

Rethinking the role of music in the neurodevelopment of autism spectrum disorder

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Abstract

Music has played a prominent role in the clinical and research literature on autism spectrum disorder (ASD) in regard to diagnosis, therapy, and behavioral observations of exceptional artistic abilities in this population. Music as therapy for ASD has traditionally focused on social interaction, communication skills, and social-emotional behaviors. However, recently, there has been an increased research focus on the role of motor and attention functions as part of the hallmark features of ASD, which may have significant implications for the role of music as an intervention for individuals with autism. The purpose of this article is to provide a critical appraisal of new research developments for therapists and researchers to potentially reassess the role of music as intervention to support healthy neurodevelopment in individuals with ASD and expand the current clinical scope of practice in music therapy for autism. Our argument is based upon compelling research evidence indicating that motor and attention deficits are deeply implicated in the healthy neurodevelopment of socio-communication skills and may be key indicators of structural and functional brain dysfunction in ASD. In light of this evidence, we suggest that music-based developmental training for attention and motor control may receive a critical new functional role in the treatment of autism due to the significant effect of auditory-motor entrainment on motor and attention functions and brain connectivity.

Keywords

Attention, autism spectrum disorder, intervention, music therapy, motor control

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Autism spectrum disorders (ASD) is the term used for a diverse group of developmental conditions that affect one's ability to relate to and communicate with others (Walsh, Elsabbagh, Bolton, & Singh, 2011). These conditions (henceforth also referred to as "autism") are characterized by two cardinal clinical features: persistent deficits in social communication and social interaction, and repetitive/stereotyped behaviors, including hyper- or hypo-reactivity to certain sensory aspects of the environment (American Psychiatric Association, 2013). In addition to these hallmark features, individuals with ASD also consistently display several other debilitating impairments, including motor and attention deficits (Allen & Courchesne, 2001; Bhat, Landa, & Galloway, 2011; Fournier, Hass, Naik, Lodha, & Cauraugh, 2010). Indeed, recently emerging research evidence demonstrates that motor impairments and attention deficits are deeply implicated in socio-communication and interaction behaviors, opening

new avenues for clinical research with broad implications for the role of music as an intervention for individuals with ASD.

The clinical application of music to mediate the developmental and therapeutic processes in autism has a long history (for review, see Reschke-Hernandez, 2011). Most therapy practices including music-based techniques have been traditionally centered on outcomes considered primary features of autism: communication, social interaction,

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and emotional skills. In this article, we propose a reassessment of the role that music can play in interventions to support healthy neurodevelopment in ASD and suggest, based on newly emerging research evidence, that music-based developmental training for attention and motor control may receive a critical new functional role in the treatment of autism. To support this argument, we begin with an overview of recent behavioral and neuroimaging research on preserved musical-related skills in individuals with autism. Next, we provide a critical overview of the current state of clinical research into music therapy for people with autism centered on results from recent controlled clinical studies examining the effectiveness of music-based interventions to address communication, social and emotional skills. In the subsequent section of the article, we present research evidence demonstrating that motor and attention deficits have direct implications to socio-communication and interaction skills and that these impairments may be key indicators of structural and functional brain dysfunction in ASD. To conclude, we provide a theoretical framework to support the application of rhythm-based interventions in the treatment of autism.

Music-related skills in autism

There is robust research evidence that music is a domain of preserved skills and interest in individuals with ASD. Empirical behavioral research has demonstrated that individuals with autism often have intact or superior pitch and timbre processing abilities (Bonnell et al., 2003; Heaton, 2005, 2009; Heaton, Hermelin, & Pring, 1998; Heaton, Williams, Cummins, Happé, & Håppe, 2007; Mottron, Peretz, Menard, & Ménard, 2000), enhanced melodic memory (Heaton, 2003), preserved abilities to understand the rules of Western musical harmony and process melodic complexity (Heaton et al., 2007; Thaut, 1988), and intact rhythm synchronization capacity (Tryfon et al., 2017). One particularly intriguing research finding in the ASD auditory research literature is that exceptionally good pitch information processing commonly appears in autism (for review, see Heaton, 2009). It has been shown, for instance, that autistic children without musical training are often able to accurately associate musical tones to their corresponding note labels – a skill known as absolute pitch, a rare ability to identify or produce the pitch of a tone without reference to an external standard (Heaton, 2003; Heaton, Pring, & Hermelin, 2001; Heaton, Williams, Cummins, & Happé, 2008). This enhanced ability to process simple auditory stimuli such as musical tones contrasts with a generally diminished ability to process social and more complex sounds such as speech; a paradox that has served as a model to study atypical sensory processing in ASD (Chowdhury et al., 2017; Just, Cherkassky, Keller, Kana, & Minshew, 2007; Mottron, Dawson, Soulières, Hubert, & Burack, 2006; Mottron et al., 2000; Oumet, Foster, Tryfon, & Hyde, 2012). Importantly, although hypersensitivity to

some sounds and loud noises has been described in this population (Danesh, Lang, Kaf, Andreassen, Scott, & Eshraghi, 2015; Demopoulos & Lewine, 2016; Funabiki, Murai, & Toichi, 2012; O'Connor, 2012), research suggests that this abnormality is not associated with hypersensitivity of the auditory pathways but with difficulties in the higher cortical processing systems (Funabiki et al., 2012).

Emerging evidence also emphasizes the role of music stimuli in studying emotion processing in ASD. Several studies have shown, for instance, that individuals with autism are able to properly identify the positive and negative valence of emotional musical stimuli (Brown, 2017; Gebauer, Skewes, Westphael, Heaton, & Vuust, 2014; Heaton, Hermelin, & Pring, 1999; Quintin, Bhatara, Poissant, Fombonne, & Levitin, 2011). These findings are consistent with neuroimaging reports indicating that cortical and sub-cortical circuits underlying affect and reward processing are preserved in individuals with ASD (Caria, Venuti, & De Falco, 2011). Interestingly, a recent study found that although emotional responses to music are preserved in ASD, autistic individuals with comorbid alexithymia (a disorder characterized by an absence of cognitive insight into one's emotions) have difficulties ascribing affective labels to these emotions (Allen, Davis, & Hill, 2013; for review, see Bird & Cook, 2013; Hill, Berthoz, & Frith, 2004; Molnar-Szakacs & Heaton, 2012). Therefore, these studies collectively indicate that, although individuals with ASD have significant deficits in processing complex emotional cues within the social context, their ability to identify the emotional content of complex nonsocial affective stimuli such as music is generally preserved.

Despite speech disabilities in autism, recent neuroimaging research has demonstrated that speech-analog music abilities are frequently preserved (Lai, Pantazatos, Schneider, & Hirsch, 2012; Sharda, Midha, Malik, Mukerji, & Singh, 2015). A recent neuroimaging study investigating speech and song processing in low-functioning children with ASD found that the Broca's area (left inferior frontal gyrus) – which is typically under-activated during speech processing in children with autism relative to controls – was significantly activated during song processing, which indicates that children with ASD may be more effectively engaged in musical stimuli (Lai et al., 2012). Another imaging study expanded this finding by showing that while frontotemporal connectivity is significantly disrupted during spoken-word perception, this network is preserved during sung-word processing (Sharda et al., 2015). These findings suggest that alternate mechanisms of speech processing may be recruited in individuals with ASD through singing, which may be due to functional and structural differences between speech and song (e.g., singing being non-reciprocal, structured and ritualized, often metric and slower than speech, and having only associated semantic meaning).

Collectively, this growing body of research evidence corroborates anecdotal reports that music has a profound

impact on children with autism, and demonstrates that music-related skills in domains such as memory, auditory perception, emotion, and language, are significantly preserved in ASD. In addition, these findings suggest that music may be a particularly resourceful therapeutic approach for autism with strong potential to promote and facilitate functional changes in non-musical brain and behavioral functions.

Current state of clinical research

Traditionally, clinical and research practices in music therapy have focused predominantly on outcomes considered primary features of autism: communication, social interaction, and emotional skills. The following overview and critical appraisal of the current research literature focus on randomized controlled trials and controlled clinical trials published in peer-reviewed journals between 2000 and 2017. For systematic and narrative reviews of recent clinical studies in music therapy for autism, including case studies and single-group studies, see Geretsegger, Elefant, Mössler, and Gold (2014) and James et al. (2015).

Communication outcomes

Social communication, language and speech deficits in autism are traditionally the primary target areas in music therapy. Speech production was the main treatment target goal investigated in a few recent randomized clinical studies. Lim (2010) addressed acquisition of target words using a Neurologic Music Therapy technique called “developmental speech and language training through music (DSLTM)” (Thaut & Hoemberg, 2014). The DSLTM technique is designed to use developmentally appropriate musical materials and experiences to enhance speech and language development through singing, chanting, playing musical instruments, and combining music, speech, and movement. In this study, pre-recorded videos of songs composed by the music therapist to include the target words were presented to children with ASD with various levels of impairment. The control conditions were pre-recorded videos of the speech stimuli using only the text of the songs or no treatment. The intervention was administered twice a day for three days, and post-tests were completed after only six training sessions. Results indicated that high and low-functioning participants in both music training and speech training increased verbal production in the post-intervention assessment. Interestingly, low-functioning children seemed to have greater gains in the music condition. In a subsequent study, Lim and Draper (2011) added music to an applied behavioral analysis verbal behavioral approach, a method that focuses on teaching children to associate a word or phrase to its functional meaning, including making requests, labeling objects, following instructions, and completing sentences. The music intervention consisted of singing the verbal instructions and

songs composed by the music therapist to include the target words and phrases to be learned, whereas in the speech control condition the therapists spoke the same texts for the sentences and directions. Children with ASD, who were verbal or preverbal, received both music and speech training for three days per week for two weeks (the order of the intervention was counterbalanced). The results indicated that there were no differences between the treatment groups since both music and speech training had a significant effect on verbal operant production compared to the no-training condition. The only measure in favor of the music training condition was echoic production of speech.

Similar results were observed in other studies comparing the effectiveness of infant-directed speech intervention with infant-directed song intervention on communication skills. Simpson and colleagues (Simpson, Keen, & Lamb, 2013, 2015) tested whether sung instructions embedded into a computer-based communication intervention developed to teach receptive labeling would facilitate engagement and learning outcomes. Twenty-two children with limited communication skills were randomly allocated to five weeks of infant-directed song intervention or infant-directed speech intervention (participants crossed over and completed the other intervention after the follow-up assessment). Pre-recorded sung or spoken instructions directed children to label garden creatures depicted in pictorial form. Researchers found that, although children were more engaged during the infant-directed singing condition (Simpson et al., 2013), there were no significant differences between the interventions regarding the improvement of receptive labeling skills (Simpson et al., 2015).

Social outcomes

The main intervention approach to address social communication skills in autism is musical improvisation (Geretsegger et al., 2015; Wigram & Gold, 2006). Within this therapeutic approach, music is utilized as a medium for self-expression, communication, and interaction, and for the development or rehabilitation of appropriate socio-emotional functioning.

Kim, Wigram, and Gold (2008) investigated the effects of improvisational music therapy on joint attention behaviors. Pre-school children with autism undertook 12 weekly improvisational music therapy sessions and 12 weekly play sessions with toys as the control condition (the order of interventions was counterbalanced with a one-week wash-out period). The study reported improvement in initiating joint attention bid, joint visual attention, eye contact duration, and alternating eye contact during and after the treatment sessions in the music therapy condition but not in the control condition. In a subsequent analysis of this data, Kim, Wigram, and Gold (2009) focused on the social-motivational aspects of the interaction between the child and the therapist during improvisational music therapy. For that, behavioral microanalysis of video recordings of the

therapy sessions assessed outcomes such as frequency and duration of the participant's emotional and motivational responsiveness (joy, emotional synchronicity, initiation of engagement). Results indicated that emotional and responsiveness behaviors were significantly more frequent and longer in duration in the music therapy intervention than in the toy play condition. Therefore, the findings of these two studies are in favor of the use of improvisational music therapy to address joint attention and pro-social behaviors. However, replication is usually a problematic matter in improvisational music therapy given the subjectivity and lack of protocol structure, which are characteristic of some improvisational music therapy methods. To address this issue, future clinical studies should provide open access to the musical activities administered in the study, supplemented with thorough descriptions of the intervention protocols and justifications as to why the various musical features were used to promote the desired non-musical behavior and/or experience.

Other controlled studies investigated the effect of improvisational music therapy on verbal, nonverbal and social communication skills. In Gattino, Riesgo, Longo, Leite, and Faccini (2011), unstructured music improvisation intervention was administered weekly for 16 weeks to a group of children diagnosed with autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger's syndrome, while participants in the control group did not receive music therapy treatment in addition to standard care. Results revealed no statistically significant differences between groups in all outcomes assessed. However, a subgroup analysis indicated that non-verbal communication significantly increased after music intervention only for children with autism (but not PDD-NOS and Asperger's). Given the small sample of children with autism in the experimental group, limited conclusions can be made, warranting further investigation. In LaGasse (2014), children with autism received either music therapy or a non-musical social skills intervention for five weeks. The music therapy intervention consisted of structured group musical experiences to promote cooperative play and communication, whereas the control group participated in similar group experiences with games and non-musical activities. Social outcome measures focused on eye gaze, joint attention, and communication. Results indicated that children in the music therapy group significantly improved in measures of joint attention with peers and eye gaze towards other persons in relation to the control group. However, the study did not find significant differences between groups in measures of communication, and the lack of standardized treatment protocols makes it difficult to interpret and replicate the positive results. A family-centered music therapy intervention was also used to assess social engagement in children with severe ASD (Thompson, McFerran, & Gold, 2014). In this study, parents were encouraged to actively participate in home-based music therapy sessions and to collaborate with the therapist in the

musical activities. The intervention consisted of structured music activities designed to address shared attention, turn-taking, response and initiation of joint attention, whereas the control group did not receive music therapy in addition to standard care. Primary outcome measures were based on parent-report assessments. Results showed that parents perceived a significant improvement in the quality of their child's social skills after the music therapy intervention in relation to the control condition. Assessment of video recordings also suggested improvement in the level of interpersonal engagement within music therapy sessions. Although encouraging, these findings must be interpreted with caution given that the results were predominantly based on parental assessment, which is prone to bias.

Although these studies collectively provide some encouraging results supporting the use of musical improvisation in the treatment of social communication skills in individuals with ASD (for a systematic review, see Geretsegger et al., 2014), a recent large randomized controlled trial cast doubt on this conclusion (Bieleninik et al., 2017). This study evaluated the effects of improvisational music therapy on the generalized social communication skills of 364 children with ASD. Children allocated to the music therapy group received five months of weekly individual therapy sessions consisting of joint musical activities aimed to develop and enhance social skills such as affect sharing and joint attention. Children allocated to the control group did not receive music therapy in addition to standard care. The study found no significant differences in social communication skills among children in the improvisational music therapy group when compared with standard care alone. The authors acknowledged that the music therapy intervention was not tightly controlled and perhaps not consistently implemented across multiple centers, corroborating our comment regarding replication of musical improvisational intervention protocols.

Emotional outcomes

Although social communication and interaction skills have historically been the primary focus of music therapy intervention for ASD, self-awareness, emotional expression and understanding have also been targeted with music therapy (for review: Geretsegger et al., 2014; James et al., 2015). For instance, Allen and Heaton (2010) proposed a music-based intervention based on associative learning to help individuals with ASD and comorbid alexithymia to develop a vocabulary to express their experiences of music-evoked emotions and to transfer this vocabulary and related socio-emotional skills to non-musical situations in everyday life. Although promising, there is a paucity of controlled clinical studies investigating the potential use of music therapy to facilitate emotional understanding in children with ASD. Katagiri (2009) studied the effectiveness of a music-based intervention to facilitate understanding of four different emotions: happiness, sadness, anger, and fear. In the music

therapy instrumental improvisational condition, structured improvisations referencing the targeted emotions were pre-recorded and presented to the participant while the therapist gave verbal instructions about each of the emotions. In a second music therapy condition, the emotions were taught by singing a song composed by the therapist which included lyrics referencing the targeted emotions. The control conditions included verbal instructions only or no purposeful teaching of the targeted emotion. Results suggested that participants' emotional understanding improved from pre-test to post-test in all conditions, with no clear indication that the music therapy conditions were superior to control conditions in facilitating emotional expression and understanding.

Expanding the clinical scope of practice in music therapy for autism

The overview of recent controlled clinical studies provides an inconclusive scenario. While some studies support the use of music therapy to improve joint attention and general pro-social behaviors, a recent rigorous multicenter study did not arrive at the same conclusion (Bieleninik et al., 2017). Moreover, there is no clear indication that the music therapy interventions tested to date are superior to standard care with respect to improving speech production, verbal/non-verbal communication and emotional understanding.

Based on the current state of the clinical research on this topic we propose a reassessment of the role that music can play in interventions to support healthy neurodevelopment in ASD, and suggest an expansion of the clinical scope of practice in music therapy for autism. This expansion refers to the need to address motor control impairments and attention deficits as additional key treatment targets. Our argument is based on newly emerging research evidence that motor and attention deficits are directly implicated in the development of socio-communication and interaction skills and may be key indicators of structural and functional brain dysfunction in ASD.

Implications of motor control deficits to socio-communication and interaction skills

Parents and clinicians often report that children with autism display significant and pervasive motor impairments that are not associated with motor stereotypies. Motor deficits in autism include impairment in basic motor control such as clumsy gait (Fournier et al., 2010), poor balance and postural control (Bhat et al., 2011), delayed motor development (Fatemi et al., 2012; Wang, Kloth, & Badura, 2014), impairments to reaching and grasping (Sacrey, Germani, Bryson, Zwaigenbaum, & Morris, 2014), and poor manual dexterity and coordination (Kindregan, Gallagher, & Gormley, 2015; Kushki, Chau, & Anagnostou, 2011). Evidence gathered in recent research suggests that motor impairments are not only co-occurring neurological

symptoms but may be one of the earliest identifiable and most prevalent features of autism (Bo, Lee, Colbert, & Shen, 2016; Dziuk et al., 2007; Hilton et al., 2007; Hilton, Zhang, Whilte, Klohr, & Constantino, 2012; Ming, Brimacombe, & Wagner, 2007).

Researchers examining home videos of infants who were later diagnosed with autism noted that these children exhibited significant motor development delays and higher frequency of unusual motor behaviors as early as in the first six to nine months of life (e.g., problems in sequencing movements to grasp, crawl or walk) (Ozonoff, Heung, Byrd, Hansen, & Hertz-Picciotto, 2008; Teitelbaum, Teitelbaum, Nye, Fryman, & Maurer, 1998; Weiss, Moran, Parker, & Foley, 2013). Studies of infants at risk have also demonstrated that early motor deficits are reliable predictors of autism. For instance, manual-motor abilities such as grabbing and exploring objects (Gernsbacher, Sauer, Geye, Schweigert, & Hill Goldsmith, 2008; Libertus, Sheperd, Ross, & Landa, 2014; Sacrey et al., 2014), postural instability and delayed posture development (Minschew, Sung, Jones, & Furman, 2004; Nickel, Thatcher, Keller, Wozniak, & Iverson, 2013), poor muscle tone and motor imitation (Brian et al., 2008; Landa, Gross, Stuart, & Bauman, 2012; Rogers, 2009), and being delayed in the onset of walking (Iverson & Wozniak, 2007), are consistently reported in infants at risk for ASD. Furthermore, according to Sutra et al., 2007, motor skills at the age of two years are the best predictors of later ASD diagnosis.

Motor development is closely intertwined with socio-emotional and cognitive development (Jones, Gliga, Bedford, Charman, & Johnson, 2014; Leonard & Hill, 2014). Recent studies have demonstrated that early motor impairments are strong predictors of social-communication deficits developed later in childhood. Oral and manual motor impairments in infancy and toddlerhood have been linked to communication delays (Bhat, Galloway, & Landa, 2012; Flanagan, Landa, Bhat, & Bauman, 2012; Lebarton & Iverson, 2013; Libertus et al., 2014), speech fluency deficits (Gernsbacher et al., 2008), and difficulties in processing emotional facial expressions (Leonard, Bedford, Pickles, & Hill, 2015; Leonard & Hill, 2014).

There is also increasing evidence that motor control is deeply implicated in social cognition (Cook, 2016; Mostofsky & Ewen, 2011; Trevarthen & Delafield-Butt, 2013). Social skills depend on one's performance of skilled and goal-oriented movements (praxis) as well as the understanding of others' movements and associated intentions. Through observation and imitation of others' actions, we build internal representations that are used as a template to interpret and predict other people's intentions (Mostofsky & Ewen, 2011). Researchers have found that dyspraxia is correlated with core social, communicative and behavioral features of autism (Dowell, Mahone, & Mostofsky, 2009; Dziuk et al., 2007). The correlation between abnormal praxis development with social/communicative impairments in ASD suggests that "similar mechanisms may

underlie impaired development and execution of both motor skills and social/communicative skills in autism” (Mostofsky & Ewen, 2011, p. 439). Additionally, new methods of analysis have recently emerged allowing examination of micro-movements (Torres & Denisova, 2016; Torres et al., 2013). Torres and colleagues suggested that deficits in micro-movements are associated with difficulties in building internal representations of one’s own movements, which in turn can affect the interpretation and prediction of other people’s intentions.

Therefore, this growing body of research indicates that the earliest observable symptoms of autism may involve motor behavior and that impaired motor functions in ASD are strong predictors of core social, communicative and behavioral features of autism. These findings collectively demonstrate that the motor system – which is known to be trainable – is a promising target for early intervention to improve outcomes for individuals living with ASD.

Implications of attention deficits to socio-communication and interaction skills

Cognitive deficits are also widely observed in ASD, although generally regarded as secondary impairments or comorbidities. New research evidence indicates, however, that attention dysfunction in ASD should be reconsidered as a primary feature due to its role in impairments in language and socio-emotional areas. Attention is critically involved in all cognitive functions as the gateway to voluntary control of thoughts, emotions, and actions (Fan, 2013, p. 281). There is accumulating evidence from behavioral and neuroimaging studies that individuals with ASD display a wide range of attentional deficits across the many domains of attention functions (for review, see Allen & Courchesne, 2001; Fan, 2013). Abnormal spatial orientation of attention has been extensively reported in autism literature. Researchers have noted, for instance, that individuals with autism have limited capacity in disengaging and shifting attention from a stimulus or task to another (Landry & Bryson, 2004; Wainwright-Sharp & Bryson, 1993). Orientation deficits have also been observed in tasks requiring rapid shifting of attention between sensory modalities (Courchesne et al., 1994), between object features (Rinehart, Bradshaw, Moss, Brereton, & Tonge, 2001), and between spatial locations (Townsend, Harris, & Courchesne, 1996). Orientation to human faces and social information have also been well-studied in ASD. Evidence suggests that individuals with autism have particular difficulty attending to and processing social stimuli (e.g., facial expressions, gestures) (Dawson et al., 2004; Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Jones & Klin, 2013). Orientation and executive control functions of attention are essential during the normal exchange of information and turn-taking, which happens rapidly, frequently, and often unpredictably (Fan, 2013). Therefore, difficulties

in orienting and shifting attention can lead to severe challenges in social and communication engagement.

Individuals with ASD also have difficulties with selective attention, which is the ability to attend selectively to meaningful sources of information while ignoring task-irrelevant ones. Selective attention deficits have been demonstrated in tasks where the targets are defined by different shapes or colors (Allen & Courchesne, 2001, 2003), or in tasks including competing distractors (Belmonte & Yurgelun-Todd, 2003; Burack, 1994). The impaired ability to filter task-irrelevant information and control shifts of attention may be directly associated with a variety of commonly observed autistic features, such as stimulus overselectivity, perseveration, and narrowed interests (Courchesne et al., 1994).

Studies have also found that children at risk and with ASD display significant impairments in initiating and responding to joint attention (Presmanes, Walden, Stone, & Yoder, 2007; Stone, McMahon, Yoder, & Walden, 2007; Sullivan et al., 2007). Infant-initiated joint attention or directing attention, refers to a child’s use of gestures, gaze shifts, pointing and other cues to initiate a shared experience with others, whereas responding to joint attention or attention following, reflects the infant’s ability to orient attention in response to a cue, such as someone’s gaze, head turn, point, or attention-directing utterance. Sullivan and colleagues (2007) examined responses to joint attention (RJA) in children at risk of developing ASD at 14 months and 24 months of age and found that 14-month-olds at risk already displayed significant deficits in responding to gaze shift cues and/or pointing cues. At 24 months of age, children at risk completely failed to respond to any RJA opportunity, indicating little developmental improvement in response behaviors in children at risk between 14 and 24 months. Moreover, the study reported that response to joint attention performance predicted later receptive and expressive language performance, and reliably predicted later ASD diagnoses.

Finally, comorbid attention deficit hyperactivity disorder (ADHD) is common and persists with age in individuals with ASD (Gargaro, Rinehart, Bradshaw, Tonge, & Sheppard, 2011; Yoshida & Uchiyama, 2004). Although previous diagnostic guidelines precluded diagnosing ASD and comorbid ADHD, researchers have long reported rates of comorbidity between autism and ADHD within the range of 14–78% (Corbett & Constantine, 2006; Johnston et al., 2013; Sinzig, Walter, & Doepfner, 2009). A shared cognitive phenotype is inattention. Sustained attention is consistently reported as one of the main deficits in ADHD (Corbett & Constantine, 2006; Sinzig et al., 2009) and has also been reported in ASD (Allen & Courchesne, 2001; Murphy et al., 2014; Johnson et al., 2007). A recent neuroimaging study sought to elucidate commonalities and differences in the underlying neurofunctional substrates of adolescents with ADHD or ASD during a vigilance task (Christakou et al., 2013). Results demonstrated that while

both disorders displayed the same type of underactivation relative to controls in brain regions such as left-hemispheric dorsolateral prefrontal cortex (DLPFC) and superior parietal cortex, ADHD patients showed a more severe DLPFC dysfunction associated with poorer performance measures in the sustained attention task, whereas patients with ASD specifically presented dysregulation of the fronto-striato-cerebellar circuitry.

In sum, an examination of the performance of individuals with autism across a variety of attentional operations reveals a wide range of deficits, including difficulties to rapidly re-allocate attention to new spatial locations or target features, to filter task-irrelevant information, to share attention with others, and to coordinate attention between people and objects – especially in social contexts. It is clear that deficits of attention affect one's ability to attend, engage, reciprocate, and learn, thus significantly impacting social development.

The role of the cerebellum and dysfunctional brain connectivity

There is strong evidence suggesting that the cerebellum is a key player in the complex neural underpinning of ASD with behavioral implications beyond the motor domain (Becker & Stoodley, 2013; D'Mello & Stoodley, 2015; Fatemi et al., 2012; Koziol et al., 2014; Wang et al., 2014). Histopathological changes in the cerebellum have been observed in post-mortem studies where a decrease in the number of Purkinje cells in regions such as folia, vermis and cerebellar hemispheres have been recurrently reported (Becker & Stoodley, 2013; Fatemi et al., 2012). Structural imaging studies of the cerebellum have repeatedly demonstrated that autism is associated with significant white matter differences, abnormally lower cerebellar vermal volumes, and reduced size of cerebellar hemispheres in children and adults with ASD (Chukoskie, Townsend, & Westerfield, 2013; Wang et al., 2014). Functional imaging research has also revealed task-dependent differences in cerebellar activation in a wide range of tasks (Anagnostou & Taylor, 2011; Philip et al., 2012).

There is ample evidence at multiple levels of inquiry that abnormalities in the structure and function of the cerebellum are associated with impaired neurobehavioral function. Bolduc and colleagues (2012) showed in a cohort of children between the ages of one and six years that reduced vermis volume was associated with impairment of global development, cognition, expressive language, gross and fine motor skills, behavioral problems, and higher scores in autism spectrum screening tests. Studies have also reported that lesions in the cerebellum hemispheres at earlier ages can result in language delay, whereas damage to the vermis results in withdrawn social behavior, impaired gaze, anxiety and stereotyped behavior (Riva & Giorgi, 2000; Wells, Walsh, Khademian, Keating, & Packer, 2008). In autism, reduced vermal VI–VII is

associated with symptoms such as reduced exploration and increased stereotyped and repetitive moments (Kaufmann et al., 2003), whereas lesions in the cerebellar lobules I–V are linked with vestibular, gross and fine motor control (Fatemi et al., 2012; Gowen & Miall, 2007; Nayate, Bradshaw, & Rinehart, 2005). These studies collectively demonstrate that cerebellar lesions directly interfere with a number of behaviors, including motor, cognitive and affective functions.

The cerebellum has been long known for its importance in motor learning, motor coordination and timing due to its crucial role in prediction and adaptation mechanisms (Manto et al., 2012). That is, the cerebellum is key in establishing sensory prediction errors by processing signal discrepancies between the expected sensory consequences of a stimulus or movement and the actual sensory input. These error signals are essential for sensorimotor control and motor adaptation learning because they allow rapid adjustments in the motor output and refinement of future sensory predictions in order to reduce the variability of subsequent actions (Allen, Müller, & Courchesne, 2004; Bastian, 2006; Koziol et al., 2014; Middleton & Strick, 2000; Sokolov, Miall, & Ivry, 2017). Therefore, cerebellum abnormalities would impair this prediction mechanism resulting in slower, more variable, inaccurate, and effortful responses (Allen & Courchesne, 2001; Courchesne et al., 1994; Diamond, 2000; Sokolov et al., 2017). This assumption has been confirmed in several studies showing, for instance, that patients with cerebellar lesions exhibit increased temporal variability in the production of periodic movements such as simple finger tapping (Diedrichsen, Criscimagna-Hemminger, & Shadmehr, 2007; Ivry & Keele, 1989; Spencer, Ivry, & Zelaznik, 2005). Studies have also found evidence of atypical movement preparation in participants with autism characterized by a failure to adjust the motor preparation time in response to an “expected” versus “unexpected” movement, suggesting a deficit in anticipatory preparation of movement (Rinehart et al., 2006; Rinehart, Bradshaw, Brereton, & Tonge, 2001).

In addition to motor behavior, current research has firmly established the cerebellum's critical role in modulating cognitive functions (Buckner, 2013; Doya, 2000; Koziol et al., 2014; Sokolov et al., 2017). Evidence of the involvement of the cerebellum in attention has emerged from functional imaging studies demonstrating, for instance, that attention and motor performance activate distinct cerebellar regions – attention tasks engage areas located in the superior posterior cerebellar hemispheres and those involved in motor tasks are located in the anterior cerebellar hemisphere (Allen, Buxton, Wong, & Courchesne, 1997; Allen & Courchesne, 2003; see also Mosconi, Mohanty, Greene, Cook, Vaillancourt, & Sweeney, 2015). Studies have also shown that people with autism and patients with acquired cerebellar lesions are similarly impaired in tasks requiring rapid voluntary shifts of

attention between stimuli, which indicates that cerebellum abnormalities result in deficits in the timely and accurate control of the direction of attention (Akshoomoff & Courchesne, 1994; Courchesne et al., 1994). Structural and functional cerebellar abnormalities in autism have been also linked to deficits in spatial orientation (Harris, Courchesne, Townsend, Carper, & Lord, 1999), selective attention (Allen & Courchesne, 2003) and sustained attention (Christakou et al., 2013; Murphy et al., 2014). Another important aspect of the cerebellum, in addition to cognition, is its role in affective responses. An important network loop connects the vermal regions in the cerebellum associated with emotional functions to several cortical and subcortical systems, among them the ventral insula, which is also highly involved in emotional functions. Therefore, the cerebellum may also be considered an important component in a subcortical network for subjective and social emotion processing in ASD (Bird et al., 2010; Reetz et al., 2012).

Studies often report that abnormal cerebellar activity is associated with atypical activation of cortical regions, suggesting that cerebellar abnormalities disrupt optimization of both structure and function in specific cerebro-cerebellar circuits (D'Angelo & Casali, 2013; D'Mello & Stoodley, 2015; Middleton & Strick, 2000). The cerebellum is interconnected with several different regions of the cerebral cortex by discrete circuits or "loops" that connect a diverse set of cerebral cortical areas with the cerebellum and the basal ganglia (for review, see D'Angelo & Casali, 2013; D'Mello & Stoodley, 2015; Middleton & Strick, 2000). This extensive connectivity provides anatomical substrates by which dysfunctional cerebro-cerebellar connectivity could be involved in the large spectrum of symptoms that comprise ASD (D'Mello & Stoodley, 2015). Studies have repeatedly reported significant overconnectivity in networks between the cerebellum and motor cortices (D'Mello & Stoodley, 2015; Khan et al., 2015; Mostofsky & Ewen, 2011) and underconnected prefrontal-cerebellar attention networks in individuals with ASD in relation to healthy controls (Belmonte, 2004; Fitzgerald et al., 2015; Keown et al., 2013; Murphy et al., 2014). Dysfunctional connectivity between the cerebellum and cerebral cortical brain regions has been demonstrated in tasks involving finger sequencing (Mostofsky et al., 2009), visual processing (Villalobos, Mizuno, Dahl, Kemmotsu, & Müller, 2005), language (Hodge et al., 2010; Just, Cherkassky, Keller, & Minshew, 2004), attention (Allen et al., 1997; Belmonte & Yurgelun-Todd, 2003; Murphy et al., 2014), social processing (Jack & Pelphrey, 2015; Sokolov et al., 2012), and executive function (Gilbert, Bird, Brindley, Frith, & Burgess, 2008; Koziol et al., 2014) (for review, see Stoodley & Schmahmann, 2009). These findings therefore strongly indicate that inefficient connectivity may be a hallmark of ASD.

In light of these findings, attention and motor deficits in ASD could be considered critical indicators of cerebellar dysfunction and abnormal cortico-cerebellar connectivity.

If this is indeed the case, then music-based developmental training for attention and motor control may receive a critical new functional role based on evidence that the cerebellum is significantly involved in virtually all music-related tasks, and that music increases synchronized activation of widespread networks in the brain.

Music, like other higher cognitive tasks, requires the activation of different cortical and subcortical regions in an organized and synchronized way. Research has demonstrated that listening to auditory rhythmic sequences such as music increases connectivity in extensive reciprocal cortico-subcortical projections (Alluri et al., 2017; Bhattacharya & Petsche, 2005; Ohnishi et al., 2001; Paraskevopoulos, Chalas, & Bamidis, 2017; Thaut, Trimarchi, & Parsons, 2014) and induces cortico-cortical coherence in auditory and motor areas (Fujioka, Trainor, Large, & Ross, 2012; Lee & Noppeney, 2011; Nozaradan, 2014). Listening to one's favorite song alters connectivity between auditory brain areas and the hippocampus (Wilkins, Hodges, Laurenti, Steen, & Burdette, 2014). There is also growing evidence that auditory rhythmic stimuli processing (Nozaradan, Schwartz, Obermeier, & Kotz, 2017; Teki, Grube, & Griffiths, 2012) and auditory-motor entrainment tasks rely heavily on extensive cortico-subcortical-cortical functional networks, including cortico-cerebellar circuits (Chauvigné, Gitau, & Brown, 2014; Thaut et al., 2009). Moreover, recent imaging research has indicated that the cerebellum is not only involved in temporal perception and sensorimotor synchronization tasks, but that the cerebellum has a critical role in processing melodic properties and speech information (e.g., prosody) (Callan, Kawato, Parsons, & Turner, 2007; Parsons, Petacchi, Schmahmann, & Bower, 2009; Thaut et al., 2014). Putting together a new framework that links the neural basis of music processing to a new look at the behavioral and neurological deficits in the developing brain in ASD, some more specific directions towards the use of music in therapy for autism may be finally laid out.

Neurobiological foundations of rhythm-based interventions

Auditory rhythm has a profound effect on the motor system. The auditory system is well known for its ability to detect temporal patterns in auditory signals with extreme precision and rapidly construct stable temporal templates (for review, see Thaut & Kenyon, 2003). Moreover, the auditory system has richly distributed fiber connections to motor centers from the spinal cord upward on to brain stem, subcortical, and cortical levels (Felix, Fridberger, Leijon, Berrebi, & Magnusson, 2011; Koziol & Budding, 2009; Schmahmann & Pandya, 1995). This distributed and reciprocal connectivity between the auditory and motor systems explains why auditory rhythmic cues entrain motor responses.

Auditory-motor entrainment occurs when the firing rates of auditory neurons, triggered by auditory rhythm such as music, entrain the firing patterns of motor neurons. For example, it has been demonstrated that finger and arm movements instantaneously entrain to the period of a rhythmic stimulus (e.g., metronome beat) and maintain phase synchrony to the metronome even when subtle tempo changes are introduced (Thaut, Miller, & Schauer, 1998). The clinical importance of auditory-motor entrainment is that the continuous time reference provided by the rhythm of the music primes the motor system into a state of readiness by providing anticipatory time cues that allow movement anticipation and motor planning to occur based on expectations of the duration of the time cues, thus increasing response quality (Thaut & Hoemberg, 2014; Thaut, McIntosh, & Hoemberg, 2015).

The ability to use rhythm to prime the motor system and re-program the execution of a motor pattern has opened the possibility of using complex auditory stimuli such as music and rhythm-based interventions for movement therapy and rehabilitation (Thaut, Miltner, Lange, Hurt, & Hoemberg, 1999). Rhythm-based techniques use rhythmic patterns to provide a continuous time reference and generate expectations for when an object will occur or when a movement needs to be performed, thus allowing preparation and increasing the quality and precision of the responses. For instance, rhythm-based interventions such as Rhythmic Auditory Stimulation (RAS) involve the utilization of rhythmic cues (metronome or rhythmically accentuated music with embedded metronome clicks) to facilitate gait and improve the kinematic stability of walking movements (Thaut & Hoemberg, 2014). There is a strong body of research evidence that RAS improves movement in patients with movement disorders (for review, see Thaut, 2015; Thaut & Abiru, 2010; Thaut et al., 2015). Specifically, it has been demonstrated that rhythmic auditory cues have immediate effects on gait by increasing speed, stride length, and improving symmetry and stability (Arias & Cudeiro, 2010; McIntosh, Brown, Rice, & Thaut, 1997; Thaut et al., 1996; Thaut et al., 1999; Thaut, McIntosh, & Rice, 1997). In upper limb rehabilitation, rhythmic cueing is effective to improve spatiotemporal control, reduce movement variability, smooth reaching trajectories, and reduce reliance on compensatory movements (Malcolm, Massie, & Thaut, 2009; Thaut, Kenyon, Hurt, McIntosh, & Hoemberg, 2002; Luft et al., 2004).

Rhythmic entrainment extends beyond motor control. Music is inherently temporal and sequential, and the regularity of rhythmic pulses generates temporal expectations that allow us to predict when the next beat of the music will occur and consequently direct our attention to a particular moment in time (Honing, Bouwer, & Háden, 2014; Large & Palmer, 2002). There is a large body of research demonstrating that rhythm is key in tuning and modulating attention (Drake, Jones, & Baruch, 2000; Jones, 1992). According to dynamic attending theory (Large & Jones,

1999; Jones et al., 1982), internal fluctuations in attentional energy entrain with the temporal patterns of external events, generating expectations about when future events will occur. Consequently, if an event coincides with this attention peak, its processing is facilitated. Indeed, people are most accurate in judging pitch changes when they occur on the beat of the music than at unexpected time points (Honing et al., 2014; Jones, 1992; Lange, 2010; Schmuckler & Boltz, 1994). Studies have also shown that the capacity to focus attention on relevant stimuli while ignoring distracting information is possible due to an anticipatory attentional mechanism that suppresses the processing of distracting information (Fu et al., 2001; Johnson & Zatorre, 2005). It is possible, therefore, that the rhythmic structure of the music modulates these anticipatory mechanisms, facilitating the process of attentionally relevant information. The impact of rhythmic entrainment on attention has been examined in cross-modal and cross-domain studies. Recently emerging electrophysiological and behavioral evidence indicates that auditory rhythmic cues can entrain visual attention and facilitate processing of visual stimuli (Bolger, Trost, & Schön, 2013; Escoffier, Herrmann, & Schirmer, 2015; Miller, Carlson, & McAuley, 2013; Sacrey, Clark, & Whishaw, 2009). Indeed, when one is listening to an auditory rhythmic sequence, processing of visual stimuli presented on the beat is facilitated, supporting the idea that entrainment of neuronal oscillations is a general mechanism through which the brain uses predictive cues to optimize attention and stimulus perception (Bolger et al., 2013).

Evidence of the effects of rhythmic entrainment on attention has supported the development of therapy techniques such as Musical Attention Control Training (MACT), which involves perceptual and structured musical exercises built on rhythmic, melodic and harmonic patterns to train sustained, selective, divided, focused, and shifting attention (Thaut & Hoemberg, 2014). A recent pilot study tested whether this intervention would be effective to improve attention functioning in adolescents with neurodevelopmental delays, including autism (Pasiali, LaGasse, & Penn, 2014). The study found significant improvements in measures of selective attention and rapid shifting of attention after eight treatment sessions. This promising result is based on a small sample and a relatively short intervention period, encouraging replication in larger controlled trials.

The effect of auditory rhythm has also been demonstrated in the speech domain (Cason, Astésano, & Schön, 2015; Cason & Schön, 2012; Fujii & Wan, 2014; Schön & Tillmann, 2015). In a recent study, participants listened to a metrical sequence immediately followed by a word or a sentence and were asked to detect whether the last syllable of the sentence contained the sound [a]. It was reported that reaction times were faster when the rhythmic cueing matched the prosody of the sentence (Cason & Schön, 2012). In a subsequent study, researchers used the same protocol, however, one group of participants received

audio-motor training before the task, which consisted of reproducing the cueing rhythmic patterned vocally using different sounds to distinguish between strong and weak beats (e.g., “ba ba KA”). Results indicated that rhythmic audio-motor training enhanced the priming effect of the rhythmic cues (Cason et al., 2015). This theoretical framework was also applied in the development of therapeutic interventions that combine intonation (singing) and the use of a pair of tuned drums to facilitate speech output (e.g., Thaut, 1984; Wan et al., 2011). For instance, in an initial proof-of-concept study (Wan et al., 2011), six non-verbal children with autism participated in music therapy sessions wherein the therapist introduced the target word or phrase to be learned by simultaneously singing the words and tapping the drums. The child would then repeat and reproduce the target word/phrase on their own. Results showed that participants significantly improved in their ability to articulate words and phrases after the intervention, suggesting that auditory-motor training may be effective in facilitating speech production, thus warranting replication in a larger controlled study. These studies collectively demonstrate that auditory-motor entrainment may facilitate and improve language processing and acquisition, suggesting that audio-motor rhythmic training may be particularly effective in language rehabilitation.

Conclusion

The purpose of this article is to provide a critical appraisal of new research developments for therapists and researchers to potentially reassess the role of music as an intervention to support healthy neurodevelopment in individuals with ASD and expand the current clinical scope of practice in music therapy for autism. More specifically, we suggest that motor control impairments and attention deficits should be addressed as key treatment targets. Our argument is based upon compelling research evidence indicating that motor and attention deficits are deeply implicated in the healthy neurodevelopment of socio-communication and interaction skills, and may be key indicators of structural and functional brain dysfunction in ASD. In light of this evidence, we suggest that music-based developmental training for attention and motor control may receive a critical new functional role in the treatment of autism due to the significant effect of auditory-motor entrainment on motor and attention functions and brain connectivity. Our argument is corroborated by recent studies suggesting that the inclusion of rhythmic-motor components in music therapy interventions have resulted in significant improvements in motor control, selective attention, speech production, and language processing and acquisition. These promising initial results indicate that targeting motor and attention functions may be particularly effective to support healthy neurodevelopment of individuals with ASD, warranting further investigation. We hope that the substantial evidence provided here ignites further research to better

understand the potential impact of addressing motor and attention deficits to the healthy neurodevelopment of persons with ASD.

Contributorship

MT and TBJ conceived the article. TBJ researched the literature and wrote the first draft of the manuscript. Both authors reviewed and edited the manuscript and approved the final version of the manuscript.

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