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Extensive Piano Practicing has Regionally Specific Effects on White Matter Development in Autism?

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Abstract

The pervasive developmental disorders are a group of neurodevelopmental disorders that include autistic disorder, Asperger's disorder, pervasive developmental disorder - not otherwise specified (PDD-NOS), childhood disintegrative disorder (CDD), and Rett's disorder. All feature childhood onset with a constellation of symptoms spanning social interaction and communication and including atypical behavior patterns.

Autism spectrum disorder (ASD) is typified as a brain connectivity disorder in which white matter abnormalities are already present early on in life.

White matter abnormalities have been described in autism spectrum disorder (ASD) with mounting evidence implicating these alterations in the pathophysiology of the aberrant connectivity reported in this disorder.

Autism is a developmental disorder that manifests itself in early childhood. Autism is characterized by inability to acquire social skills, repetitive behaviors and failure of speech and nonverbal communication development.

Piano-training was associated with balanced interhemispheric interactions both at rest and during motor activation. Piano training, in a short timeframe, may reshape local and inter-hemispheric motor cortical circuits.

Key Words: Autism, Piano, White matter.

Autism and Related Disorders

The pervasive developmental disorders are a group of neurodevelopmental disorders that include autistic disorder, Asperger's disorder, pervasive developmental disorder - not otherwise specified (PDD-NOS), childhood disintegrative disorder (CDD), and Rett's disorder. All feature childhood onset with a constellation of symptoms spanning social interaction and communication and including atypical behavior patterns. The first three disorders (autistic disorder, Asperger's disorder, and PDD-NOS) are currently referred to as autism spectrum disorders, reflecting divergent phenotypic and etiological characteristics compared to Rett's disorder and CDD [1].

Autism is a set of heterogeneous neurodevelopmental conditions, characterized by early-onset difficulties in social communication and unusually restricted, repetitive behavior and interests. The worldwide population prevalence is about 1%. Autism affects more male than female individuals, and comorbidity is common (>70% have concurrent conditions). Individuals with autism have atypical cognitive profiles, such as impaired social cognition and social perception, executive

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dysfunction, and atypical perceptual and information processing. These profiles are underpinned by atypical neural development at the systems level. Genetics has a key role in the aetiology of autism, in conjunction with developmentally early environmental factors. Large-effect rare mutations and small-effect common variants contribute to risk. Assessment needs to be multidisciplinary and developmental, and early detection is essential for early intervention. Early comprehensive and targeted behavioral interventions can improve social communication and reduce anxiety and aggression. Drugs can reduce comorbid symptoms, but do not directly improve social communication. Creation of a supportive environment that accepts and respects that the individual is different is crucial [2].

Autism is a developmental disorder that manifests itself in early childhood. Autism is characterized by inability to acquire social skills, repetitive behaviors and failure of speech and nonverbal communication development. Recent studies have shown that genetic mutations occur in majority of individuals with autism. These mutations cause a variety of disorders that ultimately lead to brain disorders. It is noteworthy that all mutations do not follow the same pattern. They encompass various kinds of mutations. Autism needs to be treated during childhood as untreated patients usually do not progress to the later stages of development. In this regard, many studies have been performed and numerous treatments have been proposed to improve the outcome of this disease [3].

Autism spectrum disorders are not rare; many primary care pediatricians care for several children with autism spectrum disorders. Pediatricians play an important role in early recognition of autism spectrum disorders, because they usually are the first point of contact for parents. Parents are now much more aware of the early signs of autism spectrum disorders because of frequent coverage in the media; if their child demonstrates any of the published signs, they will most likely raise their concerns to their child's pediatrician. It is important that pediatricians be able to recognize the signs and symptoms of autism spectrum disorders and have a strategy for assessing them systematically. Pediatricians also must be aware of local resources that can assist in making a definitive diagnosis of, and in managing, autism spectrum disorders. The pediatrician must be familiar with developmental, educational, and community resources as well as medical subspecialty clinics [4].

Music Improves Social Communication and Auditory-Motor Connectivity in Children with Autism

Music has been identified as strength in people with Autism Spectrum Disorder; however, there is currently no neuroscientific evidence supporting its benefits. Given its universal appeal, intrinsic reward value and ability to modify brain and behaviour, music may be a potential therapeutic aid in autism. Here we evaluated the neurobehavioural outcomes of a music intervention, compared to a non- music control intervention, on social communication and brain connectivity in school-age children. Fifty-one children aged 6-12 years with autism were randomized to receive 8-12 weeks of music (n = 26) or non-music intervention (n = 25).

The music intervention involved use of improvisational approaches through song and rhythm to target social communication. The non-music control was a structurally matched behavioral intervention implemented in a non-musical context. Groups were assessed before and after intervention on social communication and resting- state functional connectivity of fronto-temporal brain networks. Communication scores were higher in the music group post-intervention (difference score = 4.84,P = .01). Associated post-intervention resting-state brain functional connectivity was greater in music vs. non-music groups between auditory and subcortical regions (z = 3.94, P < .0001) and auditory and fronto-motor regions (z = 3.16, P < .0001). Post- intervention brain connectivity was lower between auditory and visual regions in the music compared to the non-music groups, known to be over-connected in autism (z = 4.01, P < .00001). Post-intervention brain connectivity in the music group was related to communication improvement (z = 3.57, P < .0001).

This study provides the first evidence that 8-12 weeks of individual music intervention can indeed improve social communication and functional brain connectivity, lending support to further investigations of neurobiologically motivated models of music interventions in autism [5].

The central impairments of people with autism spectrum disorder (ASD) affect social interaction and communication. Music therapy uses musical experiences and the relationships that develop through them to enable communication and expression, thus attempting to address some of the core problems of people with ASD. The present version of this review on music therapy for ASD is an update of the original Cochrane review published in 2006.

To assess the effects of music therapy for individuals with ASD.

We searched the following databases in July 2013: CENTRAL, Ovid MEDLINE, EMBASE, LILACS, PsycINFO, CINAHL, ERIC, ASSIA, Sociological Abstracts, and Dissertation Abstracts International. We also checked the reference lists of relevant studies and contacted investigators in person.

All randomised controlled trials (RCTs) or controlled clinical trials comparing music therapy or music therapy added to standard care to 'placebo' therapy, no treatment, or standard care for individuals with ASD were considered for inclusion.

Two authors independently selected studies, assessed risk of bias, and extracted data from all included studies. We calculated the pooled standardised mean difference (SMD) and corresponding 95% confidence interval (CI) for continuous outcomes to allow the combination data from different scales and to facilitate the interpretation of effect sizes. Heterogeneity was assessed using the I^2 statistic. In cases of statistical heterogeneity within outcome subgroups, we examined clients' age, intensity of therapy (number and frequency of therapy sessions), and treatment approach as possible sources of heterogeneity.

We included 10 studies (165 participants) that examined the short- and medium- term effect of music therapy interventions (one week to seven months) for children

with ASD. Music was superior to 'placebo' therapy or standard care with respect to the primary outcomes social interaction within the therapy context (SMD 1.06, 95% CI 0.02 to 2.10, 1 RCT, n = 10); generalized social interaction outside of the therapy context (SMD 0.71, 95% CI 0.18 to 1.25, 3 RCTs, n = 57, moderate quality evidence), non-verbal communicative skills within the therapy context (SMD 0.57, 95% CI 0.29 to 0.85, 3 RCTs, n = 30), verbal communicative skills (SMD 0.33, 95% CI 0.16 to 0.49, 6 RCTs, n = 139), initiating behavior (SMD 0.73, 95% CI 0.36 to 1.11, 3 RCTs, n = 22, moderate quality evidence), and social-emotional reciprocity (SMD 2.28, 95% CI 0.73 to 3.83, 1 RCT, n = 10, low quality evidence). There was no statistically significant difference in non-verbal communicative skills outside of the therapy context (SMD 0.48, 95% CI -0.02 to 0.98, 3 RCTs, n = 57, low quality evidence). Music therapy was also superior to 'placebo' therapy or standard care in secondary outcome areas, including social adaptation (SMD 0.41, 95% CI 0.21 to 0.60, 4 RCTs, n = 26), joy (SMD 0.96, 95% CI 0.04 to 1.88, 1 RCT, n = 10), and quality of parent-child relationships (SMD 0.82, 95% CI 0.13 to 1.52, 2 RCTs, n = 33, moderate quality evidence). None of the included studies reported any adverse effects. The small sample sizes of the studies limit the methodological strength of these findings.

The findings of this updated review provide evidence that music therapy may help children with ASD to improve their skills in primary outcome areas that constitute the core of the condition including social interaction, verbal communication, initiating behavior, and social-emotional reciprocity. Music therapy may also help to enhance non-verbal communication skills within the therapy context. Furthermore, in secondary outcome areas, music therapy may contribute to increasing social adaptation skills in children with ASD and to promoting the quality of parent-child relationships. In contrast to the studies included in an earlier version of this review published in 2006, the new studies included in this update enhanced the applicability of findings to clinical practice. More research using larger samples and generalized outcome measures is needed to corroborate these findings and to examine whether the effects of music therapy are enduring. When applying the results of this review to practice, it is important to note that the application of music therapy requires specialized academic and clinical training [6].

Autism spectrum disorder (ASD) affects approximately one in 68 children, substantially affecting the child's ability to acquire social skills. The application of effective interventions to facilitate and develop social skills is essential due to the lifelong impact that social skills may have on independence and functioning.

Research indicates that music therapy can improve social outcomes in children with ASD. Outcome measures are primarily assessed using standardized nonmusical scales of social functioning from the parent or clinician perspective.

Certified music therapists may also assess musical engagement and outcomes as a part of the individual's profile. These measures provide an assessment of the individual's social functioning within the music therapy session and generalizability to nonmusical settings [7].

Autism Spectrum Disorder (ASD) refers to a group of neurodevelopmental disorders including autism, Asperger's syndrome (AS) and pervasive developmental disorder- not otherwise specified (PDD-NOS). The new diagnostic criteria of ASD focuses on two core domains: social communication impairment and restricted interests/repetitive behaviors. The prevalence of ASD has been steadily increasing over the past two decades, with current estimates reaching up to 1 in 36 children. Hereditary factors, parental history of psychiatric disorders, pre-term births, and fetal exposure to psychotropic drugs or insecticides have all been linked to higher risk of ASD. Several scales such as the Childhood Autism Rating Scale (CARS),

The Autism Spectrum Disorder-Observation for Children (ASD-OC), The Developmental, Dimensional, and Diagnostic Interview (3di), are available to aid in better assessing the behaviors and symptoms associated with ASD. Nearly 75% of ASD patients suffer from comorbid psychiatric illnesses or conditions, which may include attention-deficit hyperactivity disorder (ADHD), anxiety, bipolar disorder, depression, Tourette syndrome, and others. Both pharmacological and non- pharmacological interventions are available for ASD. Pharmacological treatments include psychostimulants, atypical antipsychotics, antidepressants, and alpha-2 adrenergic receptor agonists. These medications provide partial symptomatic relief of core symptoms of ASD or manage the symptoms of comorbid conditions. Non- pharmacological interventions, which show promising evidence in improving social interaction and verbal communication of ASD patients, include music therapy, cognitive behavioral therapy and social behavioral therapy. Hormonal therapies with oxytocyin or vasopressin receptor antagonists have also shown some promise in improving core ASD symptoms. The use of vitamins, herbal remedies and nutritional supplements in conjunction with pharmacological and behavioral treatment appear to have some effect in symptomatic improvement in ASD, though additional studies are needed to confirm these benefits. Developing novel disease-modifying therapies may prove to be the ultimate intervention for sustained improvement of symptoms in ASD [8].

Music therapy may facilitate skills in areas affected by autism spectrum disorder (ASD), such as social interaction and communication.

To evaluate effects of improvisational music therapy on generalized social communication skills of children with ASD.

Assessor-blinded, randomized clinical trial, conducted in 9 countries and enrolling children aged 4 to 7 years with ASD. Children were recruited from November 2011 to November 2015, with follow-up between January 2012 and November 2016.

Enhanced standard care (n = 182) vs enhanced standard care plus improvisational music therapy (n = 182), allocated in a 1:1 ratio. Enhanced standard care consisted of usual care as locally available plus parent counseling to discuss parents' concerns and provide information about ASD. In improvisational music therapy, trained music therapists

sang or played music with each child, attuned and adapted to the child's focus of attention, to help children develop affect sharing and joint attention.

The primary outcome was symptom severity over 5 months, based on the Autism Diagnostic Observation Schedule (ADOS), social affect domain (range, 0- 27; higher scores indicate greater severity; minimal clinically important difference, 1). Prespecified secondary outcomes included parent-rated social responsiveness. All outcomes were also assessed at 2 and 12 months.

Among 364 participants randomized (mean age, 5.4 years; 83% boys), 314 (86%) completed the primary end point and 290 (80%) completed the last end point. Over 5 months, participants assigned to music therapy received a median of 19 music therapy, 3 parent counseling, and 36 other therapy sessions, compared with 3 parent counseling and 45 other therapy sessions for those assigned to enhanced standard care. From baseline to 5 months, mean ADOS social affect scores estimated by linear mixed-effects models decreased from 14.08 to 13.23 in the music therapy group and from 13.49 to 12.58 in the standard care group (mean difference, 0.06 [95% CI, -0.70 to 0.81]; P = .88), with no significant difference in improvement. Of 20 exploratory secondary outcomes, 17 showed no significant difference.

Among children with autism spectrum disorder, improvisational music therapy, compared with enhanced standard care, resulted in no significant difference in symptom severity based on the ADOS social affect domain over 5 months. These findings do not support the use of improvisational music therapy for symptom reduction in children with autism spectrum disorder [9].

In pediatric health care, non-pharmacological interventions such as music therapy have promising potential to complement traditional medical treatment options in order to facilitate recovery and well-being. Music therapy and other music-based interventions are increasingly applied in the clinical treatment of children and adolescents in many countries world-wide. The purpose of this overview is to examine the evidence regarding the effectiveness of music therapy and other music- based interventions as applied in pediatric health care. Surveying recent literature and summarizing findings from systematic reviews, this overview covers selected fields of application in pediatric health care (autism spectrum disorder; disability; epilepsy; mental health; neonatal care; neuro rehabilitation; pain, anxiety and stress in medical procedures; pediatric oncology and palliative care) and discusses the effectiveness of music interventions in these areas. Findings show that there is a growing body of evidence regarding the beneficial effects of music therapy, music medicine, and other music-based interventions for children and adolescents, although more rigorous research is still needed. The highest quality of evidence for the positive effects of music therapy is available in the fields of autism spectrum disorder and neonatal care. Music therapy can be considered a safe and generally well-accepted intervention in pediatric health care to alleviate symptoms and improve quality of life. As an individualized intervention that is typically provided in a person-centered way, music therapy is usually easy to implement into clinical practices. However, it is important to note that to exploit the potential of music therapy in an optimal way, specialized academic and clinical training and careful selection of intervention techniques to fit the needs of the client are essential [10].

Preliminary studies have indicated that music therapy may benefit children with autism spectrum disorders (ASD).

To examine the effects of improvisational music therapy (IMT) on social affect and responsiveness of children with ASD.

International, multicentre, three-arm, single-masked randomised controlled trial, including a National Institute for Health Research (NIHR)-funded centre that recruited in London and the east of England. Randomization was via a remote service using permuted blocks, stratified by study site.

Schools and private, voluntary and state-funded health-care services.

Children aged between 4 and 7 years with a confirmed diagnosis of ASD and a parent or guardian who provided written informed consent. We excluded children with serious sensory disorder and those who had received music therapy within the past 12 months.

All parents and children received enhanced standard care (ESC), which involved three 60-minute sessions of advice and support in addition to treatment as usual. In addition, they were randomized to either one (low-frequency) or three (high- frequency) sessions of IMT per week, or to ESC alone, over 5 months in a ratio of 1 : 1 : 2.

The primary outcome was measured using the social affect score derived from the Autism Diagnostic Observation Schedule (ADOS) at 5 months: higher scores indicated greater impairment. Secondary outcomes included social affect at 12 months and parent-rated social responsiveness at 5 and 12 months (higher scores indicated greater impairment).

A total of 364 participants were randomized between 2011 and 2015. A total of 182 children were allocated to IMT (90 to high-frequency sessions and 92 to low- frequency sessions), and 182 were allocated to ESC alone. A total of 314 (86.3%) of the total sample were followed up at 5 months [165 (90.7%) in the intervention group and 149 (81.9%) in the control group]. Among those randomized to IMT, 171 (94.0%) received it. From baseline to 5 months, mean scores of ADOS social affect decreased from 14.1 to 13.3 in music therapy and from 13.5 to 12.4 in standard care [mean difference: music therapy vs. standard care = 0.06, 95% confidence interval (CI) -0.70 to 0.81], with no significant difference in improvement. There were also no differences in the parent-rated social responsiveness score, which decreased from 96.0 to 89.2 in the music therapy group and from 96.1 to 93.3 in the standard care group over this period (mean difference: music therapy vs. standard care = -3.32, 95% CI -7.56 to 0.91). There were seven admissions to hospital that were unrelated to the study interventions in the two IMT arms compared with 10 unrelated admissions in the ESC group.

Adding IMT to the treatment received by children with ASD did not improve social affect or parent-assessed social responsiveness.

Other methods for delivering music-focused interventions for children with ASD should be explored [11].

For young children on the autism spectrum, the inclusion of shared parent-child music activities in everyday life may provide additional opportunities for social interactions in the home. However, no psychometrically validated assessment exists to measure the extent of shared music activity within family or community contexts.

This study aimed to develop and test the reliability of a self-report assessment to measure the use of Music in Everyday Life (MEL) by parents with young children on the autism spectrum.

A total of 45 mothers of children with autism aged between 4 and 7 years completed the MEL questionnaire. Internal consistency and item-total correlation were examined.

Analysis confirmed the reliability of two predetermined subscales: Music in Everyday Life-Joint Activities using Music (MEL-JAM) and Music in Everyday Life-Routine Activities using Music (MEL-RAM). Internal consistency (Cronbach's alpha 0.63 and 0.75) and positive item-total correlation (Pearson's r between .23 to .62 for MEL-JAM and between .30 to .67 for MEL-RAM) were demonstrated.

The reliability of the MEL assessment to measure the use of music in everyday life by parents with their children with autism was confirmed, filling an important gap in the availability of assessment tools [12].

Autism spectrum disorder (ASD) is characterized by social and interpersonal communication disabilities and repetitive motor activities. A deficit in social interaction may be due to motor and synchronization disabilities in individuals with ASD. These disabilities serve as a hindrance for the progression of day-to-day life. ASD individuals are known to have variations in the neural network contributing to changes in their oral-motor activity. As the brain has experience-dependent structural plasticity, these changes in the neural network can probably be reversed with appropriate treatment Music playing a universal role in human life has been studied for its therapeutic potential in rehabilitation of ASD individuals. Music and rhythm have shown a significant potential in improving the oral-motor activities of people affected by ASD. Music based interventions are being used for children diagnosed with ASDs to improve their social communication and motor skills. This article represents the possible role of rhythmic cueing for sensorimotor regulation in ASD individuals. This can serve as a base for further research for the impact of musical therapy on coordination and oral-motor synchronization of individuals diagnosed with ASD [13].

The existing methodological weakness in conducted researches concerning music therapy (MT) for children with autism led to ambiguity and confusion in this scope of studies. The aim of the present research is to identify the effectiveness of MT method in improving social skills of children with autism and its stability, as well.

In the form of a clinical trial study with design of pretest/posttest/follow-up with control group, among the children with autism in community of Tehran city, on the basis of childhood autism rating scale, 27 children with mild to moderate autism were chosen and were divided into two groups of experiment (n = 13), and control (n = 14). Social skills' level of both groups was measured and recorded with the help of social skills rating system scale. The children of the experiment group participated in MT programs of Orff-Schulwerk for 45 days in 12 sessions (two sessions of 1-h/week), whereas the control group received no intervention. The data were analyzed with Statistic Package For Social Science (SPSS) software t-test and analysis of covariance was used to compare groups.

In posttest, the results of covariance analysis showed a significant increase in social skills' scores of the experiment group ($P < 0.001$). Also, results of the paired-sample t-test showed that the effectiveness of MT has been persistent up to the follow-up phase.

The study showed that MT is an effective method with deep and consistent effects on improving social skills of children with autism [14].

Using Equivalence-Based Instruction to Teach Piano Skills to Children

The purpose of the current study was to evaluate the effects of equivalence-based instruction (EBI) on learning to play individual notes and simple songs on the piano.

Participants were 4 typically developing children and 4 children with a diagnosis of autism spectrum disorder (ASD). They were exposed to a series of auditory-visual matching-to-sample procedures using musical stimuli. Following training, participants were tested on the emergence of novel untrained relations and generalization in the form of playing two songs on a keyboard. Results suggest that the EBI was effective in teaching piano playing skills with both typically developing children and children with ASD. The success of this procedure is indicative of the wide-ranging applications of EBI to novel and creative domains [15].

Perfect pitch, also known as absolute pitch (AP), refers to the rare ability to identify or produce a musical tone correctly without the benefit of an external reference. AP is often considered to reflect musical giftedness, but it has also been associated with certain disabilities due to increased prevalence of AP in individuals with sensory and developmental disorders. Here, we determine whether individual autistic traits are present in people with AP. We quantified subclinical levels of autism traits using the Autism-Spectrum Quotient (AQ) in three matched groups of subjects: 16 musicians with AP (APs), 18 musicians without AP (non-APs), and 16 non-musicians.

In addition, we measured AP ability by a pitch identification test with sine wave tones and piano tones. We found a significantly higher degree of autism traits in APs

than in non-APs and non-musicians, and autism scores were significantly correlated with pitch identification scores (r = .46, p = .003). However, our results showed that APs did not differ from non-APs on diagnostically crucial social and communicative domain scores and their total AQ scores were well below clinical thresholds for autism. Group differences emerged on the imagination and attention switching subscales of the AQ. Thus, whilst these findings do link AP with autism, they also show that AP ability is most strongly associated with personality traits that vary widely within the normal population [16].

Co-occurrence of preserved musical function with language and socio- communicative impairments is a common but understudied feature of Autism Spectrum Disorders (ASD). Given the significant overlap in neural organization of these processes, investigating brain mechanisms underlying speech and music may not only help dissociate the nature of these auditory processes in ASD but also provide a neurobiological basis for development of interventions. Using a passive-listening functional magnetic resonance imaging paradigm with spoken words, sung words and piano tones, we found that 22 children with ASD, with varying levels of functioning, activated bilateral temporal brain networks during sung-word perception, similarly to an age and gender-matched control group. In contrast, spoken-word perception was right-lateralized in ASD and elicited reduced inferior frontal gyrus (IFG) activity which varied as a function of language ability.

Diffusion tensor imaging analysis reflected reduced integrity of the left hemisphere fronto-temporal tract in the ASD group and further showed that the hypoactivation in IFG was predicted by integrity of this tract. Subsequent psychophysiological interactions revealed that functional fronto-temporal connectivity, disrupted during spoken-word perception, was preserved during sung-word listening in ASD, suggesting alternate mechanisms of speech and music processing in ASD. Our results thus demonstrate the ability of song to overcome the structural deficit for speech across the autism spectrum and provide a mechanistic basis for efficacy of song- based interventions in ASD [17].

Data on the potential behavioral effects of music therapy in autism are scarce.

The aim of this study was to investigate whether a musical training program based on interactive music therapy sessions could enhance the behavioral profile and the musical skills of young adults affected by severe autism.

Young adults (N = 8) with severe (Childhood Autism Rating Scale >30) autism took part in a total of 52 weekly active music therapy sessions lasting 60 minutes. Each session consisted of a wide range of different musical activities including singing, piano playing, and drumming. Clinical rating scales included the Clinical Global Impression (CGI) scale and the Brief Psychiatric Rating Scale (BPRS). Musical skills-including singing a short or long melody, playing the C scale on a keyboard, music absorption, rhythm reproduction, and execution of complex rhythmic patterns-were rated on a 5-point Likert-type scale ranging from "completely/entirely absent" to "completely/entirely present."

At the end of the 52-week training period, significant improvements were found on both the CGI and BPRS scales. Similarly, the patients' musical skills significantly ameliorated as compared to baseline ratings.

Our pilot data seem to suggest that active music therapy sessions could be of aid in improving autistic symptoms, as well as personal musical skills in young adults with severe autism [18].

Piano Training Enhances the Neural Processing Of Pitch and Improves Speech Perception in Children

Musical training confers advantages in speech-sound processing, which could play an important role in early childhood education. To understand the mechanisms of this effect, we used event-related potential and behavioral measures in a longitudinal design. Seventy-four Mandarin-speaking children aged 4-5 y old were pseudorandomly assigned to piano training, reading training, or a no-contact control group. Six months of piano training improved behavioral auditory word discrimination in general as well as word discrimination based on vowels compared with the controls. The reading group yielded similar trends. However, the piano group demonstrated unique advantages over the reading and control groups in consonant-based word discrimination and in enhanced positive mismatch responses (pMMRs) to lexical tone and musical pitch changes. The improved word discrimination based on consonants correlated with the enhancements in musical pitch pMMRs among the children in the piano group. In contrast, all three groups improved equally on general cognitive measures, including tests of IQ, working memory, and attention. The results suggest strengthened common sound processing across domains as an important mechanism underlying the benefits of musical training on language processing. In addition, although we failed to find far-transfer effects of musical training to general cognition, the near-transfer effects to speech perception establish the potential for musical training to help children improve their language skills. Piano training was not inferior to reading training on direct tests of language function, and it even seemed superior to reading training in enhancing consonant discrimination [19].

Patients with cerebral palsy with severe motor disabilities are limited not only in everyday life activities but also in choice of their hobbies. Playing a musical instrument is for the majority not possible, even though music constitutes a central component of many relaxation activities for people with disabilities. To give affected patients the opportunity to make music and to learn piano playing through somatosensory perception, a prototype of piano jacket was developed.

A cycling jacket was equipped with boxes, each representing a musical note, incorporated into the sleeves. Each box contains vibration motors and LEDs. These can be used to translate the sequences of piano key presses performed at an external E-piano. An additional operation mode allows the user to actively play a melody himself by

touching the same boxes that also incorporate touch sensor components.

A working prototype of the piano jacket was developed.

The sensory piano jacket provides patients with cerebral palsy and contractures the possibility to develop sensorimotor skills, motor abilities and participation in music- related activities. The jacket is planned to be used in music lessons. Implications for Rehabilitation The system is suitable even for patients with severe motor disabilities and especially joint contractures. Excellent handling through large easily accessible communication buttons. All building blocks are held in a garment, which allows for easy portability and gripping comfort [20].

Motor lateralization is viewed as anatomical or functional asymmetry of the two sides of the body. Functional motor asymmetry can be influenced by musical practice. This study explored whether piano playing experience modulates motor asymmetry and leads to an altered pattern of hand selection, reflecting an altered handedness. We asked two groups of right-handed participants-piano players and non-piano players-to reach targets in their frontal space with both arms, and we tested the motor performance of each arm on this task and then on an arm preference test. As musical practice can decrease motor asymmetry between arms, we hypothesized that participants with piano playing experience would display less interlimb asymmetry and that this, in turn, would change their arm preference pattern, compared with participants without piano playing experience. We found support for both hypotheses, and we conclude that arm selection (preference) is not biologically fixed, but, rather, can be modulated through long-term piano playing [21].

Playing a musical instrument demands the integration of sensory and perceptual information with motor processes in order to produce a harmonic musical piece. The diversity of brain mechanisms involved and the joyful character of playing an instrument make musical instrument training a potential vehicle for neurorehabilitation of motor skills in patients with cerebral palsy (CP). This clinical condition is characterized by motor impairments that can affect, among others, manual function, and limit severely the execution of basic daily activities. In this study, adolescents and adult patients with CP, as well as a group of typically developing children learned to play piano for 4 consecutive weeks, having completed a total of 8 hours of training. For ten of the participants, learning was supported by a special technical system aimed at helping people with sensorimotor deficits to better discriminate fingers and orient themselves along the piano keyboard. Potential effects of piano training were assessed with tests of finger tapping at the piano and tests of perception of vibratory stimulation of fingers, and by measuring neuronal correlates of motor learning in the absence of and after piano training. Results were highly variable especially among participants with CP. Nevertheless, a significant effect of training on the ability to perceive the localization of vibrations over fingers was found. No effects of training on the performance of simple finger tapping sequences at the piano or on motor-associated brain responses were registered.

Longer periods of training are likely required to produce detectable changes [22].

Using diffusion tensor imaging, we investigated effects of piano practicing in childhood, adolescence and adulthood on white matter, and found positive correlations between practicing and fiber tract organization in different regions for each age period. For childhood, practicing correlations were extensive and included the pyramidal tract, which was more structured in pianists than in non-musicians. Long-term training within critical developmental periods may thus induce regionally specific plasticity in myelinating tracts [23].

Gray Matter Density and White Matter Integrity in Pianists' Brain

The current study combined structural magnetic resonance imaging (sMRI) and diffusion tensor MRI (DT-MRI) to investigate both gray matter density (GMD) and white matter integrity (WMI) in 18 pianists and 21 age-matched non-musicians. The pianists began their piano training at a mean age of 12. Voxel-based morphometry of the sMRI data showed that the pianists had higher GMD in the left primary sensorimotor cortex and right cerebellum. Voxel-based analysis of the DT-MRI data showed that pianists had higher fractional anisotropy (FA) (indicating higher WMI) in the right posterior limb of the internal capsule. The sMRI and DT-MRI results indicate that both the GMD and WMI of pianists may exhibit movement-related increases during adolescence or even early adulthood compared with non-musicians [24].

To establish if listening to Mozart's Sonata for two pianos in D major (K448) has an anti-epileptic effect on the EEGs (electroencephalograms) of children.

Forty five children (2-18 years; mean 7 years 10 months) who had epileptiform activity on EEG were recruited from those attending for scheduled EEG investigations. Mozart's Sonata for two pianos in D major (K448) and an age- appropriate control music were played during the EEG. There were five consecutive states during the record, each lasting 5 min; before Mozart music (baseline), during Mozart music, after Mozart music/before control music, during control music and after control music. Epileptic discharges were counted manually and the mean frequency of epileptic discharges calculated in each state.

A significant reduction ($p < 0.0005$) in the frequency of epileptic discharges was found during listening to the Mozart music compared to the baseline. No evidence of a difference in mean epileptic discharges was found between the baseline and the other three states or between listening to the Mozart music and control music.

This study confirms an anti-epileptic effect of Mozart music on the EEG in children, which is not present with control music. The role of 'Mozart therapy' as a treatment for drug-resistant epilepsy warrants further investigation [25].

We explored the effects of playing the piano on patients with cognitive impairment after mild traumatic brain injury (mTBI) and, addressed the question if this approach would

stimulate neural networks in re-routing neural connections and link up cortical circuits that had been functional inhibited due to disruption of brain tissue. Functional neuroimaging scans (fMRI) and neuropsychological tests were performed pre-post intervention.

Three groups participated, one mTBI group (n = 7), two groups of healthy participants, one with music training (n = 11), one baseline group without music (n = 12). The music groups participated in 8 weeks music-supported intervention.

The patient group revealed training-related neuro-plasticity in the orbitofrontal cortex. fMRI results fit well with outcome from neuropsychological tests with significant enhancement of cognitive performance in the music groups. Ninety per cent of mTBI group returned to work post intervention.

Here, for the first time, we demonstrated behavioural improvements and functional brain changes after 8 weeks of playing piano on patients with mTBI having attention, memory and social interaction problems. We present evidence for a causal relationship between musical training and reorganization of neural networks promoting enhanced cognitive performance. These results add a novel music-supported intervention within rehabilitation of patients with cognitive deficits following mTBI [26].

The neuronal mechanisms involved in brain plasticity after skilled motor learning are not completely understood. We aimed to study the short-term effects of keyboard training in music-naive subjects on the motor/premotor cortex activity and interhemispheric interactions, using electroencephalography and transcranial magnetic stimulation (TMS). Twelve subjects (experimental group) underwent, before and after a two week-piano training: (1) hand-motor function tests: Jamar, grip and nine-hole peg tests; (2) electroencephalography, evaluating the mu rhythm task-related desynchronization (TRD) during keyboard performance; and (3) TMS, targeting bilateral abductor pollicis brevis (APB) and abductor digiti minimi (ADM), to obtain duration and area of ipsilateral silent period (ISP) during simultaneous tonic contraction of APB and ADM. Data were compared with 13 controls who underwent twice these measurements, in a two-week interval, without undergoing piano training. Every subject in the experimental group improved keyboard performance and left-hand nine-hole peg test scores. Pre-training, ISP durations were asymmetrical, left being longer than right. Post-training, right ISPAPB increased, leading to symmetrical ISPAPB. Mu TRD during motor performance became more focal and had a lesser amplitude than in pre-training, due to decreased activity over ventral premotor cortices. No such changes were evidenced in controls. We demonstrated that a 10-day piano-training was associated with balanced interhemispheric interactions both at rest and during motor activation. Piano training, in a short timeframe, may reshape local and inter- hemispheric motor cortical circuits [27].

White Matter and Cognition

Whereas the cerebral cortex has long been regarded by neuroscientists as the major locus of cognitive function, the white matter of the brain is increasingly recognized as equally critical for cognition. White matter comprises half of the brain, has expanded more than gray matter in evolution, and forms an indispensable component of distributed neural networks that subserve neurobehavioral operations. White matter tracts mediate the essential connectivity by which human behavior is organized, working in concert with gray matter to enable the extraordinary repertoire of human cognitive capacities. In this review, we present evidence from behavioral neurology that white matter lesions regularly disturb cognition, consider the role of white matter in the physiology of distributed neural networks, develop the hypothesis that white matter dysfunction is relevant to neurodegenerative disorders, including Alzheimer's disease and the newly described entity chronic traumatic encephalopathy, and discuss emerging concepts regarding the prevention and treatment of cognitive dysfunction associated with white matter disorders. Investigation of the role of white matter in cognition has yielded many valuable insights and promises to expand understanding of normal brain structure and function, improve the treatment of many neurobehavioral disorders, and disclose new opportunities for research on many challenging problems facing medicine and society [28].

Autism spectrum disorder (ASD) is typified as a brain connectivity disorder in which white matter abnormalities are already present early on in life. However, it is unknown if and to which extent these abnormalities are hard-wired in (older) adults with ASD and how this interacts with age-related white matter changes as observed in typical aging. The aim of this first cross-sectional study in mid- and late-aged adults with ASD was to characterize white matter microstructure and its relationship with age. We utilized diffusion tensor imaging with head motion control in 48 adults with ASD and 48 age-matched controls (30-74 years), who also completed a Flanker task. Intra-individual variability of reaction times (IIVRT) measures based on performance on the Flanker interference task were used to assess IIVRT-white matter microstructure associations. We observed primarily higher mean and radial diffusivity in white matter microstructure in ASD, particularly in long-range fibers, which persisted after taking head motion into account. Importantly, group-by-age interactions revealed higher age-related mean and radial diffusivity in ASD, in projection and association fiber tracts. Subtle dissociations were observed in IIVRT- white matter microstructure relations between groups, with the IIVRT-white matter association pattern in ASD resembling observations in cognitive aging. The observed white matter microstructure differences are lending support to the structural underconnectivity hypothesis in ASD. These reductions seem to have behavioral percussions given the atypical relationship with IIVRT. Taken together, the current results may indicate different age-related patterns of white matter microstructure in adults with ASD [29].

Both autism spectrum disorder (ASD) and schizophrenia are often characterized as disorders of white matter integrity. Multimodal investigations have reported elevated metabolic rates, cerebral perfusion and basal activity in various white matter regions in schizophrenia, but

none of these functions has previously been studied in ASD. We used 18fluorodeoxyglucose positron emission tomography to compare white matter metabolic rates in subjects with ASD (n = 25) to those with schizophrenia (n = 41) and healthy controls (n = 55) across a wide range of stereotaxically placed regions-of-interest. Both subjects with ASD and schizophrenia showed increased metabolic rates across the white matter regions assessed, including internal capsule, corpus callosum, and white matter in the frontal and temporal lobes. These increases were more pronounced, more widespread and more asymmetrical in subjects with ASD than in those with schizophrenia. The highest metabolic increases in both disorders were seen in the prefrontal white matter and anterior limb of the internal capsule. Compared to normal controls, differences in gray matter metabolism were less prominent and differences in adjacent white matter metabolism were more prominent in subjects with ASD than in those with schizophrenia. Autism spectrum disorder and schizophrenia are associated with heightened metabolic activity throughout the white matter. Unlike in the gray matter, the vector of white matter metabolic abnormalities appears to be similar in ASD and schizophrenia, may reflect inefficient functional connectivity with compensatory hypermetabolism, and may be a common feature of neurodevelopmental disorders [30].

Autism Spectrum Disorder (ASD) symptoms have been hypothesized to result from altered brain connectivity. The 'disconnectivity' hypothesis has been used to explain characteristic impairments in socio-emotional function, observed clinically in ASD. Here, we review the evidence for impaired white matter connectivity as a neural substrate for socio-emotional dysfunction in ASD.

Studies were identified using a sensitive search strategy in MEDLINE, Embase and PsycINFO article databases using the OvidSP database interface. Search terms included database subject headings for the concepts of pervasive developmental disorders, and DTI. Seventy-two published DTI studies examining white matter microstructure in ASD were reviewed. A comprehensive discussion of DTI studies that examined white matter tracts linking socio-emotional structures is presented.

Several DTI studies reported microstructural differences indicative of developmental alterations in white matter organization, and potentially myelination, in ASD. Altered structure within long-range white matter tracts linking socio-emotional processing regions was implicated. While alterations of the uncinate fasciculus and frontal and temporal thalamic projections have been associated with social symptoms in ASD, few studies examined association of tract microstructure with core impairment in this disorder.

The uncinate fasciculus and frontal and temporal thalamic projections mediate limbic connectivity and integrate structures responsible for complex socio-emotional functioning. Impaired development of limbic connectivity may represent one neural substrate contributing to ASD social impairments. Future efforts to further elucidate the nature of atypical white matter development, and its relationship to core symptoms, may offer new insights into etiological mechanisms contributing to ASD impairments and uncover novel opportunities for targeted intervention [31].

White matter abnormalities have been described in autism spectrum disorder (ASD) with mounting evidence implicating these alterations in the pathophysiology of the aberrant connectivity reported in this disorder. The goal of this investigation is to further examine white matter structure in ASD using proton magnetic resonance spectroscopy ((1) H MRS). Multi-voxel, short echo-time in vivo(1)H MRS data were collected from 17 male children with ASD and 17 healthy age- and gender-matched controls. Key (1)H MRS metabolite ratios relative to phosphocreatine plus creatine were obtained from four different right and left white matter regions. Significantly lower N-acetylaspartate/creatine ratios were found in the anterior white matter regions of the ASD group when compared to controls. These findings reflect impairment in neuroaxonal white matter tissue and shed light on the neurobiologic underpinnings of white matter abnormalities in ASD by implicating an alteration in myelin and/or axonal development in this disorder [32].

Conclusion

Piano-training is associated with balanced interhemispheric interactions both at rest and during motor activation. Piano training, in a short timeframe, may reshape local and inter-hemispheric motor cortical circuits in Autism spectrum disorder (ASD) patients.

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