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A repetitive movement detector used for automatic monitoring and quantification of scratching in mice

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Abstract

We have designed an economical non-invasive movement detector for small animal studies and used it for monitoring and quantifying itch in mice. The system is based on a sensitive force transducer positioned below a recording platform holding a lightweight polystyrene recording box in which an animal is placed. A programmed micro-controller is used to discriminate between non-specific movement, grooming behaviour, and scratching movements made by the animal's hind limb. Following sub-dermal injection of histamine receptor agonists into the neck of a mouse, dose-related scratching occurred which was detected and quantified. There was 91% correlation between bouts of scratching as counted manually from playback of the video recording and recorded by the detector. The detector was also able rapidly to count the individual scratch movements of the hind limb that comprise a bout, with 95% accuracy in comparison with manual counting during slow motion playback of video tape, something that is impossible for an unaided observer to achieve because individual scratch movements are too fast to discriminate by eye. Separate detectors were used for the efficient non-invasive study of four animals simultaneously, and this number could easily be increased by adding more platforms. The system could also be modified to record the animal's position within the box, which would be of value in studies involving exploratory behaviour.

In summary, the non-invasive multichannel repetitive movement detector will be very useful for accurate measurement of scratching during pruritus studies in small animals, with considerable savings in staff time and effort. It should therefore be a valuable tool for helping to investigate pruritus and in the evaluation of anti-pruritic drugs.

Keywords: Itch; Pruritus; Histamine; Mouse; Scratching; Automated detector

1. Introduction

Itch (pruritus) is operationally defined as an unpleasant sensation, which provokes the desire to scratch (Ekblom, 1995). Itch is commonly the result of primary skin disease but is also a major clinical feature of a variety of systemic disorders including obstructive liver failure, chronic renal failure and haematological malignancies (McMahon and Koltzenburg, 1992).

Although itch is a subjective symptom, scratch, as an objective correlate, has provided one way in which to assess therapy and disease pathophysiology (Savin, 1998). Unfortunately, with the exception of potent histamine H1 receptor antagonists that are useful for a limited range of disorders such as chronic idiopathic urticaria in which histamine is involved, the pathophysiological mechanisms and endogenous mediators responsible for most of the common causes of itch are unknown, which makes it very difficult to develop anti-pruritic drugs. This in part, reflects the absence of suitable animal models in which to establish the causative neurophysiological and inflammatory pathways and to test pharmacological agents. Animals cannot report a subjective sensation but they do scratch in response to agents, such as

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histamine, that also evoke scratching and itching in man. In the past, scratching was regarded as a response to low threshold stimulation of nociceptive (pain) afferents (see review by McMahon and Koltzenburg, 1992) but itch is now known to be a distinct sensation with its own sensory receptors (pruritoceptors) and neural pathway (Schmelz et al., 1997).

Itch is generally studied in laboratory animals by the application of exogenous pruritogens to the skin (Kuraishi et al., 1995). The level of scratching evoked is taken as a measure of itch. Measurement of scratching by observing and counting is a labour intensive procedure that is limited to studying a few mice simultaneously in real-time. It is normally only possible to count "bouts" or episodes of scratching because individual scratch movements within a bout are too rapid to discriminate by eye. A video recorder with slow playback facility can be used to count individual scratch movements within a bout but this slow playback approach requires an observer and is very time consuming, tedious and expensive.

During studies on scratch/itch in mice (Bell et al., 2004), the value of automating the detection and counting of scratching in order to reduce the considerable time spent on data analysis was highlighted. The aim of this study was to develop a relatively simple inexpensive automated detector using non-invasive techniques to measure and quantify scratching in small laboratory animals such as mice.

2. Materials and methods

2.1. Force platform

A force platform was constructed using two parallel aluminium plates (20 cm × 30 cm) joined by plastic hinges at one end and separated at the other end by a force transducer (see Fig. 1C). This simple design of force platform exhibits varying sensitivity to movement forces depending on distance of the animal from the hinge but in practice that has little effect, as the activities being monitored are restricted to a narrow area of the upper plate, distal from the hinge. Other factors, such as the direction of the repetitive movement being monitored, also affect the forces measured by the platform (see below).

2.2. Theory

In designing the system we considered the forces that would be generated by a repetitive movement of a small mass such as the hind limb of a mouse. Consider a mass (m) of 1 g moving vertically sinusoidally with a frequency (f) of 12 Hz and amplitude (D) of 5 mm.

$$\text{Displacement}\,(x) = D\sin(2\pi f\,t)$$

where t is the elapsed time (s)

$$\text{Acceleration}\,(a) = -4D\pi^2 f^2 \sin(2\pi f\,t)$$

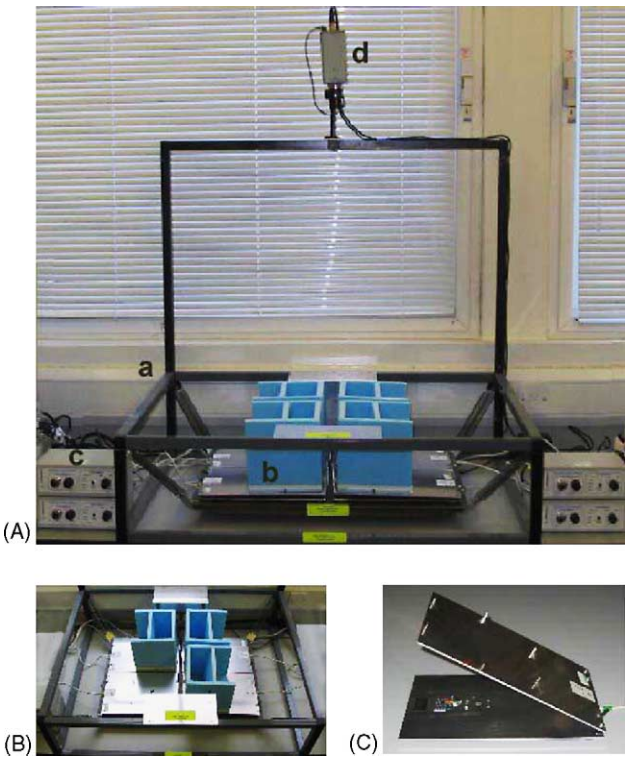

Fig. 1. (A) Overall view of apparatus showing the supporting framework (a) for the anti-vibration table, (b) the four force platforms with animal boxes, (c) the associated repetitive movement detector electronics and (d) the overhead video camera; (B) aerial view of the four force platforms with one animal box removed. Studies could be conducted on four mice simultaneously and (C) force platform with hinged plates separated to show the force transducer.

The corresponding force (F) measured by the force platform would be

$$F = ma$$

The amplitude of this force would be

$$|F| = 4\,\text{m}D\pi^2 f^2 = 4\times10^{-3}\times5\times10^{-3}\times144\times\pi^2$$
$$= 28.4\,\text{mN} = 2.9\,\text{gf}$$

This would be observed as 5.8 gf peak-to-peak.

If the sinusoidal movement was not vertical but at an angle of θ to the vertical then the force exerted on the platform would be reduced by the factor $\cos(\theta)$.

2.3. Design

Complex designs of force platform were considered during the early stages of development. For example, using three force transducers it would be possible to obtain an accurate measure of the vertical force and also the position of the animal within the platform-mounted cage. In practice, the much simpler less expensive design described here provides appropriate data for use in measuring scratch in rats or mice, but the system could be enhanced to include information about the animal's position in the cage, if this was needed.