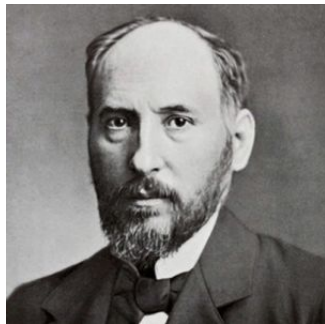# Estimating the contribution of new neurons to behaviour using Bayesian graphical models

Stanley E. Lazic, PhD

3 Sept 2015
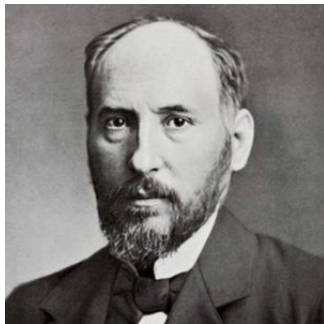
Adult hippocampal neurogenesis

"Once the development was ended, the founts of growth and regeneration of the axons and dendrites dried up irrevocably. Everything may die, nothing may be regenerated."
–*S. Ramón y Cajal*

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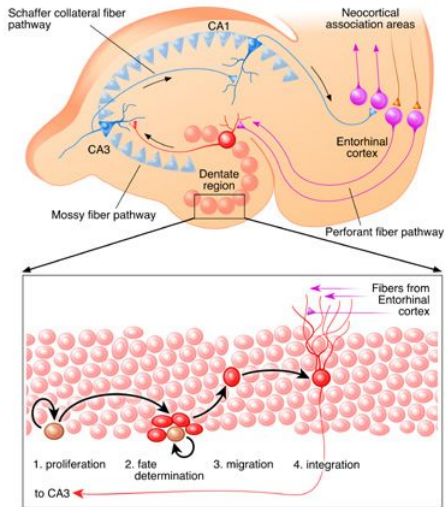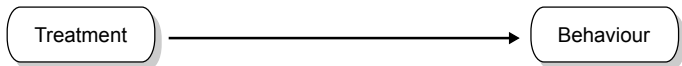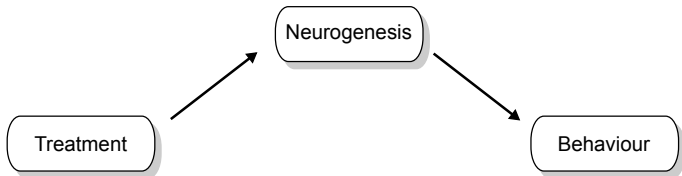–*S. Ramón y Cajal*

http://www4.utsouthwestern.edu/HsiehLab/

Graphical models
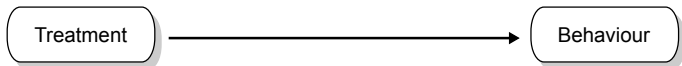
Graphical models

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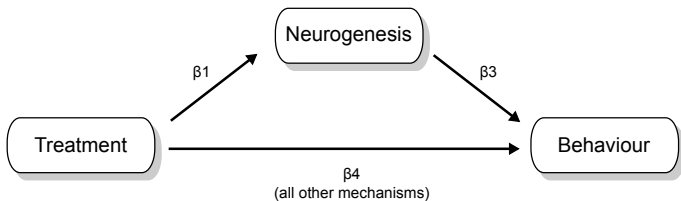
Are other mechanisms at work?

Affects neurogenesis	Off-target effects
Exercise	Spine density
	Synaptic proteins
	Glutamate receptors
Stress/Corticosterone	Dendrites/spines
	GR/MR expression
Environmental Enrichment	Dendrites/spines
	BDNF
MAM	General health
	Locomotor activity
Imipramine	Dendrites/synapses
Fluoxetine	Dendrites/spines
Irradiation	NMDA receptors
	Inflammation/vasculature
	DNA damage
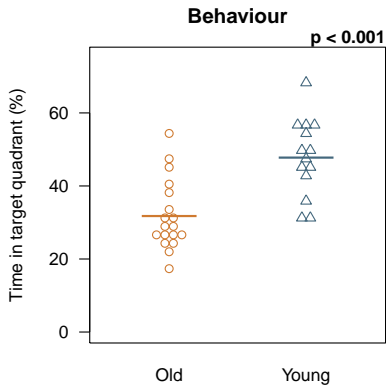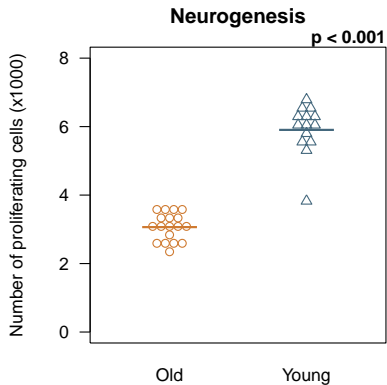
Age and spatial memory

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Hassler & Thadewald (2003) Nonsensical and biased correlation due to pooling heterogeneous samples. *J R Stat Soc: Series D* 52:367.
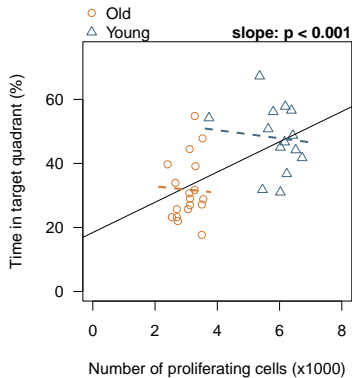
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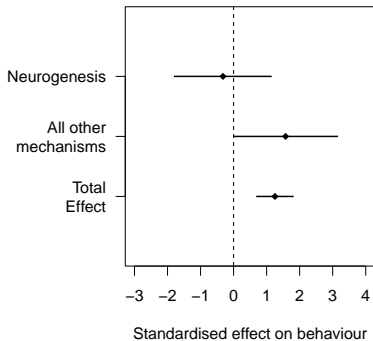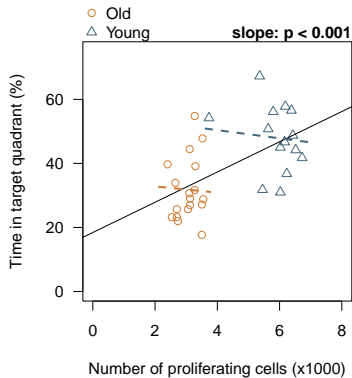
Systematic review and meta-analysis
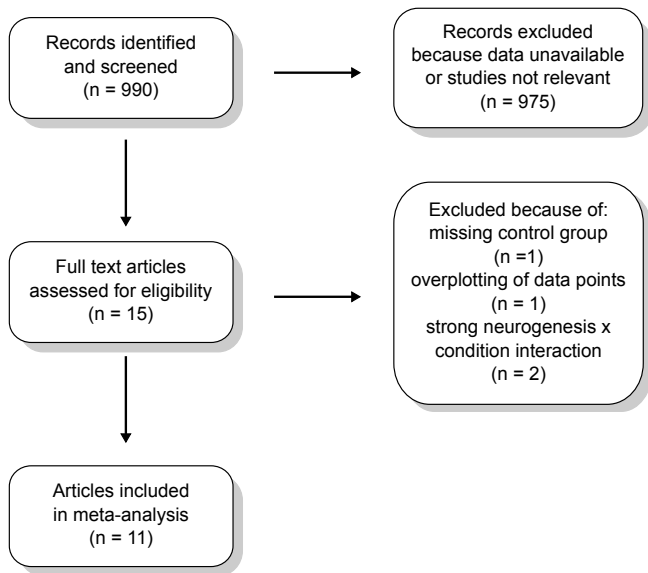
Systematic review and meta-analysis

PMID	Species	Condition	Behavioural test
24582851	Rat (Wistar)	CB1 agonist	MWM
20133882	Mouse (C57BL/6)	Exercise	Pattern separation
23567812	Rat (Wistar)	Ethanol	OF/Locomotion
19452518	Mouse (C57BL/6)	Exercise	OF/ LDB
11005874	Rat (SD)	Stress	MWM
20875841	Mouse (C57BL/6)	Enrichment	FST
12640670	Rat (F344)	Age	MWM
19100662	Rat (DA)	Age	MWM (latency)
17587610	Canine	Antiox + Enrich	Reversal + spatial errors
22795793	Rat (F344)	Enrichment	MWM
23078985	Rat (F344)	Exercise	MWM
23643842	Mouse (C57BL/6)	Down's + Choline	MWM

Meta-analysis: effect of other mechanisms

PMID	Species	Condition	Test	Histology	n	
24582851	Rat (Wistar)	CB1 agonist	MWM	DCX	9	
20133882	Mouse (C57BL/6)	Exercise	Pat sep	BrdU/NeuN	20	
23567812	Rat (Wistar)	Ethanol	OF (72 days)	DCX	17	
23567812	Rat (Wistar)	Ethanol	OF (114 days)	DCX	23	
11005874	Rat (SD)	Stress	MWM	BrdU	10	
20875841	Mouse (C57BL/6)	Enrichment	FST	BrdU	19	
12640670	Rat (F344)	Age	MWM	BrdU	32	
19100662	Rat (DA)	Age	MWM	DCX	16	
17587610	Canine	Antiox+Enrich	B/W	BrdU/DCX	21	
22795793	Rat (F344)	Enrichment	MWM	Multiple	16	
23078985	Rat (F344)	Exercise	MWM	Multiple	11	
23643842	Mouse (C57BL/6)	Down's + Choline	MWM	DCX	21	

Overall estimate:
(p < 0.0001)

Standardised effect of other mechanisms

Meta-analysis: effect of neurogenesis

PMID	Species	Condition	Test	Histology	n
24582851	Rat (Wistar)	CB1 agonist	MWM	DCX	9
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Overall estimate:
(p = 0.128)

Standardised effect of neurogenesis

A more complex experiment

Condition	Neurogenesis	Behaviour
Control	Baseline	Baseline

A more complex experiment

Condition	Neurogenesis	Behaviour
Control	Baseline	Baseline
Exercise	↑	↑

A more complex experiment

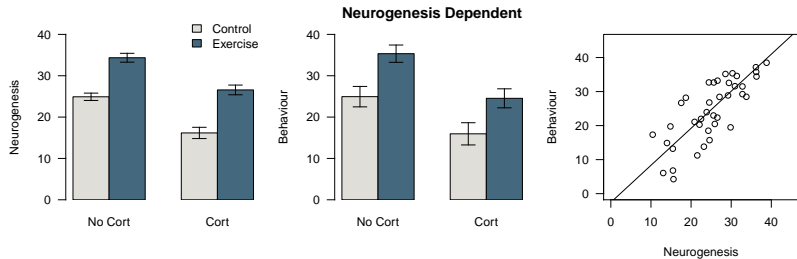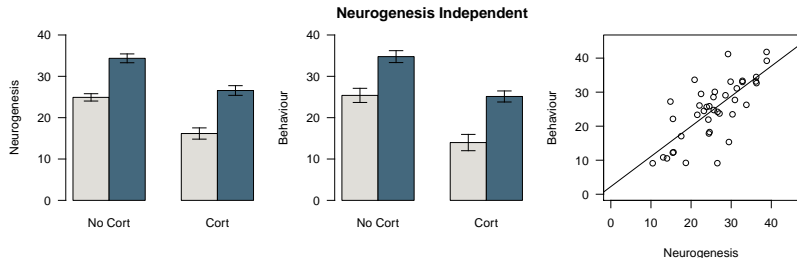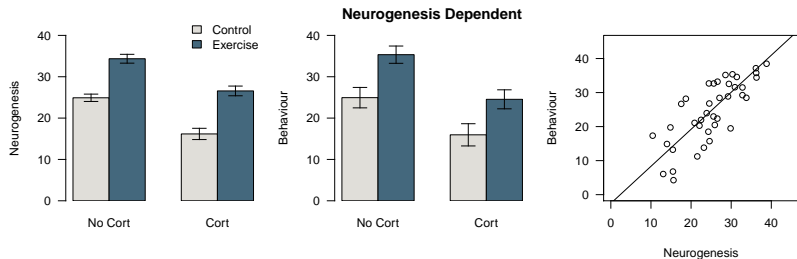| Condition	Neurogenesis	Behaviour
Control	Baseline	Baseline
Exercise	↑	↑
Exercise + CORT	↔	↔

A more complex experiment: simulation study
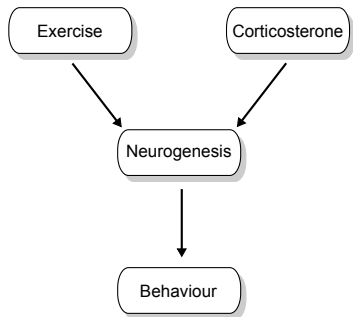
A more complex experiment: simulation study
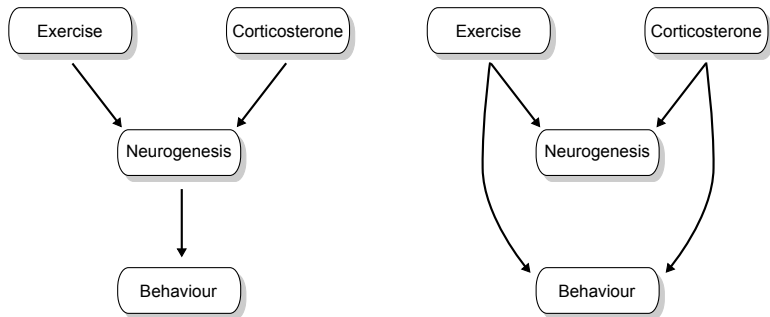
More complex experiments

More complex experiments

Conclusions

- Graphical models are useful to describe and test relationships in the data.
- Most studies provide no evidence for a causal neurogenesis–behaviour relationship because of
  1. inferential leaps that are unsupported by the data, and
  2. other mechanisms that are known to exist and can explain the results.
- Data underlying conclusions are unavailable.
- Neurogenesis has limited involvement in behaviour.

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Acknowledgements

Prof Peter Gass & Dr Johannes Fuss
Central Institute of Mental Health, Mannheim, Germany

References

1) **Lazic SE**, Fuss J, Gass P (2014). Quantifying the behavioural relevance of hippocampal neurogenesis. *PLoS ONE* 9(11):e113855.

2) **Lazic SE** (2012). Using causal models to distinguish between neurogenesis-dependent and -independent effects on behaviour. *J R Soc Interface* 9(70):907–917.

3) **Lazic SE** (2010). Relating hippocampal neurogenesis to behavior: the dangers of ignoring confounding variables. *Neurobiology of Aging* 31:2169–2171 (discussion 2172–2175).