Available online at www.sciencedirect.com

SCIENCE DIRECT

Brain Research 1039 (2005) 37–42

BRAIN RESEARCH

www.elsevier.com/locate/brainres

Research report

Age dependence of strain determinant on mice motor coordination

Bertrand Bearzatto[a], Laurent Servais[a,b], Guy Cheron[b,c], Serge N. Schiffmann[a,*]

[a]Laboratory Neurophysiology CP601, Université Libre de Bruxelles, route de Lennik 808, 1070 Brussels, Belgium
[b]Laboratory of Electrophysiology, Université Mons-Hainaut, Mons, Belgium
[c]Laboratory of Movement Biomechanics, Université Libre de Bruxelles, Brussels, Belgium

Accepted 12 January 2005

Abstract

Evaluation of motor coordination and motor learning in mice remains a challenge as many factors may interact with the different tests used. Among these factors, genetic background has been reported to be a major determinant of mice performances in motor coordination tests. However, it is not known if the strain dependence of motor coordination and motor learning remains constant through life. In order to assess this point, we tested during 5 days male and female mice of three different strains (NMRI, C57BL/6J, and C57BL/6J × 129OlaHsd) in runway, rotarod, and thin rod tests at juvenile (first day of testing = postnatal day 19) and adult (3 months) age. We found a strong strain effect on motor performances and motor learning at juvenile age (C57BL/6J performing more poorly than the two other strains), whatever the tests used. Interestingly, the C57BL/6J mice were the best performing mice at the adult age. These strain rankings were observed either in male and female groups. These results demonstrate that the strain determinant on mice performances and motor learning is highly age dependent.

Theme: Motor systems and sensorimotor integration
Topic: Cerebellum

Keywords: Motor coordination; Strain; Age; Mice

1. Introduction

Ataxia is a common characteristic in many neurological disorders. As cerebellum plays a central role in motor control and especially in the fine tuning of movements [17,18,22], ataxia and other impairment of motor coordination are often associated with cerebellar dysfunction although other brain regions, such as vestibulum, motor cortex, striatum, or spinal cord, may also be involved. Quantifying motor coordination in mice models of ataxic disorders is crucial in the evaluation process of the model or of subsequent therapeutic approaches. Moreover, impairment of motor coordination in mice may be impossible to detect in standard rooming environments and appears when mice are challenged in tests designed to specifically evaluate motor coordination [1,2,19]. Accelerated rotarod, where the mice have to stay as long as possible on an accelerating rod, is the most commonly used test in this purpose [4,9]. Runway (where the mice have to run along a thin bar without slipping) and stationary horizontal thin rod test (where the mice have to stay as long as possible on a thin bar) have also been used recently [14]. The sometimes subtle differences between normal and impaired mice complicate the choice of an adequate test. Indeed, the discrimination between normal and slightly impaired mice requires a test which as to be not too easy for the impaired, but not too difficult for the normal mice. If these two conditions are not fulfilled, normal and impaired mice may wrongly appear similar, even with perfectly matched test groups. It is thus very important to know the factors that

* Corresponding author. Fax: +32 2 555 41 21.
E-mail address: sschiffm@ulb.ac.be (S.N. Schiffmann).

0006-8993/$ - see front matter
doi:10.1016/j.brainres.2005.01.044

may potentially interfere with the different tests and the possible interactions between these factors. Among them, strain [7,8,10,15,20] has received much attention these last 10 years because of the employment of different mouse strains in transgenic technology. For instance, C57BL/6J, a frequently used strain, is considered to perform very well in motor coordination test in comparison with other strains, but it is not known if this superiority is constant for both genders and through ages. The importance of strains in genetic engineering goes far above motor coordination or behavioral performances, as different mutations may appear very impairing in certain genetic background and nearly asymptomatic in others [3]. Indeed, if gender and age [11,20] also appear to interact with motor coordination evaluation, their interactions with strain have not yet been reported to our knowledge. The choice and the interpretation of motor coordination test according to the strain, age, and gender of the evaluated mice remain thus widely empirical. To assess this point, we evaluated 3 currently used mice strains at juvenile and adult ages through 3 different motor coordination tests. The tests were performed during 5 consecutive days in order to evaluate the motor performances and the motor learning ability of the mice. We found that the strain determinant on motor performances is largely dependent on the age of the tested animals.

2. Materials and methods

Naive male and female juvenile (at the first day of the test the animals are P19) and naive adults (3 months old) of C57BL/6J (B6) (Iffa Credo, France), NMRI (Iffa Credo, France) strains, and 129/OlaHsd × C57BL/6J F2 crosses (129B6) (inbred strains were obtained from Harlan and Iffa Credo, France) were used in this study. The animals were housed in the same sex groups of three to four animals per cage in clear plastic cages maintained in a temperature- and humidity-controlled room on a 12-h light–dark schedule with food and water provided ad libitum. All experiments were conducted in the light phase of circadian cycle between 9:00 AM and 4:00 PM. Every day, animals were sequentially subjected to the following tests: runway, stationary horizontal thin rod, and accelerating rotarod test as described below. The study was approved by the Institutional Ethical Committee of the School of Medicine, Université Libre de Bruxelles, Belgium.

2.1. The runway test

In this test, mice ran along an elevated runway with low obstacles intended to impede the progress of mice. The runway was 100 cm long, either 1.2-cm or 0.7-cm width for adults or juvenile mice, respectively. We used two different sizes for the width of the runway test in order to adapt the test to the size of the mice. Using a 1.2-cm width test for the juvenile mice, this one was too easy and not discriminating enough. Obstacles being of 1-cm diameter wood rod took place every 10 cm along the runway, the width of the obstacles being adjusted to the width of the runway. The number of slips of the right hind legs was counted. Mice were placed on one brightly illuminated extremity of the runway and had to run to the other side where they retrieve their cage. Animals were given four trials per day during 5 consecutive days.

2.2. The stationary horizontal thin rod test

This test consists of a horizontal fixed thin rod of wood (diameter 0.6 cm) placed 30 cm above the cage of the animals. Mice were transversely placed on the rod and their latency to fall was measured. Animals staying during 60 s were taken from the rod and recorded as 60 s. Mice were given four trials per day during 5 consecutive days.

2.3. The accelerating rotarod

The rotarod apparatus (accelerating model Ugo Basile) consisted of a plastic roller (3 cm in diameter) with small grooves running along its turning axis. On the first day, mice were given a training session. During this training session, every mouse was placed on the rotarod at a constant speed (4 rpm) for a maximum of 60 s. Afterwards, mice received four trials per day during 5 consecutive days. During each test session, animals were placed on the rod rotating at a constant speed (4 rpm) and, as soon as all the animals were placed on the rod, the rod started to accelerate continuously from 4 to 40 rpm over 300 s. The latency to fall off the rotarod was recorded. Animals staying during 300 s were taken from the rotarod and recorded as 300 s.

2.4. Statistical procedure

As all strains presented strong motor learning through days, strains were compared every day by a one-way ANOVA test and for all days by a two-way repeated measures ANOVA test. The same procedure was used for single-gender groups. In addition, two-way non-repeated measures ANOVA tests (Strain × Gender) were also used to compare mice every day.

Results are expressed as mean ± SEM and were considered significant if $P < 0.05$. All analyses were performed on Statistica 6.0.

3. Results

3.1. Accelerating rotarod

At juvenile age, a strong effect of genetic background was observed on rotarod performances from day 1 to 5 ($F(2,38) = 19.99$, $P < 0.000001$ compared with one-way ANOVA, day 1) (Fig. 1A). The highest performance at