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Review Article

Raga Therapy for Autism

Neelima Chauhan [1,*], Mahesh Kale[2], Neeta Naik[3]

[1] Department of Pediatrics, University of Illinois, at Chicago, VA Healthcare System, Chicago, IL, USA. Email: nchauhan51@gmail.com.

[2] Indian Classical Music and Arts Foundation, Mahesh Kale School of Music, San Francisco, CA, USA. Email: mahesh@maheshkale.com.

[3] EN1 Neuro Services Pvt. Ltd. Mumbai, India. Email: neeta.naik2@gmail.com.

***Corresponding author**

Neelima Chauhan,
Department of Pediatrics, University of Illinois at Chicago, 840 Wood Street, Chicago, Illinois 60121;
Phone: 312-569-7747;
Fax: 312-569-8114;
E-Mail: nchauhan51@gmail.com

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Abstract

Autism spectrum disorder (ASD) is a global health crisis. There is an increasing prevalence of ASD not only in US but throughout the world mainly affecting children and adolescents. ASD exhibits compromised quality of life characterized by persistent deficits in two core areas of functioning including social communication and interaction, and restricted/repetitive patterns of motor activities. These aberrances arise from overall brain underconnectivity coupled with local over-connectivity within specific brain regions. Normal brain connectivity is modulated by a neurohormone called oxytocin. Deficiencies in oxytocin either due to genetic or non-genetic causes, results in dysfunctional brain connectivity leading to the development of ASD. Based on these facts, restoration of oxytocin has been attempted considering current limitations of ASD pharmacotherapy. Oxytocin treatment by systemic or central routes of administration have produced mixed outcomes and therefore non-pharmacological oxytocin-boosting alternatives are increasingly considered. One of such alternatives is music therapy. Music therapy not only to boosts oxytocin levels but also targets the core socioemotional deficits observed in ASD. The uniqueness of North Indian Classical Music in advancing its therapeutic potential is presented.

Key Words:

Autism Spectrum Disorder, Insular Cortex, Mirror Neuron System, Large Neural Network, Classical Music, Oxytocin, Brainwaves, Brain Entrainment.

Abbreviations:

ABA: Applied Behavioral Analysis
ADHD: Attention Deficit Hyperactivity Disorder
ADDM: Autism and Developmental Disabilities Monitoring
AVP: Arginine Vasopressin
AS: Asperger's Syndrome
ASD: Autism Spectrum Disorder
ADDM: Autism and Developmental Disabilities Monitoring
CDC: Centers for Disease Control
CEN: Central Executive Network
CBT: Cognitive Behavioral Therapy
DMN: Default Mode Network
DSM: Diagnostic and Statistical Manual of Mental Disorders
Hz: Hertz
IN: Insula
IC: Insular Cortex

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ID: Intellectual Disability
EEG: Electroencephalography
ERPs: Event-Related Potentials
OT: Oxytocin
MRI: Magnetic Resonance Imaging
MNS: Mirror Neuron System
MT: Music Therapy
NDD: Neurodevelopmental Disorders
NICM: North Indian Classical Music
OT: Oxytocin
OTR: Oxytocin Receptor
PDDs: Pervasive Developmental Disorders
PDD-NOS: Pervasive Developmental Disorder-Not Otherwise Specified
SN: Salience Network
SBT: Social Behavioral Therapy

Autism Spectrum Disorder

Autism spectrum disorder (ASD) is a group of developmental disabilities that can cause significant social, communication and behavioral aberrations, characterized by persistent deficits in two core areas of functioning [1] social communication/interaction, [2] restricted/repetitive patterns of motor activities [1,2,3,4]. Abnormal development is usually present before the age of 3 years showing affected children with developmental regression and loss of previously acquired skills [5]. Approximately, one third of the children with ASD tend to develop epilepsy and the rest may develop depression, anxiety, attention deficit hyperactivity disorder (ADHD), mental retardation, etc. [5,6]. Although, no unifying genetic or non-genetic causative factor(s) have been identified for ASD, deficient oxytocin (OT) signaling [7,8], and aberrant methylation or mutations in the oxytocin receptor (OTR) gene, are increasingly recognized as fundamental trigger to the development of ASD [9,10,11]. Oxytocin is a key mediator of socioemotional behavior [12], which regulates connectivity of insular cortex (IC) and large-scale brain networks [13]. The OT deficiency disrupts IC and large-scale brain network connectivity in ASD [14] leading to social, communication and behavioral [11,14,15], and neurophysiological [11,16,17] deficits typical of ASD. Thus, OT deficiency is the prime therapeutic target for ASD treatment.

Dysfunctional Brain Connectivity in Autism

Altered intrinsic dysfunctional connectivity is a hallmark of ASD [11] showing a pattern of overall brain underconnectivity, coupled with local over-connectivity within frontal and occipital regions [3], affecting sensory processing [15,18]. The functional connectivity of frontotemporal and frontoparietal regions, the amygdala-hippocampal complex, basal ganglia, cerebellum, and cingulate cortex are compromised in ASD [2]. Insular cortex acts as a "hub" in orchestrating large-scale brain network with different brain regions [14,19]. Large-scale brain network includes Salience Network (SN), Default Mode Network (DMN), and Central Executive Network (CEN) [14,19]. IC-SN detects and filters salient stimuli, integrates sensory, emotional, cognitive information and significantly contributes to social communication, behavior, and self-awareness [20]. Therefore, dysfunctional connectivity of IC-SN produces dissociation of social communication, behavior, and self-awareness [20,21]. IC-DMN is a large-scale brain network that is most active at rest and involved in various domains of social and cognitive processing [22]. Dysfunctional connectivity of IC-DMN compromises social and cognitive processing in ASD [22,23]. IC-CEN is involved in sustained attention, complex problem solving, and working memory [22]. Dysfunctional connectivity of IC-CEN impairs attention, problem-solving, and working memory processing in ASD [21,22]. In summary, both hypo- and hyper-dysfunctional connectivity of IN-SN/DMN/CEN, "breaks" large-scale brain network circuits impairing verbal/non-verbal social communication, social and cognitive processing including parent/peer-bonding/interaction/attachment in ASD [24-27].

Neurophysiological Aberrations in Autism

The most consistently observed pattern indicates that compared to controls that do not have ASD, individuals with ASD show a U-shaped pattern of spectral power with excessive slow (delta/δ/0.5-4Hz; theta/θ/4-8Hz) and/or fast (beta/ß/12-30Hz, gamma/γ/>30Hz) frequency bands, but significantly reduced neutral/mid-range (alpha/α/8-12Hz) frequency band [11,16,17,28]. The underconnectivity of frontotemporal and subcortical networks, and overconnectivity of sensory networks underly neurobehavioral deficits observed in ASD [11,29]. Deficits in sensory processing disrupt neural inhibition/excitation and sensory gating leading to compromised emotional response, mental activity, attention, and cognitive processing in ASD [30].

Neurochemical Aberrations in Autism

Neurochemical aberrations of ASD include altered levels and mis-signaling of serotonin, dopamine, endorphins, and oxytocin [31,32,33]. Significant increases in the levels of serotonin and serotonin transporters (SERT) [34] and altered serotonin signaling [35,36] are observed in ASD. Increased serotonin reduces oxytocin levels, indirectly producing OT deficits [36]. A dysfunctional midbrain dopaminergic system [37,38,39], mutations in dopamine transporter protein [40], and perturbations in dopamine signaling [37,41,42] contribute to central executive deficits observed in ASD [43]. Endorphins (endogenous opioid system) play a key role in enhancing the rewarding properties of dopamine and therefore observed deficits of endorphin in ASD indirectly reduce dopamine, adding to the effects of dopamine deficiency in ASD [32]. Oxytocin is a key neural substrate that interacts with central dopamine systems and hence implicated in mediating mesolimbic dopamine pathways [42]. Thus, serotonin and dopamine both are linked to oxytocin deregulation, making oxytocin a key neural substrate contributing to ASD [44]. The role played by oxytocin in regulating social/affiliative behavior by mediating brain OT release in psychiatric disorders including ASD have been well recognized [45,46,47,48]. Oxytocin modulates IN-SN/DMN/CEN functional connectivity and salience processing [13,49,50], and hence regarded as prime causative factor for ASD [7,51].

Positive Effects of Music on Social Activities, Communication Skills and Key Symptoms of ASD

Music is innately present in humans and therefore regarded as a universal system for socio-emotional communication owing to its power to evoke emotions [52,53,54]. Musical emotions are processed by a large-scale network that includes insula, orbitofrontal, cingulate, prefrontal, temporal and parietal cortices, amygdala, hippocampus, and subcortical mesolimbic system [55]. Emotions emerge through a combined activation of emotional and motivational brain systems such as reward pathways, and several other areas including motor, attention, and memory [56]. In addition to the emotional impact of music on the brain, listening to music is linked to the induction of neurohormones i. e. dopamine, serotonin, endorphins, oxytocin, etc. [55]. There is a growing body of evidence showing benefits of music therapy in different neurological disorders such as Stroke [57], Parkinson's disease [58], Alzheimer's disease [59,60], dementia [61], epilepsy [62], and many other neurological conditions [2,63], including ASD [1,4,64]. Since music is engaging, emotional, physical, social, and persuasive tool, it promotes synchronization of various brain functions [2], it has a distinct ability to target ASD-specific core disabilities [36,65,66]. Despite altered intrinsic connectivity, individuals with ASD often enjoy music perception and can achieve a high level of music proficiency [67,68]. Given the ability of music to modify neurophysiological responses [65,69], and perceptions [64], music can be a great alternative in treating ASD. Scientists have shown that a 30-min singing lesson increased blood OT levels [70], listening to slow-tempo and soothing music increased salivary OT levels [71,72]. Besides OT elevation, music listening activated IN-SN/DMN/CEN networks [14,73]. Presentation of happy music was observed to enhance insular cortex, superior temporal lobe, and caudate putamen associated with awareness of emotions [74,75]. ASD-induced reduction of OT and suppression of neutral (alpha/α/8-12Hz) brain waves, was restored after OT treatment [51]. Although peripheral OT administration produced mixed results, direct brain targeting of OT via nasal route improved emotion, recognition [76], social cognition [77,78], eye gaze/social interaction [79,80], and social anxiety [81] in ASD. Most importantly, OT promoted physiological response to music/acoustic stimuli [82], and induced the secretion of OT [52,71,72,83], indicating a physiological link between music/acoustic stimuli and OT. The fact that music gives a sense of shared affective relationship [14], the core aspects highly compromised in ASD, along with its effects on elevating OT and other key neurotransmitters (dopamine, serotonin) [35,84], involved in reward, motivation, pleasure, and social affiliation [52], makes music a potential therapeutic alternative in treating ASD [1,4,66,85]. There have been many studies on the effects of music in autism [1,6,85]. Not all randomized controlled trials of music therapy were successful [86,87], but the observed failures are attributed to a medium/high risk of bias, small sample size and mostly male participants [14,28]. Nonetheless, recent systematic reviews confirmed benefits of music therapy in neurodevelopmental disorders (NDD) including ASD and intellectual disability (ID) [28,88,89].

Therapeutic Potential of North Indian Classical Music in Treating Autism

North Indian Classical Music (NICM), by virtue of its uniqueness of its melodic structural design and improvisation, offers added advantages over afore-mentioned conventional music therapy [90,91]. "Raga" constitutes the constructive core of NICM [84,92,93]. Ragas are composed of permutations and combinations of seven basic "natural" Swaras/notes (derived from the sounds of nature - birds, animals), called "Shuddha Swara", and five "Modified" notes (Vikruta Swara), making a total of 12 notes/Swaras, composed in an ascending/descending order to create a melodic structure known as Raga [92,94,95,96]. Ragas are known to exert note-swara-specific, improvisation-specific, tempo/rhythm-specific, circadian-specific, and season-specific emotional effects, indirectly indicating the activation of pertinent brain regions [92,94,95,96].

Swara Effects

All Swaras used to construct Ragas play important roles in exerting Raga-specific emotional effects [92,94,95,96]. Specific arrangement of Swaras and combination of tonal intervals are capable of evoking/magnifying/modifying distinct emotions [94,95]. If the frequency of a given note is more than its mean value, then it is termed to be a Tivra Swara (Western sharp note) [90,91]. Similarly, if frequency of a given note is decreased below the mean value, then it is called Komal Swara (Western soft/flat note) [90,91,92]. Predominance of Shuddha Swaras (pure notes) makes the Raga "Happy" and "Cheerful", while incremental predominance of Komal Swaras (soft/flat notes) makes the Raga progressively sentimental, elevating emotional seriousness from happiness to sympathy to sad/sorrow/tensed to peace and tranquility [90,91,92,93,94,95,98,99]. The use of Komal Re, creates tension and longing and Komal Dha, produces seriousness and calmness [94, 95, 99], while Komal Ga and Komal Ni, create the mood of compassion, submission, sorrow [92, 93, 97], and Tivra Ma, intensifies the inherent emotions of accompanying note(s)/Swara(s) [93]. In NICM emotional valence systematically varies along with the tonal ratios of each Raga, varying not only systematically, but incrementally, in finer gradations of emotions from happy -to- peace -to- tranquility/devotion [92, 100], rather than binary notions of "positive/negative" "happy/sad" ascribed to consonance/dissonance effects on emotion [95].

Stages of Raga and Rhythm Effects

Besides, the use of specific Raga with specific emotional signature, various stages of Raga presentation, such as an arhythmic introductory phase (Aalap), a rhythmic phase (Gat), and tempo, all are capable of modifying emotional output [84,94,97,98]. As reported by Mathur et al., the "Aalap" and "Gat" components of Raga Yaman revealed change in emotion from "Calm" (Aalap) to "Happy" (Gat) [94]. In addition, use of different tempos (Laya) i. e.

Vilambit (slow), Madhya (medium), Drut (fast), have differential emotional effects within a Raga such as Vilambit Laya with calm effect; Madhya Laya with pleasant/happy/cheerful effects; and Drut Laya with excitement [84,94]. The rhythm of Raga, known as "Taal" is the cyclic patterns of beats within a rhythmic cycle that repeats on itself. The cyclic nature of Taal is another unique feature of NICM which is represented as beats per minute (bpm). Both Raga and Taal are open frameworks for creativity and allow theoretically infinite number of possibilities. By and large, the Ragas with bpm lower than the heart rate (< 70-75 bmp) produce calming/soothing effects, Ragas with bpm equal to the heart rate (=70-75 bpm) create joy/happiness/cheerfulness/pleasant feelings, while Ragas with bpm greater than the heart rate (> 70-75 bpm) produce excitement or energizing effects [90,91,92].

Circadian and Seasonal Selectivity

Based on the belief that human state of mind is affected by nature's rhythms, Ragas have circadian and seasonal selectivity, meaning certain Ragas exert more prominent effects when specifically sung/performed during specific time of the day, and certain Ragas are specific for certain seasons [90,91,92].

Improvisational Effects

An artist of NICM is not strictly confined to reproduce a fixed composition, rather an NICM artist explores beyond fixed composition to produce artistic pleasure with his/her own individual talent without changing the core features of Raga [90,91,92]. Each Raga provides a musical framework within which the musician can improvise [94]. Improvisation by the musician involves creating sequences of notes allowed by the Raga while maintaining Raga-specific rules. Raga can be improvised by changing the sequence of ascending/descending Swaras (notes), emphasizing any single note, and integrating catch phrases in the Raga [90,91,92]. For example, Raga "Bhimpalasi" and Raga "Dhanashri" have the same notes and sequence, the only difference being that in Raga "Dhanashri", Swara "Pa" (Perfect Fifth-note) is used as the tonic most sonant and important musical note, while in of Raga "Bhimpalasi", the Swara "Ma" (F-Note) is used as the most sonant and important musical note [90,91]. Thus, NICM is an open-ended and flexible improvisational system which has an ability to modify/intensify/subdue inherent emotional effects of Raga/Swara, via neurochemical [52] and neurophysiological [51] modulations, making Raga the more personalized and tailored neurotherapy [84,94,95,98], compared to conventional music therapy. Ragas containing all/majority of consonant notes (Shuddha Swaras), along with their circadian rhythmic specificity, are known to elicit joy/happiness that tend to increase dopamine [56] and oxytocin [101]. Recently, a case study by Panda et al. showed that the Ragas containing majority of Shuddha Swaras, namely Raga Pilu, Raga Bahar and Raga Khamaj, used for treating autistic children, showed positive results [102]. In summary, Raga Therapy has great scope of customization based on its afore-mentioned unique qualities. This uniqueness makes NICM as an effective neurotherapy [84,94,96,103].

Conclusions

The prevalence of ASD has been increasing over past two decades and about 1 in 36 children has been identified with ASD according to the estimates from Centers for Disease Control (CDC) Autism and Developmental Disabilities Monitoring (ADDM) Network. There is no single effective therapy for treating ASD. Currently practiced pharmacological treatments include the use of psychostimulants, atypical antipsychotics, anti-depressants, and α-2 adrenergic receptor agonists for treating ASD. These medications provide partial symptomatic relief but not a complete cure and are associated with adverse side effects [14]. Given the failure of FDA-approved pharmacological treatments with limited benefits and many side effects, reliance on non-pharmacological integrative treatments is emerging [6]. Most people with ASD respond best to highly structured and specialized non-pharmacological treatments. Non-pharmacological interventions for ASD include applied behavioral analysis (ABA), cognitive behavioral therapy (CBT), social behavioral therapy (SBT) and music therapy (MT). According to the Cochrane database, MT has been postulated to be the effective therapy for ASD [28]. Presently discussed Raga therapy may be more effective based on its unique structural and improvisational ability to produce desired health effects.

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