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RHYTHMIC AUDITORY STIMULATION IN REHABILITATION OF MOVEMENT DISORDERS: A REVIEW OF CURRENT RESEARCH

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PHYSIOLOGICAL RESEARCH HAS SHOWN THAT AUDITORY rhythm has a profound effect on the motor system. Evidence shows that the auditory and motor system have a rich connectivity across a variety of cortical, subcortical, and spinal levels. The auditory system—a fast and precise processor or temporal information—projects into motor structures in the brain, creating entrainment between the rhythmic signal and the motor response. Based on these physiological connections, a large number of clinical studies have researched the effectiveness of rhythm and music to produce functional change in motor therapy for stroke, Parkinson's disease, traumatic brain injury, and other conditions. Results have been strong in favor of rhythmic auditory stimulation (RAS) to significantly improve gait and upper extremity function. Comparative studies also have shown RAS to be more effective than other sensory cues and other techniques in physical rehabilitation.

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OVER THE PAST TWO DECADES RESEARCHERS have begun to elucidate the neural basis of music in the human brain. One of the core elements of any musical 'language structure,' rhythm has always been one of the primary foci of these research efforts. The study of the neurobiology of rhythm was also the first area in which new research insights helped to establish a new role for music in rehabilitation, moving from a more social science and cultural value driven approach that emphasized 'well being' and 'relationship building' to a neuroscience based understanding of music to retrain and re-educate the injured brain.

Although throughout cultural history music and movement were always recognized as having a close and mutually influencing relationship, the concepts usually were confined to emotional, motivational, or purely artistic concepts of expression and aesthetics. However, although only poorly understand until a few years ago, there is indeed a rich physiological basis for the influence of auditory rhythm on the motor system. This basis has increasingly become into clearer focus and understanding. Early landmark studies by Paltsev and Elner (1967), Rossignol and Melvill (1976), and Ermolaeva and Borgest (1980) were among the first to shed light on the rich connectivity between auditory and motor areas in the brain and what role sound and auditory rhythm could play in priming and timing of movement.

We now know that the rich connectivity between the auditory rhythm and movement interfaces in distributed and parallel fashion throughout the brain. Research has shown evidence on the brain stem level for the existence of audio-motor pathways via reticulospinal connections. Rossignol and Melvill (1976) demonstrated priming and timing of motor responses via this audiospinal path using sound cues and musical rhythms. Auditory projections into the cerebellum also have been demonstrated via pontine nuclei. As one of the nuclei in the ascending auditory pathway, the inferior colliculus is a source of auditory information via thalamic projections to the striatum of the basal ganglia (Koziol & Budding, 2009). The striatum in turn projects to the globus pallidus as the output system of the basal ganglia whose projections reach cortical motor structures such as supplementary motor area and premotor cortex. Auditory association areas also project back to the basal ganglia, reciprocally influencing basal ganglia function in regard to sequencing, timing, and behavioral response selection. These pathways may play a critical role, for instance, in the facilitative effect of music and auditory rhythm on motor output in Parkinson's disease (McIntosh, Brown, Rice, & Thaut, 1997). Ermolaeva and Borgest (1980) mapped auditory fiber connectivity to determine terminal zones relative

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to motor projections, finding rich connections between primary and secondary auditory cortices and motor cortex. In an MEG-study investigating motor synchronization (finger tapping) to tempo shifts in metronome cues above and below the level of conscious awareness (Tecchio, Salustri, Thaut, Pasqualetti, & Rossini, 2000), we showed that the magnitude of the auditory field potentials (neural responses to time variations) covaried in magnitude with the temporal size of the tempo shift, indicating a spatial and temporal neural coding process for rhythmic time measurements. The source for these neural responses was located in primary auditory cortex. These findings, in conjunction with Ermolaeva and Borgest's earlier data, suggest that the immediate motor adaptations to these tempo shifts in order to maintain synchronization were at least in part also mediated by cortical auditory-motor pathways.

Other lines of research, especially from psychophysics, have shown that auditory (musical) rhythm may be a useful stimulus to cue motor function, due to the speed and high resolution of time processing in the auditory system. Taken together, conceptual understanding of these research findings have converged on an oscillator-entrainment model where rhythmic processes in neural motor networks become entrained to rhythmic time-keeper networks in the auditory system. The time-keeper networks are driven peripherally from rhythmic inputs, such as metronome or music.

Early studies to investigate these models clinically were carried out by Safranek, Koshland, and Raymond (1982; modulatory effect of rhythmic cuing on EMG in arm movements) and Mandel, Nymark, Balmer, Grinnell, and O'Riain (1990; rhythmic feedback vs. EMG feedback in stoke gait rehabilitation). In our research, we first studied the effect of rhythmic cuing on EMG activations in arm movements (Thaut, Schleiffers, & Davis, 1991) and stride parameters and electromyography (EMG) patterns in the gait of normal individuals (Thaut, McIntosh, Rice, & Prassas, 1992a). We found improvement in stride symmetry and also in EMG patterns, especially the amplitude variability in muscle contractions across the movement cycle. Similar results were seen in measurements with individual stroke, cerebellar, and transverse myelitis patients (Thaut, McIntosh, Rice, & Prassas, 1992b). Based on these observations we began to study Rhythmic Auditory Stimulation (RAS) as a rehabilitation technique in motor therapy. We developed standard protocols for RAS as a gait training technique, which now has become standard in neurologic music therapy (NMT) and other rehabilitation disciplines. Extensions of RAS to techniques dealing with upper extremity and coordination training have been developed successfully and are clinically employed (Thaut, 2005).

RAS Gait Rehabilitation Post CVA

In a first rehabilitation study with 10 hemiparetic stroke patients who were post CVA from 4 weeks to 24 months, we used a frequency entrainment design to study the effect of RAS on gait patterns (Thaut, McIntosh, Rice, & Prassas, 1993). Five of the participants had either thrombotic or hemorrhagic events affecting right cerebral hemisphere, typically in the middle cerebral artery distribution. Patients walked for six meters at free speed to determine their baseline walking ability. During the second walk RAS was matched to their baseline gait cadence to determine if immediate entrainment effects would occur without interference from practice. The same trial was repeated three times with each trial spaced a week apart. Results from this study showed a clear pattern of auditory-motor synchronization emerge for most participants. Stride time symmetry as well as stride length symmetry improved significantly, as well as weight bearing time on the paretic side ($p < .05$). Stride time variability decreased to a significant degree. Participants also showed a more balanced muscular activation pattern on EMG between the paretic and non-paretic limbs. Furthermore, a decrease in integrated amplitude variability of EMG was noted on the paretic side ($p < .05$). Other gait kinematic improvements with RAS included significant increase in center of mass vertical displacement and a significant reduction in lateral displacement, resulting in a smoother forward gait trajectory (Prassas, Thaut, McIntosh, & Rice, 1997).

The potential therapeutic effect of RAS subsequently was studied in a six-week daily training study with 10 stroke patients in a RAS gait training group, and a matched control group of 10 patients using conventional physical therapy gait training (Thaut, McIntosh, & Rice, 1997). Patients entered the study within an average of 15 days post CVA, as soon as they could walk for five meters with hand-held assistance. Results showed a significantly stronger ($p < .05$) improvement in gait velocity and stride length for the RAS group and a nonsignificant trend for improved stride symmetry. Gait velocity in the RAS group had improved by 164% over pretest vs. 107% in the control group. Stride length had improved by 88% with RAS vs. 34% with conventional physical therapy. Symmetry improvements were 32% for RAS and 16% for the control group. Also, the reduction of variability of EMG activation patterns in the gastrocnemius muscle was significantly stronger at posttest in the RAS group (69%) than in the control group (33%). We replicated the study in a multicenter international gait rehabilitation project implementing three weeks of daily gait training (Thaut et al., 2007). Results for velocity, swing symmetry, stride length, and step frequency showed significant results in favor of RAS over NDT/Bobath based gait training. However, the magnitude of improvement for both conditions was reduced for all gait parameters by about 30%, compared to the six-week training, which indicates strongly that significant gains in early post stroke gait training can still be made after three weeks of intervention. Significant results for RAS also were found by Schauer and Mauritz (2003) and Schauer, Steingrueber, and Mauritz (1996) with hemiparetic stroke patients using RAS during treadmill facilitated gait training. A study by Ford, Wagenaar, and Newell (2007) found significant improvements for RAS on gait and associated arm swing patterns in patients with stroke.

In Japan, a number of neurorehabilitation hospitals have started to apply NMT in addition to conventional rehabilitation approach as a special service (Abiru, Mihara, & Yoshii, 2009; de L'Etoile, Abiru, & Yoshii, 2007). RAS is among the most widely used of neurologic music therapy techniques in Japan, and has been shown as beneficial to stroke patients with lesions in the putamen, cerebellum, and thalamus (Abiru et al., 2007a; Abiru et al., 2007b; Abiru et al., 2008; Abiru et al., 2009; Abiru et al., 2010; Nakano et al., 2010). In the study by Nakano et al., in addition to conventional gait training by physical therapy (60 min, 7 times a week), RAS (30 min, 5 session a week) was implemented 18.3 ± 9.3 times. Cadence, stride length, step length of paralyzed side and unparalyzed side, velocity, and symmetry index were measured by a three-dimensional motor analysis device (VICON612, VMS Ltd). As a result, after RAS, all gait parameters except symmetry index showed significant improvement for all patients ($p < .05$). However, the improvements of the symmetry index of stroke patients with thalamic lesions were different among individuals. Especially stroke patients with thalamus lesions and severe sensory impairment showed excessive movement of hip joint to compensate for lack of movement of ankle joint. These data indicate that the severity of paresis and sensory impairment in stroke also needs to be taken into consideration when RAS is implemented.

The effects of rhythmic motor training also have been extended to upper extremity rehabilitation in stroke. Positive outcomes have been reported in studies by Whitall, McCombe, Waller, Silver, and Macko (2000), Thaut, Schicks, McIntosh, and Hoemberg (2002), Luft et al. (2004), Jeong and Kim (2007), Schneider, Schoenle, Altenmüller, and Muente (2007), and Malcolm, Massie, and Thaut (2009). The evidence base of RAS in gait rehabilitation has been reviewed, for example, by Jeffrey and Good (1995), Hummelsheim (1999), Mauritz (2002), and Hoemberg (2005).

It is important to note that the comprehensive gait pattern changes with RAS in immediate entrainment, as well as in therapeutic training, lead us to assign a more substantial contribution to RAS in motor control than a pure pacemaker role. Significant changes in the total pattern of gait movement suggest that RAS—by augmenting timing as the primary coordinative control structure in the generation of the complex movement sequences—also influences and improves positional and muscular control.

RAS Gait Training in Patients with Parkinson's Disease

The successes of RAS in stroke rehabilitation stimulated investigations into other patient groups, most notably Parkinson's disease (PD). In one of the first studies of its kind we studied entrainment effects of RAS on gait with 21 PD patients on medication, 10 PD patients off medication, and 10 healthy age matched elderly participants as a control group (McIntosh et al., 1997). Patients walked initially at free velocity, then with RAS matched to the free velocity cadence and with RAS 10% faster than baseline, and immediately following without RAS to test for short-term carry-over effects. Faster RAS produced significant improvements ($p < .05$) in mean gait velocity, cadence, and stride length over walking without RAS in all groups. Of specific interest was the large improvement rate of 36% for velocity in the PD on medication group and 25% in the off medication group. Since a persistent feature of walking patterns in PD is the reduction of stride length, it is of special importance to note that the velocity improvements in both groups were caused by substantial increases in stride length (18.6% for on medication, 18.9% for off medication), which were proportionally larger than accelerations in gait cadence. Furthermore, close rhythmic synchronization between RAS and step frequency for both PD groups suggests the ability to utilize auditory rhythmic input to improve gait function even in the presence of basal ganglia dysfunction.

In a follow up study on longer term clinical results we investigated the potential therapeutic effect of RAS on gait training over a period of three weeks (Thaut et al., 1996). Fifteen PD patients participated in a three-week at-home based walking program of 30 minutes daily.

Again, gait velocity improved significantly ($p < .05$) by 25% with even increases in stride length (12%) and cadence (10%). A significant reduction in amplitude variability ($p < .05$) was seen in the anterior tibialis and vastus lateralis muscles. In a control group that followed the same walking program as the RAS group without any sensory facilitation, gait velocity improved insignificantly by 7%, mainly driven by changes in stride length. A control group without any gait training decreased in gait velocity by 7%. A more in-depth physiological analysis of EMG patterns, using Latency-Corrected Ensemble Averages (LCEA) showed that RAS training produced significant decreases in tibialis anterior shape variability and asymmetry, and gastrocnemius shape variability with more normal gait, possibly reflecting improved feedback adaptability of muscle activity, which may be useful in generating more stable gait patterns (Miller, Thaut, McInotsh, & Rice, 1996).

After these initial investigations, numerous studies on RAS in PD have been conducted. Pacchetti and colleagues (1998, 2000) found significant results for a comprehensive neurologic music therapy program on motor and cognitive functions in PD. Del Olmo and colleagues (2003, 2005, 2006) confirmed RAS-effects on PD gait, and extended the findings on freezing gait in several studies. Hausdorff et al. (2003), Suteerawattananon, Morris, Etnyre, Jankovic, and Protas (2004), and Willems et al. (2006) also determined RAS effects specifically in regard to regulating freezing episodes. Many other studies (e.g., Bernatzky, Bernatzky, Hesse, Staffen, & Ladurner, 2004; Freedland et al., 2002; Howe, Lovgreen, Cody, Ashton, & Oldham, 2003; Lim et al., 2005; Nieuwboer et al. 2007; Rochester et al. 2005; Willems et al. 2006;) have confirmed RAS as a viable gait therapy technique in PD. Among other variables, these studies also compared the effectiveness of auditory rhythm vs other sensory cues, the viability of home-based RAS programs, and the benefits of RAS cuing during divided attention tasks. In a longitudinal pilot study, McIntosh, Rice, Hurt, and Thaut (1998) found that after three weeks of home-based RAS training, improvements in gait were maintained for 3-4 weeks after training was discontinued before gradual decreases in gait performance reemerged.

RAS Gait Training with other Patient Groups

RAS investigations have been extended to a limited group of other patient populations. For example, an exploratory study with eight TBI patients 6 to 24 months post injury was carried out using an entrainment and a therapeutic training design (Hurt, 1998). Patients in this study were assessed as making no more progress in physical therapy gait training. Entrainment effects of RAS on TBI gait were highly variable, depending on the patients' initial level of gait ability. However, significant increases ($p < .05$) in gait velocity (51%) were found after five weeks of training. Also, the two patients with the slowest baseline velocity, and who could not entrain to faster RAS frequencies, were able to utilize RAS as a training stimulus and improved their walking speed by 35.6%. Mathematical analysis of knee angle displacement across the gait cycle of one of the most severely impaired patients showed a significant reduction in positional tremor (Kenyon & Thaut, 2000)

A study with 27 HD patients showed that metronome stimuli facilitated significant gait velocity modulation to slower and faster tempos in mild, moderate, and severe stages of the disease (Thaut et al., 1996). Music as a rhythmic cue only produced small and non-significant speed adaptations and became highly ineffective with increasing severity of the disease. This observation and the very stable synchronization patterns with the rhythmic cue further point to the well documented deterioration of complex sensory perception as well as the more putative effect of disturbance of time processing in the basal ganglia even early on in the disease process.

Several pilot investigations (e.g., Malherbe, Breniere, & Brill, 1992; Thaut, Hurt, Dragan, & McIntosh, 1998) into effects of RAS on gait training for children with cerebral palsy showed positive effects; however, the limited number of studies and small study samples make further research an important priority. Furthermore, precise phase synchronization ability seems to be linked to stages of sensorimotor development. However, these children do respond positively in their gait to tempo cues imbedded in the musical rhythms.

Conclusions

Taken together, research demonstrates a strong facilitating effect of RAS on gait performance in several patient groups with gait disorders. The effects have been most widely investigated in patients with stroke and PD. The consistency in facilitation across various patient groups is somewhat surprising because the various gait deficits have very different kinematic features and brought about by differing neuropathologies. We therefore assume that rhythmic auditory stimulation uses multiple auditory-motor pathways to access and entrain central motor processors that respond and couple to rhythmic time information to stabilize motor control independent of specific neuropathologies.

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