

PHYSIOPATHOLOGIE EN NEUROLOGIE ET PSYCHIATRIE

Lundi 24 Novembre

Durée total de l'examen : 2 heures

Vous devez répondre aux deux sujets. PENSEZ à indiquer votre numéro d'étudiant sur les deux feuillets de réponse (pages 2 et 3).

Total examination duration: 2 hours

You must respond to the two exams topics. REMEMBER to indicate your student number on pages 2 of this examination paper.

Numéro étudiant/
Student number : _ _ _ _ _

MCQ exam (20 pts)
Test duration: 1 hour

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This exam contains 40 multiple choice questions, each worth 0.5 points.

Indicate with a cross the correct response(s) for each question. Each question could have several correct answers. Make sure that your answer is clearly marked.

MCQ exam

Mark your answers on the answer sheet (page 2 of the second document)

1. Multiple sclerosis is a disease :

- a) with a chronic course.
- b) affecting the peripheral nervous system.
- c) Inflammatory.
- d) inherited.
- e) affecting preferentially the elderly.

2. Cognitive disturbances in multiple sclerosis :

- a) occur usually in the later stages of the disease.
- b) increased the risk of unemployment.
- c) concern mainly language.
- d) are characterized by information processing speed impairment.
- e) spared executive functions.

3. Cognitive impairment in multiple sclerosis:

- a) can be detected by asking questions about cognition to the patient.
- b) can be detected in many patients by a single test assessing information processing speed.
- c) can be detected in many patients by a single test assessing working memory.
- d) can be assessed by the Mini Mental Status (MMS).
- e) is more frequent in patients with a lower educational background than in more educated people with the same burden of disease lesions on MRI.

4. Cognitive disturbances in multiple sclerosis :

- a) correlate weakly with lesion load on MRI.
- b) do not correlate strongly with brain atrophy at the early stages of the disease on MRI.
- c) correlate with diffuse white matter involvement at early stages of the disease on MRI.
- d) do not correlate with deep gray matter and cortical atrophy on MRI at late stages.
- e) correlate specifically with frontal lobe lesion load on MRI.

5. Brain activity during a cognitive task performed normally by a patient with multiple sclerosis:

- a) is characterized by an increased activity in the brain area associated with the task.
- b) is associated with the same pattern of recruitment of brain areas than healthy subjects.
- c) is characterized by additional recruitment of cerebral areas normally not involved in the task.
- d) is dependant of the extent of diffuse brain tissue injury.
- e) is limited in complex tasks.

6. Which enzyme induced by cytokines is responsible for the catabolism of tryptophan within the kynurenine pathway?

- a) Tryptophan hydroxylase (TPH).
- b) Indoleamine 2,3-dioxygenase (IDO).
- c) Monoamine oxydase (MAO).
- d) Kynurenine aminotransferase (KAT).
- e) Tetrahydrobiopterin (BH4).

- 7. In which of the following aspects, sickness behavior resembles major depression?**
- a) Intensity/severity.
 - b) Duration.
 - c) Symptoms dimensions.
 - d) Adaptive response to help the body to recover from pathogens.
 - e) Requires treatment with antidepressants.
- 8. Recent clinical and animal studies demonstrate that blockade of tumor necrosis factor (TNF- α) by etanercept or infliximab has a behavioral effect. Which one?**
- a) It induces depressive symptoms.
 - b) It is responsible for the development of treatment-resistant depression.
 - c) It has an antidepressant effect.
 - d) It induces sickness behavior.
 - e) It increases appetite.
- 9. What is neopterin?**
- a) A pro-inflammatory cytokine.
 - b) An anti-inflammatory cytokine.
 - c) An antidepressant.
 - d) A metabolite of kynurenine.
 - e) A marker of macrophage activation.
- 10. One of the following non-exclusive mechanisms has not been described as underlying the depressive effects of pro-inflammatory cytokines. Which one?**
- a) Activation of the hypothalamic-pituitary-adrenal (HPA) axis.
 - b) Alteration of neurotransmitter system and function.
 - c) Effects on neurocircuitry.
 - d) Alteration of the enzymatic pathways involved in the metabolism of monoamines.
 - e) Analgesic processes.
- 11. The following propositions characterize Quinolinic Acid, except one. Which one?**
- a) A NMDA receptor agonist.
 - b) Associated with depressive symptoms in patients with cytokine-induced depression.
 - c) A NMDA receptor antagonist.
 - d) A downstream product of the kynurenine pathway.
 - e) Produced in activated macrophages/microglia.
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- 12. Which functional and structural changes correspond to PTSD:**
- a) Hypoactivation of the prefrontal cortex.
 - b) Hyperactivation of the prefrontal cortex.
 - c) Reduced hippocampal volume.
 - d) Increased amygdala volume.
 - e) Hyperactivation of the amygdala.
- 13. Risks factors for PTSD:**
- a) Blood cortisol levels.
 - b) Previous traumatic experience.
 - c) Hyperactivation of the amygdala.
 - d) Family history of PTSD.
 - e) History of drug abuse.

14. What are perineuronal nets:

- a) A subpopulation of excitatory neurons.
- b) A highly organized form of proteoglycans.
- c) A subpopulation of inhibitory neurons.
- d) Glial cells.
- e) Elements of the extracellular matrix.

15. Principal therapies for PTSD:

- a) Cognitive and behavioral therapies.
- b) Hypnosis.
- c) Eye movement desensitization and reprogramming.
- d) Antidepressant/antipsychotic.
- e) Electroconvulsive shocks.

16. Principal anxiety disorders:

- a) Psychosis.
- b) Post-traumatic stress disorder.
- c) Schizophrenia.
- d) General anxiety disorder.
- e) Obsessive compulsive disorders.

17. Fear extinction in adults:

- a) Is an inhibitory associative learning.
- b) Represents an erasure of the original fear memory.
- c) Is a new learning of the CS- no us association.
- d) Is an habituation process.
- e) Allows the reconsolidation of fear memories.

18. At brain level, functional MRI technique (fMRI) allows to directly measure:

- a) Electric activity.
- b) Hemodynamic response.
- c) Glucose consumption.
- d) Oxygen consumption.
- e) All the answers (A, B, C and D).

19. The main inconvenient of the functional MRI technique (fMRI) are:

- a) Its invasive nature.
- b) Its signal coming only from the venous system.
- c) Its low temporal resolution.
- d) Its low spatial resolution.
- e) All the answers (A, B, C and D).

20. At cerebral network level, what are the possible compensatory phenomena?

- a) A diaschisis.
- b) The lack of recruitment of counterpart areas.
- c) The increase of recruitment of brain areas which are not usually relevant for the motor or cognitive function studied in the protocol.
- d) The increase of recruitment of brain areas which are relevant for the motor or cognitive function studied in the protocol.
- e) All the answers (A, B, C and D).

- 21. At brain level, the Diffuse Tensor Imaging technique (DTI) is useful because it allows to:**
- Make the difference between isotropic and anisotropic environments.
 - Make the difference between oxygenated and deoxygenated blood.
 - Make the difference between the connection fibers integrity between healthy subjects and patients with neurological diseases.
 - Make the difference between mobile and motionless protons.
 - All the answers (A, B, C and D).
- 22. In MCI patients:**
- There is a correlation between hippocampic activation decrease and cognitive decline.
 - The DTI sequence shows greater loss of fiber integrity than in Alzheimer's disease patients.
 - There is an hypoactivation of hippocampic structure.
 - There is an hyperperfusion of hippocampic structure.
 - All of the answers A, B, C and D.
- 23. At the beginning of Multiple Sclerosis disease (MS), the increase in tissue damage is associated with:**
- No modification in cerebral networks connectivity.
 - A decrease in BOLD signal in the counterpart areas.
 - A decrease in BOLD signal in brain areas which are relevant for the motor or cognitive function studied in the protocol.
 - The preservation of the same cerebral pattern of activation than in healthy subjects.
 - None of the answers A, B, C and D.
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- 24. Major depression is classically associated with profound disturbances in the functioning of the HPA axis, including:**
- a blunted increase in plasma ACTH concentrations in response to hCRF injection.
 - a marked reduction in plasma CRF concentrations in baseline conditions.
 - a more pronounced reduction in plasma cortisol concentrations in response to dexamethasone administration.
 - a more pronounced increase in plasma cortisol concentrations in response to spironolactone administration.
 - a more pronounced increase in plasma cortisol concentrations in response to combined dexamethasone/CRF administration.
- 25. Major depression is classically associated with profound anatomical disturbances, including:**
- a lower number of CRF neurons in the hypothalamus.
 - a higher number of CRF neurons in the hypothalamus.
 - a higher number of AVP neurons in the hypothalamus.
 - a lower number of AVP neurons in the hypothalamus.
 - a higher number of CRF neurons coexpressing AVP in the hypothalamus.
- 26. Chronic stress is classically associated with profound disturbances in the functioning of the endocannabinoid system in laboratory animal models, including:**
- a marked increase in the CB1 receptor density in the hippocampus.
 - a marked decrease in the 2-AG content in the hippocampus.
 - a marked decrease in the CB1 receptor density in the hippocampus.
 - a marked increase in the 2-AG content in the hippocampus.
 - a marked increase in the anandamide content in the hippocampus.

27. Inactivation of CB1 receptors causes several modifications in emotional behaviors in laboratory animal models, including:

- a) a marked reduction in anxiety levels.
- b) a marked increase in anxiety levels.
- c) a marked increase in depressive-like symptoms.
- d) a marked reduction in feeding.
- e) a marked increase in feeding.

28. Deficit in behavioral inhibition in OCD is classically associated with profound disturbances in the functioning of several cortical regions, including:

- a) a marked reduction in the metabolic activity of the anterior cingulate cortex.
- b) a marked reduction in the metabolic activity of the orbitofrontal cortex.
- c) a marked increase in the metabolic activity of the supplementary motor area.
- d) a marked decrease in the metabolic activity of the dorso-lateral prefrontal cortex.
- e) a marked increase in the metabolic activity of the posterior cingulate cortex.

29. Deficit in cognitive flexibility in OCD is classically associated with profound disturbances in the functioning of several cortical regions, including:

- a) a marked reduction in the metabolic activity of the anterior cingulate cortex.
 - b) a marked reduction in the metabolic activity of the ventro-lateral prefrontal cortex.
 - c) a marked increase in the metabolic activity of the supplementary motor area.
 - d) a marked decrease in the metabolic activity of the dorso-lateral prefrontal cortex.
 - e) a marked increase in the metabolic activity of the posterior cingulate cortex.
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30. The prefrontal cortex encompasses different regions :

- a) Anterior cingulate cortex.
- b) Anterior temporal cortex.
- c) Dorsolateral prefrontal cortex.
- d) Insular cortex.
- e) Orbitofrontal cortex.

31. The dorsolateral prefrontal cortex is involved in :

- a) Episodic memory.
- b) Short term memory.
- c) Information upholding to consciousness.
- d) Procedural learning.
- e) Decision-making.

32. Lesions of the dorsolateral prefrontal cortex may induce:

- a) Reasoning troubles.
- b) Disruption of behavioral strategies.
- c) Apraxic disorders.
- d) Disruption of the phonological loop.
- e) Impairment of long term memory.

33. The orbitofrontal cortex:

- a) Encompasses areas 11,12,13.
- b) Encompasses areas 41 and 44.
- c) Is involved in motivational aspects of behavior.
- d) Its lesion may induce aphasic disorders.
- e) Its lesion may induce disinhibition in social behavior.

34. The anterior cingulate cortex:

- a) Is located in the most anterior part of the brain.
 - b) Is involved either in the processing of motor, cognitive and emotional information.
 - c) Its lesion may induce apathy.
 - d) Is involved in the detection of errors.
 - e) Is disrupted in Tourette's syndrome.
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35. The central dopaminergic pathways comprise:

- a) The striatonigral pathway.
- b) The meso-accumbens pathway.
- c) The cortico-striatal pathway.
- d) The meso-cortical pathway.
- e) The nigro-striatal pathway.

36. Among the following symptoms which are less or no responsive to levodopa:

- a) Tremor.
- b) Postural instability.
- c) Akinesia.
- d) Gait and balance dysfunction.
- e) Dementia.

37. The plasma half-life of levodopa is:

- a) 1 – 1.5 h
- b) 3 – 5 h
- c) 5 – 8 h
- d) 10 – 15 h
- e) 20 – 60h

38. Rasagiline is:

- a) A selective dopamine D2 receptor antagonist.
- b) An amphetamine derivative.
- c) A reversible MAO-B inhibitor.
- d) A reversible MAO-A and MAO-B inhibitor.
- e) An irreversible monoamine oxidase (MAO)-B inhibitor.

39. Which of the following statements about monoamine oxidase (MAO) enzyme distribution are true?

- a) MAO-B are highly represented in the brain.
- b) MAO-A are highly represented in the brain.
- c) MAO-A are highly represented in the gastrointestinal tract.
- d) MAO-B are highly represented in blood platelets.
- e) MAO-A are not present in the liver.

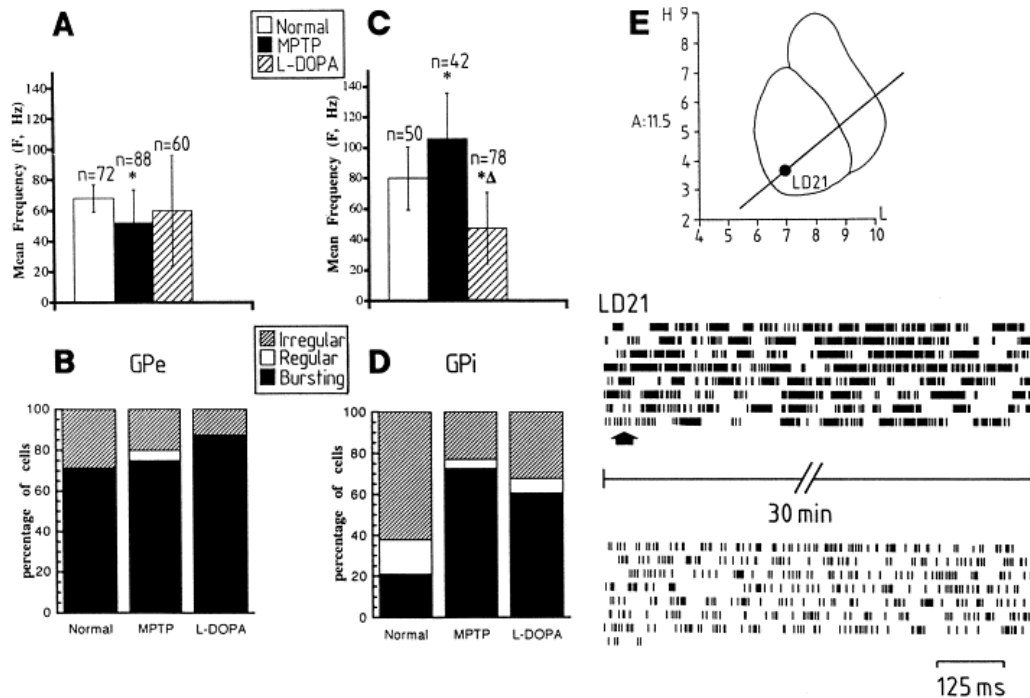
40. Which of the following statements concerning the Catechol-O-methyltransferase (COMT) enzyme are true?

- a) COMT degrade dopamine into 3-O-methyldopa.
- b) COMT participate in the metabolism of levodopa and dopamine.
- c) COMT degrade levodopa into 3-O-methyldopa.
- d) 3-O-methyldopa facilitates the transfer of levodopa across the blood brain barrier.
- e) Selegiline is a selective COMT inhibitor.

From clinic to functional anatomy of extrapyramidal syndromes

D. Guehl

Test duration: 60 minutes



- Electrophysiological activity of the GPe (A, B).
 (A) Mean firing frequency [F:spikes/s (Hz)±S.D.] of neurons in the three experimental situations (n =number of neurons). White column: normal situation, black column: after MPTP injection, shaded column: after L-DOPA treatment.
 (B) Graphic presentation of percentage distribution of the different patterns of discharge (irregular, regular, bursting) in the three experimental situations.
 - Electrophysiological activity of the GPi (C, D).
 (C) Same legend as in A. (D) Same legend as in B.
 *significance as compared to normal (Student's t-test), Δsignificance as compared to MPTP (Student's t-test).
 - (E) Continuous recording of a GPi neuron in an MPTP-treated monkey from before the oral administration of L-DOPA until the beginning of the 'best on' period 30 min later. (Top) position on a schematic frontal plane (A: 11.5, H: depth, L: laterality) of the electrode track in the GPi. The black dot corresponds to the recording site of the neuron (LD 21) presented below. (Bottom) raster display before and after the administration (arrow) of L-DOPA. Thirty minutes after drug intake (horizontal broken line), a decrease in firing activity is visible on the raster display.

1) Describe and comment the figure extracted from an article entitled «Effects of L-DOPA on neuronal activity of the globus pallidus externalis (GPe) and globus pallidus internalis (GPi) in the MPTP-treated monkey»

2) What are the effects of L-Dopa on neuronal activity of both parts of the pallidum?

3) Based on your knowledge of basal ganglia circuitry, indicate what could be the consequences of these pallidal activity changes on motor thalamus activity and on the cortical activity?