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Influence of music therapy on the rehabilitation of children with severe brain damage

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Abstract

The aim of this experiment was to test for the efficiency of a music therapy (MT) program implemented at the Centro Internacional de RestauracionNeurologica (CIREN), La Habana, Cuba. All the children who participated in this study had severe neurological disorders and were involved in an intense neuro-restoration program for 4 to 8 weeks. Children were randomly assigned to the MT group or to a control group. Overall results from questionnaires filled in by the occupational and speech therapists showed that all children improved from Week 1 to Week 4 on three dimensions (motor, social and emotional behaviours).Importantly, improvements on the motor behaviour dimension were larger for children in the experimental MT group than for children in the control group. Moreover, results in the MT group revealed that improvements on musical tests were larger after 8 weeks than after 4 weeks of MT. Finally, although analyses of the Event-Related brain Potentials (ERPs) showed large inter-individual variability, it was nevertheless possible to isolate subgroups of children with similar patterns of results (P250 vs N300 components). Taken together, these results are encouraging in showing that the use of different methodologies can provide complementary information on the efficiency of neuro-restoration and MT programs

1. Introduction

Music Therapy (MT) defined as the use of music for clinical purposes has been used for a long time (e.g., Van de Wall, 1946) and MT is often recommended as a treatment for infantile autism, for instance (Accordino, et. al. 2006). Until the past ten years, however, empirical support for MT was relatively scarce and not entirely convincing for several reasons. First, support was mainly coming from case studies conducted by music therapists with limited use of controlled research methodologies. Second, when conducting group studies, a number of factors were not controlled. For instance, groups involved in MT were often heterogeneous without control groups matched on age, sex, level of school education, socio-economic status of the family etc... Patients were not randomly assigned to the experimental (MT) or control group. Data were not always analyzed using appropriate statistical tools and the number of participants was often too small to obtain statistically reliable results (Mrazova&Celec, 2010). Finally, and may be most importantly, these first studies were not theoretically-based and the reasons for using MT in clinical settings were not explicitly described.

Importantly, these shortcomings have been fully considered and rigorously controlled studies have been conducted in the past ten years to test for the effects of MT in different groups of patients (see Robb et al. 2011; Robb & Carpenter, 2009 for reviews of music-based interventions and Wan et al. 2010, for a review of singing therapy). For instance, Särkämo (Särkämö et al., 2008) and collaborators tested a group of 60 stroke patients with acute middle cerebral artery stroke in left or right hemisphere to determine whether music listening improved cognitive recovery and mood. Patients were randomly assigned to music listening (20 patients), audiobook listening (20 patients) or to a control group (20 patients). Brain magnetic activity, Magnetoencephalography (MEG) was recorded and the Mismatch Negativity (MMNm) was analyzed. The MMN is considered as a good index of preattentive auditory processing (Näätänen et al. 1978). The main advantage of the MMN is that it can be recorded under passive listening conditions from many different types of patients without requiring any specific action from their part (Kujala & Naatanen, 2010). Patients typically watch a silent movie while a sequence of sounds is delivered that comprises standard and deviant stimuli. The MMN is computed by subtracting the Event-Related Potentials (ERPs) to the standard stimulus from the ERPs to the deviant stimuli. Results of Särkämo et al. showed that both music and audiobook listening enhanced recovery of auditory sensory memory functions as reflected by enhanced amplitude MMNm compared to the control group. However, only music listening improved cognitive recovery (verbal memory and focused attention) and prevented depression in the 6 months following the stroke. In a subsequent study from the same group (Forsblom et al. 2010), the authors tried to disentangle two factors that may have contributed to improved cognitive recovery and mood in the stroke patients tested by Särkämo (Särkämö et al., 2008), namely enhanced neuronal plasticity and stimulation or emotional and psychological factors related to the music listening experience. Using a phenomenological approach based on the analysis of the patients' own narratives, they found that both types of activities were considered as refreshing stimulations and that both evoked thoughts and memories. However, only music listening was considered as favoring relaxation and increased motor activity and as contributing more than audiobook listening to recovery and positive mood changes.

Still with stroke patients, Rodriguez-Fornells and collaborators (Grau-Sanchez et al., 2013; Rodriguez-Fornells et al., 2012), tested the hypothesis that by improving auditory-motor coupling (e.g., Bangert et al., 2006; Baumann et al., 2007; Lahav et al. 2007), playing a musical instrument can promote neuroplastic changes in the motor cortex and the restoration of motor abilities. Patients were involved in a Music-Supported-Therapy (MST) program (Schneider, et al. 2007) during 4 weeks (20 individual sessions of 30min each) in which they trained on a MIDI-piano for fine movements and on an electronic drum set for gross movements. Improvements in motor abilities were monitored using 3D movement analysis and clinical motor tests. The authors also employed different brain imaging methods, functional Magnetic Resonance Imaging (fMRI) coupled with functional connectivity analyses and Trans-Magnetic Stimulation (TMS). Patients involved in MST showed restored activation in different brain regions (primary auditory cortex, precentralgyrus, inferior frontal regions and supplementary motor area) as well as increased functional connectivity between these different brain regions. Moreover, applying TMS revealed changes in the excitability of the motor cortex and in the organization of sensori-motor cortex accompanied by a reduction of motor deficits. The authors suggested that MST may restore the inherent dynamics of the auditory–motor loops involved in music processing. While these results are highly promising, one caveat is that no patients were involved in another activity as interesting and motivating as MST that would allow controlling for attention and motivation. This is important insofar as neuroplasticity may depend on the motivational value of the activity (Sanes& Donoghue, 2000).

MT has also been used with Alzheimer patients. For instance, Narme (Narme et al., 2012) compared musical (12 patients) vs non-musical (painting: 10 patients or cooking, 5 patients) interventions (2 hours, twice a week) in 27 patients with moderate to severe dementia (Mini-mental state: 3-18/30). The largest improvements in emotional states were found in the music group both immediately and 2 weeks after the interventions. Särkämo and collaborators, (Särkämö et al., 2013) tested a larger number of patients (89) with mild to moderate dementia and involved in singing (n = 30), music listening (n = 29) or in usual care (control group, n = 30) for 10 weeks. Results showed positive changes in the mood and the quality of life of the patients immediately after the musical intervention and 6 months after. Results of neuropsychological assessments also revealed improvements in general cognition, orientation, short-term memory, attention and executive functions after singing and music listening. They concluded that simple musical activities that are easy to implement can have positive long-term cognitive, emotional, and social benefits in mild/moderate dementia. Another example of cost-effective music-based interventions is provided by the results of Janata (2012) showing that playing individually-selected music programs in the rooms of patients with moderate-to-severe dementia, several hours per day each day for 12 weeks reduced the average levels of agitation and depression among the residents.

Music listening was also shown to facilitate motor activities and the initiation of walking in Parkinson patients (McIntosh et al. 1997) as well as to reduce the speech deficits often associated with Parkinson disease (see Wan et al., 2010, for review). More generally, Stahl et al (2013) showed that singing and rhythmic therapies in non-fluent aphasic patients did facilitate the production of formulaic phrases but only standard therapy allowed transfer to the production of unknown phrases (non formulaic language). These results led the authors to conclude that propositional (left perilesional brain regions) and formulaic speech (right corticostriatal areas) may rely on different neural pathways. Similarly, recent results from Schlaug and collaborators (Vines et al. 2011; Wan et al., 2010) showed that combining singing therapy with trans-Direct Current Stimulation (t-DCS), to increase the excitability of the right posterior inferior frontal gyrus known as a key region for the recovery of aphasia, improved the fluency of speech in non fluent aphasic patients. To our knowledge, only a few controlled randomized studies have tested the effects of MT in children. For instance, Kim and collaborators (Kim et al. 2008; Kim et al. 2009) employed a single subject comparison design to investigate social interactions between children with autism and the therapist during improvisational music therapy and toy play. Within these two conditions they measured emotional, motivational and inter-personal responsiveness in the children during joint engagement episodes using video recordings (analyses of facial expressions, eye contacts…). Results indicated more and longer events of joy, ‘emotional synchronicity’ and ‘initiation of engagement’ behaviors in improvisational music therapy than in toy play sessions.

In sum, this short review of the literature shows that the number of well-controlled studies, including random assignment of patients to experimental or control groups and large groups of patients is rapidly increasing. Overall, results are positive and encouraging but this may also result from a publication bias with negative results remaining unpublished. Importantly, mechanisms underlying the positive influence of MT in several pathologies as described above are currently investigated using different behavioral and brain imaging methods.. Several hypotheses have been proposed. For instance, music listening and performance engage extensive brain networks that are also involved in other perceptual, cognitive and motor activities. Moreover, many results have shown that music training promotes neuroplastic changes in different brain regions (see Münte et al. 2002, for review) including auditory (e.g., Meyer et al. 2007) and motor-related brain areas (e.g., Bangert et al., 2006; Baumann et al., 2007; Lahav et al., 2007), thereby enhancing auditory-motor coupling (Rodriguez-Fornells et al., 2012). It has also been proposed that the preservation of the medial prefrontal cortex may explain why familiar music is still remembered and able to evoke emotions in persons with severe and advanced dementia (Janata, 2012). The short-term positive effects of music on mood and arousal are possibly mediated by the dopaminergic mesolimbic [reward] system and noradrenaline system (Särkämö & Soto, 2012). Finally, results of epidemiological studies have shown that stimulating cognitive activities (and cognitive reserve) in late life have protective effect against dementia (Verghese et al., 2003) and can slower cognitive decline in dementia (Hall et al., 2009; Treiber et al., 2011). Findings from Alzheimer transgenic mice are interesting in this respect: they showed that enriched environments can protect against cognitive impairment, decreased beta-amyloid deposition, and increased hippocampal synaptic immunoreactivity (Cracchiolo et al., 2007). Following Mrazova and Celec (2010), "The ultimate goal of mechanistic research is the molecular understanding of music therapy". While this goal may still require time to be reached, important progress is made in this direction (e.g., Gomez-Pinilla & Hillman, 2013).

The aim of the present research project was to implement an experiment aimed at investigating the influence of MT in children with severe brain damages. These children were patients from the "Centro Internacional de RestauracionNeurologica (CIREN)", directly dependent from the Ministry of Health of Cuba. This center is well-known for receiving patients (adults and children) from all over the world and, in particular from Latin America (but also Portugal, Spain, United States…). The general procedure is similar for all incoming patients. The first week is dedicated to complete evaluation of the patient by a multi-disciplinary team of neurologists, neuropsychologists, neurophysiologists and clinicians to establish a diagnostic. Based upon this diagnostic, individualized therapies are implemented to fulfill the specific needs of the patients (e.g. motor, cognitive, speech, memory etc…). Typically, patients are involved in these different therapies from 8:30 until 12:00 am and from 2:00 until 5:30 pm every day except Sundays (Saturday from 8:00 to 12:00). Each therapy session lasts for one hour minimum. Importantly, at least one member of the family remains at the CIREN during the entire stay of the patient to take care of him(her) when (s)he is not involved in the therapies. The neuro-restorative program lasts for a minimum of 4 weeks but may last longer depending upon the patient needs and the family economic situation.

We took advantage of the organization of the neuro-restorative program at the pediatric clinic of the CIREN to implement a protocol based on a Test – Training – Retest procedure. We had three main objectives. First, we aimed at testing whether 10 to 15 min of MT would increase children's attention and motivation in the subsequent speech and cognitive therapies that they received several times a day. Second, it was of importance to determine whether music therapy improved musical abilities, social behavior (verbal and nonverbal) and the quality of life of the children enrolled in the program and of their parents. To reach the first and second aim, speech and occupational therapists were asked to fill in questionnaires specifically designed for this experiment based on standard questionnaires (see methods) and parents expressed their opinions in interviews. Finally, we aimed at testing the feasibility of recording the Mismatch Negativity (MMN) from these children. As mentioned above, the MMN is recorded under passive listening conditions and is taken to reflect preattentive auditory processing (Kujala & Näätänen, 2010; Näätänen et al., 1978). In this project, we implemented a typical MMN design with sequences of standard syllables intermixed with deviant syllables varying in pitch, duration and Voice Onset Time (VOT, a phonological parameter that allows differentiating "Ba" from "Pa", for instance). Our aim in recording the MMN from a sample of the children included in the present experiment was to gain objective information on the specific acoustic cues (pitch, duration or VOT) that the child would be most sensitive to and thereafter use this cue to orient subsequent speech therapy. For instance, if one child is most sensitive to frequency, this is interesting information for the speech therapist that can then use voice frequency modulations in the speech therapy program. Moreover, it was also of specific interest to examine changes in MMN amplitude and/or latency before and after the restorative program and the MT.

2. Materials and methods

2.1. Participants

A total of twenty-seven children participated to this project that lasted from January to October 2013. The inclusion criteria were as follows: participation in the neuro-restorative program at CIREN for at least 4 weeks, age between 3 and 12 years old; Spanish as native language; functional Auditory Brainstem Responses (ABRs) and parents' consent. Out of the 27 children, all from Latin American countries (Argentina, Chile, Mexico and Venezuela), 17 were randomly assigned to the experimental group (7 girls) and 10 to the control group (3 girls). The mean age of the children was not significantly different in the experimental (mean=6.83, SD=3.22) and in the control group (mean=6.80, SD=3.77; U-Mann Whitney test for independent samples: p= 0.44). The socio-economic background of the family was assessed based on the family income as determined from the parent(s) profession (scale from 1 to 4: Working class=1, Low middle class=2, Middle class=3, Upper middle class=4) and was not significantly different between the experimental (mean = 2.66, SD= 1.18) and control groups (mean=2.55, SD=1.13; p=0.71). The level of education of the parents was also assessed based on the number of years of education (including primary school) and was again not significantly different between the experimental (mean= 14.3 years, SD=4.14) and control groups (mean= 13.1 years, SD=4.9; p=0.36).

During the first evaluation week, a comprehensive battery of standard psychometric and neuropsychological tests (Progressive Matrices Test (Raven et al.1998), Wechsler intelligence scale children WISC-r (Wechsler, 1974), Brunet-Lezine psychomotor scale (Brunet & Lezine, 1978), Children neuropsychological scale ENI (Rosselli et al. 2001), as well as routine ElectroEncephaloGram (EEG) recordings and neuroimaging (structural anatomy using Magnetic Resonance Imaging (1.5 T MRI) were performed to establish or to confirm neurological diagnosis and to propose individualized neuro-restorative programs. Screening included search for associated epilepsy, mental retardation, ophthalmologic and/or hearing impairments, speech and language disorders as well as oral-motor dysfunctions. Cognitive assessments revealed a high proportion of mental and psychomotor retardation (n=6), apraxia (n=12) and attention (n=16) impairments. Moreover, out of the 27children with brain damage, 19 suffered from Static Lesions of the Central Nervous System (SLCNS; 12 in the experimental group and 7 in the control group) of prenatal and/or perinatal origins that were expressed in cerebral palsy (n=12, with spastic diparesia subtype) or in cognitive and/or language disorders (n=9). Seven children (5 in the experimental group and 2 in the control group) were diagnosed with other disorders including Autistic Spectrum Disorder (ASD, n=2), generalized dystonia (n=1), neurofibromatosis (n=1) and paraplegia due to spinal cord injury (n=2). Finally, 12 children showed abnormal EEG, 6 children had unilateral impairments in the Auditory Brainstem Responses (ABRs) and MRI showed that 22 children had brain structural abnormalities (see Table 1).While we are aware that ideally, homogenous groups of patients should be included in such an experiment, this was not possible considering the heterogeneity of the specific lesions and associated behaviors of the children who were enrolled at CIREN.

2.2. Ethics

This study was approved by the scientific council of CIREN and received necessary support from the direction of the hospital. The project was conducted in accordance with norms and guidelines for the protection of human subjects. Informed consent from the doctors and therapists of the neuro-pediatric clinic was granted before the start of the project. Parents were informed in details of the procedure (see below) and on the music training program that was described as an interesting and rewarding experience for their children. Parents who agreed with the project signed an informed consent form.

2.3. Occupational and speech therapy questionnaires

The study comprised three phases: Test – Rehabilitation –ReTest.

During the evaluation week (Week 1), the occupational and speech therapists met the child and filled a questionnaire build from standard questionnaires (MacArthur-Bates Inventario I and II, (Jackson-Maldonado et al. 2003); Escala Autónoma Asperger-Autismo, (Belinchon et al., 2008); CUMANIN, (Portellano Perez et al. 2000) around three main dimensions: motor behavior, social behavior and emotional behavior. The therapists received specific training to use the quantitative scale (no reaction= 1, relevant reaction= 5 best). Both therapists filled the same questionnaires again at Week 4 (and at Week 8 for the children that remained at CIREN for 8 weeks).

Data Analysis: Data from the questionnaires filled in by the occupational and speech therapists were analyzed first, by computing the means and standard deviation related to the three dimensions. These data were then submitted to non-parametric Sign-tests and to the Kruskal Wallis one way ANOVA to compare results in the Experimental MT group and in the Control group.

The parent's questionnaire was administered by a specialist in Physical Medicine and Rehabilitation in an interactive interview that took around one hour and that was conducted twice, once at Week 1 (evaluation week) and once at the end of the restoration program (Week 4 or Week 8, depending upon how long the children remained at CIREN). The overall aim was to determine whether the parents observed changes in the behavior of their children (from MT or control groups) and how they evaluated different aspects of the rehabilitation program. Moreover, parents from children included in the MT program were also asked whether they felt that their children was happy to participate in the MT and whether they considered that MT increased the quality of life of their children.

2.4. Music Therapy

MT was implemented three times a day, three days per week during 4 to 8 weeks for 10 to 15 min. before the speech and cognitive therapies (Total MT=360 min after 4 weeks and 720 minutes after 8 weeks). Musical stimuli were presented to the children in a quiet, dedicated room, using a computer and external speakers. MT involved active music listening: while listening to the different musical excerpts the music therapist played games with the children to orientate their attention toward specific aspects of the music and to favor their active participation (e.g. throwing a ball to other child when changing from one music excerpt to the other, clapping hands/feet/fingers/moving head in rhythm with the music, etc…). Four different sequences of musical excerpts were prerecorded and each was used in different sessions to avoid habituation. Musical pieces with different characteristics (rhythm, melody, intensity and timber) were selected based on a pilot study conducted in the same clinical settings at CIREN (April to July 2012) with a sample of 17 pediatrics patients (the list of musical pieces is available upon request and included excerpts from, Vivaldi, Benny More, Mozart, Piazzola, etc.). Each sequence was built in such a way as to start with quiet music pieces, continue with more dynamic, entraining musical pieces and end with more quiet pieces.

Children in the control group were not involved in extra activity equivalent to MT, but they received more of the classic neuro-restoration program. Ideally, it would have been important for children in the control group to participate in an extra activity to control for attention and motivation but this was not possible to implement for practical reasons.

2.5. Evaluation of children in the music therapy group

The level of performance of the children in the experimental group was evaluated by the music therapist by using three different tests. ***Performance Scale*****:** this scale comprised 5 domains: motor ability, attention, emotion, imitation and communication. At the end of each MT day, the therapist filled a 5 points scale for each child (from 0 -poor level of performance- to 5 -high level of performance). Averaged individual scores were computed weekly (i.e., over 9 MT sessions). Comparisons are reported between Week 1, Week 4 (all children) and Week 8 (for the subset of children who stayed for 8 weeks).

Rhythm test (subtest of CUMANIN, (Portellano Perez et al., 2000): children were asked to reproduce a rhythmic sequence played by the therapist by clapping her hands. The number of taps and their grouping increase in difficulty (from level 1 to 7). Rhythmic performance was evaluated using a 5 points scale (0 poor and 5 exact reproduction). For data processing, a score equal or superior to 4 was considered as an index of successful rhythmic reproduction.

"Musical" test: this test was developed by KMM & MB to evaluate the orientation response, perceptual discrimination and attention. Fifteen music excerpts were presented twice to the children, once in their original version and once in a modified version that included abrupt changes in timber, harmony and melody. This test was presented twice, under implicit and explicit conditions. In the implicit condition, the music therapist watched the child reaction (1:no reaction and 5: child clearly reacted to the changes). In the explicit conditions, children were given the following instructions: "We are going to play a little game. You listen to the music and you raise a finger/arm/foot/leg/move your head… if you hear something surprising" (scores varied from 1: (no reaction to 5: (detect surprising events at the right time).

The Rhythm and "musical" tests were administered to each child individually at different time points during the therapy (Week 1, Week 4 and Week 8) and scores corresponding to the three time points were compared using pairwise nonparametric Sign Tests and Kruskal Wallis one-way ANOVA.

2.6. Electrophysiology experiment

Stimuli: Children were presented with a sequence of syllables (Consonant-Vowel structure) with the syllable "Ba" serving as standard stimulus and deviant stimuli in vowel frequency, vowel duration and Voice Onset Time (VOT; the syllable "Pa"). The standard stimulus "Ba" had a fundamental frequency (F0) of 103 Hz, vowel duration of 208 msec and VOT of−70msec for a total duration of the stimulus of 278 msec. For frequency deviant syllables, the F0 of the vowel was increased to 155 Hz using Praat (Boersma & Weenink, 2001). For duration deviant syllables, vowel duration was shortened by 75 msec using Adobe Audition, for a total syllabic duration of 203 msec. Finally, for VOT deviant syllables, the VOT was 70 msec. shorter than for the standard syllable for a total duration of 208 msec.

Procedure: The EEG was recorded from a subset of 12 children (out of 17) from the experimental MT group (mean age 7.78, SD 3.01; 5 girls) and from 6 children (out of 10) from the control group (mean age 7.47, SD 3.7; 2 girls; see Table 1). Children who required anesthesia for EEG recordings during the first evaluation week were not included in the subgroup because we did not want to repeat the anesthesia at the end of the MT program (Retest session, see below). Thus, EEG was recorded pre and post training without anesthesia. During EEG recordings, children were told to watch a silent movie without paying attention to the sounds that were presented through headphones. Standard syllables and frequency, duration, and VOT deviant syllables were randomly presented within the auditory sequence with a fixed Stimulus Onset Asynchrony of 600 msec. A total of 920 stimuli were presented binaurally and pseudo-randomly (at least one standard stimulus between each deviant stimulus) with76% standard stimulus and 8% for each type of deviant stimulus. All stimuli were presented within a single block that lasted for 8 min.

Recordings: EEG was recorded continuously at a sampling rate of 200 Hz using a MEDICID IV amplifier system (Neuronic, Cuba) from 19 active Ag-Cl electrodes at standard positions of the International 10/20 System (Jasper, 1958): Fp1, Fp2, F7, F8, F3, F4, C3, C4, T5, T6, T3, T4, P3, P4, O1, O2, Fz, Cz, Pz and nose. Data were re-referenced off-line to the algebraic average of the left and right mastoids and filtered with a bandpass of 1-30 Hz (12 dB/oct).

Data analyses: EEG data were analyzed using EEGLab(Delorme & Makeig, 2004)and the Neuronic Analysis software (Version 3.0.2.0;www.Neuronicsa.com). EEG recordings were segmented into 600 msec. epochs (from -100 msec. until 495 msec. post-stimulus onset) time-locked with stimulus presentation. Epochs with electric activity exceeding baseline activity by ±100 µV were considered as artifact and were automatically rejected from further processing. The percent of rejected trials was calculated by experimental condition (25% standard, 24% frequency, 22% duration, 25% VOT). The selected EEG artifacts free trials of each child were averaged for the four types of stimuli (standard, frequency, duration and VOT) in the PRE and POST conditions.

3. Results

3.1. Comparison between Experimental MT group and Control group

Results are reported for the comparisons between Week 1 (before therapies started) and Week 4 (after therapies started). The number of children who remained at CIREN for 8 weeks was too unbalanced (Occupational therapy: MT n=8 and Control n=4) or too small (Speech therapy: MT n= 3 and Control n =3) to conduct further analyses.

Occupational therapy: This questionnaire relates to all children involved in the neuro-restoration program (MT: n= 17 and Control = 10). Using pairwise Sign-tests, results showed significant improvements on motor behavior: Week 1 (mean=3.30) and Week 4 (mean=3.76, z=2.69, p=0.007), social behavior: Week 1 (mean=2.64) and Week 4 (mean=3.33, z=3.20, p=0.001) and emotional behavior: Week 1 (mean=3.07) and Week 4 (mean=3.60, z=2.91, p=0.003).

Using the Kruskal Wallis non parametric one way ANOVA, results showed that the main effect of Group was only significant for motor behavior (ChiSq(2) = 3.84, p<.04) with larger improvements from Week 1 to Week 4 in the experimental MT group (0.66) than in the control group (0.35). No significant between-groups differences were found on the other dimensions.

Speech therapy: This questionnaire relates to the subset of children who followed speech therapy (MT: n= 9 and Control = 8). For the three main dimensions that were considered, motor behavior, social behavior and emotional behavior, results of pairwise Sign-tests showed that the improvement between Week 1 and Week 4 was significant for motor behavior (z=2.75, p<0.005) but not significant for the other dimensions.

Using the Kruskal Wallis non parametric one-way ANOVA, results showed that the main effect of Group was also significant for motor behavior (ChiSq=4.5, $p<.03$): the improvement between Week1 and Week 4 was larger in the MT group (1.0) than in the control group (.69).

Evaluation of the parents' interview: Complete information was obtained from 18 parents (MT, n= 15 and Control, n = 3). Because of the unbalanced number in the two groups, it was not possible to conduct quantitative analyses. Qualitative observations are reported below.

In the initial interview, all parents (n=18) reported that their children enjoyed music and were able to pay attention to music. They also believed that music can help their children in their everyday life. Only one question, related to rhythmic movement associated with music, was negatively rated by parents (n=4) of children with spasticity or dystonia. The majority of children had previous experiences with different types of music therapy in their countries and parents generally agreed on the importance of this intervention.

In the final interviews, the positive aspects noted by parents of children in the MT group (n=15) were related to increased motivation, sociability and auditory attention. In particular, they noted that MT improved motivation so that children more easily engaged in functional games during the speech and occupational therapies, were less angry and less irritable and were more likely to allow facial massages. Related to sociability, parents noted that their children were more understanding and complying with complex requests and that the collaboration with adults was improved. Overall, children seemed more communicative and more relaxed. Finally, related to auditory attention, parents noted that their children listened more carefully to adult' speech, that they tend to apply during speech and occupational therapies the listening strategies learned during MT and that they paid more attention to music outside the MT therapy. Some children spontaneously started singing songs to their parents. May be most importantly, parents noted that their children were very happy to go to the music therapy sessions.

The positive aspects noted by the parents of children in the control group (n=3) were mainly related to social behavior (e.g., improved verbal and nonverbal communication, increased contact with other children and adults). Finally, two parents (from one child in MT group and from one child in control group) also mentioned negative aspects related to increased irritability in their children, possibly because children were taking new anti-epileptic medications.

3.2. Evaluation of children in the experimental MT group

Behaviour: the music therapist did evaluate the level of performance of the children at Week 1 (n=17), Week 4 (n=17) and at Week 8 (n=9) on five psychological scales related to motor ability, attention, emotional behaviour, imitation and communication. Using pairwise Sign tests, results revealed significant improvements from Week 1 to Week 4 on all dimensions (all $p<0.005$,) and from Week 1 to Week 8 (all $p<0.04$) but only marginally significant improvements from Week 4 to Week 8 (all $p<0.08$; see Table 2).

Using Kruskal Wallis tests, results showed that the main effect of Session was significant for each dimension (p<.00l, see Table 2). Moreover, results of post hoc Tukey HSD tests revealed that the improvements from Week 1 to both Week 4 and Week 8 were significant for each dimension ($p<.05$) but improvements from Week 4 to Week 8 were not significant ($p>.05$) except for the attention and communication dimensions ($p<.05$; see Table 2).

Specific music tests: Three children could not perform either the rhythm reproduction tests or the "musical" test. The rest were tested at Week 1 (n=14), at Week 4 (n=14) and at Week 8 (n=9).

Rhythm reproduction test (subtest of CUMANIN): Using pairwise Sign-tests, results showed that the improvement was not significant from Week 1 (mean=0.43, Std=1.16, median=0) to Week 4 (mean=1.43; std=2.14, median=0; z=1.22, p>.22) and from Week 1 to Week 8 (mean=2.75, std=1.83, median=2.50; z=1.51, p>.13). However, the improvement was significant from Week 4 to Week 8 (z=2.27, p<.03), that is for the subset of children (n=9) that remained longer.

Using the Kruskal Wallis test, results showed that the main effect of Session was significant (ChiSq(2) = 10.13, p<.007). Results of post hoc Tukey HSD tests showed significant improvements from Week 1 (0.43) to Week 8 (2.75, p<.05). However, mean scores in Week 4 (1.43) were in between and not significantly different either from Week 1 or from Week 8 (both p>.05).

Explicit "musical" test: Using sign tests, results showed increased level of performance from Week 1 (mean score = 23.57, Std = 11.48, median = 19.00) to Week 4 (mean score =34.00; std= 14.28, median=29.50; z=2.60, p<0.01), from Week 1 to Week 8 (mean score =46.88, std=12.14, median=47.00; z=2.47, p<0.02) and from Week 4 to Week 8 (z=2.47, p<0.02).

Using the Kruskal Wallis non parametric test, results showed that the main effect of Session was significant (ChiSq(2) = 12.17, p<.003). Results of post hoc Tukey HSD tests showed significant improvements from Week 1 to Week 8 (p<.05). However, mean scores in Week 4 were in between and not significantly different from Week 1 or Week 8 (p>.05).

Implicit "musical" test: Using pairwise Sign-tests, results showed increased level of performance from Week 1 (mean score=29.43, std=11.61, median=27.50) to Week 4 (mean score=41.21, std=16.33, median=42.50; z=2.77, p<.006), from Week 1 to Week 8 (mean score=54.13, std=13.34, median=53.50; z=2.47, p<.02) and from Week 4 to Week 8 (z=2.47, p<.02).

Using the Kruskal Wallis non parametric test, results showed that the main effect of Session was significant (ChiSq(2) = 11.49, p<.004). Results of post hoc Tukey HSD test showed improvements from Week 1 to Week 8 (p<.05). Again, mean scores in Week 4 were in between and not significantly different from Week 1 or Week 8 (p>.05).

Finally, results of pairwise Sign-tests showed that implicit mean scores were higher than explicit mean scores at Week 1 (z=3.18; p<.0002), Week 4 (z=3.18; p<.0002) and Week 8 (z=2.47; p<.02). Results of the Kruskal Wallis test also showed that mean scores in the implicit musical test were significantly higher than mean scores in the explicit test (ChiSq(1) = 4.32, p<.04).

3.3. Correlation analyses between different instruments

To determine whether results at the different scales and questionnaires employed in our study were correlated, we compared scores at Week 1 and at Week 4 using one-tailed Spearman correlation coefficient. Importantly, results revealed significant correlations between the social behavior subscale of the parent's interview and the subscales of the occupational therapy questionnaire: social behavior (p=0.009), emotional behavior (p=0.04) and motor behavior (p=0.05). Thus, the improvements noted by the parents were in agreement with the ratings of the occupational therapists. Turning to results in the MT group, scores on emotional behavior were significantly correlated in MT performance and speech therapy subscales (r=0.528, p=0.02).

3.4. ERPs data

Close examination of the ERPs data revealed large inter-individual variability which was expected due to the heterogeneity of the various brain lesions and neurological disorders of the children tested in this study. No clear pattern emerged from a quantitative comparison of the experimental and control group. Nevertheless, on the basis of visual inspection of the data, two suggestive patterns emerged, independently of whether children belonged to the experimental or to the control groups:

For a group of children, called the “P250 responsive group”, ERPs were more positive between 200 and 300 ms post-stimulus onset (P250 component) after the neuro-restoration and MT programs than before this intervention.
For the other group of children, called the “N300 responsive group”, ERPs were more negative between 300 and 400 ms post-stimulus onset (N300 component) after the neuro-restoration and MT programs than before this intervention.
Thus, we computed separate averages for these two sub-groups of children both in the experimental and in the control groups.

For the P250 responsive group, as can be seen in Figure 1, the ERPs to standard stimuli and VOT deviant stimuli overlap for the experimental and control subgroups before the start of the restoration and MT programs. By contrast, after the programs, the amplitude of the P250 components elicited by standard stimuli and VOT deviant stimuli were clearly larger in the experimental than in the control group. The parietal scalp distribution of this positive component is an indication that this component may belong to the P3 family (P3b) and may reflect increased auditory reactivity after the MT program.
For the N300 responsive group, as can be seen on Figure 2, the pattern of results is quite different from the P250 responsive group. Again, there is good overlap of the ERPs to standard stimuli and VOT deviant stimuli in the experimental and control subgroups before the start of the restoration and MT programs. By contrast, after the programs, a negative component peaking around 300 ms (N300) developed after both standard stimuli and VOT deviant stimuli, with larger amplitude in the experimental than in the control group.
While these observations are encouraging for further studies, the small number of children included in the subgroups (from 3 to 6), precluded to conduct further analyses

4. Discussion

Overall results of this experiment showed that all children improved from Week 1 to Week 4 on the three dimensions (motor, social and emotional behaviors) that were tested through the occupational and speech therapies questionnaires. Children from the experimental MT group only differed from children in the control group on the motor behavior dimension. Moreover, children in the MT group showed improvements on the five dimensions (attention, emotion, imitation, communication and motor behavior) of the psychological scales with larger improvements from Week 1 to Week 4 than from Week 4 to Week 8. By contrast, overall results of the specific music tests (rhythm reproduction and explicit and implicit “musical” tests) showed significant improvements from Week 1 to Week 8 but not from Week 1 to Week 4. Importantly, in the MT group and for the emotional dimension, scores on the psychological scale were correlated with scores in the speech therapy questionnaire. More generally, results of correlation analyses showed that the improvements noted by the parents were correlated with those reported by the occupational therapist on the social, emotional and motor behavior subscales. Finally, results of parents’ interviews revealed that they considered that MT had a positive influence on their children motivation, sociability and auditory attention. These different aspects are considered in turn in the following discussion.
Considering first results from the occupational and speech therapies questionnaires for all children enrolled in the experiment, the finding of significant improvements from Week 1 to Week 4 on the three dimensions that were tested (social, emotional and motor behaviors) shows the positive impact of the neuro-restoration program implemented at the neuro-pediatric clinic of the CIREN. However, one can argue that since the occupational and speech therapists were involved in the rehabilitation, there is a potential bias toward obtaining positive results. While this may be the case, correlation

analyses showed that the improvements noted by the occupational therapist were correlated with those reported by the parents (who tend to be more critical because of their high expectations regarding the outcome of the program) on the social, emotional and motor behavior subscales. Even if results converge in showing improvements on these dimensions, it will be important in future experiment for children to be tested by occupational and speech therapists that are not directly involved in the neuro-restoration program at CIREN.

Results from the occupational and speech therapies questionnaires revealed significant between-groups differences for the motor behavior dimension with larger motor improvements in the MT group than in the control group. The neuro-restoration program includes motor rehabilitation and all children involved in the experiment were receiving this therapy to variable extents depending upon their specific impairments. However, dancing (or moving any part of the body) was encouraged during music therapy and children very much enjoyed this aspect. Thus, MT provided increased motor training possibly linked to an increased motivation to move due to the entraining function of music (e.g., salsa, tango etc...). These two effects may contribute to the further improvement found in the MT group. This interpretation is in line with results of McIntosh et al. (McIntosh et al., 1997) showing that music facilitates initiation of walking in Parkinson patients. Forsblom et al (Forsblom et al., 2010) also showed that the stroke patients tested in their study considered music listening as favoring engagement in motor activity. Based on these results, it would be useful to implement motor rehabilitation programs associated with entraining musical pieces.

Turning to children in the MT experimental group, results also showed improvements on the five dimensions (attention, emotion, imitation, communication and motor behavior) of the psychological scales. Several results in the psychology of music and neuroscience of music literature have shown that music training is associated with increased attentional abilities (Tervaniemi et al., 2009); see Besson et al. (2011) for a review). For instance, recording brain electrical activity and analyzing ERPs, Marie (Marie et al. 2011) reported shorter latency and larger amplitude of ERP components associated to categorization and decision processes (N2/N3 and P3b components, respectively) in adult French musicians compared to nonmusicians in a same-different task on tone and segmental variations in Mandarin Chinese. These results were interpreted as reflecting enhanced auditory cognitive and attentional abilities in musicians. Similarly, Bauman (Baumann et al., 2007) showed that focussed attention on sine wave tones was associated with an early negative component in musicians but not in nonmusicians which again suggested that music training influenced top-down attentional processes. Moreover, Särkämo(Särkämö et al., 2008) also reported enhanced focussed attention in stroke patients after music listening. While fewer studies have been conducted with children, Chobert (Chobert, et al. , 2011) reported enhanced preattentive processing of French syllables varying in pitch, duration and VOT in musician than in nonmusician children.

The relationship between music and emotion has been extensively studied and it is common knowledge that different types of music can induce different emotions and mood. Importantly, and as mentioned in the introduction, Forsblom(Forsblom et al., 2010) found that music listening contributed more than audiobook listening to recovery and positive mood changes in stroke patients and Särkärmo (Särkämö et al., 2008) showed that only music listening prevented depression in the 6 months following the stroke. Moreover, Narme(Narme et al., 2012) showed that music interventions were associated with larger improvements in emotional states than painting or cooking interventions. Similarly, Särkämo and collaborators (Särkämö et al., 2013) showed positive changes in the mood and the quality of life of Alzheimer patients immediately after and 6 months after the music intervention and Janata (Janata, 2012) reported reduced level of agitation and depression in Alzheimer patients listening to music programs several hours per day. Finally, our results showed that MT improved imitation and communication possibly because the music therapist encouraged children to reproduce the movements that she performed on-line with the music (e.g., clapping hands in rhythm with the music, rising hands or fingers or moving the head with melodic changes in the musical excerpts, etc…). Children were also encouraged to share with each other's the emotions and movements induced by the music.

However, and as discussed above for the results of the occupational and speech therapies questionnaires, the music therapist was at the same time providing the MT interventions and filling up the questionnaires to test for the results of the therapy. Even if the therapist performing the therapy is probably the best person to evaluate changes in children's behavior because she worked with them regularly three days per week, there is a potential bias toward obtaining positive results. However, two sets of results provide evidence that such a bias is not the unique explanatory source. First, correlation analyses showed that for the emotional dimension, scores on the psychological scale were correlated with scores in the speech therapy questionnaire and the two therapists did not discuss results together. Moreover, analyses of the parents' interviews also revealed that they considered that MT had a positive influence on motivation, sociability and auditory attention. Second, results showed larger improvements from Week 1 to Week 4 than from Week 4 to Week 8 which is not expected based on the hypothesis of a positive bias toward "more music therapy better results". Note that the reasons why the effects of MT were smaller during the second month of the intervention are unclear but it may be that children tend to habituate to the music sessions with decreased positive effects of MT with longer therapy. Based on these results, it would be of interest in future experiments to test for the effect of an On-Off music therapy program (e.g., On for 4 weeks, Off for 2 weeks, On for 2 weeks...). It would also be important to compare the results obtained by the music therapist performing the therapy and those obtained by another therapist not directly involved in the rehabilitation program.

It is interesting to note that in contrast to results showing larger improvements from Week 1 to Week 4 than from Week 4 to Week 8 on the several dimensions of the psychological scales, results of the rhythm reproduction test (CUMANIN) showed significant improvements from Week 1 to Week 8 but not from Week 1 to Week 4.Thus, a rather long period of training is necessary for the improvement in rhythmic reproduction to be significant. The level of performance of the children in Week 1 was 0.43, a score close to what reported for children with Down syndrome (0.36, SD= 0.50; (Barba Colmenero & Robles Bello, 2012)). In the subset of children who stayed for 8 weeks, the level of performance increased to 2.75 (SD= 1.83) which should not, however, be considered as normal level (2.72, SD = 1.70) (Barba Colmenero & Robles Bello, 2012) because level 4 rather than level 7 was considered as correct reproduction and some of the children were older than in the Barba Colmenero 2012 study. That music therapy improved the reproduction of rhythmic patterns with increasing complexity was expected based on several results showing that musicians are more sensitive to several aspects of the music rhythmic structure than nonmusicians(e.g, (Vuust et al., 2006). However, it is important that similar results can be obtained from children with severe neurological impairments as those tested in the present study.

Turning to the "musical" test, results were somewhat different depending upon the statistical test that was used to conduct the analyses (Sign-tests vs Kruskal Wallis tests). While results from the Sign-tests revealed significant improvements from Week 1 to Week 4, results of the more conservative Kruskal Wallis tests only showed significant improvements from Week 1 to Week 8. Thus, more than one month of MT seems to be necessary for the children tested here to increase their sensitivity to abrupt changes (i.e., a combination of timber, harmonic and melodic changes) in the musical pieces. Finally, while similar results were obtained in the explicit and implicit music tests, mean scores in the implicit test were higher, as expected, than mean scores in the explicit test.

In sum, results of this experiment are encouraging in showing effects of music therapy both on specific music tests (rhythm reproduction and detection of timber, harmonic and melodic changes in the musical pieces) and on more general aspects of the children behavior, in particular motor

behavior. In line with the literature, we used questionnaires to assess the effectiveness of music therapy (Mrazova & Celec, 2010). However, two caveats are in order. First, while the questionnaires that we used were built from questionnaires published in the literature (MacArthur-Bates Inventario I and II, (Jackson-Maldonado et al., 2003); Escala autónoma Asperger-Autismo, (Belinchon et al., 2008), they were not normalized with children without neurological problems. Second, our results are based on the analyses of questionnaires filled by therapists actively involved in the neuro-restoration program or the MT so that these measures may not be objective. Moreover, the use of questionnaires may not be sensitive enough to detect subtle changes in the children's behavior. However, because the group of children involved in this program was very heterogeneous, including children with different types of brain damage and diverse etiologies (see methods and Table 1), it was not possible to find an experimental test that can be performed by all of them. Moreover, the number of children was not sufficiently larger to allow making subgroups of children with similar neurological problems.
In an attempt to find an objective measure of the influence of the neuro-restoration and MT programs, we analyzed the ERPs from a subset of children at Week 1 (evaluation week) and at Week 4 (end of the neuro-restoration and MT programs). While the sample of children was too small to compute statistical analyses and to draw firm conclusions from these data, they nevertheless lead to interesting observations. First, while individual averages were highly variables from one child to the other, it was nevertheless possible to note differences between Week 1 and Week 4. Furthermore, in some children it was also possible to detect the type of deviants they were more sensitive to. While these individual differences are difficult to quantify, it is our hope that new methods are developed for analyzing clinical data (e.g., (Aarts et al., 2014)and for allowing the use of electrophysiological measures as biomarkers bof the prognosis and the efficacy of the therapeutic intervention. Second, even if the individual data were variable, it was nevertheless possible to identify two sub-groups of children with similar patterns of results (i.e., the P250 responsive group and the N300 responsive group). While the small number of children in these subgroups precluded further analyses, these between-group differences are encouraging us to collect more data in this experimental design.
In conclusion, results of this study provided clear indications that MT had a positive influence on motor behavior, possibly because the children in the MT group benefitted from the entraining and motivational effects of music. Moreover, they are encouraging in showing that the use of different methodologies based on the analyses of questionnaires, specific tests and recording of the ERPs provide complementary information on the efficiency of the neuro-restoration and MT programs.

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7. Figure legends

Figure 1.Sub-averages for the "P250 responsive group". ERPs elicited by Standard stimuli (left side) and deviant stimuli in Voice Onset Time (VOT) before and after rehabilitation are compared in the Control (blue trace) and Experimental (red trace) groups. After rehabilitation, the amplitude of the parietally-distributed P250 component was larger in the Experimental than in the Control group. Time is in abscissa and the amplitude of the effects is in ordinate in microvolt (µV).

Figure 2.Sub-averages for the "N300 responsive group". ERPs elicited by Standard stimuli (left side) and deviant stimuli in Voice Onset Time (VOT) before and after therapy are compared in the Control (blue trace) and Experimental (red trace) groups. After rehabilitation, amplitude of the frontally-distributed N300 component was larger in the Experimental group than in the Control group.

8. Tables

Table 1. Clinical Characteristic of the Children

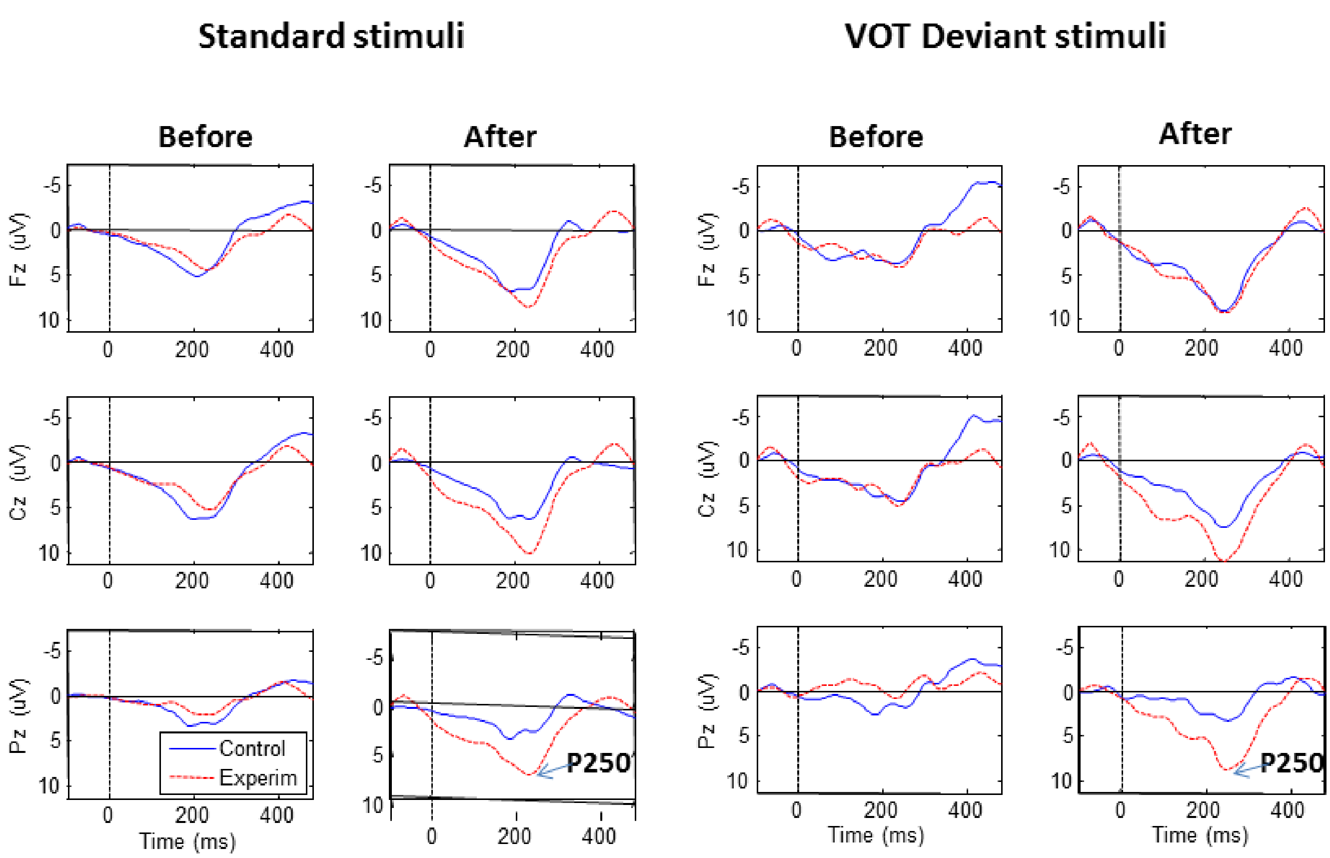
Patient/gender	Age	Nationality	Type of disease	Expressed by	MRI	EEG/ MMN	ABRs
Experimental Group							
D.F./f	6.85	Argentina	SLCNS	Cognitive Deficit	Dysplasia in left temporal region	EA /MMN	Ok
A.J./f	9.93	Chile	SLCNS	Cerebral Palsy	Cortical atrophies in insular region. Vascular lesion at left occipito- mesial area. Lesion at caudate nucleus	MMN	Abn.
A.E.V. */f	9.22	Mexico	SLCNS	Cognitive deficits	Bilateral atrophy of hippocampus.	Abn /MMN	Ok
C.A.P./m	8.79	Mexico	SLCNS	Spastic Cerebral Palsy	Cortical heterotopias deforming lateral ventricles at oval centers. Hypoxia signs.	MMN	Abn.
Y.D./m	5.43	Venezuela	SLCNS	Cerebral Palsy	Left fronto-parietal sulci absents	EA /MMN	Abn.
A.Y.H./m	7.67	Venezuela	SLCNS	Cerebral Palsy	Subcortical lesions adjacent to upper lateral ventricles. Mild bilateral hippocampal atrophy. Pineal gland cyst.	MMN	Ok
B.A.A. */f	11.6	Mexico	SLCNS	Cerebral Palsy	Cortical heterotopias deforming lateral ventricles. Right frontal atrophy.	MMN	Ok
D.A. */m	8	Mexico	Neurodevelop ment Disorder	Non-verbal Learning Disability	Mild right fronto-temporal atrophy	EA /MMN	Ok
C.G.*/m	4	Mexico	SLCNS	Language impairment	Ok	MMN	Ok
A.H.H./m	3.2	Venezuela	SLCNS	Cerebral Palsy	Hypoxic lesions in peri- ventricle areas	MMN	Ok
S.C./m	3.1	Venezuela	SLCNS	Cerebral Palsy	Subcortical lesions adjacent to lateral ventricles. Mild atrophy left temporal lobe. Hypoplasia Corpus Callosum	MMN	Ok
X.B.L. */f	7	Mexico	SLCNS	Cognitive deficit	Ok	Abn/ MMN	Ok
A.S.N./f	6	Venezuela	Spinal Cord Lesion	Paraplegia	Ok	No	Ok
L.Y.T./f	11	Venezuela	Idiopathic Dystonia		Cortical atrophy (temporal lobe). *Cavum vergae*. Brainstem hypoplasia	No	Ok
M.S./m	7	Angola	Neurofibromat osis		Tumor. Frontal atrophy.	EA	Abn.
D.F.*/m	4.2	Mexico	SLCNS		Bilateral atrophy hippocampus.	EA	Ok
O.E.T.*/m	5.8	Mexico	ASD		Left occipital lesion related to heterotopia area	EA	Abn
Control Group							
D.N.Q./f	9.48	Venezuela	SLCNS	Cerebral Palsy	Cortical atrophy. *Cavum vergae*.	Ok/ MMN	Ok
A.J.B./m	12	Venezuela	Spinal Cord Lesion	Paraplegia	Ok	No/ MMN	Ok
E.C./m	4.71	Mexico	SLCNS	Cognitive deficits	Left occipital lesion (heterotopia)	EA /MMN	Ok
S.G.*/f	3.99	Mexico	ADS	Rett Syndrome	Mild cortical atrophy more evident at temporal lobes.	EA /MMN	Abn
J.P.M./m	3.95	Venezuela	SLCNS	Cerebral Palsy	Periventricular heterotopias	MMN	No
K.P.R.*/f	9.64	Mexico	SLCNS	Cerebral Palsy	Ok	SW /MMN	Ok
L.A.C./m	3	Venezuela	SLCNS	Cerebral Palsy	Periventricular heterotopias. Corpus Callosum hypoplasia		No
A.A.M.*/m	4.96	Mexico	SLCNS	Language Disorder	Diminished cranial diameter. Temporal Operculum atrophy	EA	Ok
E.H.S./m	12	Mexico	SLCNS post surgery	Cognitive Deficit	Generalized cortical atrophy. Hypoxic lesion at basal ganglia	Abn.	Abn
J.P.R.*/m	4.6	Mexico	SLCNS	Cerebral Palsy	Periventricular heterotopias	EA	ok

SLCNS: Static Lesions of the Central Nervous System (when not explicit is by prenatal and/or perinatal causes); ASD: Autistic Spectrum Disorder. ABRs: Auditory Brainstem responses. * = quit after 4 weeks. Sex f=feminine, m=masculine. EEG/MMN: EA indicates Epileptiform abnormalities, SW: predominant slow waves, Abn: abnormal EEG or ABRs.

Table 2. Results of questionnaires related to five dimensions administered in the MT group. Means, Standard deviations (STD) as well as p-values from the non-parametric Kruskal-Wallis test and from post hoc Tukey HSD tests (correcting for multiple comparisons) are reported to compare scores in Week 1 (17 children), Week 4 (17 children) and Week 8 (9 children).

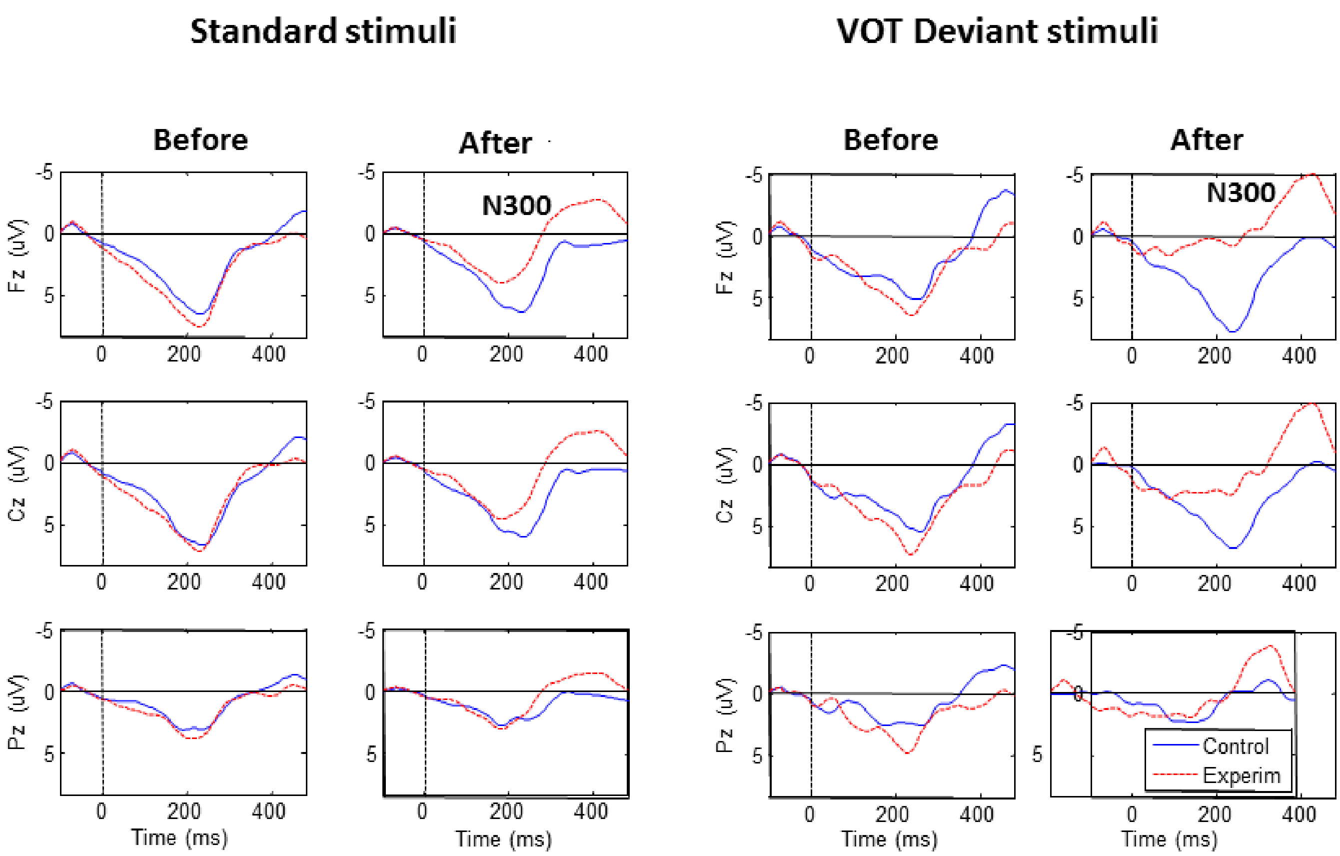
	Week 1		**Week 4**		**Week 8**		**K-W**	**W1**	**W1**	**W4**
Item	**Mean (STD)**	**Median**	**Mean (STD)**	**Median**	**Mean (STD)**	**Median**	**ChiSq(2)(pval)**	**vs. W4**	**vs. W8**	**vs. W8**
Motor ability	1.95 (0.39)	1.79	3.42 (0.80)	3.38	4.48 (0.52)	4.63	30.01 (<4e-07)	<0.05	<0.05	**>0.05**
Attention	1.69 (0.48)	1.83	3.17 (1.10)	3.17	4.64 (0.55)	4.88	26.63 (<2e-06)	<0.05	<0.05	<0.05
Affection	2.74 (0.75)	3.20	3.77 (0.70)	3.88	4.60 (0.64)	4.99	21.69 (<2e-05)	<0.05	<0.05	**>0.05**
Imitation	1.45 (0.40)	1.67	3.73 (0.71)	3.95	4.58 (0.58)	4.75	33.81 (<5e-08)	<0.05	<0.05	**>0.05**
Communication	1.58 (0.48)	1.75	2.85 (0.98)	3.10	4.45 (0.64)	4.75	26.94 (<2e-06)	<0.05	<0.05	<0.05

Figure 1.TIF



Standard stimuli
VOT Deviant stimuli
Before
After
Before
After
Fz (uV)
Cz (uV)
Pz (uV)
-5
0
5
10
0
200
400
Time (ms)
Control
Experim
P250
P250

Figure 2.TIF



Standard stimuli
VOT Deviant stimuli
Before
After
Before
After
N300
N300
Fz (uV)
Cz (uV)
Pz (uV)
-5
0
5
0
200
400
Time (ms)
Control
Experim