

## Overture for the Octogenarian – concertos and clinical practice harmonising together at last.

A concept predating democracy, music therapy was once an integral part of medicine. Historically the healing power of music was well known, advocated by intellectuals such as Plato and Pythagoras<sup>1</sup>; with its therapeutic uses documented as far back as four thousand years BC in cuneiform writings from Mesopotamia.<sup>2</sup> However with the advance of medical science, music therapy rapidly faded into the background culminating in its relegation to the chorus line of alternative therapies. Even in recent years, music therapy has been confined to playing second fiddle in the shadow of its virtuoso cousin, the prodigy promising ‘Mozart Effect’.

This infamous theory proposed in 1993 by Rauscher et al<sup>3</sup> controversially proclaimed that listening to Mozart’s Sonata for two pianos (K448) for ten minutes a day increases spatial IQ by an average of eight to nine points. Since then others have failed to match their success<sup>4</sup>; those who have been able to prove a link report the increase is only a modest 2.5 points at best.<sup>5</sup> Far from producing a new generation of geniuses, the failings of the ‘Mozart Effect’ have left clinicians sceptical to the value of music in clinical practice. However it is well documented how music directly affects reward and motivational mechanisms in the basal forebrain and in certain brainstem nuclei, actively recruiting cortical areas involved in emotional evaluation.<sup>6</sup> This harmless collection of notes exerts powerful and profound responses in millions of people every day. Surely such a powerful phenomenon has a greater medical destiny than enhancing our pencil and paper maze skills?<sup>7</sup> K448 and spatial IQ aside, it appears the full repertoire that music therapy has to offer is just being uncovered. As its voice is re-discovered, this essay discusses its value as an instrument to today’s physician in geriatric medicine.

Across the medical spectrum, music therapy is having a dramatic impact on both doctors and patients. Music is improving communication scores in autistic children in Paediatrics,<sup>8</sup> symptom scores of schizophrenics in Neurology<sup>9</sup> and increasing the speed surgeons perform mental subtraction tasks in theatre.<sup>10</sup> So what is music doing for the ever increasing geriatric population? Far from being deaf to the suffering of the elderly, music therapy is opening exciting new avenues of research and treatment options in areas of elderly care that have been neglected in the past; and its not the first time music has performed on the geriatric stage. One of the earliest musical therapy interventions in the elderly is recorded in the Old Testament of the Bible, in which David plays music to treat King Saul’s depression. ‘David would get his harp and play it. The evil spirit would leave and Saul would feel better and be alright again.’<sup>11</sup>

Over two thousand years later music can again be of assistance. Recent literature has revealed shocking holes in the rehabilitation of stroke victims; an area previously lacking in limelight. Whilst Kreisel et al 2006 make it clear that maximum progress in stroke recovery is made during rehabilitation,<sup>12</sup> a study by De Witte et al 2005 shows the majority of patients spend more than 72% of this crucial time inactive and

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isolated in their rooms.<sup>13</sup> Music therapy may offer a novel solution, facilitating both cognitive and emotional recovery in a non-invasive and inexpensive way.

After a stroke the brain undergoes dramatic, structural 'plastic' changes<sup>14</sup> that are heavily influenced by the environment. Furthermore neurological recovery can be enhanced by additional environmental stimulation instead of motor stimulation alone; and it's been shown that a variety of different stimuli such as auditory, visual and olfactory stimuli are more effective than purely concentrating on motor aspects.<sup>15</sup>

Music has been used as part of stroke recovery in speech therapy with advocates such as Belin et al<sup>16</sup>; however its full therapeutic potential only began to emerge when it was described anecdotally by Magee and Davidson<sup>17</sup>. They discovered music had an emotional analgesic effect and directed negative attention away from the traumatic experience, reducing anxiety and helping the patient cope with the emotional stress. Music's role in stroke rehabilitation was further increased when Ayotte et al<sup>18</sup> showed that the parts of the brain supplied by the middle cerebral artery were activated by music. This led Sarkamo et al<sup>19</sup> to theorise that in someone who has suffered a middle cerebral artery stroke, music would stimulate the part of the brain that had suffered the lesion as well as the opposite side of the brain, speeding up neurological recovery. They also took into account research by Kriesal, who found post stroke the opposite side of the brain is subject to greater adaptability<sup>12</sup>, and hypothesised stimulation to this side by music this would enhance overall neurological recovery. Their findings recently released in 'Brain'<sup>19</sup> strongly support their theories and showed that patients who listened to their favourite music for one to two hours a day had a greater improvement in verbal memory and attention than patients who did not. Exposed patients also experienced less depression and fewer moments of confusion than patients with no additional therapy.

That such a simple intervention could have such positive results is astounding, but what are the neural pathways that music has an influence on? There are many theories to explain the different neurological affects music has. Thompson et al propose the 'Arousal and Mood Hypothesis' which states that any enjoyable stimulus like listening to favourite music has a positive effect on mood and arousal, and its these changes that lead to improved cognitive performance<sup>20</sup>. Functional neuro-imaging studies have pieced together the complicated pathways listening to music activates. A vast interconnected system is uncovered consisting of sub cortical and cortical brain regions including the ventral striatum, the nucleus accumbens (NAc), amygdala, insula, hippocampus, hypothalamus, ventral tegmental area (VTA), anterior cingulate and the orbito-frontal cortex<sup>21,22</sup>. The dopamine producing VTA has extensive connections to the limbic system, in particular to the locus ceruleus, amygdala, hippocampus, prefrontal cortex and anterior cingulate<sup>23</sup>; which is thought to be a major factor in mediating the emotional response to music. Music's ability to increase arousal is thought to be due to connections between the locus ceruleus and the hypothalamus whilst its analgesic and pain suppressive properties can be attributed to a collaboration between the ventral tegmental area and the nucleus accumbens which block nociceptive stimuli.<sup>24</sup> Increasing the dopamine level in the human brain has been shown to significantly increase alertness, attention, speed of processing and memory<sup>25</sup>. While this dopamine increase occurs in animal brains as a direct result of listening to music it has yet to be proven in humans.<sup>26</sup> Overall music

activates an extensive conglomerate of neural systems that form a dopaminergic mesocorticolimbic system which controls our emotion, reward, memory and executive function pathways.<sup>23</sup>

While it may be premature to start composers on a 'Movement for the Middle Cerebral Artery', music induces some intriguing post stroke structural changes that may be beneficial. Kim et al's study<sup>27</sup> found that music exposure increased neurogenesis in the hippocampus, modified the expression of the glutamate receptor GluR2 in the auditory cortex and in the anterior cingulate. Angelucci et al<sup>28</sup> showed that exposure to music increased brain derived neurotrophic factor BDNF in the hippocampus and hypothalamus whilst Chikahisa et al<sup>29</sup> demonstrated an increase in the BDNF receptor, tyrosine kinase receptor b (TrkB). These plastic changes are also part of natural brain remodelling, essential in stroke recovery<sup>30</sup> and Sarkomo et al 2008 attribute their findings to music enhancing these changes in the brains of their patients given musical rehabilitation therapy.

Music does not bow out here, but has a final movement to play in the extensive symphony of stroke rehabilitation. Hommel et al 1990 have specifically isolated a further use for music, finding it a useful instrument in detecting visual neglect in patients post stroke.<sup>19</sup>

The use of music in stroke rehabilitation is an exciting and intriguing new area of research and treatment. However this impressive use is simply the first act. In stroke patients music deals with the aftermath, improving cognitive and emotional progress; but can it influence known pathology? Here we see a return of the 'Mozart Effect' which is finding a new audience and clinical application in epileptics.

The risk of developing epilepsy increases with age<sup>31</sup>. In the frail elderly it can have life threatening consequences, making epilepsy a particularly burdensome condition. It is here Mozart's Sonata for two pianos K448 makes a dazzling return. In a study of twenty nine patients, all with focal discharges or bursts of generalised spike or wave complexes, Hughes et al 1998 found that twenty three showed a significant decrease in epileptiform activity after listening to the sonata<sup>31</sup>. Patients unconscious with status epilepticus showed spectacular improvement; In two, continuous bilateral spike and wave complexes were recorded 90-100% of the time, which dramatically reduced to 50% five minutes after the sonata started playing. In one male, ictal patterns were recorded 62% of the time; once the sonata began they dropped to 21%. The fact that these patients were unconscious during the sonata shows that something more than plain appreciation of the duet is going on. Encouraged by their success Hughes et al extended their investigation to look at more long-term effects, with equally exciting results. In 1999 they played the D major duet once every waking hour to an eight year old girl with Lennox-Gastaut Syndrome, a notoriously difficult form of epilepsy to control. By the time the day was over, the number of fits had drastically decreased from nine in the first four hours to just one in the last four. The duration of the fits had nearly halved, lasting an average of 178 seconds compared to the previous 318.<sup>32</sup> Some investigations into the sonata have been carried out to try and unlock its neuroleptic properties with limited success. A study in healthy volunteers showed listening to the complex duet enhanced the synchrony of firing pattern in the right frontal and left temporoparietal areas.<sup>33</sup> Another showed increased beta spectrum power on the electroencephalogram in these areas.<sup>34</sup>

However, it is still unknown whether these changes are responsible for the remarkable therapeutic effect the sonata induces in epileptic patients. Other pieces have similar properties and it is an area of considerable interest. With compositions such as Mozart's Piano Concerto no 23 in A major K488 looking to follow K448's success,<sup>35</sup> clinicians are building up a formidable repertoire in contrapuntal complimentary therapy.

In what maybe its most exciting clinical application yet, music is making its debut in the field of Alzheimer's. An article featured in the Lancet in 2001, documented the astonishing findings that playing music while interviewing dementia patients aided recall of personal facts.<sup>36</sup> The results showed a significant increase in all types of memory, with participants recalling the remote past easier than the present (88% of the time compared to 48%). The study lead authors to conclude that music (they recommended Vivaldi's Four Seasons') should be played to all dementia patients during interview, and it should actively be included in their daily activities. Similar reports have been published in medical literature with the most interesting being published in 'Geriatric Nursing' hailing music as not just an interventional therapy but also as a means of communication and facilitating social interaction. The study carried out by Sambandon et al<sup>37</sup> showed patients increased their interactions with others through words and gestures and exhibited more social and animated behaviour after the music sessions. Their findings echo the results of Pollack and Namazi<sup>38</sup>, and support the findings of Olderog-Millard and Smith who found group singing decreased agitation and promoted functional social behaviour.<sup>39</sup> Sambandon et al conclude with the use of music therapy in facilitating communication and its use as an emotional trigger of memories. They also demonstrate the ease with which it can be implemented by less skilled care givers at little financial cost. The use of music to reach emotions and memories that have been thought lost is an idea some have elaborated on. In his report on to the U.S Senate's Special Committee on Ageing, Sacks described the memory loss associated with Alzheimer's as 'not an actual loss but a loss of access – and music above all can provide the key for opening the door to the past, a door not only to specific moods and memories but to the entire thought structure and personality of the past'.<sup>40</sup>

With current efforts focused on music's effects in Alzheimer patients an unexpected discovery has been made. Some Alzheimer patients appear to have their musical memory spared. A remarkable case study presented by Crystal et al<sup>41</sup> describes an eighty two year old patient who had trained and worked as a professional musician. Her piano playing ability remained with her throughout the course of her Alzheimer's until the very final stages. Others have reported similar patients manifesting similar memory traits, even in amateur musicians and people with only a recreational familiarity with music. Two such authors, Cuddy and Duffin<sup>42</sup> concluded that their findings are reproducible in other patients, only our current assessment methods are inadequate in detecting remaining musicality.

The choice of Vivaldi's Four Seasons in the study carried out by Valentine mentioned earlier is interesting. The effect of that particular piece on the human brain in healthy elderly volunteers was unknown at the time of the study. However recently it has emerged that listening to 'Spring' on a regular basis improves cognitive performance and memory in healthy elderly adults.<sup>43</sup> The authors attribute these results to the famous nature of the piece and the cultural familiarity the

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average lay person has with the piece leading to a positive response improving cognitive skills, an interpretation that fits in well with Thompson et al's 2001 'Arousal and Mood Hypothesis'.<sup>20</sup>

One therapy that's proving effective in the early stages of Alzheimer's is hormone therapy involving oestrogens.<sup>44</sup> It has also been shown that hormones can affect neurological systems, high levels of cortisol are known to damage neurons and oestrogen and testosterone play important roles in the regeneration, repair and protection of neurons.<sup>45</sup> Oestrogen regulates brain derived neurotrophic factor (BDNF) and suppresses amyloid beta production and testosterone elevates nerve growth factors which decrease amyloid beta levels. With this hormonal influence in mind, Japanese researchers Fukui and Toyoshima recently proposed the hypothesis that music can regenerate and repair cerebral nerves by adjusting the secretion of steroid hormones.<sup>44</sup> As they have yet to carry out any clinical research, both the medical and musical world will have to wait to see if art can succeed where science has so far failed.

The opposite problem has arisen in another aspect of elderly care. Music therapy has long been a part in caring for terminal elderly patients in hospices. However an unexpected and unexplainable phenomenon is arising. Studies such as the one carried out by Hilliard in 2004 show that patients receiving music therapy live significantly longer than those who do not.<sup>46</sup> There are many studies documenting similar results and as yet no thorough explanation has been offered. It also begs the question, with medical science being able to offer patients so little at the end of their lives aside from pain relief, why isn't music therapy an inexpensive successful alternative not available in all hospices and care homes?

So far this essay has focused on music's effect on the mind. What physiological effects does music have on the human body and how can they be used to benefit the elderly?

Music has always been associated with the theatre but it is now the operating theatre where music is taking centre stage. 1998 saw the debut of the analgesia sparing properties of music hitting the literature. A study by Koch et al 1998 showed patients listening to their favourite music required significantly less propofol to achieve the same level of sedation as control patients. Their analgesic requirements also decreased, needing 44% less opioids than controls<sup>47</sup>. These remarkable findings have been attributed to the 'Gate Control Theory of Pain' and music's biochemical influence generating an anxiolytic affect. In the 'Gate Control Theory' the perception of pain is controlled by the strength of the sensory input. Interestingly it is thought the pain and auditory pathways cancel each other out<sup>48</sup>, and the authors link the activation of the auditory cortex with the blocking of nociceptive stimuli. As mentioned earlier in the essay, the connections between the ventral tegmental area and the nucleus accumbens both of which are activated by music may play a role in blocking such stimuli. Neuroanatomy aside, the potential benefit to the elderly of such an idea is staggering. Many elderly patients are not considered for surgery as the stress of going under anaesthesia is considered too great. Although at the moment we are still struggling to hit the correct notes, we get glimpses of the melody which offers the possibility that in the future the quality of life of elderly patients may be significantly improved, as music makes vital surgical procedures viable.

Koch et al 1998 mention changes in endorphin levels in response to music, however the full neuroendocrine nocturne does not end on such an imperfect cadence. A study by Conrad et al 2007 shows a selection of slow movements from Mozart's piano sonatas causes a significant decrease in IL6 production and a marked increase in growth hormone secretion<sup>49</sup>. IL6 is thought to be an important activator in the adrenocortical and sympathoadrenal axis<sup>50</sup>. Music's reduction of IL6 secretion is thought to be one of the main stress relief mechanisms and has an important anti hypertensive effect. Regular listening may improve blood pressure, giving music therapy an important role in alternative therapy for cardiovascular disease. This could be exceptionally beneficial to the elderly, many of whom are victims of polypharmacology taking numerous medications and still suffering poorly controlled blood pressure. In a similar vein, Emery et al 2003 have found music to be beneficial in the treatment of coronary artery disease.<sup>51</sup> Cardiovascular disease is the main killer of the elderly that costs the government billions of pounds each year; an inexpensive anxiolytic and anti hypertensive complimentary therapy is urgently needed. Has it been hiding in the performing arts, recreation and religion all this time?

The increase in growth hormone leads to less clinical but equally intriguing possibilities. Research shows a definite link between neuroendocrine and immune systems<sup>52</sup>. It has been suggested that the increase in growth hormone secretion influenced by music inhibits fas-induced apoptosis in activated B and T lymphocytes<sup>53</sup>. Both the declining release of growth hormone and the decline of the immune system are well documented in the elderly and associated with the ageing process<sup>54</sup>. Could music play a part in defeating time and holding off ageing? An unlikely concept, but it does throw up interesting and as yet unanswered questions.

Music is immortal; as long as we exist music will thrive. So do its cellular benefits stretch to longevity? Unfortunately this is where current understanding plays out and speculation takes over. Amongst those studying longevity a question is emerging. Why do symphonic conductors generally live so long? No doubt their profession involves a high degree of cognitive processing and requires mental and physical coordination potentially continuing well beyond retirement age, but so do other jobs. A MetLife study followed 437 conductors from 1956 until 1975 during which 118 of them had passed away. The study found that 20% of them had died aged 80 and above, and found the death rate amongst the group to be 38% below that of the general population. In the 50-59 age group the death rate was found to be 56% less than the rest of the population of the same age<sup>55</sup>. Although this study is open to numerous biases, such as the small sample group it does raise the question is the key to conductors longevity on the very staves they work with every day?

Whether music has a part to play in longevity has yet to be established. However it is clear that music exerts remarkable effects from which the elderly can benefit; a tune even the healthy can sing along to. Janata et al 2002 found from brain imaging studies that listening to music actively recruited bilateral, frontal, temporal and parietal neural circuits involved in attention, working memory, semantic and syntactic processing and imagery<sup>56</sup>. Their work has been extended in the last couple of years with the conclusion that regularly listening to music improves attention, creativity (Schellenberg et al)<sup>57</sup> and verbal fluency (Thompson et al)<sup>58</sup>.

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Although we are still struggling with explanations, music therapy is proving to be a valuable alternative therapy with very real effects. How a non-invasive everyday procedure such as listening to one's favourite music can have such startling clinical benefits should not be forgotten in groups such as the elderly who are extremely frail and taking numerous medications.

Can an art as fundamental and abstract as music be an effective complimentary therapy? Music may provide the missing link and be for medicine what superstring theory is to physics. Where string theory attempts to unify general relativity with quantum mechanics, music elegantly unites clinical medicine with art facilitating both healing and creativity.

As we get older we become more health conscious. Generally we change our diet, attempt to adopt healthier eating habits and try to exercise on a regular basis. While these are excellent changes to make health wise, maybe we should go a step further and think about what we are exposing our mind to. With music having such profound mental effects maybe it is time to swap Iron Maiden for the occasional Mozart sonata. There may not be a medically certified 'Aria for the Ageing' however the quest to be forever young may yet turn out to be a musical. It is clear from the literature that whatever genre of music suits your taste regular listening is the key. Finally, think twice before describing an annoying pop song as mind numbing, it may play a role in preserving your faculties in the future!

Word count: 4182

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