Rodent Big Brother: Optimal Location and Orientation of the Subcutaneous RFID microchip Transponder for Home Cage 24/7 Monitoring in Rats

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Introduction

- Rodent Big Brother (RBB, ActualHCA™, Actual Analytics Ltd, UK) allows continuous detection of temperature and activity of individual animals in a group-housed, home cage environment.
- Temperature and activity are detected via a passive subcutaneous radiofrequency identification (RFID) transponder, which is read by a baseplate containing 12 antennae, located beneath the cage.
- The purpose of this study was to select the optimum implantation site for future studies.
- The criteria for selection were based on signal strength, dark/light phase differences in temperature and activity, correlation between ambulatory activity detected by the baseplate and the animal's actual locomotion from an overhead webcam, ease of implantation, and histological examination of the skin surrounding the implant.

Methods

- Han Wistar rats (220-270g) were implanted with a single temperature sensing RFID transponder (Biothermo13, Biomark). Four different sites were investigated: interscapular; flank in the horizontal orientation; flank in the vertical orientation; ventral midline (n=3/cage, n=6/site; Fig 1).

Figure 1: Four implantation sites investigated to optimise the location for the RBB subcutaneous RFID transponder

- All 4 sites were initially tested before magnetic shielding patches were fitted to the underside of the baseplates to increase the field strength of the antennae. Following the shielding, ventral midline and flank in vertical orientation were re-tested.
- Temperature and the animal's location are detected by the baseplate. The theoretical maximum read rate for each baseplate is 0.93Hz (red line on Fig 3).

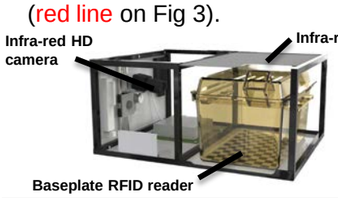

Figure 2: A schematic diagram of a RBB enclosure set up in a standard IVC cage rack.

- Activity data is derived from baseplate readings via a filtering algorithm that prevents duplicate sequential readings being registered as spurious movement.
- Animals were recorded continuously for 7 days for all implantation sites.
- To correlate between ambulatory activity from the baseplate and an animal's actual locomotion, a temporary webcam was set up above a cage with the food hopper grid removed. Actual locomotion was based on the bird's eye view footage from the webcam, annotated manually (Fig 5).

Results

Signal strength

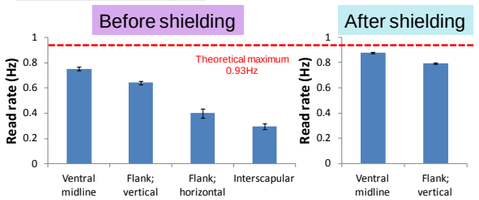

Figure 3: Average read rates for each implantation site before shielding of the baseplates. Ventral midline and flank in vertical orientation were re-tested after shielding (n=6/site; n=5 for ventral midline before shielding).

Dark phase and light phase differences

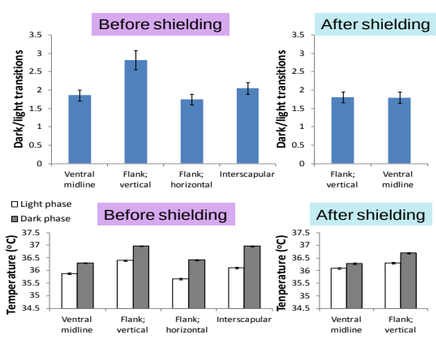

Figure 4: a) activity – mean ratio from dark to light phases; b) temperature – mean temperature from dark and light phases, before and after shielding of the baseplates (n=6/site; n=5 for ventral midline before shielding).

Bird's eye analysis

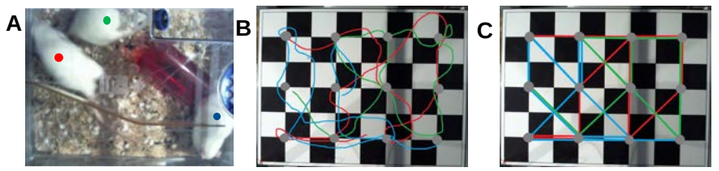

Figure 5: An overview of the bird's eye analysis A) view from the webcam set up above the cage showing the bird's eye view of 3 animals. B) schematic of the actual locomotion of 3 rats around the cage on the baseplate. C) schematic of the activity of 3 rats detected by the antennae of the baseplate. Individual rats are distinguished by colour (red, green and blue). Grey dots represent the location of the antennae

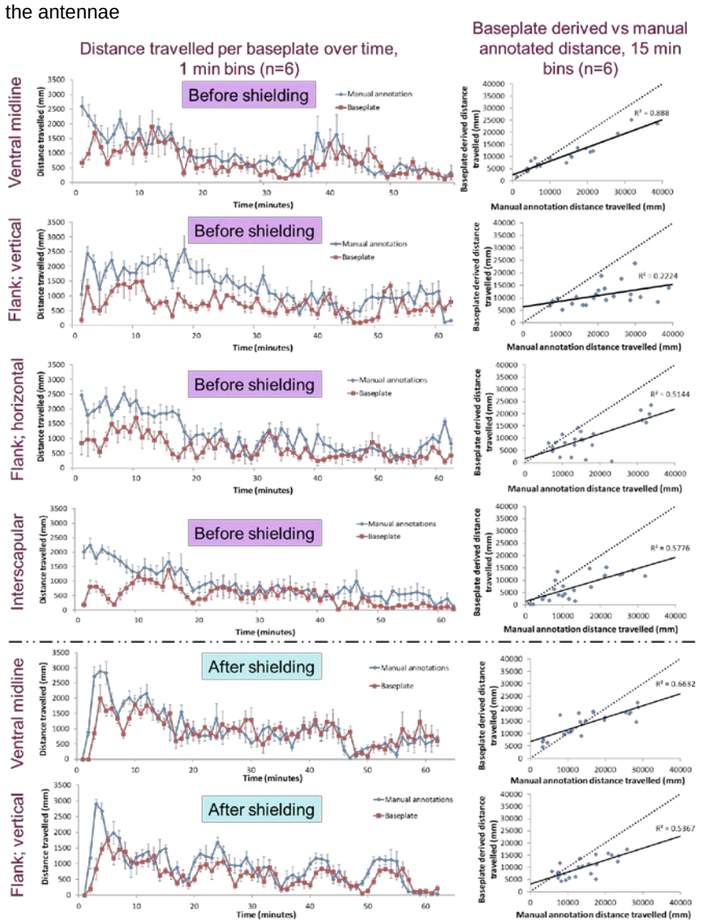

Figure 6: Baseplate derived against manual annotated distance travelled. A-D) Mean (±SEM) distance plotted in 1-minute bins over 1h. E-H) Correlation plot from raw data in 15-minute bins. The solid line represents the linear correlation of the data and the dashed line represents a 1:1 ratio.

	Before shielding				After shielding	
	Ventral midline	Flank (vertical)	Flank (horizontal)	Interscapular	Ventral midline	Flank (vertical)
Signal strength	++++	+++	++	+	++++	+++
Dark/light phase ratio	+++	++++	++	+++	+++	+++
Baseplate activity readout vs. bird's eye	++++	+++	++	+	++++	+++
Ease of implantation (assessed by experimenter)	++ - n=1 inadvertently injected IP	++ - n=1 found in testicular fat	+++	++++	+++	+++ Improved implantation method
Histopathology at implantation site (assessed by pathologists)	++++	++++	++++	++++	++++	++++

Table 1:Summary of all the criteria to select the optimum implantation site. The implantation method for both vertical flank and ventral midline was refined.

Conclusions

- Ventral midline and flank in vertical orientation gave the highest signal strength from the baseplate. Also, the shielding improved the signal strength of the baseplates.
- Ventral midline and flank in vertical orientation showed consistent dark/light phase ratio in activity. The activity of group-housed rats detected by the baseplate was 1.75 x higher in the dark phase. Single-housed rats have been reported to have ~4x higher activity in the dark[1,2]. Future studies can investigate the impact of single-housing on circadian activity. The temperature range from ventral midline is similar to from flank in horizontal orientation, which reflects the core temperature[3].
- Ventral midline showed the best correlation in activity detected by baseplate vs. motion detection and animal's actual motion.
- Improvements to the implantation methods had increased the accuracy of transponder location.
- Histopathology of skin surrounding the implants showed no inflammation for all 4 sites.
- Overall, the two best implantations sites were ventral midline and flank in the vertical orientation. The site chosen for further pharmacological validation is **ventral midline**.

References

[1]McDermott C and Kelly JP. 2008. Progress in Neuro-Psychopharmacology & Biological Psychiatry 32: 1816 -1823
[2]Terrón MP et al. 2013 Physiology & Behaviour 118: 8-13
[3]Prior H et al. 2012 J Pharmacol Toxicol Methods 66: 192

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