Neurophysiological Correlates of Musical Giftedness in Autism Spectrum Disorders

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Abstract
Despite their social deficits and behavioral abnormalities, individuals with autism may frequently display unexpected and unusual areas of interest and giftedness in music. In the present work, we discuss the natural predisposition to music shown in autism using a neurophysiological framework, exploring the possible correlations between the musical experience and the connectivity alterations of the autistic brain. After a brief description of the complex cerebral organization in autism spectrum disorder (ASD), the article focuses on the microcircuit alterations, in particular on the excess synaptic excitation and minicolumnopathy, which are strongly linked to the peculiar attention in detecting, processing, and focusing on detail, widely described by the weak central coherence theory. Superior pitch discrimination, labeling, and memory, demonstrated in ASD, even seem to derive from these complex mental processes. The connectivity alterations seem to be also present in the cerebellum, where they damage the timekeeper function and produce severe dysfunctions in rhythmicity and synchronization of thoughts and emotions. We propose that music might restore the natural rhythmicity in the cerebellum of patients with ASD and that this could explain the natural predisposition to music seen in this condition. Finally, we focus on the usefulness of music for rehabilitative purposes.

Keywords
autism, music, connectivity, music therapy

Autism is a lifelong disabling condition that dramatically affects social interaction and communication¹ and is often accompanied by severe behavioral abnormalities² and intellectual disability.³ Despite these social and behavioral abnormalities, individuals with autism may frequently display unexpected and unusual areas of interest and giftedness in music.⁴ They may present enhanced pitch memory and discrimination,⁵,⁶ are sensitive to the affective components of music,⁷,⁸ and occasionally show an extraordinary musical talent.⁹ Additionally, they have been found to display a similar taste in music as healthy individuals.¹⁰ Moreover, music may produce cognitive and affective improvements in people with autism and is frequently used in autism for therapeutic purposes.¹¹-¹³ In the present work, we discuss the natural predisposition to music shown in autism using a neurophysiological framework, exploring the possible correlation between the musical experience and the connectivity alterations of the autistic brain.

Autism Spectrum Disorder: A Complex Form of Cerebral Organization
Autism spectrum disorder (ASD), affecting 6 in 1000 people with a 4:1 prevalence in young males compared to females,³ is clinically defined by a basic triad of symptoms comprising impairments on communication and language, reduced social interaction, and repetitive and stereotyped patterns of behaviors and interests.¹⁴,¹⁵ As highlighted by the term spectrum, the intensity and severity in clinical manifestations and symptoms are variable and produce multiple phenotypes, ranging from severe hypo- to hyperfunctional conditions.¹

Although behaviorally defined, ASD is now agreed to be a neurobiological disorder, and its pathogenesis is determined by multiple factors. Genetics play a key role and multiple genes are likely to be involved.¹⁵ In humans, genotypic screening based on blood analysis has revealed that numerous genes and chromosomal alterations are involved in ASD.¹⁵ Most of the risk alleles are present in the general healthy population, where they exert an adaptive function, for example, enhancing focused attention and other neuropsychological functions. The disorder may emerge when multiple gene alterations are

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This means that each genetic variant that is innocuous by itself may be pathological in concert. However, the 60% concordance for ASD diagnosis in identical twins highlight the role of environmental interactions in its pathogenesis. Autism spectrum disorder may represent the end point of several organic etiologies including prenatal insults, untreated metabolic disorders, localized lesions as in tuberous sclerosis, and postnatal infections and encephalitis.

The specific interactions between genetic, environmental, and developmental factors may contribute to the complexity of the disorder. Developmental compensatory processes may sometimes mask or reduce primary dysfunctions with the effect of normalizing behavior or, in other cases, may induce activity-dependent secondary dysfunctions, disrupting behavior in additional ways. Accordingly, ASD has been recently conceptualized as a complex form of cerebral organization, specifically developed to compensate and contrast the core features of the disorder. The results of similar processes are patterns of severe behavioral abnormalities and atypical cognitive styles of ASD.

Microcircuit Alterations: Excess Synaptic Excitation and Minicolumnopathy

In vitro investigations and molecular genetics have uncovered specific cellular abnormalities related to the manifestation of autism in humans and animal models. In all cases, the common theme seems to be exaggerated activation of certain receptor subtypes at glutamatergic synapses, providing the molecular substrate for local hyperexcitability. These abnormalities could produce a pervasive alteration of neural processing, which, interacting with environmental and developmental factors, contributes to the complexity of the disorder and results in different phenotypes.

In autism, circuit mechanisms in the cerebral cortex underlying local hyperactivity have been described by Casanova et al who defines autism as a minicolumnopathy. Minicolumns, which are the basic functional units of the brain, are more numerous and narrower than are normal ones in the frontal cortex of people with ASD. Narrow minicolumns seem to be the most prominent in the peripheral neuropil compartment, a space rich in unmyelinated projections of some interneurons. These alterations could be linked to a deficit of lateral inhibition in autism. The lateral inhibition is the capacity of an excited neuron to reduce the activity of its neighbors; lateral inhibition sharpens the spatial profile of excitation in response to a localized stimulus. Normally, an activated minicolumn presents a central area of excitation limited by a peripheral area of lateral inhibition, which creates a typical Mexican hat profile of excitation/inhibition. In autism, the pathological minicolumns with lateral inhibition deficit show a large excitation area that is not limited and tends to activate an entire module, resulting in a stovepipe hat profile. A consequence of this local overactivation is the generation of patterns of weak, long-range connectivity.

The exaggerated activation of the glutamatergic synapses, providing the molecular substrate for local hyperexcitability, seems to be related to a dysfunction of common inhibitory cell types, that is, the gamma-aminobutyric acid neurons.

It has been highlighted how altered connectivity/structure in early maturing regions will compound developmental disruptions in subsequently developing areas. A wide range of atypical or adaptive behaviors is associated with these changes, including the alterations in communication, the social isolation, and the behavioral abnormalities that characterize autism. However, as described in the following section, the same connectivity alterations may well provide a basis for compensatory or developmentally enhanced functions.

Minicolumnopathy and Musical Giftedness in Autism

Sometimes the interactions between functional abnormalities, environment, and cognitive and developmental compensatory processes may, as in the case of low-functioning people with ASD, result in severe dysfunctions, including disruptive behavior and severe learning disabilities.

In other cases, the complex interactions may have a relatively positive effect on cognition and behavior, at the same time reducing the primary core dysfunctions of autism. This is the case in Asperger syndrome (AS) and high-functioning autism, where the local networks, hyperfunctioning and isolated, may acquire novel functional properties leading to the formation of enhanced functions including musical skills.

The enhanced skills found in patients with ASD, already described by H. Asperger (1944), have been explained by the special mental processes. In 1999, Happé in “Autism: Cognitive Deficit or Cognitive Style?” discussed the role of the weak central coherence (CC) in determining autistic genius and talent. The weak CC is a peculiar detail-focused processing style that characterizes autism. This elaborated and important work focuses on the strength areas of autism and opens a new trend on autism research that overcomes the reductionist perspective represented by the analysis of the severe deficits that this condition shows. Several authors are in agreement with this recent trend. The weak CC is demonstrated in autism in various domains and at different levels, including the perceptual, visuospatial, constructional, and verbal semantic ones. The autistic mind, appreciating the parts more than the whole, may access details that are not normally considered. This peculiar attention in detecting, processing, and focusing on detail may be considered strongly linked to the neurophysiology of autism, in particular the hyperconnectivity of the local cerebral circuits.

Superior pitch discrimination, labeling, and memory, demonstrated in ASD, may derive from this peculiar mental functioning. In particular, absolute pitch may be learned normally before 6 years of age. After 6 years of age, there is a shift from perceiving individual features to perceiving relations among features and this makes it impossible to acquire absolute pitch. In autism, the pervasive local processing bias explains the high frequency of absolute pitch and superior pitch discrimination at later ages.
Happe\textsuperscript{22} stresses the importance of weak CC in the organization of cerebral functioning in people with autism and highlights the advantages they derive from it; rather than a deficit, these individuals’ weak CC seems to represent a peculiar cognitive style. Accordingly, patients with ASD may be able to generate unexpected connections between the diverse parts of disparate systems, finding novelty within a familiar space.\textsuperscript{28} Autistic creativity, including musical giftedness and talent, derives from these processes.

In recent years, the discussion on musical giftedness in autism has been enriched by the more complex theories of Mottron et al’s Enhanced Perceptual Functioning (EPF)\textsuperscript{29} and Baron-Cohen et al’s Hyper-systemizing Theory.\textsuperscript{30} The EPF theory accounts for atypical lateral inhibition phenomena characterizing the autistic brain,\textsuperscript{18,31,32} the abnormal involvement of primary and associative perceptual areas,\textsuperscript{33-35} and the functional autonomy of perceptual operations from top-down processing influences.\textsuperscript{36} A consequence of EPF is an increased ability to recognize patterns in highly organized cognitive domains. Such a capacity includes the ability to complete and fill in missing information in memorized or perceived units or structures.\textsuperscript{37} Similarly, Baron-Cohen et al\textsuperscript{30} discuss hyper-systemizing capacities evidenced by superior pattern recognition and increased awareness of rules inherent within different cognitive domains.\textsuperscript{36} The autistic hyper-systemizing ability probably derives from the excellent attention to detail and sensory hypersensitivity typically shown in this condition.\textsuperscript{37}

Considered within the context of music, these theories are convincing. As in the case of the weak CC, hyper-systemizing capacity and hypersensitivity may be the consequences of the intrinsic characteristic of the autistic brain, including the overconnectivity in the local cerebral circuits.\textsuperscript{17}

A beneficial consequence of enhanced pattern detection is that it allows stabilizing associations between labels and precise values within continuous dimensions, which individuals without an autistic condition are poorly able to memorize. For pitch perception, people without an ASD are able to easily discriminate 2 distinct pitches as well as to maintain an absolute pitch value in short-term memory. The musical performance in autism encompasses both superior local perception (absolute pitch) and the ability to perceive, perform, transpose, improvise on, and enhance global aspects of musical structure. Additionally, the cognitive processes in autism are more independent and result in regularities within and among patterns being detected and manipulated; this generates a scale of very large structures and is strongly related to the autistic talent.

### Music in Autism: Rhythm for the Brain

The rhythm in music creates the explicit architecture of time, allowing musical elements to emerge in meaningful patterns.\textsuperscript{38} In a similar way, rhythm organizes and coordinates global brain functioning, favoring the learning, development, and performance of motor and cognitive functions.\textsuperscript{39} Rhythm formation is assured by the cerebellum, the timekeeper of the whole brain,\textsuperscript{40} which integrates sensory perception and motor entrainment into cognitive operations and motor transformations.\textsuperscript{39} The connectivity alterations in autism also seem to be present in the cerebellum, damaging its timekeeper function. This produces peculiar and severe dysfunctions in rhythmicity and synchronization of thoughts (dysmetria of thought) and emotions. Therefore, as well as being a pathology of connectivity, autism also seems to be a pathology of central rhythms.

Patients with ASD show a particular interest in music, sometimes accompanied by enhanced pitch memory and discrimination and relevant musical skills,\textsuperscript{5,28} as described earlier. The link between music and autism is something mysterious and fascinating. It has been suggested that music could be processed by cerebral mechanisms that do not seem to be damaged by the autistic pathology.\textsuperscript{4} Alternatively, considering the alterations in brain rhythms and organization seen in autism, we propose that natural predisposition to music seen in this condition might derive from the capacity of music to restore the natural rhythmicity that was altered by the pathology.\textsuperscript{41} In other words, music, as an external source of rhythm, may produce synchronization and organization within the abnormal circuits in the autistic brain, partially compensating for the dysmetria of thoughts and emotions and promoting neuronal plasticity.

### Music Therapy in Autism

Markram and Markram\textsuperscript{24} define autism as an “intense world” of feelings, thoughts, emotions, and abilities. However, with the word \textit{intensity}, they also highlight the extreme behavioral patterns that characterize such condition and are a real challenge for parents and caregivers working in this field.

An appropriate pharmacological treatment that is recommended in managing aberrant behaviors\textsuperscript{42,43} must always be accompanied by an adequate rehabilitative intervention.\textsuperscript{44} In particular, Howlin et al\textsuperscript{45} highlight the crucial role of early intensive rehabilitative interventions in determining a positive outcome in autism. The behavioral approach is considered a \textit{conditio sine qua non} of any comprehensive program, especially in the early years.\textsuperscript{45} However, an efficacious intervention also requires other elements specifically focusing on social development, communication, and joint social interactions.\textsuperscript{45} Music therapy is a promising tool in the field of rehabilitation, but as highlighted by Gold et al,\textsuperscript{11} more relevant scientific and rigorous studies are needed in this field.

Music may produce affective and cognitive improvements and may exert positive effects on deficits in initiating and sustaining joint attention.\textsuperscript{46} Additionally, the musical experience may stimulate attention, engagement, interaction, and reciprocal play.\textsuperscript{47,49}

A rationale for the use of music with rehabilitative purposes is based on the occurrence of musical dialogues between mother and infant soon after birth.\textsuperscript{50,51} The sensitivity of very young infants to the musical dimensions of maternal speech demonstrates that humans are born ready to engage with the “communicative musicality” of conversation.\textsuperscript{52}
**Conclusion**

Music is a mysterious and fascinating entity that shows numerous potentialities in autism. It represents an area of “shared play” and favors the expression of emotions, promoting enjoyment and pleasure and stimulating creativity and concentration.

It may therefore be particularly important for autism because it represents a privileged way to understand the specific aspects of this condition. We have highlighted how, despite their severe social and communication deficits, individuals with ASD present an intense world of emotions and feeling that may be efficaciously explored through music. Additionally, music may be important to provide interventions within rehabilitative contexts.

In this work, we have explored a neurophysiological approach to discuss the natural predisposition to music of people with ASD. The neurophysiologic findings presented in this article substantiate these conclusions, highlighting how music may be considered a real “window into the world of autism.”

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