Physiology week 3 – Nerves VIVAs

5. a) In the synapse, where can inhibition occur? b)What are the mechanisms involved?	Post-synaptic: direct or indirect (refractory periods, after-hyperpolarisations) Pre-synaptic: mediated by neurons that end on excitatory endings (axo-axonal synapsss). i Increased Cl^- conductance – reduces Ca^{2+} influx and amount of excitatory transmitter released ii. Voltage-gated K^+ channels – K^+ also decreases Ca^{2+} entry iii. Direct inhibition of excitatory transmitter release, independent of Ca^{2+} influx	Must give pre-synaptic and post-synaptic Must give reduction in Ca^{2+} influx

QUESTION: 5. Catecholamines

Question	Required response [Key items marked with*]	To Pass
Which catecholamines act as neurotransmitters?	*Noradrenaline, *Adrenaline and Dopamine	* to pass
Describe the sequence of events at a **noradrenergic synapse**, following stimulation of a sympathetic nerve. *Prompts:* *How is noradrenaline released?* *How is noradrenaline removed from the synaptic cleft?* *What enzymes are involved in the breakdown of noradrenaline?*	Noradrenaline, which has been **stored in granulated *vesicles**, is released into the synaptic cleft by ***exocytosis.** Noradrenaline acts on postsynaptic and to a lesser extent presynaptic and glial receptors. In addition to binding to receptors, Noradrenaline is also removed from the synaptic cleft by: • ***Reuptake** into presynaptic neuron (via a Neuro Transmitter Transporter (NTT)) and then is broken down to inactive product by Monoamine Oxidase (MAO) located on mitochondria • **Broken down** to inactive product by Catechol-O-methyl transferase (COMT) located on the postsynaptic membrane	* to pass

Question 5: Serotonin (Ganong pp 106-107, 262-263)	i) What are the functions of serotonin?	a) Regulation of **vomiting reflex** b) Regulation of **mood** c) Control of respiration d) Platelet aggregation and smooth muscle contraction e) Facilitate GI secretion and peristalsis f) Regulation of circadian rhythms	C
	ii) What are the steps in synthesis and catabolism of serotonin?	i) Hydroxylation and decarboxylation of tryptophan to form serotonin ii) Released serotonin from serotonergic neurones is recaptured by an **active re-uptake mechanism and inactivated by MAO** to form 5HIAA iii) (5-hydroxyindoleacetic acid) iv) 5HIAA is excreted as a urinary metabolite	C

TOPIC: Noradrenergic neurotransmission _____ **NUMBER:** _____

OPENING QUESTION	Please describe the synthesis and release of noradrenaline at a synapse? You may draw a diagram.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1 Draw synaptic nerve ending or describe	1	
	2	2	
	3	3	
	4	4	
	5	5	
	6	6	
SECOND QUESTION (if needed)	Once it is released, how is the effect terminated?		
POINTS REQUIRED	1 Diffusion	1	
	2 Reuptake	2	
	3 MAO	3	
	4 COMT	4	
	5	5	
	6	6	
	7		
THIRD QUESTION (if needed)	What types of noradrenergic receptors are there?		
POINTS REQUIRED	1 Alpha and beta	1	

TOPIC: _____ **NUMBER:** _____

OPENING QUESTION	Please describe the synthesis and release of acetyl choline at a nerve synapse. You may draw a diagram	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1	1	
	2	2	
	3	3	
	4	4	
	5	5	
	6	6	
SECOND QUESTION (if needed)	Once it is released, how is the effect terminated?		
POINTS REQUIRED	1 Diffusion	1	
	2 Acetylcholinesterase	2	
	3	3	
	4	4	
	5	5	
	6	6	
	7		
THIRD QUESTION (if needed)	What types of cholinergic receptors are there?		
POINTS			

TOPIC: Neuromuscular transmission _____ **NUMBER:** _____

OPENING QUESTION	Describe the synthesis and release of acetyl choline at the neuro-muscular junction? You may draw a diagram.	**PROMPTS**	**COM**
POINTS REQUIRED	1 Acetyl choline formed From acetyl coenzyme A and choline, by enzyme Choline acetyl transferase at Presynaptic terminal Stored in synaptic vesicles With ATP and proteoglycan	1	
	2	2	
	3	3	
	4	4	
	5	5	
	6	6	
	7	7	
	8		
SECOND QUESTION (if needed)	Once it is released, how is the effect terminated?		
POINTS REQUIRED	1 Diffusion	1	
	2 Acetylcholinesterase	2	

	[Key items marked with*]	
What are the steps in synthesis of noradrenaline at a nerve ending? *Prompt:* *What is noradrenaline made from?*	1 **Tyrosine transported in and converted to Dopa** by tyrosine hydroxylase **(rate-limiting)** in presence of tetrahydrobiopterin 2 **Dopa converted to Dopamine** by dopa decarboxylase 3 **Dopamine** enters granulated vesicles and **converted to Noradrenaline** by dopamine beta hydroxylase 4 Noradrenaline inhibits tyrosine hydroxylase (feedback inhibition)	
What happens to noradrenaline released into a synapse? *Prompt:* *How is the effect terminated?*	1 Binds to post-synaptic receptors 2 Binds to pre-synaptic receptors 3 **Reuptake** into pre-synaptic neurons 4 **Catabolism** by monoamine oxidase (A or B) (nerve endings) and catechol-o-methyl transferase (post synaptic membrane, liver, kidneys, muscles)	
What happens to acetylcholine released into a synapse? *Prompt:* *How does it differ from noradrenaline?*	1 **No acetylcholine reuptake** 2 **Catabolism by acetyl cholinesterase** 3 Reuptake of choline 4 Catabolism by pseudocholinesterase	SPARE

TOPIC: Synthesis and fate of catecholamines at synaptic junction **NUMBER:** _____

OPENING QUESTION	**Describe the biosynthesis and storage of norepinephrine at the synaptic junction.**	**COMMENTS**
POINTS REQUIRED	1. dietary **tyrosine** mostly (some formed from phenylalanine)	
	2. tyrosine transported into catecholamine-secreting neurones by concentrating mechanism	
	3. tyrosine → **dopa** by tyrosine hydroxylase [this is the rate-limiting step & is subject to feedback inhibition by dopamine and norepinephrine] → **dopamine** by dopa decarboxylase in cytoplasm	At least 4 in correct order
	4. dopamine enters granulated vesicles → **norepinephrine** by dopamine β-hydroxylase (DBH)	
	5. norepinephrine stored bound to ATP, with protein **chromogranin A**	
PROMPTS		
SECOND QUESTION (if needed)	**How is Norepinephrine removed from the synaptic junction?**	
POINTS REQUIRED	**1. norepinephrine is removed from the synaptic junction by:** **i. binding to postsynaptic receptors** **ii. binding to presynaptic receptors** **iii. reuptake into presynaptic neurons** iv. **catabolism (MAO)**	Bolded to pass
	2. catabolism at noradrenergic nerve endings is catalysed by MAO (monoamine oxidase) and COMT (COMT mainly in liver, also at postsynaptic noradrenergic nerve endings)	
	3. norepinephrine → DOMA (3,4-dihydroxymandelic acid) & DHPG (3,4-dihydroxymandelic aldehyde) → VMA (vanillylmandelic acid) & MHPG (3-methoxy-4-hydroxyphenylglycol) by systemic COMT. These deaminated derivatives are physiologically inactive.	
PROMPTS		

.

4 a).Outline the steps in the synthesis of catecholamines	TyOHylase Tyrosine→ DOPA ↓ DOPA Decarboxylase Dopamine ↓ Dopamine βhydroxylase Adrenaline← Nor Adrenaline PNMT (adrenal medulla, some central) Adrenaline/Noradrenaline	Tyrosine to dopamine to noradrenaline, plus one of the synthesis enzymes
4 b).What happens to noradrenaline after it is released into the synaptic cleft?	Removed by post-synaptic and pre-synaptic binding, reuptake and catabolism IC) MAO ↓ COMT (EC) VMA	Three out of four processes

TOPIC: Synthesis and fate of catecholamines at synaptic junction_____ **NUMBER**: _____

OPENING QUESTION	Describe the synthesis and release of catecholamines at synapses.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	1. All neurotransmitters are synthesised in synaptic vesicles, manufactured in cell body: catecholamines are made in small, dense core vesicles. **(For an MCQ, there are 3 types of presynaptic vesicles:** • Small, clear – Ach, glycine, GABA, glutamate • Small, dense core – catacholamines • Large, dense core – neuropeptides.)		
	MCQ: Details for **Noradrenaline (NAd),** which is found at most sympathetic post ganglionic endings: 1. Phenylalanine → Tyrosine (phenylalanine hydroxylase) 2. → dops **(tyrosine hydroxylase** – subject to feedback inhibition and is the **rate limiting step**) 3. → dopamine (dopamine decarboxylase). 4. Dopamine then enters vesicles. 5. Dopamine → NAd (dopamine beta hydroxylase)		Tyrosine → dops step is essential, including its significance
	2. Released in response to action potential • AP reaches pre-synaptic terminal • Opens voltage gated calcium channels • Calcium influx • Fusion with the synaptic membrane and exocytosis is aided by several proteins including synaptobrevin and syntaxin • Vesicle fuses with cell membrane and releases neurotransmitter • Calcium removed by calcium/sodium antiport • **MCQ:** Synaptic delay = 0.5ms		
SECOND QUESTION	How is catecholamine's action at the synapse **terminated**?		

POINTS REQUIRED	1. Reuptake from the synaptic cleft is the major factor 2. Catabolism 3. Binding to receptors		Essential
	Using Noradrenaline (NAd) as the classic example, catabolism is via oxidation and methylation by MAO and COMT – catachol O methyl transferase		