

LOCATION: SWANSEA

LLEOLIAD: ABERTAWE

LEVEL 5

LEFEL 5

EXAMINATION PERIOD
MAY 2024

CYFNOD ARHOLIADAU
MAI 2024

MODULE CODE: ECPS5003
THE BRAIN, BIOLOGY, AND COGNITION

TIME: 2 HOURS

THIS PAPER CONSISTS OF THREE SECTIONS. YOU SHOULD:

ANSWER FOUR QUESTIONS OUT OF FIVE IN SECTION A

ANSWER THREE QUESTIONS OUT OF FIVE IN SECTION B

ANSWER TWO QUESTIONS OUT OF FIVE IN SECTION C

ALL answers must be written in your exam booklet.

Please clearly indicate the section and question number of each question attempted.

Equipment or materials required – None

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SECTION A: ANSWER FOUR QUESTIONS OUT OF FIVE

1. List any five major external features of a neuron (5 marks).

- Any five of the following: Cell membrane, Dendrites, Axon Hillock, Myelin, Nodes of Ranvier, Cell body, Buttons, Synapse.

2. List any five structures of the eye (5 marks).

- Any five of the following: Eye muscle, Ligament, Iris, Pupil, Lens, Cornea, Ciliary muscle, Sclera, Retina, Optic nerve, Blind spot, Fovea

3. List the five major classes of anxiety disorders (5 marks).

- Generalised, Phobic, Panic, Obsessive-compulsive, Posttraumatic stress

4. List the five main symptoms of Grand mal seizures (5 marks).

- Grand mal: Loss of consciousness, loss of equilibrium, Tonic-clonic convulsions, Rigidity (tonus), Tremors (clonus).

5. List any five tests from the Common Neuropsychological Test Battery (5 marks).

- Any of the following: The Wechsler Adult Intelligence Scale (WAIS), or any of the WAIS sub tests, Digit span, Token test, Sodium Amytal test, dichotic listening

SECTION B: ANSWER THREE QUESTIONS OUT OF FIVE

1. Describe the process for conducting clinical trials to test new medication (10 marks).

- Translational research – basic research (discovery of the drug, efficient synthesis, testing with animal models – 5 years) - then approval from government agency (1 year), then 3 phases to human clinical trials: screening for safety and finding max safe dose (1.5 years), establishing testing protocol – effective doses and schedule of treatment – 2 years), and final testing (clear demonstration drug is therapeutic – 3.5 years). Then application to begin marketing and review results of clinical trials by government agency (1.5 years), then sell to the public with recovering development costs and continue to monitor safety.

2. Compare and contrast Positron Emission Tomography (PET) with functional Magnetic Resonance Imaging (fMRI) to examine the brain (10 marks).

- fMRI provides images of brain structure and activity, uses strong magnetic field, two properties of oxygenated blood allow it to work. 1. Active areas of the brain take up more oxygenated blood than needed. 2. Oxygenated blood has magnetic properties through the iron, Structure is imaged using waves emitted by hydrogen ions, Function is imaged using signal created from interaction between oxygen and iron in the blood: Blood Oxygenated Level Dependent (BOLD) signal, Good spatial and temporal resolution, Produces 3D images of activity over the whole brain, But only provides indirect measure of neural activity through BOLD, Also, the 2 to 3 seconds to create image is too slow to capture neural responses e.g., action potentials that happen in milliseconds.

3. Describe the four main methods used to lesion the brain (10 marks).

- Aspiration lesions: lesion to an area accessible to the eyes and instruments of the surgeon, cortical tissue is drawn off by suction through a glass pipette.
- Radio-frequency lesions: place radio-frequency current through tissue from an electrode. Heat from the current destroys tissue, with the size & shape of lesion determined by duration & intensity of current.
- Knife cuts: involves cutting nerves or tracts. Blade enters & swivels out to make the cut.
- Cryogenic blockade: involves implanting cryoprobe in brain then pumping coolant through the system. Neurons are cooled to such a degree that they stop firing, but temperature is maintained above freezing to avoid structural damage. When tissue is allowed to warm back up, normal neural activity resumes.

4. Describe the neuropathology of Alzheimer's Disease (10 marks).

- Three defining characteristics: Neurofibrillary tangles, amyloid plaques, neuron loss, especially in amygdala, entorhinal cortex, and hippocampus.
- Neurofibrillary tangles: thread tangles of protein in neural cytoplasm.
- Amyloid plaques: clumps of scar tissue of degenerating neurons and a protein called amyloid.
- Both prevalent in medial temporal lobe structures (amygdala and hippocampus - role in memory).
- Both prevalent in inferior temporal, posterior parietal, and prefrontal cortex (complex cognitive functions).
- Genetic component & acetylcholine decline is early sign

5. Explain how lateral inhibition assists us in our perception of edges (10 marks).

- Edges define extent and position of all objects - where 2 different areas of a visual image meet.
- Perception of edge is perception of contrast between 2 adjacent areas in the visual field.
- To enhance contrasts, our visual system creates non-existent stripes called:
- Mach bands
- Makes edges easier to see
- Consequence of lateral inhibition
- Intensity graph shows what is there:
- Series of stripes of differing intensities.
- But we see brightness changing from darker to lighter.
- Next to each edge, brighter stripe looks brighter than is & darker stripe looks darker.
- When receptor is illuminated by light, it fires & inhibits other receptors around it from firing.
- Contrast enhancement is firing rate of receptors on each side of edge.
- E.g., receptor D fires more than others intensely illuminated (A,B,C) because it's next to edge between intense & dim light.
- While E fires less than others (F,G,H) because it's next to edge between 2 types of lighting but on dim side.

SECTION C: ANSWER TWO QUESTIONS OUT OF FIVE

1. Describe the symptoms of schizophrenia and critically discuss the dopamine theory of schizophrenia (25 marks).

“Splitting of psychic functions” • Breakdown of integration of emotion, thought, action

- Affects ~1% of the population
- Diverse & complex: multiple types with varied profiles
- Can overlap with other psychiatric disorders & even change during progression.
- Symptoms can be classed as either:
 - Positive: represent an excess or distortion of normal function
 - Negative: represent a reduction or loss of normal function.

• Positive symptoms: 1. Delusions (of being controlled, persecution, or grandeur), 2. Hallucinations (imagine voices), 3. Inappropriate affect (incorrect emotions for context), 4. Incoherent speech/thought, 5. Difficulty performing everyday tasks, 6. Lack of personal hygiene

• Negative symptoms: 1. Affective flattening (absence of emotional expression), 2. Alogia (no speech), 3. Avolition (absence of motivation), 4. Anhedonia (unable to experience pleasure).

Causal Factors in Schizophrenia • Evidence for a genetic contribution • Inherit an increased risk for the disorder but experience may also influence it developing • Multiple causes • Several different chromosomes implicated • Associated with various early issues – birth complications, infections, autoimmune reactions, toxins, traumatic injury, stress • Interference with usual development of susceptible individuals may lead to the disorder.

Discovery of the First Antipsychotic Drugs • Chlorpromazine: originally developed as antihistamine to counteract swelling from surgery • Surgeons noticed its calming effect, so given to calm agitated schizophrenics & to activate emotionally blunt schizophrenics • Does not cure schizophrenia, just reduces severity. • Reserpine: also found to be effective, but no longer used due to dangerous side effects. • Although chemical structure of both were different, their effects were similar (i.e., no effect for 2-3 weeks, also Parkinson-like motor effects were seen), suggesting they were both working through the same mechanisms.

Dopamine Theory of Schizophrenia • 1960 – link between dopamine and Parkinson’s disease established • Striatum depleted of dopamine, suggesting disruption of dopaminergic transmission might produce Parkinson’s disease. • Due to this & already established relationship between symptoms of Parkinson’s & antischizophrenic effects of chlorpromazine and reserpine, it was suggested anti-schizophrenic drug effects are produced in same way. • Led to development of dopamine theory – too much dopamine causes schizophrenia & conversely, anti-schizophrenic drugs exert effects by decreasing dopamine levels.

• Supported by fact that: • Reserpine depletes brain of dopamine and other monoamines by making vesicles leaky • Chlorpromazine antagonizes dopamine activity by binding and blocking dopamine receptors – So, both antagonize transmission of dopamine but in different ways. Lack of activity at postsynaptic receptors sends feedback signal to presynaptic cells to increase release of dopamine. • This led to revision of the dopamine theory • Instead of high dopamine levels, the main factor is the high levels of activity at dopamine receptors. • 1970s: degree to which various antischizophrenia drugs bind to dopamine receptors was assessed. • Radioactively labelled dopamine added to samples of dopamine-receptor-rich neural membrane obtained from calf striatum • Unbound dopamine molecules rinsed away & amount of radioactivity left was measured to obtain number of dopamine receptors. Drugs ability to block binding of radioactive dopamine was assessed - assumed drugs with high affinity for dopamine receptors would leave fewer sites available for the dopamine. • Chlorpromazine & others

had high affinity for dopamine receptors whereas ineffective drugs had low affinity..... • Except for haloperidol: very potent but had low affinity. • Solution: came from discovery that dopamine binds to more than one receptor subtype – 5 have been identified. • Chlorpromazine & others bind effectively to D1 & D2 receptors, whereas haloperidol bind effectively to D2 but not to D1. • This discovery led to further revision suggesting schizophrenia is caused by hyperactivity at D2 receptors rather than dopamine receptors in general. Limitations of the Dopamine Theory • Four key discoveries about the neural basis of schizophrenia cannot be explained by the D2 theory. 1. Other receptors are involved: glutamate, GABA, serotonin. • Evidence from studies on LSD, which produce schizophrenia-like symptoms by acting on serotonin & glutamate receptors. • Atypical neuroleptics, such as clozapine has affinity for D1, D4, & serotonin receptors but not for D2. 2. Neuroleptics block D2 receptors within hours but it takes weeks to alleviate symptoms. • Time difference suggests blockage of D2 receptors is not only aspect involved. Limitations of the Dopamine Theory 3. Schizophrenia is associated with widespread brain damage, & meta-analysis of studies has shown reduced volume in 50 different brain regions. • Two aspects about pattern of brain damage observed that causes problems for the dopamine theory: A. Little evidence of damage to dopamine circuits B. Theory does not explain why there is diffuse damage 4. Neuroleptics only marginally effective. • If dopamine theory was correct neuroleptics should be effective to treat all patients. • They only help with some symptoms not others: • Conventional neuroleptics (D2 blockers) are effective for positive symptoms, while negative symptoms might be caused by brain damage.

2. Critically discuss the effects of drugs, such as Heroin, on brain functioning and cognitive processing (25 marks).

Drug tolerance: People can become tolerant of a drug, where they experience decreased sensitivity to the drug due to repeated exposure. • Demonstrated in 2 ways: either dose has less effect than before, or it takes more of the drug to produce the same effect. • Drug tolerance = shift in dose-response curve: a graph of the magnitude of effect of different doses of the drug to the right. 3 aspects about the specificity of drug tolerance 1. Cross tolerance – one drug can produce tolerance to similar drugs – e.g., alcohol & benzodiazepines. 2. Tolerance often develops to some effects & not others of a drug. Can also have an “inverse tolerance,” or sensitization. 3. Drug tolerance is not a unitary phenomenon – no single mechanism underlies all examples of tolerance. 2 categories of changes that underlie drug tolerance: Metabolic and Functional Drug withdrawal: Sudden elimination triggers adverse physiological reaction: withdrawal syndrome • Body makes changes to compensate for drug’s presence – functions normally with drug present • Withdrawal effect is usually opposite to the initial effect of the drug • Suggests withdrawal effect may be produced by same neuronal changes that produce drug tolerance. Relation between Drug Tolerance and Withdrawal Effects Longer exposure to greater doses followed by rapid elimination produces greater withdrawal effects. Addiction: “Addicts” continue to use a drug despite adverse effects on health, cognition, and social life and despite repeated efforts to stop. Many equate addiction and physical dependence: – They see addicts as trapped in cycle of drug taking, withdrawal, & further drug taking to combat withdrawal • But this is inconsistent with evidence • Addicts sometimes take drugs to alleviate/prevent withdrawal symptoms but it is not the major factor. • However, addicts often start taking their drug again even after months or years without it.

Role of learning: Research suggests learning and cognition plays role in drug tolerance • Focus has been on two phenomena: 1. Contingent drug tolerance: tolerance develops only to drug effects that are actually experienced. 2. Conditioned drug tolerance: tolerance effects are maximally expressed only when a drug is administered in same situation it has previously been administered. Conditioned Tolerance and Withdrawal: Situational specificity of drug tolerance • Siegel et al. addicts are susceptible to lethal effects of drug overdose when the drug is administered in a new context. • Hypothesis: addicts become tolerant when repeatedly self-administer drug in same environment, thus take larger doses to counteract diminution of drug effect. • If they administer huge dose in new situation, tolerance effects are not present to counteract effects of the drug. • Research evidence: Siegel et al. many more heroin-tolerant rats died following high dose of heroin administered in a novel situation than died in the usual injection environment.

Effects of opioids: Desire to avoid withdrawal adds to motivation to use & tolerance encourages use of higher doses. • Withdrawal symptoms begin 6-12 hours after last dose & include restlessness, pacing, fidgeting, eyes watering, runny nose, yawning, sweating, sleep fits • Once awake they experience chills, shivering, nausea, vomiting, diarrhea, cramps, dilated pupils, tremor, muscle pains and spasms. • Many health hazards related to use of dirty Page 8 of 10 needles & poorly processed “street” versions. • Death from overdose by suppressing breathing. • Main treatment: Methadone (an opiate itself) • Binds to opiate receptors, but... • Produces less pleasure than heroin • Administered orally • Prevents withdrawal • Buprenorphine: similar but longer lasting • Substitute less dangerous drug for abused drug. Dopamine and drug addiction: Following research on role of dopamine in intracranial selfstimulation, studies implicated dopamine in the rewarding effects of neural reinforces and addictive drugs. • E.g., in rats dopamine antagonists blocked self administration of, or the conditioned preference for several types of addictive drugs & reduced reinforcing effects of food. • Findings from research suggest dopamine signals something similar to reward value or pleasure and the nucleus accumbens appears to play a key role in this. 1. Lab animals would self-administer microinjections of addictive drugs directly into nucleus accumbens. 2. Microinjection of drugs into nucleus accumbens produced conditioned place preference for compartment where they were administered. 3. Lesions to either nucleus accumbens or ventral tegmental area blocked self-administration of drugs into general circulation or the development of drug associated conditioned place preferences. 4. Both self-administration of addictive drugs & experience of natural reinforcers were found to be associated with elevated levels of extracellular dopamine in the nucleus accumbens. Volkow et al. administered various doses of radioactively labelled cocaine to addicts and asked to rate the high. – Used PET to measure degree to which the labelled cocaine bound to dopamine transporters. – Intensity of high experienced correlated with degree to which cocaine bound to dopamine receptors – No high was experienced unless the drug bound to 50% of the dopamine transporters. • Healthy non-addicted humans given amphetamine injection. – As dopamine levels in nucleus accumbens increased in response to injection, Ps reported increase in euphoria. But reward is a complex process with many psychological components – so what exactly is the role in reward of dopamine release in the nucleus accumbens. • Extracellular dopamine levels in the NA increase following presentation of a natural reward (e.g., food or addictive drug) • Ventral tegmental neurons, which release dopamine into the NA fire in response to a stimulus at a rate proportional to its reward value. • Dopamine released in the NA is related to the expectation of reward rather than to the experience itself. Critical review: Addiction is psychologically complex • Addicts show poor decision making & lack of self control, suggestive of prefrontal cortex role • Drug addiction may be related to other nonadaptive behaviors, e.g., compulsive eating, gambling, sexual behavior, kleptomania, etc. • Other neurotransmitters also involved: glutamate, endogenous

opioids, norepinephrine, GABA, and endocannabinoids. Current research not in complete agreement but there is consensus other areas are involved in... 1. Initial drug taking: mediated in same way as pleasure activity, with the mesocorticolimbic pathway (particularly nucleus accumbens playing a key role). – But it does not act alone – Instead it interacts with 3 other areas: • Prefrontal lobes (role in decision making); • Hippocampus: provides info about previous experiences; • Amygdala: coordinates positive and negative reactions. Craving & compulsive drug use: repeated consumption brings major changes in motivation as addict develops habit & compulsion despite adverse effects. – Due to direct neural response to repeated exposure of drug-induced pleasure and as product of conditioned response to drug-associated cues. – Several changes in brain's response contribute to development of addiction: • Change in how striatum reacts to drugs, which spreads from the NA to the dorsal striatum, which is known to play a role in habit formation. • At same time the prefrontal cortex in controlling behavior declines & stress circuits in hypothalamus begin to interact with dorsal striatum. • Development of addiction is a pathological neuro-plastic response. Relapse – thought to be triggered by 3 factors: • Stress – drug use as a coping mechanism • Priming – a single exposure leads to a relapse • Environmental cue – certain people, times, places, objects previously associated with the drug • Evidence from animal studies shows: – Prefrontal cortex mediates priming-induced relapse, – Amygdala mediates condition cue induced relapse, – Hypothalamus mediates stress-induced relapse.

3. With reference to the binding problem, critically discuss visual functional specialisation and explain what this means for visual cognition (25 marks).

Zeki's work with animals, distinction of V1,2,3,4,5, brain imaging research (both showing activity in particular brain area thought to deal with specific type of visual stimuli (e.g., present Ps with colour vs. black and white version of film to assess activity in V4), research with patients who have brain damage to specific areas and subsequently show visual deficit linked to that area (e.g., V4 Achromatopsia, V5 Akinetopsia) – but also key to discuss when there is damage to area but no corresponding visual deficit. Binding problem – the different types of binding problems (e.g., work of Treisman, Feldman) and evidence from cognitive psychology, including role of attention. Critique that there is no binding problem (DiLollo). Most importantly must always link back to the last part of the question – what does all this mean for visual cognition – how do we see in a coherent whole if different visual properties are processed in different brain areas?

4. Critically discuss whether biopsychological paradigms of animal behaviour are useful for understanding the human brain and cognition (25 marks).

Assessment of Species-common behaviours: those displayed by all members of the species: e.g., grooming, eating, building nests, etc.). • Main tests 1. Open-field test: place animal in empty chamber & record activity (does it move around or stay close to wall, how much

droppings it produces, etc.). 2. Tests of Sexual Behaviour. 3. Tests of Aggressive and Defensive Behaviour: Colony-intruder paradigm: examine no. of combat encounters between dominant alpha male of established colony & smaller male intruder. • Dominant alpha is aggressive: biting, putting hair upright. • Intruder is defensive: goes up on back legs to defend from biting & tries to push alpha away with its front paws. • Elevated plus maze: a maze mounted 50cm from the ground, two arms of maze have sides while other two do not • Amount of time rat spends in closed arms rather the open edge arms is compared. • Giving rat anti-anxiety drugs increases amount of time spent in open arms of maze: used for understanding usefulness of anti-anxiety drugs in humans? 4. Traditional Conditioning Paradigms: • We can infer about the sensory, motor, motivational, and cognitive state of an animal from its ability to learn and perform various responses. • Pavlovian conditioning (pairing an unconditioned stimulus with a conditioned stimulus) • Operant conditioning & reinforcement. Semi-natural Animal Learning Paradigms: 5. Conditioned Taste Aversion: pairing something that makes an animal ill with food so they learn to avoid it. • This really challenged traditional learning paradigms because taste aversion can be established after a single trial. 6. Radial Arm Maze: place food at the end of the same arms. • Rat learns not to bother looking in the other arms. • Shows their spatial ability is good because all the arms look the same, so they have to orientate themselves to the whole room. • When the maze is rotated their performance is disrupted. 7. Morris Water Maze: rat must find hidden escape platform in an opaque pool of water. • Even when rat is placed in different places around the pool it quickly learns route, using spatial cues from the room. • Brain lesions disrupt ability and in severe cases the rat can be swimming around in circles for a long time even if they are placed in the same starting point on a trial where they successfully found the platform previously. 8. Conditioned Defensive Burying: give rat a single aversive stimulus (e.g., a shock/blast of air) delivered from an object. • They then spray their bedding/hay at the object to cover it. • Anti-anxiety drugs decrease amount of burying behaviour.

5. With reference to the lesion paradox, critically discuss the role of the hippocampus in memory functioning (25 marks).

Spiers et al. (2001): 147 cases of amnesia with damage to hippocampus or fornix.

Episodic memory impaired in all cases

Fewer issues with semantic memory

Vargha-Khadem et al. (1997): Two patients with bilateral hippocampal damage

Poor episodic but normal range semantic memory.

Considered as stronger evidence as damage occurred at age before semantic memory developed.

Episodic memory depends on hippocampus

Semantic memory depends on entorhinal, perirhinal, and parahippocampal cortices.

Damage to hippocampus and cortices leads to episodic & semantic deficits (Vargha-Khadem et al., 1997)

Damage only to hippocampus leads to greater deficits in episodic memory (Bindschaedler et al., 2011).

Greater retrograde amnesia for episodic memory compared to semantic memory (Bayley et al., 2006)

Theory to explain retrograde amnesia:

Consolidation: Long-lasting physiological “fixing” of episodic memories in the hippocampus.

Hippocampus plays role in consolidation as removal of temporal lobes disrupts formation of new memories.

Recently formed memories still being consolidated are vulnerable to interference and thus forgetting.

Perhaps hippocampus stores memories temporarily standard consolidation theory

Over time memories stored elsewhere, which protects them from hippocampal damage.

Or perhaps hippocampus stores memories permanently, but they become “stronger” over time (Multiple-trace theory: Nadel & Moscovitch, 1997).

1990s research challenged if hippocampal damage key in medial temporal amnesia.

Bilateral removal of rhinal cortex = object-recognition deficits

Bilateral removal of hippocampus = no effects on object recognition

Bilateral removal of amygdala = no effect on object recognition

Complete removal of hippocampus = moderate deficit in object recognition

But small lesions of hippocampus lead to severe deficit

How can this be?

Ischemia-induced hyperactivity of CA1 pyramidal cells damages neurons outside hippocampus (excessive release of excitatory amino acids).

Explains ischemia-induced object recognition deficits

Whereas bilateral hippocampectomy prevents ischemia-induced deficit

Supported by fMRI where rats have induced ischemia by tying carotid artery to restrict blood flow to brain

Rhinal cortex plays role in object recognition

Hippocampus plays role in spatial location memory

Many hippocampal cells are place cells, responding when in a particular place and to other cues

Grid cells also found in hippocampus and entorhinal cortex

Similar findings in Food-caching birds:

Need to remember location of food stores hidden in their territory.

Have larger hippocampus than non-food caching birds.

Primate studies inconsistent:

Perhaps discrepancies due to different testing paradigms (navigating actual env vs. sitting still/locating on computer screen).

Cognitive map theory: hippocampus constructs and stores allocentric maps of the world:

Representations of space based on relations among external objects/landmarks.

Challenges to this theory:

Firing of place cells sometimes depends on more than spatial location

Hippocampal damage sometimes impairs behavior without spatial component

Hippocampus is large/complex and component substructures require further evaluation

Diwedd/End