

## MCQ exam

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

**1. The central dopaminergic pathways comprise:**

- a) The nigro-striatal pathway
- b) The meso-accumbens pathway
- c) The cortico-striatal pathway
- d) The thalamo-cortical pathway
- e) the nigro-thalamic pathway

**2. Among the following symptoms which are less or no responsive to levodopa**

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

**3. Which of the following statements are false? In parkinsonian patients, the association of an ICOMT and levodopa:**

- a) Increases the bioavailability of the levodopa
- b) Reduces the fluctuations of plasma-levodopa levels
- c) Provides a continuous dopamine-receptor stimulation
- d) Worsen the quality of life
- e) Reduces motor fluctuations by increasing the "OFF" periods

**4. Which of the following statements concerning Safinamide is (are) false? Safinamide**

- a) Is a selective and reversible MAO-B and DA reuptake inhibitor
- b) Is a selective and irreversible MAO-B and DA reuptake inhibitor
- c) Increases glutamate release
- d) Exerts a state-dependent blockade of voltage-dependent Na<sup>+</sup> channels
- e) Its antidyskinetic effects could be attributed to non-dopaminergic mechanisms related to decreased glutamate release

**5. Which of the following statements concerning Parkinson's disease is (are) true? Levodopa:**

- a) Improves motor symptoms
- b) Influences the course of neuronal loss
- c) Has limited effect on non-motor symptoms
- d) Has no influence on late-stage motor symptoms (e.g. dysphagia falls)
- e) Is a dopamine receptor agonist

**6. The combined dexamethasone-CRF test was largely documented to:**

- a) cause a greater cortisol response in depressed patients as compared to normal healthy subjects
- b) cause a greater cortisol response in unaffected first-degree relatives of depressed patients, as compared with normal healthy subjects
- c) predict the therapeutic response to antidepressant medications in depressed patients
- d) predict the relapsing course and poor prognosis in depressed patients
- e) predict the emotional response to the presentation of sad faces in depressed patients

**7. Strong relationships were established between cortisol awakening response and clinical symptoms in depressed patients, especially including:**

- a) anhedonia
- b) sleep disturbances
- c) anxiety
- d) cognitive impairment
- e) general distress

**8. In depressed patients, decreased sensitivity of glucocorticoid receptors is supported by:**

- a) a less pronounced memory impairment than that in normal healthy subjects after hydrocortisone administration
- b) a more pronounced memory impairment than that in normal healthy subjects after hydrocortisone administration
- c) a less pronounced reduction in plasma cortisol levels than that in normal healthy subjects after dexamethasone administration
- d) a more pronounced reduction in plasma cortisol levels than that in normal healthy subjects after dexamethasone administration
- e) a less pronounced reduction in plasma cortisol levels than that in normal healthy subjects after spironolactone administration

**9. In patients with obsessive-compulsive disorder, functional neuroimaging studies conducted during symptom-provocation paradigms have shown:**

- a) decreased functional activity within the ventromedial prefrontal cortex, as compared to normal healthy subjects
- b) increased functional activity within the supplementary motor area, as compared to normal healthy subjects
- c) increased functional activity within the putamen, as compared to normal healthy subjects
- d) increased functional activity within the subthalamic nucleus, as compared to normal healthy subjects
- e) decreased functional activity within the amygdala, as compared to normal healthy subjects

**10. In patients with obsessive-compulsive disorder, different cognitive processes were consistently found to be disrupted, especially including:**

- a) cognitive flexibility
- b) facial recognition
- c) error detection
- d) social cognition
- e) memory recall

**11. An abnormal error processing was classically found in:**

- a) patients with obsessive-compulsive disorder unresponsive to cognitive-behavioral therapy
- b) patients with obsessive-compulsive disorder responsive to cognitive-behavioral therapy
- c) unaffected first-degree relatives of patients with obsessive-compulsive disorder
- d) depressed patients unresponsive to cognitive-behavioral therapy
- e) depressed patients responsive to cognitive-behavioral therapy

**12. The pathophysiology of Parkinson's disease can involve all these mechanisms except:**

- a) The loss of dopaminergic neurons of the pars compacta of substantia nigra
- b) The loss of dopamine fibers in the striatum
- c) The loss of glutamatergic neurons in the thalamus
- d) The loss of noradrenergic neurons of the raphe nucleus
- e) The loss of GABA neurons of the striatum

**13. Among the following propositions, select the correct proposition(s). Parkinson's disease is characterized by:**

- a) Muscle rigidity
- b) Essential tremor
- c) Myoclonia
- d) Dyskinesias characterized by involuntary abnormal movements
- e) Akinesia or bradykinesia

**14. Among the following propositions, select the correct proposition(s):**

- a) L-Dopa induces a stable improvement of motor symptoms in all stages of Parkinson's disease
- b) L-Dopa induces dyskinesias during the first three years of treatment
- c) Deep brain stimulation of the subthalamic nucleus induces a stable improvement of motor symptoms in advanced stages of Parkinson's disease
- d) Deep brain stimulation of the subthalamic nucleus leads to an improvement of motor symptoms accompanied by dyskinesias
- e) Deep brain stimulation of the subthalamic nucleus improves the motor symptoms including tremor at rest

**15. Among the following propositions, select the correct proposition(s):**

- a) Deep brain stimulation of the subthalamic nucleus induces its beneficial effect by inhibiting a large part of subthalamic nucleus neurons
- b) Deep brain stimulation of the subthalamic nucleus induces its beneficial effect by exciting the pars reticulata of substantia nigra neurons
- c) Deep brain stimulation of the subthalamic nucleus increases the tissue level of glutamate in the pars reticulata of substantia nigra of 6-OHDA rats
- d) Deep brain stimulation of the subthalamic nucleus increases the tissue level of GABA in the pars reticulata of substantia nigra of 6-OHDA rats
- e) Deep brain stimulation of the subthalamic nucleus increases the tissue level of GABA in the motor thalamus of parkinsonian patients

**16. Among the following propositions, select the correct proposition(s):**

- a) In the striatum, dopamine D1 and D2 receptors are located on the same projection neurons
- b) In the striatum, dopamine D1 receptors are located on the projection neurons of the direct pathway
- c) Dopamine D2 receptors of the striatum are located on the projection neurons of the indirect pathway
- d) Activation of dopamine D1 receptors exerts an inhibitory effect on striatal projection neurons
- e) Activation of dopamine D2 receptors exerts an excitatory effect on striatal projection neurons

**17. Among the following propositions, select the correct proposition(s):**

- a) D5 receptors located in the subthalamic nucleus are a part of D1 family receptors playing a key role in the pathophysiology of Parkinson's disease
- b) Dopamine D5 receptors are characterized by their constitutive activity, which is at the origin of the bursty activity in the subthalamic nucleus of 6-OHDA rats
- c) In the context of Parkinson's disease, D2 receptors are activated to maintain the tonic neuronal firing of subthalamic nucleus neurons
- d) Local injection of D5 receptor inverse agonist into the subthalamic nucleus changed bursty activity to a tonic activity in the 6-OHDA rat model of Parkinson's disease
- e) Local injection of D5 receptor agonist into the subthalamic nucleus can be proposed as a target in the treatment of Parkinson's disease

**18. Concerning multiple sclerosis:**

- a) The disease mainly affects young women.
- b) The disease is considered as an inflammatory disorder of the central and peripheral nervous systems.
- c) The clinical evolution is relapsing remitting for most of the patients.
- d) Computed tomography (CT) is the imaging modality of choice to monitor the lesion load.
- e) Magnetic resonance imaging (MRI) can quantify microstructural alterations outside of focal lesions.

**19. In the context of translational research, in vivo imaging:**

- a) can be used to explore patients with a specific disease but also the corresponding animal model.
- b) can be helpful to test in patients a hypothesis coming from animal data.
- c) can be used in the animal model to understand the underlying histological modifications associated with signal changes observed in patients.
- d) can take advantage of several modalities such as magnetic resonance imaging (MRI), computed tomography (CT) or positron emission tomography (PET).
- e) is done under anesthesia in rodents.

**20. Diffusion weighted imaging (DWI) of the brain with magnetic resonance imaging (MRI):**

- a) Provides images sensitive to the diffusion of a contrast agent injected intra-venously.
- b) Provides images sensitive to the blood flow.
- c) Provides images sensitive to the thermal agitation of water.
- d) Can show restricted or accelerated water movements.
- e) Indirectly provides specific information on the microscopy of the tissue.

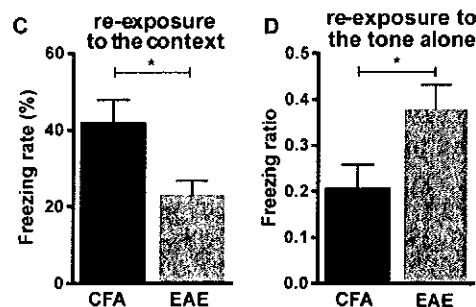
**21. Diffusion weighted imaging (DWI) of the brain with magnetic resonance imaging (MRI):**

- a) Is based on the application of symmetric gradients of diffusion on top of a standard anatomical imaging scheme.
- b) The apparent diffusion coefficient quantifies the diffusion at the voxel level.
- c) The diffusion metrics will be impacted by the isotropic or anisotropic behavior of the tissue.
- d) Fractional anisotropy is higher in isotropic tissue than in anisotropic tissues.
- e) White matter fibers are the main source of anisotropy in the brain; a property that is used for fiber tracking application.

**22. Considering that multiple sclerosis (MS) is a demyelinating disorder secondary to focal infiltration of immune cells (plaques), what could be expected from diffusion weighted imaging (DWI) in MS:**

- a) Some acute plaques could show restriction of diffusion because of water hindrance by inflammatory cells.
- b) Some acute plaques could show restriction of diffusion because of the demyelination.
- c) Some plaques could show acceleration of diffusion because of demyelination.
- d) Acceleration of diffusion, if observed, is usually driven by an increase of radial diffusivity.
- e) Acceleration of diffusion, if observed, is usually driven by an increase of axial diffusivity.

**23. In order to quantify memory performances in an animal model of multiple sclerosis, we performed a contextual fear condition paradigm in which a discrete tone is also presented but with a pseud random distribution (tone-footshock unpaired). EAE represents the group of mice with the experimental autoimmune encephalitis (the rodent model of multiple sclerosis); CFA represents the control group. Based on the results below you can conclude that:**



- a) EAE mice showed a deficit in the identification of the environment in which they previously received footshocks.
- b) EAE mice showed a deficit in the identification of the tone as the predictor of the shock.
- c) The functional integrity of the hippocampus of EAE mice might be impaired.
- d) The functional integrity of the amygdala of EAE mice might be impaired.
- e) The results cannot be interpreted because EAE mice might have motor deficit that can bias the results.

**24. Autism is a pervasive developmental disorder which appears:**

- a) after 6 years old
- b) after 9 years old
- c) after 7 years old
- d) after 10 years old
- e) during early childhood.

**25. Autism diagnosis is based on:**

- a) imaging data
- b) genetic data
- c) metabolomic data
- d) blood data
- e) clinical examination.

**26. Autism can be associated to:**

- a) genetic diseases
- b) epilepsy
- c) motor disorder
- d) language disorder
- e) hyperactive and attentional deficit disorder.

**27. In Autism:**

- a) social cognition is preserved
- b) sensori-perception can be altered
- c) eye-tracking studies can be used to measure gaze orientation
- d) eye-tracking studies can be used to measure pupil dilatation
- e) cortical ERP have evidence atypical auditory cortical activation

**28. In autism**

- a) Psychotropic drugs are used to cure autism
- b) Social rehabilitation program are proposed to young children
- c) The effectiveness of therapies is based on brain plasticity
- d) 20 % of patients have very positive outcome
- e) Pharmacological drugs can be used to treat emotional dysregulation disorder

**29. In autism**

- a) Hyporeactivity to vocal sounds is observed
- b) Lack of eye contact is one of the earliest signs
- c) 1 000 genes may be involved
- d) Abnormal brain cytoarchitecture is observed on MRI
- e) Brain overgrowth is observed in the first two years of life in some cases

**30. The prefrontal cortex encompasses different regions :**

- a) A premotor region
- b) A temporal region
- c) An orbitofrontal region
- d) A cingulate region
- e) A premotor region

**31. The dorsolateral prefrontal cortex is concerned with tasks that require :**

- a) Long-term memory
- b) Short-term memory
- c) Procedural memory
- d) Consciousness of information processing
- e) Neural mechanisms of praxis

**32. Working memory involves:**

- a) A phonological loop
- b) A visual sketchpad
- c) Auditory information processing
- d) The anterior cingulate cortex
- e) A central executive system

**33. The orbitofrontal cortex is involved**

- a) in motivational aspects of behavior
- b) in socialization
- c) in cognitive flexibility
- d) in decision-making
- e) in contest-dependent-behaviour

**34. The anterior cingulate cortex**

- a) Has a cognitive and an affective part
- b) Plays a role in explicit memory
- c) Its lesion could induce visual troubles
- d) Plays a role in attentional processes
- e) Is involved in the pathophysiology of Tourette's syndrome

**35. Attention Deficit Hyperactivity Disorder:**

- a) Is an heterogeneous disorder
- b) Is characterized by hyperactivity-impulsivity
- c) Is characterized by stereotypies
- d) Is never present during adulthood
- e) Is often comorbid with other disorders

**36. Attention Deficit Hyperactivity Disorder:**

- a) Is a neurodevelopmental disorder
- b) Has a genetic component
- c) Has an environmental component
- d) Is a social construct
- e) Can be diagnosed through neuroimaging

**37. The following comorbidities can associate with Attention Deficit Hyperactivity Disorder:**

- a) Emotional dysregulation
- b) Oppositional Defiant Disorder
- c) Depression
- d) Motor disorder
- e) Sleep disorder

**38. Evolution with age of Attention Deficit Hyperactivity Disorder:**

- a) can lead to higher rates of addictions
- b) can lead to higher rates of obesity
- c) can be associated with other neurodevelopmental disorders
- d) can be associated with higher rates of psychopathological problems
- e) Always get worse

**39. The link between Attention Deficit Hyperactivity Disorder and addictions:**

- a) Can be due to a common vulnerability
- b) Can result from reverse causality
- c) Is present only in the case of comorbid behavioral disorders
- d) Is present only in females
- e) Is rare

**40. Attention Deficit Hyperactivity Disorder and bipolar disorder:**

- a) Are never comorbid
- b) Do not overlap in their symptoms
- c) Are sometimes difficult to distinguish
- d) Can share the symptom of emotional dysregulation
- e) All answers are correct

# PHYSIOPATHOLOGIE EN NEUROLOGIE ET PSYCHIATRIE

**Vendredi 7 Décembre**

Durée totale de l'examen : 2 heures

Vous devez répondre aux QCMs et À UN SEUL des deux autres sujets (topic 1 **ou** topic 2).  
PENSEZ à indiquer votre numéro d'étudiant sur le feuillet de réponse (pages 2).

Total examination duration: 2 hours

You must respond to the MCQ exam and to ONLY ONE of the two other exams topics (topic 1 **OR** topic 2). REMEMBER to indicate your student number on page 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.

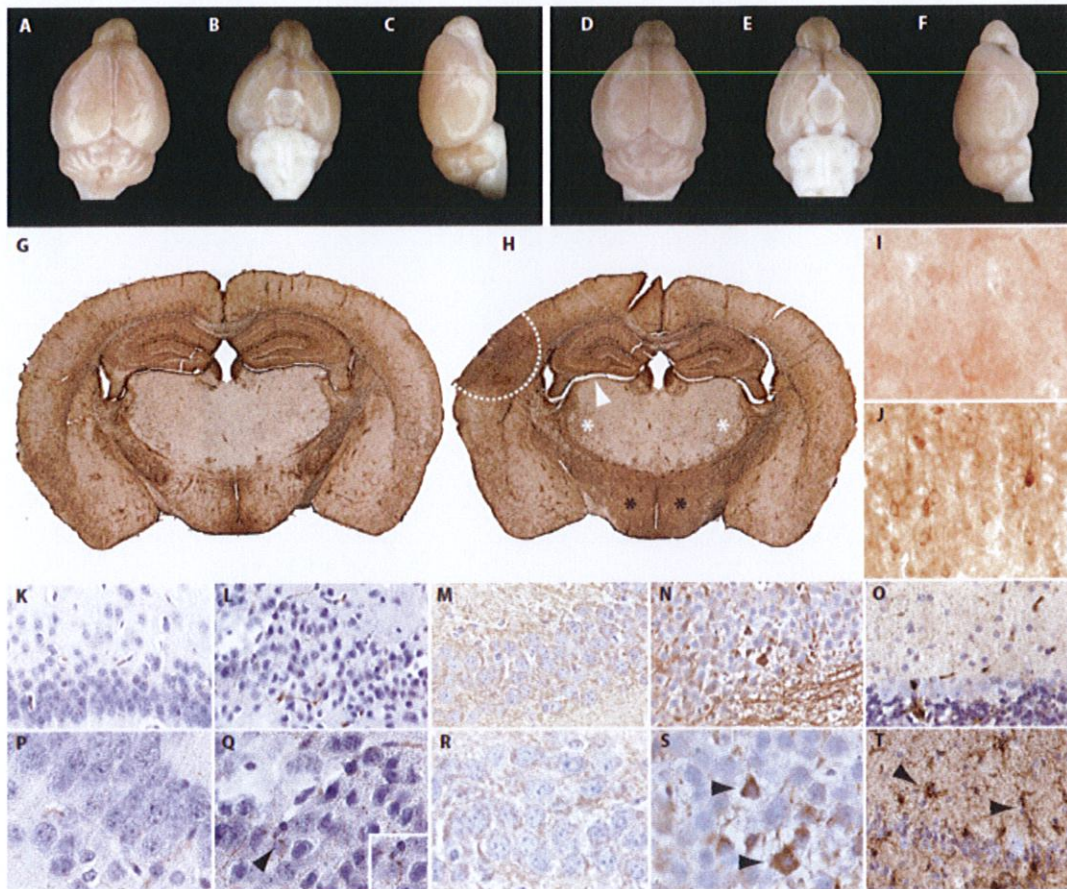
Indicate with a cross the correct response(s) for each question. Each question could have several correct answers. Make sure that your answer is clearly marked.

From Paper: Lee E Goldstein et al Sci Transl Med 4, (2012)

## RESEARCH ARTICLE

## TRAUMATIC BRAIN INJURY

### Chronic Traumatic Encephalopathy in Blast-Exposed Military Veterans and a Blast Neurotrauma Mouse Model



Downloaded from stm.sciencemag.org on May 16, 2012

**Fig. 3.** Single-blast exposure induces CTE-like neuropathology in wild-type C57BL/6 mice. (A to F) Absence of macroscopic tissue damage (contusion, necrosis, hematoma, or hemorrhage) 1 day (A to C) or 2 weeks (D to F) after exposure to a single blast. Experimental blast conditions were compatible with 100% survival and full recovery of gross locomotor function. (G) Normal astrocytic glial fibrillary acidic protein (GFAP) immunoreactivity in a mouse brain 2 weeks after exposure to sham blast. Whole-mount sections. (H) Increased astrocytic GFAP immunoreactivity in the ipsilateral cortex (area enclosed by white hash line), bilateral thalamus (white asterisks), and bilateral hypothalamus (black asterisks) 2 weeks after single-blast exposure. Parenchymal atrophy with ventricular dilation was also observed (white arrowhead). Whole-mount sections. (I) Background phosphorylated tau (CP-13) immunostaining in superficial layers of the cerebral cortex 2 weeks after exposure to sham blast. (J) Phosphorylated tau (CP-13) immunostaining in superficial layers of the cerebral cortex 2 weeks after exposure to a single blast. Increased accumulation of phosphorylated tau in the brains of blast-exposed mice was confirmed by quantitative immunoblot analysis (Fig. 5). (K and P) Background phosphorylated neurofilament

(SMI-31) immunostaining in the hippocampus 2 weeks after exposure to sham blast demonstrating normal-appearing CA1 pyramidal neurons with no detectable axonal pathology. (L and Q) Increased phosphorylated neurofilament (SMI-31) immunostaining in the hippocampus 2 weeks after exposure to single blast demonstrating pyknotic CA1 pyramidal neurons with nuclear smudging and injured axons with beaded, irregular swellings [arrowhead, (Q); enlargement shown in inset]. (M and R) Faint total tau (Tau-46) immunoreactivity in the soma and processes of pyramidal neurons in the hippocampal CA1 field 2 weeks after exposure to sham blast. (N and S) Increased total tau (Tau-46) immunoreactivity in the soma and processes of pyramidal neurons [arrowheads, (S)] in the hippocampal CA1 field 2 weeks after exposure to single blast. Biochemical abnormalities in total tau expression in the brains of blast-exposed mice were confirmed by quantitative immunoblot analysis (Fig. 5). (O) Faint activated microglial [*Ricinus communis* agglutinin (RCA)] immunoreactivity in the cerebellum 2 weeks after exposure to sham blast. (T) Increased activated microglial RCA immunoreactivity in the cerebellum indicative of brisk microgliosis [arrowheads, (T)] 2 weeks after exposure to single blast.

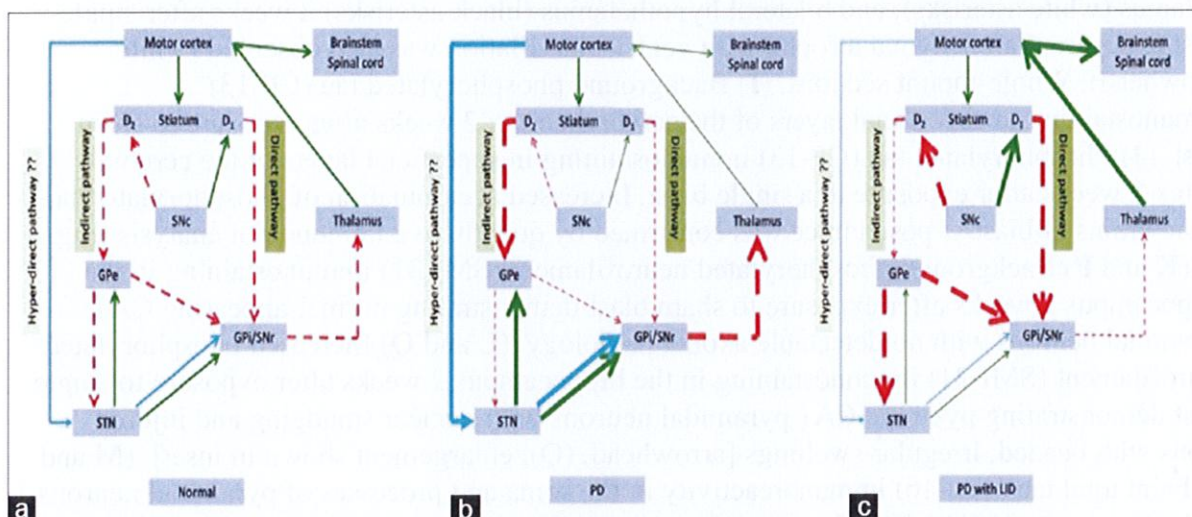
**Question:**

**Please describe the main results obtained in this plate in a model of the blast injury reproducing chronic traumatic encephalopathy (CTE). And from this description propose additional experiments supporting these observations and a discussion of these results in the scientific context linking CTE and neurodegenerative diseases.**

**You can find a copy of Fig. 3 legend on page 6 of this document.**

**Question:**

Comment this figure and briefly explain the pathophysiology of dyskinesia in Parkinson's disease. Comment more specifically the role of the hyper-direct pathway in the different schemas.



The models of basal ganglia in normal condition, Parkinson's disease and Parkinson's disease with levodopa-induced dyskinesia.

(a) The model of basal ganglia in normal condition.

(b) In Parkinson's disease (PD).

(c) After long-term administration of levodopa concomitant with more degree of loss of striatal dopamine.

PD = Parkinson's disease; LID = levodopa-induced dyskinesia; GPe = Globus pallidus externa; GPi = Globus pallidus interna; SNc = substantia nigra pars compacta; SNr = substantia nigra pars reticulata; STN = Subthalamic nucleus; Green arrow = excitatory output; Red arrow with dashed line = inhibitory output

**Fig. 3 Legend copy (from Topic n°1)**

Single-blast exposure induces CTE-like neuropathology in wild-type C57BL/6 mice. (A to F) Absence of macroscopic tissue damage (contusion, necrosis, hematoma, or hemorrhage) 1 day (A to C) or 2 weeks (D to F) after exposure to a single blast. Experimental blast conditions were compatible with 100% survival and full recovery of gross locomotor function. (G) Normal astrocytic glial fibrillary acidic protein (GFAP) immunoreactivity in a mouse brain 2 weeks after exposure to sham blast. Whole-mount sections. (H) Increased astrocytic GFAP immunoreactivity in the ipsilateral cortex (area enclosed by white hash line), bilateral thalamus (white asterisks), and bilateral hypothalamus (black asterisks) 2 weeks after single-blast exposure. Parenchymal atrophy with ventricular dilation was also observed (white arrowhead). Whole-mount sections. (I) Background phosphorylated tau (CP-13) immunostaining in superficial layers of the cerebral cortex 2 weeks after exposure to sham blast. (J) Phosphorylated tau (CP-13) immunostaining in superficial layers of the cerebral cortex 2 weeks after exposure to a single blast. Increased accumulation of phosphorylated tau in the brains of blast-exposed mice was confirmed by quantitative immunoblot analysis (Fig. 5). (K and P) Background phosphorylated neurofilament (SMI-31) immunostaining in the hippocampus 2 weeks after exposure to sham blast demonstrating normal-appearing CA1 pyramidal neurons with no detectable axonal pathology. (L and Q) Increased phosphorylated neurofilament (SMI-31) immunostaining in the hippocampus 2 weeks after exposure to single blast demonstrating pyknotic CA1 pyramidal neurons with nuclear smudging and injured axons with beaded, irregular swellings [arrowhead, (Q); enlargement shown in inset]. (M and R) Faint total tau (Tau-46) immunoreactivity in the soma and processes of pyramidal neurons in the hippocampal CA1 field 2 weeks after exposure to sham blast. (N and S) Increased total tau (Tau-46) immunoreactivity in the soma and processes of pyramidal neurons [arrowheads, (S)] in the hippocampal CA1 field 2 weeks after exposure to single blast. Biochemical abnormalities in total tau expression in the brains of blast-exposed mice were confirmed by quantitative immunoblot analysis. (O) Faint activated microglial [Ricin communis agglutinin (RCA)] immunoreactivity in the cerebellum 2 weeks after exposure to sham blast. (T) Increased activated microglial RCA immunoreactivity in the cerebellum indicative of brisk microgliosis [arrowheads, (T)] 2 weeks after exposure to single blast.