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Assignment 2.1

Differences between short- and long-term effects of the effects of neurotransmitters

Understanding how neurotransmitters produce change in the brain requires distinguishing between what happens in the moment and what persists long after. Acute neurotransmitter effects involve direct receptor activation and immediate cellular responses that fade once the substance is metabolized and cleared. Long-term effects involve structural remodeling of neural architecture through mechanisms like neuroplasticity. Psychedelics, not typically associated with simplicity, offer a surprisingly straightforward illustration of this distinction because their acute experiential effects differ dramatically from their lasting therapeutic benefits.

Every neurotransmitter produces acute effects through the same basic mechanism. Neurons communicate by releasing chemical messengers into the synaptic cleft, where they bind to receptors on the neighboring neuron and trigger an immediate cellular response (BrainFutures, n.d.). This process works like a message dispatched across a canyon between two stations. The receiving station reads the chemical message and fires an electrical signal down the road to the next canyon, continuing the chain of communication. Once the chemical message has been delivered, the sending station recalls it through reuptake.

The body's neurons constantly dispatch serotonin across multiple receptor subtypes, an in-house team serving multiple functions to keep mood, cognition, and perception operating within normal parameters. Psychedelics function more like a specialized outside contractor with equipment the in-house team does not have. Acting as agonists, they mimic serotonin at 5HT2A receptors specifically. But they overactivate those receptors far beyond normal stimulation levels (Calder & Hasler, 2023). The result is intense sensory, emotional, and cognitive disruption. In the canyon, this is a full construction crew on site with heavy equipment. But when the substance is metabolized and the crew packs up, the immediate disruption ends.

Long-term neurotransmitter effects are not about what happens while the signaling molecule is present. They are about the structural changes that persist after the neurotransmitter is gone. For example, when psychedelics activate 5HT2A receptors, the intensity of that activation triggers the release of brain-derived neurotrophic factor (BDNF), which binds to TrkB receptors and initiates structural growth (Calder & Hasler, 2023). This is the psychedelic crew's lasting contribution. As their time on site winds down, the work transitions into a new phase. The crew hands off work orders that fast-track remodeling beyond what the in-house team's daily operations would produce. New dendritic branches and synaptic connections form over the days and weeks that follow, like new roads through previously unmapped territory. Research in mice treated with psilocybin supports this. New dendritic spines formed during the window of heightened plasticity survived for at least one month, even after the rate of new growth returned to baseline (Calder & Hasler, 2023).

Part of what makes psychedelics so effective as the outside contractor is access. Psychedelics are lipophilic, meaning they can pass through the cell membrane and activate intracellular 5HT2A receptors that the body's own water-soluble serotonin cannot reach (Vargas et al., 2023). This is why the body's routine serotonin signaling maintains existing neural pathways but cannot produce the same level of structural remodeling that psychedelics can.

SSRIs offer a second example of the difference between acute neurotransmitter activity and lasting structural change. By blocking reuptake, they increase serotonin levels in the synaptic cleft almost immediately, like filling the canyon with extra chemical messengers starting from the very first dose. The antidepressant effect, however, can take up to four to six weeks to emerge because the therapeutic change depends on gradual structural remodeling, not the acute signal itself (Calder & Hasler, 2023).

Microdosing illustrates this from yet another angle. A therapeutic dose produces intense sensory, emotional, and cognitive effects, like a full crew shutting the road down for demolition and new construction. At a sub-perceptual microdose, most people continue their daily routines while gradual construction happens around them, improving the road network without ever closing it. Research suggests that even at these lower doses, the same BDNF-driven plasticity processes described above still activate (Calder & Hasler, 2023). This suggests that the lasting therapeutic value may not be a product of acute receptor activation itself, but of the structural remodeling that follows.

Acute activation sends the message. Long-term effects remodel the infrastructure that carries it. Every example explored here, from psychedelic-triggered dendritogenesis to the delayed onset of SSRIs, points to the same conclusion. The most lasting changes in the brain are not reactions to a signal. They are the structural rebuilding that continues long after the signal is gone.

References

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