FATIGUE DETERMINATION IN DRIVERS USING BIOMARKERS AND SUBJECTIVE ASSESSMENT TOOLS

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By

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CERTIFICATE

This is to certify that the work in the thesis entitled *"Fatigue determination in drivers using biomarkers and subjective assessments"* by *Ritu Mishra* in partial fulfilment of the requirements for the award of the degree of Bachelor of Technology in Biotechnology Engineering in the department of Biotechnology and Medical Engineering, National Institute of Technology Rourkela is an authentic research work carried out by her under my supervision and guidance.

To the best of my knowledge, the matter enclosed in this project work has not been submitted by any other university/institute for the award of any degree.

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Abstract

Fatigue is a condition of extreme tiredness, resulted from physical or mental stress due to prolonged monotonous and stressful work with/without sleep deprivation. It can originate centrally or peripherally due to a multitude of inducing factors like excessive physical activity, peer-pressure, undue stress, tight schedules etc. Fatigue in specific occupations like driving can be hazardous by increasing the risk of road traffic accidents. In case of drivers, it is recorded the most for the ones who drive for long distances, or drive heavy-vehicles or the ones who are seasoned drivers. The driver shows symptoms like sleepiness, loss of pleasure, slower reaction/reflex, pessimism, inattentiveness and irritation. According to WHO report, road traffic injuries are the 6th leading cause in India. And conferring to a study done by JP Research India, over a span of 2 years, fatigue was the leading cause contributing to 29% of the total accidents. But there is still no defined machinery to monitor a driver's fatigue in real time. In order to get an estimate of physical fatigue in drivers, appropriate study is essential. In the current study, an attempt was made to quantify physical fatigue in healthy non-trained subjects during simulated driving session of 12 hours at a stretch. The goal was to observe and estimate the progress of fatigue in the subjects out of driving task. Briefly, 10 male healthy subjects with mean age of 25 ± 4 years were selected. During 12 hours of driving on the simulator, blood samples were collected at 6 hours intervals from each subject, for estimation of Serotonin, CK-MB and Lactic acid. The subjective feeling of stress and fatigue was evaluated in the participants using subjective assessment tools like Epworth Sleepiness Scale, Berlin Questionnaire (for sleep apnoea) and Beck Depression Inventory (mood disturbance). All the biochemical parameters increased significantly as fatigue progressed. The subjective assessment scores also indicated the fatigue progress and strongly correlated with the biochemical parameters.

Key words: fatigue, drivers, stress, serotonin, CK-MB, lactic acid, subjective assessments

Chapter 1

Introduction

In physiological terms, fatigue is defined as the reduced capability or complete inability of an organism or one its parts to function normally [2]. It is usually due to extended hours of uninteresting work, stressful jobs, absence of proper ventilation, exposure to environmental factors like heat, noise, vibration, etc. Few major symptoms of fatigue are drowsiness, poor judgement, daydreaming, trouble in focussing, etc. The expanding number of transportation mishaps has turned into a significant issue for society. The car crashes will be generally diminished if discovering a judging standard to figure out if drivers stay alert or not, and make a notice to the drivers when they start to nod off, so it is important to research weariness location calculation which is likewise a key innovation in shrewd vehicles driving [18]. The driver weariness issue has turned into an essential component for bringing about car crashes. Driver weariness is a real reason for auto mishaps, since lethargic drivers are not able to settle on fast choices, and they may have slower response times. Therefore, numerous administrations have training system to alarm individuals to the perils of driving while tired, and drivers are urged to dodge conditions which may prompt driver weariness. Accordingly, how to direct and keep away from exhaustion and driving proficiently is one of the critical issues.

Fatigue has a very complex origin and is caused due to a combination of both central and peripheral factors. Hence, it has been neatly divided into Physical (or Peripheral) fatigue and Central Fatigue. Peripheral Fatigue (PF) occurs due to dysfunction of the muscles or impairment in neuromuscular transmission. It's caused after long hours of recreation, physical exertion, etc. Central Fatigue (CF) occurs due to specific alterations in the central nervous system and could originate because of stress, depression, boredom, sleep deprivation, etc. It basically results from impaired functioning of the central nervous system and even though it might not affect muscles directly, it reduces the capacity to work. The central fatigue starts at molecular level much before the symptoms occur. Of all the

neurotransmitters responsible for CF, Serotonin or 5-HT (5-hydroxytryptamine) is the most studied one [12]. The Serotonergic system has been suggested as an important modulator of mood, emotion, sleep, appetite, and thus has been implicated in the control of numerous behavioural and physiological functions. 5-HT is unable to cross the Blood-Brain-Barrier (BBB), therefore cerebral neurons are required to synthesise it for themselves which increases the amount of Tryptophan (TRP). TRP is the precursor for synthesis of Serotonin, hence plays an important role by synthesis and release of 5-HT in the brain [13]. This brain 5-HT is involved in control of tiredness, stimulation and mood, hence linked with central fatigue during sustained exercise. Meanwhile, Lactic acid is produced during chemical processes in the body when too little oxygen is present for usual processes (anaerobic metabolism). It serves as a major factor in muscle cramps and is produced in the tissues when conditions such as heart attack or shock reduce the blood supply responsible for carrying oxygen [16]. CK-MB is recognised as the leading cardiac serum marker and its determination has been proven to be more specific for myocardial necrosis. It is released after Myocardial Infarction and is detectable in plasma as early as 3-4 hours after the onset of symptoms. Elevated CK-MB levels have been reported in significant percentages of patients with acute skeletal muscle trauma (59%), chronic muscle disease (78%) and chronic renal failure (3.8%). This is a notable shortcoming since its determination isn't tissue-specific [17]. Any condition that causes muscle damage or interferes with muscle energy production can cause increase in CK levels.

Of the salivary segments analysed till today, Melatonin has demonstrated most encouraging as an immediate measure of circadian beat [19]. Levels of cortisol in serum and spit are known to be impacted by various figures expansion to circadian rhythms, including a mixed bag of intense and constant stressors, for example, a sleeping disorder, obstructive sleep apnoea, dejection and incessant weakness [20, 21]. Techniques to measure drowsiness have

emerged from different behavioural, electrophysiological, hereditary, proteomic and metabolomics investigations of slumber and lack of sleep. Techniques for evaluating dozing risks have been proposed in light of changes in behavioural components, for example, reaction time. After a certain tranquil period, subjects finished the Profile of Mood States (POMS) review for appraisal of exhaustion level and Stroop Color-Conflict Test (Stroop tests) for evaluation as subjective assessments [22]. While the Stroop tests are known to be affected by learning impacts, they were chosen for their simplicity of organization to gatherings of the size utilized as a part of this study.

Tiredness has more prominent impact on principle construct driving undertakings than in light of aptitude based errands, in spite of the fact that ability based assignments can't be utilized to give early markers of tired driving, deterioration of such errands may demonstrate the presence of other driving hindrances, for example, intoxication [4]. Fatigue can be treated by taking proper rest because sleep restores the normal functionality of the nervous system. And since it increases the risk of mishaps in roadways, aviation and military sector, it is essential to study the effects of sleep deprivation on performance, in order to develop methods to fight fatigue.

Chapter 2

Objective

The objectives of the study are:

- To quantify the progress of fatigue in non-trained drivers during simulated driving by using biochemical parameters (Serotonin, CK-MB, Lactic acid)

- To undertake subjective assessment of fatigue by use of subjective assessment tools namely Epworth Sleepiness Scale, Berlin Questionnaire and Beck Depression Inventory

- To make a correlation between the objective and subjective parameters

Chapter 3

Literature Survey

Over the past few years, there has been a lot of research done on occupational drivers health and work safety associated with driver's fatigue [1]. It is one of the biggest problems of roadways. The impact of drivers fatigue isn't trivial and hence there have been a lot of studies done on it. One study showed that if a person is kept awake for a night, his performance levels are as impaired as someone with high alcohol concentration in blood. There was a done by Harvard Medical School which suggested that 28% of adult drivers fell asleep during driving and 54% of them had feelings of drowsiness while they were handling the stick [5]. A study by Foret and Latin showed that train drivers feel sleepy during their work time due to their tight schedules. It deteriorated the quantity and quality of sleep which elevated their fatigue. Several other studies have advocated incidences of uncontrolled attacks of sleep during driving. There was a study that showed 50% of the road accidents were fatigue related on two of America's busiest roads [3]. An Australian road safety organisation estimated that 30% disastrous crashes, 15% fatal accidents and 6% road mishaps were due to driver's fatigue. A World Health Organisation report of 2009 suggested that more people in India died due to road accidents than anywhere else in the world. So clearly, it's an important issue which raises serious questions regarding driver's fatigue and safety.

In different nations, studies show that male youthful drivers are more inclined to rest-related crashes because of their hectic schedules and propensity to drive high mileage on roads. It was also found that sleep related accidents were at peak in the early morning hours, i.e. from 2:00 Hours to 6:00 Hours [6]. According to a study done by Horne, it was found that drivers were more prone to falling asleep at wheel at dusk than at 10 Hours. The probability of falling asleep on a monotonous road was also high in case of a long journey. New studies suggest that brain function is impaired at an equivalent level as it would be after staying awake for 17-19 hours. And the amount is equivalent to what 50-60 mL of alcohol would induce [7]. Driving for long hours is bound to be a monotonous exercise which comes with

sleep deprivation; hence it induces fatigue as it ascends gradually in cerebral metabolism [8-10].

Different blood biochemical parameters especially the neurotransmitters and their metabolic products- Lactic acid, CK-MB and Serotonin whose content in blood speaks of them either being the inducers or the result of events prompting exhaustion. These biochemical parameters suggest the gradual onset and progress of fatigue. There are also speculations of whether Serotonin levels really get affected or not with ascend in fatigue; and that if Lactate has a threshold which it jumps and then starts increasing rapidly. Hence we take samples at smaller time intervals and keep the demographics as similar as possible.

Aside from the blood biochemical parameters, the subjective evaluation of the people can likewise advocate for the level of weakness, or depression or sleepiness. These assessments give us a fuller and clearer picture of why and how fatigue affects our activities. The Beck Depression Inventory mirrors the slow increment in the depression and lethargy alongside the progress of fatigue. Aside from this Epworth Sleepiness Cycle and the Berlin questionnaire give us an idea of the sleepiness and its risks on the test subjects, according to defined scales. Hence, we get an outlook of all the changes in parameters that come alongside fatigue genesis and its following staging.

Yuan-Pang Wang and Clarice Gorenstein did an experiment to perform a systematic review of the utility of the BDI for detecting depression in medical settings, which was reformulated according to the DSM-IV criteria for major depression. They concluded that the Beck Depression Inventory-II can be easily adapted in most clinical conditions for detecting major depression and recommending an appropriate intervention [24]. Lethargy and exhaustion are thoughtfully particular however pervasively frustrated in research, estimation instruments, clinical settings, and ordinary daily language. ESS is limited to the experience of daytime sleep tendency. The vital clinical ramifications of ESS are in the capacity to recognize

"drowsiness which is not fatigue," a construct nearly identified with essential sleep disorder [25].

In this work, an effort has been made to measure the different blood biochemical parameters and subjective estimation at the same time. In every type of estimation, various variables have been examined and their connection with fatigue progression has been assessed.

Chapter-4

Materials and Methods

This chapter describes the materials, methodology and the protocols followed for the estimation of the biochemical parameters, the set-up of the simulator for the fatigue study.

4.1 Materials

- All the examine packs utilized for the investigation of the different biochemical parameters are affirmed for IVD *(in-vitro diagnosis).*

- The Serotonin ELISA pack was obtained from Labor Diagnostika Nord GmbH & Co. KG.

- The CK-MB unit was acquired from Coral Clinical frameworks and the Lactic Acid pack was obtained from Randox research centres.

- The pipettes and eppendorfs were acquired from Tarsons.

- The blood accumulation tubes and expendable syringes were acquired from BD Biosciences (India).

- For the colorimetric investigation of the blood test, a mechanized biochemical analyzer (EVOLUTION 3000) was utilized.

4.2 Simulator Setup

The test system comprise of a PC (detail), truck test system programming (EURO TRUCK), a product good guiding wheel (900º turn) with a vibration leg cushion and water driven slowing mechanism (Driving Force GT, Logitech, India), a LCD projector, a HD Sound framework (INSPIRE M 4500™, CREATIVE) and a screen. The test system module alongside the varying media unit was introduced in the PC. The projector and the screen were set in such ways that, the driver can get a reasonable vision. The entire setup was organized keeping drivers ergonomics in perspective.

4.3 Subjects

10 healthy male individuals of diverse age groups (25 ± 4) were undertaken for the study and were made to drive under stimulated laboratory environment. They were told of all the pros and cons of the study in order for them to make an informed decision. Since driver fatigue is a consequence of a few variables, for example, sporadic driving calendar, long time driving, lack of sleep, physical and mental conditions and so forth, the comparative conditions were re-enacted in the research centre environment by articulating volunteers to experience dreary activity with lack of sleep. Before the investigation, the subjects experienced strict clinical examination by enlisted therapeutic professionals and were announced sound. An educated assent in composed structure was acquired from every subject. Their blood tests were collected in occasional interims for the estimation of different blood biochemical parameters to get the genesis and dynamic phases of fatigue improvement.

4.4 Experimental Design

The trial was led under research facility stimulatory conditions with one subject in a solitary session. The whole investigation was subdivided into different stages (for each person, beginning time of different stages were: Stage1- 9:00Hrs, stage2-15:00Hrs; Stage3-21:00Hrs), and in every stage the individual was requested to perform virtual driving on test system to produce mental and also physical exhaustion. Before the analysis the people were requested that perform their typical regular movement aside from specific exercises like dozing toward the evening, any utilization of liquor, caffeine, and tobacco and so forth. Just before the beginning of the stages, every member was subjected to a progression of survey for their subjective evaluation before actuation of any weakness. Likewise, the first blood test was gathered (that serves as the control) and the second blood test was trailed by snacks. The subjects were kept conscious amid the entire session of the driving reproduction. The

progressive blood tests were gathered at 9:00Hrs, 15:00Hrs, and 21:00Hrs to watch the impact of exhaustion on biochemical parameters. In the meantime the subjective appraisal was additionally rehashed in the meantime purposes of blood gathering. They were likewise made to experience tedious activity at customary intervals consequently with lack of sleep and repetitive activity, a replica of exhaustion condition was re-enacted *in vitro*.

4.5 Blood Sample Collection

The blood sampling was done three times throughout the experiment from all the individuals. Briefly a tourniquet was wrapped around either arm (left or right arm altering at each time point) of the individual and was asked to flex the elbow as well as the fingers. From the anterior region of the elbow, 5ml of blood was collected by puncturing the brachial vein through 5ml disposable syringe fitted with 22G needles (BD Biosciences, India) after sterilizing it with a cotton swab soaked with 70% alcohol. 2ml of the blood was collected in a tube containing clot inhibitor (Na-EDTA) to obtain whole blood, and the remaining 2ml was collected in tubes containing clot activator (coated with Silicone gel, AkuSet™, Eastern Medikit Limited) to obtain serum, for the biochemical and the immunological assays. The samples were vortexed 8 times for proper mixing followed by preservation in refrigerator at 2-8ºC. Later the samples were analysed for various blood biomarkers.

4.6 Measurement of Blood Biomarkers

The blood test was centrifuged at 400 rpm for 10 minutes and afterwards the plasma was gathered.

4.6.1 Serotonin Estimation

Serotonin Estimation was done by ELISA test using the kit acquired. The concentrations were measured by competitive ELISA, after the samples were prepared according to the guidelines provided in the kit.

4.6.1.1 Procedure

Wavelength/filter: 505nm/green

Temperature: 37ºC

The standards were prepared. The sample collection was done and those were stored till further estimation. Acylation was done in acylation tubes by making three samples for each reading, namely Diluted Standard, Diluted Controls and Samples. To each tube, 25uL of acylation buffer was added. Those were mixed shortly and incubated for 15-20 hours at 2-8ºC and then washed using wash-buffer concentrate. The enzyme conjugate was added and the samples were incubated for 30mins at room temperature on a shaker. Substrate was added and again the samples were stored for 30mins at room temperature. The stop solution was added and the absorbance was read at 450nm.

4.6.2 CK-MB Estimation

CK-MB estimation was done with the assistance of a semi-automatic Biochemical Analyzer (Evolution 3000) and the required merchandized kit.

4.6.2.1 Procedure

Wavelength: 340nm

Temperature: 370 C

Clean dry eppendorfs were taken and labelled as test (T). The subsequent addition sequence was followed: 0.8mL of L1 (as named in the kit) was added to the tube, followed by 0.5mL of the sample. It was then incubated at assay temperature for 5mins. Then, 0.2mL L2 was

added and mixed well. The tubes were left for 5mins for proper reaction at room temperature. Absorbance readings were noted after every 1, 2 and 3mins.

4.6.3 Lactic Acid Estimation

The lactate concentration in blood was done by preparing the standards and samples according to the kit acquired and reading its absorbance and concentration using a micro-plate reader.

4.6.3.1 Procedure

Wavelength: 550nm

Temperature: 37°C

Two tubes were taken i.e. for Standard and Reagent. In Standard, only 10uL of the standard provided in the kit was used whereas for the Sample, 10uL of the plasma was taken. To each tube, 1000uL of the reagent (provided) was added. They were incubated for 5mins at room temperature and absorbance of sample and standard was measured within 30mins.

4.7 Subjective Assessment Tools

The subjective assessments of fatigue takes into account a set of questionnaires which were asked to every subject towards the end of every step. For this appraisal, three standard conventions were taken. To be specific, Epworth sluggishness cycle that is a subjective measure of comprehending somebody's sleepiness. Beck Depression Inventory (BDI-II), which comprises 21 multiple-choice self-reportable inquiries, have an essential aphorism to gauge the seriousness of depression and disinterest from the present undertaking in the subject; Berlin Questionnaire which is essentially used to focus the degree of torment and inability out of an intervention. All these evaluation instruments were slightly changed according to the necessity of the present study.

The inquiries were asked in a cooperative environment and the scoring was done on the consolidated perspective of the subject's self-assessment and the perception of one of the individuals from the examination group.

4.7.1 Demographics

The participants in this project work were between the ages of 21-30. All the participants in the study were Male and were tested healthy. Subsequently, a record of the demographics has been maintained. The assessments used were quite simple and understandable, so all the returned forms could be studied easily.

4.7.2 Epworth Sleepiness Scale

It is a self-directed test. It is generally utilized as a part of the field of sleep-medicine as a subjective measure of understanding someone's drowsiness. The test comprises of eight circumstances in which you rate your propensity to wind up drowsy on a size of 0, no shot of

snoozing, to 3, high risk of napping. When one completes the test, the assigned values of their reactions were summed up. The aggregate score is in view of a size of 0 to 24. The scale gauges whether subject is encountering excessive tiredness that commands any medical help.

4.7.3 Berlin Questionnaire

The Berlin Questionnaire is a basic sleep apnoea screening poll used to rapidly identify the danger (low to high) of sleep disturbed breathing, i.e. it is utilized to recognize the danger of sleeping issues and the disorders. The questionnaire comprises of 3 classes and the danger is in light of the reactions to individual questions and general scores in the symptom categories.

4.7.4 Beck Depression Inventory

Beck Depression Inventory is a set of questionnaire used for the evaluation of depression level in patients, experts and so on [11]. The latest form (BDI-II) is a nonexclusive instrument that can be utilized on various age groups over thirteen, and is made out of polls that identify with melancholy level (sadness, irritation and so on.) , perceptions (guilty feeling, self-dislike, feelings of punishment and so forth) and additionally, if any physical side effects.

Chapter-5

Results

The result section is divided in two parts.

1. Blood Biochemical measures

2. Subjective assessment Results

5.1 Blood biochemical parameters

5.1.1 Serotonin level in whole blood

The Serotonin level in blood was examined and hence, the average value of Serotonin was on decrease as the day advanced and the fatigue grew and sleep deprivation increased. It was found out to be 13.0670 ± 7.8378 at Stage 1, 69.4750 ± 48.7631 at Stage 2 and 181.0813 ± 100.7798 at Stage 3. The standard error of difference was negligible and hence the data was statistically extremely significant according to the *t-test*. Earlier researchers have found that Serotonin affects the mood and its level changes results in fatigue and bad mood.
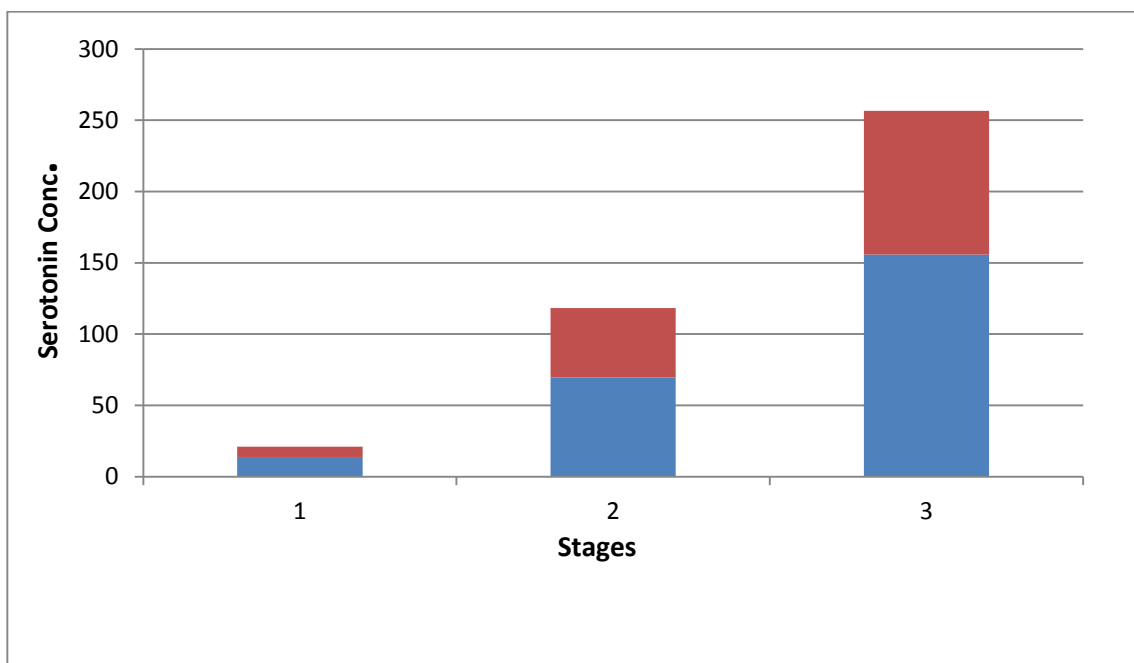
Figure 1: Serotonin levels in blood at 0, 6 & 12 hours

5.1.2 CK-MB level in plasma

The CK-MB level in plasma increased gradually with time, due to sleep deprivation. At Stage 1, it was found to be around 0.2111 ± 0.0675, at Stage 2, around 0.4678 ± 0.0616 and at Stage 3, around 0.7476 ± 0.2724. The increase in concentration of CK-MB is a critical parameter of peripheral fatigue that includes muscle damage which thus may have surcharged the kidneys. The increment in this peripheral marker indicates weariness and can be clarified by spread of steady central fatigue to the periphery which thus prompts muscle protein degradation. Any condition that causes muscle damage or interferes with muscle energy production can cause increase in CK-MB levels.
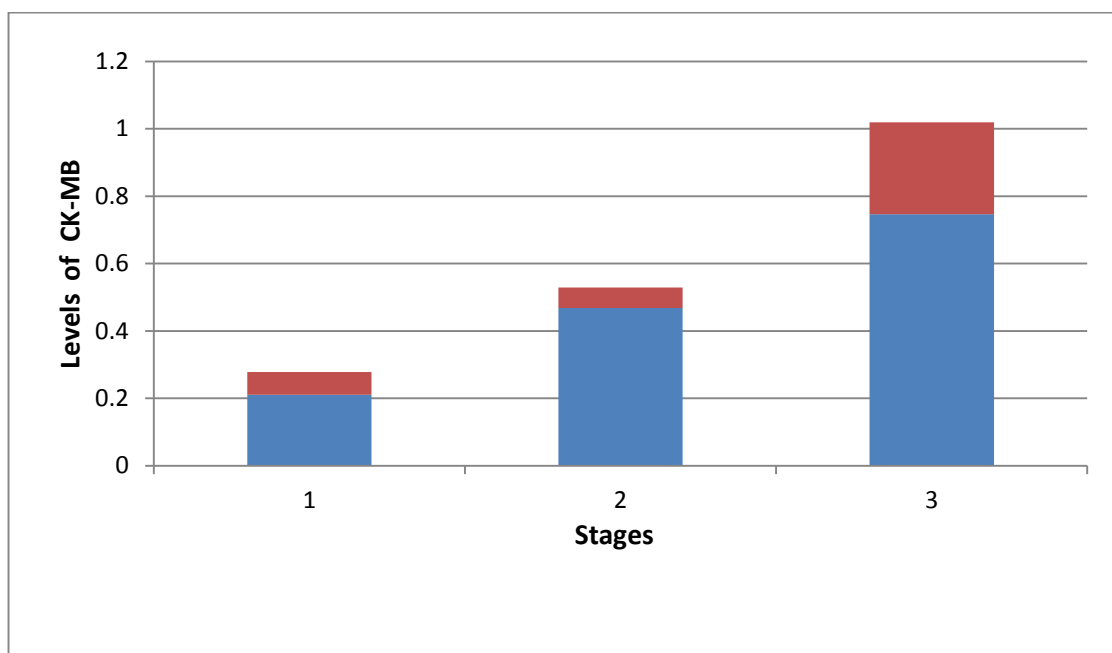
Figure 2: CK-MB levels in blood at 0, 6 & 12 hours

5.1.3 Lactic acid content in plasma

The lactic acid content in blood showed a great variation with fatigue development in the subjects. Consequently, the results were on an average of 38.4867 ± 2.6692 in Stage 1;

54.9467 ± 6.8452 in Stage 2; and 82.2344 ± 13.5272 in Stage 3. Hence we can see that lactic acid was continuously being produced as the person was getting fatigued. We know when oxygen levels are low, pyruvate converts to lactic acid. High blood lactate levels, together with decreased oxygen in tissues, now we can say is also caused by strenuous exercise or damage to the heart.
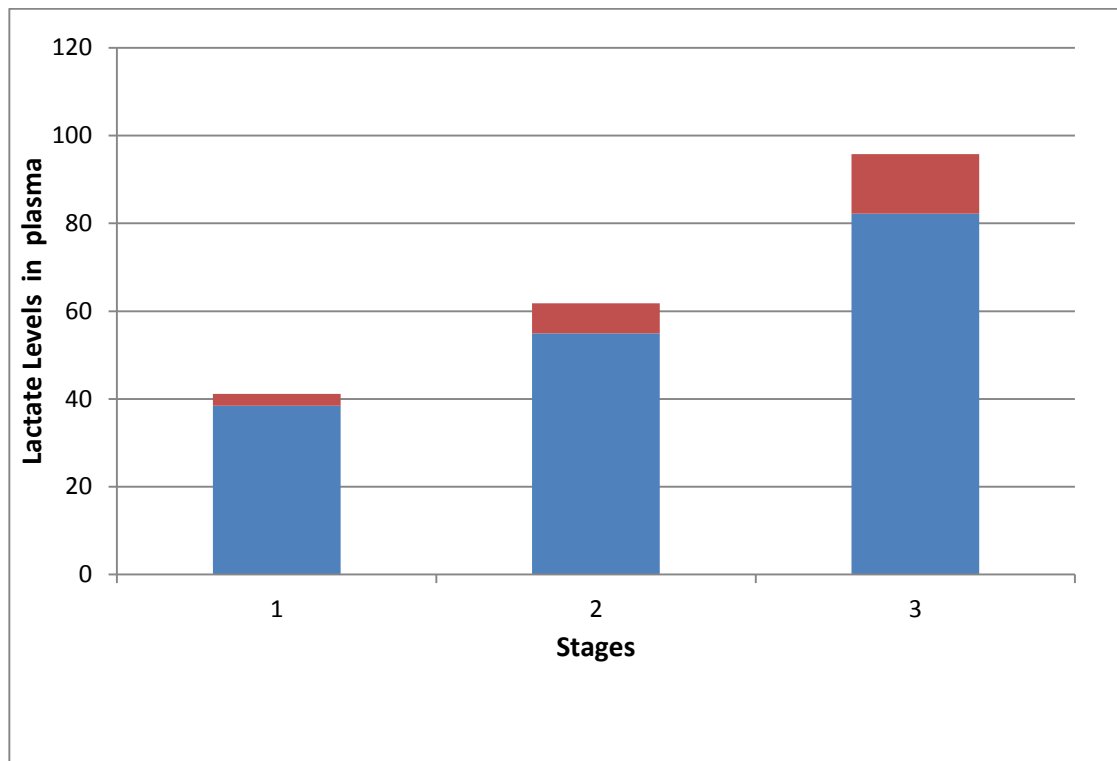
Figure 3: Lactate concentration in blood at 0, 6 & 12 hours

5.2 Subjective Assessment

5.2.1 Demographics

The test subjects of the study were between the age groups of 21 to 30; 6 of them being of 21-25 age whereas the other 4 being of the 26-30 age group. All of them were male. The experience of the majority differed as 60% of the subjects had below 1 year of experience and 40% had an experience between 1 to 5 years. 80% of the subjects had experienced fatigue before and all of them admitted to having their fatigue affect their performance at work. Some of the common reasons of fatigue were listed to be daily monotonous work, sleep debt, stress, heavy work-load, etc. None of them had been diagnosed with narcolepsy, restless leg syndrome and central sleep apnoea, prior to this experiment. The number of people who admitted that fatigue had affected their work-performance was **8**.

There were 6 subjects aged 21-25 whereas the rest 4 were between the ages of 26-30. Some study-subjects also recorded meals or late meals, tight schedule, night shifts, difficulty in sleep, disturbed sleep pattern, inadequate medical care, etc. as reasons for their fatigue.

5.2.2 Epworth Sleepiness Cycle

The average scores for people who would have high chances of dozing if they lie down in the afternoon was recorded to be the highest at 2.8, with a standard deviation of 0.4216. Then, the people who were most likely to fall asleep were the ones who would doze off during sleeping and reading or during sitting quietly after lunch. The least likely activity which would make anyone sleepy was talking to someone.

ESS Distribution Table of Test Subjects		
SITUATION	MEAN	SD
Sitting and Reading	1.5	1.1785
Watching television	0.5	0.7071
Sitting, inactive in a place	1.3	0.8232
Passenger in a car for an hour	1.5	0.7071
Lying down to rest at noon	2.8	0.4216
Talking to someone	0.2	0.4216
Sitting quietly after lunch	1.5	0.5164
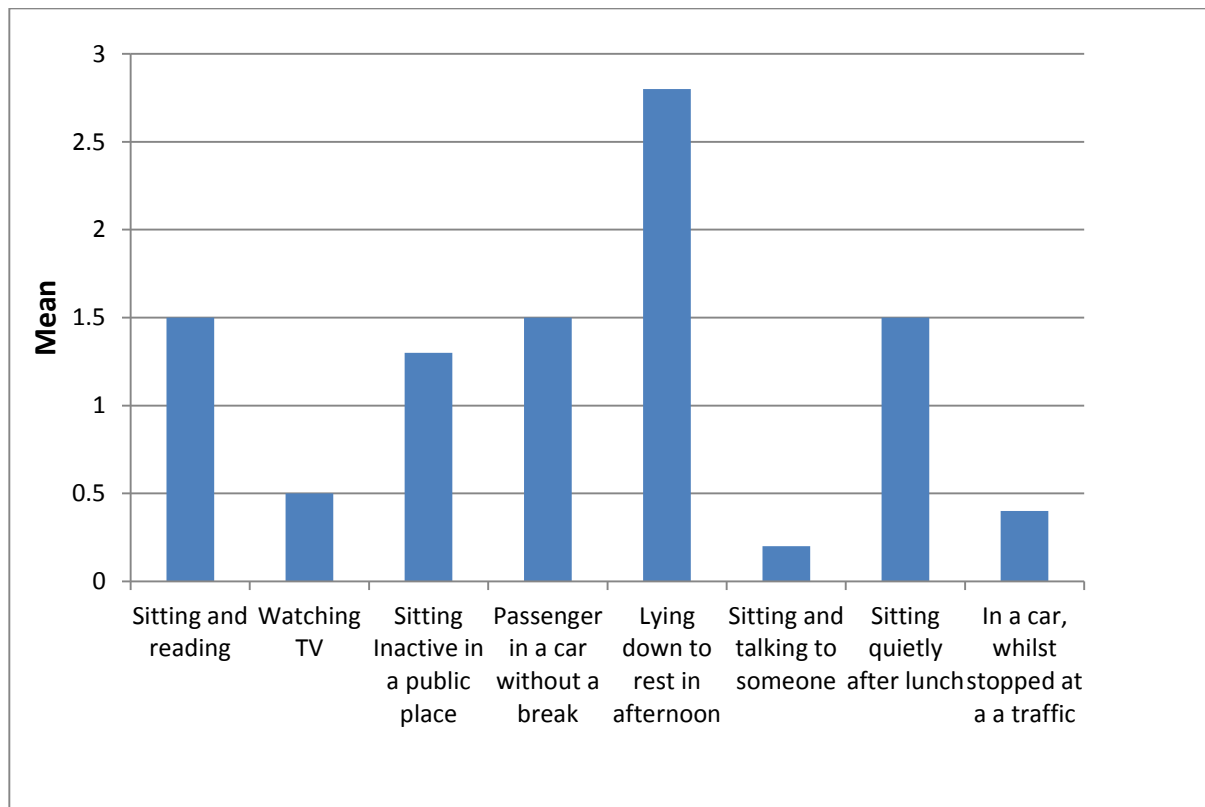
Figure 4: Mean scores of situations on Epworth Scale

5.2.3 Berlin Questionnaire

Used to test sleep apnoea, Berlin Questionnaire (BQ) has a set of 10 questions, divided into 3 categories. There is a <u>simple scoring scheme</u>:

	A	B	C	D	E
1.	1 point	--	--	--	--
2.	--	--	1 point	1 point	
3.	1 point	1 point	--	--	
4.	1 point	--			
5.	2 points	2 points	--	--	--
If Score > 2 till now, Category A is positive					
6.	1 point	1 point	--	--	--
7.	1 point	1 point	--	--	--
8.	1 point	--			
If Score > 2, Category B is positive.					
9. Answers to be noted and discussed separately					
10. Observations to be noted separately					
High Risk if 2 or more categories are positive Low risk if 1 or no category is positive					

The overall observations made showed that 40% of the study subjects were under high risk of sleep apnoea and 30% were under low risk. The mean values for people who snore and their frequency of snoring being the highest at 1.5 with standard deviations of 0.4830 and 0.4538 respectively. The rest of the distribution is shown in the table below:

Distribution Table of Berlin Questionnaire		
LIST	MEAN	SD
Do you snore?	0.7	0.4830
Loudness	0.1	0.3162
Frequency	0.7	0.4538
Bother others	0.6	0.5164
Quit breathing	0.2	0.6324
Feel tired after sleep	0.6	0.5071
Feel fatigued after waking up	0.5	0.4829
Nodded off while driving	0.2	0.4216
Frequency	0.1	0.1438
High Blood Pressure	0.7	0.4879
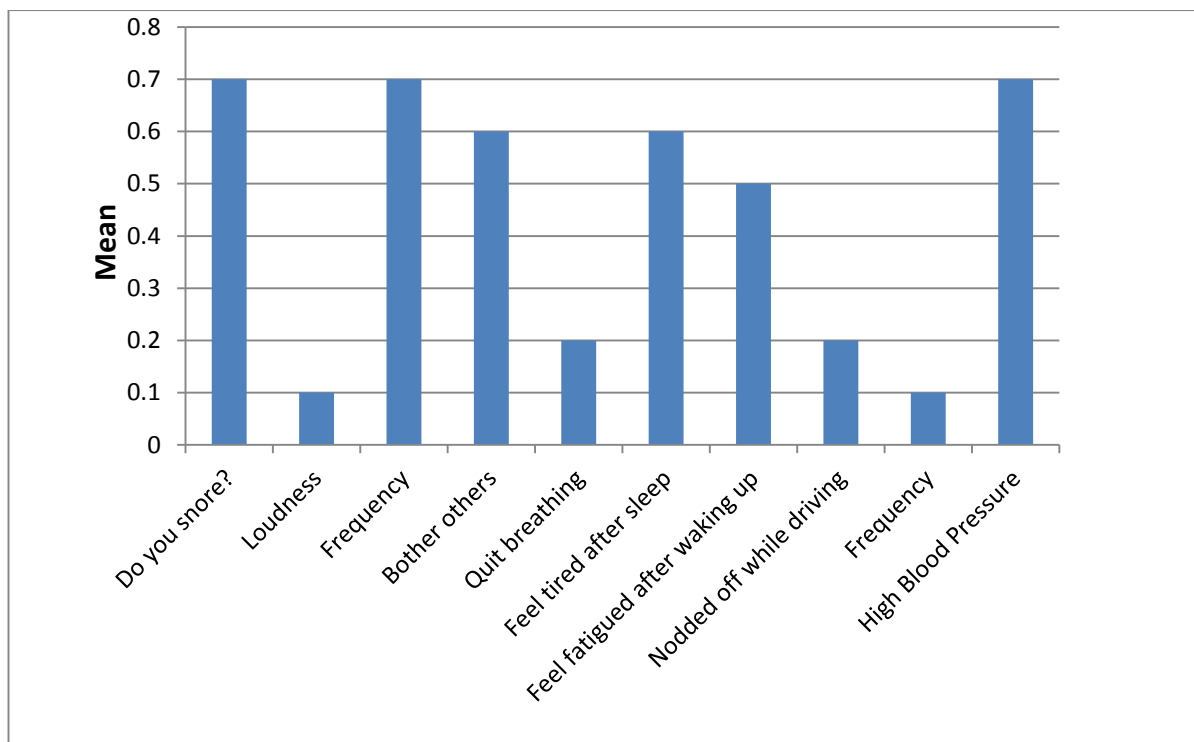
Figure 5: Mean Scores of Berlin Questionnaire

5.2.4 Beck Depression Inventory

It is a scale which tests how depressed a person is. This was very important to the study to record the change in mood and depression levels of the test subjects, during simulated driving. This would give us a bigger and clearer picture of why the biochemical parameters are affected. Most of the subjects were recorded to have mild depression at the start of the study, i.e. comprised as sample study. The results showed that 10% of the subjects had mild depression, 40% had moderate depression while the rest 50% had severe depression, towards the end of the study. According to Beck Inventory, depression has two constituents namely, Affective component which consists of eight items i.e. mood/pessimism, feelings of past failure, guilty feeling, punishment-like feeling, self-hatred, self-criticalness, worthlessness, suicidal feelings; whereas the Somatic component consists of loss of pleasure, sadness, agitation, loss of zeal and energy, sobbing, loss of interest, prickliness, change of appetite, vagueness, tiredness, concentration difficulties, change in sleep pattern and loss of interest[22][23].

Distribution Table of Beck Depression Inventory		
ATTITUDE	MEAN	STANDARD DEVIATION
Mood	1.9	0.9944
Pessimism	1.5	0.5270
Past failure	1.4	0.6992
Loss of pleasure	2.1	0.5676
Guilty feeling	1.6	0.8432
Sense of punishment	2	1.0540
Self-hatred	1.7	0.6749
Self-criticalness	1.9	0.8756

Suicidal thoughts	1.8	0.7888
Crying	2.4	1.2649
Agitation	2.2	0.9189
Loss of interest	2.1	0.9944
Indecisiveness	2.1	0.7378
Worthlessness	2.1	1.3703
Loss of energy	2.2	0.6324
Changes in sleeping pattern	2.6	1.0749
Irritability	2.3	0.9486
Changes in appetite	2	0.9428
Loss of weight	1.2	0.4216
Worried about health	2.2	0.4264

As noted above, we can see that sleeping pattern changes significantly as depression starts getting to the head, the victims find it very difficult to even break down, hence lose energy and the zeal to live, which leads to getting suicidal thoughts.

5.3 Pearson Correlation:

The Pearson Correlation was established amongst the subjective and objective parameters to represent the strength of the relationship between the variables. The ones with positive correlations were CK-MB & ESS with a score of 0.86. But correlation between Serotonin and Beck Depression Inventory was the highest at 0.99. It is almost a linear relationship and hence is highly desirable.

CHAPTER 6

Discussion

It can be observed that all the three biochemical markers follow a similar trend. The increase in the level of Serotonin indicates that it can be safely used as a parameter to test drivers' fatigue. It affects the mood significantly during driving for prolonged hours and hence leads to fatigue. The increase in concentration of CK-MB is a critical parameter of peripheral fatigue that includes muscle damage which thus may have surcharged the kidneys. The increment in this peripheral marker indicates weariness and can be clarified by spread of steady central fatigue to the periphery which thus prompts muscle protein degradation. Any condition that causes muscle damage or interferes with muscle energy production can cause increase in CK-MB levels. Lactic acid was continuously being produced as the person was getting fatigued. We know when oxygen levels are low, pyruvate converts to lactic acid. High blood lactate levels, together with decreased oxygen in tissues, now we can say is also caused by strenuous exercise or damage to the heart.

Driver fatigue could be due to a plethora of reasons like emotional disturbance or pressure or long shifts at work which could lead to diversion of their attention, depression, fatigue, absence of interest and vitality and so forth. When both kinds of fatigue (physical and mental) are consolidated with lack of sleep for a long period of time (like in case of long distance driving), it can lead psychological pain which triggers the depression levels in subjects. Like we saw in the study, the different biochemical and subjective components prove that they follow a similar pattern as they change with progression in fatigue. The decrease in Serotonin concentration shows that with an upsurge in depression levels, Serotonin is produced less. The reasons could also be lack of receptor sites to get the produced 5-HT, failure of the 5-HT to reach the sites, deficiency of Trp, etc. Obviously, Serotonin can't be the only reason for depression, it's a part of a bigger picture of which Serotonin and SSRI's are a small part. We also observed that blood lactate levels increase as the person starts to get fatigued. Amid low-intensity activity, blood lactate levels will stay

close to resting levels and then it rises exponentially due to the growth in work-intensity. Though it cannot be generalised that blood lactate accumulation happens due to increase in H^+ ion concentration, since once they clear out, it will have no negative impact. The study also ruled out any defined point after which the lactate levels take a shot up, since we see a steady increase in the levels. Normally, CK-MB levels are deficient in blood, its concentration is so low but its increase shows damage to heart tissues. It leads to unusual fatigue, disturbance in sleep pattern, etc. This cardiac marker, as can be seen from results, rises slowly after 3-4 hours of work and reaches higher peaks at the end of 12 hours or more. More diverse conditions in which drivers actually have to undergo long-distance driving (like extreme temperature, alcohol use/abuse, etc.) may lead to more acute interference in the test subjects. But the test subjects were placed under similar conditions and are of almost the same age, still the levels of CK-MB in serum vary to an extent. In some cases, it could be genetic but a pinpoint reason still remains unknown.

Discussion of Subjective assessments:

The ESS report showed that around 60% of the subjects had enough sleep which came down to approx. 10% at the end of 12 hours. The subjects felt dangerously sleepy which could pose undesirable dangers for them, their partners and the normal road users. Significant improvement was seen while 'someone was sitting and talking to them', rather than the drivers driving alone for long hours. It was also seen the risks of accidents were high if th person had had alcohol in lunch or dinner.

Now, the BQ suggested that around 4 out of the 10 test subjects were at high-risk of sleep apnoea, 3 were at low-risk and nothing could be said about the rest 3, since they were unaware of some of their health problems and had varied answers. Sleep apnoea could lead to memory loss, depression, stroke, etc. It is disturbing to find that so many individuals were at

high risks and were completely unaware of it. It was also noted that snoring is a habit amongst many subjects and that their snoring bothers other people, hence it could lead to disturb in their partners' sleep pattern too. None of the subjects nodded off or fell asleep during the driving period, so that was a relief. Though, some admitted to have had signs of moderate dozing during the lunch hours. People were also asked if they had suffered from high blood pressure and 30% of them could not give us an affirmation. Proper diagnosis was suggested to those at high risk.

The BDI questionnaire showed that 50% of the test subjects were under severe depression while 40% were under moderate depression. As the day started, their depression levels were recorded to be minimal or mild. But with the advance of the strenuous activity, their depression levels showed major changes. It was noted that once the person is depressed, the most affected criteria is one's sleeping pattern. They find it difficult to cry, even if they want to. It makes them irritated for most of the time and hence, they find it difficult to concentrate on their work. Most of them admitted that their depression state affects their quality of work and it leads to withdrawal from the job undertaken. They become indecisive, due to which they find it difficult to make any snap judgement or take reflex actions on time, once faced with a calamity or accident. These traits are highly undesirable in drivers and needs to be looked out for. The stark changes and differences of the undertaken components hence show that they can be used for medical presentation of fatigue, its causes and its effects.

Chapter 7

Conclusion

After correlation, Serotonin comparatively shows a better correlation with Beck Depression Inventory. Serotonin is also a key inducer of central fatigue during driving sessions and hence can be used for real time assessment. By combining Serotonin with peripheral biomarkers like CK-MB and Lactic Acid, a précised staging of fatigue in the occupational groups can be obtained.

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Appendix – I

(Subjective assessment

Questionnaires)

Demographics

Q1) What is your age group? (Please tick)	
1) Below 21 years	
2) 21 - 25	
3) 26 - 30	
4) 31 - 35	
5) 36 - 40	
6) 41 – 45	
7) Above 45	

Q2) What is your gender? (Please tick)	
1) Male	
2) Female	

Q3) How long have you been employed as an auto rickshaw driver?	
1) Below 1 year	
2) 1 – 5 years	
3) 5 – 10 years	
4) 10 – 15 years	
5) Above 15 years	

Q4) Have you experienced fatigue in the last 6 months?	
1) Yes	
2) No	

5. If so, what do you believe this is a result of?

Q6) Do you believe fatigue has affected your performance at work?	
1) Yes	
2) No	

Q7) Have you ever been diagnosed with narcolepsy, restless leg syndrome, obstructive or central sleep apnoea?	
1) Yes	
2) No	

Q8) If so are you being treated for this?	
1) Yes	
2) No	

Epworth Sleepiness Scale (Johns, 1991)

How likely are you to doze off or fall asleep in the following situations (rather than just feeling tired) - referring to your usual way of life in recent times. If you haven't done some of these things recently, try and work out how it would have affected you - so all questions have an answer.

Use the following scale to choose the most appropriate number for each situation 0 = no chance of dozing
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

SITUATION CHANCE OF DOZING

1. Sitting and reading

   _____

2. Watching television

   _____

3. Sitting, inactive in a public place
   (eg. in cinema or a meeting)   _____

4. Passenger in a car for an hour without a break

   _____

5. Lying down to rest in the afternoon (when circumstances permit)

   _____

6. Sitting and talking to someone

   _____

7. Sitting quietly after lunch (without alcohol)

   _____

8. In a car, whilst stopped for a few minutes in traffic

   _____

Berlin Questionnaire (for sleep apnoea) (Netzer et al., 1999)

Height _____ **cm**   **Weight** _____ **kg**

Age _____ **yrs**   **Gender M / F**

Q1) Do you snore?	
6) Yes	
7) No	
8) Don't Know	

If you snore:

Q2) Your snoring is	
1) Slightly louder than your breathing	
2) Louder than talking	
3) As loud as talking	
4) Very Loud	

Q3) How often do you snore?	
1) Almost every day	
2) 3-4 times a week	
3) 1-2 times a week	
4) Never or almost never	

Q4) Does your snoring bother other people?	
8) Yes	
9) No	

Q5) Has anyone ever noticed that you quit breathing during your sleep?	
1) Nearly every day	
2) 3-4 times a week	
3) 1-2 times a week	
4) 1-2 times a month	

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5) Never or nearly never

Q6) How often do you feel tired or fatigued after you sleep?	
1) Nearly every day	
2) 3-4 times a week	45
3) 1-2 times a week	
4) 1-2 times a month	
5) Never or nearly never	

Q7) During your wake time, do you feel tired, fatigued or not up to par?	
1) Nearly every day	
2) 3-4 times a week	
3) 1-2 times a week	
4) 1-2 times a month	
5) Never or nearly never	

Q8) Have you ever nodded off or fallen asleep while driving a vehicle?	
1) Yes	
2) No	

If Yes,

Q9) How often does this occur?	
1) Nearly every day	
2) 3-4 times a week	
3) 1-2 times a week	
4) 1-2 times a month	
5) Never or nearly never	

Q10) **Do you have high blood pressure?**	
1) Yes	
2) No	
3) Don't Know	

Beck Depression Inventory

Q1) Sadness	
1) I do not feel sad.	
2) I feel sad	
3) I am sad all the time and I can't snap out of it.	
4) I am so sad and unhappy that I can't stand it.	

Q2) Pessimism	
1) I am not particularly discouraged about the future.	
2) I feel discouraged about the future.	
3) I feel I have nothing to look forward to.	
4) I feel the future is hopeless and that things cannot improve.	

Q3) Past Failure	
1) I do not feel like a failure.	
2) I feel I have failed more than the average person.	
3) As I look back on my life, all I can see is a lot of failures.	
4) I feel I am a complete failure as a person.	

Q4) Loss of Pleasure	
1) I get as much satisfaction out of things as I used to.	
2) I don't enjoy things the way I used to.	
3) I don't get real satisfaction out of anything anymore.	
4) I am dissatisfied or bored with everything.	

Q5) Guilty Feelings	
1) I don't feel particularly guilty.	
2) I feel guilty a good part of the time.	
3) I feel quite guilty most of the time.	
4) I feel guilty all of the time.	

Q6) Punishment Feelings	
1) I don't feel I am being punished.	
2) I feel I may be punished.	
3) I expect to be punished.	
4) I feel I am being punished.	

Q7) Self Dislike	
1) I don't feel disappointed in myself.	
2) I am disappointed in myself.	
3) I am disgusted with myself.	
4) I hate myself.	

Q8) Self Criticalness	
1) I don't feel I am any worse than anybody else.	
2) I am critical of myself for my weaknesses or mistakes.	
3) I blame myself all the time for my faults.	
4) I blame myself for everything bad that happens.	

Q9) Suicidal thoughts or wishes	
1) I don't have any thoughts of killing myself.	
2) I have thoughts of killing myself, but I would not carry them out.	
3) I would like to kill myself.	
4) I would kill myself if I had the chance.	

Q10) Crying	
1) I don't cry any more than usual.	
2) I cry more now than I used to.	
3) I cry all the time now.	
4) I used to be able to cry, but now I can't cry even though I want to.	

Q11) Agitation	
1) I am no more irritated by things than I ever was.	
2) I am slightly more irritated now than usual.	
3) I am quite annoyed or irritated a good deal of the time.	
4) I feel irritated all the time.	

Q12) Loss of Interest	
1) I have not lost interest in other people.	
2) I am less interested in other people than I used to be.	
3) I have lost most of my interest in other people.	
4) I have lost all of my interest in other people.	

Q13) Indecisiveness	
1) I make decisions about as well as I ever could.	
2) I put off making decisions more than I used to.	
3) I have greater difficulty in making decisions more than I used to.	
4) I can't make decisions at all anymore.	

Q14) Worthlessness	
1) I don't feel that I look any worse than I used to.	
2) I am worried that I am looking old or unattractive.	
3) I feel permanently unattractive.	
1) I believe that I look ugly.	

Q15) Loss of Energy	
1) I can work about as well as before.	
2) It takes an extra effort to get started at doing something.	
3) I have to push myself very hard to do anything.	
4) I can't do any work at all.	

Q16) Changes in sleeping pattern	
1) I can sleep as well as usual.	
2) I don't sleep as well as I used to.	
3) I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.	
4) I wake up several hours earlier than I used to and cannot get back to sleep.	

Q17) Irritability	
1) I don't get more tired than usual.	
2) I get tired more easily than I used to.	
3) I get tired from doing almost anything.	
4) I am too tired to do anything.	

Q18) Changes in appetite	
1) My appetite is no worse than usual.	
2) My appetite is not as good as it used to be.	
3) My appetite is much worse now.	
4) I have no appetite at all anymore.	

Q19) Loss of weight	
1) I haven't lost much weight, if any, lately.	
2) I have lost more than five pounds.	
3) I have lost more than ten pounds.	
4) I have lost more than fifteen pounds.	

Q20) Tiredness or Fatigue	
1) I am no more worried about my health than usual.	
2) I am worried about physical problems	
3) I'm very worried about physical problems and it's hard to think of much else.	
4) I am so worried about my physical problems that I cannot think of anything else.	