

# Ageing at a snail's pace

NDA workshop, London March 2008

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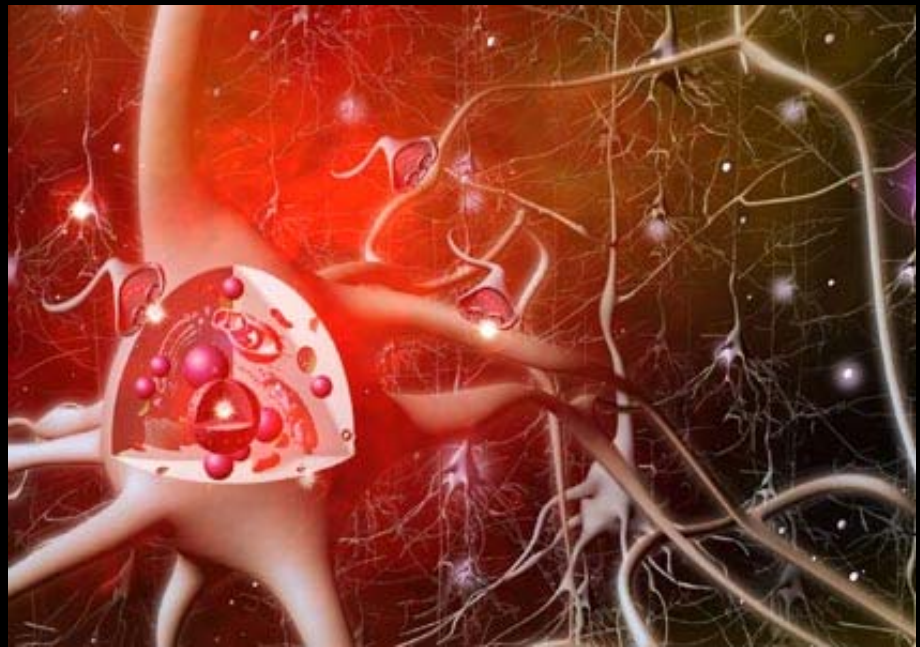
University of Brighton

# What happens in normal brain ageing?

- Alterations in the strength of connections



- Decreases in connectivity

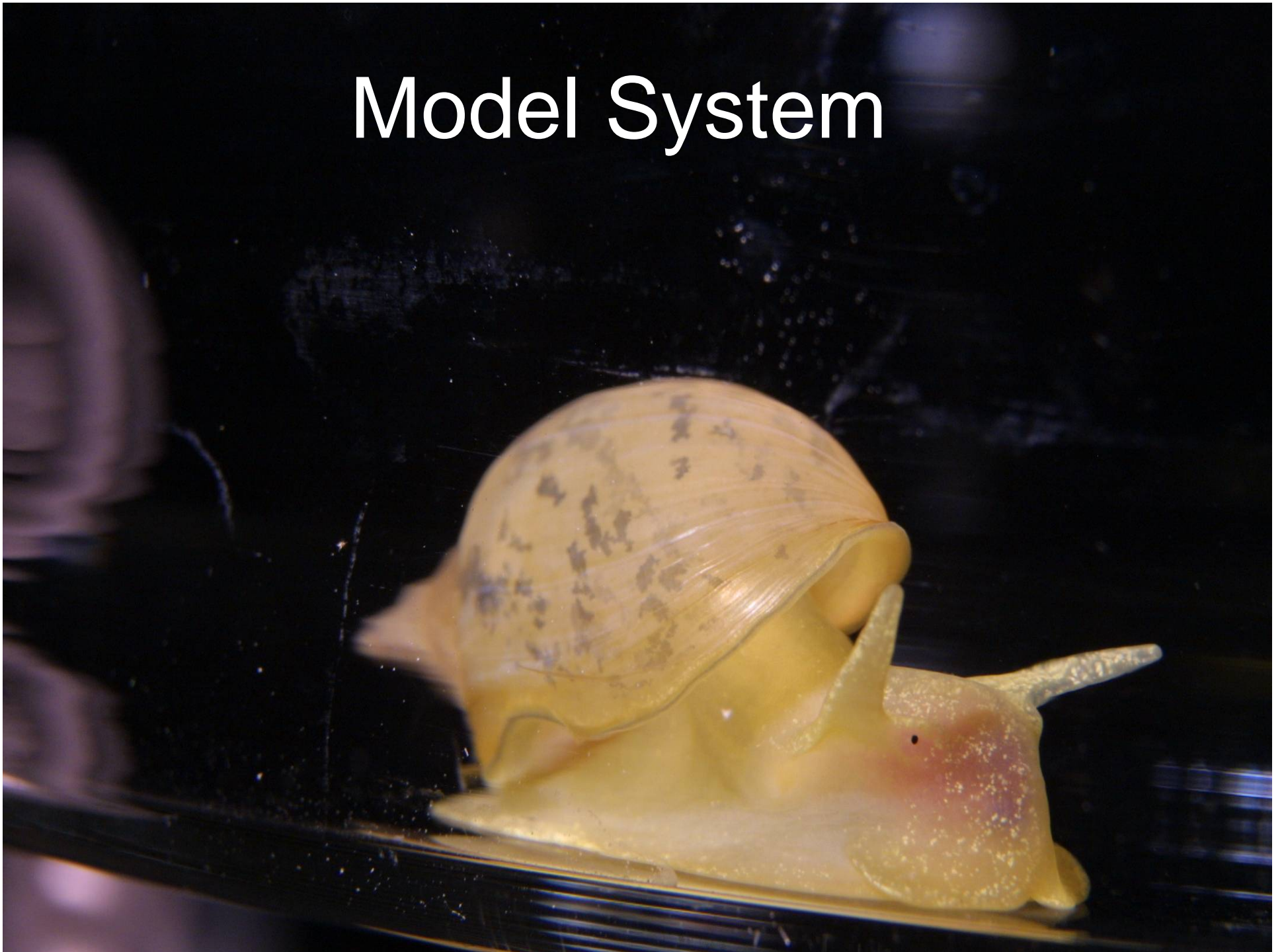


# Potential problems associated with normal brain ageing

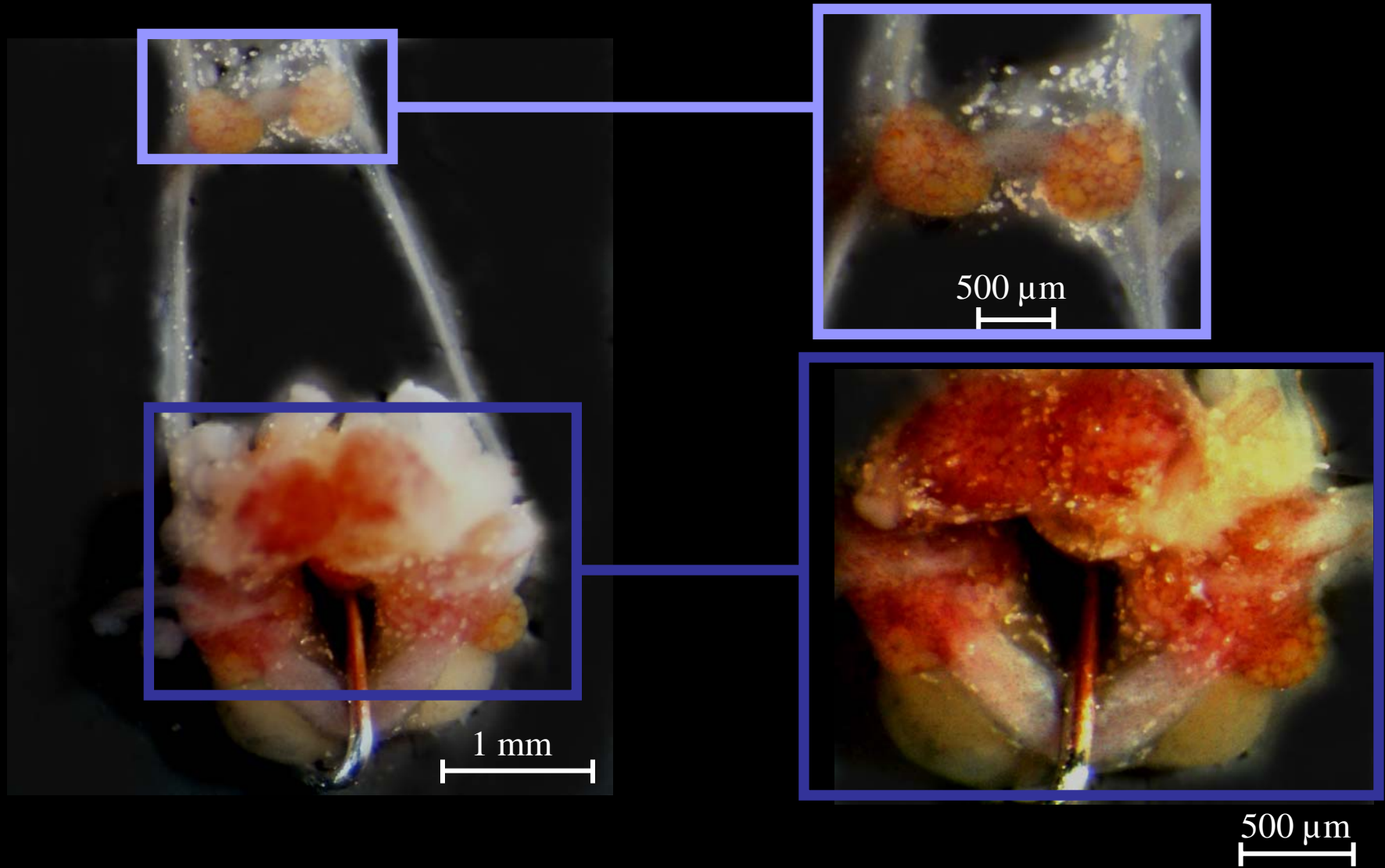
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- Dysphagia
- Impaired cognition

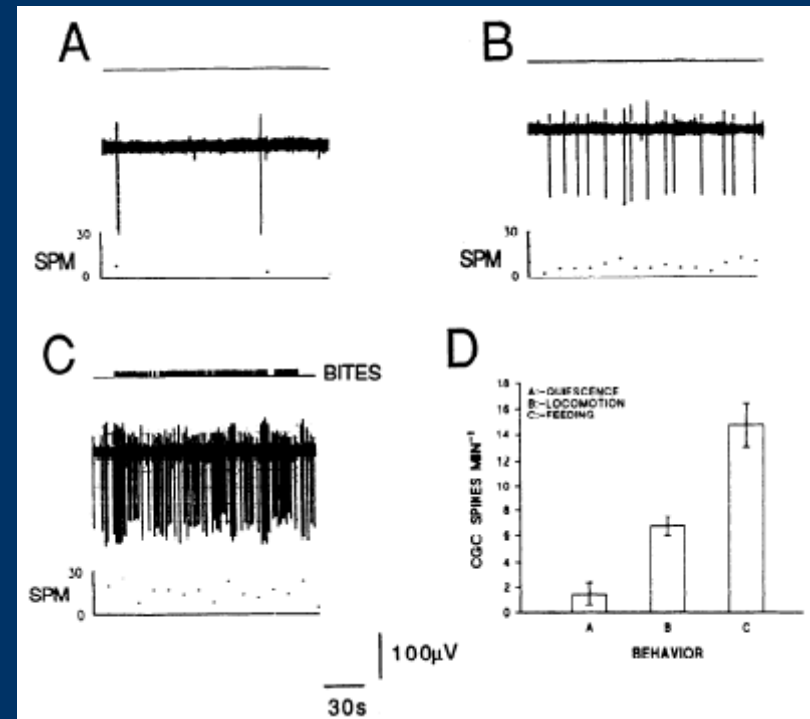
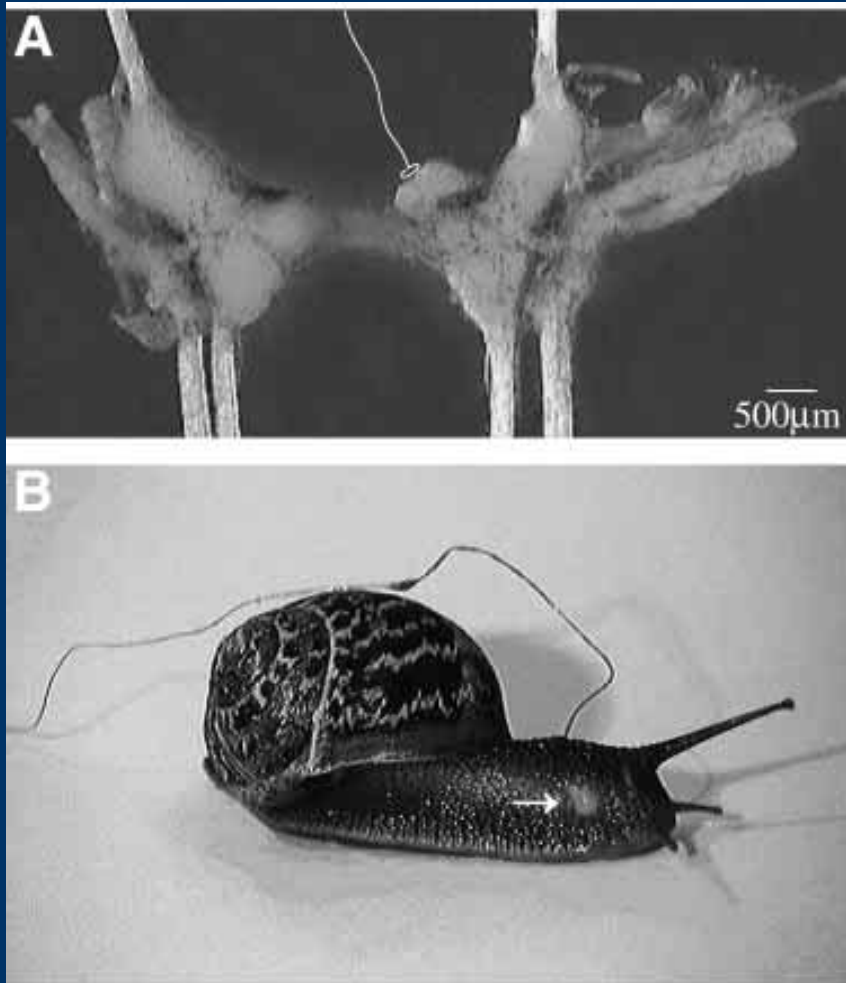
# Model System



# Snail Brain

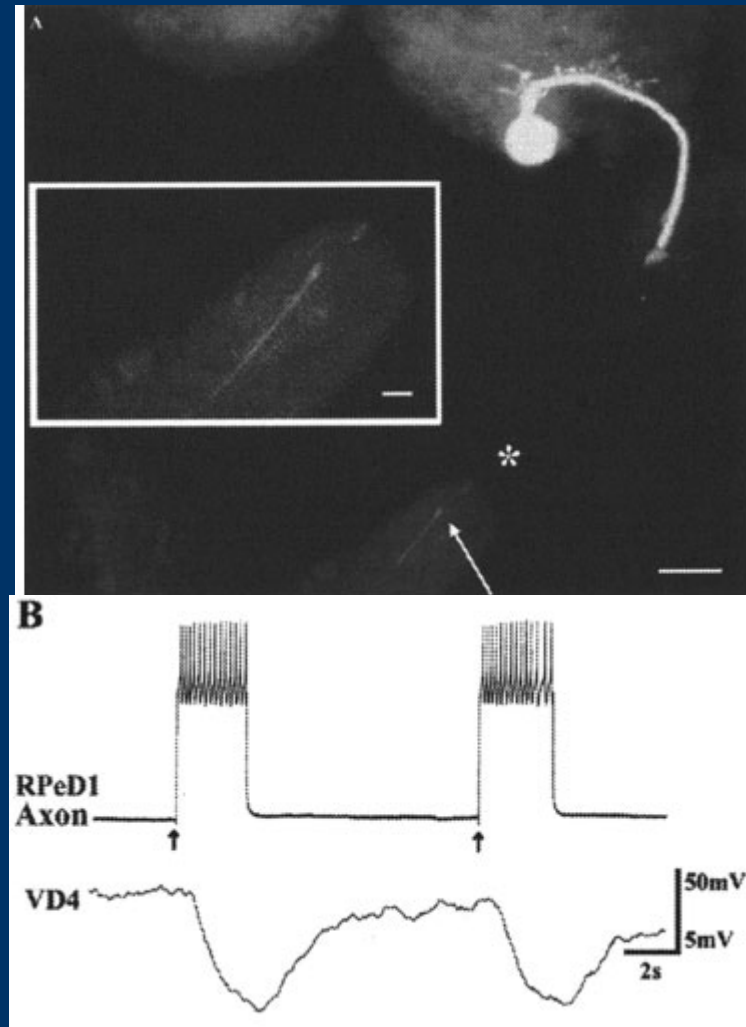
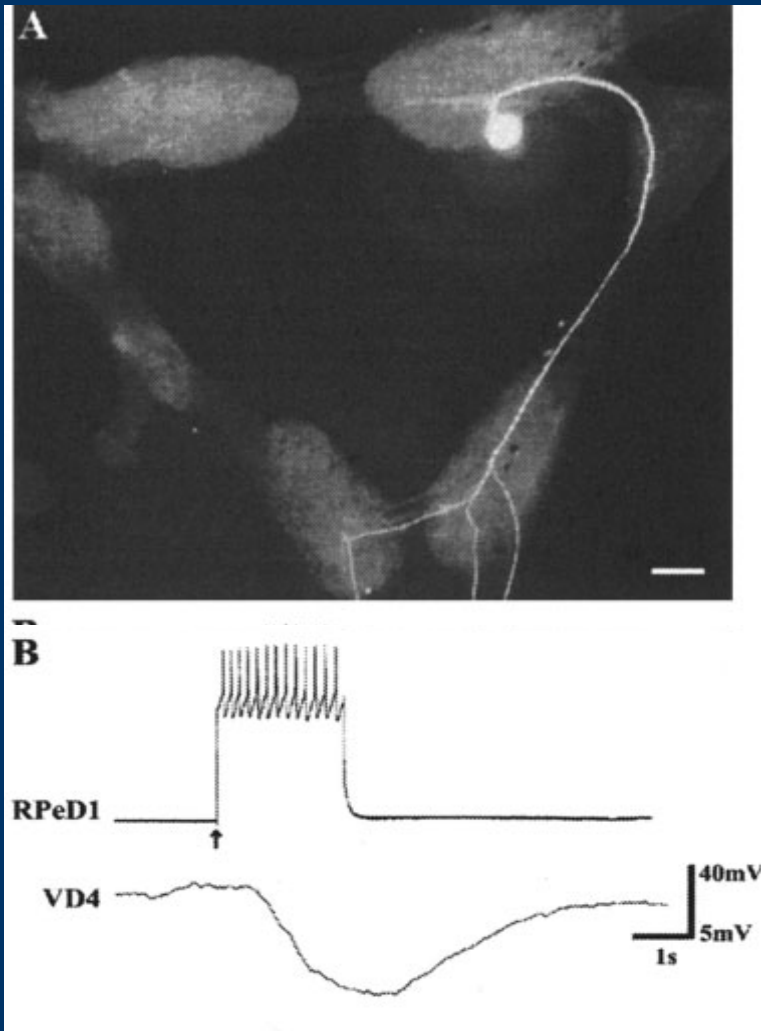


# *In vivo* recordings



Yeoman et al. *J. Neurophysiol.* 1994

# Transplantation of individual neurones is possible



From Lee and Syed, Synapse 2004.

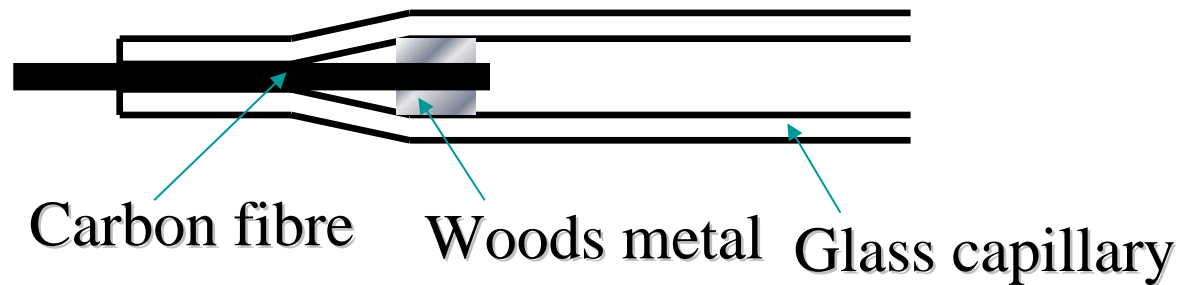
# Patch Clamp Amperometry



- 7  $\mu\text{m}$  carbon fibre electrodes used
- Tip insulated with electrophoretic paint and then cut to expose a disc

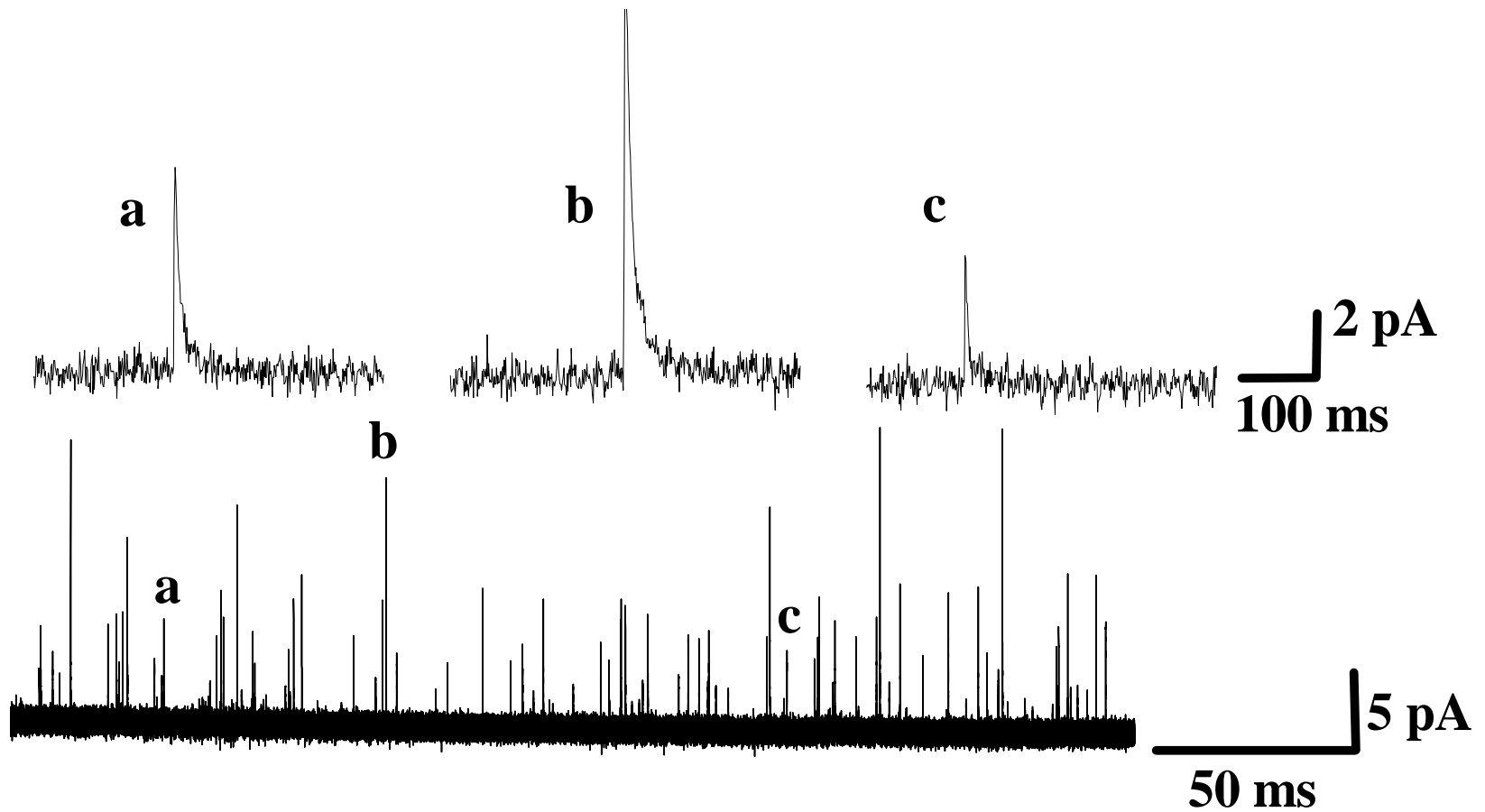


Silver wire

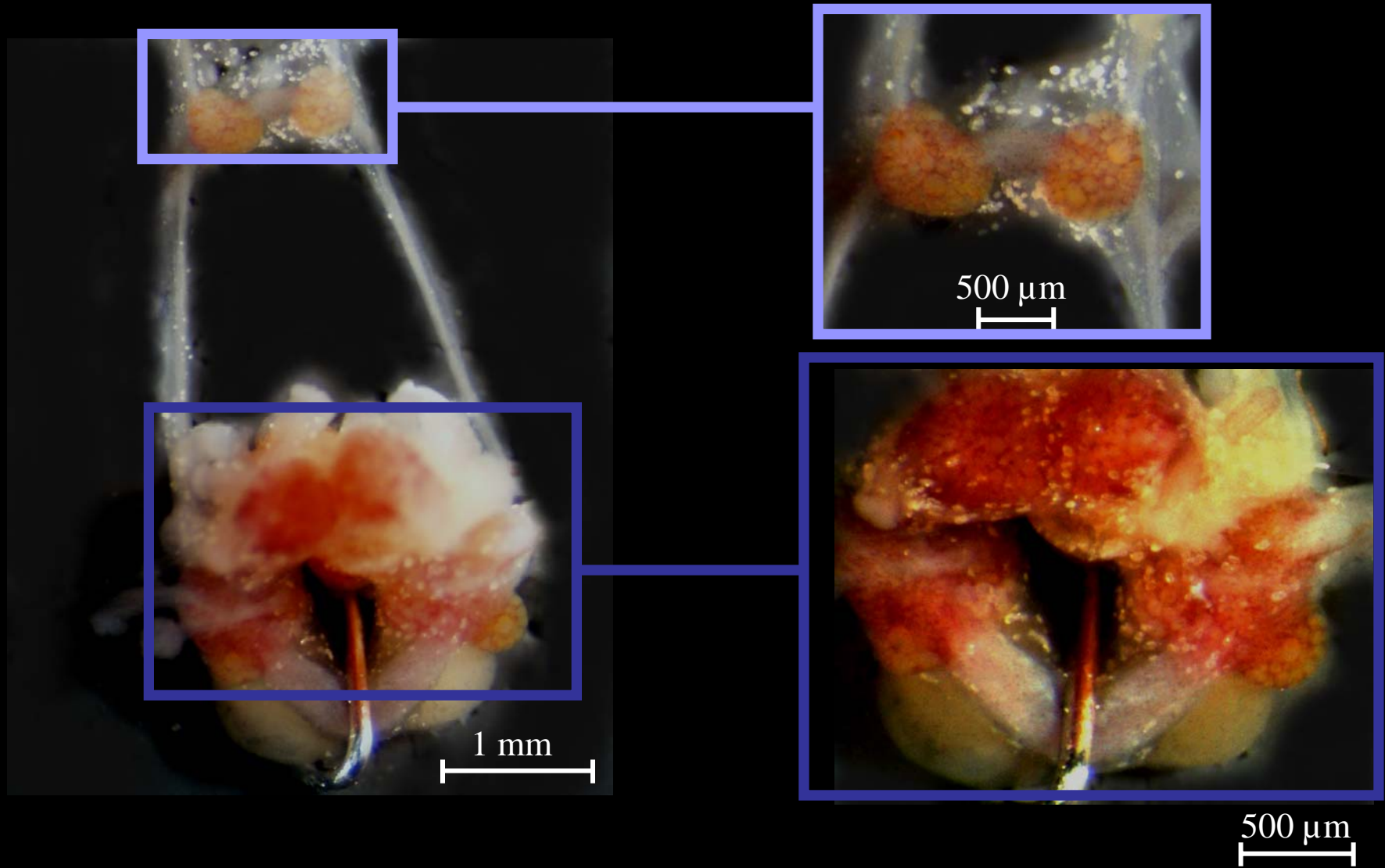


# Quantal Release of serotonin

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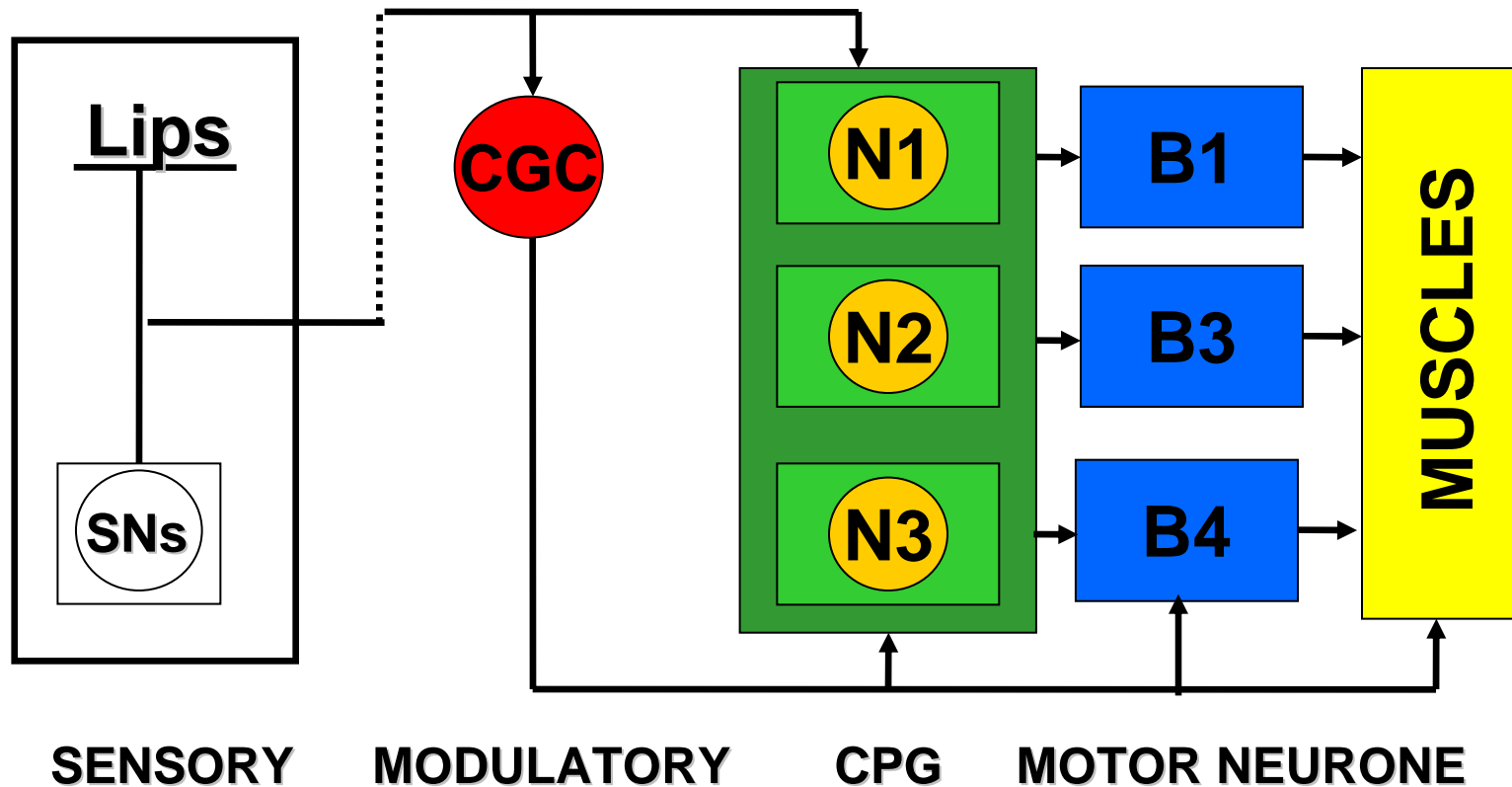


# Snail Brain



# Feeding Network

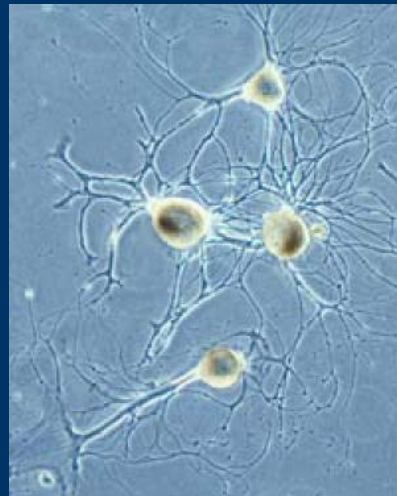
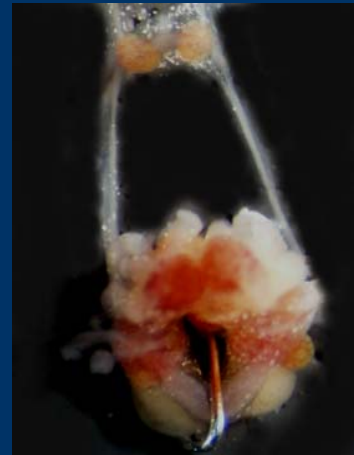
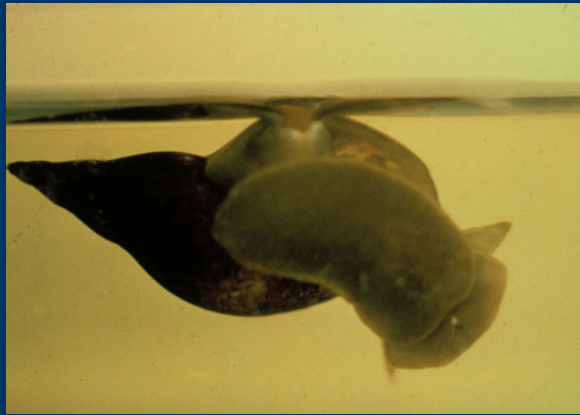
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# Snails offer a unique opportunity to ageing research

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# Do their CNSs show similar changes to those of higher organisms?

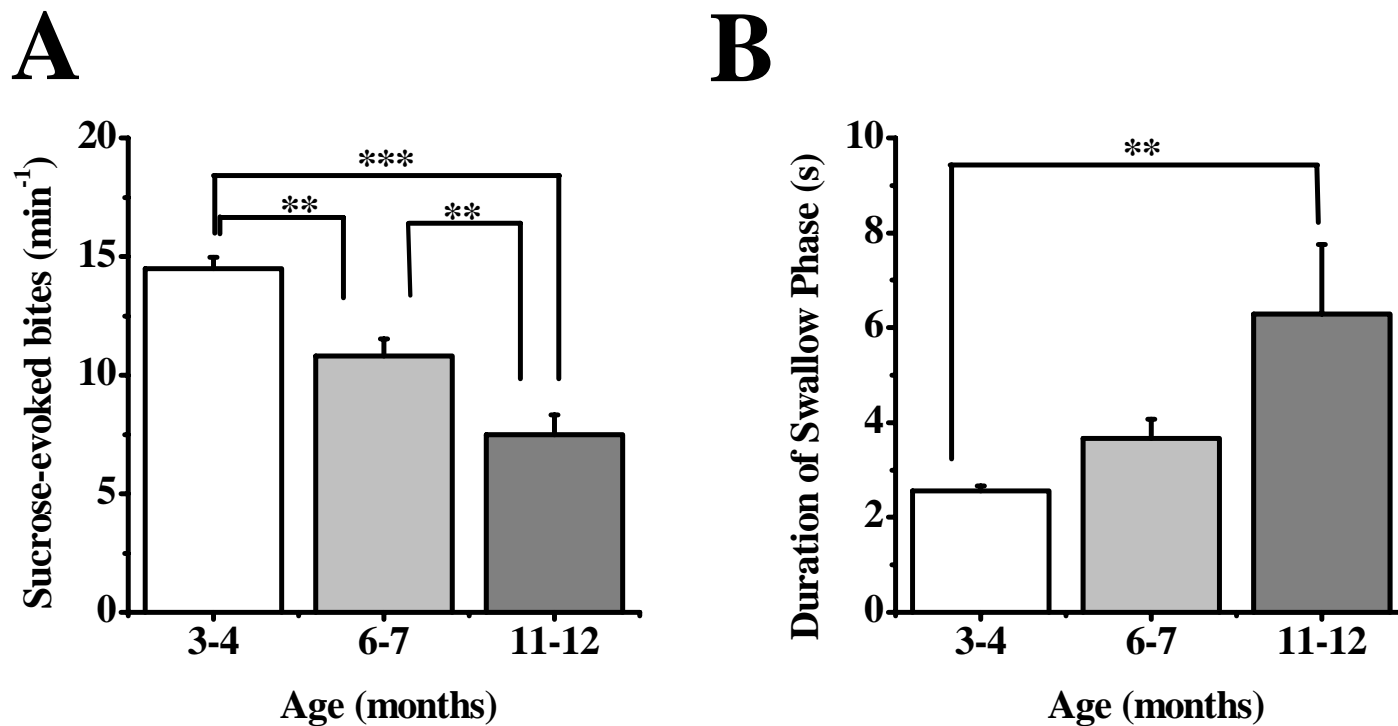
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- Is swallowing impaired in aged snails?
- Do snails suffer from cognitive decline as they age?

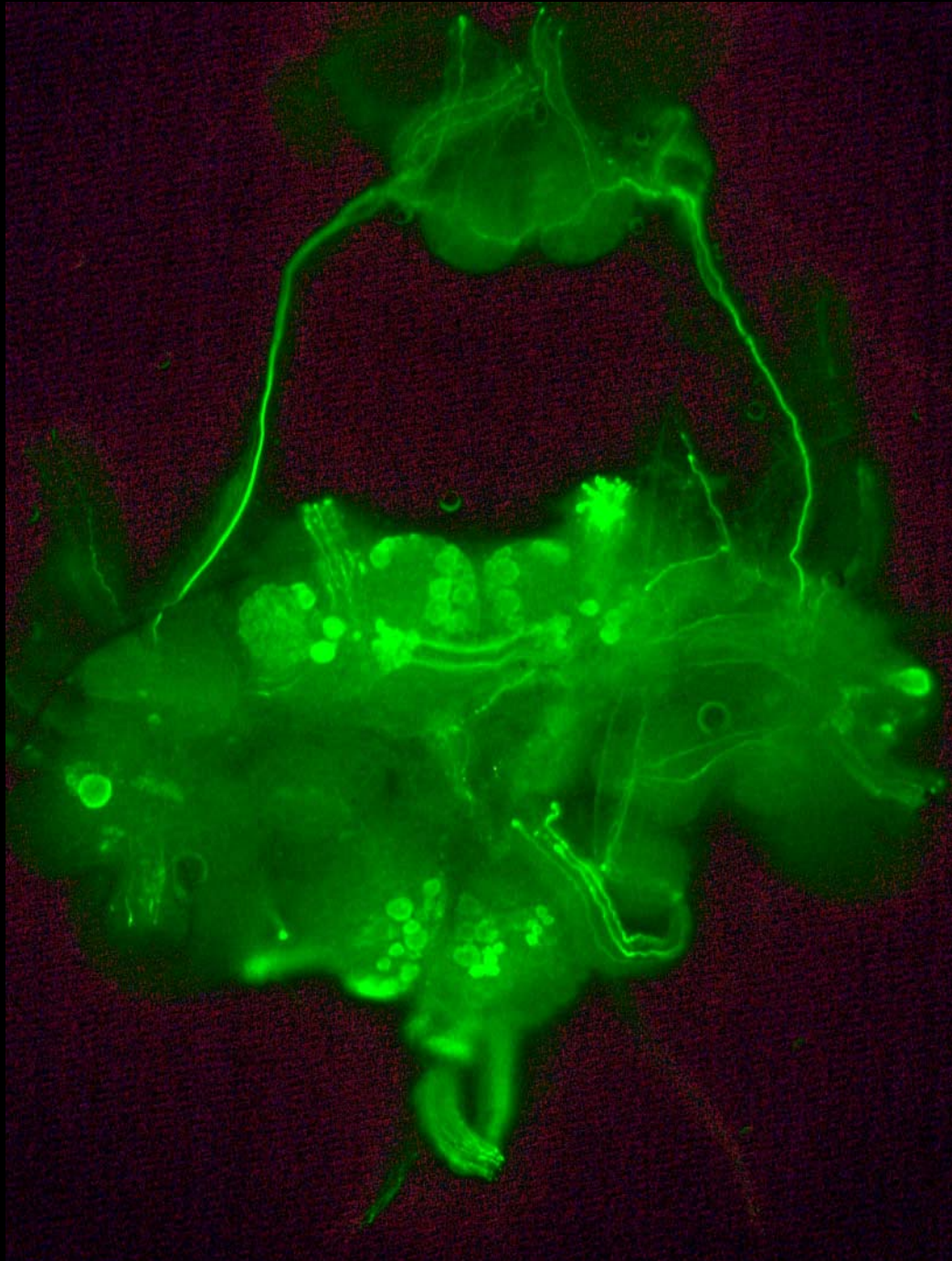
Do snails suffer from age-related decreases in motor function?

# Changes in Short-Term Feeding

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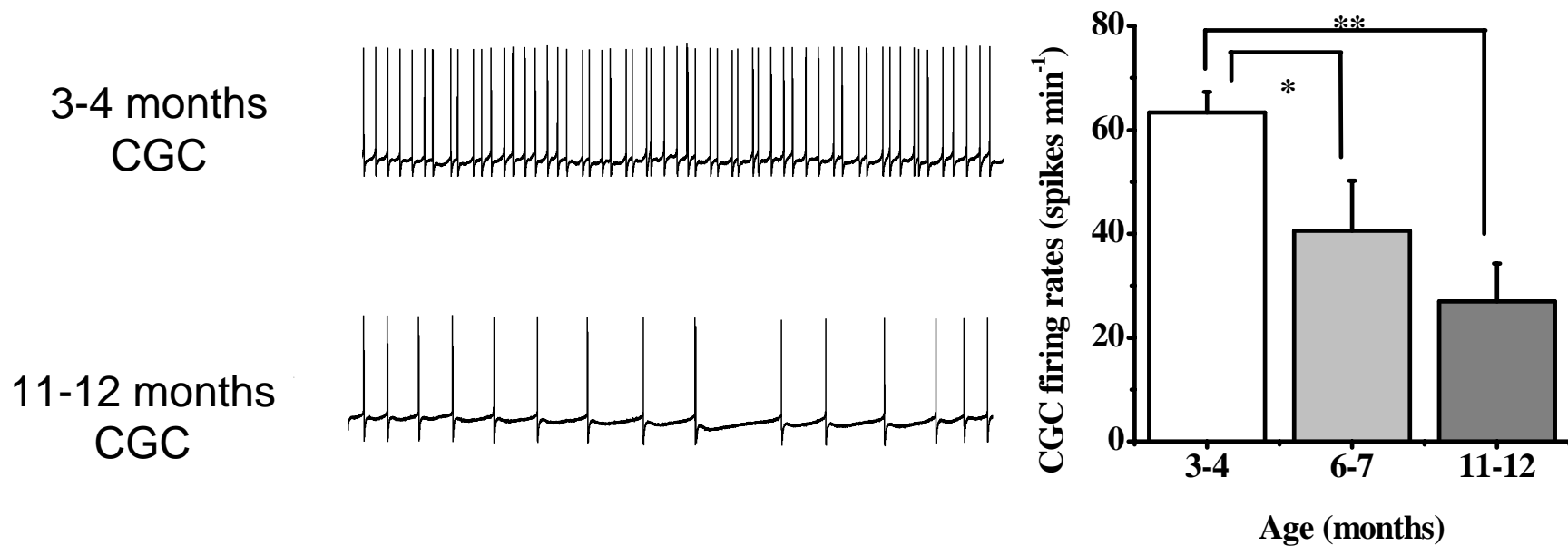


From Arundell, Yeoman et al. 2006, Neurobiology of Aging



# Increasing age decreases cerebral giant cell (CGC) firing rate

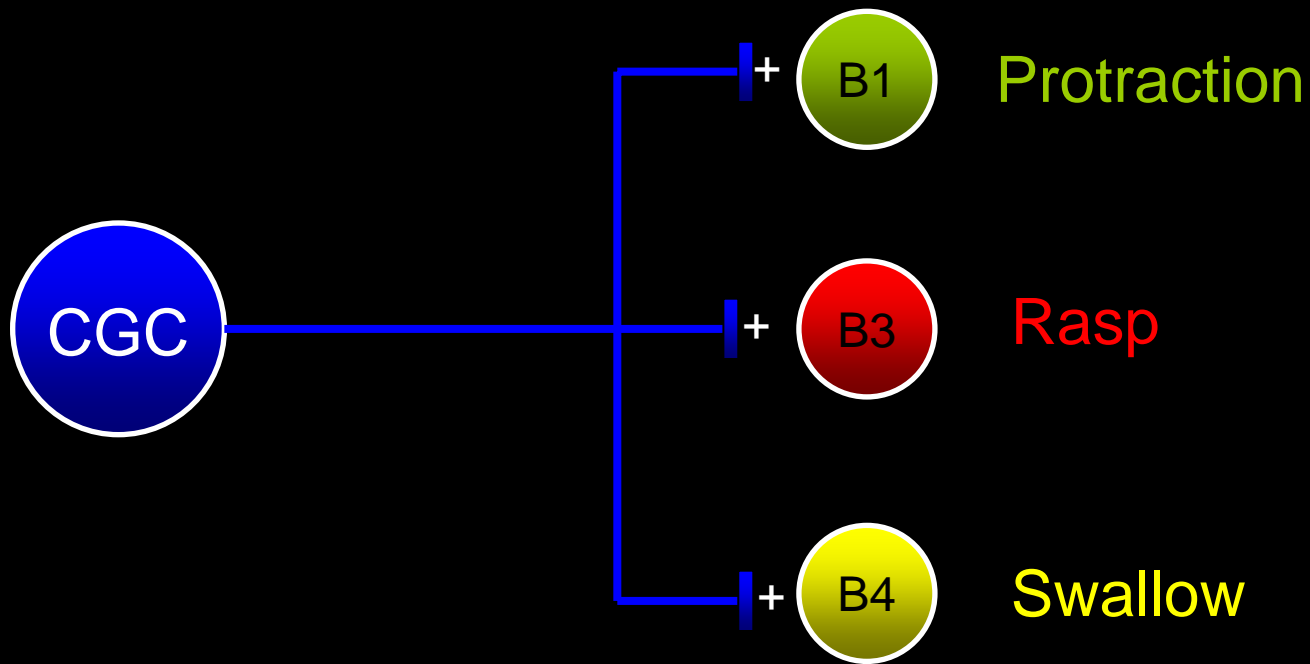
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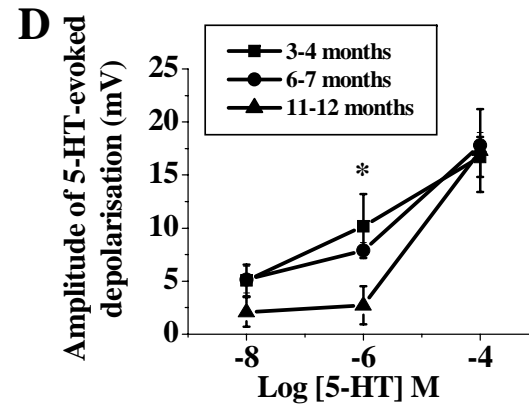
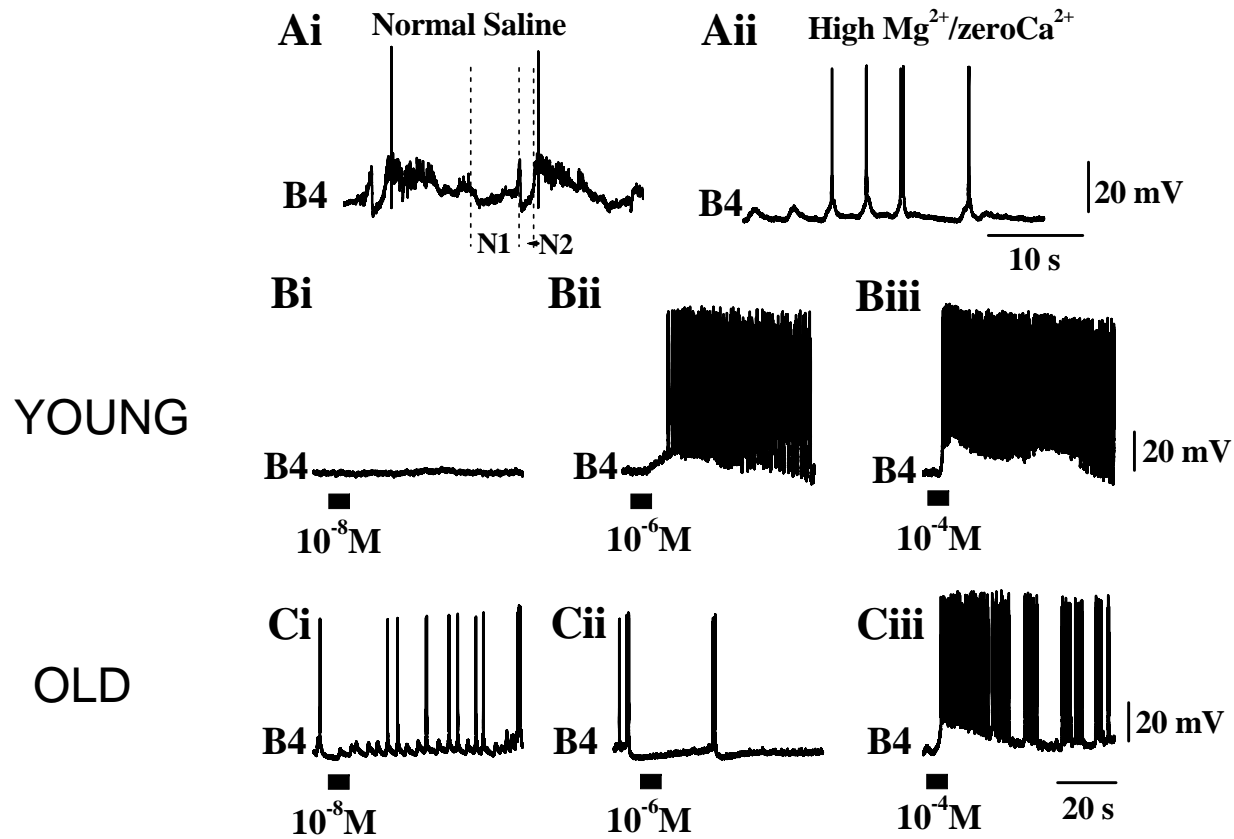


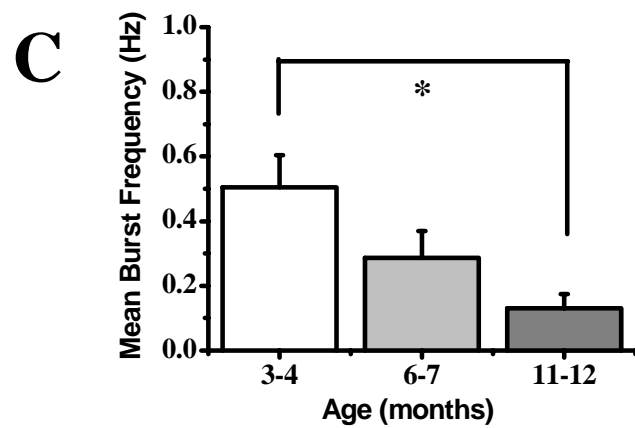
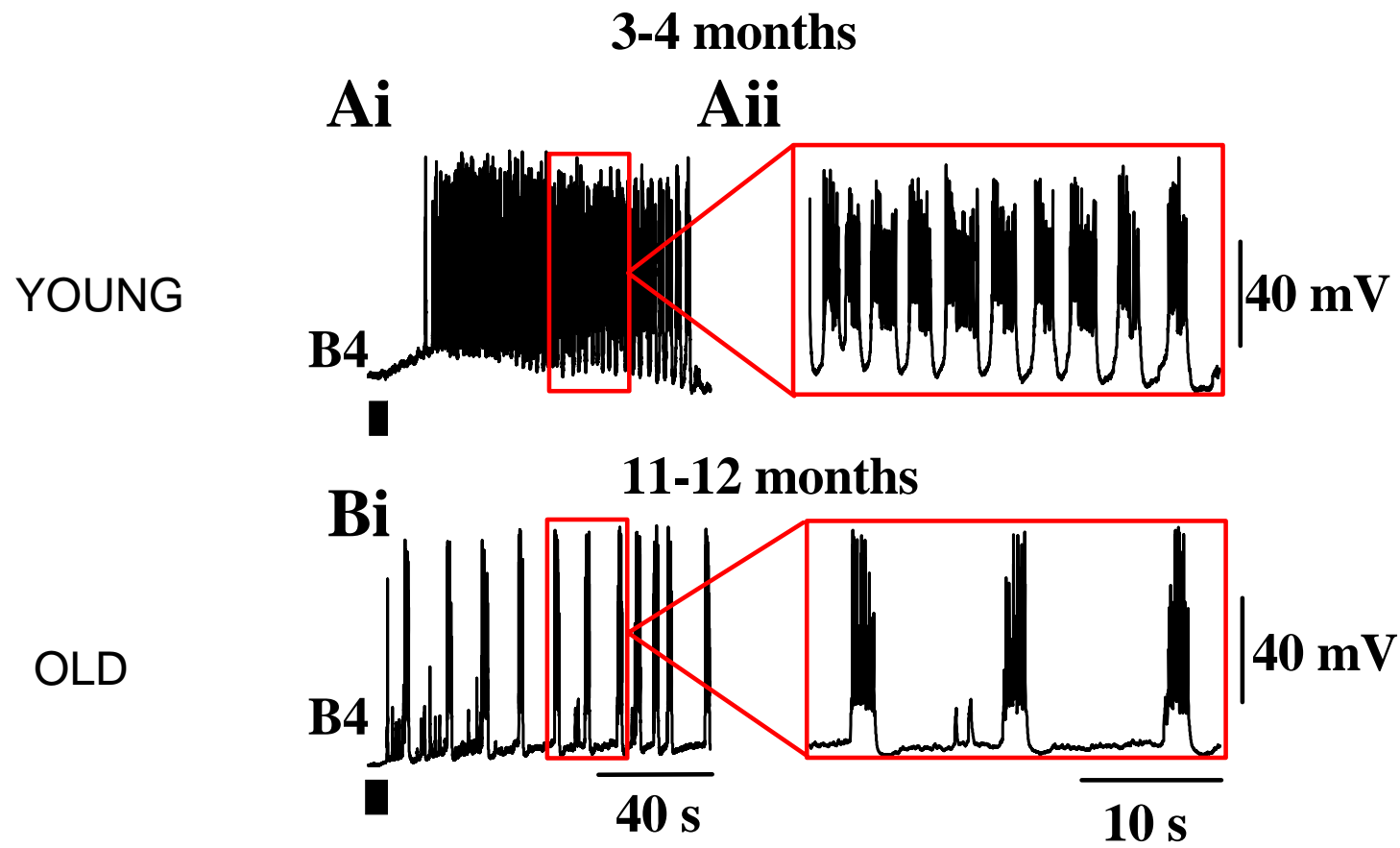
From Patel, Yeoman et al. 2006, Neurobiology of Aging

# Connectivity

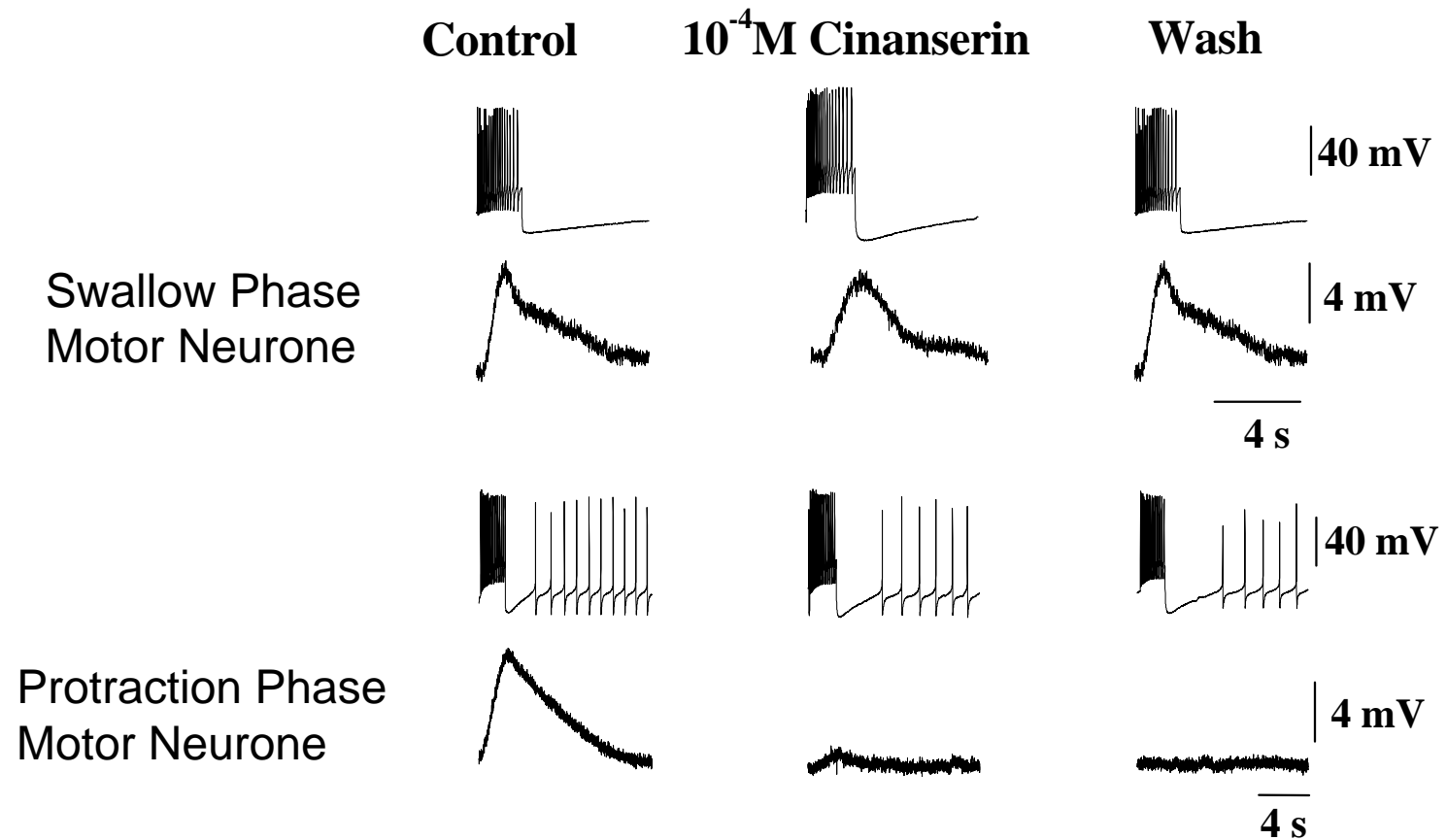
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# The Pharmacology of the Synapses are Different



Yeoman et al. submitted  
J. Neurochem.

# Summary

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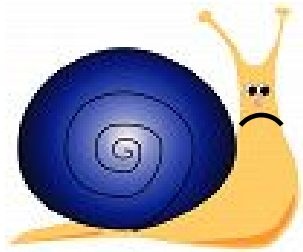
- Differences in the pharmacology of the synapse maybe an important determinant for age sensitivity.
- Unique opportunity to study the mechanisms of brain ageing and to understand why age targets certain connections but not others.

Can snails learn and does ageing  
impair learning and memory  
formation?

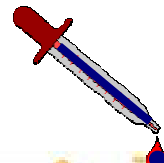
# Snails Can Learn and Remember?

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Day1



No feeding +

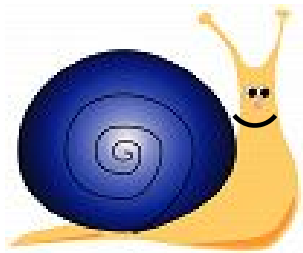
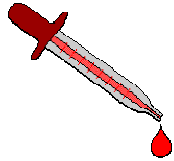


feeding

Amyl Acetate

Sucrose

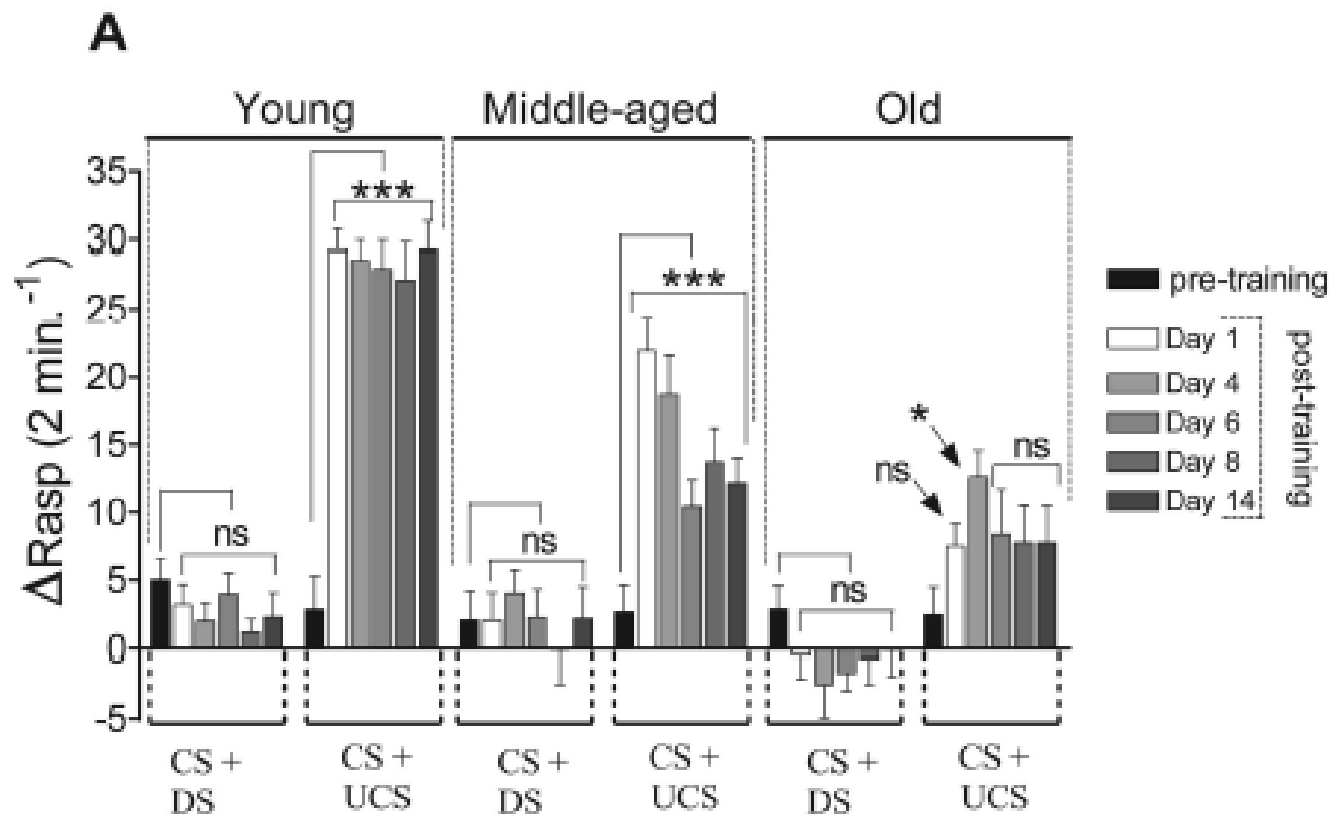
Day2



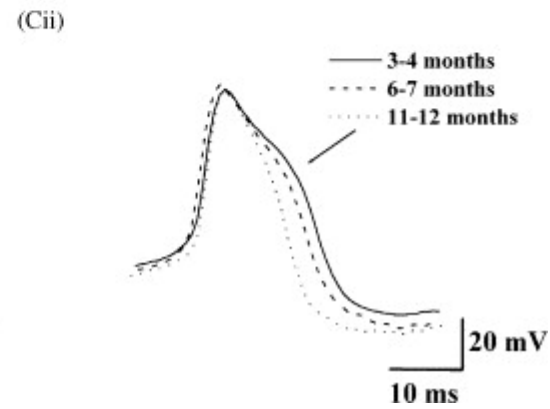
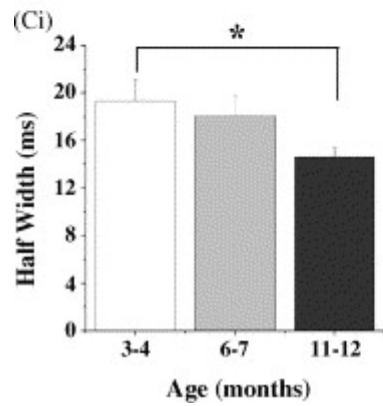
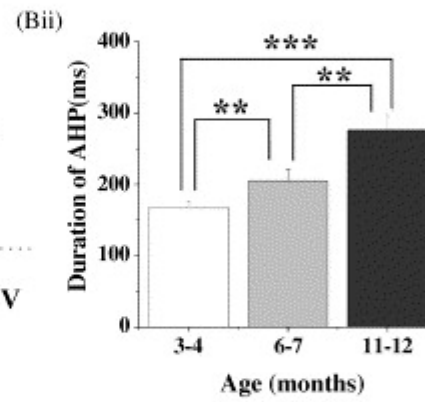
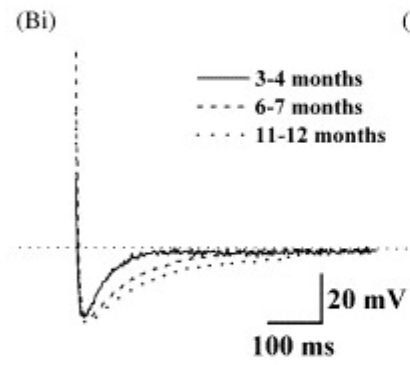
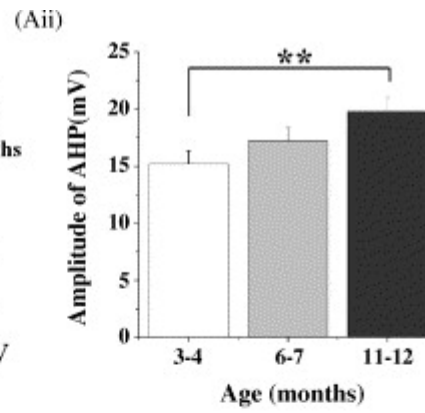
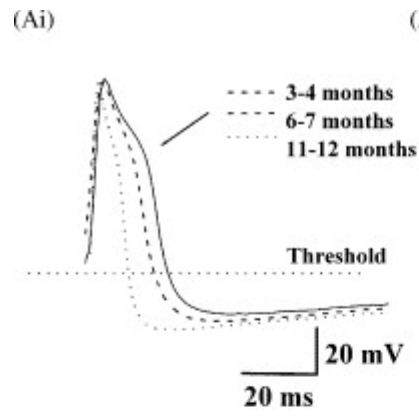
feeding

Amyl Acetate

# Long-term associative memory is impaired in aged snails

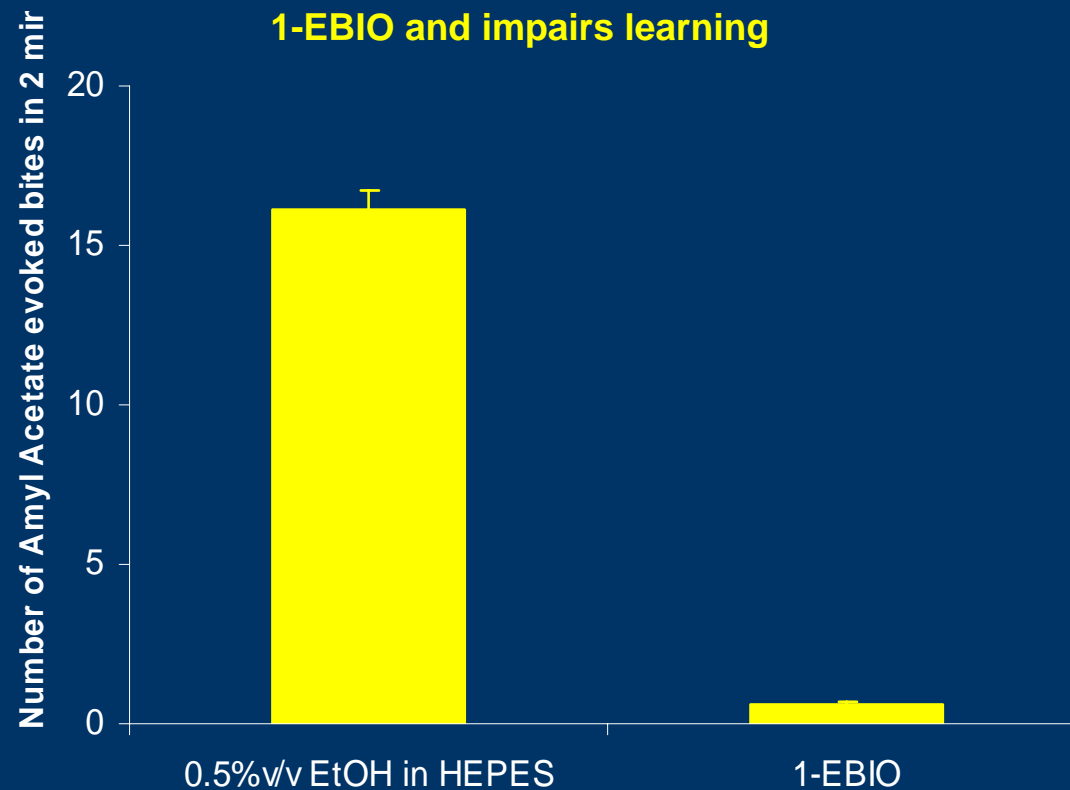


From Hermann et al. 2007, Behavioural Neuroscience



# 1-EBIO Impairs Learning in Young snails

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# Summary

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- Learning in snails involves LTP and additional processes that are distinct from those currently known to occur in mammals.

Do commonly used  
pharmacological agents have  
differential effects on young and old  
neurons?

# Postoperative Cognitive Dysfunction

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- Impaired memory or concentration.
- Not detected until days or weeks after anaesthesia
- Duration of several weeks to permanent

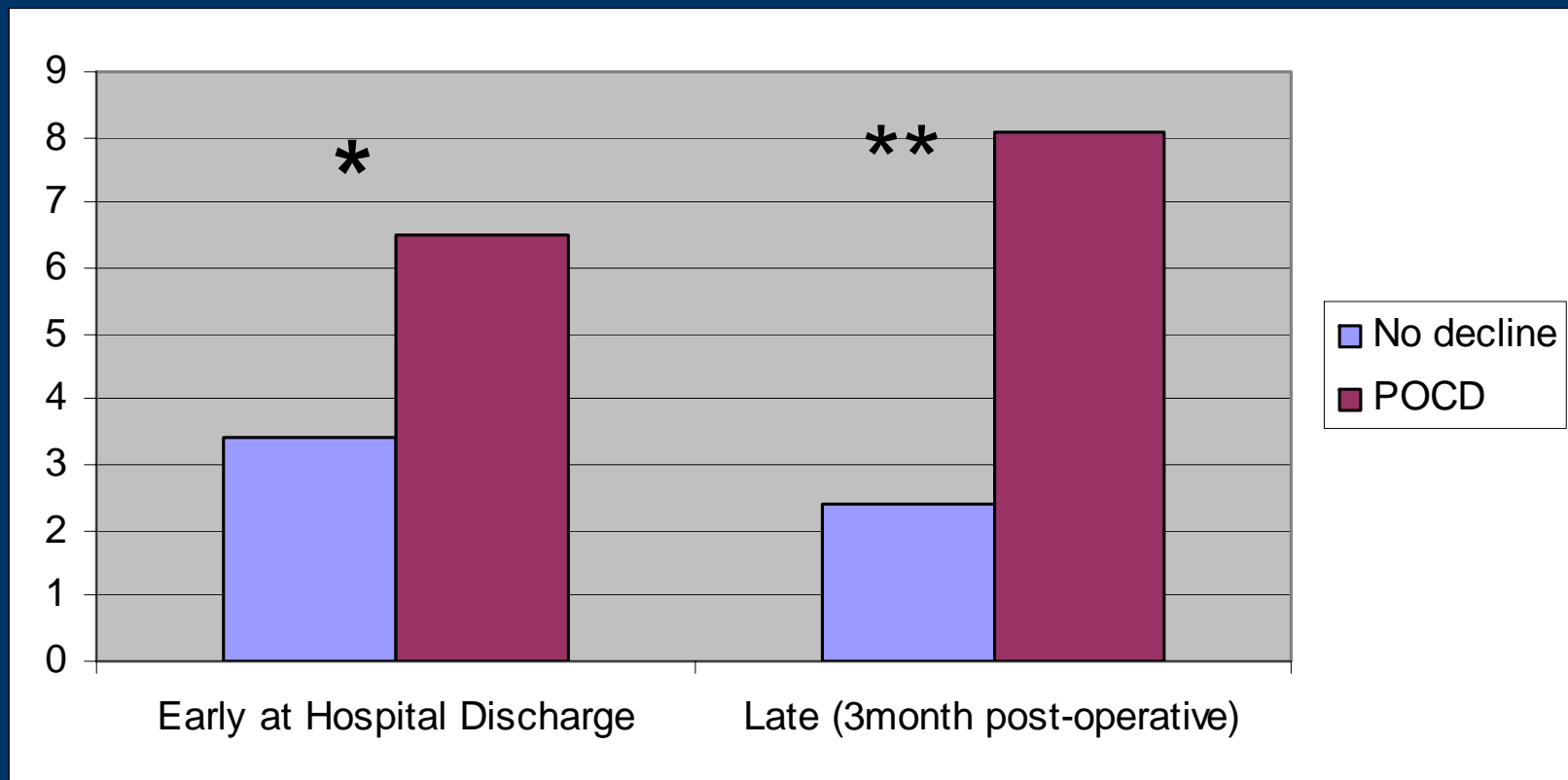
# Implications of Postoperative Neurocognitive Disorder

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- Abrupt decline in cognitive function heralds:
  - Loss of independence
  - Withdrawal from society
  - Death

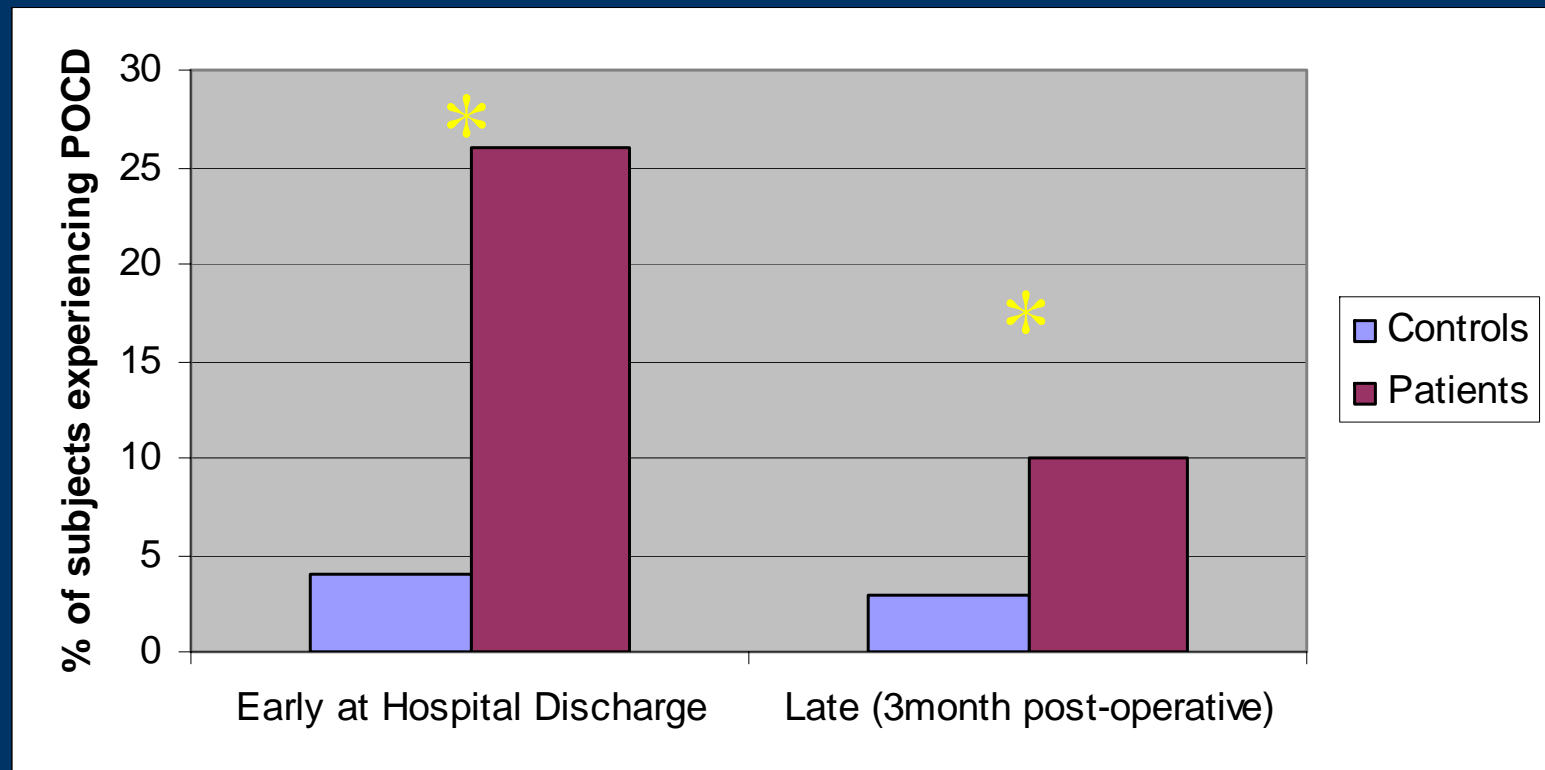
Seattle Longitudinal Study of Aging  
Berlin Aging Study

# One-Year Mortality Rate by Cognitive Status



\* P = 0.027 vs. No Decline; \*\* P = 0.014 vs. No Decline

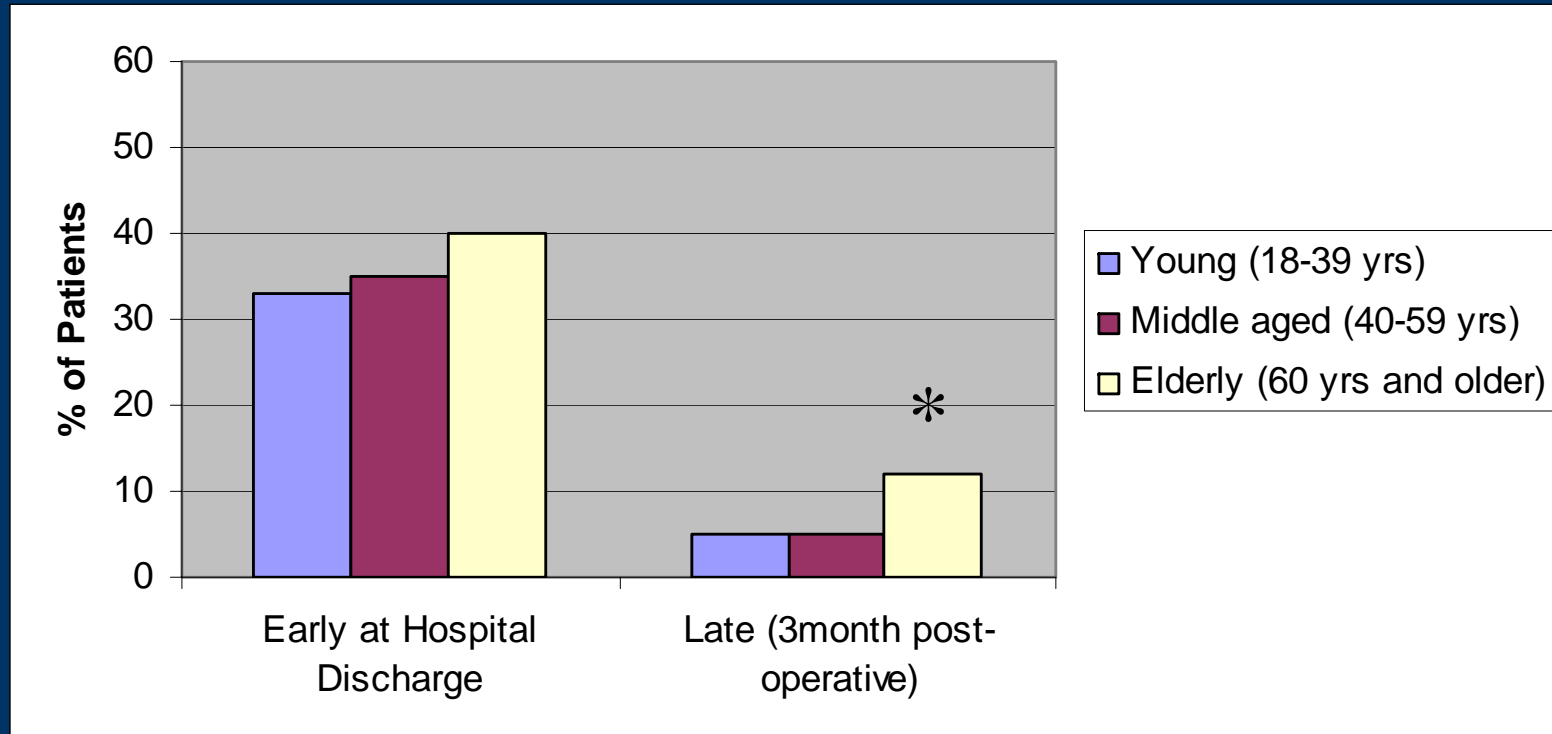
# Incidence of POCD in Patients and Controls



\*  $p < 0.004$

Lancet 1998; 351:857

# Incidence of POCD in Adult Patients:



*\*p < 0.05*

Monk et al. *Anesthesiology* 2001; 95: A-50

# Incidence of POCD

# Effects of volatile anaesthetics on *Lymnaea* neurones

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- Inhibit ACh signalling (Dickinson et al 1995)
- Alter synapse formation (Onizuka et al. 2005).
- Preliminary evidence that anaesthetics impair memory formation in *Lymnaea*.

# Summary

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- Examine the molecular actions of anaesthetics at a cellular level
- Determine how these change with age
- Most importantly how this affects learning and memory.

# Overall Summary

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- Started trying to understand the basic biology of normal brain ageing
- Developed a model that will allow to us to further understand key issues that may affect the quality of lives of older people.

# Acknowledgements

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**Bhavik Patel, Martin Arundell and Danny O'Hare, Imperial College, London.**

**Karen Dolphin, Erin Johnson, Greg Scutt  
University of Brighton  
EPSRC LSI  
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