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Journal of Neuroscience Methods 116 (2002) 197–213

JOURNAL OF NEUROSCIENCE METHODS

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Gait analysis as an objective measure in a chronic pain model

Paul Coulthard [a,*], Barbara J. Pleuvry [b], Mike Brewster [c], Kevin L. Wilson [d], Tatiana V. Macfarlane [a]

[a] *University Dental Hospital of Manchester, Higher Cambridge Street, Manchester M15 6FH, UK*
[b] *School of Biological Sciences, The University of Manchester, Oxford Road, Manchester M13 9PT, UK*
[c] *F. Hoffman-La Roche AG, Pharmaceuticals Division, Pharma Research Non-Clinical Safety, CH-4070 Basel, Switzerland*
[d] *Roche Products Ltd, Broadwater Road, Welwyn Garden City AL7 3AY, UK*

Received 5 December 2001; received in revised form 27 February 2002; accepted 1 March 2002

Abstract

The aim of this study was to investigate objective characterisation of gait as a marker of the chronic pain of adjuvant arthritis (AA). Video recorded images of spontaneous rat ambulations were analysed to quantify various temporal and spatial parameters and compare these between the AA and control groups. Changes were also recorded after the administration of a single dose of buprenorphine (15 μg). Individual temporal parameters were significantly reduced (velocity ($P = 0.05$), stride length ($P = 0.007$), single stance time ($P < 0.001$), swing time ($P = 0.001$)), or increased (dual stance time ($P < 0.001$)) at 10 days in the AA group compared to control. The rear paws showed reduced ground contact and the fore paws an increase in proximal pad and decrease in digit area, although these changes were not all statistically significant. Some of the gait parameters showed significant reversal following administration of buprenorphine (velocity ($P < 0.001$) and stride length ($P < 0.001$) were increased and single stance time ($P = 0.014$) reduced). It is proposed that changes in gait are a marker of AA chronic pain in this model. These behavioural changes were significant at a very early stage (day 10), before the development of physical deformities and increase in paw volume and might permit an earlier detection of pain than other models.

Keywords: Chronic pain; Pain measurement; Adjuvant arthritis; Gait

1. Introduction

There are few models of chronic pain. Adjuvant arthritis (AA) in the rat has been the classic model used to more closely mimic inflammatory pain, and has been extensively used to study pain processes and evaluate potential analgesic strategies. However, despite many advantages of this model, the severe systemic changes associated with the disease provoke ethical concern and for this reason, several workers have developed limited forms of this arthritis model. Iadarola et al. (1988) described a model of monoarthritis that follows the injection of Freunds adjuvant into the footpad of a rat rather than the usual tailbase site. Many research teams have turned to this or variants of this model, but if it is allowed to persist for use in chronic pain investigations, polyarthritis develops, with all the ethical disadvantages of the systemic disease. Butler et al. (1992) produced a predictable stable monoarthritis that was stable from weeks 2 to 6 post injection of *Mycobacterium butyricum* into the tibiotarsal joint of a rat, and more recently, Calvino et al. (1996) described ultrasonic vocalisation as a useful marker of chronic pain in the classic AA model. The aim of our study was to investigate objective characterisation of gait as a marker of the chronic pain of AA that might permit an earlier detection of pain than other models.

2. Methods

This experiment was carried out in accordance with UK animal welfare guidelines (Animals Scientific Procedures Act, 1986) and received Local Ethical Committee approval. Forty female Alan and Hanberies Hooded

* Corresponding author. Tel.: +44-161-275-6650; fax: +44-161-275-6631.
E-mail address: paul.coulthard@man.ac.uk (P. Coulthard).

0165-0270/02/$ - see front matter
PII: S0165-0270(02)00042-0

Ren, 1999), it is proposed that gait analysis is a suitable marker for the measurement of chronic pain.

4.2.7. Buprenorphine analgesia

Buprenorphine (15 μg) administration as a single dose had a dramatic effect on animal locomotion with only 2 out of 20 animals walking prior to administration and 18 animals walking after administration in the arthritic group. There were significant changes in gait toward baseline in the arthritic group and no changes in gait in the control group. There was therefore evidence of inhibition of AA associated gait changes following the administration of an opioid analgesic. It would be difficult to explain such a rapid and dramatic reversal of gait changes in terms of reduction in tibiotarsal joint inflammatory oedema or cartilage change, which may potentially have restricted movement. The effect of buprenorphine on gait therefore supports the hypothesis that gait changes may be a marker of AA chronic pain.

Costa et al. (1981) suggested that for a model of animal chronic pain to be accepted as such, it should fulfil the following criteria: rats should show changes in behaviour that can be quantified; these behavioural changes should be reversible with morphine and these behavioural changes should be present for at least 1 month. The last of these suggested criteria is now controversial. As discussed earlier, in chapter one, one of the objectives of this research is to develop a limited AA model by measuring pain at an earlier stage and so minimise suffering. The development of novel animal models which do this are now being encouraged by the 'European Centre for Validation of Alternative Methods' and the 'Home Office', that regulates animal experimentation in the UK. The results described above indicate that there are behavioural changes in gait associated with AA and that these can be quantified. The first criterion suggested by Costa's group is therefore fulfilled. The inhibition of these changes in gait by buprenorphine satisfies the second of Costa's criteria.

5. Conclusions

Significant changes in gait were observed in arthritic rats and these were objectively measured. These behavioural changes were significant at a very early stage (day 10) before the development of physical deformities and before a significant increase in volume of left rear paw. Arthritic rats showed a reduction in velocity, stride length and dual stance time and an increase in single stance time. The temporal measures of gait showed more significant change than spatial measures of gait but the latter showed some evidence of change and are therefore considered to be worthy of further investigation. The rear paws showed a reduction in ground contact and the fore paws an increase in proximal pad and decrease in digit area, although these changes were not all statistically significant. As a hypothesis it can be proposed that changes in gait are a marker of AA chronic pain. An argument for this hypothesis is the fact that buprenorphine blocked these changes. Velocity and stride length were increased and single stance time reduced in the arthritic animals following administration of buprenorphine. The method of gait analysis showed good evidence of repeatability and reliability.

Acknowledgements

This study was supported by a grant awarded by the British Association of Oral and Maxillofacial Surgeons, The Royal College of Surgeons of England.

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