3. AUTOMATED TECHNIQUES FOR IDENTIFYING DEPRESSION FROM EEG

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1 INTRODUCTION

The modern period is often called "the age of melancholy" [1]. Depression or melancholy is one of the common underdiagnosed diseases in clinical psychiatry [2]. Primary (i.e. which has no other associated cause) disorders of affect (mood) and thought are considered psychobiologic manifestations of abnormal brain mechanism. However, patients may also present with depression secondary to metabolic derangements, drug toxicity (e.g. antihypertensive drugs like reserpine, alpha methyl dopa, clonidine, propranolol; other drugs like levo-dopa, corticosteroids and amphetamine withdrawal may precipitate depression), influenza, hyperthyroidism, focal cerebral lesions, epilepsy or degenerative brain diseases [3]. There is some commonalty in the overt emotional behavior in all mammalian species from mouse to man. Burghardt [4] urges neuroscientists to join the collective effort to address the entire issue of mentalism, especially to use electroencephalography for comparing humans to animals where specific animal behavioral models of human mental states are known or can be developed. In most cases, before performing experiments with human beings, it is customary to test the validity of the results in lower animals. Several valid animal models of depression have been developed [5–7] which mimic most of the somatic symptoms of clinical depression.

Electroencephalography (EEG) reflects the spontaneous electrical activity of the brain during the various states of sleep and wakefulness. It is recorded usually with scalp electrodes in human beings. The presence of "Brain waves" (undulations in

the recording potentials) in animals, was discovered by Richard Caton in 1875. In 1929, Hans Berger of Germany developed the first practical EEG machine. In his honor, the "Alpha" rhythm of EEG is also called the "Berger rhythm". EEG, in its present applied form, does not assist much either diagnostically or prognostically in determining the extent of depression [3,8]. Development in the field of evoked EEG responses to stimuli have made possible greater detailed study of deviations in perception among psychological patients. Instead of analyzing only the frequency and amplitude changes, obtaining power spectra by fast Fourier transform of EEG signals conveys more information [9]. Gale and Edwards [10] believe that as a correlate of the ongoing behavioral and experiential stream, the EEG has no competitor.

Automated techniques are mailnly based on rule based expert systems and artificial neural networks (ANNs). Computerization has led to more sophisticated use of EEG, even in affective disorders, where perceptual processes are significantly distorted [11]. ANNs are also now being used to automatically recognize EEG patterns in various sleep states [12]. One may question the need of automated diagnosis from EEG recordings. The answer lies in the following. EEG paper recordings have not only great inter-observer variations, but also a lot of intra-observer variations. Unlike ECG (Electro-cardiography for heart), it is not very specific either. For a long time, qEEG has been trying to overcome these problems. As all these computer-assisted reports are being generated, the roles of visual estimation and pure analog signals as obtained on the direct paper recordings of EEG, are being sidelined. Another point against EEG paper recording is that an EEG strip-chart paper (a page of standard dimensions of $11'' \times 14''$), at 30 mm/s movement, for 16-channel recording will hold only 10-s sample. In other words, in 24 h, it will be 1.6 miles (2.6 km) long. If two multichannel monitors are used, approximately 50 miles of hardcopy per day will be generated, i.e. about 276 boxes of 1000-sheet EEG paper, weighing more than 2 tons. The cost (1992, USA) would have come to \$20 per box = \$5, 520 per day = > \$2millions per year [13].

Sleep is an active action of the brain on which, about 200 years back, Samuel Johnson [14] had commented: "Sleep is a state in which a great part of every life is passed . . . Yet this change, so frequent, so great, so general and so necessary, no searcher has yet found the efficient cause, or can tell by what power the mind and body are chained down . . . or what benefits the animal receives from this alternate suspension of its active powers." Sleep research has also advanced very much and is presently an important constituent of psychophysiological experiments. Sleep has an essential or obligatory function which is helpful in combating stress, and thereby affecting mood, by reorganizing the unpleasant memories [15]. Aserinsky and Kleitman [16] had termed REM (Rapid eye movement, fast, paradoxical, dreaming, desynchronized or D) and NREM (Non-rapid eye movement, orthodox, synchronized or S) sleep. Later Dement and Kleitman [17] further classified sleep into REM, Stage 1 (Drowsiness), Stage 2 (Light Sleep), Stage 3 (Deep Sleep) and Stage 4 (Very Deep Sleep). Stages 3 and 4 together are also called Slow Wave sleep or SWS [9]. REM and NREM sleep can be differentiated by simultaneous recording of EEG, EMG (electromyogram) and EOG (electrooculogram) [16,18]. REM sleep is dominated by hippocampal "theta"(θ)

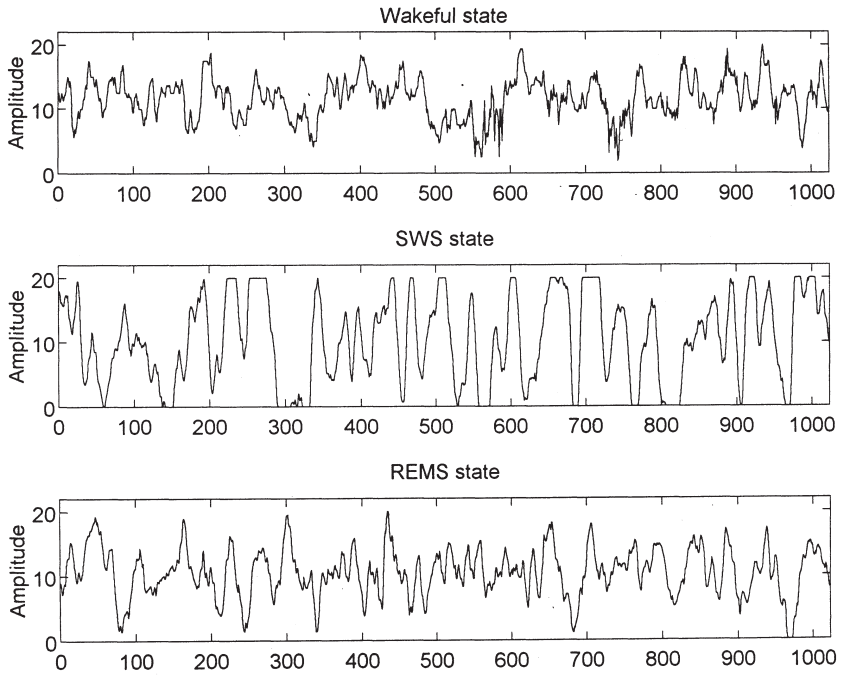

Figure 3.1. Digital EEG tracings during wakeful, SWS and REM sleep states.

rhythm, which correlates with "search behavior" in waking. Hippocampal θ rhythm is obtained by EEG tracing from the hippocampus of the animal. It is a rhythmic slow activity, sinusoidal, with frequency ranging from 5–10 Hz in rats, 4–7 Hz in cats and dogs. It is found in voluntary, appetitive, instrumental, purposive, operant, or "theta" behavior [19]. International Federation of Societies for Electroencephalography and Clinical Neurophysiology (IFSECN, 1974) [9] standardized the nomenclature. The characteristic EEG tracings (in wakeful and REM/NREM sleep states) are shown in Figure 3.1.

In depression, the most marked changes in sleep patterns are: short REM latency, increased REM density, increased sleep-onset latency, reduced total sleep time and efficiency, decreased stages 2 and 3 as percent total sleep time and an early temporal distribution of REM sleep [20,21]. There is also a decrease of SWS and Slow Wave Activity [22]. In other words, we dream more in depression [23].

The behavioral changes (food, sleep and work habits) are quite conspicuous in depression. During mood disorders, there are behavioral deficits like psychomotor retardation, in animals as well. These changes too can be quantified and correlated with the EEG findings [24].

"All work and no play, makes Jack a dull boy" is an age old adage. Modern medical management is also echoing the same thought. As another aphorism goes, "Prevention is better than cure", chronic (long-term) regular moderate physical exercise has been found to have beneficial effects in preventing cardiovascular, especially hypertensive disorders; metabolic and endocrine (hormonal) disorders like diabetes mellitus and also mood disorders like depression [25]. Regularly performed exercise helps in coping with environmental stress in humans and animals [26–28]. Therefore exercise is now being recognized as an effective antidepressant measure, in stress related mental disorders. Regular moderate physical exercise often reverses the EEG changes found in depression [24,29].

The notion, that the two cerebral hemispheres of the brain have different functions, has come into limelight in the last two decades. There is now hardly any doubt that affective (emotional) functioning is lateralized in the brain. It is generally recognized that the left hemisphere (LH) is superior for cognitive functions, and albeit less well defined, the right hemisphere (RH) is superior for emotional functions [30]. The lateralization effects of depression are evident both behaviorally and electrophysiologically [31].

By now it must be evident that depression is not only caused by multifactorial agents but it also has got multifarious manifestations [3,32]. Therefore, for any automated system, at the present state of knowledge, it will not be possible to identify all sorts of depression in every case. However, it may be surmised that with the growth of technology, advancement in the knowledge of understanding depression will also be achieved as newer insights will be gained.

The next section describes different automated techniques for EEG classification, followed by a description of the EEG changes in depression in Section 3. Finally, Section 4 summarizes the conclusions.

2 AUTOMATED TECHNIQUES FOR EEG CLASSIFICATION

This review will follow the basic approach to EEG analysis assuming that the EEG signals are stochastic. In this context, various statistical pattern recognition techniques, segmentation procedures, syntactic methods, knowledge-based approaches and ANN models have been developed with different levels of success. However, only the investigations referring to EEG analysis in depression or related conditions will be reviewed here. Another fundamentally different approach to automated EEG analysis, assuming the EEG signals as the output of a deterministic system of relatively simple complexity, but containing non-linearities is gradually gaining grounds [33]. Albeit there are studies [34] following non-linear approaches in determining depression from EEG, perhaps some more time will be required to incorporate them into chapters like this. A point to note is that ANNs are essentially non-linear discriminant function generators, and newer connectionist expert systems can also include the contextual information as a readily interpretable knowledge-base within the networks. Moreover, new rules may be generated by using these networks [35–38].

Model-based approaches for EEG interpretation may also produce information not obtained otherwise [33,39]. This is either to describe the lumped properties of a particular system of the brain or to describe the relationship between the cellular firing and the population rhythmic waves of a specific brain region in detail [40,41]. In other words, stochastic, deterministic and neural model based approaches, for electroencephalographically identifying various psychiatric disorders including depression, may act complementarily. But, reviewing all the approaches, at the present state of the art, is beyond the scope of this article.

2.1 Expert systems

The nature of EEG being (pseudo-)random, comparison between two EEG intervals was initially based on stochastic techniques like statistical pattern recognition. The necessary quantitative features extracted for this purpose are discussed in Section 2.3. To overcome the unwanted sources of variability due to non-stationarity of EEG signals, (i) time-varying modeling like autoregressive (AR) techniques and (ii) segmentation were used [9,42,43].

However, by piece-wise segmentation and clustering, the temporal relationship between elementary patterns gets lost. Spatial (across channels) and temporal contexts play a crucial role in visual EEG interpretation [44]. Temporal context may be preserved by means of transition matrices rather than profiles. The transition matrices quantify the number of times an elementary pattern of type i is followed by one of type j in long EEG intervals [45].

Spatiotemporal contextual information can be incorporated for automated EEG analysis through syntactic analysis techniques. Here, EEG is represented as a series of elementary patterns called "tokens". After subdividing an EEG tracing into 1-second intervals, a sequence of unique characters may be called a "label". The resulting sequence of "labels" is usually known as a "sentence" which is "parsed" by a definite "grammar". A grammar consists of a set of rules that governs the merging of tokens into higher-order recognizable entities in the input data [46].

A severe drawback in this approach lies in the amount of heuristics involved in writing the grammar. Also, it is almost impossible for an untrained electroencephalographer (EEGer) to inspect the grammar and make the necessary modifications. Knowledge-based approaches purvey a way of increasing the involvement of the expert (EEGer) in the design process and also allow the utilization of contextual information to a larger degree. These systems (Expert Systems or ESs) apply a body of knowledge ("knowledge-base") to the input data and subsequently derived facts ("data-base"). Typically, the knowledge base comprises IF⟨premise⟩THEN⟨action⟩ type rules which presumably reflect the human expertise. Another advantage of this type of flexible problem solving approach is that the collection of rules may be modified from time to time [47,48].

Knowledge-based enhancement of EEG signals [49] and parallel processing [50] are being employed to save time and effort, as well as to increase the accuracy of the interpretations.

2.2 Artificial neural networks

The term "neural network" has been borrowed from neurophysiological literature. The biological "neuron" is the structural and functional unit of the nervous system. Two neurons are interconnected through gap junctions or "synapses". However, the "artificial neuron" not only consists of the cell body but also the synapse and the mechanism for learning within it, unlike its biological counterpart [51]. So, an ANN has essentially three elements – a set of processing "neurons", a specific topology of interconnecting weights between them and a learning law which purveys the updating of connection weights. Artificial neural networks (ANN) [52–54] can be formally defined as *massively parallel interconnections of simple (usually adaptive) processing elements that interact with objects of the real world in a manner similar to biological systems*. The benefit of neural nets lies in the high computation rate provided by their inherent massive parallelism, thereby enabling real-time processing of huge data sets with proper hardware backing. All information is stored distributed among the various connection weights. The networks can be trained by examples (as is often required in real life) and sometimes generalize well for unknown test cases. Human beings have very large memories of visual, auditory and problem-solving episodes. One key operation in solving new problems is finding closest matches to old situations. Approximate matching is something that brain-style models seem to be good at because of the diffuse and fluid way in which knowledge is represented. Ultimately, connectionists would like to see the symbolic structure "emerge" naturally from complex interactions among simple units, just as "wetness" emerges from the combination of hydrogen and oxygen, though it is an intrinsic property of neither [55].

ANNs have been successfully used for developing many pattern recognition techniques of EEG analysis. This includes the use of an ANN (Madaline) for distinguishing the EEG power spectra in normal, depressed and exercised rats [29]. There, Madaline Rule I [51] had been used with a first layer of thirty hard-limited (signum) adalines whose outputs purveyed inputs to a second layer of majority-vote-taker. In that investigation, rules were not generated. There the results in the wakeful state was not as good as those in the sleep states. However, assessing the wakeful state is more important for long term monitoring, especially in humans. A few of the earlier investigators [45,56–58] have used neural networks and expert systems for EEG waveform analysis and topography. Some [59,60] have used AI for classifying evoked potentials. Jansen [61] has used ANN for K-complex detection and Frost [44] has used it in epilepsy. Mamelak *et al*. [12] successfully used neural nets for automated staging of sleep in cats and O'Boyle *et al*. [62] had used FFT of EEG from "eyes open" and "eyes closed" persons for distinguishing with an ANN. Klöppel (1994) has discussed Neural Networks as a useful method for EEG analysis [63]. In another common disease, hypertension, Poli *et al*. [64] had very successfully used ANN for diagnosing and treating. The ANN had three main modules – for reference generating, drug compatibility testing and therapy selecting. Each of the modules had multiple layers of neurons and it gave 94% correct diagnosis and 82% acceptable treatment prescription.

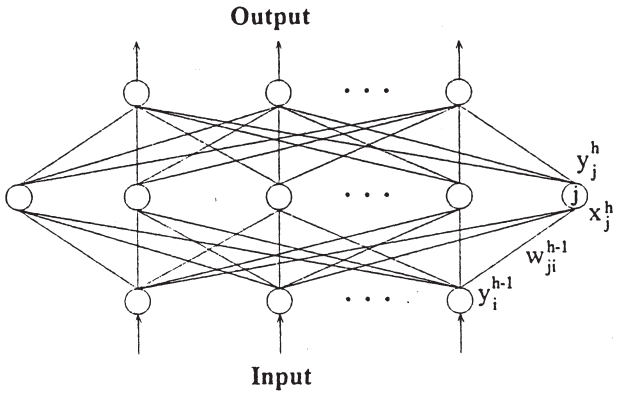

Figure 3.2. Multi-layer Perceptron.

Recently, ANNs have also been used for inferencing and rule generation in expert systems [35]. Medical experts rely on linguistic labels of any symptom or sign for reaching a proper decision. So, if an expert system can provide linguistically the rules for its inferences, it can be of great help to the clinician. Let us now describe, in detail, how rule generation can be achieved using multilayer perceptron (MLP) architecture, from its classification aspect.

The MLP [52] consists of multiple layers of simple, two-state, sigmoid processing elements (nodes) or neurons that interact using weighted connections. After a lowermost input layer there are usually any number of intermediate or *hidden* layers followed by an output layer at the top. There exist no interconnections within a layer while all neurons in a layer are fully connected to neurons in adjacent layers. Weights measure the degree of correlation between the activity levels of neurons that they connect.

Classification

An external input vector is supplied to the network by clamping it at the nodes in the input layer. For conventional classification problems, during training, the appropriate output node is clamped to state 1 while the others are clamped to state 0. This is the desired output supplied by the *teacher*.

Consider the network given in Figure 3.2. The total input x_j^{h+1} received by neuron j in layer $h+1$ is defined as

$$x_j^{h+1} = \sum_i y_i^h w_{ji}^h - \theta_j^{h+1}, \tag{1}$$

where y_i^h is the state of the i-th neuron in the preceding h-th layer, w_{ji}^h is the weight of the connection from the i-th neuron in layer h to the j-th neuron in layer $h+1$ and θ_j^{h+1} is the threshold of the j-th neuron in layer $h+1$.

The output of a neuron in any layer ($h > 0$) other than the input layer is a monotonic non-linear function of its total input and is given as

$$y_j^h = \frac{1}{1 + \mathrm{e}^{-x_j^h}}. \tag{2}$$

The Least Mean Square (LMS) error in output vectors, for a given network weight vector $\boldsymbol{w}$, is defined as

$$E(\boldsymbol{w}) = \frac{1}{2} \sum_{j,c} \left(y_{j,c}^H(\boldsymbol{w}) - d_{j,c} \right)^2, \tag{3}$$

where $y_{j,c}^H(\boldsymbol{w})$ is the state obtained for output node j in layer H in input–output case c and $d_{j,c}$ is its desired state specified by the teacher. One method for minimization of $E(\boldsymbol{w})$ is to apply the method of gradient-descent by starting with any set of weights and repeatedly updating each weight by an amount

$$\triangle w_{ji}^h(t) = -\epsilon \frac{\partial E}{\partial w_{ji}} + \alpha \triangle w_{ji}^h(t-1), \tag{4}$$

where the positive constant ϵ controls the descent, $0 \leq \alpha \leq 1$ is the damping coefficient or momentum, and t denotes the number of the iterations currently in progress.

After a number of sweeps through the training data, the error $E(\boldsymbol{w})$ in Eq. (3) may be minimized. At this stage the network is supposed to have discovered (learned) the relationship between the input and output vectors in the training samples.

Rule generation

The trained MLP is used for rule generation in *If-Then* form [35]. These rules describe the extent to which a pattern belongs or not to one of the classes in terms of antecedent and consequent clauses. For this, one has to backtrack along maximal weighted paths using the trained net and utilize its input and output activations.

After training, the connection weights of an MLP encode among themselves (in a distributed fashion) all the information learned about the input–output mapping. Therefore, any link weight with a large magnitude reflects a strong correlation between the connecting neurons. This property is utilized in evaluating the importance of an input node (feature) on an output layer mode (decision). For this one needs to compute the path weights from each output node to each input node through the various hidden nodes. Each output–input path that is maximum (through any hidden node) denotes the importance of that input feature for arriving at the corresponding output decision. Note that one or more hidden layers may be considered (if necessary) for evaluating the path weights. An increase in the number of hidden layers simply leads to an increase in the possible variety of paths being generated through the various hidden nodes in the different layers.

An input pattern $\mathbf{F}_p$ from the training set is presented to the input of the trained network and its output is computed. The consequent part of the corresponding *If-Then*

rule is generated from the output node activation. To find the antecedent clauses of the rule, one has to backtrack from the output layer to the input through the maximal weighted links.

Output layer

Let the user ask for the justification about a conclusion regarding class j. Starting from the output layer $h = H$, the process continues in a *top-down* manner until the input layer ($h = 0$) is reached. In the first step, for layer H, select those neurons i in the preceding layer that have a positive impact on the conclusion at output neuron j. Hence one has to choose neuron i of layer $H-1$ if $w_{ji}^{H-1} > 0$. Let the set of m_{H-1} neurons of layer $H-1$, so selected, be $\{a_1^{H-1}, a_2^{H-1}, \ldots, a_{m_{H-1}}^{H-1}\}$ and let their connection weights to neuron j in layer H be given as $\{\text{wet}_{a_1^{H-1}} = w_{ja_1}^{H-1}, \ldots, \text{wet}_{a_{m_{H-1}}^{H-1}} = w_{ja_{m_{H-1}}}^{H-1}\}$. For the remaining layers one can obtain the *maximum weighted* paths through these neurons down to the input layer.

Intermediate layers

Neuron i in layer $0 < h < H-1$ is selected if

$$y_i^h > 0.5, \quad \text{and} \quad \text{wet}_{i^h} = \max_{a_k^{h+1}} \left[\text{wet}_{a_k^{h+1}} + w_{a_k i}^h\right], \tag{5}$$

such that $\text{wet}_{i^h} > 0$. Let the set of m_h neurons so chosen be $\{a_1^h, a_2^h, \ldots, a_{m_h}^h\}$ and their cumulative link weights to neuron j in layer H be $\{\text{wet}_{a_1^h}, \text{wet}_{a_2^h}, \ldots, \text{wet}_{a_{m_h}^h}\}$ respectively, by Eq. (5). Note that this heuristic ensures that each of the selected m_h neurons have a significant output response y_i^h. This implies choosing a path with neurons that are currently active for deciding the conclusion that is being justified. It also enables each neuron i to lie along one of the *maximum weighted* paths from the input layer ($h = 0$) to the output node j in $h = H$, by choosing only one of the m_{h+1} previously selected paths that provides the largest net weight wet_{i^h}.

Input layer

Let the process of Eq. (5) result in m_0 chosen neurons (paths) in (from) the input layer ($h = 0$). These neurons indicate inputs that are *known* and have contributed to the ultimate positivity of the conclusion at neuron j in the output layer H. It may happen that $m_0 = 0$, such that no clear justification may be provided for a particular input–output case. This implies that no suitable path can be selected by Eq. (5) and the process terminates.

Let the set of the selected m_0 input neurons be $\{a_1^0, a_2^0, \ldots, a_{m_0}^0\}$ and their corresponding path weights to neuron j in layer H be $\{\text{wet}_{a_1^0}, \text{wet}_{a_2^0}, \ldots, \text{wet}_{a_{m_0}^0}\}$. These neurons are arranged in the decreasing order of their *net impacts*, where the net impact for neuron i is defined as

$$\text{net impact}_i = y_i^0 * \text{wet}_{i^0}$$

Then clauses for an *If-Then* rule from this ordered list are generated until

$$\sum_{i_s} \text{wet}_{i_s^0} > 2 \sum_{i_n} \text{wet}_{i_n^0}, \tag{6}$$

where i_s indicates the input neurons selected for the clauses and i_n denotes the input neurons remaining from the set $\left\{a_1^0, a_2^0, \ldots, a_{m_0}^0\right\}$ such that

$$|i_s| + |i_n| = m_0,$$

$|i_s|$ and $|i_n|$ refer, respectively, to the number of neurons selected and remaining from the said set. This heuristic allows selection of those *currently active* input neurons contributing *the most* to the final conclusion (among those lying along the maximum weighted paths to the output node j) as the clauses of the antecedent part of a rule. Hence, it enables the *currently active* test pattern inputs (current evidence) to influence the generated *knowledge base* (connection weights learned during training) in producing a rule to justify the *current* inference.

The complete *If* part of the rule is found by ANDing the clauses corresponding to each of the features.

2.3 Features commonly used

There are two contradictory conjectures for the generation of EEG signals. The most well known conjecture has been that the EEG is a very complex-looking, virtually unpredictable signal; therefore, it must be produced by a very complex system [33]. Statistical pattern recognition [42] for complex system analysis has been based on extraction of quantitative features from EEG intervals. These features are supposed to be representative of the test segment and usually include parameters related to the frequency content of the signal.

Another recent trend has been not to classify the EEG signals according to the stochastic or statistical approach, rather apply non-linear dynamics for the dimension analysis. This is in view of finding chaotic attractors in EEG signals [65,66]. So, the more recent conjecture here is that the EEG is a very complex-looking, virtually unpredictable signal, therefore, it could be produced by a relatively simple, non-linear system [33]. The basis for this conjecture is that a non-linear dynamical system with at least three degrees of freedom (or state variables) may exhibit chaotic behavior. As an example of chaotic activity, the waxing and waning of alpha EEG activity in alert subjects may be considered. Though alpha activity resembles a sinusoid, it is certainly not periodic (i.e. does not repeat itself after a period T), it is bounded (i.e. amplitudes are generally confined upto 100 microvolts) and too regular to qualify as a noise. However, as this approach has hardly been applied for identifying EEG in depression, the authors will not further elaborate in this article.

Nearly two hundred years back Joseph Fourier (contemporary of Galvani, Volta, Euler and Bernoullis) defined the Fourier Series as an expansion of a periodic function into sinusoid (i.e. sine and cosine waves) functions according to a rule. Fourier series

is a special case of Fourier Transform. The EEG signal can be considered as a function as it is composed of numerous waveforms. By this method, the original signal (amplitude as a function of time) is converted to an amplitude spectrum – a graph of amplitude as a function of frequency. Usually the amplitude values are squared to give rise to "Power (Density) Spectra" [67,68]. It may be a continuous spectrum in which the graph is a continuous line over a range of frequency or a discrete spectrum (sometimes known as a line spectrum) in which only specific frequencies are present and their amplitudes are represented by vertical lines at those points on the frequency axis. This is the discrete Fourier transform (DFT) of the signal. Cooley and Tukey [69] presented an algorithm for the computation of DFT applicable when N is a composite number (product of two or more integers) and called it FFT (fast Fourier transform) algorithm. Presently FT can be done with the help of a personal computer using the FFT algorithms [70]. The advantages of spectra are its transparency and reversibility (by Inverse DFT the original signal can be regained). A sinusoidal function $X(t)$ is completely described by three parameters – amplitude A, frequency f and the phase ϕ as $X(t) = A\sin(2ft+\phi)$, where t is the time. More generally, an epoch of EEG will be approximated by m frequency components as $X(t) = \sum_{n=1}^{m} A_n \sin(2\pi f_n + \phi_n)$, where n varies from 1 through m. Here, $3m$ parameters are needed to specify the EEG epoch. Spectral analysis is a method of calculating the amplitude A_n and phase ϕ_n corresponding to each frequency component f_n that is contained in the EEG epoch. The power spectrum of the EEG is a measure of the relative magnitudes of the A_n^2s, with no account taken of the phase information. In case of a complete direct evaluation of an N-point DFT, $4N^2$ real multiplications and $(4N^2 - 2N)$ real additions are required. For the direct computation of the DFT, the amount of computation, and thus the computation time, is approximately proportional to N^2 and can become very great for large values of N. The basic principle is decomposing the computation of the DFT of a sequence of length N into successively smaller DFT's. It may be either decimation-in-time, where the sequence $X(t)$ is decomposed into successively smaller subsequences or decimation-in-frequency, where the DFT coefficient $X(k)$ is decomposed into smaller subsequences. The decimation-in-time algorithm is best applicable when N is an integral power of 2, i.e. $N = 2^r$. The characteristic FFT from EEG tracings in the three sleep-wake states (Figure 3.1) are shown in Figure 3.3.

FFT is not superior to time-domain transforms, rather it is more informative than the conventional analog recordings which are still preferred by clinicians. Any transform, being derived from the original signal, is always likely to lose some information. However, frequency domain processing makes the findings more objective (quantified) and hence, observer independent. Power density spectra measurement is a form of quantitative EEG (qEEG), albeit not the only one. Duffy [71] discusses the role of quantified EEG or quantified neurophysiology (qNP) or neurometrics or BEAM (Brain Electrical Activity Mapping) which gives color coded topographical representation of the FFT values in different regions of the brain. The darker sides of it are that controlling the artifacts are quite difficult, huge data sets have to be managed, classic EEG and multivariate statistics are essential for proper inferences.

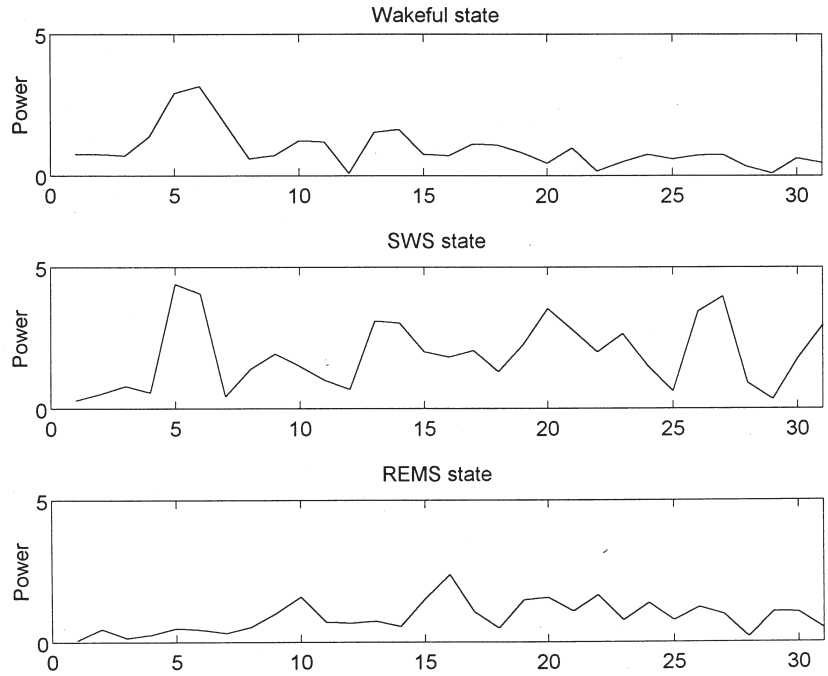

Figure 3.3. Curves of FFT coefficients of the three EEG tracings in Figure 1.

A modern tool, for the analysis of signals like EEG, "Bispectrum" [72,73], is the Fourier transform (FT) of the Third order cumulant (TOC) sequence generally used.

(a) to extract information in the signal pertaining to deviations from Gaussianity and
(b) to detect the presence of nonlinear properties and quadratic phase coupling.

Since TOC and Bispectrum are both zero for a stationary Gaussian process, bispectrum purveys a natural measure of Gaussianity. Also, bispectrum can detect phase coupling (i.e. presence of quadratic nonlinearity) and the degree of phase coupling can be quantified using the bicoherence index, i.e. a normalized bispectrum. Bispectra have been computed to detect phase coupling in the cortical and hippocampal EEG of rat during various vigilance states. For EEG recordings from the hippocampus, significant phase coupling was obtained during REM sleep between the frequency components 6–8 Hz associated with θ rhythm. During slow wave sleep, EEG from frontal cortex or hippocampus exhibit a larger deviation from Gaussian distribution than those of quiet waking and REM sleep. So, bispectral analysis yields extra information not obtainable from power spectrum.

Recently cepstrum (power spectrum of the logarithmic power spectrum) and bicepstrum analyses of EEG have also been tried [74,75] for EEG.

Apart from these, a new approach to visual evaluation of long-term EEG recordings has been based on multichannel adaptive segmentation, subsequent feature extraction, automatic classification of acquired segments by fuzzy cluster analysis (fuzzy c-means algorithm) and on distinguishing of the segments so identified by color directly in the EEG record [76].

The Lyapunov spectrum of EEG has also been analysed [77]. The FFT dipole approximation algorithm has been applied for localizing the sources of various EEG waves [78]. Another approach to measure the scalp potentials due to dipole sources has been a finite-element modeling of the human head [79].

3 CHANGES IN EEG SIGNALS IN DEPRESSION

Synchronously occurring post-synaptic potentials generate scalp EEG. Other membrane potentials like action potential do not contribute to EEG signals because of the following reasons:

(i) Membrane potential variation caused by an action potential generates a field which is equivalent to that of a single dipole perpendicular to the membrane because the piece of membrane that is depolarized at any instant of time is very small. In contrast, that of an electrotonically conducted post-synaptic potential extends, at any instant, over a larger portion of the membrane; thus generating a field corresponding to that of a dipole layer with dipoles perpendicular to the membrane surface. The latter attenuates with distance less rapidly than the former, and,

(ii) Action potentials, due to their short duration (1–2 ms), tend to overlap much less than do post-synaptic potentials (excitatory and inhibitory) which last longer (about 10–250 ms). When the action potentials do occur simultaneously (e.g. a short stimulus exciting a group of fibers), the field of the action potential may also be recorded at relatively large distances as a compound action potential. The post-synaptic potentials contribute primarily to the generation of extracellular field potentials in the cerebral cortex [80].

The main factor causing synchrony of the potentials is the structural nature of the nervous tissue (combination of interlocked excitatory and inhibitory populations). The neural masses act as a cortical macroscopic source, behaving like a dipole layer, directed perpendicular to the cortical surface. The dynamic properties of the rhythms (like frequency) depend upon the parameters of neuronal populations, viz., feedback gains, strength of connections, time properties of synaptic potentials and nonlinear properties (i.e. thresholds of saturation). The propagation of electrical activity in the cortex from small "epicenters" may cause time dilatation i.e. an EEG transient recorded at the cortex will seem to be of shorter duration than the transient recorded simultaneously at the scalp, as in epileptiform spikes. This happens as a moving dipole seen from a distance can be observed over a longer time than when seen from nearby [9]. The surface of the cerebral cortex is composed almost entirely of a mat of dendrites from neurons in the lower layers of the cortex. Dendrites may be conducting processes, but they are usually the sites of nonpropagated hypopolarizing

and hyperpolarizing local potential changes. When the excitatory endings become active, current flows into the current-sinks from the current-sources in the rest of the dendritic processes and the neuronal cell body (soma). The reverse happens in case of inhibitory impulse. The cell-dendrite relationship is that of a constantly fluctuating dipole. Current flow in this dipole would be expected to produce waveform potential changes in the volume conductor. When the sum of the dendritic activity is negative compared to the cell, the cell is hypopolarized and hyperexcitable; when it is positive, the cell is hyperpolarized and hypoexcitable. The cerebellar cortex and the hippocampus also produce characteristic fluctuations in surface potentials because of the complex, parallel dendritic processes located subpially over a layer of cells there. The brain wave intensity is closely related to the degree of activity in the thalamic or brainstem portion of the ascending reticular activating system.

The "inverse problem" which is to determine the intracerebral sources, given a measured potential distribution at the scalp, has no unique solution. According to modern approach [9] the intracerebral source is assumed to be an equivalent current dipole localized within the brain. To obtain possibly significant results, it is mandatory to use a model with inhomogeneities (i.e. with shells of different conductivities) to account for the layers surrounding the brain, viz., the cerebrospinal fluid (CSF), the skull and the scalp.

The EEG is a complex signal and its statistical properties depend on both time and space. However, the everchanging EEG signals can be analytically subdivided into representative epochs. Topographical consideration of the montages are essential for deriving useful information from the EEG.

EEG signal is said to be a realization of a stationary random or stochastic process and an average frequency or amplitude can be obtained statistically. The continuous EEG signal may be replaced by a string of numbers (set of values) $x(t_i)$ (denoted also as x), representing signal amplitude at sequential sample moments – indicated by index "i" along the time axis. The entire collection of EEG signals is called an "ensemble"; each member of the ensemble is called a sample function or realization. By "deterministic chaos", the EEG signal generated can be described using sets of nonlinear differential equations [33,65,66].

3.1 Animal studies

Thiébot *et al*. [7] say that animal behavioral models of psychiatric disorders cannot exactly simulate human psychopathology, but they can be used to evaluate the behavioral changes induced by drugs and to suggest hypotheses about the functions of the central nervous system and its involvement in psychiatric disorders. The most widely used animal for neuro-physiological research has been the albino or white Norway rat (Class: Mammalia; Subclass: Theria; Infraclass: Eutheria; Order: Rodentia; Suborder: Myomorpha; Superfamily: Muroidea; Family: Muridae; Subfamily: Murinae; Genus: Rattus; Species: norvegicus; Variant: albinus) i.e. *Rattus norvegicus* var. *albinus* [81].

Improving the understanding of the underlying neurobiological mechanism(s) of depression, is a major purpose of animal research of this kind. The sensitivity of the

behavioral changes to drugs (or other treatment like electroconvulsion or exercise), remains a principal reason for the heuristic value of the models. Drugs are invaluable tools that allow insight into the neurobiological processes of psychopathology. These symptoms are alleviated by chronic antidepressant therapy and electroconvulsive therapy. In them, RSD ("Rapid Eye Movement" Sleep Deprivation) by arousal, increases the pleasure seeking behavior like ICSS (Intra Cranial Self Stimulation). Also, chronic pharmacological RSD increases the motor, aggressive and ICSS behaviors in animal models of depression [82]. Even if the model is not an animal equivalent of human psychiatric illness, sensitivity to the same drugs may indicate that humans and animals share common neurobiological processes, which have behavioral consequences when subjected to the same constraints [83]. Feinberg *et al*. [84], using male rats with chronic implantation of electrodes, deprived them of sleep for 24 h by handling the rats gently when they became inactive. The "negative delta rebound" in these rats entailed a transient, near-total failure of delta amplitude to rise normally in response to the onset of darkness. This loss of EEG response to darkness suggests a disruption of basic sleep physiology and the negative rebound is a pathological response. The negative rebound may be caused by the massive increase in REM sleep that precedes it. These results, with TSD caused by gentle handling, confirm that TSD produces a far smaller initial delta increase than that reported for TSD with forced locomotion, indicating that a factor besides simple sleep loss contributes to the EEG response to sleep deprivation by forced locomotion.

As manual differentiation of EEG paper recordings in depression is not very helpful, the use of an ANN system to differentiate the EEG power density spectra in depressed from the normal rats was implemented [29]. The beneficial effects of chronic physical exercise in reducing the effect of stress and therefore depression was also tested by the same method. In this study, rats were divided into four groups, subjected to (i) chronic stress (D group); (ii) chronic exercise by treadmill running (EO group); (iii) exercise with stress (ES group) and (iv) handling (C group). The prefrontal cortical EEG, EMG and EOG were recorded simultaneously on paper and the digitized EEG signals were also stored in the hard-disk of a PC-AT through an ADC. The EEG power spectra was calculated by an FFT routine from the digitized and filtered signals. Three successive four-second artifact-free epochs were averaged. The REM and NREM sleep periods as well as the Awake period signals were analyzed separately. The FFT values from each of the three states, in the four groups of animals were tested by an ANN with 30 first layer neurons and a 2nd layer of a Majority-Vote-taker. The ANN could distinguish the depressed from the normal rats' EEG very well in REM (99%) sleep, NREM (95%) sleep and Awake (81%) states. In most of the cases it identified the Exercised rats' EEG as normal.

Later [38], a Multilayer Perceptron (MLP) has been used to differentiate the EEG power density spectra (qEEG), in the wakeful state, from animals (control, exercised and depressed). The qEEG from 1–30 Hz, at 1 Hz increment (thirty input features) and also as slow, medium and fast activity (represented by three ranges of frequencies at the input) have been used. After training with depressed and control qEEG only, the MLP has been found to distinguish successfully between the normal and the depressed

Table 3.1. Recognition score (%) on qEEG data with training set (30 + 30).

Model	MLP							Bayes'
Input features	30			3				3
No. of layers	3	4	5	3		4	5	—
Hidden nodes	30	5 : 5	5 : 5 : 5	5	15	5 : 5	5 : 5 : 5	—
Training (overall)	100	100	100	96.67	98.33	96.67	95	—
Testing (overall)	82.14	82.14	83.93	80.36	80.36	80.36	80.36	69.6
Depressed	100	100	100	96.67	96.67	96.67	96.67	80
Normal	61.54	61.54	65.38	61.54	61.54	61.54	61.54	57.69

Table 3.2. Recognition score (%) on qEEG data with training set (25 + 25).

Model	MLP							Bayes'
Input features	30			3				3
No. of layers	3	4	5	3		4	5	—
Hidden nodes	30	5 : 5	5 : 5 : 5	5	15	5 : 5	5 : 5 : 5	—
Training (overall)	100	100	100	100	100	100	100	—
Testing (overall)	76.8	76.8	75	82.14	82.14	80.36	80.36	69.64
Depressed	93.33	90	93.33	96.67	93.33	90	90	80
Normal	57.69	61.54	53.85	65.38	69.1	69.1	69.1	57.69

rats in more than 80% of the cases, identifying, in the process, most of the exercised groups' EEG as normal. The reduction in the dimension of input features from thirty individual frequencies to three frequency bands has produced similar results. The rules generated for making such distinctions have been found to be similar to the clinical views.

Tables 3.1–3.4 demonstrate the recognition scores obtained using MLP corresponding to the training samples' size of thirty + thirty, twenty five + twenty five, twenty + twenty and fifteen + fifteen from the depressed and normal groups, respectively, with different number of layers, the k-NN classifier and the Bayes' classifier.

Only those hidden node configurations yielding the best results have been shown in the table. Note that $n_1 : n_2 : n_3$ nodes, in the third row, refer to n_1, n_2, n_3 nodes in the first, second and third hidden layers respectively.

Here, the Bayes' classifier with multivariate normal class conditional densities and *a priori* class occurrence probabilites $p_i = |C_i|/N$ was used. Here C_i indicates the number of patterns in the ith class and N is the total number of pattern points. The covariance matrices for the pattern classes were considered to be different.

Table 3.3. Recognition score (%) on qEEG data with training set (20 + 20).

Model	MLP							Bayes'
Input features	30			3				3
No. of layers	3	4	5	3		4	5	—
Hidden nodes	30	5 : 5	5 : 5 : 5	5	15	5 : 5	5 : 5 : 5	—
Training (overall)	100	100	100	100	100	100	100	—
Testing (overall)	78.6	73.2	76.8	80.36	80.36	80.36	80.36	71.43
Depressed	86.67	80	86.67	93.33	96.67	93.33	90	83.33
Normal	69.1	65.38	65.38	65.38	61.54	65.38	69.1	57.69

Table 3.4. Recognition score (%) on qEEG data with training set (15 + 15).

Model	MLP							Bayes'
Input features	30			3				3
No. of layers	3	4	5	3		4	5	—
Hidden nodes	30	5 : 5	5 : 5 : 5	5	15	5 : 5	5 : 5 : 5	—
Training (overall)	100	100	100	100	100	100	100	—
Testing (overall)	75	75	75	78.6	76.8	78.6	78.6	80.36
Depressed	86.67	86.67	86.67	96.67	93.33	96.67	100	100
Normal	61.54	61.54	61.54	57.69	57.69	57.69	53.85	57.69

The k-nearest neighbors (k-NN) classifier [85], with $k = 1, 3, 5, 7$, was also implemented. The k-NN classifier is reputed to be able to generate piecewise linear decision boundaries and, thereby, is quite efficient in handling concave and linearly nonseparable pattern classes. Therefore, a comparison of the performance of the neural net model with that of the k-NN classifier is justified.

It may be noted that in the earlier work [29], with Madaline Rule I, with thirty input features and thirty adalines, the overall percentage recognition of the test set was 81. In the case of depressed group, it could correctly recognize only 86%, but it recognized 79.33% of the other groups as normal. However, the better recognition for the normal groups was due to the fact that the training set had hundred samples from each group.

The overall recognition scores for the training and test sets are provided along with the individual classwise performance for the test set only. It was observed that reducing the dimension of input features from thirty to three leads to no significant degradation in performance. The overall performance by the MLP was better than that by the Bayes' classifier.

Also, with fifteen + fifteen, twenty + twenty and twenty five + twenty five training samples, three features (ranges) yielded better scores than thirty features. This

indicates that the seclection of the three ranges of frequencies was reasonably good. Therefore, besides faster computation there is the added advantage of increased efficiency by reduction in input feature dimension. Only the salient points were selected from the three ranges and this is also justifiable clinically since the slow and the fast EEG activities are indeed altered in depression.

However, training with ten + ten and five + five samples did not yield good results with MLP because a very small training set does not allow the MLP to learn the input–output relationship properly. This leads to over learning and subsequent poor generalization on the test set. On the other hand, for normal densities, Bayes' classifier gives the best decision surface. Moreover, even in cases where the Bayes' classifier performed better, the recognition scores were more or less comparable to that of the MLP (e.g. in the fifteen + fifteen case).

Another interesting feature observed is that this model was able to classify most of the exercised rats' (with or without concomitant stress) qEEG as normal, as in the previous study [29].

Rule generation

Rules had been generated for the three input case according to Eq. (5). Let the three features be represented as F_1, F_2 and F_3 corresponding to EEG activity levels *slow, medium* and *fast* respectively. The rules obtained were enumerated as follows:

- If F_1 is large and $F_2 > 0$ and F_3 is small, then class 1 (Depressed).
- If F_1 is small and $F_2 < 0$ and F_3 is large, then class 2 (Normal).

Note that by Eq. (5) one can descend at input nodes having activation greater than 0.5, along the maximally weighted paths [35]. The neuronal activation is the product of the weight and signal value traveling through the path. The investigators have actually calculated the weights, as well as, the products of weights and respective signal values for deducing a particular rule. In both the cases the results have been similar. In this article the approach is modified a little bit to suit the requirement of the data domain. Here the conventional approach of n input nodes is used instead of the $3n$ linguistic input nodes as in [35]. Therefore, the product is compared as $w^0_{ji_A} y^0_{i_A}$ corresponding to F_1 and F_3, such that the feature providing a relatively lower value is assigned a linguistic label *small* while the other is defined as *large*.

It is observed that the two rules match partly with the statistical analysis of the data [24,29]. In depression, the slow wave (δ or delta) EEG activity is increased and the fast wave (β or beta) EEG activity is reduced. Incidentally the role of F_2 cannot be explained from the existing clinical ideas and the experimental findings. The reasons for this may lie in the fact that the medium EEG activity defined here encompasses two bands – θ (theta) and α (alpha) and a sub-band β_1 (beta-1) or slow beta activity.

3.2 Human studies

Horne [22] states that in normal subjects, the prefrontal cortex (PFC) is the site of greatest cortical brain work during wakefulness, with the reverse being so during human slow wave sleep (hSWS) and activity (hSWA). The delta EEG activity is most intense in the PFC. Human SWS is that form of sleep which is most positively correlated with the length of prior wakefulness and hence seems to be most likely of all sleep-EEG characteristics to be associated with recovery processes. Thus it would seem that cortical recovery, if it exists in sleep, is most likely to occur during hSWS and in the PFC. However, to date, due to lack of data, there are no empirical findings actually linking hSWS with PFC recovery. The neuropsychological effects of TSD (total sleep deprivation) in normal subjects point to some reversible PFC dysfunction. Such effects seem more pronounced than those relating to the function of other cortical areas. However, at the moment it cannot be determined whether it is the loss of hSWS itself during TSD that is specifically associated with PFC dysfunction or whether the cause is a more generalized sleep loss. Low levels of hSWS may be indicative of certain forms of PFC impairment. Such a rationale may apply to chronic depression, type 2 schizophrenia and to some extent to normal aging where there is also diminished hSWS and some symptoms indicating PFC impairment. A change in PFC function may be the result of a more subtle failing elsewhere, em e.g., in the basal ganglia and the limbic system. During wakefulness, the PFC somehow causes or facilitates the rest of the cortex to move into action, and during sleep, to move into a more profound resting state and to generate hSWS. Impaired function of PFC seems to lead to less organization of the cortex, particularly towards the tasks in hand, and a marked deterioration in hSWS throughout the cortex. Summarily, there seems to be an intriguing link between hSWS and PFC function. Riemann *et al*. [86], studying the cholinergic REM induction test with agonist RS86, found that sleep efficiency and amount of SWS decrease with age, number of awakenings and early morning awakening. The amount of stage 1 sleep (drowsiness) increases with age. The REM latency is negatively correlated with age only in major depressives. Statistically significant differences (with the controls) are present for almost all the parameters of sleep continuity in major depressives. REM latency and density are also altered in major depression.

Aeschbach *et al*. [87] studied the effects of triazolam, a minor tranquilizer/ anxiolytic (0.25 mg), on the stages of sleep in sitting position and the EEG power spectra, in healthy male subjects. There was an increase in the SWS with triazolam in first third of night, and in the morning. The sleep was also more quiet. There was a reduction in NREM EEG (1.25–10 Hz) and there was a rise in sleep spindles (12.25–13 Hz) which were present also in the last third of night. In REM, triazolam reduced the spectrum in 4.25–10 Hz range. Sitting posture itself affected the NREM spectra.

Coble *et al*. [88], conducting a study on childbearing women, found that the sleep systems of subjects with history of depression were more fragile. Those subjects showed depressive stigmata even in absence of mood disturbances.

Grunhaus *et al*. [89] observed that in depressed patients, electroconvulsive therapy (ECT) reduces REM activity and density. In 50% patients there is also sleep-onset REM.

Mendlewicz and Kerkhofs [21], conducting a WHO collaborative study, found that throughout the world, compared with controls, depressed patients showed sleep-continuity disturbances like increase in sleep-onset latency, decrease in total sleep time and in sleep efficiency. Stages 2 (light sleep) and 3 (deep sleep), as percentage of total sleep time, were reduced in depressed patients. REM latency was shortened and REM density increased.

These findings confirm the presence of specific sleep-EEG abnormalities in major depression. Earlier Vogel *et al*. [20] had also found an early temporal distribution of REM sleep period in case of endogenous depression.

3.3 Hemispheric lateralization

Interestingly, there is a greater right sided (non-dominant hemispheric) EEG abnormalities in depression due to impaired lateralization [31,90,91]. So, females are more prone (because of earlier cerebral lateralization) and males are less predisposed to depression. Therapeutically too, better antidepressant results are obtained with nondominant unilateral electro convulsive shock [92].

Shagass *et al*. [93], testing "eyes open" and "eyes closed" awake EEGs, in 12 leads, in different psychiatric patients, found that depressives, like the personality disorder group, had a low level of EEG activation. Later, they [94] had performed time series analysis of amplitude, frequency and wave symmetry. Differences between eyes open and closed were adjusted for "eyes closed" values to obtain measures of reactivity. These reactivity measures yielded the main difference between the unmedicated and non-patients. Depressives were more reactive. Reactivity differences were eliminated or reversed in medicated patients. The EEGs of unmedicated depressives were over-reactive and with medication, EEG reactivity declined.

Nyström *et al*. [95] had chosen 5-second epochs from 5-min awake-EEG recordings and averaged to a total of 60-second recordings. In primary major depressive disorder (MDD), they found an increase in "delta" amplitude and in retarded MDD, increased "delta" and "theta" amplitude along with EEG variability. In cases of recurrent unipolar MDD, a reduction of total alpha symmetry was found. Symmetry was measured by left/right ratio in amplitude values (mean amplitude = square root of power). The number of the former depressive episodes were positively correlated with "beta" amplitude and negatively correlated with EEG symmetry for "delta".

It is generally claimed that "affect" processing is a right hemisphere (RH) function. It is also claimed that RH dysfunction is characteristic of depressive illness. Both these claims are controversial and it has been found that the relationship between affect processing and affective illness, in terms of intra- and inter-hemispheric role play, is not straight forward. There is an exchange of information and action between the two hemispheres (inter-hemispheric, i.e. between left and right; intra-hemispheric, i.e. between anterior and posterior; and also cross-hemispheric coupling, i.e. similarities among the left anterior and right posterior quadrants) [31,96]. Summarily, sad mood

is a function of positive coupling (stimulation) of left posterior and right anterior areas and/or negative coupling (depression) of left anterior and right posterior areas of the brain.

3.4 Sleep changes

The sleep stages have been mentioned in the introduction (Section 1). Operationally, in animals, [97], "SWS" (Slow wave sleep) is defined when the rat lays down its head with closed eyes and high amplitude slow waves are recorded from the neocortex. "REM" (Rapid eye movement) sleep can be defined when the rat is in a sleep posture with head supported. REM sleep occurs only after a period of SWS and is characterized by neocortical desynchronized EEG, irregular respiration, body jerks, vibrissae twitches and rapid eye movements. The period during REM with muscular twitches (phasic REM) is typically recorded. Awakening from the SWS cause the neocortical EEG to become lower in amplitude. The rat typically lifts up its head suddenly and starts staring straight ahead with a fixed posture for a few seconds. Then it might make postural adjustments or lower its head back to a sleep posture; EEG during these movements are avoided.

Cai [15] purveys a new theory regarding the functions of sleep by integratively analyzing different areas of sleep research. From the phylogenetic studies and other related sleep research it can be concluded that sleep in mammals has at least one obligatory function which cannot be accomplished during waking. The hypothesis also shows that the synchronized sleep (SS) period plays a critical function in accomplishing the obligatory functions of sleep, which are related to the brain. That is, adjusting and reorganizing emotional behavior is a very important function of SS. Cai also suggests that the gradual accumulation of the variously randomly learned memories, during waking, in the limbic structure would inevitably imbalance and disorganize emotional behaviors. So, sleep should have developed in evolution to adjust and reorganize emotions and so that the function of SS for memory and emotion regulation are the obligatory functions of sleep. Albeit phylogenetic studies suggest that PS (paradoxical sleep) may not play obligatory function across all mammals, along with SS, PS also plays very important roles in memory and emotion which are different from the corresponding SS roles in those mammals possessing PS. Obviously, sleep is the only mechanism for regulating emotions, which can be of a long-lasting effect.

The symptoms during endogenous depression and distinguishing it from reactive depression involve behavioral and psychological abnormalities. Behavioral abnormalities that can be modeled in animals include [98]: loss of interest in pleasurable activity, including sexual activity, diminished irritability and hostility and a psychomotor change, either retardation or agitation. In Section 3.1 it was stated that REM sleep deprivation also increases the pleasure seeking behavior like ICSS (Intra cranial self-stimulation) which is actually mediated through the endogenous opioid system, described in the next subsection.

3.5 Behavioral changes

Klemm [83] recalls the fact that mental states are generated by neural processes that also produce an associated EEG. Thus, logically, correlations can be expected between a mental state and the EEG. The corollary is that the EEG can serve as an index of mental state, especially for animal studies, where mental states are much less accessible for objective study than in humans. Virtually all of our conclusions about mental states in animals are drawn by inference from behavioral observations, a process that is inevitably subject to anthropomorphism. Traditionally, the EEG has been used in a crude way as an objective indication of physical and behavioral state in animals. However, this has caused substantial controversy because of several situations of EEG-behavioral dissociations. Powerful new methods like, topographical EEG mapping, wavelet analysis and testing for nonlinear (chaotic) dynamical properties and short-term serial dependencies, are now available for studying the extent to which the EEG can index thinking and feeling in humans, and by extrapolation, in animals. Nandrino *et al*. [34] reports a decrease of complexity in EEG as a sign of depression. Nonlinear methods can predict major depression because of the reduced complexity. In healthy systems, there is a high level of complexity in the dynamics. The diminished complexity of brain function, in depression, may be due to low level of environmental interaction.

In humans, suffering from major depression, in the wakeful state, slow EEG activity (θ_2 and α_1 bands) is positively and fast activity (α_3 and β_2 bands) is negatively correlated with psychomotor retardation [99]. Of the four retardation subitems (motor, verbal, intellectual and emotional), motor retardation is closest correlated with slow EEG activity. In the investigation [24] with an animal model of depression, the EEG power spectra have been correlated with the behavioral tests in the Open-field and the Elevated plus-maze. Hashimoto *et al*. [100] have made an extensive comparative study on the behavioral and EEG changes induced by anxiolytic drugs (Diazepam, Buspirone and DN-2327) during the various sleep-wake stages in normal cats.

Exercise increases the SWS and now it is found that it also reduces REM sleep – both of which do alleviate depressive mood. So, exercise exerts multimodal antidepressant effect. As shown in Figure 3.4, there is a significant positive correlation between β_2 EEG activity during REM sleep and anxiolytic manifestation (ambulation in central squares) [24]. Exercise also affects the endogenous opioid system, which in turn is related to "pleasure" sensation which is almost absent in severe depression.

Hawkins [101] has reviewed the evidence that endorphins (opioid or morphine-like compounds found within the brain) form the basis of pleasure response in the context of five areas of human experience: opiate use (e.g. opium, morphine, heroin, methadone); love and sex; alcohol; food and exercise. Clearly, all such complicated and personalized experiences depend upon many mechanisms, both psychological and physical, and there are few areas of human experience that are not related to the endogenous opioid systems. As discussed in the next subsection, exercise (e.g. games and sports) does give rise to pleasure sensation, whereas, depression acts in the opposite manner. The endogenous opioid system may be an important pathway for these manifestations.

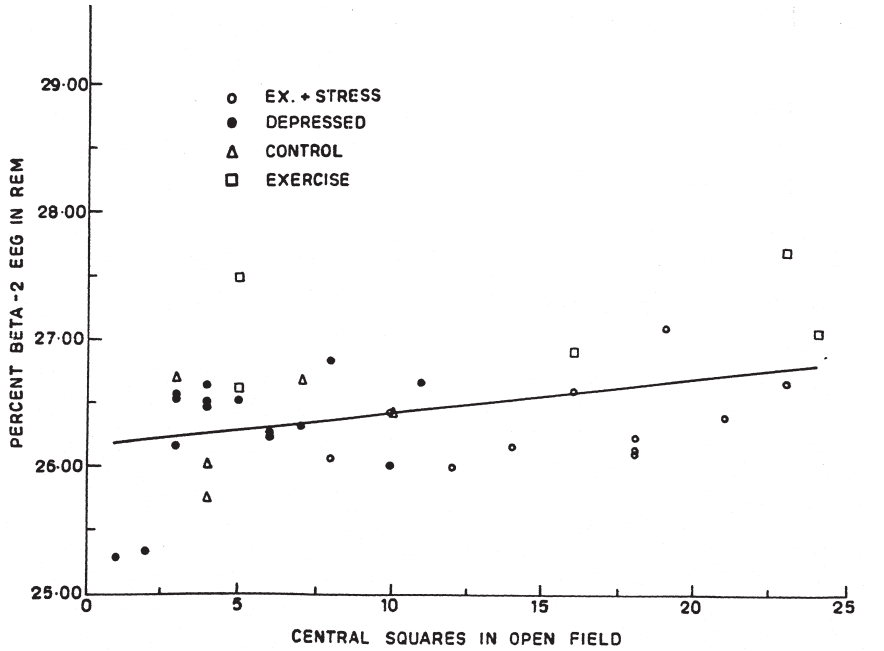

Figure 3.4. Scatterplot showing the significant positive correlation ($r = 0.3576$, $P < 0.05$) between ambulation in the central squares of the Open Field (denoting anxiolytic manifestation in the rats) and the percent power in the β_2 band of EEG during the REM sleep period, at the end of the experiment (from: [24]).

3.6 Changes in exercise

Regularly performed exercise is associated with diminished cardiovascular responses to environmental stress, even in animals [28]. However, there is a paucity of information regarding the potential mechanism(s) by which exercise training might blunt the response of stress. Exercise increases the slow wave sleep [22], which in turn, is associated with elevated mood. Again, how does exercise increase SWS and how does SWS alleviate depression, these are yet to be properly understood. Some evidences [28] suggest that physical training can alter β_1 and β_2 adrenoceptor population and reduce α-adrenergic responsiveness. Cross sectional studies based on national surveys done in the U.S.A. and Canada have shown a positive association between physical activity and affect (mood, depression, anxiety). The association seems to be most positive for self-reported and transient changes in affect and also of self-esteem [25].

Moore [102] has studied the effects of exercise on body-image, self-esteem and mood, in Australian female college students, testing with "Profile of Mood States" (and Levenson Locus of Control) Scales. Exercisers reported a higher quality of life, better mood states, greater concentration and reduced confusion. Hays [103]

advocates the use of exercise (in accordance with the need and capacity of the subject) in psychotherapy.

Schlicht [104], performing a meta-analysis of 20 studies published between 1980 and 1990, has observed 22 effect-sizes based on 1306 subjects. The age of the subjects served as a weakly moderating variable. For middle-aged (31–50 years), the relation between physical exercise and anxiety was closer than for younger adults. The marginal moderating effect of age correlated also with meta-analytical results of relationship between physical exercise and mental health. The interactions of physical activity and fitness with depression [105] have been stressed as an integral part of health.

Vogel *et al*. [20] had surmised "REM sleep deprivation" as the mechanism of action of most of the antidepressant drugs. Oniani *et al*. [82] had speculated that during active wakefulness (it can logically be extrapolated to exercise) and REM sleep, other neurobiological brain processes (particularly on the level of the forebrain) also proceed similarly, thus making these two states competitive. The impression is created that, on the one hand, episodes of forced wakefulness/activity restrict the formation of a biological need for REM sleep during SWS, and on the other, they can utilize the REM need already formed thereby reducing the depressive tendency.

4 SUMMARY AND CONCLUSIONS

An extensive review of the various modalities of EEG analysis in humans [106] and another review, on animals [83], are extant. In this article, the relative merits of some of the available techniques are discussed. ANNs have been used for sleep-wake staging [12] or for a more limited distinction between eyes open or closed, with the FFT of theta and alpha bands of EEG [62]. In normal subjects, by inducing four states (of expectation, negative event, positive event and rest period), the EEG power spectra have been measured [107]. There, sadness had reduced all powers, increased alpha band width and complexity. The conclusions were that EEG activity depicts an individual's actual emotional states.

In our recent investigation [38], we found that since the results with three reduced features (three ranges of frequencies) have been found to be comparable to those with thirty original input features (individual frequencies), one can exploit this dimension reduction capability. It will naturally make a neural net converge much faster even while dealing with huge databases and enable reaching a quicker diagnosis. The generated rules, if comprehensible clinically, will add to the diagnostic validity of automated qEEG detection in various neuropsychiatric conditions. In general, doctors deal with linguistic variables to reach a proper diagnostic decision. If the expert systems can produce such linguistic rules for discriminating between various clinical conditions, it will be of great help to the clinician. In future, such automated methodologies may also be applied to human beings. ANN can become a very useful tool in this field, leading to a greater concurrence between the diagnosticians of various laboratories, unlike now. Building up a proper database for psychiatric conditions, like depression, based on the qEEG findings and the rules generated by the ANN, may

help in realizing reliable connectionist expert diagnostic systems. In schizophrenia type 2 (with predominantly negative sysmptoms), there are behavioral similarities with depression. These may be reflected in the qEEG which can then be compared with the qEEG in depression. However, for psychiatric assessment by computers, an accompanying human clinician is essential [108]. Computerized assessments and clinical acumen are not mutually exclusive, rather they reinforce each other [109].

All the facts depicted in this article make us aware of our far from complete knowledge and understanding of definitive diagnostic and prognostic values of EEG reports. Even today the textbooks of medicine, neurology and psychiatry do not attach as much importance to EEG as they regard the ECG or Electrocardiogram. The EEG is considered to be quite nonspecific except in a few cases of epileptic disorders. Moreover the same recording elicits a different interpretation not only from different experts (inter-observer variations), but also from the same expert (intra-observer variations) at different times. On the other hand, the journals, specialized textbooks and reference books on EEG are stressing on the various new computer-aided (quantitative or qEEG) methods for analysis. As yet there is no consensus on the appropriate mathematical analysis. Each method has its inherent advantages and disadvantages. A neuropsychiatrist is less likely to afford the time to learn all of those techniques. In near future, that may lead to laboratory dependent qEEG diagnosis. Initially what had started with the aim of simplifying and standardizing the EEG interpretations, have, with time, grown into a much more complex and overexpanding exercise. However, without these computations, we could not have known the finer details of EEG and brain functions.

Spitzer *et al*. [110] had forwarded some arguments against computer-aided psychiatric diagnoses. The main constraint on the validity of computerized diagnosis is not in any inherent limitation of computer processing but rather in the limitations of the current diagnostic system itself. Improvements in computerized diagnosis await improvements in the diagnostic system, along the lines of simplification, explicit criteria, and limitation of the categories to those conditions for which validity evidence exists. The validity is determined by agreement with a clinician (expert or otherwise) or correlation with behavioral or physiological criteria or prediction of outcome or correctness of treatment assignment. Twenty years later, First [108] has discussed potential applications of computer technology to diagnostic assessment and two basic design axioms for computerized assessment. The first axiom: given the current state of computer technology, a human clinician must remain a necessary component of diagnostic procedure to ensure a sufficiently high level of diagnostic validity. The second axiom, for successful diagnostic computer program is that the clinician must understand completely the strengths and the limitations of the computer-assisted assessment procedure. Two basic approaches are the use of computers as an expert-system and the use of computers to collect data directly from patients by administering a diagnostic interview or questionnaire. Butcher [111] believes that computer-generated procedures for psychiatric assessment remove subjective bias from the interpretation process. However, computerized assessments (CAs) can also lead clinicians to make serious errors unless the potential problems are recognized and avoided. The CAs

can encourage a passive stance in clinical evaluation, mystify the assessment process and may lend an unwanted aura of scientific precision to test interpretations through impressive printouts. Also, it may not be specific or sensitive for each patient or disease. It should be considered as raw test data or hypothesis and not as final clinical evaluation.

Some of the likely problems that can be envisaged from the foregoing discussion are the following. It should be investigated whether all the results obtained from the animal experiments can be substantitated by human studies or not. Next, whether or not Depression and Schizophrenia type 2 show similar changes in EEG features deserves investigation. Further, whether there is any cerebral hemisphere-specific EEG change, in depression, which can be identified automatedly has to be found out. Another statistical point of interest may be to find out whether the behavioral, psychomotor and electrophysiological parameters, in depression and in exericse, can be significantly correlated or not. Apart from these, whether the rules generated from the learned networks can be corroborated with the clinical counterparts or even advance clinical decision making knowledge awaits confirmation.

To conclude, we can hopefully look forward to some objective and reliable automated techniques for identifying depression from qEEG in near future.

REFERENCES

1. G. Klerman. The age of melancholy. *Psychology Today* **10**: 37–88, 1979.
2. P. E. Greenberg, L. E. Stiglin, S. N. Finkelstein and R. Ernst. Depression: A neglected major illness. *J. Clin. Psychiatry* **54**: 419–424, 1993.
3. L. L. Judd, K. T. Britton and D. L. Braff. Mental disorders (Chap. 389 in Part 14.4). In: K. J. Isselbacher *et al.* (Eds), *Harrison's Principles of Internal Medicine*, Vol. 2, 13th edn, pp. 2400–2419. McGraw Hill Inc., New York, 1994.
4. G. M. Burghardt. Animal awareness. Current perceptions and historical perspective. *Am. Psychol.* **40**: 905–919, 1985.
5. P. Willner. The validity of animal models of depression. *Psychopharmacology* **83**: 1–16, 1984.
6. P. Willner. Animal models of depression: An overview. *Pharmacol. Ther.* **45**: 425–455, 1990.
7. M. H. Thiébot, P. Martin and A. J. Puech. Animal behavioural studies in the evaluation of antidepressant drugs. *Br. J. Psychiatry* **160**(Suppl. 15): 44–50, 1992.
8. R. Rosse, D. L. Warden and J. M. Morihisa. Applied Electro-physiology (Chap. 1.8). In: H. I. Kaplan and B. J. Sadock (Eds), *Comprehensive Textbook of Psychiatry*, Vol. 1, 5th edn, pp. 74–85. Williams and Wilkins, Baltimore, USA, 1989.
9. E. Niedermeyer and F. Lopes da Silva (Eds), *Electroencephalography – Basic Principles, Clinical Applications and Related Fields*. Urban and Schwarzenberg, Baltimore-Munich, 1987.
10. A. Gale and J. Edwards. The EEG and human behavior. In: A. Gale and J. Edwards (Eds), *Physiological Correlates of Human Behavior*, Vol. 2, pp. 99–127. Academic Press, New York, 1983.
11. R. Morstyn, F. H. Duffy and R. W. McCarley. Altered topography of EEG spectral content in schizophrenia. *Electroenceph. Clin. Neurophysiol.* **56**: 263–271, 1983.
12. A. N. Mamelak, J. J. Quattrochi and J. A. Hobson. Automated staging of sleep in cats using neural networks. *Electroenceph. Clin. Neurophysiol.* **79**: 52–61, 1991.

13. T. F. Collura, E. C. Jacobs, R. C. Burgess and J. P. Turnbull. The Epilog system: Automated long-term EEG monitoring for epilepsy. *IEEE Computer* **25**(9): 5–14, 1992.
14. S. Johnson. As quoted. In: D. Giannitrapani (Ed.), *The Electrophysiology of Intellectual Function*, p. 128. S. Karger, Basel, New York, 1985.
15. Z. Cai. The functions of sleep: Further analysis. *Physiol. Behav.* **50**: 53–60, 1991.
16. E. Aserinsky and N. Kleitman. Regularly occurring episodes of eye motility and concomitant phenomena during sleep. *Science* **118**: 273–274, 1953.
17. W. C. Dement and N. Kleitman. Cyclic variations in EEG during sleep and their relation to eye movements, body motility and dreaming. *Electroenceph. Clin. Neurophysiol.* **9**: 673–690, 1957.
18. A. Rechtschaffen and A. Kales (Eds). *A manual of standardized terminology. Technique and scoring system for sleep stages in human subjects*. UCLA Brain Information Service/Brain Research Institute, Los Angeles, USA, 1968.
19. C. H. van der Wolf, R. Kramis, L. A. Gillespie and B. H. Bland. Hippocampal rhythmic slow activity and neocortical low voltage fast activity: Relations to behavior. In: R. L. Isaacson and K. H. Pribram (Eds), *The Hippocampus*, Vol. 2, pp. 101–128, Plenum Press, New York, 1975.
20. G. W. Vogel, T. Roth, J. C. Gillin, W. B. Mendelson and A. Buffenstein, REM sleep and depression. In: T. Oniani (Ed.), *Neurobiology of Sleep–Wakefulness Cycle*, pp. 187–213. Metsniereba, Tbilisi, 1988.
21. J. Mendlewicz and M. Kerkhofs. Sleep electroencephalography in depressive illness. A collaborative study by the World Health Organization. *Br. J. Psychiatry* **159**: 505–509, 1991.
22. J. A. Horne. Human sleep, sleep loss and behaviour. Implications for the prefrontal cortex and psychiatric disorder. *Br. J. Psychiatry* **162**: 413–419, 1993.
23. S. N. Sarbadhikari. Let your Dreams come true through Virtual Reality. *J. Indian Med. Assoc.* **95**: 190, 1997.
24. S. N. Sarbadhikari, S. Dey and A. K. Ray. Chronic exercise alters EEG power spectra in an animal model of depression. *Indian J. Physiol. Pharmacol.* **40**(1): 47–57, 1996.
25. S. S. Harris, C. J. Caspersen, G. H. DeFriese and E. H. Estes Jr. Physical activity counseling for healthy adults as a primary preventive intervention in the clinical setting report for the US preventive services task force. *JAMA* **261**: 3590–3598, 1989.
26. T. Stephens. Physical activity and mental health in the United States and Canada: Evidence from four population surveys. *Prev. Med.* **17**: 35–47, 1988.
27. C. S. Liebowitz. To release stress – Exercise! *NY State Dent. J.* **55**: 36–37, 1989.
28. J. M. Overton, K. C. Kregel, G. Davis-Gorman, D. R. Seals, C. M. Tipton and L. A. Fisher. Effects of exercise training on responses to central injection of CRF and noise stress. *Physiol. Behav.* **49**: 93–98, 1991.
29. S. N. Sarbadhikari. A neural network confirms that physical exercise reverses EEG changes in depressed rats. *Med. Eng. Phys.* **17**(8): 579–582, 1995.
30. J. C. Borod. Interhemispheric and intrahemispheric control of emotion: A focus on unilateral brain damage. *J. Consult. Clin. Psychol.* **60**: 339–348, 1992.
31. M. K. Mandal, H. S. Asthana, R. Pandey and S. Sarbadhikari. Cerebral laterality in affect and affective illness: A review. *J. Psychol.* **130**(4): 447–459, 1996.
32. S. N. Sarbadhikari. Will the aging computer technology comfort the aging human? *Speculat. Sci. Technol., Special Issue on Computers in the Fight Against Aging* **19**(2): 131–136, 1996.
33. B. H. Jansen. Quantitative analysis of electroencephalograms: Is there chaos in future? *Int. J. Biomed. Comput.* **27**: 95–123, 1991.
34. J. L. Nandrino, L. Pezard, J. Martinerie *et al*. Decrease of complexity in EEG as a symptom of depression. *Neuroreport: Intl. J. Rap. Comm. Res. Neurosci.* **5**: 528–530, 1994.

35. S. Mitra and S. K. Pal. Fuzzy multi-layer perceptron, inferencing and rule generation. *IEEE Trans. Neural Networks* **6**: 51–63, 1995.
36. S. Mitra and S. K. Pal. Logical operation based fuzzy MLP for classification and rule generation. *Neural Networks* **7**: 353–373, 1994.
37. S. Mitra and S. K. Pal. Self-organizing neural network as a fuzzy classifier. *IEEE Transactions on Systems, Man and Cybernetics* **24**(3): 385–399, 1994.
38. S. Mitra, S. N. Sarbadhikari and S. K. Pal. An MLP-based model for identifying qEEG in depression. *Int. J. Biomed. Comput.* **43**: 179–187, 1996.
39. H. Carmesin. Statistical neurodynamics: A model for universal properties of EEG-data and perception. *Acta Physica Slovaka* **44**: 311–330, 1994.
40. R. D. Traub, R. Miles and R. K. S. Wong. Model of the origin of rhythmic population oscillations in the hippocampal slice. *Science* **243**: 1319–1325, 1989.
41. F. H. Lopes da Silva. The rhythmic slow activity (theta) of the limbic cortex: an oscillation in search of a function. In: E. Basar and T. Bullock (Eds), *Brain Dynamics Series. Induced Rhythms in the Brain*, pp. 83–102. Birkhäuser, Boston, 1992.
42. G. Bodenstein and H. M. Praetorius. Pattern recognition of EEG by adaptive segmentation. In: W. J. Perkins (Ed.), *Biomedical Computing*, pp. 20–31. Pitman Medical, London, 1977.
43. J. S. Barlow. Artifact processing in EEG data processing. In: F. H. Lopes da Silva, W. Storm van Leeuwen and A. Remond (Eds), *Clinical Application of Computer Analysis of EEG and other Neurophysiological Signals. Handbook of Electroencephalography and Clinical Neurophysiology, New Series*, Vol. 2, pp. 15–64. Elsevier, Amsterdam, 1986.
44. J. D. Frost Jr. Automatic recognition and characterization of epileptiform discharges in human EEG. *J. Clin. Neurophysiol.* **2**: 231–249, 1985.
45. B. H. Jansen and W. K. Cheng. Structural EEG analysis: An explorative study. *Int. J. Biomed. Comput.* **23**: 221–237, 1988.
46. J. R. Bourne, V. Jagannathan, B. Hamel, B. H. Jansen, J. W. Ward, J. R. Hughes and C. W. Erwin. Evaluation of a syntactic pattern recognition approach to quantitative electroencephalographic analysis. *Electroenceph. Clin. Neurophysiol.* **52**: 57–64, 1981.
47. V. Jagannathan, J. R. Bourne, B. H. Jansen and J. W. Ward. Artificial intelligence methods in quantitative electroencephalographic analysis. *Comp. Progr. Biomed.* **15**: 249–258, 1982.
48. B. H. Jansen. Quantitative EEG analysis in renal disease. In: F. H. Lopes da Silva, W. Storm van Leeuwen and A. Remond (Eds), *Clinical application of Computer Analysis of EEG and other Neurophysiological Signals. Handbook of Electroencephalography and Clinical Neurophysiology, New Series*, Vol. 2, pp. 239–260, Elsevier, Amsterdam, 1986.
49. E. C. Ifeachor, M. T. Hellyar, D. J. Mapps and E. M. Allen. Knowledge-based enhancement of human EEG signals. *IEE Proc.-F, Radar & Signal Processing* **137**: 302–310, 1990.
50. E. S. Manolakos, H. M. Stellakis and D. H. Brooks. Parallel processing for biomedical signal processing: higher order spectral analysis – an application. *IEEE Computer* **24**: 33–43, 1991.
51. B. Widrow and M. A. Lehr. 30 years of adaptive neural networks: Perceptron, Madaline and Backpropagation. *Proc. IEEE* **78**: 1415–1440, 1990.
52. D. E. Rumelhart and J. L. McClelland (Eds). *Parallel Distributed Processing: Explorations in the Microstructures of Cognition*. Vol. 1. MIT Press, Cambridge, MA, 1986.
53. J. Hertz, A. Krogh and R. G. Palmer. *Introduction to the Theory of Neural Computation*. Addison-Wesley, Reading, MA, 1994.
54. J. C. Bezdek and S. K. Pal (Eds). *Fuzzy Models for Pattern Recognition*. IEEE Press, New York, 1992.

55. E. Rich and K. Knight. *Artificial Intelligence, 2nd edn.* Tata McGraw Hill, New Delhi, 1991.
56. R. C. Eberhart, R. W. Dobbins and W. R. S. Webber. EEG waveform analysis using CaseNet. *Proc. Annual Int. Conf. IEEE, EMB Soc.* **6**: 2046–2047, 1989.
57. B. H. Jansen and B. M. Dawant. Knowledge-based approach to sleep-EEG analysis – a feasibility study. *IEEE Trans. Biomed. Eng.* **36**: 510–518, 1989.
58. A. Hiraiwa, K. Shimohara and Y. Tokunaga. EEG topography recognition by neural networks. *IEEE Eng. Med. Biol.* **9**: 39–42, 1990.
59. I. Bruha and G. P. Madhavan. Need for a knowledge-based subsystem in evoked potential neural net recognition system. In: *Proceedings of 11th Annual International Conference of IEEE-EMBS*, pp. 2042–2043. IEEE Press, New York, USA, 1989.
60. R. M. Holdaway, M. W. White and A. Marmmarou. Classification of somatosensory-evoked potentials recorded from patients with severe head injuries. *IEEE Eng. Med. Biol.* **9**: 43–49, 1990.
61. B. H. Jansen. Artificial neural nets for K-complex detection. *IEEE Eng. Med. Biol.* **9**: 50–52, 1990.
62. D. J. O'Boyle, E. W. K. Choi, G. Conroy and M. Turega. Learned classification of EEG power spectra using a neural network. In: *J. Physiol., Proceedings of the Physiological Society*, p. 345P. Sheffield Meeting, U.K., 19–20 April, 1991.
63. B. Klöppel. Neural networks as a new method for EEG analysis: a basic introduction. *Neuropsychobiology* **29**: 33–38, 1994.
64. R. Poli, S. Cagnoni, R. Livi, G. Coppini and G. Valli. A neural network expert systems for diagnosing and treating hypertension. *IEEE Computer* **24**: 64–71, 1991.
65. A. Babloyantz. Evidence of chaotic dynamics of brain activity during the sleep cycle. *Phys. Lett. (A)* **111**: 152–156, 1985.
66. F. H. Lopes da Silva. Neural mechanisms underlying brain waves: from neural membrane to networks. *Electroenceph. Clin. Neurophysiol.* **79**: 81–93, 1991.
67. A. V. Oppenheim and R. W. Schafer. *Digital Signal Processing*. Prentice-Hall of India Pvt. Ltd., New Delhi, 1989.
68. S. D. Stearns and R. A. David. *Signal Processing Algorithms*. Prentice-Hall Inc., Englewood Cliffs, New Jersey, 1988.
69. J. W. Cooley and J. W. Tukey. An algorithm for the machine calculation of Complex Fourier Series. *Math. Comput.* **19**: 297–301, 1965.
70. M. Cesarelli, F. Clemente and M. Bracale. The flexible FFT algorithm for processing biomedical signals using a PC. *J. Biomed. Eng.* **12**: 527–530, 1990.
71. F. H. Duffy. The role of quantified EEG in psychological research. In: G. Dawson and K. W. Fischer (Eds), *Human Behavior and the Developing Brain*, pp. 93–132. Guilford Press, New York, 1994.
72. T. Ning and J. D. Bronzino. Bispectral analysis of rat EEG during various vigilance states. *IEEE Trans. Biomed. Eng.* **36**: 497–499, 1989.
73. T. Ning and J. D. Bronzino. Autoregressive and bispectral analysis techniques: EEG applications. *IEEE Eng. Med. Biol.* **9**: 47–49, 1990.
74. D. Regan. *Human Brain Electrophysiology – Evoked Potentials and Evoked Magnetic Fields in Science and Medicine*. Elsevier, New York, 1989.
75. R. M. J. Cotterill (Ed.). *Models of Brain Function*. Cambridge University Press, Cambridge, 1989.
76. V. Krajca, S. Petranek, I. Patakova and A. Varri. Automatic identification of significant graphoelements in multichannel EEG recordings by adaptive segmentation and fuzzy clustering. *Int. J. Biomed. Comput.* **28**: 71–89, 1991.
77. T. Ikeguchi, K. Aihara, S. Itoh and T. Utsunomiya. An analysis on Lyapunov spectrum of EEG potentials. *Trans. Inst. Electron. Inf. Commun. Eng. E.* **E73**(6): 842–847, 1990.

78. C. M. Michel *et al*. Localization of the sources of EEG delta, theta, alpha and beta frequency bands using the FFT dipole approximation. *Electroenceph. Clin. Neurophysiol.* **82**: 38–44, 1992.
79. Y. Yan, P. L. Nunez and R. T. Hart. Finite-element model of human head: scalp potentials due to dipole sources. *Med. Biol. Eng. Comput.* **29**: 475–481, 1991.
80. E. J. Speckman and H. Caspers (Eds). *Origin of Cerebral Field Potentials*. Thieme, Stuttgart, 1979.
81. S. N. Sarbadhikari. *Neural Network Aided Analysis of Electrophysiological Signals from the Brain of an Animal Model of Depression Subjected to Chronic Physical Exercise*. Ph.D. thesis, School of Biomedical Engineering, Institute of Technology, Banaras Hindu University, Varanasi, India, March 1995.
82. T. N. Oniani, N. D. Lortkipanidze, M. M. Mgaloblishvili, L. M. Maisuradze, L. T. Oniani, M. R. Babilodze and M. G. Gvasalia. Neurophysiological analysis of paradoxical sleep deprivation. In: T. Oniani (Ed.), *Neurobiology of Sleep–Wakefulness Cycle*, pp. 19–42. Metsniereba, Tbilisi, 1988.
83. W. R. Klemm. Are there EEG correlates of mental states in animals? *Neuropsychobiology* **26**: 151–165, 1992.
84. L. Feinberg and I. G. Campbell. Total sleep deprivation in the rat transiently abolishes the delta amplitude response to darkness: Implications for the mechanism of the "negative delta rebound". *J. Neurophysiol.* **70**: 2695–2699, 1993.
85. J. T. Tou and R. C. Gonzalez. *Pattern Recognition Principles*. Addison-Wesley, London, 1974.
86. D. Riemann, F. Hohagen, M. Bahro and M. Berger. Sleep in depression: The influence of age, gender and diagnostic subtype on baseline sleep and the cholinergic REM induction test with RS 86. *Eur. Arch. Psych. Clin. Neurosci.* **243**: 279–290, 1994.
87. D. Aeschbach, C. Cajochen, I. Tobler *et al*. Sleep in a sitting position: Effect of triazolam on sleep stages and EEG power spectra. *Psychopharmocology* **14**: 209–214, 1994.
88. P. A. Coble, C. F. Reynolds, D. J. Kupfer *et al*. Childbearing in women with and without a history of affective disorder: II. Electroencephalographic sleep. *Comprehensive Psychiatry* **35**: 215–224, 1994.
89. L. Grunhaus, J. E. Shipley, A. Eiser *et al*. Sleep electroencephalographic studies after ECT. Age and clinical response. *Am. J. Geriatric Psychiatry* **2**: 39–51, 1994.
90. R. Abrams and M. A. Taylor. Differential EEG patterns in affective disorder and schizophrenia. *Arch. Gen. Psychiatry* **36**: 1355–1358, 1979.
91. M. Biondi, P. Parise, P. Venturi *et al*. Frontal hemisphere lateralization and depressive personality traits. *Perceptual & Motor Skills* **77**: 1035–1042, 1993.
92. C. M. Swartz, R. Abrams, D. Richard *et al*. Heartrate differences between right and left unilateral electro-convulsive therapy. *J. Neurol. Neurosurg. Psychiatry* **57**: 97–99, 1994.
93. C. Shagass, R. A. Roemer and J. J. Straumanis. Relationships between psychiatric diagnosis and some quantitative EEG variables. *Arch. Gen. Psychiatry* **39**: 1423–1435, 1982.
94. C. Shagass, R. A. Roemer and R. C. Josiassen. Some quantitative EEG findings in unmedicated and medicated major depressives. *Neuropsychobiology* **19**: 169–175, 1988.
95. C. Nyström, M. Matousek and T. Hällström. Relationships between EEG and clinical characteristics in major depressive disorder. *Acta Psychiatr. Scand.* **73**: 390–394, 1986.
96. A. J. Tomarken and R. J. Davidson. Frontal brain activation in repressors and non-repressors. *J. Abnorm. Psychol.* **103**: 339–349, 1994.
97. L. S. Leung, F. H. Lopes da Silva and W. J. Wadman. Spectral characteristics of the hippocampal EEG in the freely moving rat. *Electroenceph. Clin. Neurophysiol.* **54**: 203–219, 1982.
98. G. Vogel, D. Neill, M. Hagler and D. Kors. A new animal model of endogenous depresssion: A summary of present findings. *Neurosci. Biobehav. Rev.* **14**: 85–91, 1990.

99. D. Nieber and S. Schlegel. Relationships between psychomotor retardation and EEG power spectrum in major depression. *Neuropsychobiology* **25**: 20–23, 1992.
100. T. Hashimoto, C. Hamada, T. Wada and N. Fukuda. Comparative study on the behavioral and EEG changes induced by diazepam, buspirone and a novel anxioselective anxiolytic DN-2327, in the cat. *Neuropsychobiology* **26**: 89–99, 1992.
101. C. H. Hawkins. Endorphins: the basis of pleasure? *J. Neurol. Neurosurg. Psychiatry* **55**: 247–250, 1992.
102. K. A. Moore. The effect of exercise on body-image, self-esteem and mood. *Ment. Health Aust.* **5**: 38–40, 1993.
103. K. F. Hays. The use of exercise in psychotherapy. In: L. van de Creek, S. Knapp and T. L. Jackson (Eds), *Innovations in Clinical Practice*, Vol. 12, pp. 155–168. Professional Resource Press, Sarasota, FL, USA, 1993.
104. W. Schlicht. Does physical exercise reduce anxious emotions? A meta-analysis. *Anxiety, Stress & Coping: An international J.* **6**: 275–288, 1994.
105. W. P. Morgan. Physical activity, fitness and depression. In: C. Bouchard, R. Shephard and T. Stephens (Eds), *Physical Activity, Fitness and Health: International Proceedings and Consensus Statement*, pp. 851–867. Human Kinetics Publisher, Champaign IL, 1994.
106. A. S. Gevins. Quantitative human neurophysiology. In: H. J. Hannay (Ed.), *Experimental Techniques in Human Neuropsychology*, pp. 419–456. Oxford University Press, New York, 1986.
107. W. Machleidt, L. Gutjahr, A. Mugge *et al*. Evaluation of normal depressive episodes by spectral EEG-analysis. *Res. Comm. Psychol. Psychiat. Behav.* **13**: 123–127, 1988.
108. M. B. First. Computer-assisted assessment of DSM-III-R diagnoses. *Psychiatric Annals* **24**: 25–29, 1994.
109. S. N. Sarbadhikari. Medical informatics – are the doctors ready? *J. Indian Med. Assoc.* **93**: 165–166, 1995.
110. R. L. Spitzer, J. Endicott, J. Cohen and J. L. Fleiss. Constraints on the validity of computer diagnosis. *Arch. Gen. Psychiatry* **31**: 197–203, 1974.
111. J. N. Butcher. Psychological assessment by computer: Potential gains and problems to avoid. *Psychiatric Annals* **24**: 20–24, 1994.