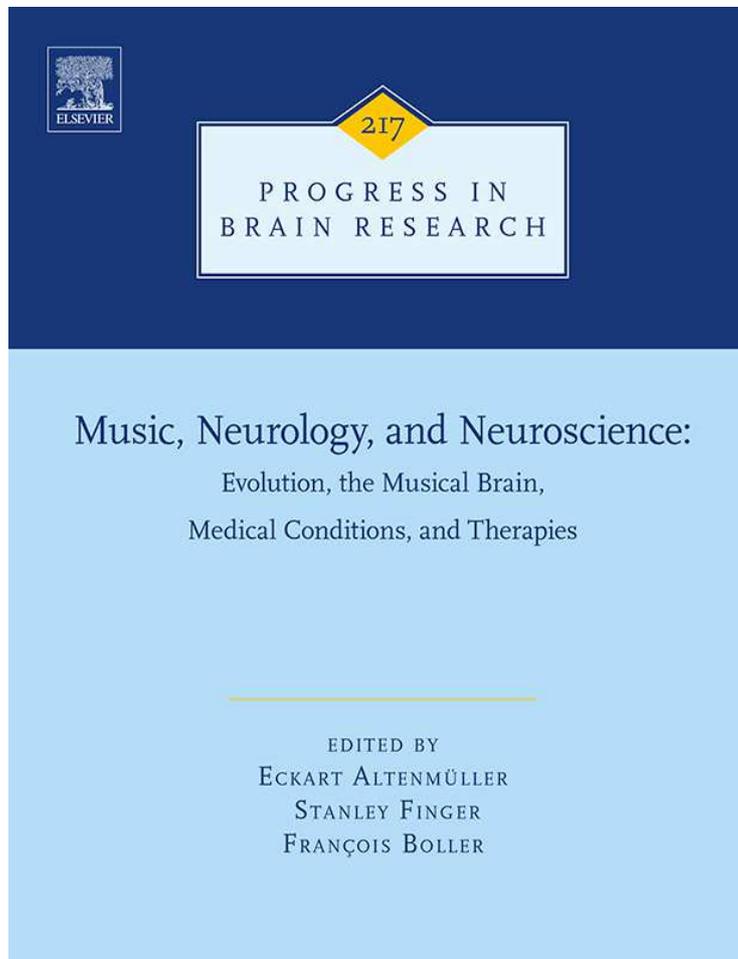


**Provided for non-commercial research and educational use only.
Not for reproduction, distribution or commercial use.**

This chapter was originally published in the book *Progress in Brain Research, Vol. 217* published by Elsevier, and the attached copy is provided by Elsevier for the author's benefit and for the benefit of the author's institution, for non-commercial research and educational use including without limitation use in instruction at your institution, sending it to specific colleagues who know you, and providing a copy to your institution's administrator.



All other uses, reproduction and distribution, including without limitation commercial reprints, selling or licensing copies or access, or posting on open internet sites, your personal or institution's website or repository, are prohibited. For exceptions, permission may be sought for such use through Elsevier's permissions site at:

<http://www.elsevier.com/locate/permissionusematerial>

From Michael H. Thaut, The discovery of human auditory–motor entrainment and its role in the development of neurologic music therapy. In: Eckart Altenmüller, Stanley Finger and François Boller, editors, *Progress in Brain Research, Vol. 217*, Amsterdam: Elsevier, 2015, pp. 253-266.

ISBN: 978-0-444-63551-8

© Copyright 2015 Elsevier B.V.

Elsevier

The discovery of human auditory–motor entrainment and its role in the development of neurologic music therapy

13

Michael H. Thaut¹

Center for Biomedical Research in Music, Colorado State University, Fort Collins, CO, USA

*¹Corresponding author: Tel.: +1-970-4915533; Fax: 970 491 7541,
e-mail address: michael.thaut@colostate.edu*

Abstract

The discovery of rhythmic auditory–motor entrainment in clinical populations was a historical breakthrough in demonstrating for the first time a neurological mechanism linking music to retraining brain and behavioral functions. Early pilot studies from this research center were followed up by a systematic line of research studying rhythmic auditory stimulation on motor therapies for stroke, Parkinson's disease, traumatic brain injury, cerebral palsy, and other movement disorders. The comprehensive effects on improving multiple aspects of motor control established the first neuroscience-based clinical method in music, which became the bedrock for the later development of neurologic music therapy. The discovery of entrainment fundamentally shifted and extended the view of the therapeutic properties of music from a psychosocially dominated view to a view using the structural elements of music to retrain motor control, speech and language function, and cognitive functions such as attention and memory.

Keywords

entrainment, neurologic music therapy, neurorehabilitation, neuroscience, rhythm

1 INTRODUCTION

Entrainment is a universal phenomenon that can be observed in physical (e.g., pendulum clocks) and biological systems (e.g., fire flies) when one system's motion or signal frequency entrains the frequency of another system. The use of entrainment for therapeutic purposes was established for the first time in the early 1990s by Thaut and colleagues in several research studies, showing that the periodicity of auditory rhythmic

patterns could entrain movement patterns in patients with movement disorders (Thaut et al., 1999). Physiological, kinematic and behavioral movement analyses showed very quickly that entrainment cues not only changed the timing of movement but also improved spatial and force parameters. We know now that anticipatory rhythmic templates are critical coordinative constraints in the brain for optimal motor planning and execution. This discovery showed for the first time that a structural element in music, i.e., rhythm, could be a successful stimulus for therapeutic purposes.

Rhythmic entrainment is one of the most important underlying mechanisms for the successful application of rhythmic-musical stimuli in motor rehabilitation for movement disorders associated with stroke, Parkinson's disease (PD), traumatic brain injury, cerebral palsy, etc. Temporal rhythmic entrainment has been successfully extended into applications in cognitive rehabilitation and speech and language rehabilitation, and thus became one of the first major neurological mechanisms linking music and rhythm to brain rehabilitation. Multiple treatment techniques in neurologic music therapy (NMT) utilize entrainment concepts in sensorimotor, cognitive, and speech/language training (Thaut and Hoemberg, 2014).

However, the discovery of structural elements in music as important mechanism facilitating therapeutic change has also motivated a previously not well-represented view to explore other elements in music as well as a language of rehabilitation: for example, the perception of melodic patterns to retrain attention and memory, singing and vocal exercises to retrain speech and language production, or elementary improvisation and composition exercises in a clinical context to train complexity thinking and facilitate executive functions. In this way, clinical rhythmic entrainment research became a model for a very different way of thinking about music in therapy and how to research it (Thaut, 2005). Approximately 25 years later, these discoveries have revolutionized how we use music successfully as a language of brain rehabilitation. The affective properties remain an important aspect of music in therapy but they are now functionally focused on dysfunctions that have critical affective and social components (Hallam et al., 2009). The clinical “music perception” model, however, has opened very new and very effective ways to apply music-based therapeutic exercises functionally to a broad range of dysfunctions of the human nervous system.

The remainder of this chapter will introduce the concept of entrainment more closely and show with examples from clinical research how profound the effects of rhythmic auditory–motor entrainment are in the rehabilitation of movement disorders. Furthermore, I will discuss why the discovery of entrainment had such a dramatic impact on changing the concepts of how music operates in therapy. Finally, illustrations will be provided how this conceptual change has led to the development of new NMT techniques in speech/language and cognitive therapy and rehabilitation.

2 WHAT IS ENTRAINMENT?

In 1666, the Dutch physicist Christian Huygens, the inventor of the pendulum clock, discovered that the pendulum frequencies of two clocks mounted on the same wall or board became synchronized to each other. He surmised that the vibrations of air

molecules would transmit small amounts of energy from one pendulum to the other and synchronize them to a common frequency (Bell, 1947; Garber, 2003). However, when set on different surfaces the synchronization effect disappeared. As it turned out, the transmitting medium was actually the vibrating board or wall. For air molecule vibrations, there would have been too much dampening of the energy transmission, as was later discovered. The effect he observed was subsequently confirmed by many other experiments and was called entrainment. In entrainment, the different amounts of energy transferred between the moving bodies due to the asynchronous movement periods cause negative feedback. This feedback drives an adjustment process, in which the energy is gradually eliminated to zero until both moving bodies move in resonant frequency or synchrony. The stronger “oscillator” locks the weaker into its frequency. When both are equally strong, the faster system slows down and the slower system speeds up until they lock into a common movement period (Pantaleone, 2002).

Technically, entrainment in physics refers to the frequency locking of two oscillating bodies, i.e., bodies that can move in stable periodic or rhythmic cycles. They have different frequencies or movement periods when moving independently, but when interacting they assume a common period. Incidentally, Huygens’ pendulums assumed a common period 180° out of phase, which he humorously called “odd sympathy.” It is now known that entrainment can occur in various phase relationships of the movement onsets of the oscillating bodies—often one can observe a stable phase relationship between the two bodies. A stable phase relationship is achieved when both bodies start and stop their movement period at the same time. However, this is not a necessary prerequisite for entrainment to occur. The deciding factor for entrainment is the common period of the oscillating movements of the two bodies. This phenomenon is of considerable importance for clinical applications of rhythmic entrainment in motor rehabilitation (Kugler and Turvey, 1987; Thaut et al., 1998a,b).

Entrainment is a common phenomenon in the physical world—e.g., coupled oscillators, fluid waves, etc. Entrainment also occurs in nature, e.g., fireflies flashing their light signal and in circadian rhythms entraining to light–dark cycles within the 24-h day period (Roenneberg et al., 2003). Unfortunately, the term entrainment is often also used loosely and has been connected to many unrelated claims—usually in the context of claims for health or healing—with little or no scientific evidence, e.g., brain wave entrainment, altered states of consciousness, trance, drum circles, or binaural beat entrainment. Therefore, it is important for the clinician who follows an evidence-based intervention model to check the scientific validity for therapeutic claims (Thaut, 2005; Thaut and Hoemberg, 2014).

3 THE AUDITORY SYSTEM AND RHYTHM PERCEPTION

The ability of the auditory system to construct stable temporal templates rapidly is well known (Thaut and Kenyon, 2003). The auditory system is superbly constructed to detect temporal patterns in auditory signals with extreme precision and speed, as

required by the nature of sound as only existing in temporal vibration patterns (Moore, 2003). The auditory system is faster and more precise than the visual and tactile systems (Shelton and Kumar, 2010). Since sound waves that are most important for speech and music and other perceptual tasks are based on periodic motions that repeat themselves in regularly recurring cycles, the auditory system is also perceptually geared toward detecting and constructing rhythmic sound patterns. However, the observation of timing in the auditory system does not stop its function there. From culture and history, we know and experience every day that the auditory and the motor system have a special relationship. For example, Thaut et al. (1998a,b) demonstrated that finger and arm movements instantaneously entrain to the period of a rhythmic stimulus (e.g., metronome beat) and stay locked to the metronome frequency even when subtle tempo changes are induced into the metronome that are not consciously perceived. These findings have been confirmed by other studies (Large et al., 2002).

Two early electrophysiological studies (Paltsev and Elnor, 1967; Rossignol and Melvill Jones, 1976) also showed how sound signals and rhythmic music can prime and time muscle activation via reticulospinal pathways. The pathway connections between the auditory and the motor system—which had not been given much emphasis when compared to visual and proprioceptive systems in motor control—have been researched much more carefully in the past 20 years, ever since our discovery between 1991 and 1993 that rhythmic entrainment in human movement is possible and can be effectively applied to improve motor function in movement disorders (Thaut et al., 1992, 1993). It is now well established that the auditory system has richly distributed fiber connections to motor centers from the spinal cord upward on brain stem, subcortical, and cortical levels (Felix et al., 2011; Koziol and Budding, 2009; Schmahman and Pandya, 2006). Clinical applications based on auditory–motor connectivity will be discussed in the next section.

4 CLINICAL APPLICATIONS OF ENTRAINMENT

In a number of experiments between 1991 and 1993, Thaut and colleagues demonstrated that auditory rhythm and music can entrain the human motor system and be used to improve functional control of movement in healthy subjects and subjects with stroke (Thaut et al., 1991, 1992, 1993). This entrainment process in human movement—especially with patients with severe motor dysfunction like stroke—was previously unknown and never applied clinically. Gait patterns in hemiparetic stroke training, however, showed massive entrainment effects resulting in highly significant improvements in velocity, stride length, cadence, and stride symmetry, as well significant reductions in variability and amplitude of motor unit recruitment (i.e., muscle activation) (Thaut et al., 1993). Based on these findings we developed a standard gait training protocol—rhythmic auditory stimulation (RAS)—which proved to be very effective when compared to traditional gait therapies (Thaut et al., 2007). Immediate entrainment effects could be translated into long-term training effects over 3 weeks (Thaut et al., 1997) and 6 weeks (Thaut et al., 2007),

respectively. Patients entered the studies in the subacute stage, approximately 2 weeks post stroke. These clinical findings have been replicated by a number of other research groups substantiating the existence of rhythmic auditory–motor circuitry for entrainment (Ford et al., 2007; Roerdink et al., 2007, 2011). RAS is now recognized among the evidence-based, state of the art motor therapies for cardiovascular accidents (Hoemberg, 2013).

Of greatest importance was the finding that the injured brain can indeed access rhythmic entrainment mechanisms. These observations led to studying rhythmic motor circuits in the brain more carefully. It is now well accepted that rhythm processing and auditory–motor interactions take place in widely distributed and hierarchically organized neural networks, extending from brain stem and spinal levels to cerebellar, basal ganglia, and cortical loops (Konoike et al., 2012; Thaut, 2003). Cortico-cerebellar networks underlying rhythmic auditory entrainment have been demonstrated by Thaut et al. (2008). Differential engagement of prefrontal (Stephan et al., 2002) and primary auditory cortex areas (Tecchio et al., 2000) have been identified mediating rhythmic motor entrainment below levels of conscious perception, depending on the magnitude of the rhythmic tempo changes. Common and distinct neural substrates for different components of musical rhythm (e.g., pattern, tempo, meter) have been described in a recent study investigating the neural basis of musical rhythm perception (Thaut et al., 2014a,b,c). The involvement of basal ganglia areas via cortico-striatal loops in the perception of harmonic changes in musical cadences was recently described for the first time by Seger et al. (2013). The involvement of the basal ganglia in auditory rhythm perception has been researched by Grahn and Brett (2009) and Grahn and Rowe (2013). Interestingly a study using rhythmic entrainment with patients with cerebellar dysfunction (Molinari et al., 2007) showed that entrainment ability, even on a subliminal level, was not affected by the presence of cerebellar damage, excluding the cerebellum as the chronometric timekeeper of the brain as had been suggested in earlier research (cf. Ivry et al., 2002).

In subsequent experiments, researchers studied rhythmic entrainment in the gaits of people with PD (McIntosh et al., 1997; Miller et al., 1996; Thaut et al., 1996). Although PD presents itself with a different neuropathology and different movement dysfunctions, we also discovered for the first time with this patient group strong entrainment effects that benefited mobility, most noticeably in improvements in bradykinesia, more stable stride symmetry and stride length, and strengthening of motor unit recruitment. Long-term maintenance of improvements over 4–5 weeks was demonstrated in a later study (McIntosh et al., 1998). RAS is now recognized as state of the art mobility treatment for PD (Archibald et al., 2013; Dietz, 2013; Hoemberg, 2005).

After successful experiments entraining endogenous biological rhythms of neural gait oscillators, a new question emerged. Can rhythmic entrainment also be applied to entrain whole body movements, especially arm and hand movements that are not driven by underlying biological rhythms? We found the answer by turning upper extremity movements, which are usually discrete and nonrhythmic by nature, into repetitive cyclical movement units which now could be matched to rhythmic time cues.

Our research group carried out two experiments studying hemiparetic arm reaching movements in patients with stroke. In one study, we investigated the immediate effect of rhythm on kinematic movement patterns, especially reaching trajectories, variability of movement timing, and elbow range of motion. Elbow range as well as both cyclical movement timing and smoothness of reaching trajectories improved significantly (Thaut et al., 2002). In a second study, we measured the effect of repetitive rhythmic arm training using a patterned sensory enhancement (PSE) protocol. Outcomes were assessed with the wolf motor function action test and the self-reporting motor activity log. Both measures were improved significantly in a within-subject design (Malcolm et al., 2009). The improvements were comparable in size to a parallel study we carried out using constraint induced therapy (CIT; Massie et al., 2009). We also compared trunk flexion and shoulder rotation in a discrete arm reaching versus cyclical reaching task cued by auditory rhythm. The rhythmic cyclical task reduced trunk flexion and increased shoulder and trunk rotation comparable to normal patterns, whereas in the discrete task subjects relied mostly on extended forward flexion of the trunk to reach the targets (Massie et al., 2009). Lastly, CIT significantly increased shoulder abduction, bringing the arm into a more circular outward motion, compared to pretest measures, whereas PSE decreased shoulder abduction, helping to bring the arm into a more forward trajectory. These findings might be interpreted as CIT being an excellent protocol to overcome nonuse of the paretic side, to stimulate associated brain plasticity, and increase quantity of movement, whereas auditory rhythm also addresses recovery of the quality of movement, such as increase in trunk rotation during reaching, which CIT does not facilitate. These findings have also been supported by similar findings in other research groups (Peng et al., 2011; Schneider et al., 2007; Whittall et al., 2000).

5 MECHANISMS OF ENTRAINMENT IN MOTOR CONTROL

The comprehensive effect of rhythmic entrainment on motor control raises some important theoretical questions as to the mechanisms modulating these changes. We know that firing rates of auditory neurons, triggered by auditory rhythms and music, entrain the firing patterns of motor neurons, thus driving the motor system into different frequency levels. However, that is not all. There are two additional mechanisms are of great clinical importance in regard to entrainment. The first is that auditory stimulation primes the motor system toward a state of readiness to move. Priming increases subsequent response quality.

The second, more specific aspect of entrainment refers to the changes in motor planning and motor execution it creates. Rhythmic stimuli create stable anticipatory time scales or templates. Anticipation is a critical element in improving movement quality. Rhythm provides precise anticipatory time cues for the brain to plan ahead and be ready. Furthermore, successful movement anticipation is based on foreknowledge of the duration of the cue period. We may remember that during entrainment two movement oscillators—in our case neurally based—of different periods entrain

to a common period. In auditory entrainment, the motor period entrains to the period of the auditory rhythm. Entrainment is always driven by frequency or period entrainment—that is, the common periods may or may not be in perfect phase lock (i.e., the onset of the motor response would be perfectly synchronized to the auditory beat). Beat entrainment is a commonly misunderstood concept. Entrainment is not defined by beat or phase entrainment—it is defined by period entrainment (Large et al., 2002; Nozaradan et al., 2011; Thaut and Kenyon, 2003).

Period entrainment offers the solution to why auditory rhythm also changes the spatial kinematic and dynamic force measures of muscle activation. For a while, we lacked a conceptual link to connect time cuing via rhythmic stimuli to spatiodynamic parameters of motor control, before the analysis of acceleration and velocity profiles of our subjects offered an intriguing explanation. Why is time cuing via period entrainment so helpful for the patients' overall motor control in space, time, and force? The answer is simple and complex at the same time: rhythmic cues give the brain a time constraint—they fix the duration of the movement. Foreknowledge of the duration of the movement period changes computationally everything in motor planning for the brain. Velocity and acceleration are mathematical time derivatives of movement position. We realized that, by fixating movement time through a rhythmic interval, the brain's internal timekeeper now has an additional externally triggered timekeeper with a precise reference interval, a continuous time reference. This time period presents time information to the brain at any stage of the movement. The brain knows at any point of the movement how much time has elapsed and how much time is left, enabling better mapping and scaling of optimal velocity and acceleration parameters across the movement interval. The brain tries to optimize the movement now by matching it to the given template. This process will result not only in changes in movement speed but also in smoother and less variable movement trajectories and muscle recruitment. We can conclude that auditory rhythm, via physiological period entrainment of the motor system, acts as a forcing function to optimize all aspects of motor control. Rhythm not only influences movement timing—time as the central coordinative unit of motor control—but also modulates patterns of muscle activation and control of movement in space (Thaut et al., 1999).

With this understanding of the underlying mechanisms of entrainment it is less important if the patients synchronize their motor responses exactly to the beat—it is important that they entrain to the rhythmic period, because the period template contains critical information to optimize motor planning and motor execution. Consequently, patients might actually move, as Huygens once worded it, in any stage of “odd sympathy” to the actual beat.

6 MORE CLINICAL APPLICATIONS OF ENTRAINMENT

Rhythmic entrainment extends beyond motor control. Speech rate control affecting intelligibility, oral motor control, articulation, voice quality, and respiratory strength could greatly benefit from rhythmic entrainment using rhythm and music. Recent

findings in aphasia rehabilitation suggest that the rhythmic component in Melodic Intonation Therapy might even be as important as the activation of intact right-hemispheric speech circuitry through singing (Stahl et al., 2011). Rate control via auditory rhythmic cues has been successfully applied to fluency disorders (e.g., stuttering, cluttering), as well improvements in intelligibility in dysarthria (Lansford et al., 2011; Pilon et al., 1998; Thaut et al., 2001; Van Nueffelen et al., 2009, 2010). NMT has an excellent standardized repertoire of evidence-based techniques for speech and language training based on rhythmic entrainment mechanisms (Thaut and Hoemberg, 2014).

Lastly, the potential of temporal entrainment of cognitive function has only recently emerged as an important driver of therapeutic change. NMT techniques in cognitive rehabilitation are relying to a large extent on the role of timing in music and rhythm. For example, in the context of new research findings the time structure of music and rhythm might be considered an effective mnemonic device to improve memory functions (Kern et al., 2007; Thaut et al., 2014a,b,c; Wallace, 1994).

7 OTHER MUSICAL ELEMENTS AS THERAPEUTIC DRIVERS

Kindled by the discovery of the clinical effects of rhythmic entrainment experimenters drawing on new research concepts began to examine other musical elements for their usefulness in rehabilitation. Especially in speech/language functions and cognitive functions, additional mechanisms in music perception beyond rhythm might be needed to address therapeutic needs.

In the area of speech and language therapies, two shared functions became important from a biomedical perspective: (1) the acoustical, anatomical, and neural perception and production features shared between spoken language and vocalization in music; and (2) the ability of both systems to embed communicative functions in the auditory modality. In the research and clinical literature underlying NMT, five areas of therapeutic mechanisms and clinical applications have emerged:

1. *Differential neurologic processing of music and speech*: the fact that the neural circuitry for speaking and singing is partially overlapping but also partially segregated has led to applications, such as Melodic Intonation Therapy, especially in regard to expressive aphasia rehabilitation, where singing could engage undamaged speech circuitry in the hemisphere contra lateral to the damage.
2. *Commonalities between speech and vocal production in music*: there is evidence that common prosodic, acoustical, and physiological production features are enhanced in music versus speech. For example, singing creates a broader overtone spectrum and a stronger fundamental voice frequency. Prosodic elements are amplified leading to enhanced oral motor ranges, better phonemic enunciation, and enhanced voice control. Singing could enhance phonation, and

enhance respiratory control and capacity, due to longer durations in sound production. Longer sound durations are the basis for the slower pace in singing versus speech. Slower pacing might enhance voice control regarding articulation and intelligibility.

3. *Verbal and nonverbal auditory communication systems*: music and speech are two auditory communication systems that—in regard to certain structural elements—have common counterparts, for example, in regard to phonology, prosody, pragmatics, and rule-based systems of composition. For example, musical patterns can simulate communication gestures found in speech: dialogic turn taking, question/answer forms, expressive statements, repeating, simultaneous expressions, etc.
4. *Enhanced auditory perception through music*: music creates an enriched, complex auditory environment that can help enhance sound perception. There is research evidence that shows how musical training enhances auditory sensitivity, which can also translate into enhanced speech perception (Strait et al., 2012).
5. *Musical development mirrors speech and language development*: very interesting parallels have been found between musical and speech/language development in early childhood, showing that engaging in both can have mutually supportive developmental effects (Brandt et al., 2012). Verbalization through singing offers an additional mode of expression and language learning, which can be further integrated into other related activities, like playing musical instruments or dancing.

The role of music in cognitive rehabilitation emerged as the last rehabilitation domain in NMT. There are two likely reasons for this. Human neurocognition research could only fully develop once noninvasive research tools to study the human brain, such as brain imaging, became available. The first focus of these research endeavors was to study the neural bases of higher cognitive functions in humans before a clinical rehabilitative perspective could be established to develop neuroscience-based intervention paradigms. Second, the traditional view of music in therapy was very much characterized by an emphasis on emotional and social factors as therapeutic mechanisms and goals. Cognitive functions, such as attention or memory, were given much less interest in more psychotherapeutically oriented concepts (Thaut et al., 2014a). However, a growing body of recent research has demonstrated intriguing links between music as a complex auditory language and higher cognitive functions, including temporal sequencing (Conway et al., 2009), temporal order learning (Hitch et al., 1996), spatiotemporal reasoning (Sarnheim et al., 1997), auditory attention (Drake et al., 2000), visual discrimination (Feng et al., 2014), hemispatial neglect (Soto et al., 2009), auditory verbal memory (Thaut et al., 2014a,b,c), emotional adjustment (Kleinstaubler and Gurr, 2006), and executive control (Thaut et al., 2009). By linking music cognition and perception research to models of music learning—and finally linking music learning to retraining the injured brain, a new model has emerged that has allowed for the development of functional intervention techniques in the cognitive domain of NMT.

8 CONCLUSIONS

In conclusion, entrainment for therapeutic purposes has been used since the early 1990s, with strong research evidence that the periodicity of auditory rhythmic patterns could improve movement patterns in patients with movement disorders. Clinical research studies have demonstrated that auditory rhythmic cues elicit changes in motor patterns in gait and upper extremity movements. Changes in motor patterns are possibly due to priming of the motor system and anticipatory rhythmic templates in the brain that allow for optimal motor planning and execution with an external rhythmic cue. The ability of the brain to use rhythmic information to anticipate and plan the execution of a motor pattern has made rhythmic entrainment a valuable tool in motor rehabilitation. More recently, temporal rhythmic entrainment has been extended into applications in cognitive rehabilitation and speech and language rehabilitation, with initial successes indicating that mechanisms of rhythmic entrainment might prove to be an essential tools for rehabilitation in all domains.

The discovery of the clinical effectiveness of rhythmic motor entrainment also brought into focus for the first time that the structural elements of music have enormous potential in clinical applications to retrain the injured brain. As such, the discovery of entrainment was not just about the usefulness of entrainment, but more importantly served as a new vantage point for researching and understanding that the complex “language architecture” structure of music contains critical stimuli for effective brain rehabilitation. The new “clinical science” of music has been the bedrock for the development of NMT. Standardized clinical techniques were developed around clusters of research evidence to address motor, speech/language, and cognitive goals in brain rehabilitation. This treatment system constitutes historically the first medically endorsed form of music therapy.

REFERENCES

- Archibald, N., Miller, N., Rochester, L., 2013. Neurorehabilitation in Parkinson’s disease. In: Barnes, M.P., Good, D.C. (Eds.), *Handbook of Neurology*. In: *Neurological Rehabilitation*, vol. 110. Elsevier, New York, NY, pp. 435–442.
- Bell, A.E., 1947. *Christian Huygens and the Development of Science in the 17th Century*. Edward Arnold & Company, London.
- Brandt, A., Gebrian, M., Slevic, R.L., 2012. Music and early language acquisition. *Front. Psychol.* 3, 327. <http://dx.doi.org/10.3389/psyg.2012.00327>.
- Conway, C.M., Pisoni, D.B., Kronenberger, W.G., 2009. The importance of sound for cognitive sequencing abilities: the auditory scaffolding hypothesis. *Curr. Dir. Psychol. Sci.* 18, 275–279.
- Dietz, V., 2013. Gait disorders. In: Barnes, M.P., Good, D.C. (Eds.), *Handbook of Neurology*. In: *Neurological Rehabilitation*, vol. 110. Elsevier, New York, NY, pp. 133–144.
- Drake, C., Jones, M.R., Baruch, C., 2000. The development of rhythmic attending in auditory sequences: attunement, referent period, focal attending. *Cognition* 77, 251–288.

- Felix, R.A., Fridberger, A., Leijon, S., Berrebi, A.S., Magnusson, A.K., 2011. Sound rhythms are encoded by postinhibitory rebound spiking in the superior paraolivary nucleus. *J. Neurosci.* 31, 12566–12578.
- Feng, W., Stoermer, V.S., Martinez, A., McDonald, J.J., Hilyard, S.A., 2014. Sounds activate visual cortex and improve visual discrimination. *J. Neurosci.* 34, 9817–9824.
- Ford, M., Wagenaar, R., Newell, K., 2007. The effects of auditory rhythms and instruction on walking patterns in individuals post stroke. *Gait Posture* 26, 150–155.
- Garber, D., 2003. *The Cambridge History of Seventeenth-Century Philosophy*. Cambridge University Press, Cambridge, UK.
- Grahn, J.A., Brett, M., 2009. Impairment of beat-induced rhythm discrimination in Parkinson's disease. *Cortex* 45, 56–61.
- Grahn, J.A., Rowe, J.B., 2013. Finding and feeling the beat: striatal dissociations between detection and prediction of regularity. *Cereb. Cortex* 23, 913–921.
- Hallam, S., Cross, I., Thaut, M.H., 2009. *Oxford Handbook of Music Psychology*. Oxford University Press, Oxford, UK.
- Hitch, G.J., Burgess, N., Towse, J.N., Culpin, V., 1996. Temporal grouping effects in immediate recall: a working memory analysis. *Q. J. Exp. Psychol. A* 49, 116–139.
- Hoemberg, V., 2005. Evidence based medicine in neurological rehabilitation—a critical review. In: von Wild, K. (Ed.), *Re-Engineering of the Damaged Brain and Spinal Cord—Evidence Based Neurorehabilitation*. Springer, New York, NY, pp. 3–14.
- Hoemberg, V., 2013. Neurorehabilitation approaches to facilitate motor recovery. In: Barnes, M.P., Good, D.C. (Eds.), *Handbook of Clinical Neurology*, vol. 110. Elsevier, New York, NY, pp. 161–174.
- Ivry, R.B., Spencer, R.M., Zelaznik, H.N., Diedrichsen, J., 2002. The cerebellum and event timing. *Ann. N. Y. Acad. Sci.* 978, 1085–1095.
- Kern, P., Wolery, M., Aldridge, D., 2007. Use of songs to promote independence in morning greeting routines for young children with autism. *J. Autism Dev. Disord.* 37, 1264–1271.
- Kleinstaub, M., Gurr, B., 2006. Music in brain injury rehabilitation. *J. Cogn. Rehab.* 24, 4–14.
- Konoike, N., Kotozaki, Y., Miyachi, S., Miyauchi, C.M., Yomogida, Y., Akimoto, Y., Kuraoka, K., Sugiura, M., Kawashima, R., Nakamura, K., 2012. Rhythm information represented in the fronto-parieto-cerebellar motor system. *NeuroImage* 63 (1), 328–338. <http://dx.doi.org/10.1016/j.neuroimage.2012.07.002>.
- Kozioł, L.F., Budding, D.E., 2009. *Subcortical Structures and Cognition*. Springer, New York, NY.
- Kugler, P.N., Turvey, M.T., 1987. *Information, Natural Law, and the Self-Assembly of Rhythmic Movement*. Erlbaum, Hillsdale, NJ.
- Lansford, K.L., Liss, J.M., Caviness, J.N., Utianski, R.L., 2011. A cognitive-perceptual approach to conceptualizing speech intelligibility deficits and remediation practice in hypokinetic dysrthria. *Parkinsons Dis.* 2011, 150962. <http://dx.doi.org/10.4061/2011150962>.
- Large, E.W., Jones, M.R., Kelso, J.A.S., 2002. Tracking simple and complex sequences. *Psychological Research* 66, 3–17.
- Malcolm, M.P., Massie, C., Thaut, M.H., 2009. Rhythmic auditory-motor entrainment improves hemiparetic arm kinematics during reaching movements. *Top. Stroke Rehabil.* 16, 69–79.

- Massie, C., Malcolm, M., Greene, D., Thaut, M.H., 2009. Effects of constraint-induced therapy on kinematic outcomes and compensatory movement patterns: an exploratory study. *Arch. Phys. Med. Rehabil.* 90, 571–579.
- McIntosh, G.C., Brown, S.H., Rice, R.R., Thaut, M.H., 1997. Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinson's Disease. *J. Neurol. Neurosurg. Psychiatry* 62, 122–126.
- McIntosh, G.C., Rice, R.R., Hurt, C.P., Thaut, M.H., 1998. Long-term training effects of rhythmic auditory stimulation on gait in patients with Parkinson's disease. *Mov. Disord.* 13, 212.
- Miller, R.A., Thaut, M.H., McIntosh, G.C., Rice, R.R., 1996. Components of EMG symmetry and variability in Parkinsonian and healthy elderly gait. *Electroencephalogr. Clin. Neurophysiol.* 101, 1–7.
- Molinari, M., Leggio, M., Thaut, M.H., 2007. The cerebellum and neural networks for rhythmic sensorimotor synchronization in the human brain. *Cerebellum* 6, 18–23.
- Moore, B.C.J., 2003. *Psychology of Hearing*. Elsevier, New York, NY.
- Nozaradan, S., Peretz, I., Missal, M., Mouraux, A., 2011. Tagging the neuronal entrainment to beat and meter. *J. Neurosci.* 31, 10234–10240.
- Paltsev, Y.I., Elnor, A.M., 1967. Change in functional state of the segmental apparatus of the spinal cord under the influence of sound stimuli and its role in voluntary movement. *Biophysics* 12, 1219–1226.
- Pantaleone, J., 2002. Synchronization of metronomes. *Am. J. Phys.* 70, 992–1000.
- Peng, Y., Lu, T., Wang, T., Chen, Y., Liao, H., Lin, K., Tang, P., 2011. Immediate effects of therapeutic music on loaded sit-to-stand movement in children with spastic diplegia. *Gait Posture* 33, 274–278.
- Pilon, M.A., McIntosh, K., Thaut, M.H., 1998. Auditory versus visual speech timing cues as external rate control to enhance verbal intelligibility in mixed spastic-ataxic-dysarthric speakers. *Brain Inj.* 12, 793–803.
- Roenneberg, T., Daan, S., Merrow, M., 2003. The art of entrainment. *J. Biol. Rhythm.* 18, 183–194.
- Roerdink, M., Lamoth, C.J.C., Kwakkel, G., van Wieringen, P.C.W., Beek, P.J., 2007. Gait coordination after stroke: benefits of acoustically paced treadmill walking. *Phys. Ther.* 87, 1009–1022.
- Roerdink, M., Bank, P.J.M., Peper, C., Beek, P.J., 2011. Walking to the beat of different drums: practical implications for the use of acoustic rhythms in gait rehabilitation. *Gait Posture* 33, 690–694.
- Rossignol, S., Melvill Jones, G., 1976. Audiospinal influences in man studied by the H-reflex and its possible role in rhythmic movement synchronized to sound. *Electroencephalogr. Clin. Neurophysiol.* 41, 83–92.
- Sarnheim, J., Von Stein, A., Rappelsberger, P., Petsche, H., Rauscher, F.H., Shaw, G.L., 1997. Persistent patterns of brain activity: an EEG coherence study of the positive effects of music on spatial-temporal reasoning. *Neurol. Res.* 19, 107–116.
- Schmahman, J.D., Pandya, D.N., 2006. *Fiber Pathways of the Brain*. Oxford University Press, Oxford, UK.
- Schneider, S., Schoenle, P.W., Altenmueller, E., Munte, T., 2007. Using musical instruments to improve motor skill recovery following stroke. *J. Neurol.* 254, 1339–1346.
- Seger, C., Spering, B.J., Sares, A.G., Quraini, S.I., Alpeter, C., David, J., Thaut, M.H., 2013. Corticostriatal contributions to musical expectancy perception. *J. Cogn. Neurosci.* 25, 1062–1077.

- Shelton, J., Kumar, G.P., 2010. Comparison between auditory and visual single reaction time. *Neurosci. Med.* 1, 30–32.
- Soto, D., Funes, M.J., Guzman-Garcia, A., Rothstein, P., Humphreys, G.W., 2009. Pleasant music overcomes the loss of awareness in patients with visual neglect. *Proc. Natl. Acad. Sci.* 106, 6011–6016.
- Stahl, B., Kotz, S.A., Henseler, I., Turner, R., Geyer, S., 2011. Rhythm in disguise: why singing may not hold the key to recovery from aphasia. *Brain* 134, 3083–3093.
- Stephan, K.M., Thaut, M.H., Wunderlich, G., Schicks, W., Tellmann, L., Herzog, H., McIntosh, G.C., Seitz, R.J., Hoemberg, V., 2002. Conscious and subconscious sensorimotor synchronization—prefrontal cortex and the influence of awareness. *NeuroImage* 15, 345–352.
- Strait, D.L., Parbery-Clark, A., Hittner, E., Kraus, N., 2012. Musical training during early childhood enhances the neural encoding of speech in noise. *Brain Lang.* 123, 191–201.
- Tecchio, F., Salustri, C., Thaut, M.H., Pasqualetti, P., Rossini, P.M., 2000. Conscious and pre-conscious adaptation to rhythmic auditory stimuli: a magnetoencephalographic study of human brain responses. *Exp. Brain Res.* 135, 222–230.
- Thaut, M.H., 2003. Neural basis of rhythmic timing networks in the human brain. *Ann. N. Y. Acad. Sci.* 999, 364–373.
- Thaut, M.H., 2005. *Rhythm, Music, and the Brain: Scientific Foundations and Clinical Applications*. Routledge, New York, NY.
- Thaut, M.H., Hoemberg, V., 2014. *Oxford Handbook of Neurologic Music Therapy*. Oxford University Press, Oxford.
- Thaut, M.H., Kenyon, G.P., 2003. Rapid motor adaptations to subliminal frequency shifts in syncopated rhythmic sensorimotor synchronization. *Hum. Mov. Sci.* 22, 321–338.
- Thaut, M.H., Schleiffers, S., Davis, W.B., 1991. Analysis of EMG activity in biceps and triceps muscle in a gross motor task under the influence of auditory rhythm. *J. Music. Ther.* 28, 64–88.
- Thaut, M.H., McIntosh, G.C., Prassas, S.G., Rice, R.R., 1992. The effect of rhythmic auditory cuing on stride and EMG patterns in normal gait. *J. Neurol. Rehabil.* 6, 185–190.
- Thaut, M.H., McIntosh, G.C., Prassas, S.G., Rice, R.R., 1993. The effect of auditory rhythmic cuing on temporal stride and EMG patterns in hemiparetic gait of stroke patients. *J. Neurol. Rehabil.* 7, 9–16.
- Thaut, M.H., McIntosh, G.C., Rice, R.R., Miller, R.A., Rathbun, J., Brault, J.M., 1996. Rhythmic auditory stimulation in gait training with Parkinson's disease patients. *Mov. Disord.* 11, 193–200.
- Thaut, M.H., McIntosh, G.C., Rice, R.R., 1997. Rhythmic facilitation of gait training in hemiparetic stroke rehabilitation. *J. Neurol. Sci.* 151, 207–212.
- Thaut, M.H., Bin, T., Azimi-Sadjadi, M., 1998a. Rhythmic finger-tapping sequences to cosine-wave modulated metronome sequences. *Hum. Mov. Sci.* 17, 839–863.
- Thaut, M.H., Miller, R.A., Schauer, L.M., 1998b. Multiple synchronization strategies in rhythmic sensorimotor tasks: phase vs period adaptation. *Biol. Cybern.* 79, 241–250.
- Thaut, M.H., Kenyon, G.P., Schauer, M.L., McIntosh, G.C., 1999. The connection between rhythmicity and brain function. *IEEE Eng. Med. Biol. Mag.* 18, 101–108.
- Thaut, M.H., McIntosh, K., McIntosh, G.C., Hoemberg, V., 2001. Auditory rhythm enhances movement and speech motor control in patients with Parkinson's disease. *Funct. Neurol.* 16, 163–172.
- Thaut, M.H., Kenyon, G.P., Hurt, C.P., McIntosh, G.C., Hoemberg, V., 2002. Kinematic optimization of spatiotemporal patterns in paretic arm training with stroke patients. *Neuropsychologia* 40 (7), 1073–1081.

- Thaut, M.H., Leins, A., Rice, R.R., Kenyon, G.P., Argstatter, H., Fetter, M., Bolay, V., 2007. Rhythmic auditory stimulation improves gait more than NDT/Bobath training in near ambulatory patients early post stroke: a single-blind randomized control trial. *Neurorehabil. Neural Repair* 21, 455–459.
- Thaut, M.H., Stephan, K.M., Wunderlich, G., Schicks, W., Tellmann, L., Herzog, H., McIntosh, G.C., Seitz, R.J., Hoemberg, V., 2008. Distinct cortico-cerebellar activations in rhythmic auditory motor synchronization. *Cortex* 45, 44–53.
- Thaut, M.H., Gardiner, J.C., Holmberg, D., Horwitz, J., Kent, L., Andrews, G., Donelan, B., McIntosh, G.C., 2009. Neurologic music therapy improves executive function and emotional adjustment in traumatic brain injury rehabilitation. *Ann. N. Y. Acad. Sci.* 1169, 406–416.
- Thaut, M.H., McIntosh, G.C., Hoemberg, V., 2014a. Neurologic music therapy: from social science to neuroscience. In: Thaut, M.H., Hoemberg, V. (Eds.), *Oxford Handbook of Neurologic Music Therapy*. Oxford University Press, Oxford, UK, pp. 1–6.
- Thaut, M.H., Peterson, D.A., McIntosh, G.C., Hoemberg, V., 2014b. Music mnemonics aid verbal memory and induce learning-related brain plasticity in multiple sclerosis. *Front. Hum. Neurosci.* 8, 395. <http://dx.doi.org/10.3389/fnhum.2014.00395>.
- Thaut, M.H., Trimarchi, D., Parsons, L.M., 2014c. Human brain basis of musical rhythm perception: common and distinct neural substrates for different rhythmic components. *Brain Sci.* 4, 428–452.
- Van Nueffelen, G., De Bodt, M., Wuyts, F., Van de Heyning, P., 2009. Effect of rate control on speech rate and intelligibility of dysarthric speech. *Folia Phoniatri. Logop.* 61, 69–75.
- Van Nueffelen, G., De Bodt, M., Vanderwegen, J., Van de Heyning, P., Wuyts, F., 2010. Effect of rate control on speech production and intelligibility in dysarthria. *Folia Phoniatri. Logop.* 62, 110–119.
- Wallace, W.T., 1994. Memory for music: effect of melody on recall of text. *J. Exp. Psychol. Learn. Mem. Cogn.* 20, 1471–1485.
- Whitall, J., McCombe Waller, S., Silver, K.H., Macko, R.F., 2000. Repetitive bilateral arm training with rhythmic auditory cuing improves motor function in chronic hemiparetic stroke. *Stroke* 31, 2390–2395.