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Do dopaminergic gene polymorphisms affect mesolimbic reward activation of music listening response? Therapeutic impact on Reward Deficiency Syndrome (RDS).

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Abstract

Using fMRI, Menon and Levitin [9] clearly found for the first time that listening to music strongly modulates activity in a network of mesolimbic structures involved in reward processing including the nucleus accumbens (NAc) and the ventral tegmental area (VTA), as well as the hypothalamus, and insula, which are thought to be involved in regulating autonomic and physiological responses to rewarding and emotional stimuli. Importantly, responses in the NAc and VTA were strongly correlated pointing to an association between dopamine release and NAc response to music. Listing to pleasant music induced a strong response and significant activation of the VTA-mediated interaction of the NAc with the hypothalamus, insula, and orbitofrontal cortex. Blum et al. [10] provided the first evidence that the dopamine D2 receptor gene (DRD2) Taq 1 A1 allele significantly associated with severe alcoholism whereby the author's suggested that they found the first "reward gene" located in the mesolimbic system. The enhanced functional and effective connectivity between brain regions mediating reward, autonomic, and cognitive processing provides insight into understanding why listening to music is one of the most rewarding and pleasurable human experiences. However, little is known about why some people have a more or less powerful mesolimbic experience when they are listening to music. It is well-known that music may induce an endorphinergic response that is blocked by naloxone, a known opioid antagonist (Goldstein [19]). Opioid transmission in the NAc is associated with dopamine release in the VTA. Moreover, dopamine release in the VTA is linked to polymorphisms of the DRD2 gene and even attention-deficit hyperactivity disorder (ADHD), whereby carriers of the DRD2 A1 allele show a reduced NAc release of dopamine (DA). Thus it is conjectured that similar mechanisms in terms of adequate dopamine release and subsequent activation of reward circuitry by listening to music might also be affected by an individual's D2 density in the VTA mediated interaction of the NAc. It is therefore hypothesized that carriers of DRD2 A1 allele may respond significantly differently to carriers of the DRD2 A2 genotype. In this regard, carriers of the D2 A1 allele have a blunted response to glucose and monetary rewards. In contrast powerful D2 agonists like bromocryptine show a heightened activation of the reward circuitry only in DRD2 A1 allele carriers. If music causes a powerful activation in spite of the DRD2 A1 allele due to a strong DA neuronal release which subsequently impinges on existing D2 receptors, then it is reasonable to assume that music is a strong indirect D2 agonist (by virtue of DA neuronal release in the NAc) and may have important therapeutic applicability in Reward Deficiency Syndrome (RDS) related behaviors including Substance Use Disorder (SUD). Ross et al. [18] found that music therapy appears to be a novel motivational tool in a severely impaired inpatient sample of patients with co-occurring mental illness and addiction.

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