

05 - 5. Serotonin

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•tryptophan → 5 hydroxy l-tryptophan → serotonin Source Source •availability of tryptophan (hence it is possible to conduct tryptophan depletion studies and manipulate 5HT system) Rate limiting step Rate limiting step •tryptophan hydroxylase Synthetic enzymes Synthetic enzymes •MAO (preferentially MAO-A) Breakdown enzymes Breakdown enzymes •5-hydroxyindoleacetic acid (5-HIAA) Breakdown product Breakdown product •Serotonin reuptake channel (tricyclics, SSRIs inhibit this) Reuptake Reuptake •mood, perception of pain, feeding, sleep-wake cycle, motor activity, sexual behaviour, and temperature regulation. Function Function •14 known subtypes of serotonin receptors (5-HT1A, 5-HT1B, 5-HT1D, 5-HT1E, 5-HT1F, 5HT2A, 5-HT2B, 5-HT2C, 5-HT3, 5-HT4, 5-HT5A, 5-HT5B, 5-HT6, and 5-HT7) •All except 5-HT3 are G-protein-coupled receptors; 5HT3 predominant in gut; associated with motility. •5-HT1A receptors – Gi coupled postsynaptic; antidepressant response; sexual behaviour •5-HT1B receptors – Gi coupled presynaptic; •5-HT1D receptors – Gi coupled - both presynaptic and postsynaptic. •5-HT2 receptors - phospholipase C coupled; postsynaptic; antagonism leads to antipsychotic response (atypicals) and sedation; LSD causes 5-HT2 stimulation; down regulation noted after antidepressant treatment / ECT. •5-HT6 may be involved in antidepressant action •5-HT7 - regulation of circadian rhythm Receptors Receptors •low serotonin levels → increased depression, aggression, suicide, and impulsivity; regulate dopamine system – role in psychosis Disorders Disorders

© SPMM Course Receptor Action 5HT1A Antidepressant (agonist), anxiolytics (partial agonist) 5HT1B Aggression 5HT1D Antimigraine (antagonist) 5HT2A Antipsychotic (antagonist); hallucinogens (agonist / partial agonist); implicated in working memory; also seen in platelets and smooth muscles 5HT2B Stimulation may produce cardiac valvular fibrosis (dexfenfluramine) 5HT2C Anxiogenic and anorexic effect (agonists) 5HT3 Antiemetic (antagonist) 5HT6 Possible antipsychotic/antidepressant action (antagonism) 5HT7 Regulation of circadian rhythm

DOPA decarboxylase (DDC) “is an enzyme implicated in 2 metabolic pathways, synthesizing two important neurotransmitters, dopamine and serotonin (Christenson et al., 1972). Following the hydroxylation of tyrosine to form L-dihydroxyphenylalanine (L-DOPA), catalyzed by tyrosine hydroxylase, DDC decarboxylates L-DOPA to form dopamine. This neurotransmitter is found in different areas of the brain and is particularly abundant in basal ganglia. Dopamine is also produced by DDC in the sympathetic nervous system and is the precursor of the catecholaminergic hormones, noradrenaline and adrenaline in the adrenal medulla”. In the nervous system, tryptophan hydroxylase produces 5-OH tryptophan, which is decarboxylated by DDC, giving rise to serotonin. DDC is a homodimeric, pyridoxal phosphate-dependent enzyme. (Excerpt from

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