NON-EVOKED PAIN TESTS IN NEUROPATHIC RATS
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INTRODUCTION
Different models of neuropathies (mechanically, chemically-induced, diabetes-associated) have been extensively established in the rat and their responsiveness to nociceptive stimulations are well described in the literature. In these models, symptoms of neuropathy are not restricted to the modification of pain sensitivity. Chronic pain can have incapacitating long-term effects which are expressed in different behaviors. The objective of this study was to determine the effects of peripheral mononeuropathies (Bennett/CCI and Chung/SNL models) in rats using a range of different behavioral tests without evoked pain (i.e. without direct nociceptive stimulation).

Rats were operated according to the Bennett or Chung protocol. Selected neuropathic rats were subjected to different behavioral tests evaluating locomotor activity and coordination (activity meter and rotarod tests) anxiety and mood (elevated plus-maze and behavioral despair tests). Neuropathic animals were also evaluated using a neurological score, classically used in trauma or ischemia models.

MATERIAL & METHODS

- **Animals:**
  - Male Wistar (Hen) rats, weighing 180-220 g (surgical day). They were supplied by Elevage Javelier, 53960 Le Genest-Saint-Isle, France.
  - 1 week (Bennett model) or 2 weeks (Chung model) post-surgery, rats were tested with an electronic von Frey to confirm the presence of tactile allodynia.

- **Bennett model of neuropathic pain:** chronic constriction injury (CCI) of the common sciatic nerve
  - Rats were anesthetized and an incision at the mid-thigh level was performed to expose the common left sciatic nerve. Four ligatures spaced 1 mm apart were loosely tied around the sciatic nerve.

- **Chung model of neuropathic pain:** tight ligature of spinal nerve (SNL)
  - Rats were anesthetized and an incision at the L4-L2 level was performed to expose the left L5 nerve. A ligature was tied tightly around the L5 nerve.

- **Activity meter test:**
  - The activity meter consists of 16 covered Plexiglas cages (40 x 25 x 25 cm) contained within a darkened enclosure. Each cage was equipped with 4 photocell assemblies, 3 cm above the floor, to measure the number of movements in the horizontal plane. Ten additional photocell assemblies were placed at even intervals 20 cm above the floor along the long wall to record rearing. The number of horizontal crossings and rears were recorded by a computer for 40 minutes.

- **Rotarod test:**
  - Habitation: rats were placed on a rod (diameter: 7 cm) rotating at a constant speed of 12 revolutions per minute for 2 minutes. If they fell off during this period, they were replaced on the rod. At the end of this period, rats were placed on the rod under the same conditions as used during the test session.
  - Test: at least 2 hours after habituation, rats were placed on the rotarod for a maximum of 3 minutes. The number of animals which fell off before the end of this period were counted and the latency to fall off was also recorded.

- **Neurological score:**
  - The neurological score was evaluated using a neurological score, classically used in trauma or ischemia models.

- **Behavioral despair test:**
  - Duration of immobility in CCI or SNL rats was similar to control rats.

RESULTS

**Activity meter test:**
- The number of crossings was significantly decreased in CCI and SNL rats as compared with control rats (20% and 32%, respectively). A more marked effect was observed on the number of rears (-37% and -45%, respectively).

**Rotarod test:**
- The drop-off time was clearly decreased in both CCI and SNL rats as compared with control rats (-26% and -36%, respectively).

**Elevated plus-maze test:**
- Total number of entries, % of entries and time spent in open arms were not significantly decreased in CCI or SNL rats as compared with control rats.

**Behavioral despair test:**
- Duration of immobility in CCI or SNL rats was similar to control rats.

CONCLUSION

These results demonstrate that both the CCI and SNL models of neuropathic pain produced behavioral changes in tests (activity meter, rotarod and neurological score) which may indicate non-evoked pain states. Assessment of standard and novel analgesic agents using these behavioral assays in CCI and SNL rats will help to determine the potential utility of these measures for non-evoked pain.

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