

Good welfare – good scientific output: Refining husbandry and procedures for primates in the laboratory

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Why primates?

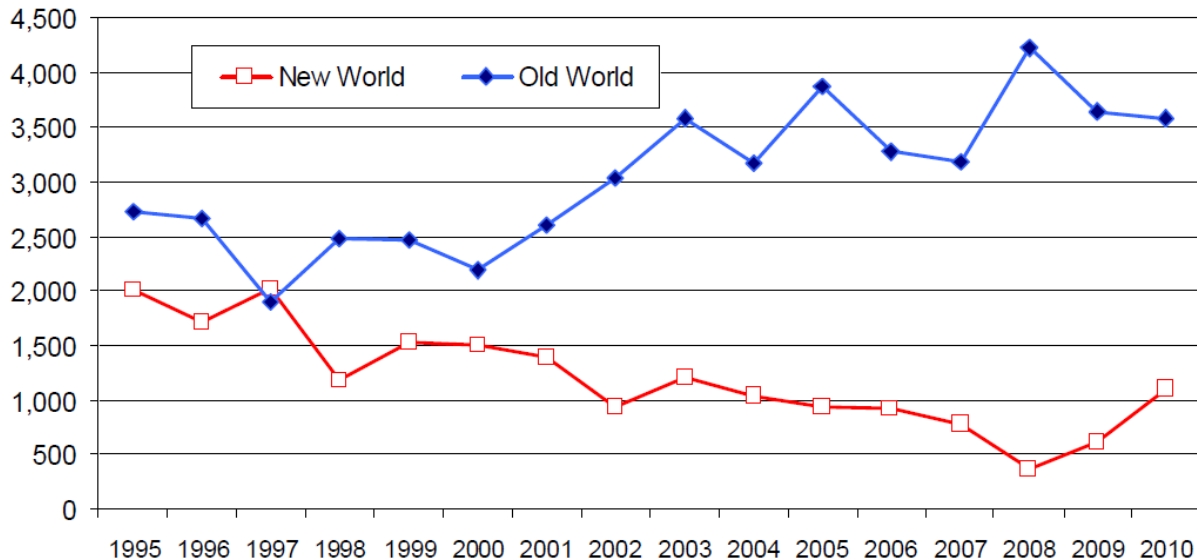
Total: 4,688 procedures in 2010, and 66% in toxicology

Same principles



Figure 4: Procedures using non-human primates, 1995-2010

Number of procedures



Refinement is about animal welfare:

"Any approach which avoids or minimises the actual or potential pain, distress and other adverse effects experienced at any time during the life of the animals involved, and which enhances their well-being" Buchanan-Smith et al., 2005



Photo credit: NC3Rs

Promoting good welfare

- Social housing
- Appropriate weaning age
- Large, complex enclosures
- Socialisation with humans
- Positive reinforcement training



Photo credit: Keith Morris



Photo credit: Keith Morris

**Socialisation
and PRT**

**Family
separation**

Enrichment



Separation

Handling

Capture

**Rearing
practices**

**Prenatal
stress**

**Rearing
Environment**



Transport

Journey



Health screening



**Behavioural
restriction**

**Laboratory
Environment**

**Study
Protocol**

**Designated
Establishment**

**Complex
enclosures**



NC3Rs

Restraint

Dosing

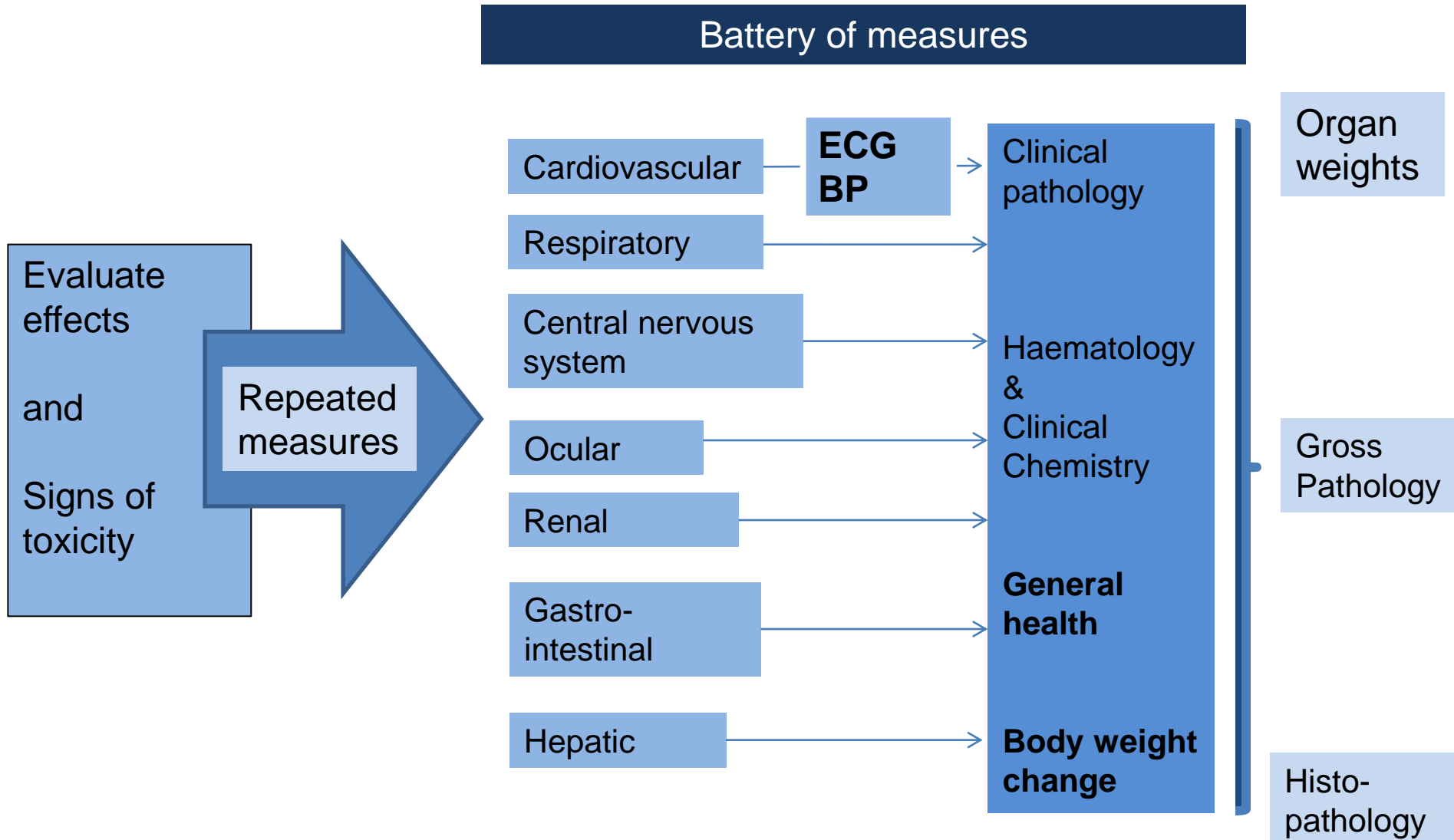
Sampling



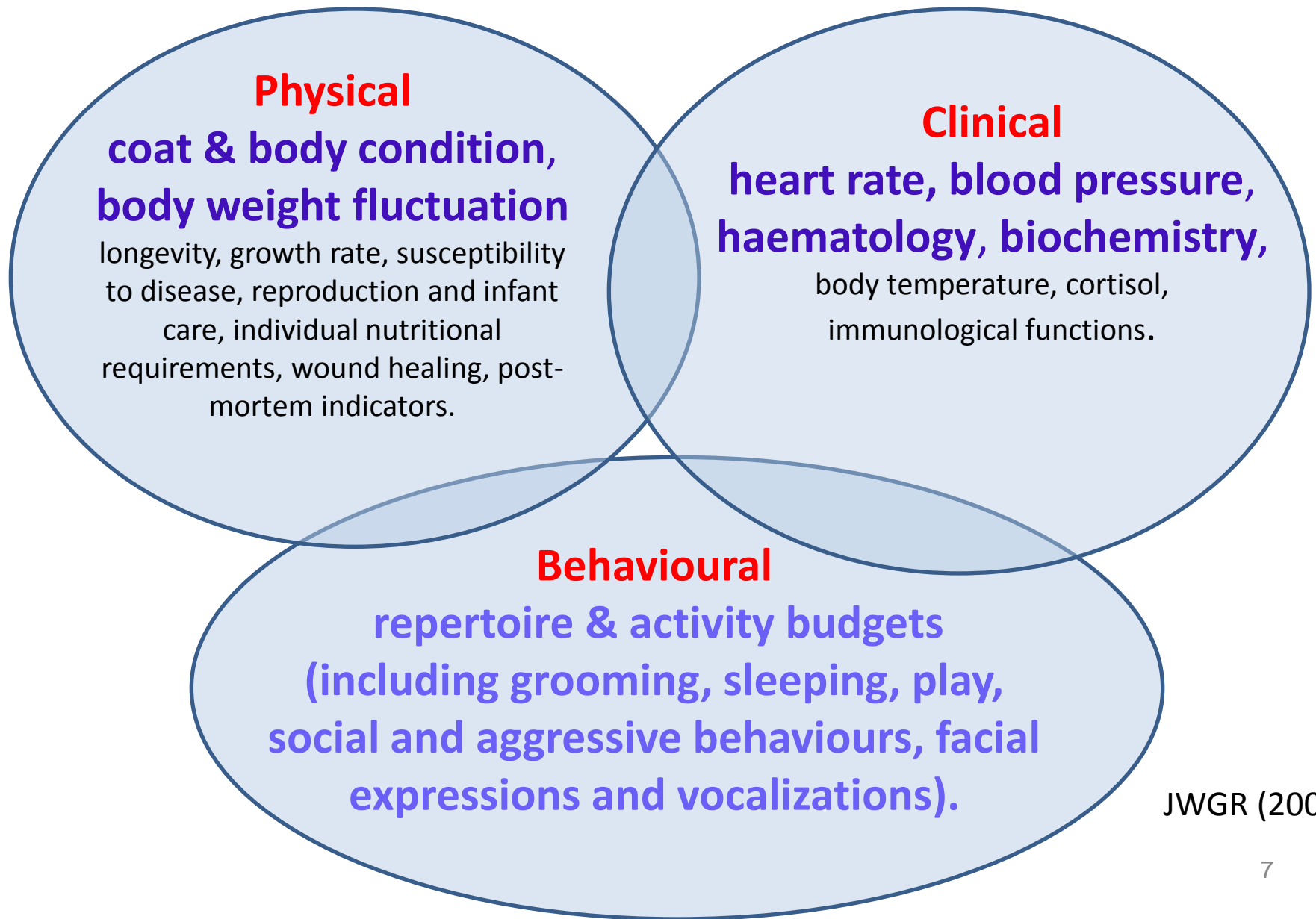
**Husbandry inc.
socialisation**

PRT

In vivo model in regulatory toxicology



Overlapping measures – toxicity and welfare



JWGR (2009)

The link between good welfare & good scientific output

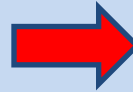
Good welfare

- Normal and stable
- Acclimatised (NRC 1996; Weed & Raber 2005)

Good scientific output

- Valid – the right measure!
- Reliable & Repeatable (precision, consistency, absence of confounding factors & unplanned variation)

BAD WELFARE



BAD SCIENCE

The link

- Compromised welfare affects behaviour, physiology and immunology
 - ➔ unreliable conclusions?
 - ➔ unwanted variation in scientific output?

Repeatability - Acclimatisation

Rhesus macaques, 6 mo acclimatisation (n=6m, 6f)

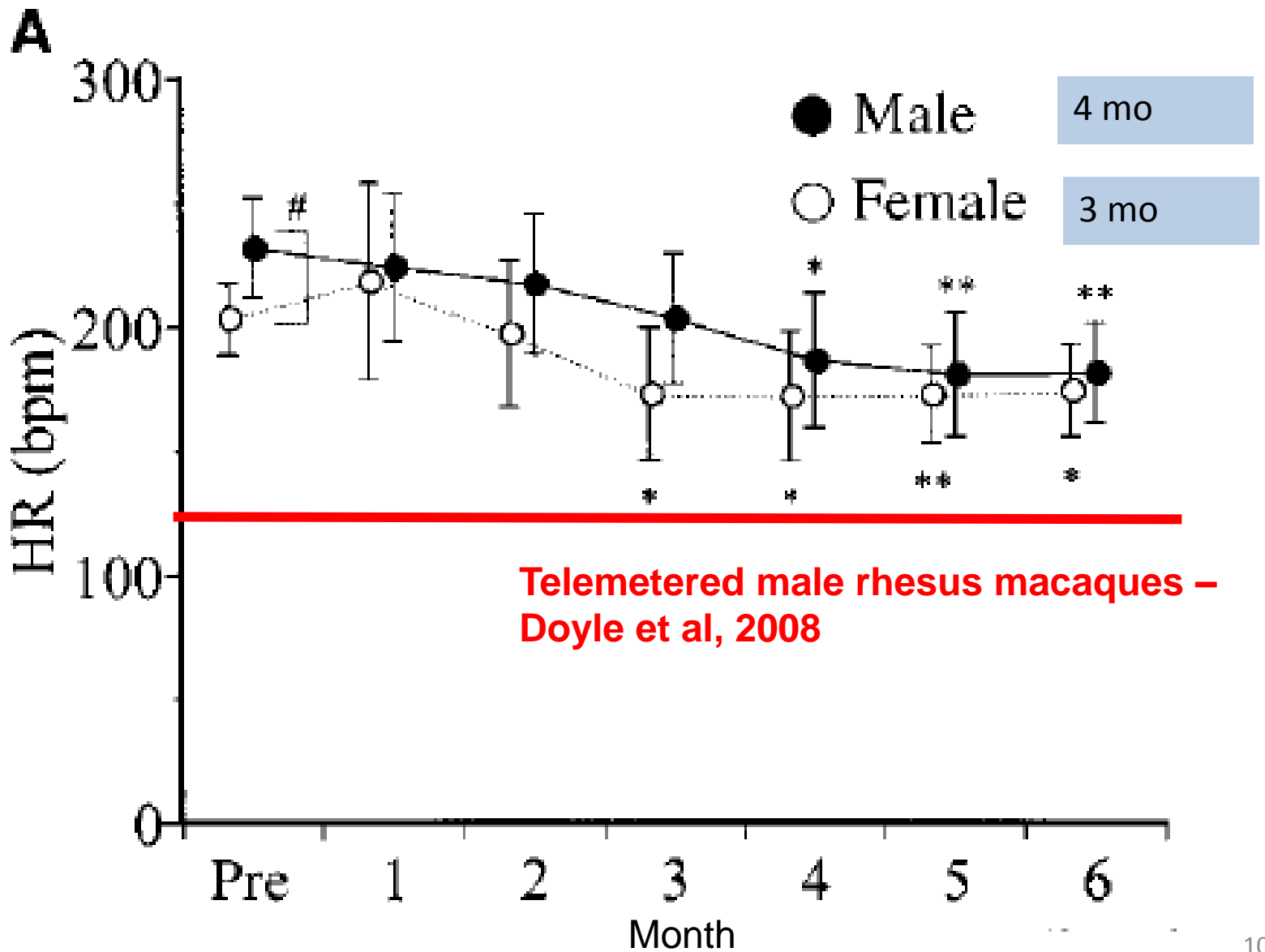
Week 1 after arrival - habituation to:

- Body-touching and hand-feeding (every day),
- 10 min chair restraint (twice a week),
- Water gavage (twice a week)
- Blood sampling and ECG recordings (every month)

Is 6 month acclimatisation period sufficient?

- Cardiac parameters
- Haematology
- Biochemistry

Repeatability - Acclimatisation



Repeatability - Acclimatisation

Blood parameter	Change over 6 mo	
	Mean value	SD
WBC		
RBC		
PLT	↓	
HGB		
HCT		↑
ALP	↓	↓
CRE	↑	↑
T-CHO	↑	↑
PL		↑
ALB		
GLU		
Na	↓	



Hassimoto et al 2004

Key:

Males & females differ

Males & females decrease

Males & females increase

RESTRAINT – a welfare problem, a science quality problem

Parameter	Change	Author
Heart rate	↑	Line et al 1991; Schnell & Wood 1993; Hassimoto & Herada 2003; Jenkins et al 2008; Kelly et al in prep
Readability/Quality of ECG trace	↓	Kelly et al in prep
Blood pressure	↑	Golub and Anderson 1986; Schnell and Wood 1993; Schmelting et al 2008; Hassimoto & Herada 2003
Respiration rate	↑	Berendt & Williams 1971
Blood – haematology*	↑ ↓	Loomis, Henrickson & Anderson 1980; Hassimoto et al 2004
Blood – biochemistry*	↑ ↓	Landi et al 1990; Hassimoto et al 2004

* Individual parameters vary

Telemetry

- Reduces research animal stress from restraint, and improves quality of data.
- Interplay 2Rs (Reduction and Refinement) and opposing effects within Refinement.
- May be +ve Refinement, +ve Reduction.

- Not feasible for all research animals
 - Surgery
 - Expense
 - Time

CHANGING RESTRAINT - to improve welfare and science

Refinement	Parameter change	Author
Socialisation with care staff	↓ Fearful behaviour towards care staff ↓ Blood pressure	Clay et al 2009 Tasker et al in prep
Restraint technique	↓ HR ↑ Trace quality	Kelly et al in prep
Habituation to restraint	↓ Blood pressure ↓ Variation	Schmelting et al 2008 Tasker et al in prep
Training (PRT)	↓ Fearful behaviour & stress-related behaviours ↓ Self-injurious behaviour ↓ Plasma cortisol ↓ Lymphocytes ↑ Neutrophils	Clay et al 2009 Bassett et al 2003 Baker et al 2003 Reinhardt 1992 Bentson et al 2003; Koban et al 2005
	↑ Cooperation	Reinhardt & Cowley 1992

Bass et al (2009)

- Assessment of the potential for cardiotoxicity, including arrhythmias, is paramount to assure appropriate monitoring for human safety.
- Sensitivity of identifying cardiac risk (arrhythmias and ventricular repolarization as seen in test article-related changes in the QT and QTc intervals) is significantly improved in non-restrained versus restrained cynomolgus macaques.

Conclusions

Improved positive socialisation with humans, and improved restraint impacts on:

Physical health

Closer to normal, stable - baseline measures

Behaviour

-  Fear responses to care staff, during handling & CV data collection

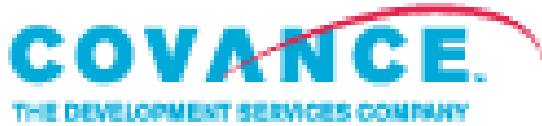
Cardiovascular (HR & BP)

- Lower baseline values
 - Greater accuracy to quantify drug-induced changes
- Fewer trace artefacts e.g. movement, vocalisation, tension
 - Cleaner traces, easier to determine arrhythmias
- Faster data collection
- Better repeatability (less variation). 5 x BP measures

**Enhanced socialisation → better welfare → better scientific output
+ improved restraint & PRT**

Acknowledgments

Meeting organisers and many helpful colleagues



Providers of images

Funders

BBSRC

Covance Laboratories Ltd, Harrogate



Just launched: <http://marmosetcare.com/>

COMMON MARMOSET CARE

HOME

IN THE WILD

CARE IN CAPTIVITY

UNDERSTANDING BEHAVIOUR

USEFUL LINKS



Welcome



**An interactive site with information on how best to care for common marmosets in captivity
– for private owners, researchers, zoo and laboratory professionals**



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Primate Society of Great Britain



National Centre for the Replacement, Refinement
and Reduction of Animals in Research