Test Exam 2024-25 BIO-499 Your Name: _____

Test-Exam for **BIO-499 (2024 - 2025** Kochubey / Schneggenburger, **Neural circuits of Motivated Behavior**)

- This test exam randomly covers 7 Units, and therefore represents ~ 60% of the true exam

- The true written exam (Thursday 26.06.2024, 15:15 - 18:15; CO120) will cover all 12 Units of the course, as follows:
1: Brain Anatomy • 2: Techniques to Study Neural Circuits • 3: The nociceptive System • 4: Learned fear, 1 • 5: Learned fear, 2 • 6: Innate defensive behaviors • 7: Internal body States: Thirst • 8: Internal body States: Hunger • 9: Instrumental Learning • 10: Social behavior: sociability and sexual behavior • 11: Social behavior: Parental behaviors and Aggression • 12: Psychiatric disease.

- For each Unit there will be:
    - 1 multiple choice question (1 point)
    - a short essay question (2, 2.5, or 3.0 points to be earned)

There will be a total of ~ 40 - 46 Points to be earned in the real exam

Important: for the real exam …

- **Write your name on top of each page (first name + last name)**

- If there is not enough space, please continue writing on the reverse page, for each Unit.

Unit 2. Techniques to study neural circuits

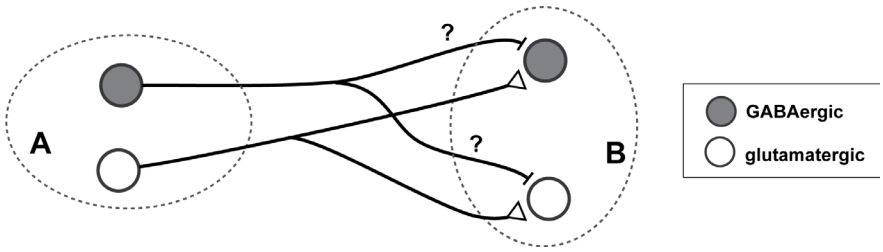
What are the correct statements regarding rabies virus? More than one answer might be possible:

- ☐ it is used for anterograde labeling of neural circuits and circuit mapping
- ☐ wild-type rabies virus spreads in the brain retrogradely via multiple trans-synaptic jumps
- ☐ rabies is well tolerated by neurons which survive for months after infection
- ☐ wild-type rabies viruses are safe to use because there are antibiotics against rabies infection
- ☐ for use of EnvA (Envelope protein of Avian sarcoma leucosis virus) pseudotyped rabies vector, one needs to infect starter cells with TVA (avian receptor for EnvA).

(1 point)

Imagine the following circuit between two brain areas (drawing). How can the specific connectivity between GABAergic neurons in brain area A, and i) GABAergic and ii) glutamatergic neurons in brain area B be studied with optogenetic tools and patch-clamp recordings in slices? In your experimental toolbox, you have the following mouse models available: VGluT2^{Flp} mice, and VGAT^{Cre} mice. Furthermore, you have any type of Flp- or Cre-dependent AAV vector of your choice available. Describe the exact viral tools, and experimental design you would use.

(3 Points)



Unit 3. Nociceptive system and nocifensive behavior

Which are the correct statements? More than one answer might be possible:
□ nociceptive axons arriving to the dorsal horn use acetylcholine as neurotransmitter
□ morphine causes analgesia by activating neurons in the periaqueductal grey (PAG), which in turn recruit neurons that project to the dorsal horn of the spinal cord
□ nociceptive axons arriving to the ventral horn use glutamate as neurotransmitter
□ in allodynia, a slight touch of an injured part of the body is subjectively felt as a painful event due to a decreased pain threshold
□ morphine causes analgesia by reducing the inflammatory response at the pain locus
(1 Point)

Describe the role of the parabrachial nucleus (PBN) in the brainstem for the processing of the emotional component of pain. i) From which central nervous system structure does the PBN receive nociceptive input? ii) To which forebrain areas do neurons of the PBN project, and iii) in which two pain-processing functions are two of these projections involved?
(**3 Points**)

Unit 4. Learned fear, 1

Which are the wrong statements? More than one answer might be possible:

- ☐ The spino-mesencephalic pathway carries nociceptive information to the midbrain
- ☐ Pavlovian conditioning always involves an association between the CS and an aversive US
- ☐ The central amygdala contains mainly inhibitory neurons, and makes a long-range inhibitory connection to the periaqueductal grey (PAG)
- ☐ Fear learning circuits exclusively utilize glutamate and GABA as neurotransmitters
- ☐ During protocols for "contextual fear learning", no auditory stimuli are presented

(**1 Point**)

Explain the auditory-cued fear conditioning paradigm, and a model of how the amygdala is involved in auditory fear learning in mice. i) Describe the experimental setup for inducing an auditory-cued fear memory using mild electric foot shocks (what and when is applied, what is measured). ii) Describe the flow of sensory information in the brain, focusing on the pathways mediating the transfer of auditory information from the auditory midbrain (inferior colliculus) to the amygdala. iii) Which part of the amygdala is thought to receive the auditory CS information, and how is this information transformed by local plasticity?
(**3 Points**)

Unit 7. Internal body states: Thirst

Which are the wrong statements? More than one answer might be possible:
□ after extensive sweating, urine volume increases to excrete extra Na^+ from the plasma
□ blood plasma and intracellular fluid have different ion composition but same osmolality
□ low-pressure baroreceptors are found in the aortic arch and in the lungs
□ cerebrospinal fluid has high [K^+] and low [Na^+] (145 mM and 3 mM, respectively)
□ AVP hormone controlling water homeostasis is released from the posterior pituitary
(1 Point)

In a thirsty animal (elevated blood osmolality), experiments suggest that the feeling of thirst is rapidly reduced when (especially cold) water, or even a cold object is placed into the mouth. i) Is such a rapid reduction of "thirst" expected from classical homeostatic regulation models, in which the blood osmolality is fed back to the brain? - please explain your answer. ii) Name the circumventricular organ which is primarily involved in the detection of blood osmolality, and briefly explain the mechanism. iii) Name the neighboring hypothalamic area which sends a feedback signal to the above-mentioned circumventricular organ, thereby causing rapid quenching of the feeling of "thirst". Explain the underlying cellular- and circuit mechanism and the involved neurotransmitter in this feedback signal.
(**3 Points**)

Unit 9. Instrumental learning

Which are the wrong statements? More than one answer might be possible:
□ in operant conditioning, the rewarded behavior is strengthened, the punished is weakened
□ the mesolimbic dopaminergic pathway is central to emotional processing of reward
□ sensory stimulus gains reflexive association with reward during operant conditioning
□ non-dopaminergic neurons in the ventral tegmental area (VTA) are mainly GABAergic interneurons that inhibit the dopamine neurons
□ all dopaminergic neurons in the brain are devoted to signal a reward prediction error
(1 Point)

Describe the concept of instrumental learning and the basic learning experiment using the "Skinner box". i) Which experiment involving instrumental learning first provided evidence for the role of VTA dopaminergic neurons in the reward signaling? ii) Illustrate the response pattern (firing rate) of VTA dopamine neurons at different stages of learning within the frame of reward prediction error theory. iii) Which brain nuclei are the main downstream targets of VTA dopamine neurons mediating reward and how is this circuit involved in the development of substance addiction?
(3 Points)

Unit 11. Social behavior: parental behaviors, aggression.

Which are the correct statements? More than one answer might be possible:
□ male mice, including experienced fathers, do not take part in caring about the pups
□ virgin females in mice can learn caregiving behaviors from experienced dams
□ galanin^{+} neurons in the medial preoptic area are required for parental behavior in mice
□ in mice, experienced mothers will kill the pups not belonging to them
□ genetic lack of oxytocin receptors does not affect maternal behavior
(**1 Point**)

i) Explain what is aggressive behavior, its evolutionary purpose, and describe the main experimental paradigm for studying neural circuits of aggression in mice. ii) Outline a simplified circuit of intermale aggression, from the sensory input up to the brain node coordinating behavioral output. iii) Which glutamatergic nucleus in this circuit is thought to be necessary and sufficient for aggressive behavior, and by which three types of experiments was this demonstrated?
(3 Points)

Unit 12. Neural mechanisms of psychiatric disorders.

Which are the wrong statements? More than one answer might be possible:
 Selective serotonin reuptake inhibitor (SSRI) - type antidepressants increase the availability of serotonin for its receptors
 The main action of antipsychotics is the block of D2-type dopamine receptors, although these drugs can also act on other molecular pathways.
 autism patients can estimate the mental state of others without looking into the eyes
 symptoms of obsessive-compulsive disorder can be relieved with the SSRI fluoxetine
 in the open field test, more anxious mice keep away from the walls
(**1 Point**)

i) Describe the main signs of childhood autism and of obsessive-compulsive disorders (OCD). ii) Which symptoms are in common and which are different? iii) Which circuit mechanism is thought to underlie OCD, and which postsynaptic receptor signaling was shown to be specifically upregulated in the Sapap3 KO genetic model of OCD?
(**3 Points**)