Potential Pharmacological Impact on Dopamine and Serotonin Receptors

Introduction

Neurotransmitters are signaling molecules that relay information affecting cellular function in the receiving cell. They are released from the presynaptic neuron into the synapse, where they bind corresponding receptors on the postsynaptic neuron and transmit the information to help activate or block cellular functions downstream.[1] Dopamine and serotonin are 2 such neurotransmitters, each with its own unique pathways and receptors.

Understanding how dopamine and serotonin signaling may be modulated by various actions of psychopharmacologic agents may help nurse practitioners to gain insight into their roles in psychiatry.

Hypothesized Mechanisms of Drug Actions on Neurotransmitter Signaling

Agonists

Agonists are compounds that are thought to bind to receptors and activate them to the full extent. They can mimic the action of the neurotransmitter and can be used to increase neurotransmitter activity when it may be deficient.[1]

Antagonists

Antagonists are thought to bind to receptors but do not activate them. Instead, they block the receptor and prevent it from being activated by agonists or neurotransmitters, thus blocking the agonist-mediated response. Antagonists can be used to inhibit excessive neurotransmitter activity.[1]

Partial Agonists

Partial agonists can act as agonists or antagonists depending on the surrounding levels of naturally occurring neurotransmitters. For example, in the absence of a full agonist, a partial agonist can act as an agonist and activate the receptor. However, the response elicited by a partial agonist is thought to be lower than that of a full agonist. In the presence of a full agonist, however, a partial agonist can act as an antagonist and help prevent the receptors from being activated.[2]

Partial agonists have a lower intrinsic activity than full agonists. When they bind to receptors, they partially activate them, producing a response that is less than that of a full agonist. Partial agonists provide responses that are intermediate from those of agonists and antagonists.[2] Partial agonists can be useful in situations where a full response is not desired.[1]

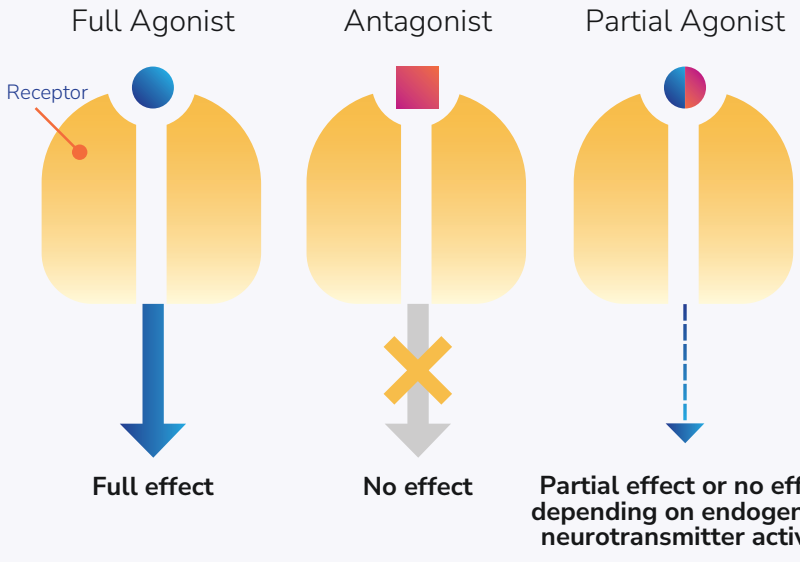

Figure 1. Drug Effect at Target Receptor. Adapted from TRC Pharmacology.[3,4]

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Example Actions and Potential Downstream Effects of Drugs Thought to Modulate Dopamine and Serotonin Activity

Drug Class	Potential Downstream Effects	Potential Adverse Effects
Dopamine Receptor Agonists	Dopamine receptor agonists are thought to help mitigate symptoms of extrapyramidal adverse effects from antipsychotics by restoring dopaminergic activity. They may also help reduce hyperprolactinemia by inhibiting prolactin release.[5]	Long-term use of dopamine receptor agonists may be associated with choreiform and dystonic movements, hallucinations, delusions, confusion, depression, and mania.[5]
Dopamine Receptor Antagonists	Dopamine receptor antagonists are thought to reduce dopamine activity. The decreased dopamine activity, particularly in the mesolimbic pathway, may help alleviate the positive symptoms of psychosis, such as hallucinations and delusions.[1]	Due to the dopamine receptor blockade in all dopamine pathways, dopamine receptor antagonists may be associated with extrapyramidal symptoms (EPS) and hyperprolactinemia.[6]
Dopamine Receptor Partial Agonists	Dopamine receptor partial agonists are theorized to act as antagonists in the mesolimbic pathway and agonists in the mesocortical pathway depending on the level and activity of endogenous dopamine in these areas of the brain. Partial dopamine agonists are also thought to be associated with reduced EPS and hyperprolactinemia since they do not completely block the dopaminergic activity in the nigrostriatal and tuberoinfundibular pathways.[2]	Dopamine receptor partial agonists may be associated with side effects such as akathisia, EPS, and metabolic changes.[7]
5-HT2A Antagonists	5-HT2A antagonists may play a role in treating dimensions of psychosis. They are thought to have an effect on negative symptoms of schizophrenia and major depression in clinical studies.[8] It is theorized that 5-HT2A receptor antagonism indirectly stimulates dopamine release in the striatum, which may potentially mitigate EPS.[1]	Glucose homeostasis may be affected by blocking 5-HT2A receptors. 5-HT2A antagonists may also be associated with weight gain and sleep disturbances.[9]
5-HT1A Partial Agonists	5-HT1A partial agonist activity is thought to have effects on negative symptoms, mood, and cognitive function in patients with schizophrenia.[2] It is believed that the activation of 5-HT1A receptors may indirectly increase dopamine release in the striatum, which may potentially help to mitigate EPS.[1] Partial agonist activity at 5-HT1A autoreceptors is thought to increase the antidepressant action of drugs that block serotonin reuptake by preventing negative feedback inhibition of serotonin release.[10,11]	The partial agonist activity of 5-HT1A receptors may lead to increased dopamine release downstream and may be associated with nausea, vomiting, and insomnia.[12,13] 5-HT1A agonists may impair memory and learning by inhibiting the release of glutamate and acetylcholine in various areas of the brain.[14] Other potential adverse effects may include dizziness, asthenia, fatigue, and headache.[15]
5-HT2C Antagonists	Blocking 5-HT2C receptors may stimulate dopamine and norepinephrine release in the prefrontal cortex and is thought to have pro-cognitive and antidepressant actions.[1]	Blockade of 5-HT2C receptors may be associated with changes in appetite and weight gain.[9]

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