Letter to Editor

Music Therapy and Social Skills in Autism: Underlying Biological Mechanisms

To the Editor,

Ghasemtabar *et al*.[1] sought to investigate the role of music therapy (MT) in the amelioration of autistic symptoms in a sample of children diagnosed with autism spectrum disorders (ASDs). The authors included 27 children with a moderate performance level on the childhood autism rating scale questionnaire. The parent's form of the social skills rating system scale-P was administered at three time points of the study: a pretest, a posttest, and at a 2-month follow-up point. The MT followed the Orff Schulwerk with the aid of two music therapists. The results of the clinical trial noted that social skills were significantly enhanced among children with autism in the MT intervention, even after 2 months of follow-up.

While Ghasemtabar *et al*.[1] have noted that musical activities are often very social in nature with significant peer and instructor interaction, which may help prime social cognitive abilities among those with ASDs. The underpinning biological basis for such a benefit was not mentioned, however, even though many peer-reviewed studies have provided evidence of the analgesic action of MT. In a highly cited work, Goldstein[2] published initial data indicating that music was particularly effective as a stimulus of "thrills" and that administration of an opioid antagonist, naloxone, significantly attenuated this effect in some subjects, indicating that MT may involve opioidergic stimulation. Subsequent studies involving surgical populations indicate reduced analgesia (i.e. mu-opioid receptor [MOR]) requirement among those exposed to MT intraoperatively.

Evidence is mounting indicating opioidergic involvement in attachment behavior and social reward. Infusion of morphine in the nucleus accumbens (NAc) of adolescent rats stimulated social play behavior, while intra-NAc infusion of the opioid receptor antagonist, naloxone, reversed the increase in social play behaviors due to systemic morphine. The actions of specific opioid receptors showed that intra-NAc infusion of the MOR agonist, D-Ala2, N-MePhe4, Gly-ol]-enkephalin (DAMGO), significantly increased priming and pouncing behavior, while the kappa-opioid receptor (KOR) agonist, U69593, significantly decreased social play behavior.[3] In mice lacking the MOR gene, Moles *et al*.[4] demonstrated a reduction in attachment behavior as indicated by decreased ultrasonic vocalizations by knockout pups when separated from the mother and an indifference to mothering cues. These data argue for the importance of opioid signaling, and specifically MOR, in the reward of socioaffiliative behaviors. It has recently suggested through empirical study that exposures to the pervasive and understudied environmental air pollutant, nitrous oxide (N_2O), may be a contributing etiological factor in neurodevelopmental disorders such as attention-deficit hyperactivity disorder and ASD.[5] A principal component of this hypothesis rests on the repeated biological evidence showing that low-dose N_2O exposure induces endogenous release of dynorphin, which is opioid peptide that acts principally as a KOR ligand. KOR activity is not depleted in MOR-knockout mice,[6] suggesting a lack of cooperativity between the two opioid receptors in many physiological domains. Although, others have argued for a multilevel antagonistic dynamic between the receptor subtypes including domains such as reward processing.[7] Therefore, it is worthy to consider that environmental exposure to N_2O may prime KOR activation, serving as a potential biological target mediating abnormal social affiliative behaviors in neurodevelopmental disorders such as ASD. Activities such as MT may activate opioidergic activity in a receptor-specific manner (i.e., MOR) so as to mitigate a heightened dynorphinergic system and KOR activation possibly induced from environmental exposures. Future research should seek to clarify the opposing actions of the opioid receptor subtypes as it relates specifically to social reward processing to better understand the biological basis for the possible socially ameliorative effect of MT in disorders characterized by impaired social interactions.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Quick Response Code:

Website: www.advbiores.net

DOI: 10.4103/abr.abr_280_16

How to cite this article: Fluegge K. Music Therapy and Social Skills in Autism: Underlying Biological Mechanisms. Adv Biomed Res 2018;7:57.