Ageing at a snail’s pace
NDA workshop, London March 2008

Dr. Mark Yeoman
Department of Pharmacology and Therapeutics
School of Pharmacy and Biomolecular Sciences
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

- Dysphagia
- Impaired cognition
Model System
Snail Brain
In vivo recordings

Transplantation of individual neurones is possible

From Lee and Syed, Synapse 2004.
Patch Clamp Amperometry

- 7 µm carbon fibre electrodes used
- Tip insulated with electrophoretic paint and then cut to expose a disc

Silver wire

Carbon fibre  Woods metal  Glass capillary
Quantal Release of serotonin

2 pA
100 ms
5 pA
50 ms

a
c
b
Feeding Network

Lips

SNs

CGC

N1

N2

N3

B1

B3

B4

MUSCLES

SENSORY

MODULATORY

CPG

MOTOR NEURONE
Snails offer a unique opportunity to ageing research
Do their CNSs show similar changes to those of higher organisms?

- 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

From Arundell, Yeoman et al. 2006, Neurobiology of Aging
Increasing age decreases cerebral giant cell (CGC) firing rate

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

CGC

B1  Protration
B3  Rasp
B4  Swallow
Amplitude of 5-HT-evoked depolarisation (mV)
The Pharmacology of the Synapses are Different

Yeoman et al. submitted J. Neurochem.
• 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?

Day1

- Amyl Acetate
  - No feeding + feeding

Day2

- Amyl Acetate
  - feeding

Sucrose
  - feeding
Long-term associative memory is impaired in aged snails

From Hermann et al. 2007, Behavioural Neuroscience
1-EBIO Impairs Learning in Young snails

Number of Amyl Acetate evoked bites in 2 min

- 0.5% v/v EtOH in HEPES
- 1-EBIO

1-EBIO and impairs learning
Summary

• 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 neurones?
Postoperative Cognitive Dysfunction

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

- 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

* 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

* 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

- Inhibit ACh signalling (Dickinson et al. 1995)

- Alter synapse formation (Onizuka et al. 2005).

- Preliminary evidence that anaesthetics impair memory formation in *Lymnaea*.
Summary

• 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

• Started trying to understand the basic biology of normal brain ageing

• Developed a model that will allow us to further understand key issues that may affect the quality of lives of older people.
Acknowledgements

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

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