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An automated system for positive reinforcement training of group-housed macaque monkeys at breeding and research facilities

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HIGHLIGHTS

- An automated positive reinforcement training system for group-housed monkeys.
- Animals can be trained with no food or fluid restriction.
- Breeding facility results may predict subsequent research facility and lab performance.

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ABSTRACT

Background: Behavioural training through positive reinforcement techniques is a well-recognised refinement to laboratory animal welfare. Behavioural neuroscience research requires subjects to be trained to perform repetitions of specific behaviours for food/fluid reward. Some animals fail to perform at a sufficient level, limiting the amount of data that can be collected and increasing the number of animals required for each study.
New method: We have implemented automated positive reinforcement training systems (comprising a button press task with variable levels of difficulty using LED cues and a fluid reward) at the breeding facility and research facility, to compare performance across these different settings, to pre-screen animals for selection and refine training protocols.
Results: Animals learned 1- and 4-choice button tasks within weeks of home enclosure training, with some inter-individual differences. High performance levels (~200–300 trials per 60 min session at ~80% correct) were obtained without food or fluid restriction. Moreover, training quickly transferred to a laboratory version of the task. Animals that acquired the task at the breeding facility subsequently performed better both in early home enclosure sessions upon arrival at the research facility, and also in laboratory sessions.
Comparison with existing method(s): Automated systems at the breeding facility may be used to pre-screen animals for suitability for behavioural neuroscience research. In combination with conventional training, both the breeding and research facility systems facilitate acquisition and transference of learning.
Conclusions: Automated systems have the potential to refine training protocols and minimise requirements for food/fluid control.

1. Introduction

Positive reinforcement training (PRT) (Skinner, 1938) represents a valuable refinement of laboratory animal husbandry (Prescott and Buchanan-Smith, 2007) and its use with non-human primates (NHPs) is recommended by the UK Home Office, International Primatology Society, National Research Council, Laboratory Animal Science Association and Medical Research Council. PRT can be used to successfully train NHPs to participate voluntarily in procedures (Laule et al., 2003; Young and Cipreste, 2004) such as injection (Priest, 1991), the collection of blood, urine or saliva samples (Priest, 1991; Coleman et al., 2008; Laule et al., 1996; Lambeth et al., 2006; Reinhardt, 2003; Tiefenbacher et al., 2003), movement within/between enclosures (Bloomsmith et al., 1998; Veeder et al., 2009) and may benefit the welfare of captive animals as a

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result of their ability to control their environment and exercise free choice (Buchanan-Smith and Badihi, 2012). In addition, improved data from co-operative subjects may further reduce the number of animals required for studies (Prescott and Buchanan-Smith, 2007). PRT can provide environmental enrichment for captive animals (Melfi, 2013; Westlund, 2014) and reduce aggression and other behavioural problems in primates (Honess and Martin, 2006; Coleman and Maier, 2010; Minier et al., 2011).

Despite widespread recognition of the benefits of PRT it remains to be universally adopted (Perlman et al., 2012), due to 'principally a lack of staff and time and a lack of confidence in ability to train' (Prescott and Buchanan-Smith, 2007). Current PRT regimes are labour intensive, particularly during early stages when it is important that operant behaviours are consistently associated with rewards and performance is systematically documented so that training can proceed at an optimal rate. Consistent daily training has been found most conducive to training success (Fernström et al., 2009).

PRT is commonly used for behavioural neuroscience experiments to train complex cognitive and motor behaviours for food or fluid reward. Animals are typically motivated by restricting corresponding food or fluid intake in the home enclosure (Prescott et al., 2010). While successful in most cases, final performance levels vary considerably across individuals. A small proportion of subjects (~1 in 10) fail to respond to this routine and must be replaced, incurring welfare costs related to unproductive training, unnecessary transport and re-housing of animals (Davenport et al., 2008; Schapiro et al., 2012).

These considerations motivated us to develop an automated operant conditioning system for unsupervised PRT of NHPs in group home enclosures. While automated systems have previously been reported for use in the training of NHPs (Rumbaugh et al., 1989; Andrews and Rosenblum, 1994; Weed et al., 1999; Spinelli et al., 2003; Mitz et al., 2001; Wilson et al., 2005; Mandell and Sackett, 2008; Fagot and Paleressompoulle, 2009; Truppa et al., 2010; Gazes et al., 2012; Calapai et al., 2016), none of these investigated automated training performance across the different settings in which animals may be trained throughout the course of a typical research project. We investigated the potential benefits of using an automated PRT system at the breeding facility (BF) *before* animals are issued to the research facility (RF) and the effect on subsequent training performance both at the research housing facility and in the laboratory. To do this we designed automated systems which were simple and inexpensive to build/operate/repair, could deliver a high volume of reward and which trained animals to perform a simple motor task using the upper limbs which would be relevant for subsequent research projects. These systems then allowed us to systematically compare animal task performance across the BF, RF and Laboratory settings.

We found automated training enabled animals to learn a high level of performance on simple tasks with minimal requirements for staff time and no food or fluid control, and thus represents a valuable refinement to the training process. In addition, we found that automated training data at the breeding facility correlated with subsequent performance at the research facility and in the laboratory. Thus, automated training records could be used to identify animals suitable for behavioural experiments and assist in optimising the training process for each individual.

2. Materials and methods

2.1. Automated training systems

We used three separate systems to collect behavioural data: one at the breeding facility (MRC Centre for Macaques facility at Porton Down, UK), a second in the housing area of the research facility (Newcastle University, UK) and a third for use in the laboratory (Fig. 1).

The systems all comprised coloured LED cues next to response buttons, although the number and physical layout varied slightly across systems (see inset panels in Fig. 1a–c). While some previous systems for automated NHP training have used touch-screens in order to facilitate progression onto tasks of increasing cognitive complexity, (Weed et al., 1999; Spinelli et al., 2003; Mandell and Sackett, 2008; Fagot and Paleressompoulle, 2009; Truppa et al., 2010; Gazes et al., 2012; Calapai et al., 2016), our priority was to design a low-cost (approx. £300 per system), robust system (self-contained and with minimal cables and in-build data storage, easy to clean and repair) that could be used at the BF with minimal support from RF staff located at a different site. Moreover, our animals progress to motor tasks that require interaction with physical devices (levers, manipulanda etc.) rather than cognitive testing. Therefore we designed our system to use robust physical buttons and LED cues, although we do not discount the utility of more advanced technologies (such as touch screens, remote supervision and centralised data storage) for later stages of training on cognitive tasks.

Both BF and RF systems allowed fully-automated training on a button press task cued by coloured LEDs. Fluid rewards (blackcurrant flavour cordial juice, using a 1/10 dilution with water) were delivered via a peristaltic pump and associated with success/error tones delivered via a built-in speaker. A control unit incorporated a microcontroller (ATMega644P, Atmel Corp., San Jose, CA, USA) to run the task, an SD card for data storage, an LCD display and USB serial port for exporting data to a PC (Fig. 2).

Whenever a LED cue was illuminated, animals received either a "success" tone and fluid reward for pressing the corresponding button continuously for a defined hold time, or an "error" tone and no fluid reward for pressing an incorrect button or releasing the correct button too soon. Following any incorrect press was an adjustable time out period where no LEDs were illuminated and no reward dispensed. The time out period was prolonged if any button presses were attempted during this time, thus enforcing the importance of the LED cues for successful reward retrieval and discouraging random button presses. Following an incorrect attempt, the same LED cue would illuminate again. This same LED would continue to illuminate until correctly pressed, to discourage stereotyped pressing of only one button. Correct and incorrect responses were recorded to an SD memory card along with the date, time and task parameters. The breeding facility system fitted directly onto an annex cage situated off the main NHP group enclosure (Fig. 1a). The research facility system was attached to a standard training chair situated off the animals' enclosure (Fig. 1b). The same training chair was subsequently used to bring animals to the laboratory (Fig. 1c). Unlike the fully-automated systems, training in the laboratory used food reward (assorted chopped fruit, dried fruit and nuts) hand-delivered by the trainer. LED cues were controlled by a PC which also provided success/error tones and recorded performance data.

The research facility system also incorporated a sub-cutaneous radio-frequency identification (RFID) reader coil to automatically identify animals as they entered the training chair. Sessions were filmed at least twice per week and we compared visual identification of animals against the electronic records to monitor the reliability of the RFID reader recognition rate, which in the short term performed at >80%. However, due to hardware issues RFID identification was only used for four animals; the remainder were individually separated for training sessions.