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Review Article

# Neurogenetics and Epigenetics of Spirituality and Religion: Seeking Genospirituality Via the Lens of Hierarchical Neuro-Spiritual Model (HNSM)

**Kai-Uwe Lewandrowski[1-4,25]*, Kenneth Blum[5-8,25]**, Morgan P Lorio[9], Alireza Sharafshah[10], Albert Pinhasov[5], Panayotis K Thanos[5,11], Catherine A Dennen[12], Igor Elman[5,13], David Baron[14-16], Alexander PL Lewandrowski[17], Alexander R Vaccaro[18], Óscar L Alves[19], Milan T Makale[20], Rajendra D Badgaiyan[21], Gianni Martire[7], Thomas Simpatico[8], Abdalla Bowirrat[5], Albert Pinhasov[5], William J Heaney[7,22], Debasis Bagchi[23], Rossano Kepler Alvim Fiorelli[24] and Sergio Luis Schmidt[25,26]**

*[1]Division of Personalized Pain Therapy Research and Education, Center for Advanced Spine Care of Southern Arizona, Tucson, AZ, USA*

*[2]Department of Orthopaedics, Fundación Universitaria Sanitas, Bogotá, DC, Colombia*

*[3]Department of Surgery, Arizona University School of Medicine, Tucson, AZ, USA*

*[4]Department of Orthopaedics, Universidade Federal do Estado do Rio de Janeiro, Brazil*

*[5]Department of Molecular Biology, Adelson School of Medicine, Ariel University, Ariel, Israel*

*[6]Division of Addiction Research and Education, Center for Sports, Exercise, and Mental Health, Western University of Health Sciences, Pomona, CA, USA*

*[7]Division of Clinical Neurology, The Blum Institute of Neurogenetics and Behavior, Austin, TX, USA*

*[8]Department of Psychiatry, University of Vermont, School of Medicine, Burlington, VT, USA*

*[9]Advanced Orthopedics, Altamonte Springs, On Behalf of the International Society for the Advancement of Spine Surgery, Orlando College of Osteopathic Medicine, Orlando, FL, USA*

*[10]Cellular and Molecular Research Center, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran*

*[11]Department of Psychology, University of Buffalo, Buffalo, NY, USA*

*[12]Department of Family Medicine, Jefferson Health Northeast, Philadelphia, PA, USA*

*[13]Department of Psychiatry and Cambridge Health Alliance, Harvard Medical School, Cambridge, MA, USA*

*[14]Division of Addiction Research and Education, Center for Sports, Exercise, and Mental Health, Western University of Health Sciences, Pomona, CA, USA*

*[15]Department of Psychiatry and Behavioral Sciences, Stanford University, School of Medicine, Palo Alto, CA, USA*

*[16]Division of Addiction Research and Education, Center for Sports, Exercise, and Mental Health, Western University of Health Sciences, Pomona, CA, USA*

*[17]Dornsife College of Letters, Arts and Sciences, University of Southern California, Los Angeles, CA, USA*

*[18]Chairman of the Department of Orthopaedic Surgery, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, Pennsylvania, USA*

*[19]Head of Neurosurgery, Hospital Lusíadas Porto, Senior Consultant in Neurosurgery, ULS Gaia Espinho, Portugal*

*[20]Department of Radiation Medicine and Applied Sciences, UC San Diego, La Jolla, CA, USA*

*[21]Department of Psychiatry, Texas Tech University Health Science Center, Midland, TX, USA*

*[22]Division of Pain Modulation, Electronic Waveform Laboratory, Huntington Beach, CA, USA*

*[23]Department of Pharmaceutical Sciences, Texas Southern University College of Pharmacy, Houston, TX, USA*

*[24]Department of General and Specialized Surgery, Gaffrée e Guinle University Hospital, Federal University of the State of Rio de Janeiro (UNIRIO), Rio de Janeiro-RJ, Brazil*

*[25]Department of Neurology, Federal University of the State of Rio de Janeiro (UNIRIO), RJ, Brazil*

*[26]University Hospital - Rua Mariz e Barros 750 - Tijuca, Rio de Janeiro, RJ, Brazil*

***Corresponding Author:** Kai-Uwe Lewandrowski, Division of Personalized Pain Therapy Research and Education, Center for Advanced Spine Care of Southern Arizona, Tucson, AZ, USA.

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## Abstract

Addictive behaviors-including the misuse of tobacco, alcohol, illicit substances, and compulsive activities such as gambling, overeating, and sexual excess-remain widespread and profoundly burdensome on both individuals and societies. Their impact is multifaceted, encompassing adverse health outcomes, increased criminal activity, and significant economic costs due to lost productivity. Addiction is a highly complex condition shaped by genetic predispositions, environmental influences, and behavioral factors, all of which contribute to disruptions in neural regulation and compulsive decision-making. While advances have been made in identifying the genetic and biochemical underpinnings of addiction and related psychiatric disorders, progress in developing broadly effective therapies has been limited.

Addiction is often characterized by feelings of fragmentation, helplessness, and existential despair-phenomena that may reflect a deeper, unmet need for personal integration, purpose, and transformation. This perspective supports the notion that spiritual yearning can be an integral part of the recovery process. Efforts to address addiction have frequently overlooked the potential therapeutic value of spirituality in fostering healing. If one accepts the premise that the brain governs both conscious and unconscious experience-including religious and spiritual phenomena-it follows that addiction, and mental illness may involve disrupted neural systems that regulate reward and suffering. We propose that individuals may have differing capacities for spiritual resilience or growth based on a dynamic interplay between their genetic architecture and epigenetic factors (e.g. life experiences, trauma, social environment). This expert opinion presents current evidence supporting this hypothesis and highlights the relevance of the Hierarchical Neuro-Spiritual Model (HNSM) as a novel framework for understanding the spiritual dimension in the pathophysiology and treatment of addiction.

***Keywords:*** *Reward Deficiency Syndrome (RDS); Genes; Dopaminergic; Reward Dependence; Spirituality; Addiction Recovery; Twelve Steps; Hierarchical Neuro-Spiritual Model (HNSM)*

## Introduction

The Hierarchical Neuro-Spiritual Model (HNSM), conceptualized by Dr. Morgan P. Lorio, offers a clinically grounded framework that integrates neuroanatomy, pastoral care, and spiritual transformation. This model presents healing as a dynamic progression through four neuro-spiritual levels, each corresponding to a specific brain region and pastoral intervention, with an ever-present spiritual overlay that flows throughout [1].


***Figure 1:*** *Rosetta stone of the hierarchical neuro-spiritual model (HNSM).*

Rosetta stone of the hierarchical neuro-spiritual model (HNSM) as developed by Dr. Morgan P. Lorio. The HNSM integrates neuroscience, pastoral care, and spiritual transformation into a four-level framework aligned with neuroanatomical structures:

1. **Safety - Brainstem (Basic regulation):** Simple pastoral acts like offering water, a blanket, or quiet presence stabilize the autonomic nervous system and foster a sense of safety.
2. **Connection - Limbic system (Emotional engagement**): Active listening and empathic presence build trust and support emotional regulation.
3. **Integration - Diencephalon (Narrative meaning-making):** Storytelling and spiritual reflection promote coherence, self-awareness, and meaning-making.
4. **Transcendence - Cortex (Higher-order thinking):** Rituals, blessings, and prayer engage higher cognition, renew identity, and deepen spiritual connection.

**Spiritual overlay (Always present):** At every stage, divine presence may be sensed or mediated through the caregiver. Healing flows upward and feeds back downward-creating a reciprocal loop of grace and neuroplasticity. The model offers a unified framework for chaplaincy, integrative care, and psycho-spiritual therapy.

At the foundational level is safety, associated with the brainstem, the most primitive part of the brain responsible for basic regulation. In times of acute distress, a simple pastoral gesture-offering a blanket, a glass of water, or quiet, nonverbal presence-can help regulate fear and activate parasympathetic calming. This stage prioritizes physiological stability and signals to the nervous system that the body is safe, laying the groundwork for deeper healing.

Once safety is established, the model progresses to connection, rooted in the limbic system, the seat of emotional processing and relational memory. Here, active listening and empathetic presence foster trust and relational security. By calming the reactive brain and facilitating emotional resonance, this stage helps clients feel seen, heard, and less alone. Connection opens the door to relational healing and belonging-critical elements for those recovering from isolation or trauma.

The third level, integration, is linked to the diencephalon, particularly the thalamus and hypothalamus, which regulate internal balance and serve as conduits for meaning-making. At this stage, caregivers help individuals engage in reflective storytelling, reframe suffering, and discover coherence in life events. Encouraging patients to narrate their spiritual or life journey allows fragmented experiences to be woven into a more unified sense of purpose. The brain, in turn, responds with increased coherence and a reduction in internal chaos.

The highest level of the HNSM is transcendence, tied to the cortex, the region responsible for abstract reasoning, self-awareness, and spiritual insight. This is the domain of hope, identity transformation, and connection with the divine. Practices such as prayer, ritual, blessing, or even shared silence invite individuals to access meaning beyond themselves. This stage affirms the human capacity for renewal, spiritual awakening, and post-traumatic growth (Figure 2).

Crucially, a spiritual overlay is always present-woven through each level of the hierarchy. Divine presence, however one defines it, may be encountered through the caregiver, the environment, or the inner stillness of the patient. The healing process in HNSM is not strictly linear; rather, it flows upward through the hierarchical levels and feeds back down, forming a feedback loop of grace and neuroplasticity-where spiritual practices can literally reshape the brain. In this model, the spiritual life is not separate from neurobiology, but rather integrated with it, forming a comprehensive framework for understanding recovery, transformation, and the sacred dimension of human healing.

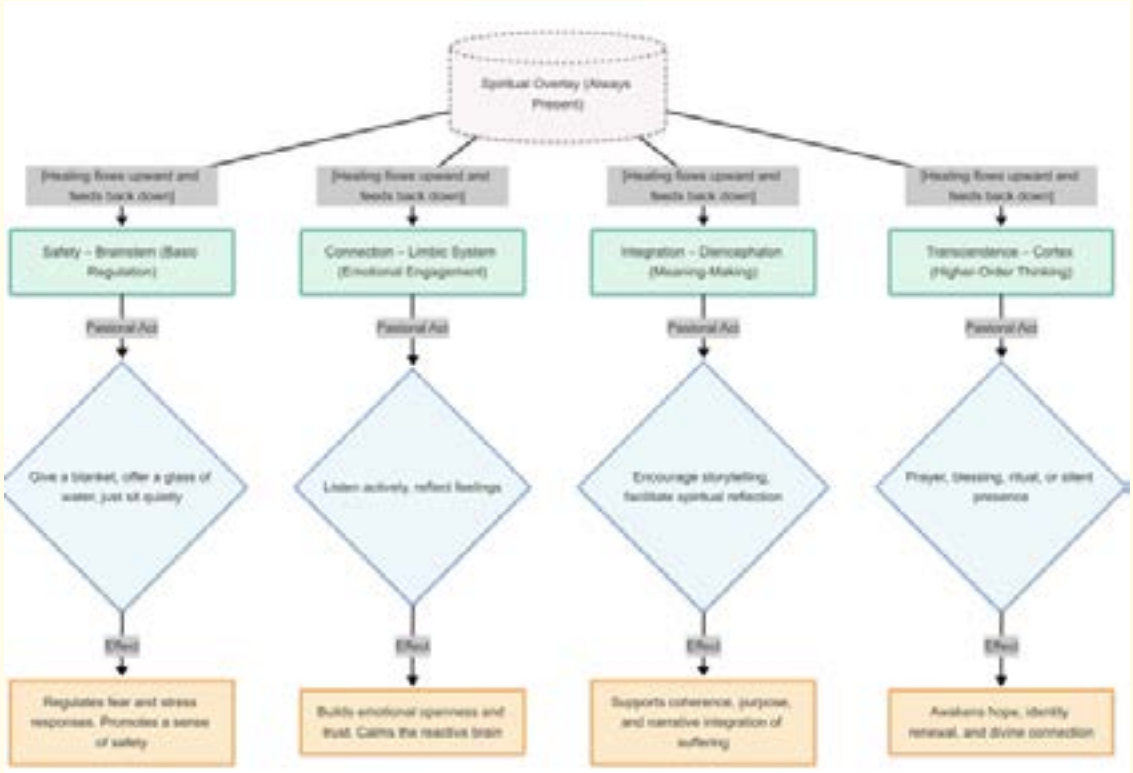


***Figure 2:*** *This flow chart illustrates the practical implementation of the hierarchical neuro-spiritual model (HNSM) as a clinical-spiritual framework aligning the four progressive levels-Safety, connection, integration, and transcendence-with corresponding brain structures. It guides pastoral care and psycho-spiritual interventions to promote healing, emotional regulation, meaning-making, and spiritual transformation. The model also intersects with the neurogenetics and epigenetics of spirituality and religion by recognizing how spiritual practices and belief systems may influence gene expression and neural plasticity. Through this lens, the HNSM bridges brain science and spiritual care within an integrated path to well-being and healing particularly useful in the treatment of addictions, anxiety, ADHD, and pain.*

## Molecular neurobiology of spirituality

Blum and colleagues explored the intersection between molecular neuroscience and the foundational elements of the twelve steps as practiced by self-help groups like alcoholics anonymous (AA) and narcotics anonymous [2]. The goal of their inquiry was not to evaluate the validity of a higher power but rather to examine how adherence to the twelve-step framework may be biologically rooted in genetic factors influencing reward circuitry.

In their publication [2], the authors provide a historical overview of the Twelve Steps, highlighting the personal struggles of co-founder William G. Wilson, known as "Bill W," and the collaborative efforts of figures such as "Dr. Bob" (Robert H. Smith) and the Oxford Group. The formation and refinement of the Twelve-Step model emerged through practical experience within these fellowships. Despite early skepticism-including lukewarm reception to the original 1939 publication of the "Big Book"-Bill W remained committed to the mission, even as he and his wife faced personal financial hardship. His perseverance helped cement the program's lifesaving impact.

Interestingly, Bill W continued to use substances like nicotine and caffeine throughout his recovery, and he remained a smoker until his death at age 76 from emphysema. From a neurobiological perspective, these substances activate dopaminergic pathways in the nucleus accumbens (NAc), part of the brain's mesolimbic reward network [2]. While AA undeniably contributed to his sustained sobriety, it is likely that the ongoing use of these dopamine-activating substances helped alleviate the depressive symptoms he experienced during his long recovery.

Blum's team also noted Bill W's openness to alternative biological approaches. His interest in LSD and Vitamin B3 (niacin) therapy as potential adjuncts for treating alcoholism stirred controversy within the fellowship but reflected his pioneering mindset and commitment to finding effective solutions.

To deepen our understanding of the neurobiological mechanisms underlying recovery [2], Blum and colleagues sought to correlate each of the twelve steps with specific aspects of molecular neurobiology and neurogenetics. Their work represents a growing effort to align spiritual recovery paradigms with emerging neuroscience, offering a more comprehensive framework for understanding how behavioral transformation in addiction may be influenced by underlying biological processes.

## Reward circuitry and addictive behaviors

Over a half century of dedicated and rigorous scientific research into the mesolimbic system has provided insight into the addictive brain and the neurogenetic mechanisms involved in the quest for happiness. In brief, a primary site in the brain where one experiences feelings of well-being is called the mesocorticolimbic reward system [2]. This is where chemical messages, including serotonin (5-HT), encephalin, gamma-aminobutyric acid (GABA), and dopamine (DA), work in concert to provide a net release of DA at the NAc [2]. It is well known that genes control the synthesis, vesicular storage, metabolism, receptor formation, and catabolism of neurotransmitters [3,4]. The polymorphic versions of these genes have certain variations that can lead to an impairment of the neurochemical events involved in the neuronal release of DA. The cascade of these neuronal events has been termed "The Brain Reward Cascade" (Figure 1a, 1b and 2) [5]. A breakdown of this cascade ultimately will lead to the dysregulation and dysfunction of DA. Because DA has been proposed as the pleasure molecule and the anti-stress molecule [4-7], any reduction in function could lead to reward deficiency and result in aberrant substance-seeking behavior and a lack of wellness (Figure 3 and 4).

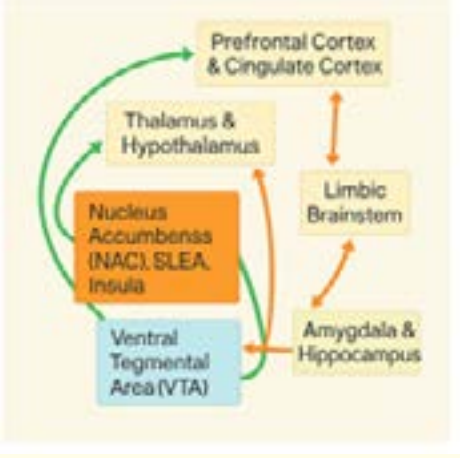


***Figure 3:*** *Shown are the core and extended pathways of the dopaminergic Brain Reward Circuitry (BRC). The ventral tegmental area (VTA) projects dopamine to the nucleus accumbens (NAc)-a key center for processing reward, motivation, and reinforcement. Supporting regions include the prefrontal cortex, anterior cingulate, substantia nigra, and hypothalamus, which modulate affect, cognition, and motor behavior. The extended network incorporates the extended amygdala (SLEA), insula, amygdala, hippocampus, thalamus, and limbic brainstem, enabling emotional, contextual, and autonomic regulation of reward. Bidirectional feedback loops integrate top-down and bottom-up signaling, reflecting the complex interplay between emotion, memory, and motivation in shaping adaptive-and maladaptive-behavior.*

Humans are innately driven to seek out food, drink, reproduction, and other naturally rewarding experiences. These behaviors are closely tied to neurobiological mechanisms designed to reinforce survival and pleasure. However, dysfunction within these reward pathways-often due to genetic polymorphisms-can result in a heightened vulnerability to impulsive, compulsive, and addictive behaviors. A growing body of evidence has identified numerous gene variants that influence mesolimbic dopamine activity, thereby predisposing individuals to intense cravings and maladaptive behavioral patterns [8-11].

Key polymorphic gene targets associated with this susceptibility include the serotonergic 2A receptor (5-HTT2a), serotonin transporter gene (5HTTLPR), dopamine receptors D2 and D4 (DRD2, DRD4), dopamine transporter (DAT1), and enzymes involved in catecholamine metabolism such as catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO). The cytochrome P450 (P400) gene family also plays a regulatory role in neurochemical processing [12].

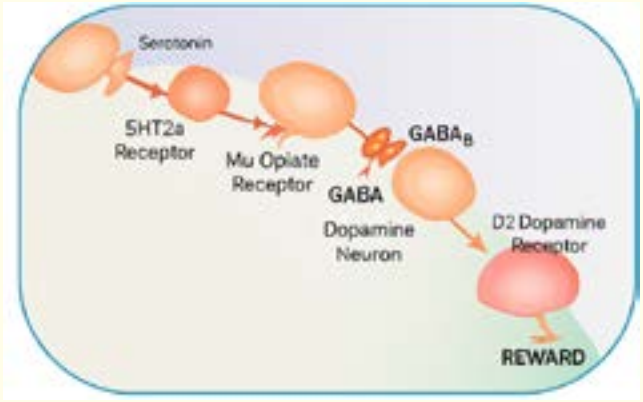


***Figure 4:*** *Interaction of neurotransmitters within the mesolimbic brain reward cascade illustrating the sequential neurochemical signaling events within the mesolimbic brain reward cascade, a key circuit underlying reward, motivation, and pleasure. The process begins in the hypothalamus with the release of serotonin, which activates 5HT2a receptors. This stimulation promotes the release of enkephalins, which bind to mu-opioid receptors on GABAergic neurons in the substantia nigra. Binding of enkephalin inhibits GABA release, reducing inhibitory tone on dopamine neurons located in the ventral tegmental area (VTA). This disinhibition permits dopamine release into the nucleus accumbens (NAc). GABA receptors (including GABA_B) are also shown exerting inhibitory control along the cascade. Ultimately, dopamine binds to D2 receptors in the NAc, generating the sensation of reward. This cascade highlights the intricate balance between excitatory and inhibitory neurotransmission, with serotonin, opioid peptides, GABA, and dopamine interacting to regulate the brain's response to rewarding stimuli. Dysregulation of this system is implicated in various neuropsychiatric conditions, including addiction and reward deficiency syndrome.*

Beyond these receptor and enzyme-related polymorphisms, other molecular contributors such as transcription factors DeltaFosB and CREB, components of the ERK signaling cascade, brain-derived neurotrophic factor (BDNF), and glutamatergic neurotransmission have been implicated in the neuroadaptations that underpin addiction vulnerability. These findings support the concept that genetic and molecular diversity shapes individual differences in reward sensitivity and addiction risk.

Gold and colleagues initially introduced the concept of a functional dopamine (DA) deficiency to account for the neurochemical basis of cocaine abstinence and later extended this model to explain opioid withdrawal symptoms as well [13-16]. In 1996, Blum's group formally conceptualized this broader neurobiological impairment under the term Reward Deficiency Syndrome (RDS), which encompasses a range of conditions linked to impaired dopaminergic signaling (Figure 5) [9].

Among the most studied genetic contributors to RDS are polymorphisms in the dopamine D2 receptor gene (DRD2), which have been associated with increased risk for impulsive, compulsive, and addictive behaviors [17-19]. Individuals with reduced density or sensitivity of dopamine and serotonin receptors-often due to inherited gene variants-may also display elevated dopamine catabolism, particularly if they possess high-activity alleles of the catechol-O-methyltransferase (COMT) gene or exhibit increased monoamine oxidase (MAO) activity.


***Figure 5:*** *Behavioral categories associated with reward deficiency syndrome (RDS) based on converging evidence from genetic, neurobiological, and clinical studies are shown in this mind map. The central blue node ("Behavioral Categories") branches into four color-coded domains: Addictive behaviors (yellow - include severe alcoholism and drug abuse, poly-substance abuse, smoking, and obesity), impulsive behaviors (light green - ADHD, Tourette syndrome, and autism), compulsive behaviors (lavender - pathological gambling, internet gaming, and aberrant sexual behavior), and personality disorders (pink - antisocial personality, conduct disorder, and aggressive behaviors). These behavioral phenotypes are unified by underlying dysfunctions in the mesolimbic dopaminergic reward system, often involving polymorphisms in key genes such as DRD2, 5HTTLPR, and COMT. This framework provides a neurogenetic rationale for understanding the common pathways across diverse psychiatric and behavioral disorders.*

As a result of this neurochemical imbalance, such individuals are more likely to engage in self-reinforcing behaviors or consume substances that elevate dopamine transmission. These include, but are not limited to, alcohol, opioids, stimulants, nicotine, sugar, gambling, sexual activity, and compulsive internet use [6,20,21]. This body of research underscores the role of genetic predisposition in shaping vulnerability to a wide spectrum of reward-seeking behaviors (Figure 5).

The consumption of various addictive substances, including alcohol, is known to stimulate dopamine (DA) release within the brain's mesocorticolimbic or reward circuitry [22] (Figure 6). This dopaminergic activation elicits sensations of pleasure and reinforcement [15,23,24]. In contrast, diminished dopamine signaling-commonly referred to as hypodopaminergia-has been implicated in the emergence of compulsive drug-seeking behavior [25]. Genetic polymorphisms can contribute to such dysfunction by reducing dopamine receptor availability, dampening dopaminergic responsiveness, or accelerating dopamine degradation along reward pathways [26]. Additionally, abrupt discontinuation after prolonged substance use may further exacerbate this hypodopaminergic state, reinforcing the cycle of craving and relapse as the brain attempts to mitigate withdrawal discomfort [27].

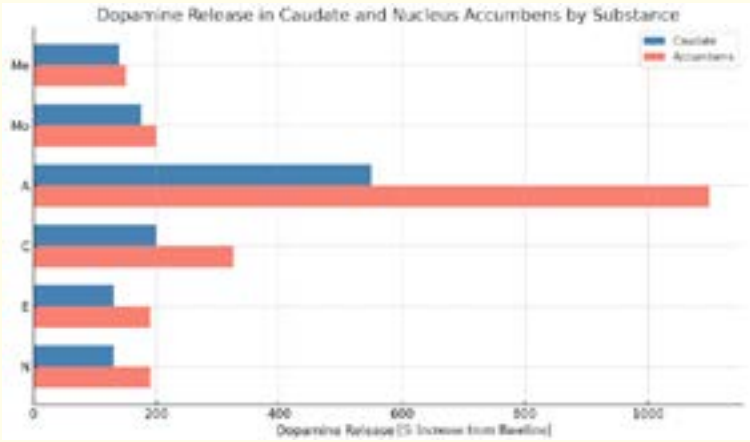


***Figure 6:*** *Dopamine release in the caudate and nucleus accumbens following administration of commonly abused substances shown in percent output from baseline. This horizontal bar graph compares extracellular dopamine levels in two key regions of the brain's reward system-the caudate and nucleus accumbens-after acute administration of various substances: Nicotine (N), Ethanol (E), Cocaine (C), Amphetamine (A), Morphine (Mo), and Methadone (Me). Blue bars represent dopamine release in the caudate, while salmon-colored bars indicate release in the nucleus accumbens. Amphetamine (A) triggers the most robust dopaminergic response, particularly in the nucleus accumbens, highlighting its strong addictive potential. The nucleus accumbens consistently exhibits higher dopamine activation than the caudate across all substances, underscoring its central role in the development of reward, reinforcement, and addiction. Abbreviations: Me = Methadone; Mo = Morphine; A = Amphetamine; C = Cocaine; E = Ethanol; N = Nicotine [22].*

Although short-term use of substances such as methadone, morphine, amphetamines, cocaine, ethanol, and nicotine can produce transient feelings of euphoria, long-term consumption leads to adverse effects including toxic highs, desensitization, emotional blunting, and the development of tolerance and dependency [28]. Individuals carrying the DRD2 A1 allele, which is associated with reduced dopamine receptor density, are particularly vulnerable to compulsive drug-seeking behavior due to an increased craving drive. In contrast, those with typical levels of D2 receptors tend to exhibit lower levels of craving and better self-regulation.

Preventative strategies aimed at mitigating substance abuse or controlling sugar overconsumption in genetically susceptible populations may benefit from approaches that promote dopamine D2 receptor upregulation [29]. Laboratory studies have demonstrated that chronic, low-dose activation of D2 receptors by specific agonists can lead to significant increases in D2 receptor density-even in models predisposed to lower receptor expression [30]. This receptor upregulation appears to be mediated through feedback mechanisms that stimulate mRNA expression in the mesolimbic system, promoting D2 receptor proliferation.

Translational evidence from animal models supports this concept. For example, targeted overexpression of DRD2 receptors via gene therapy has been shown to significantly reduce craving-like behaviors related to alcohol and cocaine intake [31-34]. These findings lay the groundwork for future interventions that aim to enhance dopamine signaling naturally, with the goal of reducing vulnerability to addiction in at-risk individuals.

These insights form the foundation of a theoretical framework for understanding compulsive drug-seeking behavior and continued substance use. Central to this framework is the hypothesis that a deficiency in dopamine signaling-a hypodopaminergic state-serves as

a primary biological driver of addictive tendencies, irrespective of whether the deficit originates from chronic drug use, genetic factors, or environmental stressors. Genetic polymorphisms that impair dopamine transmission may therefore constitute a critical inherited risk factor for persistent substance use and relapse vulnerability [29]. Consequently, long-term therapeutic strategies aimed at restoring dopaminergic balance may prove effective in managing a range of behaviors under the umbrella of Reward Deficiency Syndrome (RDS), including substance misuse, attention-deficit hyperactivity disorder (ADHD), and metabolic disorders like obesity.

Dopamine (DA) is the principal neurotransmitter associated with the brain's reward mechanisms and has been consistently linked with experiences of pleasure and emotional regulation [35]. Upon release, dopamine activates several receptor subtypes (D1 through D5), resulting in enhanced mood and decreased stress. Of particular importance is the DRD2 gene, which encodes the dopamine D2 receptor and has been extensively studied in relation to addiction, psychiatric illnesses, and other dopamine-related conditions [36,37].

Understanding motivated behavior necessitates familiarity with the brain circuits responsible for reinforcing actions and stimuli [38]. Positive reinforcers are defined as outcomes that increase the likelihood of a behavior being repeated, and substances of abuse are often considered more potent reinforcers than innate stimuli such as nourishment or reproduction [39-41]. It is important to distinguish between natural reinforcers-those fulfilling biological imperatives-and unnatural reinforcers, which are typically learned behaviors and represent acquired drives [42,43]. The latter category includes alcohol and drug use, gambling, and risk-taking behaviors that trigger pleasure-seeking responses [44,45].

The nucleus accumbens (NAc), situated within the ventral striatum, plays a key role in mediating the pleasurable effects of both drugs and natural stimuli. It has been identified as a central hub for processing reinforcement associated with substances like cocaine [46], alcohol [47], nicotine [48], highly palatable foods [49] and even music [50]. Beyond its involvement in substance-related reinforcement, the NAc regulates essential motivational behaviors, including food and fluid intake, sexual activity, and exploratory movements. A core principle of reward learning is that actions followed by pleasurable outcomes are more likely to be repeated. Disproportionate 'liking' of rewarding stimuli may promote compulsive behavior patterns, contributing to RDS pathology. This convergence of neurobiological processes supports a unified theory of motivation that applies to a broad range of hedonic behaviors [51].

In this context, we have summarized the interplay of neurochemical and genetic influences implicated in the emergence of addictive behaviors [52]. Our proposed hypothesis suggests that these behaviors are manifestations of underlying deficits in brain reward circuitry. This neurogenetic perspective helps clarify why some individuals are more vulnerable to addiction and relapse than others.

Building on the preceding discussion, we suggest that individuals with impaired dopaminergic signaling may be more inclined to engage in maladaptive behaviors as a compensatory response to their reduced capacity for experiencing reward. This inclination likely stems from a neurobiologically rooted drive to attain pleasure or alleviate emotional discomfort, which may contribute to the emergence of compulsive or destructive behavioral patterns. In the subsequent section, we examine whether similar neurochemical pathways associated with reward processing also influence the human inclination toward spiritual engagement. Specifically, we clarify how we conceptualize "spirituality" within this framework, assess its potential role in the recovery process, and explore scientific findings that implicate genetic factors and neurobiological stability in spiritual predisposition and resilience.

## Defining the ineffable

Before exploring the possibility that spirituality may be rooted in human genetics, it is important to define how the term is used in this context. By "spirituality," we do not refer to religion, which typically encompasses structured belief systems regarding specific truths or doctrines, nor are we referencing supernaturalism-the philosophical stance that posits realities beyond natural phenomena, inaccessible to empirical investigation. While elements of spirituality may be present within religious or supernatural frameworks, our current focus is not to validate or critique these paradigms.

Instead, we conceptualize spirituality as a domain of meta-meaning, closely tied to an individual's fundamental sense of purpose and personal significance. It relates to the interpretation of objects, experiences, or events in ways that transcend surface-level meaning, pointing toward a deeper understanding of one's place and value in the world.

In this sense, spirituality encompasses the full spectrum of thoughts, beliefs, perceptions, experiences, and behaviors concerning realities that lie beyond the self. Central to many spiritual frameworks is the idea of self-transcendence-extending one's awareness beyond ego-centric perspectives. Thus, spirituality becomes not only a lens through which one views life but also a way of engaging with the world. Importantly, this orientation can manifest in either constructive or harmful forms, depending on its expression and influence on well-being.

On this view, Jerome Dollard says, "Spirituality is a lot like health. We all have health; we may have good health or poor health, but it's something we can't avoid having. The same is true of spirituality: every human being is a spiritual being. The question is not whether we 'have spirituality' but whether the spirituality we have is a negative one that leads to isolation and self-destruction or one that is more positive and life-giving".

Having clarified our interpretation of spirituality, we suggest that some individuals may possess a genetic inclination toward what might be described as "spiritual well-being." This perspective is further supported by experiential and observational evidence suggesting a meaningful connection between spiritual orientation and patterns of addiction. We hypothesize that the capacity for healthy spiritual engagement may arise more naturally in certain people due to a distinctive interplay between their genetic makeup and environmental influences.

In the sections that follow, we explore emerging research that supports this proposition. For the purposes of this discussion, we introduce the term genospirituality to describe the intersection between genetic factors and spiritual propensity.

## Spirituality, addiction, and recovery

Individuals struggling with addiction frequently describe a profound inner fragmentation, a sense of being trapped, and an absence of meaning or purpose. This existential distress has often been interpreted as a form of spiritual longing-a deep yearning for wholeness, liberation, and transformation. Etymologically, the word "addict" stems from Latin, implying a voluntary submission, as if one has willingly surrendered autonomy through repeated acts of devotion. Over time, the compulsive pursuit of the temporary escape or self-transcendence offered by a substance or behavior becomes the dominant force in a person's life. What once seemed to offer freedom from the constraints of the self ultimately evolves into an all-consuming dependency-a "rapacious creditor" that drains the individual of self-direction and the strength to resist its demands [2].

Addiction constrains freedom in a unique way: not necessarily by compelling people to act against their will, but by distorting their desires-causing them to crave what they ultimately wish to avoid [3]. This cycle of obsession eventually dismantles the person's inner coherence, reducing their capacity to exert control. Recognizing this loss of control-often described as powerlessness-is a deeply personal realization, one that may surface existential or spiritual questions. For many, this acknowledgment marks the first step on the path to recovery and authentic freedom.

This experiential understanding reveals an intrinsic connection between addiction and spirituality [2]. Psychiatrist Carl Jung poignantly illustrated this idea in his correspondence with Alcoholics Anonymous co-founder Bill Wilson: "You see, Alcohol in Latin is 'spiritus'-the same word used for both the highest form of religious inspiration and the most destructive intoxicant. Thus, the remedy is: "spiritus contra spiritum". Philosopher William James echoed a similar theme in The Varieties of Religious Experience, writing: "The only radical remedy I know of for dipsomania is religiomania".

Neuroscientist Patrick McNamara has provided compelling support for the connection between spirituality and psychological integration. In The Neuroscience of Religious Experience, McNamara argues that religion may have emerged evolutionarily to help unify the divided aspects of the human psyche through spiritual encounters [53]. He suggests that the same inner drive for cohesion, self-understanding, and liberation-often misdirected toward substance use or compulsive behaviors-can instead lead individuals toward meaningful spiritual or religious engagement.

This theoretical framework finds contemporary relevance in mutual-help movements such as alcoholics anonymous (AA) and its twelve step program. AA describes itself as a fellowship where individuals share "their experience, strength, and hope" with one another in the pursuit of sobriety. As quoted by Thomas Prugh, Jerome Dollard captured this essence in his reflection on alcohol, spirituality, and recovery, emphasizing the central goal of recovery through shared purpose and mutual aid. This collective intention not only helps individuals maintain sobriety but also contributes to redefining their sense of identity and life purpose.

A major factor in AA's transformative impact is its emphasis on narrative. Members are encouraged to recount their journeys-describing who they were, what transpired, and who they've become. These personal stories serve both as a cathartic reminder of past suffering and a testament to progress. By continuously revisiting this narrative arc, individuals begin to reinterpret their lives, developing gratitude for their recovery and resilience. The act of storytelling becomes a powerful cognitive and emotional exercise, reframing one's self-perception and fostering lasting behavioral change.

Additionally, the twelve steps are designed to nurture deeper awareness and introspection. They call for a reevaluation of one's behavior and interpersonal dynamics, encouraging individuals to take responsibility for their actions and to consider the wellbeing of others. This moral inventory becomes a spiritual discipline in itself, aligning personal development with ethical consciousness. In this way, the Steps provide a structured pathway for achieving the kind of spiritual awakening long advocated by many of the world's major religious traditions.

## Spirituality and the brain

At a basic intuitive level, the interplay between addiction, spirituality, and brain function becomes evident when one considers that individuals often seek altered states of consciousness-and ultimately positive emotional experiences-through substances that chemically affect the brain. This intuitive understanding raises a compelling question at the heart of our current exploration of genospirituality: How do addictive substances undermine spirituality, and conversely, how might spiritual practices counteract addiction?

To begin addressing this question, it is crucial to acknowledge a foundational premise: that the brain is central to all experiences, both conscious and unconscious, including those considered spiritual. In religious and spiritual experiences, Wesley J. Wildman introduces this concept as the neural mediation hypothesis [54]. He asserts, "the mind does nothing we can detect that is not exhaustively mediated by and expressed in the brain." While debates around this perspective continue in some circles, Wildman contends that the weight of scientific evidence has shifted the burden of proof onto those who deny the brain's essential role in facilitating spiritual experiences. According to this view, any serious discussion of the biological underpinnings of spirituality must begin with the brain.

This understanding sets the stage for a deeper examination of how specific neurochemical and genetic factors involved in addiction may also influence the capacity for spiritual engagement-and how spirituality, in turn, might serve as a buffer against compulsive behaviors linked to reward dysregulation.

## Genospirituality

Nilsson and colleagues [55] explored the relationship between spirituality and genetic variation in adolescents, finding notable associations between specific genotypes and traits such as self-transcendence and spiritual acceptance. Among boys, there was a negative

correlation between these spiritual traits and the short allele of the 5-HTTLPR polymorphism, while a positive correlation emerged with the short variant of the AP-2β gene. In both boys and girls, an interaction between 5-HTTLPR and AP-2β genotypes revealed that individuals carrying the short 5-HTTLPR and homozygous for the long AP-2β scored significantly lower on these spiritual measures. These findings are in line with earlier research by Comings and associates, who also identified polymorphisms associated with spirituality [56].

In The God Gene, Hamer [57] proposed that dopaminergic genes related to spirituality may have been selected for their role in fostering innate optimism-an adaptive trait promoting perseverance, reproduction, and survival in the face of mortality [58]. Additional studies link this optimistic outlook to improved health outcomes and quicker recovery from illness, reinforcing its evolutionary value. Newberg [59], however, offered a complementary hypothesis, suggesting that the neural architecture supporting spiritual transcendence evolved from circuits within the limbic system originally involved in sexual behavior. This aligns with existing data connecting dopamine-regulating genes to reward, stress reduction, and affective states [60].

Research by Comings., *et al*. has further implicated the dopamine D4 receptor gene (DRD4), known for its role in novelty seeking, as a genetic marker associated with spiritual expression. This personality trait is part of Cloninger's temperament and character inventory [61], and *in vitro* findings have associated the DRD4 polymorphism with disrupted dopamine signaling [62]. Despite this, in studies focused on individuals with substance use disorders, novelty seeking did not strongly correlate with spirituality. However, a significant link was observed between spiritual acceptance and specific DRD4 gene variants [63,64].

Another gene of interest is the dopamine vesicular monoamine transporter (VMAT2), which has also been linked to spiritual tendencies. That both DRD4 and VMAT2-genes influencing dopamine release-are associated with spirituality suggests that dopaminergic tone may underlie some individuals' spiritual responsiveness. This could explain the widespread emotional comfort and existential meaning that people derive from religious or spiritual beliefs [65].

Comings and his collaborators [56,65] also observed that individuals with high scores in self-transcendence were less likely to engage in alcohol or drug misuse. This observation supports the idea that spiritually engaged individuals may be less inclined to stimulate their reward systems through external substances, relying instead on endogenous mechanisms activated through spiritual practice-a core tenet echoed in Alcoholics Anonymous' Twelve Step framework [2].

In related findings, Borg., *et al*. [66] at Sweden's Karolinska Institute demonstrated that individuals with elevated self-transcendence scores showed reduced ethanol binding in the brain, implying heightened serotonin activity. They also found a significant association between the serotonin1A receptor gene and spiritual traits. Given that LSD shares structural similarities with serotonin and modulates serotonergic pathways during psychedelic spiritual experiences, it is unsurprising that Bill Wilson-the co-founder of AA-experimented with LSD as a potential aid for treating alcoholism [2].

Moreover, various botanicals used throughout human history contain psychoactive compounds-serotonergic, opioid, and catecholaminergic-that intensify spiritual experiences. Comings [56] emphasized the foundational role of such entheogens in shaping early religious thought and facilitating belief in divine entities. Finally, Bachner-Melman [67] hypothesized that serotonergic function may serve as a key mediator in spiritual and religious experiences in humans. Building on this, we suggest that the interaction of AVPR1a and SLC6A4 may help explain the behavioral and social elements of the "dancing phenotype," which includes not only motor coordination but also communal bonding and spiritual expression.

The process of holistic healing appears to be intimately linked to gene expression, which in turn governs neurogenesis and stem cell activity. This perspective positions regenerative cellular processes as a foundational mechanism behind the effectiveness of rehabilitative

therapies, including physical and occupational interventions, as well as various mind-body modalities. Rossi [68] proposed that re-experiencing emotionally enriching and meaningful life events-through channels such as art, music, dance, theater, humor, literature, poetry, spirituality, and cultural rituals-can evoke what he termed the "novelty-numinosum-neurogenesis" effect. These creative and symbolic experiences promote consciousness, deepen interpersonal relationships, and facilitate healing by influencing gene activity. This framework parallels the psychogenomic underpinnings of both conventional and complementary medicine, suggesting that psychological arousal and awe-as encountered in culturally embedded rites of passage (e.g. birth, marriage, illness, healing, and death)-may play a vital role in promoting cellular repair and emotional well-being.

When considering the intersection of spirituality, genetics, and behavioral outcomes, research into religious behavior and gene-environment interactions has provided intriguing insights. Kendler and Myers [69] reported that as individuals age, their temperaments-which are partially genetically influenced-begin to shape their social choices, including religious engagement. During youth, frequent participation in religious services often reflects familial and environmental structures that mitigate substance use. However, in adulthood, sustained church attendance may instead reflect intrinsic, genetically rooted traits associated with resilience against substance use disorders.

This gene-environment dynamic was further explored by Boomsma., *et al*. [70], who examined the relationships between personality traits, affective disorders, and religious behavior in Dutch families. They found that upbringing had a moderating effect on sensation-seeking tendencies, particularly among male twins. In parallel, Koopmans., *et al*. [71] studied how religiosity might moderate genetic and environmental contributions to the onset of alcohol use. In a sample of 1,967 twin pairs, they hypothesized-and found evidence supporting-that individuals raised in less religious households demonstrated higher heritability for alcohol initiation, while shared environmental factors played a larger role among those raised in religious environments. Specifically, genetic influence explained 40% of variance in alcohol use initiation among nonreligious females, but none among their religiously raised counterparts. In contrast, shared environment accounted for 54% of the variance in the nonreligious group and 88% in the religious group. Although similar trends were observed in males, they did not reach statistical significance.

Haber and colleagues [72] provided further nuance, identifying religiosity/spirituality (RS) as a protective factor during the early stages of alcohol exposure, such as initiation. However, once alcohol consumption had begun, genetic factors appeared to play a more dominant role in sustaining alcohol dependence (AD), with RS exerting less influence during this maintenance phase. These findings are echoed by Levin [73] and Rosmarin [74] and support early RS-based interventions in families with known predispositions to alcoholism as a preventive measure.

### Molecular neurobiology of religion

Over the past six decades, efforts to elucidate the complex causes of disease and the variability in treatment responses have highlighted the influence of physical, chemical, and social determinants on health. These factors disproportionately affect certain vulnerable groups, particularly socio-environmentally disadvantaged (SED) populations. Emerging research in translational medicine has illuminated how adverse interactions between genetic predispositions and environmental exposures-known as aberrant epigenomic modulation-can disrupt gene expression. This occurs through dysregulation of messenger RNA (mRNA), leading to irregular protein production and impaired cellular development and specialization.

In light of this, our laboratory has turned its attention to exploring how specific polymorphisms in neurotransmitter-related genes, when considered alongside an individual's acceptance or rejection of spiritual frameworks (defined here as belief in a higher power), might influence the initiation and relapse patterns associated with substance use disorders. Drawing on two distinct datasets-the National Institute on Drug Abuse (NIDA)-funded Drug Addiction Treatment Outcome Study (DATOS) and follow-up data from a holistic

rehabilitation program based in North Miami Beach, Florida-we observed a consistent and significant inverse association: stronger spiritual beliefs correlated with lower rates of relapse across both independent cohorts [75]. Ongoing analysis will further examine the potential genetic underpinnings of these findings, particularly focusing on how specific gene polymorphisms may contribute to both spiritual orientation and substance use outcomes.

The link between religiosity/spirituality and behavioral deviance, including addiction, can be traced back to the foundational work of Émile Durkheim. He introduced the concept of "anomie" to describe the breakdown of social norms and argued that religious and spiritual engagement helps reinforce normative behaviors and strengthen social cohesion. From this perspective, the absence of structured belief systems may contribute to deviant behaviors, such as substance misuse. Given that Reward Deficiency Syndrome (RDS) has been associated with dysfunctional reward pathways and behavioral dysregulation, it is reasonable to hypothesize that heightened spiritual commitment may serve as a protective buffer-potentially reducing the likelihood of relapse and promoting recovery in individuals at risk for or struggling with addiction.

The Drug Addiction Treatment Outcome Study (DATOS) conducted by the National Institute on Drug Abuse (NIDA) was utilized to retrospectively analyze relapse patterns among 2,947 individuals assessed 12 months post-treatment intake, categorized by five distinct measures of spirituality [75]. The primary findings presented by Schoenthaler and colleagues suggest a robust inverse relationship between spiritual engagement and relapse rates-those reporting higher levels of spirituality demonstrated greater remission across substances including heroin, cocaine, alcohol, and marijuana, with crack cocaine as the sole outlier. Statistically significant associations emerged in relation to religious belief strength ($\chi^2 = 15.18$, $p = 0.028$; logistic regression = 10.65, $p = 0.006$), frequency of attending services ($\chi^2 = 40.78$, $p < 0.0005$; logistic regression = 30.45, $p < 0.0005$), reading religious texts ($\chi^2 = 27.19$, $p < 0.0005$; logistic regression = 17.31, $p < 0.0005$), viewing religious programming ($\chi^2 = 19.02$, $p = 0.002$; logistic regression = ns), and meditation or prayer frequency ($\chi^2 = 11.33$, $p = 0.045$; logistic regression = 9.65, $p = 0.002$). Individuals with higher spirituality reported between 7 - 21% lower substance use than their non-spiritual counterparts. Notably, crack cocaine users who reported minimal religious engagement paradoxically used less than those with stronger spiritual orientations. Among the spirituality indicators, regular religious service attendance showed the strongest correlation with remission, aligning with Durkheim's social integration theory.

A separate investigation by Zhen-Duan., *et al*. [76] explored the epigenetic impact of religion and spirituality (R&S) on DNA methylation across 14 CpG sites in four HPA-axis genes among 992 adults in the Hispanic Community Health Study. The analysis focused on methylation differences by nativity status and genotype. Results revealed that, among immigrants carrying the FKBP5 CC genotype, higher spirituality scores were linked to significantly lower methylation levels compared to their U.S.-born peers. Furthermore, increased organizational religious participation correlated with elevated FKBP5 methylation in immigrant subgroups, indicating that R&S may differentially influence stress-regulatory gene expression depending on cultural context.

Reducing activity in the Default Mode Network (DMN)-especially in ego-centered regions like the amygdala-has been posited as a central benefit of spiritual or meditative experiences [77]. Meditation practices (MPs), integral to Eastern spiritual healing systems, are now being examined in Western medicine for their potential to induce epigenomic modifications. Zahir's review detailed how practices such as yoga, mindfulness, and other meditative disciplines produce consistent downregulation of stress-related genes. Early high-resolution epigenetic assays confirm MPs can dynamically modulate the human genome. For instance, using 11C-raclopride PET imaging, Kjaer., *et al*. demonstrated a 7.9% reduction in radiotracer binding in the ventral striatum during Yoga Nidra, corresponding to a 65% increase in endogenous dopamine release-a neurochemical change linked to relaxation and enhanced mood [78].

Parallel work by Koepp., *et al*. using 11C-raclopride and PET scanning similarly demonstrated increased dopamine release during goal-oriented tasks such as video gaming [79]. A notable decrease in radioligand binding to D2 receptors in the striatum, particularly the

ventral region, was strongly correlated with task performance, reinforcing the idea that both spiritual practices and engaging activities can trigger meaningful dopaminergic changes.

Holmes., *et al*. [80] extended this dialogue by reviewing how social and spiritual support systems-conceptualized as the Spiritual Network Support System (SNSS)-can affect gene expression. Drawing parallels to environmental stressors such as bereavement, low socioeconomic status (SES), and early life adversity, they posited that SNSS may mitigate the expression of pro-inflammatory or maladaptive genes by engaging the sympathetic nervous system and HPA axis. Gene pathways such as the conserved transcriptional response to adversity (CTRA) and NR3C1 were implicated in these processes. Their findings suggest practices like prayer, meditation, and yoga may provide genomic resilience against stress, with implications even in conditions like cancer.

For over three millennia, psychedelics have been used in ritualistic settings to enhance spiritual awareness, community bonding, and healing. In recent years, there has been renewed scientific interest in psychedelic-assisted therapies for mental health disorders. Our lab has recently proposed that Borderline Personality Disorder (BPD) and Post-Traumatic Stress Disorder (PTSD) share common neurobiological features-particularly reward deficiency and stress-linked anti-reward circuitry-and may benefit from overlapping therapeutic strategies. This led us to suggest reconceptualizing BPD as a "Traumatic Personality Stress Disorder" (TPSD), thereby aligning it more closely with PTSD in treatment frameworks. Martire., *et al.* [81] proposed that psychedelic-assisted therapy (PAT) could be effective for trauma-related personality dysfunctions by stabilizing dopaminergic systems and facilitating emotional integration. Reframing BPD as TPSD may reduce stigma, offer improved clinical outcomes, and foster personalized care strategies across related diagnoses characterized by anhedonia, emotional dysregulation, and dissociation.

Psychedelics predominantly exert their psychoactive effects through serotonin 5-HT2A receptor binding, although many also interact with dopaminergic pathways. Recently, Fan., *et al*. [82] provided structural insights into LSD's interaction with the dopamine D1 receptor (DRD1) using cryo-electron microscopy. The findings revealed a unique binding orientation involving the ergoline moiety and an unusually rapid dissociation rate mediated by extracellular loop 2 (ECL2) flexibility. Additionally, G protein interaction was shown to stabilize this conformation, influencing downstream signaling dynamics. These data not only elucidate the pharmacokinetics of LSD but also pave the way for broader applications of GPCR-targeted therapeutics in mental health, particularly those that impact dopaminergic tone.

Unlike traditional psychotropic medications commonly used in psychiatric practice, psychedelic compounds introduce a multifaceted complexity. These agents do more than bind to receptors-they modulate entire neural networks, potentially triggering transformative experiences often described as mystical or spiritual in nature. This unique capacity to evoke altered states of consciousness has reignited interest in the intersection of psychiatry, consciousness studies, and spirituality.

The serotonin (5-hydroxytryptamine or 5-HT) receptor system, particularly the 5-HT2-family, represents a central pharmacological target for classic psychedelics such as lysergic acid diethylamide (LSD) and psilocybin. While the primary psychoactive effects are mediated via the 5-HT2A receptor (HTR2A), the closely related 5-HT2B receptor (HTR2B) serves as a structural model for investigating psychedelic drug-receptor activation due to its expression profile and pharmacologic similarities to HTR2A [83].

Despite ongoing challenges in pinpointing the full mechanisms of action for LSD and psilocybin, progress is being made in understanding their influence on monoaminergic and glutamatergic pathways, neuroplasticity, and epigenetic regulation. Psychedelics also appear to modulate large-scale brain networks, including the default mode network (DMN) and cortico-striato-thalamo-cortical loops, which are implicated in self-referential thinking and executive function. These complex effects invite a reimagining of psychiatric frameworks, potentially integrating neuroscientific and spiritual domains in novel ways [84].

Amid these neuropsychiatric advances, there remains a lack of sustained dialogue between scientific and religious communities-particularly concerning ethical considerations in precision medicine and genetic technologies. Modell., *et al*. [85] explored these perspectives in a participatory dialogue between scientists and faith leaders. While scientists emphasized adherence to professional standards, religious figures prioritized empathy and familial considerations. The collaboration revealed common ground and suggested that interdisciplinary engagement could guide ethical implementation of public health genetics.

From a historical and theological standpoint, morality has long been used as a societal tool to moderate behavior. The Christian tradition, for example, identifies seven cardinal sins-pride, greed, lust, anger, gluttony, envy, and sloth-each paired with a corresponding virtue. These moral constructs aimed to prevent societal chaos and promote individual accountability, with sin understood as a deviation from spiritual freedom or divine will [86]. Philosophical and neuroscientific inquiry into the origins of such behaviors suggests that morality, and its violations, may be partially rooted in neurobiological and genetic underpinnings-creating an interdisciplinary platform to explore the "neurobiology of sin".

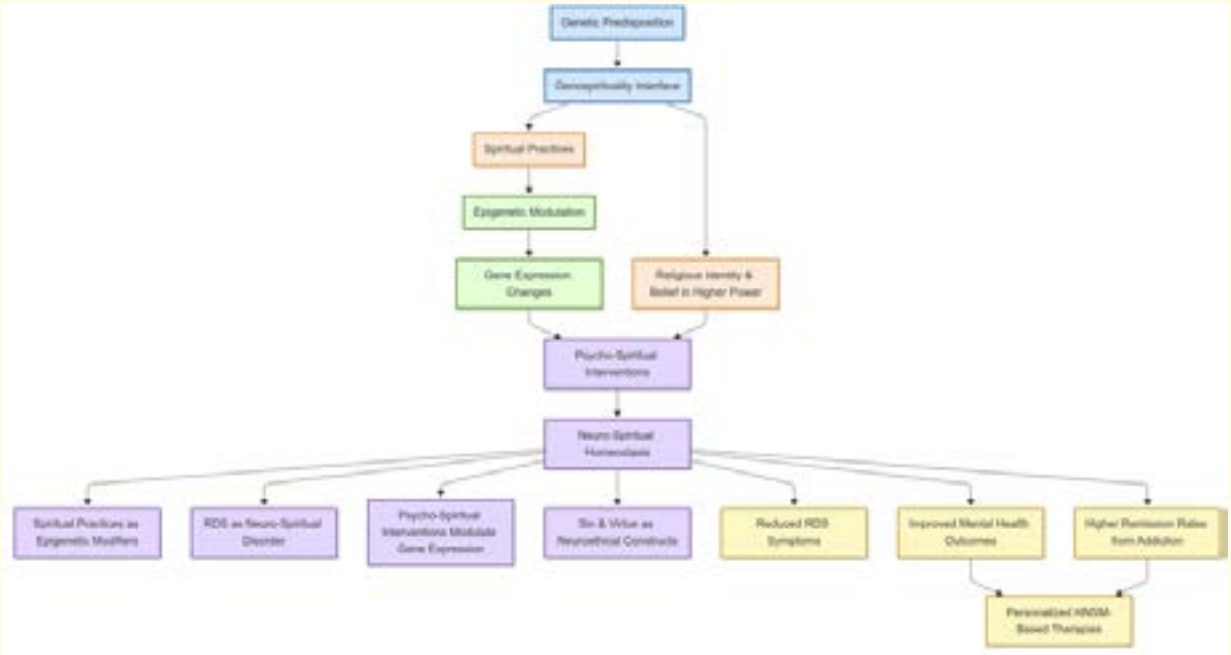

***Figure 7:*** *Hierarchical neuro-spiritual model (HNSM) is an integrative framework linking genospirituality, reward neurobiology, and addiction recovery outcomes:*

*a) The model begins with an individual's genetic predisposition, which interacts with spiritual practices and religious identity through the Genospirituality Interface-a conceptual bridge between genomic traits and spiritual engagement.*

*b) On the left side of the diagram, spiritual practices initiate epigenetic modulation, resulting in downstream gene expression changes that can influence neuroplasticity and resilience. On the right, belief in a higher power (distinct from religious affiliation) also contributes to downstream processes. Together, these elements converge on psycho-spiritual interventions, such as meditation, prayer, communal rituals, and therapeutic storytelling, which support adaptive neural and psychological functioning.*

This emerging field seeks to decode how molecular, epigenetic, and evolutionary factors shape moral behavior and judgment. Such inquiries blend insights from both ancient philosophy and modern neuroscience, reflecting on humanity's ongoing struggle between instinct, conscience, and free will-what Estévez metaphorically described as the "path between Prometheus and Descartes" [86].

Interestingly, analogous efforts to harmonize science and spirituality are evident in Islamic scholarship. Ghareeb [87] demonstrated that numerous passages in the Qur'an and ḥadīth reflect principles resonant with modern genetics-including ideas related to inheritance patterns, chromosomal sex determination, gene-environment interactions, and cytoplasmic inheritance. This alignment encourages a re-evaluation of religious texts in light of contemporary scientific paradigms and supports the notion that spirituality and science need not exist in opposition.

In sum, the convergence of psychedelic neuroscience, morality, genetic science, and spiritual traditions opens fertile ground for new models of mental health, human behavior, and ethical reflection. These evolving frameworks may help bridge scientific inquiry with ancient wisdom-paving the way for a more integrated understanding of healing, purpose, and consciousness (Figure 7).

## Future Perspective

This expert opinion explores the emerging field of neuro-spirituality by examining whether it is scientifically feasible-or even ethically desirable-to apply genetic engineering techniques to enhance human spiritual and religious experience. Such "gene-spirituality" interventions might help humanity better cope with escalating global challenges. Charlson., *et al*. [88] estimated the global prevalence of mental health disorders-including depression, anxiety, PTSD, bipolar disorder, and schizophrenia-at 22.1% (95% UI: 18.8-25.7). Within this population, comorbidity-adjusted, age-standardized prevalence rates were 13.0% (95% UI: 10.3-16.2) for mild conditions, 4.0% (95% UI: 2.9-5.5) for moderate cases, and 5.1% (95% UI: 4.0-6.5) for severe disorders.

This inquiry delves into the neurobiological underpinnings of spirituality by assessing links between reward genes, hypodopaminergic states (commonly described as Reward Deficiency Syndrome or RDS), the mirror neuron system, and the default mode network (DMN). Targeting these neurobiological frameworks may support a novel intervention model based on the Purpose and Meaning of Life as Reward (PMLR), especially within addiction medicine and behavioral health interventions [89].

The concept of Reward Deficiency Syndrome (RDS) was first introduced by Kenneth Blum in 1995 as a unified framework describing the dopaminergic dysregulation underlying various mental health conditions. The presence of the DRD2 Taq A1 polymorphism, which can reduce D2 receptor density by up to 40%, was initially proposed as a key marker. Unlike the categorical structure of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), which tends to isolate disorders, the RDS framework advocates for an integrative model acknowledging overlapping neurobiological mechanisms across psychiatric conditions.

Indeed, critiques of DSM-based nosology-such as those voiced by former NIMH Director Steven Hyman-emphasize the need to shift toward etiologically informed psychiatric research [90]. The NIMH's Research Domain Criteria (RDoC) initiative reflects this paradigm shift by promoting investigations into five core domains of brain function that transcend traditional diagnostic categories.

In alignment with this model, the RDS Consortium has taken up the challenge of refining psychiatric diagnostics by anchoring them in neuroscience and genetics [89,91,92]. As of March 2025, more than 1,600 publications on "Reward Deficiency" and over 270 specifically referencing "RDS" appear in PubMed. Since Blum and Noble's seminal discovery linking the DRD2 A1 allele to severe alcoholism, more than 700 genes have been implicated in RDS-related behaviors. A comprehensive "deep silico" GWAS meta-meta-analysis and pharmacogenomic mining effort has since narrowed this list to a predictive panel of 29 genes. Of these, 15 are functionally interconnected, with core candidates including DRD2, DRD4, OPRM1, COMT, and 5-HTTLPR.

Building on these findings, the RDS Consortium is actively developing novel gene-editing platforms, such as Transplice molecular genetic technology, with the long-term goal of mitigating or potentially correcting RDS phenotypes at the genomic level. The vision is not merely to alleviate neuropsychiatric pathology but to explore whether similar genomic interventions could enhance spiritually salient experiences as characterized by the Hierarchical Neuro-Spiritual Model (HNSM).

Although these applications remain in the conceptual and preclinical stages, the potential to shape mental health and spiritual fulfillment at the genetic level presents both extraordinary promise and profound ethical challenges. Such ambitious pursuits will demand rigorous research and collective collaboration from the global scientific community-what the authors describe as requiring "all hands on deck".

## Conclusion

This landmark paper provides the foundational biological language that grounds HNSM in genospirituality. It allows us to encode spiritual practices as epigenetic modulators, clarify Reward Deficiency Syndrome (RDS) as a neuro-spiritual diagnosis, and open the door to precision psycho-spiritual interventions.

Greater engagement in spiritual or religious beliefs and consistent practices has been strongly correlated with higher remission rates from substance use disorders-excluding crack cocaine. For individuals struggling with addiction, participating in weekly religious services of their choosing appears to have a similarly positive influence as having a supportive sponsor. This suggests that structured spiritual involvement fosters meaningful social connections and provides accountability, both of which are valuable assets in recovery. These findings underscore the therapeutic importance of spirituality and its associated community bonds in addiction treatment frameworks.

In parallel, an ongoing dialogue among scholars has examined how genetic factors intersect with religious identity across various faith traditions, including Judaism, Christianity, Islam, and others. These discussions are increasingly shaping our understanding of the biological and cultural dimensions of religiosity and how they influence human behavior and sense of purpose. Regardless of specific doctrines or affiliations, a growing body of evidence supports the view that optimal well-being results from an intricate interplay between genetic predisposition, spiritual engagement, religious rituals, and environmental influences-especially epigenetic factors.

Interestingly, belief in a higher power, rather than mere affiliation with a particular religious group, has been linked to more favorable short-term outcomes in psychiatric treatment. This finding reinforces the potential therapeutic value of personal spirituality beyond institutional religion. Taken together, these insights provide strong justification for extending and deepening the Hierarchical Neuro-Spiritual Model (HNSM). Specifically, they allow us to conceptualize HNSM as biologically grounded in "genospirituality"-the interface of genes and spirituality. Within this model: Spiritual practices are recognized as potential epigenetic modifiers:

- Reward Deficiency Syndrome (RDS) is reframed as a neuro-spiritual disorder;
- Psycho-spiritual interventions are positioned as modulators of gene expression;
- Constructs such as "sin" and "virtue" are explored as neuroethical phenomena.

Ultimately, these conceptual advances offer a blueprint for developing HNSM-based diagnostic tools and integrative treatment approaches-bridging neuroscience, genetics, and spiritual health into a unified framework for understanding and enhancing recovery.

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