



Managing Dopa Induced Involuntary Movements with Neurologic Music Therapy



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Abstract

Parkinson disease is neuro-degenerative movement disorder which progress slowly over time and affects a person's activity of daily living. The cause and cure has not been found yet. There are some treatments available, which can slow down the progression of the disease by countering the symptoms. Long-term use of medications results in involuntary movements, which becomes a problem for the person as well as for the clinician as the medication cannot be taken off. In the recent times a new rehabilitation discipline known as Neurologic Music Therapy has shown significant improvement in the Parkinson's disease symptoms. This paper provides a review of Parkinson's disease and the Neurologic Music Therapy techniques used in Parkinson's disease. The paper also attempts to provide the management of medication induced involuntary movements in Parkinson's disease by using Neurologic Music Therapy.

Keywords: Substantia nigra; Dopamine; Neurologic music therapy; Pattern sensory enhancement; Rhythmic auditory stimulation; Therapeutic instrumental music performance

"Music can make you move.... It can initiate movement... Music can make you dance... It can make patterns of movements... That is the power of music."

-Anand KS

Introduction to Parkinson's Disease

Parkinson's disease is a degenerative condition of the central nervous system, which majorly affects the motor system. The condition progresses slowly over time causing symptoms like tremors, rigidity, slowness of movement and difficulty in walking in the beginning and dementia follows along with these symptoms in the advanced stages as the disease progresses. There are four cardinal motor symptoms in Parkinson's disease, which are tremor, rigidity, bradykinesia and gait instability. There is no cure for Parkinson's disease but certain treatments are available which slows down the progression of the disease by countering the symptoms [1]. There is also surgical management of implanting electrode for deep brain stimulation, which reduce these motor symptoms. However the underlying cause of Parkinson's disease is not well understood.

Mechanism of Parkinson's Disease

Parkinson's disease (PD) is a degenerative neurological condition that progresses over time due to the degeneration

of a part of the brain called Substantia Nigra, that produces dopaminergic neurons. Substantia Nigra consists of two parts Pars Reticulata and Pars Compacta. These parts constitute to the direct and indirect pathways of movements. Loss of dopamine neurons due to Substantia Nigra degeneration is one of the major pathological sign of PD [2]. Neurons in Substantia Nigra release dopamine neurotransmitters, which are excitatory in nature and they excite neurons in Dorsal Striatum, which on receiving input from Substantia Nigra release gamma amino butyric acid (GABA) neurotransmitters which are inhibitory in nature, thus sends inhibitory command to the internal Globus Pallidus (GPi) or Pars Reticulata and further to the thalamus which initiates the movement [3]. Pars Compacta plays a major role by stimulating striatum and constitutes to the indirect pathway of movement. It plays the most prominent function in motor control [4]. Thus the role of Substantia Nigra remains indirect in motor control and it can be observed that direct electrical stimulation of Substantia Nigra does not result in a motor response. This is the reason that while modeling basal

ganglia circuits or the motor control system, the Substantia Nigra should be considered as hidden layer.

Consider this Substantia Nigra like a tap on a barrel of beer. When you want to have beer you open the tap and fill your mug with beer. Now consider this that because of some cause this tap broke and the beer is just flowing down and you cannot stop it, besides just watching it flowing on the floor and getting wasted. This is the kind of mechanism that underlies in initiation of our movements like that of rotation of the lever of tap where when the required task is done and the goal is achieved like that of when the mug is filled, you close the tap again by rotating the lever. Now what happens in Parkinson Disease is that this tap stops working and does not close down. So this Substantia Nigra works like a 'on and off' switch, which switch on the movement and stop it when the task is done.

As this Substantia Nigra starts to degenerate and dopamine production decreases it causes involuntary movements as the Pars Compacta becomes unable to send enough signals to striatum to produce enough inhibitory signals required for inhibition of a movement. Ultimately, this causes the cardinal symptoms of Parkinson's disease.

Levodopa/Carbidopa in the Management of Parkinson's Disease

There are various medications available to manage the symptoms of PD. But the combination of Levodopa and Carbidopa is widely used for PD's management because of its better response over other drugs.

Levodopa (L-DOPA) is the oldest treatment available for PD which available now for more than 40 years. Levodopa gets converted into dopamine by dopa decarboxylase. Furthermore, it release and increases the concentration of dopamine in the Substantia Nigra and counters the motor symptoms [5]. It is usually 5-10% of levodopa, which crosses the blood-brain barrier and reaches the targeted area in the brain. The remaining 90-95% of levodopa is usually metabolized in the peripheral system causing side effects like nausea, arrhythmias, hypotension, dyskinesia, joint stiffness and others.

In order to counter some of these side effects and to increase the effectiveness of Levodopa, another drug called Carbidopa is mostly given in combination with L-DOPA. Carbidopa inhibits the metabolism of L-DOPA in the peripheral system, which allows more proportion of L-DOPA to reach the brain to the targeted area instead of L-DOPA alone, which in turn becomes much more effective than L-DOPA alone.

Long-term use of these drugs leads to development of motor complication called Dyskinesia and some other involuntary movements. This indeed becomes a problem in clinical neurosciences while managing PD. This also becomes the reason to keep the L-DOPA dose as low as possible and considering other dopaminergic agonists. But as the disease progresses, the neurons

continue to die and all these medications becomes less and less effective and the condition become more and more complicated [6]. Thus other therapies are generally considered along with medications.

"Music is alive... Music shares grounds with the ultimate Circadian Rhythm... the element of life... Music can take control over your autonomic nervous system..."

-Harshdeep Singh

Why Neurologic Music Therapy?

Music has long been a part of every culture known to exist on this planet. It is the language of nature. It is the story of silence. Music as a medicine has long been known to exist in the world of tribes practice as a healing ritual [7] long before the industries have started to produce it for recreation.

Moreover music has tremendous effects on the motor system. It is discovered that listening to music results in dopamine release [8]. Now considering our switch or the tap on beer barrel, which is impaired in Parkinson's disease, music can surely be of help. As the pathological result of loss of dopamine in PD, music can be used to release dopamine. Thus music bears high potential for a therapeutic purpose.

Neurological music therapy (NMT) is the standardized paradigms taken out of music therapy, which are empirically evidential by pure scientific methods. Thus, NMT uses such standardized techniques as interventions, which can be incorporated in the medical settings being based on scientific evidence [9]. The techniques used in NMT helps increasing the brain plasticity [10] and provide the therapeutic application of music to sensory, motor and motor networks, which are dysfunctional because of neurological conditions.

This paper focuses on some of the NMT's techniques, which are used widely for Parkinson's diseases' motor symptoms. The evidence from various studies show promising result in improved motor symptoms of PD. People with PD have shown to improve on many aspects though NMT. The next three sections of this paper contain the general views of techniques used in NMT. These techniques are used in clinical settings to improve PD symptoms and other problems associated with PD.

Rhythmic Auditory Stimulation (RAS) for Gait Instability

Rhythmic Auditory Stimulation (RAS) is a technique based on purely neuro-rehabilitation paradigms, which is used for the rehabilitation of movement, which are biologically rhythmic in nature by default through timing the movement [11]. Any layman can observe the rhythmic movements in everyday life. There is rhythmic movement in the heart when it beats, in the blood as it flows, in the joints as one moves and finally in the gait when one walks. Music has the biological force of being alive. Music is alive. Music is based on rhythm and harmony. Thus music shares the

grounds with Circadian Rhythm, which is the element of life. Music can take control over the autonomic nervous system, which a person is not capable of doing that.

RAS is the method that is applied using the physiological effects of auditory rhythm on the motor system to improve control of movements, which are rooted in gait patterns and otherwise are impaired in the patients of PD. RAS is thus used extensively for gait problems in PD. In RAS application where the rhythmical auditory stimuli are applied [11-13] and the patient is asked to synchronize their movement or steps with the stimulus. The basic criterion of RAS is to provide external auditory rhythmic cues. There are various kinds of cues that are used like somatosensory or visual or auditory. RAS can consist of rhythmic beats, which are basically of three kinds of categories in the methodology. First one contains of using a metronome for providing the auditory cues. Second methodology consists of using much complex stimulus like music [14]. The last one consists of using both the stimuli together.

Patients of PD show certain gait problems, which are, characterized as slow speed, feet dragging, stooped posture, short steps, short step width and length and decreased arm swing. Decreased arm swings are characterized as the main the feature of bradykinesia [15-16]. Thus RAS contains of certain parameters, which are focused in its application. These parameters are step length, walking speed, arm swings and camptocormia (vertebral posture).

Studies have showed a tremendous effect of RAS in PD. RAS has shown significant results in improving gait performances [13,17]. In particular gait speed has also been shown to increase with higher stimulation frequencies. M. Thaut has provided a full systematic review of the studies on RAS [18].

Pattern Sensory Enhancement (Pse)

Pattern Sensory Enhancement (PSE) is a technique, which uses the rhythmic cues. Here the music is used in a rhythmic, melodic, dynamical acoustic and harmonic way used as spatial and temporal cues for the movement which are not rhythmical or cyclic in nature and are more than just temporal cues alone, along with the physiological exercises. PSE was developed in order to improve the quality of movement. This technique focuses on the cyclic or rhythmic nature of gait. The concept usually focuses mostly on upper extremity interventions i.e. upper trunk, shoulder, arms, wrist, and hands. Thus it is used to structure functional movement patterns and sequences in a certain space, time and force [19]. Functional movements like reaching, grasping, sitting, standing, lifting, pushing, pulling etc. are modified in PSE.

This technique of PSE is quite similar to RAS beside just one difference, which is that PSE is more functionally operated in a multidimensional perspective than RAS as the later is based solely on time cueing where as the earlier is used for spatial, force and other kinds of cueing. PSE is mostly used in strokes or cerebral palsy patients. One of the studies, which has focused on discrete and

cyclic reaching through auditory cueing found in stroke patients, the researcher have found that the cyclic reaching in stroke survivor was immediately improved [20]. Massie et al. in a study conducted in 2012 found that motor performance requires afferent feedback to generate movements [21]. This afferent feedback is provided by auditory cues that are presented at training. Number of other studies focusing on upper limbs with metronome cueing or auditory cueing has been implemented. All the studies have led to various clinical applications of PSE.

Therapeutic Instrumental Playing/ Music Performance (Timp) In Pd

Therapeutic Instrumental Music Performance (TIMP) is the method where instrument are played as an exercise to facilitate movement patterns which are affected in PD. Music instruments are selected according to the condition and is used a therapeutic manner to improve hand movements, finger dexterity, tremors, limb coordination endurance strength and range of motion [19]. Instrumental playing facilitates both fine and gross motor skills as well as the ability to process sensory information. TIMP also entails attention skills and other executive functioning skills. Moreover it is powerful tools for enhancing response inhibition, as music training frequently requires inhibiting response to produce sequential patterns.

TIMP focuses on improving limb coordination, endurance, strength and other ranges of motions. It also improves supination, pronation, adduction, abduction, rotation, grasp and finger dexterity. The choice of the music instrument depends on the condition and the type of motor impairments. Evidence form various studies are in support for using TIMP as a neuro rehabilitation technique as it is the most promising. Besides being used as a rehabilitation technique it is a well-known fact that musical training leads to plasticity in sensory and motor areas of the brain [22]. It has also been discovered that cognitive or motor learning both of which are highly involved in music training changes the structural and functional mechanisms of brain. Musician' brains have been discovered to carry more gray matter than the non-musicians [23].

Instrumental music playing has been seen to activate widely distributed cortical and subcortical networks in the brain related to sensory-motor and cognitive functions [23,24]. In Parkinson's disease (PD) listening to music has been significantly shown to improve arm accuracy and finger movements significantly [25].

Managing Dopa Induced Involuntary Movements with Neurologic Music Therapy

Long-term use of L-Dopa/Carbidopa leads to some complication which affects a person's life dramatically. After long-term use of L-Dopa use, motor complication like dyskinesia or other involuntary movements starts to occur. Indeed dopa induced involuntary movements becomes problem for clinicians also as it gets hard to manage as these involuntary movement occurs as a side affect to the dopaminergic drugs which cannot be taken off as they show the

best response to PD treatment. Dopaminergic drugs like L-Dopa especially induce chorea or tics like movements [26].

Most of the Parkinson's disease patients who respond to L-Dopa start to develop involuntary movements based on drug program. The reason behind this is that the drug is metabolized mostly in the peripheral system and just some proportion of the drug reaches in the brain as the molecules of the drugs are too big to cross blood brain barrier. Nano-medicine is focusing majorly on making these molecules small so it can reach brain by crossing blood-brain barrier [27]. These movements first start occurring in the foot especially to the most affected side of the body. The problem is more prominent in young onset of PD. There are two majorly types involuntary movements which are induced by L-Dopa:

A. Peak-dose dyskinesia- It is regarded as the involuntary movements which starts at about an hour after taking the dose, the patients starts to make writhing twisting movements prominent in upper extremity mostly, in the head, trunk and proximal limbs. When it starts the patients is often unaware of these movements. These movements lasts for about two to three hours and then wears off the as the drugs starts wearing off, but gets worse after the patient takes another dose.

B. End-dose dystonia- As the drug starts to wear off it results in painful cramping of the toes which makes the walking more difficult. It is countered by taking another dose of L-Dopa.

Dopa induced involuntary can managed by Neurologic Music Therapy. The methodologies described above can be modified and put in practice to counter the dopa induced involuntary movements and other problems associated with it that the patients of PD on L-Dopa face.

RAS can be used in end-dose dystonia when it affects the walking. Also it can be help as the freezing starts to occur after the drug starts to wear off. Especially synchronizing along with walking on music can take care of the cramping of foot while walking at the end dose dystonia and also of the freezing, which starts to occur later on. PSE, on the other hand can be applied on a regular basis to manage the problems associated with L-Dopa. The music is strong enough to motivate a brain. Thus the application of PSE besides just being used in strokes and cerebral palsy can also be used for the affected muscles tone, which becomes a problem for the PD patients. It can also the provide relief from the rigidity which affects their activity of daily living. The person can also be cued to counter these involuntary movements faced after taking the drug, by proving the same musical stimulus later on after taking the drugs on which the person has been cued. It might turn out to be helpful in such cases. Ultimately, TIMP can be used in multidimensional ways in the case of PD and Dopa induced involuntary movements. Instruments playing to counter tremors in PD have already been established as an effective tool. It can also be used to counter dopa induced involuntary movements.

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