

Neurobiology and Spirituality in Addiction Recovery

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Abstract

This commentary explores the neurobiology of spirituality and asks whether it is possible or desirable to apply genetic engineering to increase human spiritual and religious experience - (gene-spirituality) to deal better with the ever-increasing catastrophes that face humanity? Neurological connections between spirituality and reward genes, reward deficiencies (RDS) (hypodopaminergia), the mirror neuron system, and the default mode network are examined. Some interventions from addiction medicine that may be useful to enhance the neuro-spirituality connectome identified as a cornerstone of the Purpose and Meaning of Life as Reward (PMLR) are identified as reasonable targets for interventions to treat RDS and balance DMN activity.

Keywords: Purpose and Meaning of Life as Reward (PMLR)

Introduction

Spirituality is an important topic, especially as it relates to the notion of medical genetic engineering. Humanity is faced with ever-increasing catastrophes due to climate change, foreign and domestic terrorism, war, population displacement, quarantine for the viral pandemic; the daily challenge to survive begs for new ways to induce happiness [1]. Is it possible or desirable [2] to apply genetic engineering to increase human spiritual and religious experience - (gene-spirituality) [3]? These days, everything from intelligence to developing superhero bodies can be a medical genetic engineering target. Tucker, *et al.* demonstrated the possibility of genetic editing to modulate motor activity, increase metabolism and decrease body weight, adiposity and alter longevity in rodents [4].

Possible?

Gene expression changes are affected by ribonucleic acid (RNA) that modify humans during evolution, as much as changes in gene variant frequencies. The encoded gene's functional products require location- and time-specific triggers, which genes cannot provide. Genes are present in every cell during the individual's life. The time-specific triggers are necessary and non-genetic, either internal developmental events and conditions or external environmental events and conditions. Consequently, learned traits have no connection with genes but may, as for any trait, influence evolution. Socially learned traits, like organic traits generally, can be selected positively or negatively, for they likewise influence survival and reproduction [5].

Recent technologies such as gene editing like CRISPR [6] may be capable of altering human religiosity or spiritual sensitivity [3]. Thus, in the future, repairing the target gene or reprogramming it to encode any gene of interest may be a way to engineer genetic spiritual and religious behaviors if a faulty spirituality gene can be identified.

Identifying spirituality genes

Consistent with dopaminergic gene function that increases pleasure and decreases stress [7], Blum, *et al.* [8] pointed to Hamer's [9] suggestion that the ability of dopaminergic genes to produce innate optimism drives their responsibility for spirituality. Studies have shown that optimism, the "feel-good" sense, relates to the will to keep living and procreating, despite death's inevitability. Also, optimism promotes the positive selective value of better health and

quicker recovery from disease [10].

Comings, *et al.* had identified the specific role of the DA D4 receptor (DRD4) gene in spirituality [10]. The DRD4 gene associates with Novelty-Seeking (NS) [11]. Although they identified a correlation of the DRD4 gene with Self-Transcendence, the association with NS did not emerge in their sample of substance abusers [12]. Comings did find that those individuals who scored high on Self-Transcendence were less likely to abuse alcohol or drugs [13].

Nilsson, *et al.* [14] explored Self-Transcendence and its subscale Spiritual Acceptance in 200 individuals matched for age, gender, and risk behaviors. Among boys, examined serotonin transporter polymorphism 5-HTTLPR from blood samples. They found Self-Transcendence and Spiritual Acceptance were negatively correlated with the short 5-HTTLPR genotype and positively correlated with the short AP2beta genotype. The significant interactive effects between 5-HTTLPR and AP-2beta genotypes concerning self-transcendence measures and spiritual acceptance were found among boys and girls. In contrast, the homozygosity for the long AP-2beta genotype combined with the short 5-HTTLPR scored significantly lower on self-transcendence and spiritual acceptance [14].

Borg, *et al.* found a significant association of the serotonin1A receptor gene with self-transcendence scale scores and with the substance of spiritual acceptance. They also found lower ethanol binding and higher serotonin levels in those with the highest self-transcendence scores [15]. Melman [16] speculated that serotonergic neurotransmission in some human studies appeared to mediate human religious and spiritual experiences.

Comings suggested that the feel-good nature of dopaminergic neurochemistry may explain why most people derive happiness and comfort from belief in a god and why spirituality has a powerful role in the human condition [13].

Desirable?

It is also possible that by using new genetic engineering tools in this realm, there could be a trade-off for enhanced spirituality, such as individuals becoming less 'driven' to seek status and monetary rewards, and selfishness. Selfishness is showing an excessive concern with oneself and a lack of concern for others. Understanding

others as 'ourselves' is a unique function of mirror neurons posited to interact with the default mode network (DMN) [17].

Mirror neurons

The mirror neuron system, an execution-observation matching system [18], is thought to be the neuronal basis of all social-cognitive processes. Schmidt, *et al.* found activation in the inferior frontal gyrus, inferior parietal cortex, fusiform gyrus, posterior superior temporal sulcus, and amygdala when investigating fMRI of 75 healthy participants performing imitation, empathy, and theory of mind tasks. Their findings supported the assumption that the mirror neuron system is the heart of humanity's interpersonal understanding [19].

The DMN

The DMN, initially identified in 1998 [20] as low-frequency oscillations, is active when the brain is at rest; however, when the brain engages in a goal-directed task, the default network deactivates. The DMN includes the medial temporal lobe, which associates with memory; the medial prefrontal cortex, which associates with empathy; the ability to recognize others as having thoughts and feelings similar to one's own; and the posterior cingulate cortex involved in integrating different kinds of internal thoughts [21].

All of life is biology, so why are humans driven to search for meaning? It is unclear if humans are the only animal so driven, but the evolution of brain capacities that has been necessary for survival can provide some of the answers. Herculano-Houzel posits that the simplest explanation is that the massive increase in cognitive capacity has provided humanity with new connectivity patterns and new functions in the expanded brain areas [22]. However, the DMN can magnify the importance of self to the point of interference with happiness and function.

The DMN is related to, and may even result from, the development of language which enables us to communicate about the non-present [23], the sense of self, mind wandering; mental time travel, remembering past events and of imagining future ones and the ability to share memories, plans, and ideas. The ability to future-think, project the future onto the now, and perform mental simulations is definitional in man's evolution. These abilities are the work of the DMN, but if overactive, they can be associated with worry, anxiety, depression, and uncertainties. The activity of the DMN diminishes when someone is engaged in focused, intentional activity,

and DMN activity increases when people are idle or at rest. This may be why persistent activity is the norm for humans, even after the achievement of survival and comfort.

Although somewhat neglected, we do know from the scientific literature that, regarding the connection between dopamine and spirituality, for example, in the addiction medicine field, the concept of gene-spirituality and subsequent engineering, while not as yet accomplished, seems prudent in terms of reducing relapse and should be supported during recovery [24].

Spirituality

The pursuit of spirituality includes an effort to explain the unexplainable and to find wholeness and acceptance. There are many definitions of spirituality, some that evoke religion and some that do not. They have in common the search for the love of self and others, emotional comfort, and connection with the transcendent. Throughout history, this search has resulted in the development of strategies such as religion and certain practices of philosophy to guide that search. Throughout history, every culture and most individuals have held beliefs and actively engaged in practices to achieve spiritual growth.

In general terms, gene-spirituality could transpose the world into a better place, where people who cannot aspire to religious beliefs based on differential gene expression could begin to achieve unconditional love for all people independent of ethnicity and religious fervor [2,25].

Self-reference evolved in humans to value those actions and characteristics that predict survival and often to overvalue those actions or a desire for those actions. The result is the potential for selfishness, dishonesty, resentment, fear, envy, gluttony, greed, lust, pride, sloth, and wrath. But does engagement in those wishes and behaviors produce love of self and others, emotional comfort, and connection with the transcendent? Not usually, maybe not ever. Moreover, are those survival-driven attributes all a description of self-centeredness? Of course, our survival instincts are necessary for survival, but how can one find the right place between self-care and self-centeredness? It is probable that the answer is to intentionally engage in spiritual practices that will right-size the ego.

One example is the idea of shamanism [26], induction of states of altered consciousness (e.g., trances, delirium, or dreams); the

shaman may also undergo the experience of transformations, 'soul journeys,' and contact with a spirit realm. Akin to the concept of how a dreamer can shut off or on his/her dream to potentially increase or decrease the likelihood of direct religious experience like 'revelation' [27]: the subjective experience of communication from the deity.

Another, Buddhism strives for the removal of self or ego. In this scenario, it may be possible that, unlike in today's hustling power-driven world, those highly moral, altruistic, peaceable, and principled behaviors might become more prevalent. Understanding the neurobiology of spirituality may emphasize the value and validate the quest for a world where like Bhutan, joyousness and happiness are considered the gross national product instead of power and possessions [28].

Galanter, in the Textbook of Addiction Medicine, 6th Edition pg. 1101 [29] suggests some characteristics of spiritual health for people with addiction:

- Affect
 - A sense of wellbeing
 - Contentment with one's life circumstances
 - Positive affect
 - Feelings of support
- Existential variables
 - Meaningfulness in one's life.
- Flow
 - Ability to use highest strengths and abilities
- Spirituality
 - Non-material issues that give personal meaning and purpose in life
- Personality
 - Classification of Strengths
- Mutual help participation
 - AA or other affiliation

Some of the components of spirituality that may result in the achievement of spiritual health seem to have common themes. The practice of love, compassion, tolerance, forgiveness, responsibility, altruism, and kindness have in common the embrace of behavior

that is different from self-centeredness. A decision to understand and embrace humility and aim at right living can result in a feeling of wellbeing more satisfying than the possible result of acquisitive, self-centered effort.

However, whereas it is possible to will oneself to acquire knowledge, it is impossible to will oneself to have wisdom. It is possible to will oneself to experience pleasure; it is not possible to will oneself to be happy. It is possible to decide to be meek, but not to decide to be humble; you can make yourself go to bed, but you cannot make yourself go to sleep [30]. Often, the goals of spiritual health are not responsive to direct action, but paradoxically, to intentional efforts to reduce ego – to diminish the focus on control of others and the environment and to the practice of being of service. Perhaps engaging in practices that involve manipulation of the activity of the DMN are the same thing.

Several human conditions, ADHD, Depression, Anxiety, and Addiction, are associated with increased activity of the DMN. The activity of the DMN is often dysphoric; to quote James Kingsland, "We have evolved into an ape that takes things personally" [31]. ADHD and Addiction are involved directly with increased DMN activity [32, 33]. The findings of Tomasi, *et al.* suggest that the beneficial effects of stimulant medications (increase dopamine by blocking DAT) in inattention reflect in part their ability to facilitate the deactivation of the DMN [33]. Anxiety and depression are involved indirectly with an associated decrease in dopamine tone in the Nucleus Accumbens and Ventral Tegmental Area, a condition known as Reward Deficiency Syndrome (RDS) [34,35]. Tomasi has demonstrated that blocking the dopamine transporter (DAT), resulting in an increased dopamine tone, is associated with reducing activity in the DMN [33]. So, there is reason to believe that activities and medications that increase dopamine tone will reduce the activity of the DMN. However, will reduced activity of the DMN alone result in spiritual health or spirituality? It may well be that such accomplishment will result in less need for spiritual healing through neurobiological approaches. Would there be a concurrent increase in love, compassion, tolerance?

Spiritual practice, such as meditation, has been shown to decrease the activity of the DMN [36], perhaps due to practices that increase focus. Such practices are almost always associated with activities and commitments that value the outcomes of right living.

Prayer, also known to disrupt the activity of the DMN [35,37-39], is frequently associated with a commitment to embrace selflessness and altruism. These activities of top-down regulation of DMN activity have the advantage of goals that are valuable both to the practitioner and to the community of all humans. Fortunately, meditation and prayerfulness have in common that they value kindness, honesty, responsibility, and concern for the welfare of others.

In summary, Reward Deficiency Syndrome (RDS), along with genetic antecedents [23,40], to all addictive behaviors including but not limited to alcohol, illicit drug misuse, smoking, and behaviors like gambling, overeating, sex, and gaming, are prevalent worldwide. Due to criminality, lost productivity, and health consequences, these behaviors are highly destructive and costly to individuals and society. Unquestionably, genetic vulnerability [40], environmental or epigenetic exposures, compulsive tendencies, and some uniquely individual behaviors contribute to brain dysfunction. Although much has been learned about neurogenetic consequences of biochemical imbalances of neurotransmission across the brain reward circuitry associated with addictions [32], research leading to effective treatments and prophylaxis has been slow. RDS and its subsets, often accompanied by an inner sense of disintegration, enslavement, and meaninglessness, can be viewed in terms of a spiritual craving for wholeness, freedom, and transformation [41]. Eric R. Braverman, has identified the neuro-spirituality connectome (map) as a cornerstone of the Purpose and Meaning of Life as Reward (PMLR) and a reasonable target for interventions to treat RDS and balance DMN activity.

Arguably, progress towards safe and effective treatment has been retarded by insufficient attention to understanding the role of spirituality in helping to heal people with Substance Use Disorders [42]. Assuming one accepts the belief that the brain mediates all conscious and unconscious experiences, including spiritual experiences: healing, reward deficiencies, can mend the processes by which the human brain is organized for controlling pleasure and pain [43].

We like-minded addiction scientists and physicians [8] hypothesize that a healthy spirituality may come more naturally to some individuals because of the unique interaction of their genes and their environments, maybe engineered epigenetically now and in the future, using pro-dopaminergic behaviors, nutrients, and per-

haps gene editing to assist in the induction of dopamine homeostasis [44]. With spiritual enhancement, people can embrace the concept "Love Needs Care", as encouraged by David E Smith in the summer of love during the development of the free clinic move-

Figure 1: Schematic of Geno-spirituality and a model of the "Purpose and Meaning of Life as Reward (PMLR)

ment in San Francisco [45]. We have learned from Addiction Science that Spirituality is imperative in healing and that in the future, interventions between the DNA and the mRNA may be possible.

Figure of spirituality and neurobiology

Conclusion

Neurological connections between spirituality and reward genes, reward deficiencies (RDS) (hypodopaminergia), the mirror neuron system, and the default mode network are examined. Some interventions from addiction medicine that may be useful to enhance the neuro-spirituality connectome identified as a cornerstone of the Purpose and Meaning of Life as Reward (PMLR) are

identified as reasonable targets for interventions to treat RDS and balance DMN activity.

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Contribution of Authors

The initial draft was developed by KB and all authors commented and approved.

Conflict of Interest

K.B. is the inventor of GARS and Pro-dopamine regulator (KB220) either owned and or licensed to his various companies (Geneus Health L.L.C., Synaptamine, Ivitalize). K.B. is supported in part by Ivitalize. There are no other conflicts to report. R.J. and R.G. receive support from Ivitalize. All positions on the Kenneth Blum Behavioral & Neurogenetic Institute are on a volunteer basis, no

Bibliography

- Zhou L and Foster JA. "Psychobiotics and the gut-brain axis: in the pursuit of happiness". *Neuropsychiatric Disease and Treatment* 11 (2015): 715-723.
- Neitzke AB. "On the genetic modification of psychology, personality, and behavior". *Kennedy Institute of Ethics Journal* 22.4 (2012): 307-343.
- Charlton BG. "Genospirituality: genetic engineering for spiritual and religious enhancement". *Medical Hypotheses* 71.6 (2008): 825-828.
- Tucker K., et al. "Kv1.3 gene-targeted deletion alters longevity and reduces adiposity by increasing locomotion and metabolism in melanocortin-4 receptor-null mice". *International Journal of Obesity* (2005) 32.8 (2008): 1222-1232.
- Wells DA. "Plasticity-Led Evolution and Human Culture". *Integrative Psychological and Behavioral Science* (2021).
- Higashijima Y and Nangaku M. "The Nobel Prize in chemistry in 2020: genome editing tools and their immeasurable applications for humankind". *Kidney International* 98.6 (2020): 1367-1369.
- Asghari V., et al. "Modulation of intracellular cyclic AMP levels by different human dopamine D4 receptor variants". *Journal of Neurochemistry* 65.3 (1995): 1157-1165.
- Blum K., et al. "The Molecular Neurobiology of Twelve Steps Program and Fellowship: Connecting the Dots for Recovery". *Journal of Reward Deficiency Syndrome* 1.1 (2015): 46-64.
- Hamer D. "The god gene". New York: Doubleday (2004).
- Newberg A. "The brain and the biology of belief: An interview with Andrew Newberg, MD. Interview by Nancy Nachman-Hunt". *Advances in Mind-Body Medicine* 24.1 (2009): 32-36.
- He Y., et al. "Candidate genes for novelty-seeking: a meta-analysis of association studies of DRD4 exon III and COMT Val-158Met". *Psychiatric Genetics* 28.6 (2018): 97-109.
- Cohen MX., et al. "Connectivity-based segregation of the human striatum predicts personality characteristics". *Nature Neuroscience* 12.1 (2009): 32-34.
- Comings DE., et al. "A multivariate analysis of 59 candidate genes in personality traits: the temperament and character inventory". *Clinical Genetics* 58.5 (2000): 375-385.
- Nilsson KW., et al. "Genes encoding for AP-2beta and the Serotonin Transporter are associated with the Personality Character Spiritual Acceptance". *Neuroscience Letters* 411.3 (2007): 233-237.
- Borg J., et al. "The serotonin system and spiritual experiences". *The American Journal of Psychiatry* 160.11 (2003): 1965-1969.
- Bachner-Melman R., et al. "AVPR1a and SLC6A4 gene polymorphisms are associated with creative dance performance". *PLoS Genetics* 1.3 (2005): e42.
- Schmidt SNL., et al. "The human mirror neuron system-A common neural basis for social cognition?" *Psychophysiology* (2021): e13781.
- Buccino G., et al. "The mirror neuron system and action recognition". *Brain Lang* 89.2 (2004): 370-376.
- Schmidt SNL., et al. "The human mirror neuron system-A common neural basis for social cognition?" *Psychophysiology* 58.5 (2021): e13781.
- Hsiao FJ., et al. "Altered oscillation and synchronization of default-mode network activity in mild Alzheimer's disease com-

- pared to mild cognitive impairment: an electrophysiological study". *PLoS One* 8.7 (2013): e68792.
21. Raichle ME. "The brain's default mode network". *Annual Review of Neuroscience* 38 (2015): 433-447.
 22. Herculano-Houzel S. "The human brain in numbers: a linearly scaled-up primate brain". *Frontiers in Human Neuroscience* 3 (2009): 31.
 23. Corballis MC. "Wandering tales: evolutionary origins of mental time travel and language". *Frontiers in Psychology* 4 (2013): 485.
 24. Schoenthaler SJ, et al. "NIDA-Drug Addiction Treatment Outcome Study (DATOS) Relapse as a Function of Spirituality/Religiosity". *Journal of Reward Deficiency Syndrome and Addiction Science* 1.1 (2015): 36-45.
 25. DeGrazia D. "Ethical Reflections on Genetic Enhancement with the Aim of Enlarging Altruism". *Health Care Analyst* 24.3 (2016): 180-195.
 26. Singh M. "The cultural evolution of shamanism". *Behavioral and Brain Sciences* (2017): 1-83.
 27. Stokstad E and Vogel G. "Revelations about rhythm of life rewarded". *Science* 358.6359 (2017): 18.
 28. Oishi S and Schimmack U. "Culture and Well-Being: A New Inquiry Into the Psychological Wealth of Nations". *Perspectives on Psychological Science* 5.4 (2010): 463-471.
 29. Galanter M. "Textbook of Addiction Medicine". 6th ed (2020): 1101.
 30. Ernest Kurtz and Katherine Ketchum. *The Spirituality of Imperfection*. Bantam Books (1992).
 31. Kingsland James. *Siddhartha's Brain*: Harper Collins Publishers (2015).
 32. Kühn S and Gallinat J. "Common biology of craving across legal and illegal drugs - a quantitative meta-analysis of cue-reactivity brain response". *The European Journal of Neuroscience* 33.7 (2011): 1318-1326.
 33. Tomasi D, et al. "Dopamine transporters in striatum correlate with deactivation in the default mode network during visuo-spatial attention". *PLoS One* 4.6 (2009): e6102.
 34. Blum K. "Reward Deficiency Syndrome". In: Wenzel A, editor: *The Sage Encyclopedia of Abnormal Clinical Psychology*. Pennsylvania: Sage Publications (2017).
 35. Gold MS, et al. "Neurological correlates of brain reward circuitry linked to opioid use disorder (OUD): Do homo sapiens acquire or have a reward deficiency syndrome?" *Journal of the Neurological Sciences* 418 (2020): 117137.
 36. Andrews-Hanna JR. "The brain's default network and its adaptive role in internal mentation". *Neuroscientist* 18.3 (2012): 251-270.
 37. Carhart-Harris RL, et al. "Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin". *Proceedings of the National Academy of Sciences of the United States of America* 109.6 (2012): 2138-2143.
 38. Raffone A, et al. "The exploration of meditation in the neuroscience of attention and consciousness". *Cognitive Processing* 11.1 (2010): 1-7.
 39. Rim JL, et al. "Current Understanding of Religion, Spirituality, and Their Neurobiological Correlates". *Harvard Review of Psychiatry* 27.5 (2019): 303-316.
 40. Blum K, et al. "Biotechnical development of genetic addiction risk score (GARS) and selective evidence for inclusion of polymorphic allelic risk in substance use disorder (SUD)". *Journal of Systems and Integrative Neuroscience* 6.2 (2020).
 41. Blum K, et al. "Genospirituality: Our Beliefs, Our Genomes, and Addictions". *Journal of Addiction Research and Therapy* 5.4 (2013): 162.
 42. Beraldo L, et al. "Spirituality, Religiosity and Addiction Recovery: Current Perspectives". *Current Drug Research Reviews* 11.1 (2019): 26-32.
 43. Wuyts EM, et al. "Between Pleasure and Pain: A Pilot Study on the Biological Mechanisms Associated With BDSM Interactions in Dominants and Submissives". *The Journal of Sexual Medicine* 17.4 (2020): 784-792.

44. Blum K., *et al.* "Should We Embrace the Incorporation of Genetically Guided "Dopamine Homeostasis" in the Treatment of Reward Deficiency Syndrome (RSD) as a Frontline Therapeutic Modality?" *Acta Scientific Neurology* 4.2 (2021): 17-24.
45. Smith DE and Seymour RB. "Addiction medicine and the free clinic movement". *Journal of Psychoactive Drugs* 29.2 (1997): 155-160.

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