BSc / Masters Degree Examinations 2018-9

Department:

Biology

Title of Exam:

Neuroscience

Time Allowed:

2.5 hours

Allocation of Marks:

Total marks available for this paper: 100

Instructions for Candidates:

Answer all questions

Do not write on this booklet before the exam begins
Do not turn over this page until instructed to do so by an invigilator
1. a) How are mitochondria transported to synapses that might be over one metre from the neuronal cell soma? (2 marks)

b) Briefly describe how you could observe mitochondrial transport in live cultured neurons. (3 marks)

c) It has been observed that the delivery of mitochondria to specific synapses increases when those synapses release neurotransmitter. Provide a reason for this observation. (2 marks)

2. a) Describe the experimental procedure you would use to record an action potential from a hippocampal pyramidal neuron. (2 marks)
b) You next wish to study the voltage-gated Na⁺ channels in this neuron. Describe how you would use the voltage clamp to achieve this. (2 marks)
d) Below are Na\textsuperscript{+} currents recorded from a wildtype neuron and a mutant neuron from an individual with a mild form of epilepsy.

Wildtype:

Mutant:

i) What is the peak inward current?  

ii) What is the time to reach peak current?
e) Given your knowledge of voltage-gated Na$^+$ channel gating, in what part of the protein do you think the mutation resides? (2 marks)

3. An experimental setup using an \textit{in vitro} nerve muscle preparation is shown below. An extracellular electrode was used to stimulate the axon of a motor neuron innervating a muscle fibre. An intracellular microelectrode inserted into the muscle fibre was used to record the postsynaptic response of the muscle. The preparation was bathed in a low concentration of curare, an antagonist of acetylcholine receptors, such that a fraction of the acetylcholine receptors was blocked. This prevented the postsynaptic cell from firing an action potential and allowed recording of excitatory postsynaptic potentials.

Following stimulation of the motor axon (depicted by an S on the trace below) the recording electrode was used to measure the end-plate potential (EPP) shown in (i). Miniature end-plate potentials (MEPPs) shown in (ii) were recorded in the absence of any stimulation.
a) What two types of ion flow through the acetylcholine receptor on the postsynaptic muscle cell to generate the EPP?  

b) What would happen to the EPP if extracellular Ca\(^{2+}\) is removed from the bathing solution and why?  

c) What do miniature end-plate potentials (MEPPs) represent?  

d) What would happen to the MEPPs if extracellular Ca\(^{2+}\) is removed from the bathing solution?  

e) What would happen to the EPP and the MEPPs if an inhibitor of acetylcholine uptake is included in the bath solution?
f) You have discovered a new compound X, which when included in the bath, prevents any EPP being recorded from the electrode after stimulation of the motor axon. What are the possible mechanisms by which compound X could be preventing EPPs? (4 marks)

4. A patient complains about visual problems in their left visual field only. The physician suspects that this is a result of brain damage. Which area of the brain is likely to be affected and how would you investigate for neuronal activity in this brain region? (3 marks)

5. Researchers involved in clinical trials for a new anti-depressant drug, drug J, suspect that the drug may be having side effects and could be addictive. They decide to investigate the addictive properties of the drug in mice.

a) Describe the behavioral paradigm that can be used to test whether drug J is addictive. (4 marks)
b) In the behavioral paradigm the researchers find that the drug causes dependence. They therefore compare the effects of drug J in wild-type mice with its effects in D2 dopamine receptor (D2R) knockout mice. Why do they compare wild-type mice with D2R knockout mice? (2 marks)

c) The D2R knockout mice are resistant and do not develop drug dependence. What can you conclude about the possible mechanisms of action of drug J? Design an experiment to test one of your proposed mechanisms. (4 marks)

6. The cartoon below shows a voltage clamp experiment in cultured neurons, where stimulation of a presynaptic neuron elicits a post-synaptic response.
a) What is the neurotransmitter and receptor(s) that have generated the post-synaptic response shown? Justify your answer.  

(3 marks)

b) Complete the table by drawing an appropriate post-synaptic response for each stimulation/treatment and justify your answers.  

(1 mark for each trace; 1 mark for each justification)

<table>
<thead>
<tr>
<th>Stimulation/treatment</th>
<th>Post-synaptic response</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application of TTX prior to presynaptic action potential stimulation</td>
<td></td>
<td>(2 marks)</td>
</tr>
<tr>
<td>Application of NMDA (without action potential stimulation)</td>
<td></td>
<td>(2 marks)</td>
</tr>
<tr>
<td>Application of 50 mM KCl (without action potential stimulation)</td>
<td></td>
<td>(2 marks)</td>
</tr>
</tbody>
</table>

7. Both vertebrates and invertebrates use the G-protein coupled receptor rhodopsin as the primary molecule to detect light. After this point, how do the two processes differ?  

(4 marks)
8. Nociceptors are polymodal. What are the three major modalities that operate in nociceptors? (3 marks)

9. a) Using a simple diagram, identify the principal components of the machinery necessary for touch sensation in the cuticle of *C. elegans*. (3 marks)

b) What behavioural deficits might you expect to observe in *C. elegans* deficient for any of this machinery? (3 marks)
10. Researchers studying insect olfaction recorded from a specific type of olfactory neuron in *Drosophila*, in the presence or absence of an odorant chemical, with EGTA or GDP. The data are shown below:

<table>
<thead>
<tr>
<th>Control</th>
<th>Odorant</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>odorant</td>
</tr>
<tr>
<td>control + EGTA</td>
<td>odorant + EGTA</td>
</tr>
<tr>
<td>control + GDP</td>
<td>odorant + GDP</td>
</tr>
</tbody>
</table>

a) Which electrophysiological technique has been used to acquire the data above? (1 mark)

b) Based on the data in Figure 1, describe the properties of the olfactory receptor and justify your reasoning. (6 marks)
c) Next, the research group cloned two *Drosophila* genes (or47a and or83b/orco) that they propose are subunits of the olfactory receptor recorded above. Briefly outline an experiment to test their hypothesis.  

11. a) A typical symptom in Huntington’s disease is chorea. What does this represent?  

b) Which medium spiny neurons (MSNs) are the first to degenerate in Huntington’s disease?  

c) Huntington’s disease is a genetic disorder caused by mutations in the gene encoding Huntingtin. Describe this mutation.  

d) Patients with Huntington’s disease will often develop problems with personality at the later stages of the disease. Why?
12. You have developed a new mouse model of Parkinson’s disease expressing a G309D mutation in [redacted]. This mutation occurs in familial cases of Parkinson’s disease.

a) Based on the figure below, what is the protein mutated in the animal model. (1 mark)

b) Describe a series of experiment to determine whether this mouse has behavioural phenotypes that resemble those seen in Parkinson’s disease. (4 marks)
13. a) Discuss the experimental conclusions based on the figure below. (3 marks)

[Title redacted]. (A) Representative maps of Lewy Body-like pathology (red dots) as assessed by phosphorylated α-Synuclein (pSyn) staining in wild-type (wt) mice that received a single inoculation of α-Synuclein preformed fibrils (PFFs) in the dorsal striatum (gray circles). Mice were sacrificed at 30, 90, or 180 days post inoculation. (B) Quantification of Tyrosine Hydroxylase (TH)-immunoreactive neurons in the substantia nigra par compacta (SNpc) of mice after intrastriatal PFF or PBS injection. PBS is an inert, control solution that has no adverse effects on neurons. Data represent mean cell number ± SEM (n = 3 mice per group). *P < 0.05, one-way ANOVA with Bonferroni post-hoc test.
b) Discuss the experimental conclusions based on the figure below. (3 marks)

[Title redacted]. (A) Representative phosphorylated α-Synuclein (pSyn) staining and quantification in the substantia nigra par compacta (SNpc) of WT and lymphocyte-activation gene 3 (LAG3) knockout mice (LAG3−/−) sacrificed at 30 and 180 days after intrastriatal α-Synuclein preformed fibrils (PFF) injection. Data are the means ± SEM, n = 5 to 9 mice per group, one-way ANOVA with Sidak’s correction. (B) Stereology counts from Tyrosine Hydroxylase (TH) immunostaining and Nissl staining of SNpc dopaminergic neurons of WT and LAG3−/− mice at 180 days after intrastriatal α-syn PFF or PBS injection. Data are the mean number of cells per region ± SEM, n = 5 to 9 mice per group, one-way ANOVA with Dunnett’s correction.

14. a) Which white matter tract contains the axons of corticospinal motor neurons? (1 mark)
b) In what part of the brain do the axons of most corticospinal neurons switch to the contralateral side of the CNS? (1 mark)

c) Draw a diagram to show how corticospinal motor neurons control agonist and antagonist muscles. (4 marks)
15. How does dopamine affect the function of the glutamatergic synapses on medium spiny neurons (MSNs)? (4 marks)