



Multicentre Preclinical Animal Research Team

Multi-PART

Work Package 3 – Experimental Design

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WP 3

Purpose of WP 3 – Experimental design

- to develop strategies to maximise both the internal and external validity of the studies performed within Multi-PART or other multi-centre research consortia



WP 3

Topics to discuss

- Database issues
- Experimental design issues



WP 3 – Database issues

Experimental variables

Drug under investigation		Intervention under investigation	text
	drug/vehicle/saline		
	Weight		
	Age		
Strain		Strain	text
Sex		Sex	text

Study descriptors

Filter Top		Filter Top	Yes/No
Food Deprivation		Food Deprivation	Yes/No
Food Deprivation Schedule		Food Deprivation Schedule	Text
Handling		Handling	Text
Health Check		Health Checks	Yes/No
Health Check Frequency		Health Check Frequency	Number
Lid Brand		Lid Distributor	Text
Lid Type		Lid Type	Text



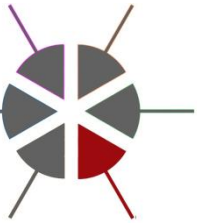
WP 3 – Database issues

Variables listed in the database

Acclimatization Period		Acclimatization Period	Number
Acoustic Background		Acoustic Background	Text
Additional Species in Lab		Additional Species in Lab	Yes/No
Additional Species in Building		Additional Species in Building	Yes/No
Bedding Material		Bedding Type	Text
Cage Brand		Cage Distributor	Text
Cage Type		Cage Type	Text
Cage Size		Cage Size	Number

Variables not listed in the database

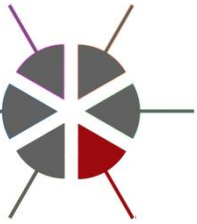
Pets held by care takers		Pets held by care takers	Text
Color of lab walls		Color of lab walls	Text
Lab coat colour		Lab coat colour	Text
Water bottle brand, size, ...		Water bottle brand, size, ...	Text
Cage rack material, height, ...		Cage rack material, height, ...	Text
...	



WP 3 – Database issues

The listing fallacy (Würbel 2002 Genes Brain Behav)

- There exist many more variables than are listed
- Selection of listed variables is arbitrary
- Many variables are unknown and unlistable
- Listed variables are no more likely to explain results than unlisted variables



WP 3 – Database issues

The listing fallacy (Würbel 2002 Genes Brain Behav)

“Such lists may in fact divert attention away from highly relevant factors that were not considered, were considered to be irrelevant, were too difficult to assess, or simply cannot be listed.”

- Therefore, such lists may induce interpretation bias

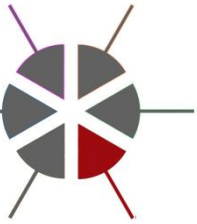


WP 3 – Database issues

What should be listed?

- Experimental design variables
- Descriptors to be reported in the papers' methods section
- Variables relevant for meta-analyses

However: All “variables” not varied within studies are confounded with “study” (i.e. with all other fixed aspects – listed or unlisted – of that study)



WP 3 – Database issues

Revision of database

Include variables only if they are:

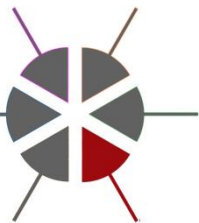
- Potential experimental design variables
- Relevant descriptors of the study method
- Variables relevant for meta-analyses



WP 3 – Experimental design issues

Main factors of the experimental design

- **Surgery** (surgery, sham surgery, no surgery)
- **Intervention** (drug, saline, vehicle)
- **Stroke Model** (intraluminal filament, distal MCAO electrocoagulation, ...)
- **Animal Species** (rat, mouse, macaque,)
- **Lab** (Macrae, Dirnagl, Planas,)
- **Conditions** (standardised or heterogenised)
(**Animals** (strain, age, sex, comorbidities, ...), **Housing & Care** (group size, cage size, enrichment, ...), **Procedures** (test protocol))



WP 3 – Experimental design issues

Template for the experimental design

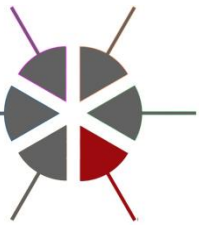
Surgery	Intervention	Stroke Model	Animal Species	Lab	Conditions
Yes	drug	Model 1	rat	Macrae	standardised
Sham	vehicle	Model 2	mouse	Dirnagl	heterogenised
No	saline	Model 3	macaque	Planas	
...	...	Model 4	...	Vivien	
		Model 5		Howells	
		Model 6		Abc	
			Def	
				Ghi	
				...	



WP 3 – Experimental design issues

Experimental design 1: Multi-lab study

Surgery	Intervention	Stroke Model	Animal Species	Lab	Conditions
Yes	drug	Model 1	rat	Macrae	standardised
Sham	vehicle	Model 2	mouse	Dirnagl	heterogenised
No	saline	Model 3	macaque	Planas	
		Model 4		Vivien	
		Model 5		Howells	
		Model 6		Abc	
				Def	
				Ghi	



WP 3 – Experimental design issues

Experimental design 2: Multi-model study

Surgery	Intervention	Stroke Model	Animal Species	Lab	Conditions
Yes	drug	Model 1	rat	Macrae	standardised
Sham	vehicle	Model 2	mouse	Dirnagl	heterogenised
No	saline	Model 3	macaque	Planas	
		Model 4		Vivien	
		Model 5		Howells	
		Model 6		Abc	
				Def	
				Ghi	



WP 3 – Experimental design issues

Experimental design 3: Multi-lab-multi-model study

Surgery	Intervention	Stroke Model	Animal Species	Lab	Conditions
Yes	drug	Model 1	rat	Macrae	standardised heterogenised
Sham	vehicle	Model 2	mouse	Dirnagl	
No	saline	Model 3	rat	Planas	
		Model 4	macaque	Vivien	
		Model 5	mouse	Howells	
		Model 6	rat	Abc Def Ghi	



WP 3 – Experimental design issues

Optimise experimental design

- Use existing data to analyse different designs
- Model trade-offs between variation of different factors
- Model trade-offs between sample size and external validity



WP 3 – Experimental Design

Deliverables

- **Month 12:** Preliminary solutions for randomisation and blinding for further discussion and refinement
- **Month 18:** Preliminary solutions for sample size calculation and systematic variation for further discussion and refinement
- **Month 24:** Final report describing the most appropriate design of future preclinical trials (randomisation, blinding, sample size calculations, systematic variation)