishable from their normal ($+/+$) littermates by means of color characteristics even before the gross cerebellar defects can be detected. This mutant, therefore, should serve as an excellent model in which to study the early etiology of cerebellar dysgenesis.

Résumé. Le cervelet des souris hétérozygotes de la mutation «lurcher» (*Lc*) présentent des anomalies. Il est réduit et déformé, en particulier l'uvula vermis. On peut détecter ces anomalies chez le nouveau-né de 3 jours avant l'apparition des aberrations du comportement.

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Isolation of Highly Purified Glomerular Complexes from Rabbit Cerebellum

Gentle disruption of brain tissue has been increasingly employed during the development of methods for large scale isolation of neuronal and glial cells[1-5]. Softening of the tissue through incubation of slices at 37 °C, followed by passage of tissue through nylon mesh of decreasing pore size, results in the recovery of larger and more intact cellular units than are generally obtained by homogenization in cold sucrose media.