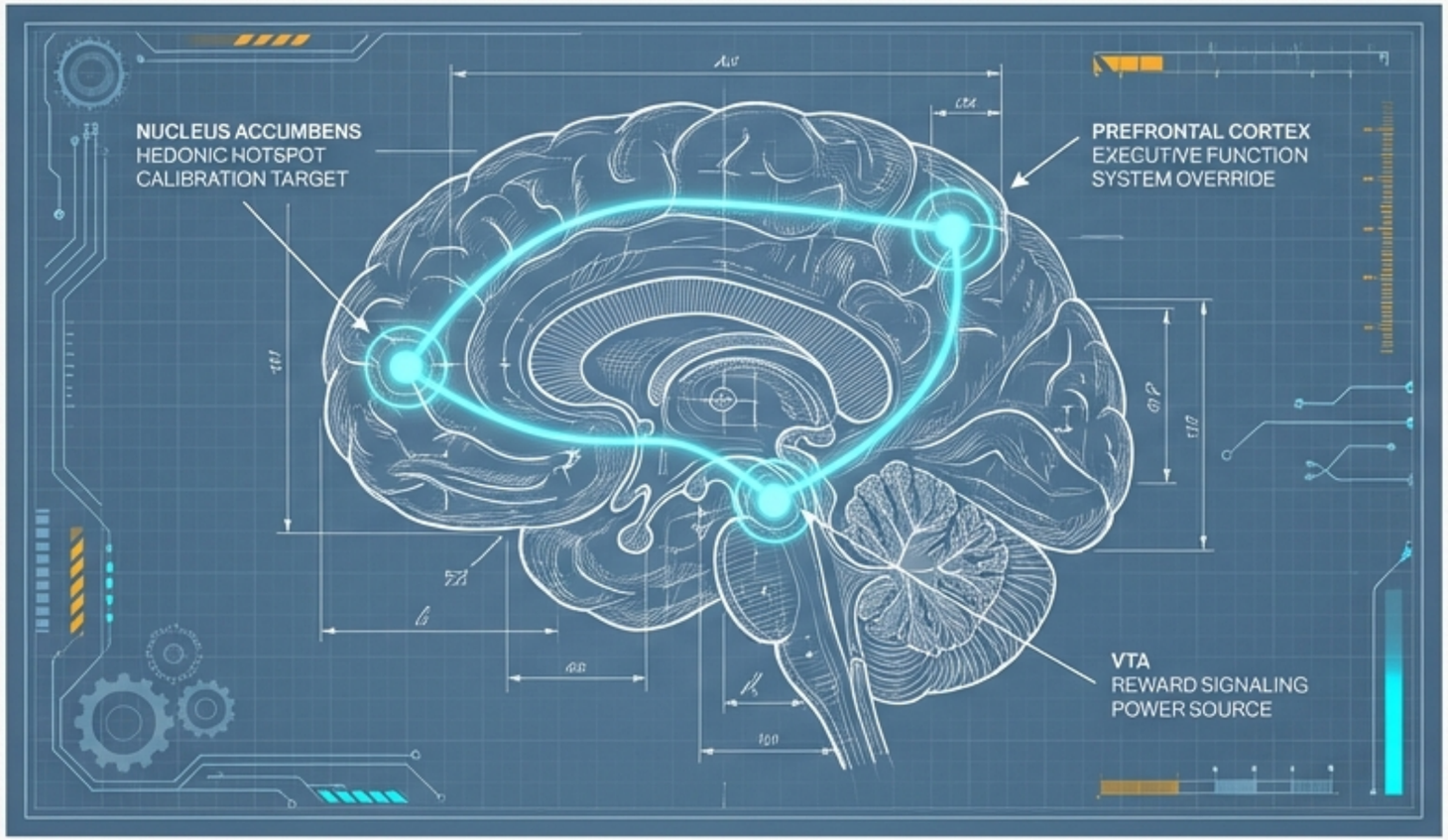
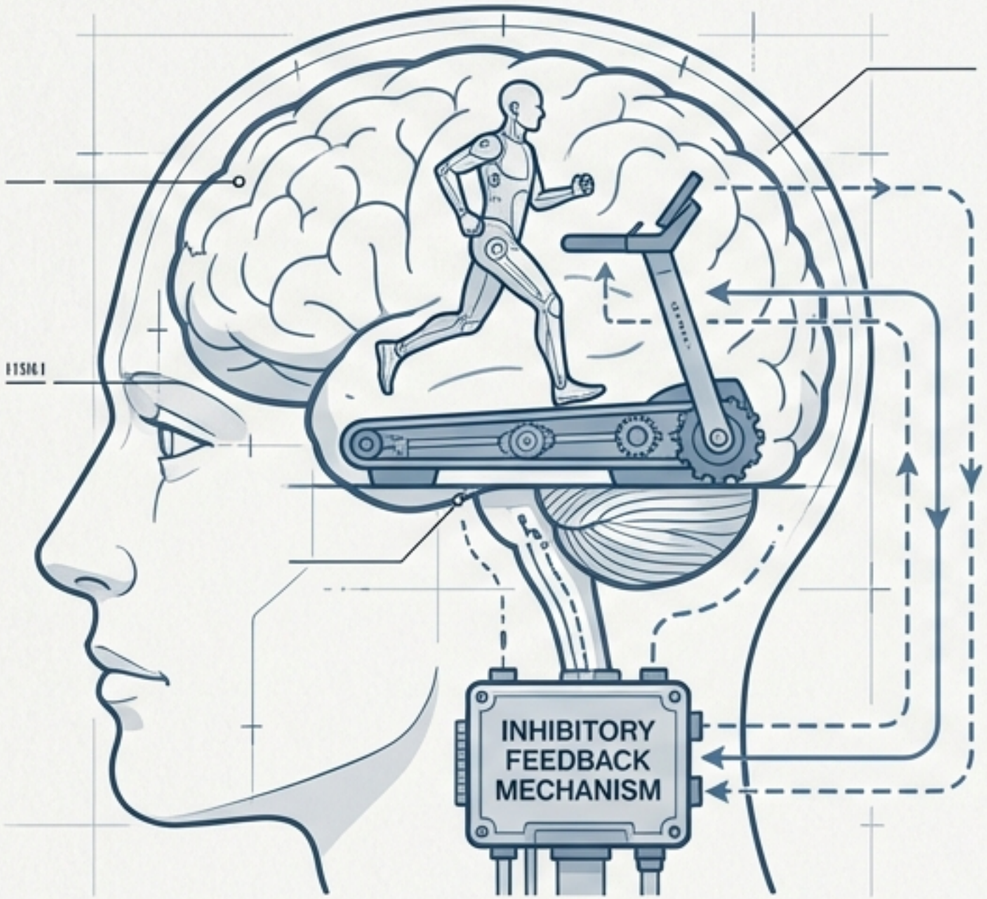
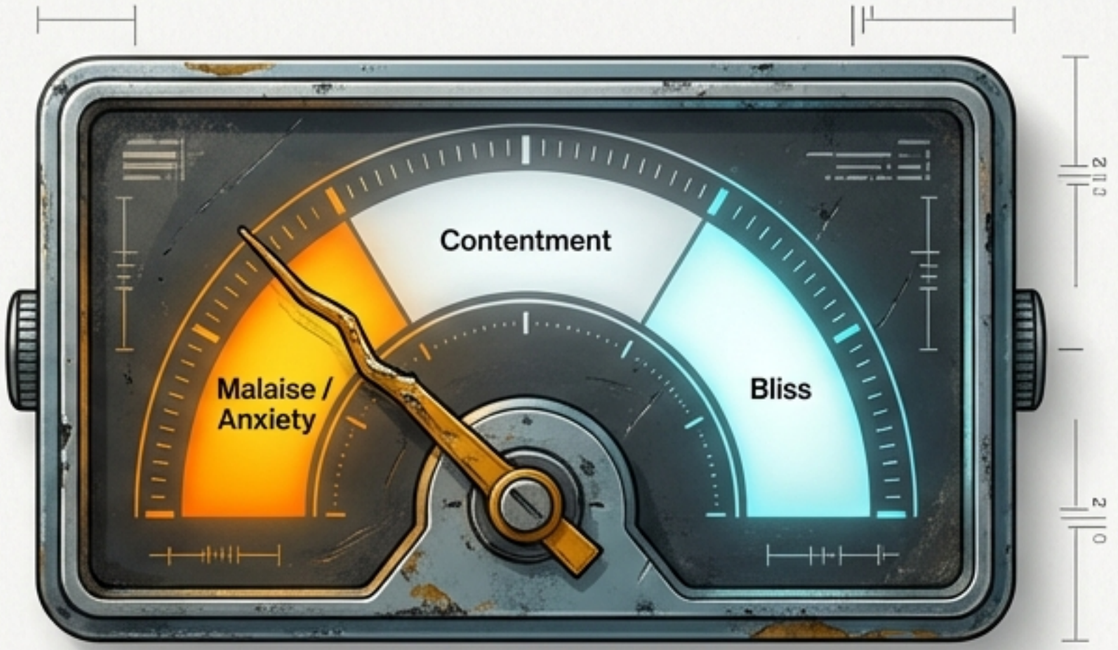
The Good Drug Guide: A Critical Path to Biohappiness



Recalibrating Our Darwinian Wetware for the 21st Century and Beyond

We are engineered for survival, not for happiness.





Our brains operate on a genetically predisposed 'emotional thermostat' that consistently reverts to a baseline of malaise. This is an evolutionary adaptation for survival in our ancestral environment. All attempts at life enrichment—from socio-economic reforms to talk therapy—ultimately fail because they do not subvert the brain's powerful inhibitory feedback mechanisms, the **hedonic treadmill**.

"If the quality of our lives is to be significantly enhanced...the genetically predisposed set-point of our emotional thermostats needs to be recalibrated."

The wells of information are poisoned.

Finding unvarnished facts is nearly impossible due to a dual information crisis:

1. **Official Sources:** Biased by commercial interests, cloaked in reputable disguise, and shaped by puritanical norms. Language is warped; socially taboo drugs are ‘abused,’ while lab animals are ‘sacrificed.’
2. **Counter-Culture Sources:** Often lack the methodological rigor of professional journals, making it difficult to separate signal from noise.

Thought Experiment: How would an everlasting-happiness drug be described in scientific literature?
“Substance x induces severe, irreversible structural damage to neurotransmitter subsystem y. Its sequelae include mood-congruent cognitive delusions, treatment-resistant euphoria, and toxic affective psychosis.”

Happiness.

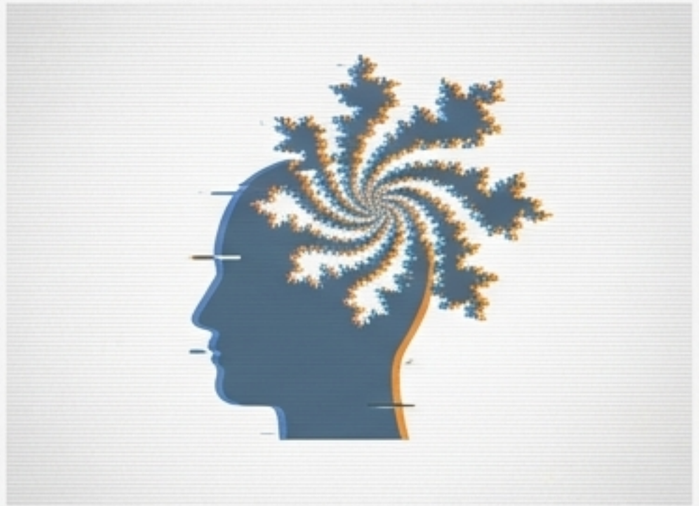
The illusion of unsustainable highs.

Power drugs and dreamlike escapes fail to deliver long-term benefits because they don't cheat the hedonic treadmill. They are spectacularly incompetent routes to a lifetime of happiness.

	PSYCHOSTIMULANTS	OPIOIDS
THE PROMISE	 "Power drugs." Short-term elevation of mood, motivation, energy, and self-confidence.	 Directly target the pleasure-pain axis, offering unsurpassed pain relief and extraordinary emotional well-being.
THE REALITY	 The central nervous system re-regulates genes and receptors in response. No long-term benefit is derived.	 Flawed by tolerance, physiological addiction, and a "dreamily contented disengagement from the problems of the world." They diminish the drive for constructive activity.

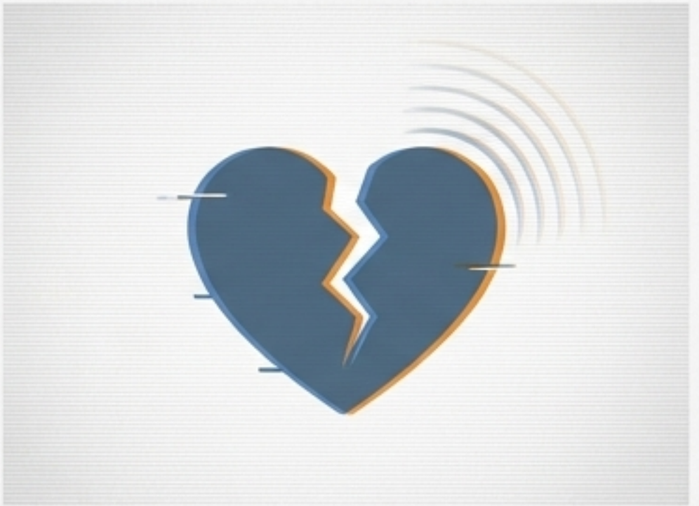
Glimpses of the sublime are not a life strategy.

Many agents alter consciousness without reliably raising one's hedonic set-point. Their effects are too exotic, unpredictable, or carry too high a cost to be integrated into a responsible life.



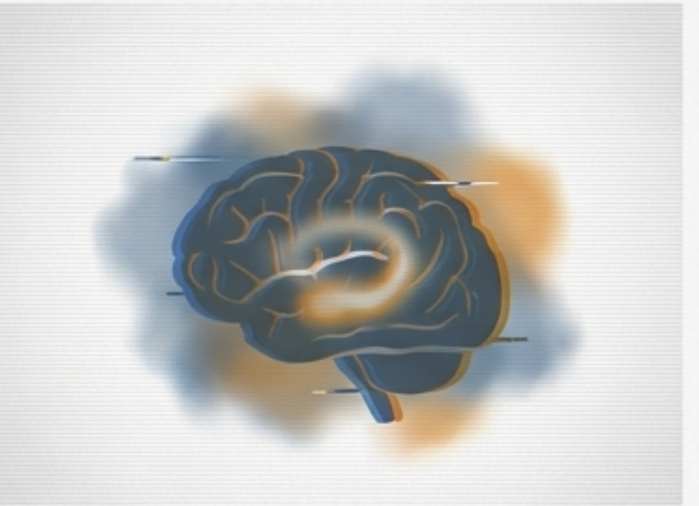
Psychedelics (LSD, Psilocybin)

Too unpredictable and bizarre. They don't directly stimulate pleasure centers and can induce "nightmarish freak-outs" in troubled minds. Their study is for a future when well-being is genetically hardwired.



MDMA ("Ecstasy")

Offers a "wonderfully warm, sensuous, loving" peak experience, but is neurotoxic to serotonergic axons. Most users never fully recapture the magic of their first trips.

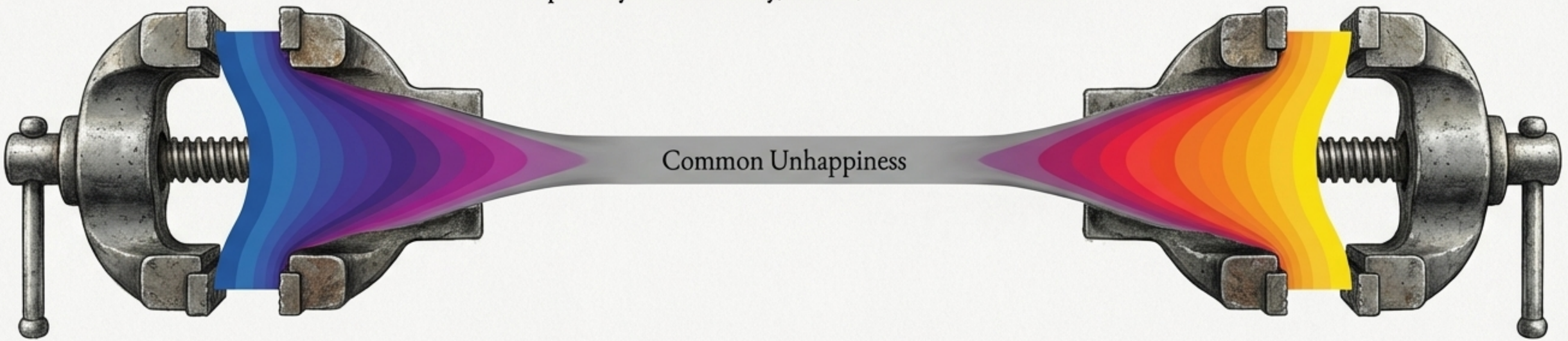


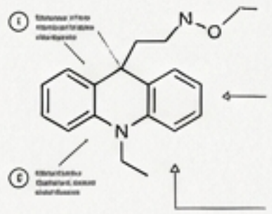
Marijuana

Interferes with memory formation by disrupting long-term potentiation in the hippocampus. "Choosing deliberately to ingest an amnestic agent for long periods is scarcely an ideal life-strategy."

Mainstream psychiatry aims to manage misery, not engineer joy

The goal of traditional pharmacotherapy is limited, aspiring only "to transform hysterical misery into common unhappiness." Its primary tools are dirty, flawed, and lack ambition.



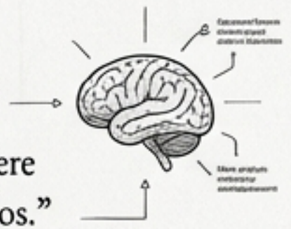


Tricyclics (e.g., Imipramine)

Relatives of the "chemical cosh" chlorpromazine. Dirty drugs with anti-cholinergic effects that harm memory and concentration, and anti-histamine action that induces sedation. "Cheap, nasty and usually best avoided."

SSRIs (e.g., Prozac, Zoloft)

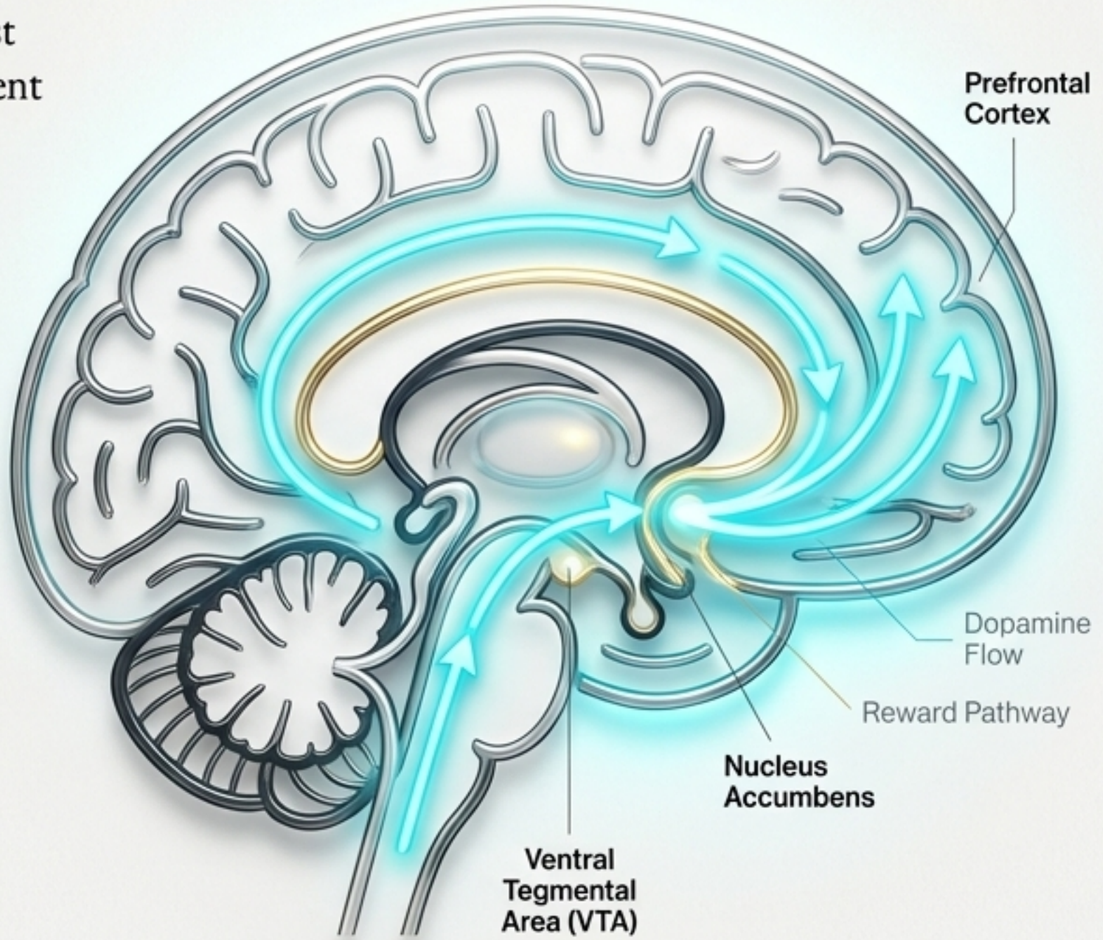
A cleaner profile, but often cause affective flattening ("emotional anesthesia") and sexual dysfunction. A meta-analysis of drug-company data showed they were "scarcely more effective as antidepressants than placebos."



The final common pathway for pleasure, motivation, and reward.

The crucial element missing from most treatments is the therapeutic enrichment of hedonic tone. This requires prolonged, sustainable stimulation of the meso(cortico-)limbic dopamine system.
Enhanced responsiveness of post-synaptic dopamine D2/D3 receptors is vital to long-term emotional well-being.

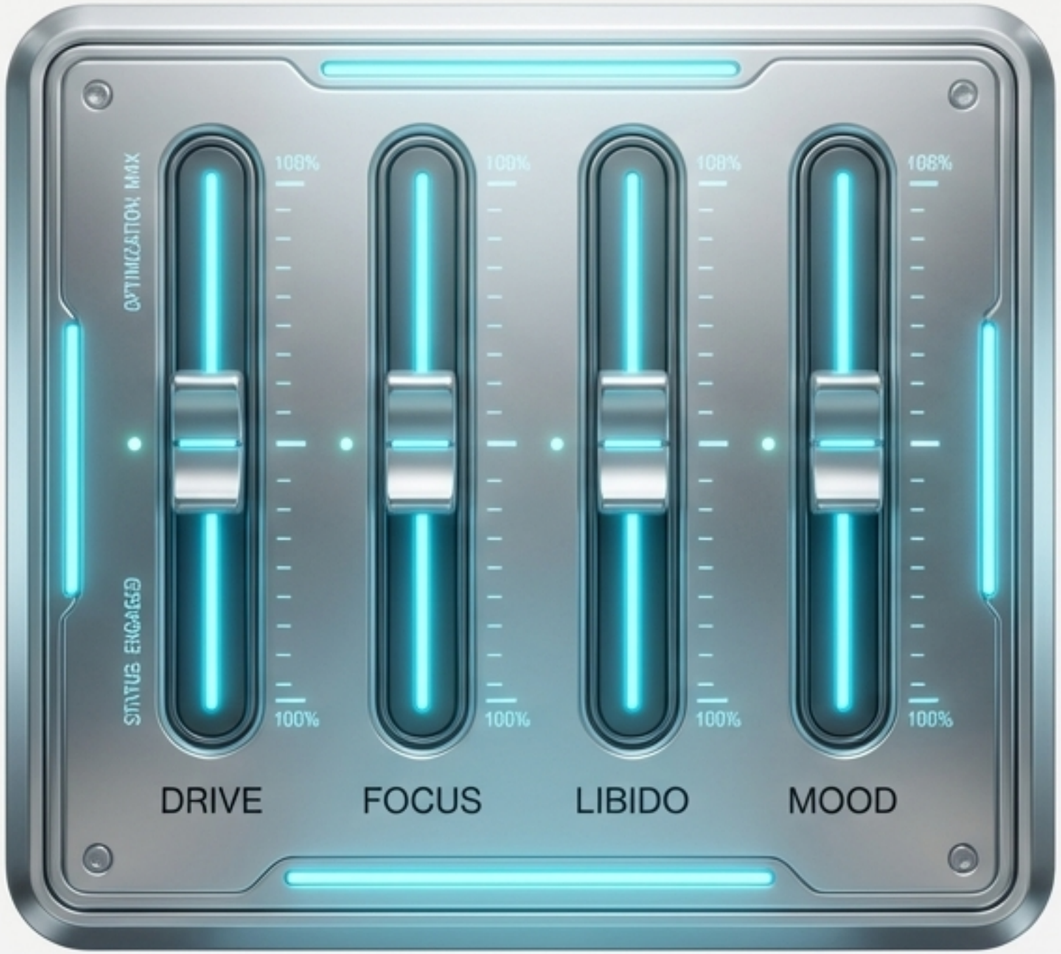
Even serotonergic and noradrenergic drugs, insofar as they work, eventually act on this pathway.



KEY INSIGHT

The mesolimbic dopamine system mediates reward-signaling, incentive salience, and a sense of urgency and significance.
It enriches the intensity of experience, increases pleasure and libido, and boosts cognitive performance.

Targeting drive, motivation, and libido.

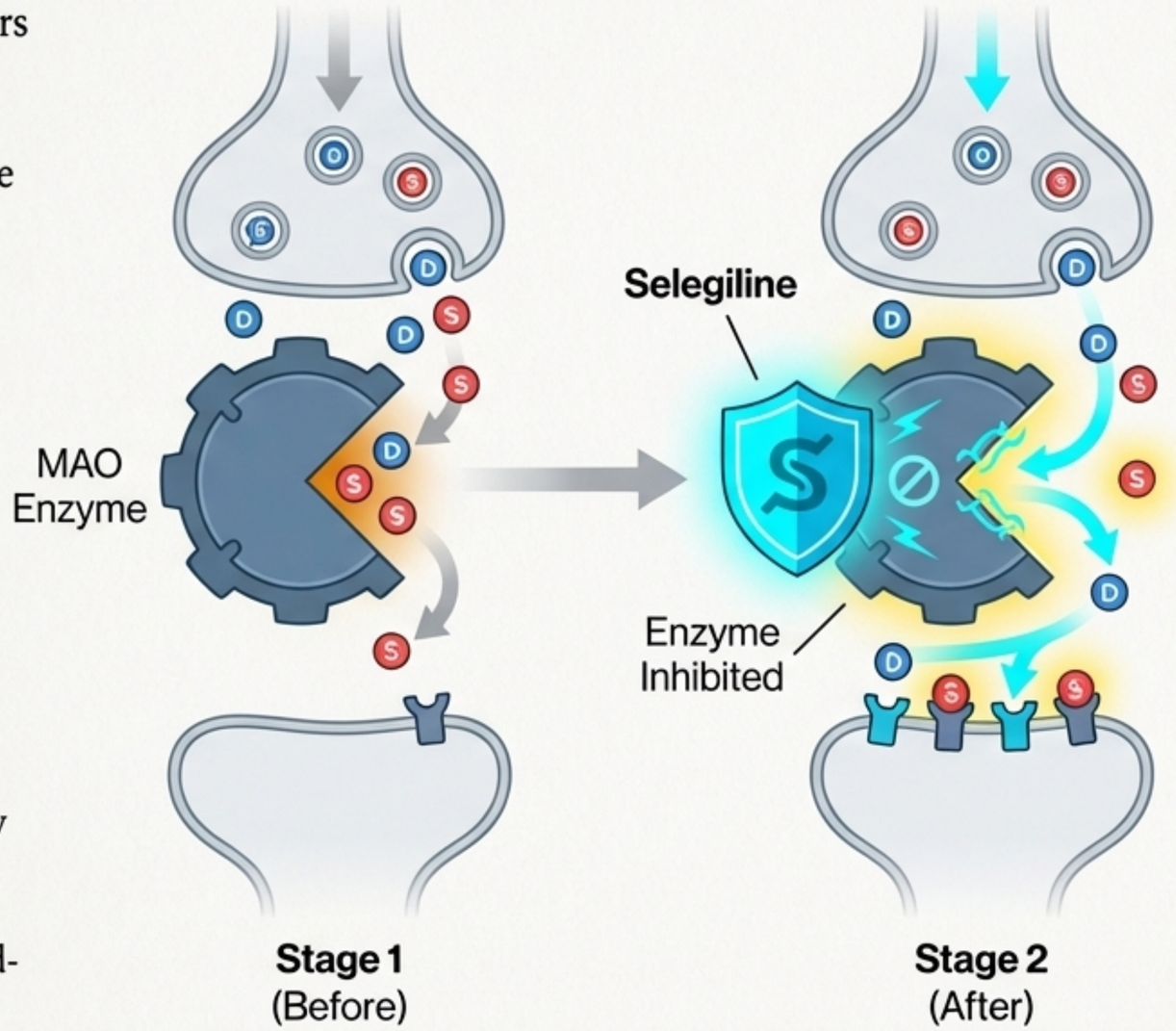


A look at more effective agents that lack the dulling or anti-sexual side effects of the SSRI/tricyclic class.

- **Bupropion (Wellbutrin):** Weakly blocks dopamine reuptake. Lacks the adverse sexual effects of SSRIs; in women, it may increase libido, arousal, and orgasm intensity.
- **Amineptine (Survector):** A selective dopamine reuptake blocker. Pro-sexual, fast-acting, and a mild psychostimulant. Withdrawn from many markets due to fears of "abuse-potential," despite no recorded cases of abuse in the USA.
- **Modafinil (Provigil):** A "eugeroic" (good arousal) agent. An alpha1-adrenergic agonist that brightens mood and sharpens mental focus, boosting alertness, memory, and motivation with remarkably few side-effects.

A potent, misunderstood class of mood-brighteners.

Monoamine oxidase inhibitors (MAOIs) were discovered by chance in the 1950s but fell out of favor. Modern selective MAOIs offer powerful benefits.



Mechanism Explained:
MAO-A preferentially breaks down serotonin and noradrenaline; MAO-B primarily metabolizes dopamine. Inhibiting these enzymes increases the availability of mood-enhancing neurotransmitters.

Featured Agent: Selegiline (EMSAM patch)

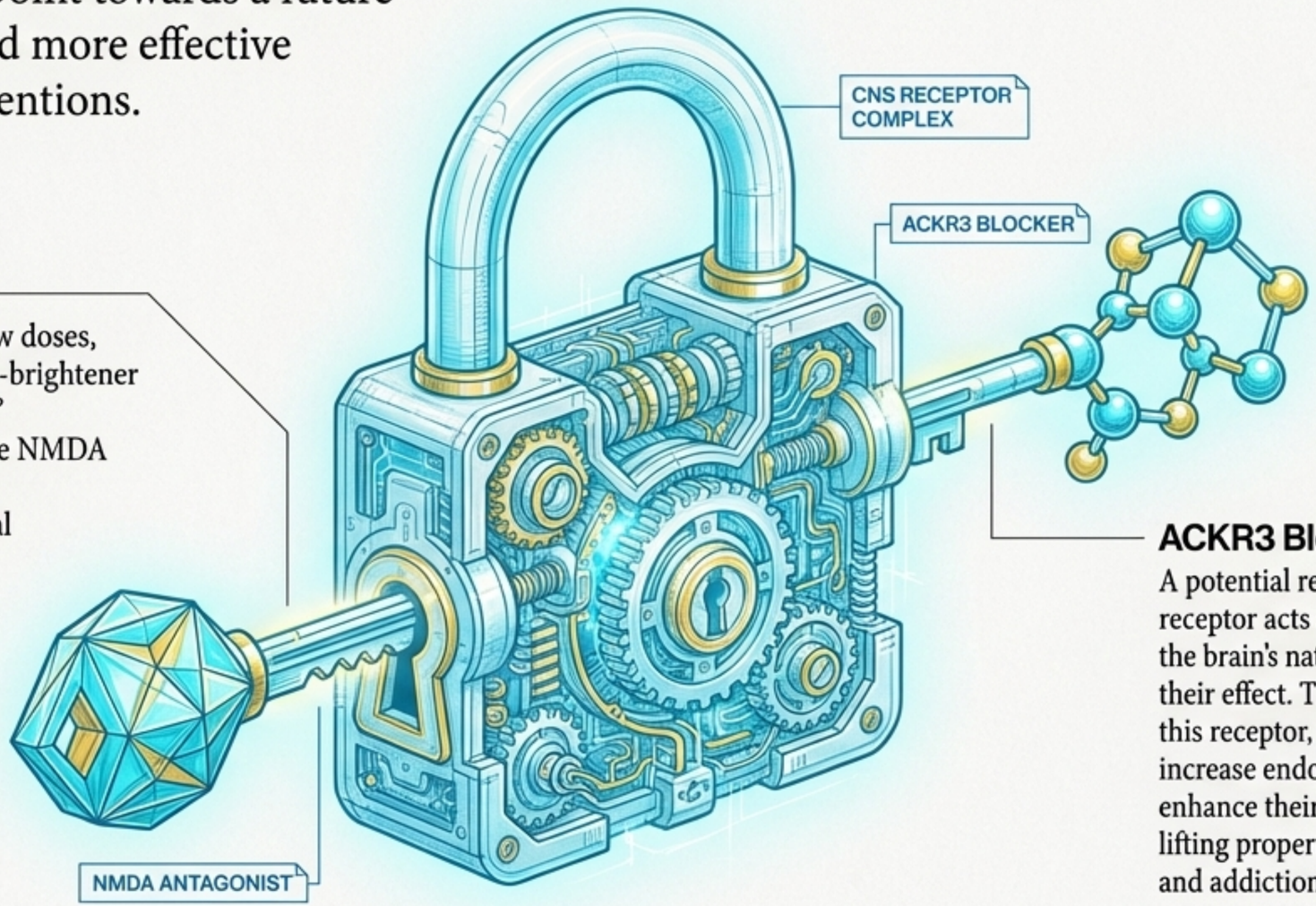
- **Neuroprotective:** The brain's dopamine cells die off at ~13% per decade. Selegiline has an anti-oxidant, immune-boosting, and dopamine-cell-sparing effect.
- **Life-Enhancing:** Enhances drive, libido, motivation, and cognitive performance. Low doses extended life-expectancy in rats by over 20%.
- The EMSAM patch avoids significant inhibition of gut MAO-A, eliminating the 'cheese effect' at low doses.

Tranylcypromine (Parnate) is a more stimulating, non-selective MAOI, potent for deep melancholy.

New targets, new mechanisms, new hope.

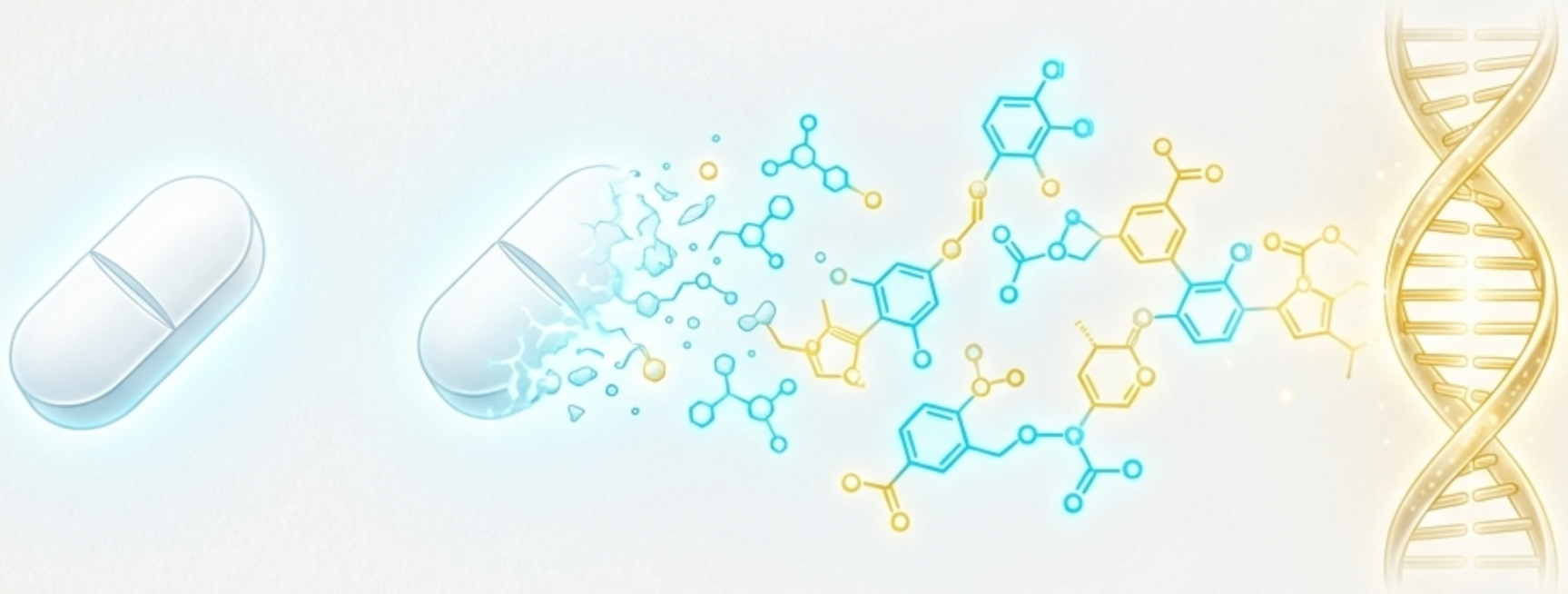
Recent breakthroughs point towards a future of radically different and more effective pharmacological interventions.

Ketamine (and Esketamine/Spravato):
A dissociative anesthetic that, at low doses, acts as a rapid and sustained mood-brightener for 65-75% of "treatment-resistant" depressives. Its primary target is the NMDA glutamate receptor, representing a complete departure from traditional monoamine theories.



ACKR3 Blockers (LIH383):
A potential revolution. The ACKR3 receptor acts as a "scavenger," trapping the brain's natural opioids and diminishing their effect. The molecule LIH383 blocks this receptor, promising to sustainably increase endogenous opioid levels and enhance their pain-killing and mood-lifting properties *without* the tolerance and addiction of traditional opioids.

The ultimate goal is not a better drug, but a better brain.



Pharmacology is a temporary stopgap. The true, lasting solution is to transcend our Darwinian legacy by editing our genetic source code for life-long well-being. We must fix the problem at its origin rather than continuously treating the symptoms.

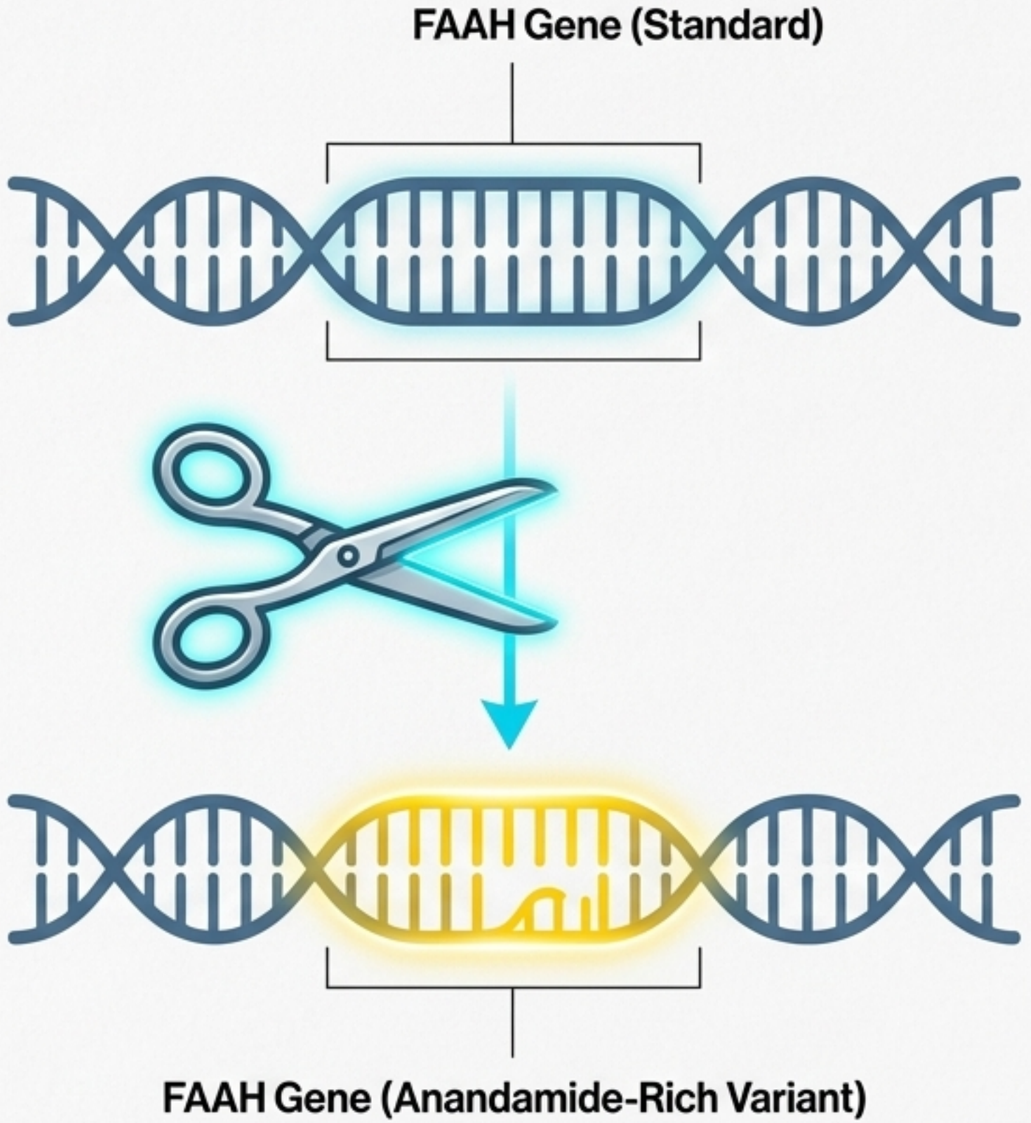
"When gradients of heavenly well-being become the genetically predestined norm of mental health, then the very notion of tampering with our newly won 'natural' condition…may come to seem immoral."

Intravenous gene therapy is no longer science fiction.

In 2021, a breakthrough trial marked a watershed moment: CRISPR-Cas9 was used via a one-time intravenous infusion to edit genes directly inside the human body, successfully treating a life-threatening disease.
This technique—using lipid nanoparticles to deliver genetic "scissors" to target cells—opens the door to systemic genetic fixes.

A Human Blueprint for Bliss: Jo Cameron

A retired teacher with a rare dual FAAH and FAAH-OUT gene mutation. She feels no anxiety, depression, or pain. Her body produces exceptionally high levels of anandamide (from the Sanskrit for "inner bliss"). She provides a living example of a potential target for universal genetic enhancement.



Does hurting make us human? If so, let's become transhuman.

Suffering is not a virtue. It exists only because it was evolutionarily advantageous for our selfish genes, not for us. Conditionally-activated negative emotions were fitness-enhancing in the ancestral environment. Apologists for mental pain are the "innocent mouthpieces of the nasty bits of code which spawned them." We now possess the tools to transcend this biological legacy.

The Vision: The "Abolitionist Project" aims to build a future animated by "information-sensitive gradients of bliss," where involuntary suffering is biologically obsolete.

The issue is not drugs vs. no drugs. It is allowing people the choice to opt for *better* ones.

While we work towards a drug-free, genetically-engineered future, we must fight for cognitive liberty in the present. In a society society where 80% of the population uses substances like alcohol and tobacco, the argument against enhancement rings hollow. People shouldn't be legally robbed of the right to use the best available tools to enhance their own well-being.

Explore the Source

Author

David Pearce

Primary Manifestos

- The Hedonistic Imperative
- The Abolitionist Project

Web Resources

- HedWeb (hedweb.com)
- BLTC Research (bltc.com)