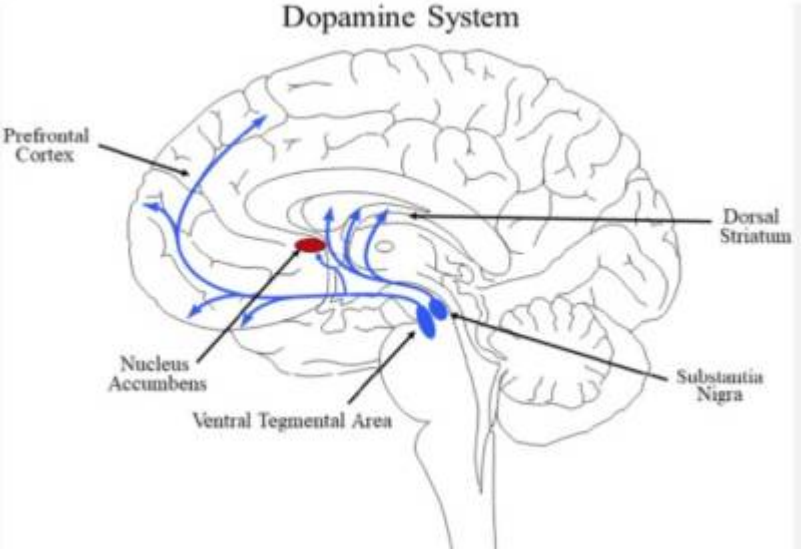
Dopamine system



The ventral tegmentum (tegmentum is Latin for covering), also known as the ventral tegmental area of Tsai (VTA), or simply ventral tegmental area (VTA), is a group of neurons located close to the midline on the floor of the midbrain (mesencephalon).

The VTA is the origin of the dopaminergic cell bodies of the mesocorticolimbic dopamine system and is widely implicated in the drug and natural reward circuitry of the brain. It is important in cognition, motivation, orgasm, drug addiction, intense emotions relating to love, and several psychiatric disorders. The VTA contains neurons that project to numerous areas of the brain, from the prefrontal cortex (PFC) to the caudal brainstem and several regions in between.

During adolescence, dopamine terminals, which have migrated from the ventral tegmental area, pause in the nucleus accumbens, before segregating by either forming local connections or growing towards the prefrontal cortex (PFC). This developmentally late and lengthy process renders adolescent dopamine axon pathfinding vulnerable to disruption by substance use. Indeed, exposure to stimulant drugs in adolescent male mice, but not females, triggers dopamine axons to mistarget the nucleus accumbens and to grow ectopically to the PFC. Some evidence suggests that at this novel site, the functional organization of the ectopic dopamine axons mirrors that of the intended target. The structural rewiring dysregulates local synaptic connectivity, leading to poor impulse control ability, deficits of which are a core symptom of substance-use disorders. Avramescu et al. argue that different substances of abuse induce dopamine mistargeting events with the off-target trajectory prescribed by the type of drug, leading to psychiatric outcomes later in life [1].

1)
Avramescu RG, Hernandez G, Flores C. Rewiring the future: drugs abused in adolescence may predispose to mental illness in adult life by altering dopamine axon growth. J Neural Transm (Vienna). 2023 Dec 1. doi: 10.1007/s00702-023-02722-6. Epub ahead of print. PMID: 38036858.