Journal of Neuroscience Methods 257 (2016) 134–138

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Basic neuroscience

Versatile 3D-printed headstage implant for group housing of rodents

R.C. Pinnell[a,*], R.K. Almajidy[a,b,c], U.G. Hofmann[a]

[a] Medical Centre - University of Freiburg, Department of Neurosurgery, Section for Neuroelectronic Systems, Freiburg, Germany
[b] Institute for Signal Processing, University of Lubeck, Lubeck, Germany
[c] College of Medicine, University of Diyala, Baqubah, Diyala, Iraq

HIGHLIGHTS

- A novel 3D-printed headstage was developed for protecting skull-mounted implants in rodents.
- The socket allowed for successful chronic pair-housing of rats following stereotaxic surgery.
- Rats were able to carry out a range of normal behaviours, with no significant implant damage observed.
- This implant can help to improve the well-being of post-surgical rats, whilst reducing the cost of rodent upkeep.

ARTICLE INFO

Article history:
Received 12 May 2015
Received in revised form
15 September 2015
Accepted 28 September 2015
Available online 9 October 2015

Keywords:
Isolation
Well-being
Rodents
Skull implant
Social environment
Pair housing

ABSTRACT

Background: An unfavourable yet necessary side-effect of stereotaxic surgery involves the social isolation of post-surgery rats, in order to protect their wound site or skull-mounted implant from damage. Social isolation can cause a myriad of behavioural and physiological changes that are detrimental to the well-being of rats, with potential negative implications for a range of experimental paradigms.

New method. Female Sprague Dawley rats ($n = 40$) were implanted onto the skull with a novel 3D-printed headstage socket that surrounded an electrode connector. The socket accommodated a removable stainless-steel headcap for the purposes of protecting the implant. Rats were pair-housed following surgery, and their behaviour was monitored for up to several weeks under two experimental conditions that involved EEG recording and deep-brain stimulation, as well as behavioural test sessions inside an open-field maze. Rat weights were compared between individually- and pair-housed rats at up to 3 weeks post-surgery.

Results: These experiments were successfully carried out using pair-housed rats, with no damage or complications observed regarding the implant and its headcap. Rats were able to carry out a range of normal behaviours including running, grooming, foraging and sleeping. Compared to individually-housed rats, pair-housed rats gained less weight over the 3 weeks post-implantation period.

Comparison with existing method(s). This method offers additional protection compared to group-housed post-surgical rats that lack the protective headcap. It is also potentially more practical and versatile than a fully-implantable device for the safe post-surgery group housing of rodents.

Conclusions: This implant design can reduce the cost of rodent upkeep, whilst potentially avoiding a myriad of behavioural and physiological changes that are known to result from social isolation.

1. Introduction

It has long been established that social isolation in rats during either weaning or adulthood facilitates marked behavioural and physiological changes, which are detrimental to their well-being (Patterson-Kane, 2004). Rats area naturally social species, and numerous lines of evidence have pointed to behavioural and physiological changes that occur from solitary housing. Social isolation in rats has been shown to result in increased heart-rate and blood pressure (Sharp et al., 2002), adrenal hyper- and hypotrophy (Westenbroek et al., 2005), a reduced density of striatal dopamine receptors (Bean and Lee, 1991), altered c-fos expression in various limbic regions (Westenbroek et al., 2003), as well as reductions in the levels of plasma triglyceride (Perez et al., 1997); all of which have been associated with chronic stress. Furthermore, individually-housed rats are known to be more aggressive and difficult to handle (Hatch et al., 1963; Valzelli and Bernasconi, 1976).

* Corresponding author. Tel.: +49 15751309758.
E-mail address: rpinne@gmail.com (R.C. Pinnell).

http://dx.doi.org/10.1016/j.jneumeth.2015.09.027
0165-0270/

One particularly noticeable change that is consistent among singly-housed rats, is their dietary habits. Numerous studies over the past few decades have noted that individually-housed rats tend to eat and weigh more than their group-housed counterparts (Fiala et al., 1977; Levitsky, 1970a,b; Perez et al., 1997; Lopak and Eikelboom, 2000a,b). More recently, Zaias et al. (2008) had demonstrated a weight gain in adolescent rats which was attributed to both a socially and/or novelty impoverished environment. Numerous reasons have been put forward for these changes in dietary habits, including competition for food, increased activity, and decreased food consumption.

In addition to physiological changes that occur, social isolation is known to alter rat behaviour. For instance, isolated rats have been shown to display disruptions in prepulse inhibition (PPI) of the acoustic startle response (Wilkinson et al., 1994). In addition, reductions in exploratory behaviour in the elevated X-maze, reduced (novel) object manipulating behaviour (Einon and Morgan, 1976), as well as an increase avoidance of bright light in a two-compartment shuttlebox (Stanford et al., 1988) have also been observed. Generally speaking rats have a strong preference for companionship, as demonstrated in an experiment that measured the escape-related behaviours in rats housed individually when compared with group-housed controls (Hurst et al., 1999). Furthermore the presence of another rat can potentially ameliorate chronic stress; for instance pair-housing female rats has been shown to normalise stress-induced increases in FOS activity (Westenbroek et al., 2003) in the paraventricular nucleus of thalamus (PVN). Finally, there are suggestions that wound-healing is improved in group-reared as opposed to isolation-reared rats (Levine et al., 2008a,b). Taken together, social isolation in rats produces a widespread array of physiological and behavioural changes that may be detrimental to the study taking place, and the group housing of rodents may provide therapeutic benefits during periods of stress inducing experimentation.

Unfortunately many neuroscience-based experimental paradigms necessitate the individual housing of rats, in order to protect their post-operative wound site from damage through various social behaviours including grooming, playing and fighting. This is of particular importance when skull-mounted implants are used for the purposes of interfacing brain-implanted electrodes/cannula with outside recording/injection systems. For instance during chronic EEG recording or deep-brain stimulation experiments, rats typically feature an implant fixed to their skull which houses a connector for recording/stimulation cables. A fully-implantable system may be considered for post-surgery group housing, however they may not be the appropriate choice in many experiments due to functionality, availability, practicality and cost constraints. For many of the reasons previously described, it is desirable to devise a means of being able to group-house rats under these scenarios, in particular since many of these rats will ultimately participate in experiments in which their performance may be influenced by solitary housing conditions. Furthermore, group housing of rats can alleviate some of the cost/space considerations in an animal facility, which in practice may offer a greater flexibility regarding the design of an experimental paradigm.

In this study, a 3D-printed headstage socket was developed for use in rodents to accommodate a protective stainless-steel head-cap. The aim of this implant was to protect an embedded electrode connector from damage that may otherwise have resulted from social housing conditions. The performance of the device was verified in rats that were reunited following the surgery recovery period, and behavioural observations were made throughout the experimental period. Two groups of rats were assessed: a small (proof-of-concept) group for 5-weeks following surgery, with weekly EEG recording sessions; and a larger group which underwent an intensive daily behavioural test paradigm for a week. In addition, the weights of pair-housed rats were compared with a separate group of individually-housed rats that underwent a similar stereotaxic surgery procedure albeit without the head-cap/thimble, and also underwent weekly EEG recording sessions.

2. Materials and methods

2.1. Protective head-cap design

A headstage socket was designed using Solid Edge ST6 (Siemens PLM Software) and manufactured using polyamide with selective laser sintering (Beta Layout, Ireland). The headstage is a 5 mm-high cylinder with an internal diameter of approximately 13.5 mm and an outer diameter of 15.6 mm at the base and 14.3 mm at the top (Fig. 1). Similarly the wall thickness varies from 1.4 mm at the base to 0.65 mm at the top. Two feet protrude at 2-mm from the base of the socket and contain screw-holes for the attachment of stainless-steel skull-mounting screws (0–80 × 1/8; Plastics One) during surgery. The corresponding protective thimble is an

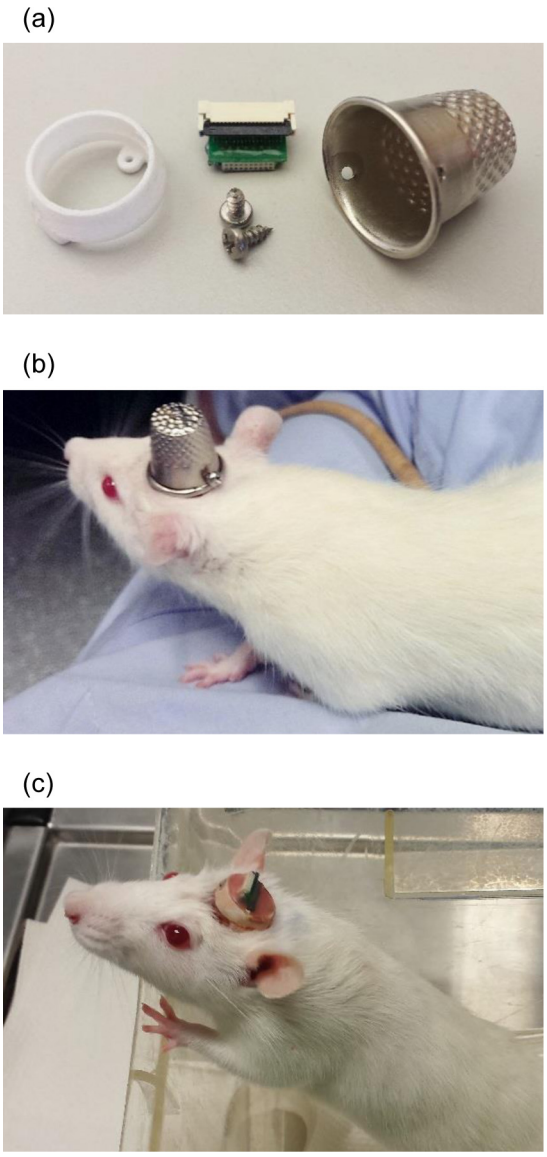

Fig. 1. Headstage socket and protective headcap. A polyamide head-stage socket is shown with its connecting stainless steel thimble and screws, and also a PCB connector which is placed inside during surgery (a). When implanted onto the skull of a rat, the thimble can be removed to reveal the electrode connector (b).