Chapter 5

5. DISCUSSION

Glycated haemoglobin reduced by 0.98 in yoga group, 0.42 in the music group and 0.59 in the control group at the end of six months. All three groups showed approximately double of reduction at 3 months which indicate that life style modification programs do show gradual change in HbA1c however, changes in yoga groups is higher than music and control group. A previous study has also shown similar result in HbA1c at the end of 9 months.(55) Another study done by Balaji et al had shown a larger change in HbA1c where Type II DM subjects were classified as only on Oral Hypoglycemic agents (OHA) and OHA with insulin compared to a control group.(56)

In our study FBS showed a mean change of 171.7 at the end of 3 months and 211.8 at the end of the six months in yoga group. However, this change was lesser in music group (140.7 at the end of the 3 months and 193.7 at the end of 6 months), and control group (116.8 at the end of 3 months and 164.5 at the end of 6 months). Changes in all the groups are statistically as well as clinically significant. PPBS changed by 232.9 and 265.6 in yoga group, 169.0 and 236.9 in the music group and 124.7 and 196.7 in control group at 3 months and 6 months respectively. Changes in yoga group were more but all the groups showed clinically significant changes at 3 months and 6 months. These changes in all the groups can be attributed to the fact that standard care was common for all the groups which comprised of prescribed physical activity and dietary changes. However, yoga does also show added benefits in controlling blood glucose levels. Previous studies have shown similar results,
however baseline values of subjects and duration of the yoga based intervention was different in all the studies.(37, 55, 57-58)

In this study Lipid profile showed a significant change in all the groups. TC reduced by 8.0 and 22.2,7.2 and 25.7,9.5 and 12.5 in yoga, music and control group at 3 and 6 months respectively. TGs changed by 5.9 and 71.8 in yoga group, 0.5 and 113.3 in music group , 4.3 and 98.4 in control group at the end of 3 and 6 months. LDL reduced by 8.3 and 13.7 in yoga group , 9.1 and 12.1 in music group and 5.9 and 14.1 in control group whereas HDL raised by 8.2 and 17.9 in yoga group, 2.2 and 5.7 in music group and 0.78 and 1.6 in control group at the end of 3 and 6 months. There was a higher change in music group for TC and TGs at the end of 6 months while LDL has reduced better in control group after 6 months from comparatively lesser change at 3 months. These variations in changes cannot be commented with full evidence but a strict adherence to exercise program or diet restriction may influence the results. However, HDL also called as good cholesterol has increased more in yoga group as compared to other two groups. In previous studies by Nagrathna, Yang and Balaji have shown improvement of lipid profile through similar parameters in their study.(55, 58-59)

In our study there was a reduction in state anxiety by 15.3, 10.4 and 4.5 at the end of 6 months, whereas trait anxiety reduced by 5.7, 3.5 and 3.0 at 6 months with total reduction in anxiety by 21.2 in yoga group ,13.9 in music group and 7.5 in control group at the end of 6 months A previous study by Nidhi Gupta has also shown significant reduction in state and trait anxiety only in 10 days of yoga intervention.(60) Interestingly, music group has also shown good reduction in anxiety more than control group which reinstate usefulness of the music in reducing anxiety. Though music has not been studied for the reducing anxiety in Type II DM, but its efficacy has been proved in reducing anxiety in COPD, Asthma, Heart disease, mechanically ventilated patients etc.(16, 61)
In this study depression evaluated by BDI reduced by 8.6 and 14.0 in yoga group, 9.0 and 13.7 in music group and 4.0 and 8.5 in control group at the end of 3 months and 6 months. In this study yoga shows promising effect on depression in Type II DM. Yoga has not been extensively studied for reducing depression in Type II DM but its efficacy in reducing depression has been studied in other populations.

In recent past, studies have shown strong correlation between stress, anxiety, depression and pathophysiology of Type II DM,(62) which are interrelated. Control of these psychosocial comorbidities may also show better glycemic control and lipid control in Type II DM subjects by heightening subjects’ interest in engaging exercise activity, good dietary habits as well as life style changes. Music has shown equivalent efficacy in reducing depression in Type II DM. Music has been studied to reduce depression in other populations but not in DM.(30)

DQOL improved by 37.7, 9.2 and 9.4 in Yoga, Music and Control group respectively at the end of 6 months. Effect of Yoga on quality of life in diabetics has not been studied extensively however a study has shown positive effect of yoga on quality of life in diabetics with cardiac complication.(63) In our study Yoga has shown a very important benefit i.e. QOL and even at 3 months Yoga based program showed higher changes in DQOL which could not be marked in Music and Control group even at 6 months. This change is very important and requires lot of discussion. Yoga has greater potential in bringing change in outlook of diabetic subjects toward their life and it provides wholesome holistic benefits to subjects who are not provided by exercises program alone or a Music Therapy. This also redirects our attention to include yoga as an important tool in life style modification program/standard care guidelines of Type II DM. This scale has been validated in Indian population in middle and higher income groups. Our base line data shows in Table 4.1 that most of our subjects belonged to this socio economic group. Further, higher socio economic groups are
ready to accept Yoga as important life style program and Yoga may be launched as a community program to prevent and control diabetes.

Type II DM is directly related to overweight and obesity. In this study also subjects in all groups were overweight but not obese. Type II DM subjects have exhibited poor adherence to physical activity and exercise programs and difficulty in initiating life style changes based on diet and exercise. In this study, Exercise self efficacy (ESE) improved by 19.2 at 3 months and 34.6 at 6 months in yoga group, 1.1 at 3 months and 19.6 at 6 months in music group as well as 2.2 and 18.7 at 3 months and 6 months in control group. Yoga is highly promising in improving motivation of diabetic subjects to change, come out of inertia of physical inactivity and adhere to active, exercise related program with other necessary life style modifications. A previous study by Yang has also reported similar change in exercise self efficacy of diabetic subjects after yoga intervention.(58) This was one of the important assumptions of our study which gets proved that Yoga is helpful in changing people positively towards exercise based program. Further, Yoga is an important tool which can be added to exercise programs to get increased benefits without increasing intensity of resistance and aerobic exercise programs, which is one of the reason for drop out of diabetic subjects from exercise based programs.

Our subjects were overweight in all groups with comparable mean height in all groups as shown in table 4.1. Weight reduced by 5.4 and 11.3 in yoga group, 2.0 and 4.2 in music group and 2.3 in control group at the end of 3 and 6 months. BMI reduced by 2.1 and 4.4 in yoga, 0.81 and 1.6 in music as well as 0.92 and 0.95 in control group at 3 and 6 months respectively. Our study shows Yoga is effective in reducing risk factors like weight and BMI more than music and control groups. It again shows better promising effect than general life style modification programs based on exercises and dietary restriction without yoga. Previous studies by Balaji and Yang have also reported reduction in weight and BMI after Yoga based programs.(58-59)
There were significant changes in SBP and DBP by 4.3 and 1.6 in yoga group, 3.7 and 1.3 in Music group and 1.8 and 1.7 in Control Group at the end of 6 Months respectively. Our subjects were pre hypertensive and not hypertensive in all the groups and they were not on any anti-hypertensive medications. This mean change is significant and yoga has good effect on modifying important risk factor of blood pressure. Music group also showed important benefit in reducing BP which can be attributed to its relaxing effect on body as reported in previous studies.

5.1 Mechanisms of Action of Yoga in Type II Diabetes

Abnormal increase in sympathetic activity and reduction in parasympathetic activity has been associated with Type II DM. Chronic stress; anxiety and depression have already been implicated in pathogenesis as well as the after math of diabetes. Some studies have shown positive effects of yoga intervention over these negative affective states like stress and anxiety. (60)

Yoga researches provide a convincing evidence for its effectiveness over autonomic nervous system. (64) Bagchi and Wenger reported that yogic meditation induces inner relaxation of ANS without inducing sleep as well as raise immune levels in the body without exaggerating physiologic manifestation against outside stimuli, thereby providing a balance between body and outside world.(65)

Yoga has a direct effect on optimizing sympathetic hormones like cortisol and catecholamine secretion, thereby improving parasympathetic activity and reducing metabolic rate. (66) Type II DM has been correlated with stress mechanisms. Stress suppresses body’s immune system and neuro-humoral actions thereby affecting psychological state. Stress is related to elevation
of gammaglobulins in psychiatric illness, IgM, IgA and gamma globulins elevation in anxiety. It would not be wrong to state that correlation of diabetes with stress, anxiety and other psychologic factors are bidirectional and make understanding co-relational mechanisms difficult.(67-69) In such a situation, yoga proves to be promising as it helps the body to bring back to balanced state of physical and emotional congruence. A previous study has reported the influence of stress in disturbing neuroendocrine and hypothalamus function that further affects immune modulation and immune homeostasis. Another study has reported incorporation of stress in human information processing pattern (HIP).(70-71)

Kulkarni and Bera, 2009 reported HIP as a method of neuropsychology to understand role of cortex and stimulus information processing. HIP has been theorized in to five steps namely detection of stimulus, discrimination, decision, memory and reaction time. These steps succinctly explain processing of cognitive stimuli with a meaningful motor output. (70)

Its conjugation with stress can be understood as stress is result of withdrawal of attention and reduces attention sensitivity thereby influencing detrimental over health. Since the limbic system is the seat of emotion, any stressful event diverts cortical aspects of attention process to affective response. This in turn negatively affects the HPA axis. Ultimately the immune system is also negatively affected. (72) This pathophysiologic phenomenon is represented in a schematic diagram (Figure 5.1).
Abnormal HIP-PNE Model

<table>
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<tr>
<th>Stress</th>
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<td>Affects HPA &amp; endocrine functions</td>
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<td>Stress Related Psychosomatic disorders</td>
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Fig. 5.1: Schematic diagram showing pathophysiology of Stress and Stress related disorders due to abnormal HIP-PNE model

**Abbreviations:** HIP-PNE model (Human Information Processing-Psychoneuroendocrine information Model), HPA (Hypothalamo-pituitary-adrenal axis)

Yoga acts via downregulating the HPA axis which gets hyperactivated as a response to abnormal physical or psychological demand (stressor). This stressful situation affects balance between sympathetic and parasympathetic systems by release of increased cortisol and catecholamines. This response is classic ‘fight or flight’ syndrome which is encountered by hypermobilization of energy needed to combat the stressor. This constant state of hyper vigilance resulting from repeated firing of HPA axis leads to dysregulation of normal body system leading to stressogenic diseases like diabetes, depression, obesity and cardio vascular diseases. Yoga attenuates this stress cascade by reducing the perception of stress. Yoga decreases physiologic manifestations by reducing heart rate, blood pressure and respiratory rate.(73-74) A study by Smith et al showed increased pain tolerance and lowered pain related brain activity during MRI in yoga practioners.(75) Tooley et al found significantly higher
plasma melatonin levels in yoga meditators. (76) Harinath et al found increased melatonin, improved psychological and cardio respiratory profiles in yoga practitioners after 3 months of practice. (77)

Reduction of cardiovascular risk factors in diabetes is a hallmark of successful diabetes management. (78-80) Mechanism of action of Yoga can be hypothesized under two pathways: first, action of yoga by vagal stimulation and second, by parasympathetic activation and HPA axis modification. (24) First mechanism explains Yoga’s action through vagal stimulation by improving baroreflex sensitivity, reducing inflammatory cytokines, and thereby reducing blood pressure and resting heart rate. (24, 78, 81-83) It improves endothelial function and reduces risks for cardiovascular diseases in Type II DM. (24)

Second postulated mechanism of action of yoga is through parasympathetic activation and associated anti stress mechanisms. It reduces perceived stress and HPA axis activation, thereby improving overall metabolic and psychologic profiles, increasing insulin sensitivity, and improving glucose tolerance and lipid metabolism. (24) These pathways are shown in Figure 5.2.
Fig. 5.2: Postulated pathways of Yoga benefits in reducing Cardiovascular risk factors in pathogenesis of Type II DM through autonomic nervous system.

**Yoga Intervention**

- **Parasympathetic activation**
  - 1. Reduced inflammatory cytokines
  - 2. Reduced heart rate and blood pressure
  - **Enhanced metabolic and psychologic profiles**
    - Increased insulin sensitivity
    - Increased glucose tolerance
    - Improved lipid profile
    - Improved mood, anxiety, depression

- 1. Reduced Stress perception
- 2. Reduced activation of sympatho adrenal system and HPA axis

- 1. Reduced oxidative stress
- 2. Improved endothelial functions
Stress is a root of diseases. (84) Figure 5.3 portrays the pathophysiologic cascade of stress and disease. Through constant deregulation of HPA axis and the sympatheic nervous system, stress keeps the entire mechanism in chaos with dysregulation of hormones like Cortisol, catecholamines etc. Their increased stimulation over a period becomes causative of disease like Type II diabetes. Yoga acts in an opposite manner by bringing balance to both the
autonomic nervous system and the HPA axis. It reduces secretions of cortisol, catecholamines, inflammatory cytokines, rennin and anti-inflammatory factors.(85) A previous study has revealed preponderance of alpha waves in yogis recorded through EEG. Physiology of neural plasticity is a great discovery which has provided the basis for understanding rehabilitation science and the regaining of lost functions after neurologic insult. The ability of neural structures to repair their functions, reorganize structures through flexibility in neural structure, is known as neural plasticity. It mainly comprises developmental, experience related and regeneration related. Yoga asanas and yogic practices involve both motor movements and sensory experiences. Thus, it may be hypothesized that yogic practices utilize neural plasticity to bring about sustained changes in structure and function of the brain. Although neural connections and structures are more dependent on genetics and development, experience related neural plasticity seem to play a greater role in reshaping neural structures. These theoretical considerations may explain how pathophysiology of Type II DM and regeneration of beta cells in pancreas may be positively affected by Yoga.(35)

Yoga practice is directly related to improved insulin sensitivity to glucose signals in Type II DM. It attenuates the negative relationship between factors causing insulin resistance like obesity, increased waist circumference, dyslipidemia etc.(86) Yoga also improves sensitivity of beta cells of pancreas to glucose signals. Manjunatha et al have stated that there is reduction in brisk release of insulin when glucose level tends to fall whereas there is increased insulin release when glucose tends to rise in blood.(87) This mechanism gets support from a previous study of Sahay who observed a fall in fasting insulin level when glucose level is at minimum level. Yoga optimizes insulin secretion as per bodily requirement through its neuro-endocrinal effects and there by bringing normalcy to the Insulin/Glucose
ratio which is suggestive of better peripheral utilization of Insulin and reduced insulin resistance. (3)

5.2 Possible Benefits of Yoga on Immune System- Emerging Hypotheses

In response to stress, activation of Hypothalamo-Pituitary-adrenal Axis (HPA) results in secretion of Corticotrophin-Releasing Factor (CRF) from hypothalamus. CRF stimulates the secretion of ACTH from pituitary, which further activates the adrenal glands to produce glucocorticoids, which are powerful immune regulators. The effects of glucocorticoids on cellular and humoral immune responses is quite complex. Although the overall effect of glucocorticoids on immune responses at the cellular level is immunosuppressive, this effect may result from suppression of many stimulatory components of immune cascade and stimulation of some immunosuppressive or anti-inflammatory elements. The relatively greater sensitivity of components of cellular immunity to glucocorticoid suppression tends to shift immune response from a cellular to humoral pattern during stress.(88-89)

No well designed experimental study has been reported concerning the effects of yoga on diabetics’ immune systems. However, studies have reported the efficacy of yoga in different populations, especially cancer patients.(64) Findings of these studies can be extrapolated to diabetes and immunology because some of the pathways of its mechanism of action are similar. A study by Ronson reported allostatic load as a cause of dysregulation of immune system in cancer patients due to dysfunction of the HPA axis as a result of the stress of oncologic pathophysiology. Although that study concerned cancer patients, dysregulation of HPA axis has been reported by many authors as cause of co-morbidities in Diabetics. (90)
There was decrease in natural killer cells in advanced breast cancer patients following yoga practice as reported by author which is a predictor of survival. (67) Recent studies reported that Relaxation elicitation, particularly after long-term practice, may evoke health benefits by improving mitochondrial energy production and utilization and thus promoting mitochondrial resiliency through upregulation of ATPase and insulin function. Mitochondrial resiliency might also be promoted by Relaxation induced downregulation of NF-κB-associated upstream and downstream targets that mitigates stress. NF-κB pathway genes are known to have a prominent role in inflammation, diabetes, stress, trauma and cancer, which were suppressed after relaxation response elicitation. (68, 91)

In a study by SuQu et al, a yoga program had a rapid and significantly greater effect on gene expression in peripheral blood mononuclear cells (PBMCs) compared to the control group who were given only walking exercise with relaxing music. They suggested that gene expression alteration may be the basis for long term higher level health effects. (71) Another study reported increase in cortisol level as a stress marker in examinees but this rise was less in the group of examinee who practiced yoga. Further, the yoga group showed attenuation of increase in cortisol due to examination stress which was attributed to relaxing effects of yoga on mind, in turn reducing stimulus to hypothalamus and anterior pituitary there by reducing secretion of cortisol. This study also reported mean plasma IL-4 rise and serum IFN-γ decrease with examination stress. Decrease in serum IFN-γ was significant in control group and non-significant in yoga group. Decrease in serum IFN-γ is a marker of reduced cellular immunity. This study found yoga to exert a buffering effect on cellular immunity. (92) It was conducted on a group of students with perceived examination-stress, however pathways of stress have been same as in diabetics therefore, the finding is relevant to be discussed here.
5.3 Possible Mechanisms of Action of Music Therapy in Type II DM

Evaluation of anxiety and depression is not common in diagnosed diabetics whereas research studies reveal that diabetics are twice at risk of suffering from anxiety and depression than general population. Undiagnosed anxiety and depression leads to poor clinical outcomes even if anti diabetes treatment is in right direction and glycemic control is good.(93)

Psychological entities like chronic stress, anxiety and depression can not be neglected as it not only affects Health related quality of life (HRQOL) but also has negative impact on psycho-neuro-endocrine and immune systems. It activates hypothalamic-pituitary-adrenal axis (HPA), sympathetic system and increases inflammatory reactions, platelet aggregation, thereby reducing insulin sensitivity, poor glycemic control and increasing cardiovascular risk factors as shown in Fig.5.4.(94-95)

![Diagram](image)

Fig.5.4: shows negative effects of stress and its effect on sympathetic system
These subjects are ought to fall prey to bad life style habits like sedentary life, inactivity, smoking and drinking and high fat diet which further compromises clinical outcomes in DM. It is completely evident that anxiety and depression are alarming situations in DM and how to manage these co-morbidities are a matter of brainstorm and research. Diabetes subjects are already laden with series of drugs and further addition of anti-depressants and anxiolytics may not be reasonable at initial stages. These drugs have their own side effects which may further compromise activity level of subjects due to its sedative side effects. When such unclear solution arises then looking back to published research with similar outcomes may be one scientific way to find rationale solution to the question. (96)

Music has been used for centuries to promote relaxation and alleviate anxiety and pain. Music is older than mankind and it has its presence in every religion and divine books. There is special mention of music as a method of healing in Vedas. In modern medicine music has been used as a therapy in 1800s. In 1990, Thaut proposed that music stimuli have biological effects on human behavior by engaging specific brain functions involved in memory, learning, and multiple motivational and emotional states. Music affects right cerebral hemisphere whereas left brain plays as an analyzer by interpretation of musical effects. Music is an auditory perception with its deep effects in brain as it affects central auditory center in temporal lobe which then recruits and signals thalamus, midbrain, pons, amygdale and hypothalamus. (97) Weeks 1991 elucidated that music therapy is a powerful tool especially for treatment of anxiety, pain and depression but its mechanisms are unclear or not well researched. However there is a plethora of research published in last decade which has brought music therapy to evidence based intervention. (98)

Despite of clear evidence of effectiveness of music for anxiety, depression, chronic stress, pain, mood and dyspnea, its utility has not been studied in DM. But, there are several
research findings indicating high prevalence of psychological co-morbidities like anxiety, chronic stress and depression in DM. These co-morbidities not only contribute to poor disease outcome but also compromise quality of life aiding to mortality. This study aims to understand mechanisms of benefit of MT elucidated for other conditions and if they have similarities then a possibility to explore effectiveness of Music therapy in controlling stress and psychiatric co-morbidities in Type II diabetes.

5.4 Theoretical Underpinnings of Effect of Music Therapy

There are several schools of thought describing rationale use of music therapy in medicine. One school believes that music has got healing power due to its potential to create transcendent awareness of self. This transcendence brings mind, body and spirit in to equilibrium. This theory has been advocated by some previous researchers. There is limited acceptance of this thought due to lack of empirical and clinical evidences to support this theory. However, such theories are based on realizations and transcendence awareness which can not be proved by increase or decrease of some biomarker which usually happens in clinical trials.(99)

The other theory advocates use of music to promote relaxation, reduce anxiety, and reduce pain and breathlessness which is more specific with clinical interventions for patients. This is more acceptable and often experimented over patients to prove efficacity of Music Therapy as shown in Fig.5.5.
Fig. 5.5: shows relaxation effects of music

The other theory is Roger’s Unitary Model which defines unitary human being as indivisible energy field that is integral with outside environmental energy. Human being is in constant interaction with environment and it has patterns. Roger’s three principles of homeodynamics are helicacy, integrality and resonancy. He believes that anxiety, stress, dyspnea and depression should be viewed as manifestation of disturbance in human energy field pattern. Music is representation of external environmental energy field which when applied in scientific way and rationale manner then it has got ability to disrupt vicious cycle of stress-anxiety perception and may promote relaxation supporting roger’s principle of integrality (1990) as interaction between subject and music to gain balance of psychological state. (44)
5.5 Psychological Responses to Music

Psychological response to music therapy depends on the listener’s ability to identify with it. It can be even subjects’ imagery, ability to associate him with musical experience and let the worries evaporate. Music works at ego and super ego levels. Music helps to release and control the emotions, satisfy the desire through aesthetic and spiritual experiences. Psychological effect of music on individual can be succinctly summarized as individual’s ability to communicate with music, identify his being and associate with pleasant experience of music, transfer himself in to a better world through imagery, express his worries and be able to be more self knowledgeable by increased self awareness.(44) Fig. 5.6 presents a schematic diagram of positive effects of music on physical, psychological and autonomic responses.

![Diagram: Positive effects of relaxing Music]

- DECREASED ANXIETY
- RELAXATION RESPONSE
- DECREASED DYSPNEA
- DECREASED BP, PR, RR

Fig.5.6: shows cascade of positive effects of relaxing Music
5.6 Physical Responses to Music

It is difficult to measure emotional and psychological effects of music scientifically, and even if done these is more often based on subjective experiences. Therefore, evaluation of physiological responses provides effective clues about physical responses to Music. First perception of music is through auditory apparatus. It sets nervous system in motion and carries its effects through thalamic and cortical pathways. Even without involving cortical pathways, it can arouse or calm the autonomic nervous system (ANS). Selection of music is paramount to know its effects. Relaxing music activates parasympathetic wing of ANS and induces relaxation. Music also causes involuntary reflexes. At times feelings of increased breath or calmed breathing sensation is due to activation of involuntary reflex due to music. Relaxation effect through these involuntary reflexes can be obtained by relaxing music only. Podolsky and Winold have agreed that music can influence electrical conductivity of human body due to reflex mechanisms. Thayer Gaytson reported music as a mean of generating physical strength. Music stimulates muscular action and induces bodily actions. Certain primitive dances e.g. African war dance was performed to gain vigor and physical energy before war. Music has been used for ages to alleviate fatigue. (100)

Singing has known beneficial effect on respiration and digestive system which may affect individual’s whole physical health. Man’s body is resonant like a rhythmical instrument which is sensitive to music. Inventions of musical instruments are extension of self physical impulse to discover man’s own identity. (101)
5.7 Effect of Music in Disease Conditions

Music is known to relieve anxiety and dyspnea due to its relaxation effects. Effectiveness of Music Therapy has been used in various respiratory disease conditions, illness states and symptom relief. It has been used as distractive stimulus to enhance exercise capacity in COPD subjects as well as an effective mean to induce relaxation and there by decrease symptoms like dyspnea, anxiety and pain. Mechanism of action of music has been explained as a parallel processing of breathing information, dyspnea, and distress. The sensory stimuli like dyspnea are processed at preconscious level as shown in Fig.2.3. If preconscious level is flooded with pleasant experience of music then dyspneagenic elements can not reach conscious level and there are reductions in dyspnea and related anxiety.(102)

Vijay et al reported two music therapy sessions across a single day in morning and afternoon was sufficient to reduce anxiety and dyspnea along with physiologic measures such as SBP, PR and RR in two sessions in COPD patients hospitalized with exacerbation but stabilized after medications. In this study reductions in music group was more as compared to the progressive muscle relaxation (PMR) group. Authors recommended that Reductions in physiologic parameters such as SBP, HR and RR should not be viewed as a separate entity. Sympathetic arousal and increase in vital parameters like BP, RR, PR are physiologic manifestation of anxiety and hence reduction in anxiety could lead to reduction in these measures.(16) Another study has shown that music is effective in reducing anxiety and dyspnea of COPD subjects who live at home.(103) A study on asthmatic subjects concluded that music was helpful as relaxation agent in decreasing asthma symptoms. Listening to music produced a greater decrease in peaks of tension than PMR, and produced greater compliance with relaxation practice, but without specific therapeutic effects.(10)
Music has been shown to be effective in relieving state anxiety in cardiac patients. A Cochrane review evaluated effect of Music therapy in cardiac disease subjects. This review included 26 trials (1369 subjects) which revealed that there is moderate reduction in anxiety with some benefits over stress. Among cardiac disease, MI patients showed better response to music with anxiety reduction by 6, reduction in heart rate by 3.4, reduction in respiratory rate by 2.5, reduction in systolic BP by 5.5, and moderate reduction in pain thereby improving quality of sleep. Authors have also elucidated some mechanisms behind these benefits like subjects get to focus their attention on pleasant experience of music away from stressful event. Music also provides aesthetic experience that inoculates comfort and peace. It also induces relaxation by calming ANS and CNS responses. Music suppresses sympathetic nervous system and reduces adrenergic activity thereby reduces neuromuscular arousal and acts as anxiolytic effect. Music triggers limbic system in brain and causes release of endorphins which reduces pain and improves sense of well being.(104)

A classic study reported one session of 30 minute music was sufficient to bring changes in anxiety and physiologic measures in mechanically ventilated subjects.(11) A Cochrane systematic review reported Pre recorded relaxing Music listening has beneficial effect on heart rate, respiratory rate, and anxiety in mechanically ventilated patients. Most studies included in this meta-analysis examined the effects of listening to pre-recorded music with relaxing effect. Authors reported that Mechanical ventilation causes major distress and anxiety in patients, which could be related to increase in complications secondary to distress and anxiety. Analgesics and sedatives are usual choices to take care of these symptoms and in turn it may lead to the prolongation of mechanical ventilation days which results in longer length of hospitalization, increased cost and Ventilator related complications. Therefore, non-pharmacological interventions have been proposed to be considered as methods for anxiety
and stress management. This review included eight randomized and quasi-randomized controlled trials with a total of 213 participants. The findings suggested that music listening may have a beneficial effect on heart rate, respiratory rate, and state anxiety in mechanically ventilated patients. While evidences for effect of music was not clear for blood pressure or oxygen saturation level because most of the studies did not had these parameters as outcome measures. (105)

A study reported efficacy of Music therapy in depression. This was a Cochrane review and authors included five RCTs which compared Music therapy with standard care. Authors reported that depressed subjects accept music therapy as intervention for depression and it improves their state of mood. Since studies were methodologically poor with wide variety of samples and non-adherence to standard reporting protocol like CONSORT a generalizable result can not be penned. Whereas, four out of five individual studies clearly reported reductions in symptoms of depression due to Music therapy.(30) However, all these possible mechanisms have direct influence from stress and proposed abnormality of Human Information Processing-Psychoneuroendocrine information Model (HIP-PNE model) and Hypothalamo-pituitary-adrenal axis (HPA). On analyzing these pathologic pathways and mechanisms, published literature also provide clues to levels at which Music therapy can work and provide treatment effect thereby bringing positive effect in vicious chain of stress and its pathomechanisms, music therapy may work in different ways leading to activation of parasympathetic system and suppression of sympatheic system, reducing stress, improving metabolic and physiologic profile resulting to harmony among various systems via relaxation and neuro-endocrine mechanisms.
Music promotes healing and is reflected by a balanced state of mind, body, and spirit. Commonly accepted theory of efficacy of music in pain, anxiety, stress and depression due to any pathological condition is either physical or psychological where music acts as a positive distracter which diverts patients’ attention to pleasant and encouraging musical stimulus by pushing subjects’ attention away from the trap of negative vicious circle of heightened sympathetic arousal. Definitely, music works through complex psycho-neuro-endocrine mechanisms by positively affecting the brain and thereby inducing relaxation. Music therapy is a powerful non-pharmacologic intervention that has been shown to be effective promoting relaxation and reducing anxiety in patients with cardiopulmonary, metabolic, psychiatric, neurologic and endocrine disorders. This therapy has not been well researched in Type II DM, but published literature do show a promising alternate adjunct therapy to control co-morbidities like stress, anxiety, depression and therefore achievement of optimal glycemic control.

5.8 Effect of Physical Activity and Its Mechanisms in Type II DM

There are clinically significant achievements in group which practiced standard care alone. Main components of standard care are diet restrictions and regular physical activity. These two alone are important factors in diabetes care especially type II DM. Visceral adiposity plays a key role in the subsequent manifestation of type II DM. The present article sustains the hypothesis that obesity, diabetes, and the metabolic syndrome are increasing mainly because people no longer need to be physically active in their daily lives (106-110). There is enough evidence in literature demonstrating that physical inactivity is the main cause of the type II DM. Gerald Reaven in a recent review on the metabolic syndrome concludes: “Obesity is not a component of syndrome X, because in contrast to the other variables, it is not a consequence of insulin resistance but only increases the likelihood of an
individual becoming insulin resistant and developing the associated adverse consequences. In the same vein, physical inactivity acts similarly to obesity in increasing the likelihood that insulin resistance will develop, and results of prospective studies have shown that physical inactivity seems to be as potent as obesity, if not more so, in increasing risk of developing type 2 diabetes mellitus"(111-112). Accordingly, there is enough evidence in literature demonstrating that physical activity is an effective therapeutic tool for prevention and management of type 2 diabetes mellitus. Intervention trials have demonstrated that in subjects with impaired glucose tolerance diet plus exercise programs reduce by ~60% the risk of developing diabetes (113-114). In subjects with overt type 2 diabetes, diet and exercise produce greater weight loss and allow greater reductions in hypoglycemic medications than diet alone(115-116). Many studies have shown that maintaining Exercise reduces blood glucose through an increase of insulin-dependent and insulin-independent glucose transport to working muscles (117). Exercise increases the translocation of glucose transporter 4 (GLUT 4) to the surface of muscle cells(118).There is evidence for the presence of two distinct pools of GLUT4 in skeletal muscle, one responding to exercise and one responding to insulin(119-120). Muscle contraction increases AMP/ATP and creatinine/phosphocreatinine ratios, which rapidly activate adenosine monophosphate protein kinase (AMPK), a key mediator of fatty acid oxidation (117) and glucose transport (121) in mammalian cells. During muscle contraction, AMPK appears to produce the translocation of GLUT 4 of either the insulin-dependent (122) or the insulin independent (123) pools. In type 2 diabetic subjects, physical training increases insulin-stimulated nonoxidative glucose disposal (124-125), presumably activating glycogen synthesis. The beneficial effects of regular physical activity on insulin sensitivity appear to be the final result of specific effects of exercise on GLUT 4 content, oxidative capacity, and capillary density of skeletal muscle. Preliminary data suggest that insulin-independent glucose transport, induced by exercise, is promoted by
augmented endothelial and muscle production of nitric oxide (126-127). Since impaired nitric oxide production often complicates type 2 diabetes mellitus, physical exercise might be utilized to improve insulin sensitivity and endothelial dysfunction as well. The effects of exercise on endothelial function might also be responsible for the reduction of blood pressure induced by regular physical activity.

A central role of exercise in the prevention and treatment of the Type II DM is the exquisite sensitivity of visceral fat to physical activity. Abdominal fat is quickly released to sustain ATP production during moderate intensity aerobic exercise (128). Thus, constant physical activity results in a reduction of visceral fat and an improvement of the features of the metabolic syndrome (106).

Despite the evidence about the benefits of exercise, many diabetologists do not spend time and efforts convincing type 2 diabetic subjects to practice physical activity. It is likely that the limited diffusion of exercise as a standard therapeutic tool among endocrinologists is caused by the poor adherence of older adults to comply with their recommendations. Survey studies have shown that adults with diabetes are less likely than adults in general to engage in regular physical activity (129) and that only 23% of older adults with type 2 diabetes reported >60 min of weekly physical activity (130). There is the need for simple and reproducible strategies of counselling to motivate type 2 diabetic patients to the practice of exercise. Recently, we have demonstrated that using an individual behavioural approach, primarily based on the social learning theory (131), it is possible for physicians to motivate the majority of type 2 diabetic subjects to long-term practice of exercise (132). The intervention consisted in a first counselling of at least 30 min conducted by an endocrinologist and designed to advise physical activity, followed, after 1 month, by home calling and every 3 months by an ambulatory visit of about 15 min (133). The intervention was effective in reducing BMI, HbA1c, coronary risk, and treatment costs with a significant correlation between the amount
of voluntary physical activity and the beneficial effects (134). The demonstration that physical activity counselling can motivate most diabetic subjects to increase their levels of voluntary energy expenditure (EE) (135) outlines the importance of instituting physical activity programs as an essential part of therapy for type 2 diabetes mellitus. The ADA (American Diabetes Association) emphasizes the benefits of regular physical activity in the prevention and treatment of type 2 diabetes mellitus, referring to proposals given to general population by several scientific societies (136). These recommendations advise individuals to engage in 30 min or more moderate-intensity physical activity on most (preferably all) days of the week. To maintain long-term weight loss, data from several studies suggest that more physical activity (60-75 min/day) is needed (137). In our study we have followed same guidelines to prescribe 150 minutes of weekly engagement in physical activity of moderate intensity. A rationale use of physical activity to prevent and treat type 2 diabetes mellitus requires the information about the amount of voluntary EE required to obtain significant benefits and about the minimum improvement in physical fitness that is associated with reduced mortality rates in diabetic and obese individuals. Both targets, EE and physical fitness, can be quantified using as a unit of measure the metabolic equivalent (MET). MET is nothing but a measure of intensity i.e. how hard a patient should work in a given time to achieve positive results desired for his/her condition. Apart from MET, oxygen consumption (VO2), heart rate reserve (HRR) and rating of perceived exertion (RPE) are reliable and valid methods to prescribe dosage of exercise to a subject. One MET corresponds to the consumption of 3.5 ml·kg⁻¹·min⁻¹ of oxygen, which is the average amount utilized by the human body in the resting state. Physical activity increases VO2 by contracting muscles in relationship to the quantity of activated muscles and exercise intensity. Thus, measuring VO2, it is possible to calculate the multiples of MET required for different activities in humans (138). METs can be used either to describe the status of physical fitness by
measuring the work load that a person can achieve before exhaustion (VO2max) or the amount of EE consumed through physical activity over a period of time. The latter measure is commonly expressed as METs-h/week and calculated as the product of the duration (hours x week) of the different activities weighted by an estimate of MET intensity of each activity. Increased levels of EE can be achieved either through structured leisure-time physical activity or by focusing on easy-to-perform daily activities such as walking the dog, washing the car, or avoiding the elevator as often as possible, etc. The total amount of EE will be the result of physical activity duration (PAD) and the intensity at which it is performed. It has been proposed to classify physical activities in moderate (3-6 METs), vigorous (6-9 METs) and very vigorous (>9 METs). However, such a categorization cannot be generalized because the intensity of physical activity is strictly related to the VO2max of subjects. For instance, an intensity of 10 METs is a moderate effort for elite athletes in aerobic sports who are able to maintain intensities over 20 METs for more than 1h. In order to better individualize the levels of intensity of physical activity a practical approach might be to compare the rates of perceived exertion, using the Borg’s scale (138), with the objective measurement of METs achieved. Therefore, in this study we have used RPE and HRR as a measure of exercise prescription intensity.

Regularly performed endurance exercise has a number of health benefits, including improvements in cardiovascular function, muscle metabolism, and increased work capacity. The increase in endurance is a result of greater oxygen delivery and extraction by the exercising muscle. Oxygen extraction is a result of an improved capillary-to-fiber ratio, as well as a higher mitochondrial content within muscle. The increase in mitochondrial content is a well-established and dramatic adaptation within the exercised muscle, but the molecular mechanisms underlying this change in muscle phenotype are just beginning to be clarified. An understanding of the cellular processes involved could help in the development of
therapeutic applications other than exercise, and may help us better comprehend the pathology of type II DM. This increase in mitochondrial content which occurs as a result of regular exercise is referred to as mitochondrial biogenesis. The process is complex because mitochondria are composed of proteins encoded by both nuclear and mitochondrial DNA (mtDNA). The major steps involved include: (1) signaling events leading to transcription, brought about by each exercise bout; (2) transcriptional regulation of nuclear-encoded genes encoding mitochondrial proteins, mainly mediated by the coactivator PGC-1α; (3) control of mitochondrial DNA gene expression by the transcription factor Tfam; (4) mitochondrial fission and fusion mechanisms; (5) import of nuclear-derived gene products into the mitochondrion via the protein import machinery; and (6) assembly of nuclear- and mitochondrially-encoded subunits into functional holoenzyme complexes. An additional complicating factor in mitochondrial biogenesis is the fact that mitochondrial structure differs markedly among cell types, and even within different regions of a specific cell type. For example, in skeletal muscle, mitochondrial properties differ between those organelles located under the sarcolemma [subsarcolemmal (SS) mitochondria] and those between the myofibrils [intermyofibrillar (IMF) mitochondria]. (140-141) It is now known that exercise can modify the rates of several of the steps leading to mitochondrial biogenesis, thus establishing exercise as an extremely useful model for understanding the underlying mechanisms involved in organelle synthesis. Recently, several breakthroughs in our understanding of the initiation of mitochondrial biogenesis have occurred, with the discovery of an important overall regulator of the process, PGC-1α. In this paper we will review our current understanding of mitochondrial regulatory proteins, the signals leading to mitochondrial biogenesis during exercise, as well as mitochondrial biogenesis during aging and muscle disuse. A number of other related reviews have also recently been published on this topic (142).
PPARγ coactivator-1α (PGC-1α) has been termed the “master regulator” of mitochondrial biogenesis because of its ability to induce mitochondrial biogenesis in a variety of experimental models. In mouse C2C12 skeletal muscle cells, ectopic PGC-1α expression increases mitochondrial content and oxygen consumption (143). In addition, over expression of PGC-1α in skeletal muscle of transgenic mice is sufficient to coordinate a host of muscle adaptations reminiscent of endurance exercise training, including increased mitochondrial content, increased proportion of Type I muscle fibers, and a corresponding increase in muscle fatigue resistance (144).

Data of literature showing that modest increments of physical fitness in diabetic subjects reduce by twofold the risk of overall mortality support the establishment of physical activity programs in the cure of type 2 diabetes mellitus. Since it is possible to motivate the majority of persons with diabetes to engage in the long-term practice of physical activity, it is time to move exercise from theory to daily ambulatory practice. In a recent web document WHO (World Health Organization) states: “Physical inactivity is estimated to cause 2 million deaths worldwide annually. Globally, it is estimated to cause about 10%-16% of cases each of breast cancer, colon cancers and diabetes, and about 22% of ischemic heart disease.” We have to do our best to direct our patients to use human genes for the scope they have been selected over millions of years: physical activity. (144)

This study clearly indicates same theories as stated above. Physical activity has shown improvements in all outcome measures but lesser as compared to yoga group. Yoga is very beneficial in motivating people to engage in exercise based programs and benefit all components of health.