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$1/f^{\beta}$-Fluctuations in Bipolar Affective Illness

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Abstract

Temporal fluctuations which cannot be explained as consequences of statistically independent random events are found in a variety of physical and biological phenomena. These fluctuations can be characterized by a power spectrum density $S(f)$ decaying as $1/f^{\beta}$ at low frequencies with an exponent $0.5 \leq \beta \leq 1.5$. We present a new approach to reveal $1/f^{\beta}$-fluctuations in manic and depressive episodes in bipolar affective illness using published data from patients for whom daily records were obtained applying a 7-point magnitude category scale. This time series $\{R(t_i)\}$ was described as a point process by introducing discriminating rating levels r and s for the occurrence of $R(t_i) \geq r$ ('mania') and $R(t_i) \leq s$ ('depression'). For $\beta < 1$ a new method to estimate the low frequency part of $S(f)$ was applied using counting statistics without applying Fast Fourier Transform. The method reliably discriminates these types of fluctuations from a random point process with $\beta = 0.0$. It is very tempting to speculate that the neuronal/humoral mechanisms at various levels of the nervous system underlying the manic and depressive episodes in bipolar affective illness are expressions of a self-organized critical state. But the most important result of the present study is the finding of a scaling region $1d \leq \Delta t \leq 200d$ for the 'manias' and 'depressions' where $S(f)$ is decaying as $1/f^{\beta}$ with $\beta \approx 0.8$. Therefore, based on the monitored ratings for a given time period it should be possible to predict future episodes with a certain probability by applying methods of nonlinear time series analysis or modified feed-forward neural networks learning with the backpropagation algorithm. This could result in an improvement of the treatment of patients.

Keywords

$1/f^{\beta}$-fluctuations, affective illness, biological rhythms, self-organized criticality, chaos

1 INTRODUCTION

A variety of phenomena in nature exhibit temporal fluctuations in the absence of intentional stimulation which cannot be explained as consequences of statistically independent random events. It has been shown that temporal fluctuations found in phenomena as different as currents through cell membranes, earthquakes, sunspot activity, light emitted from quasars, sand falling through an hour glass, traffic flow, heart beat or breathing activity can be characterized by their power spectrum density $S(f)$ decaying as $1/f^{\beta}$ at low frequencies with $0.5 \leq \beta \leq 1.5$. This behavior of the temporal fluctuations of a system described by its $S(f)$ is called $1/f$-noise.

Recently, Bak, Tang and Wiesenfeld (Bak, 1987) suggested that the large fluctuations in time characterized as $1/f$-fluctuations and the self-similarity in space might both be manifestations of a self-organized critical state. Self-organized criticality (SOC) describes the tendency of some open dissipative many-body systems to drive themselves spontaneously to a critical state with no characteristic time or length scales without any fine-tuning by external fields: hence the criticality is self-organized. This is in contrast to the criticality of equilibrium systems undergoing phase transition only at a critical external field, such as temperature, pressure, electrical or magnetic fields. The idea provides a unifying concept for large scale behavior in systems with many degrees of freedom operating persistently far from equilibrium at or near a threshold of instability, so to speak at the 'border to chaos' (Bak, 1990).

The SOC phenomenon is expected to be universal and we assume that it is the underlying principle of some biological many-body systems. The present paper uses methods and presentations published earlier for fluctuations in the subjective intensity of well-being (Kniffki, 1993), (Kniffki, 1994).

2 METHODS

Data from 7 patients were analyzed from a longitudinal study (Squillance, 1984). The patients met the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III). The intensity of the recurrent affective illness was rated as: 0 = normality, +1 = mild mania, +2 = moderate mania, +3 = severe mania, −1 = mild depression, −2 = moderate depression, −3 = severe depression. Fluctuations of the mental state within a day were not monitored and were therefore neglected in this analysis. The time series of the daily ratings $R(t_i)$ (Figure 1) can be described as a point process by introducing discriminating rating levels for the occurrence of $R(t_i) \geq r$, e.g. for the occurrence of 'manias' (cf. Figure 2) and $R(t_i) \leq s$, e.g. for the occurrence of 'depressions', cf. Fig. 3; data of another patient.

Usually $S(f)$ is obtained by Fast Fourier Transform (FFT). To avoid the well-known problems in using FFT for the obtained point process, we used a new simple method based on counting statistics (Meesmann, 1993) to analyze the low frequency part of $S(f)$ of the monitored ratings. After the introduction of a discriminating rating level, the series of ratings is considered to be a point process described as

$$y(t) = \sum_{i=1}^{n} \delta(t - t_i), \tag{1}$$

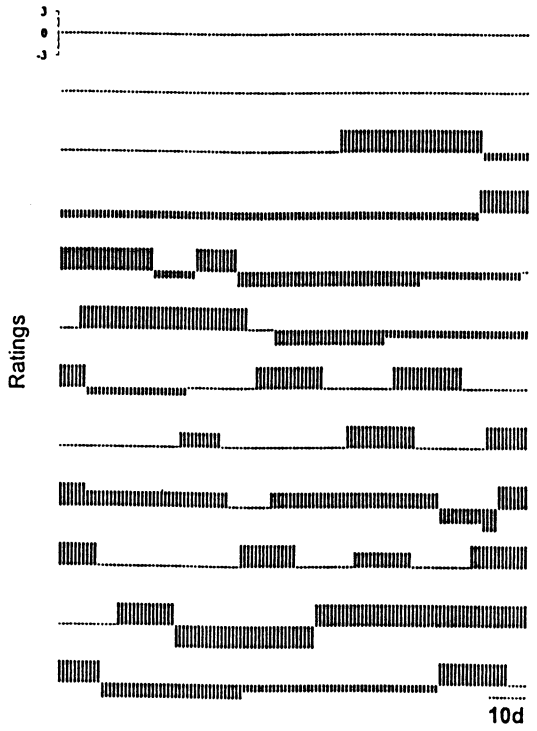

Figure 1 Bipolar affective illness. Daily ratings of the intensity of the recurrent affective episodes using a 7-point magnitude category scale. Subset of raw data taken from the entire set published in (Squillance, 1984).

in which $\delta(t - t_i)$ represents Dirac's delta function, and t_i is the time of occurrence of a particular $R(t_i) \geq r$ or $R(t_i) \leq s$ within the train of n events. In the absence of severe intentional stimulation $y(t)$ is assumed to be statistically stationary. Another statistical variable derived from Eq. (1) is the actual number of events $N(\Delta t)$ occurring in a time interval Δt ranging from t_1 to t_2. Thus, $N(\Delta t)$ can be expressed as

$$N(\Delta t) = \int_{t_1}^{t_2} \sum_{j}^{\nu} \delta(t - t_j)\, dt. \tag{2}$$

The variance of counts $Var[N(\Delta t)]$ is the so-called variance-time curve. Its second time derivative is related to the auto-covariance function of y, $C_y(\Delta t)$ by

$$C_y(\Delta t) = \frac{1}{2}(Var[N(\Delta t)])'' \tag{3}$$

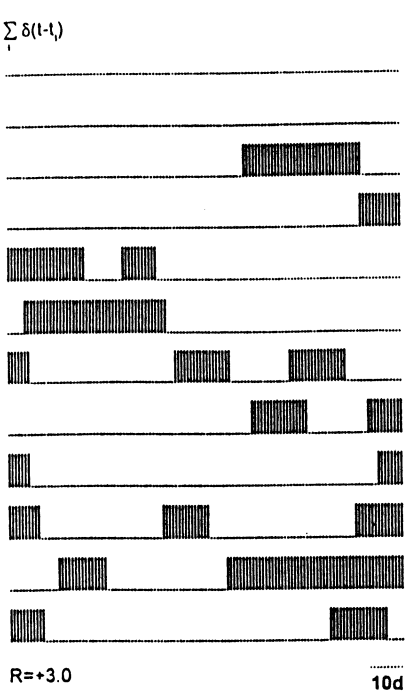

Figure 2 Occurrence of ratings of the recurrent affective episodes with $R(t_i) = +3$ (severe mania) of the data set shown in Figure 1. The corresponding days are indicated by Dirac's delta functions $\delta(t - t_i)$.

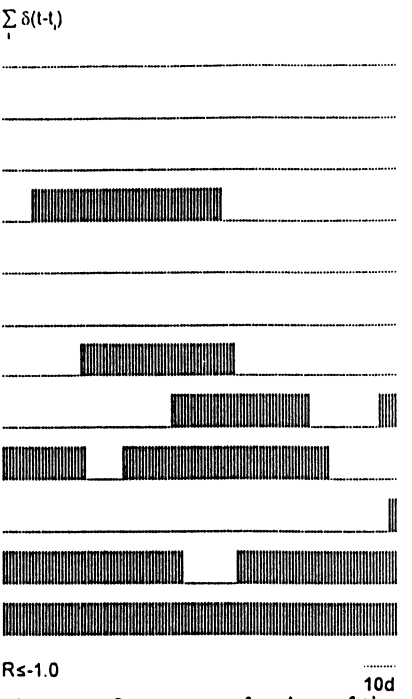

Figure 3 Occurrence of ratings of the recurrent affective episodes of another patient with $R(t_i) \leq -1$ (mild to severe depression). The corresponding days are indicated by Dirac's delta functions $\delta(t - t_i)$.

(Cox, 1980) and therefore the key to determine the low frequency part of the spectrum $S_y(f)$ is to experimentally obtain $Var[N(\Delta t)]$ (Meesmann, 1993). If the variance-time curve follows within certain limits the power law

$$Var[N(\Delta t)] \propto (\Delta t)^{1+\beta} \text{ with } \beta < 1, \tag{4}$$

then it can be shown using the Wiener-Chinchin theorem that the spectrum $S_y(f)$ scales as

$$S_y(f) \propto 1/f^{\beta} \tag{5}$$

within $f_{min} < f < f_{max}$ (Korutchev, in press), (Scharf, in press).

The variance-time curve is defined by the variance of counts for time intervals of length Δt as

$$Var[N(\Delta t)] = \langle N^2(\Delta t)\rangle - \langle N(\Delta t)\rangle^2 \tag{6}$$

with $\langle ...\rangle$ denoting expectation values. For estimating $Var[N(\Delta t)]$, the entire observation time T is divided into k non-overlapping counting windows of duration Δt with $T = k\Delta t$ and the variance of counts is determined for this particular window Δt. This is repeated for different values of Δt. The results were plotted as $Var[N(\Delta t)]$ versus Δt on a log-log scale and fitted by linear regression using the least-square method.

3 RESULTS

In Figure 1 a part of the whole data set of one patient is shown, i.e., the daily ratings $R(t_i)$ for 48 months. It is obvious from the data that the variation in intensity of the recurrent affective episodes, taken as a whole, is not just a simple oscillation but exhibits fluctuations of certain endogenic dynamics. This was true for all the 7 patients' data studied.

By introducing discriminating levels for the occurrence of $R(t_i) \geq r$ to reveal the fluctuations in the 'manias' or $R(t_i) \leq s$ for the 'depressions', the data set shown partly in Figure 1 was transformed into a point process. To obtain Figure 2 the discriminating rating level was set to $r = +3$, i.e. the point process shows the occurrence of the severe manias. Similar point processes for other discriminating rating levels were obtained for all 7 data sets and analyzed. In particular, for determining the fluctuations of the occurrence dynamics of the depressions $s = -1$ was chosen (Figure 3).

For all discriminating rating levels r or s, the resulting point processes exhibited a certain clustering of events individually described as $\delta(t - t_i)$ (cf. Figures 2 and 3). In order to characterize the clustering more precisely one use the clustering function $g(t)$ which was defined for earthquakes (Olami, 1992) as follows:

$$g_{r,s}(t) = \langle n(t)\rangle_{t_i} - t\overline{n}, \tag{7}$$

where $\langle n(t)\rangle_{t_i}$ is the number of events in the interval $(t_i, t_i + t]$ averaged over all t_i in the temporal sequence $\mathbf{S}_r = \{R(t_i) \in \mathbf{S} \mid R(t_i) \geq r\}$ or $\mathbf{S}_s = \{R(t_i) \in \mathbf{S} \mid R(t_i) \leq s\}$ and $\mathbf{S} = \{R(t_i)\}$, describing the total temporal sequence (cf. Figure 1). $\overline{n}$ is the average density of events, i.e. the number of events within $\mathbf{S}_r$ or $\mathbf{S}_s$ divided by the total observation time. The clustering function $g_{r,s}(t)$ should measure the expected different clustering for the 'manias' and 'depressions' inherent in the data sets of the patients. In general, for all discriminating levels r and s analyzed, $g_{r,s}(t)$ is positive and non-decreasing, contrary to a homogeneous Poisson point process for which $g(t) = 0$ for all t. After introducing a certain r or s, for the resulting point process $\mathbf{S}_r$ or $\mathbf{S}_s$, the low frequency part of the corresponding spectrum $S(f)$ was determined by using counting statistics as described in Methods. Figure 4 shows the results of the point processes shown in Figures 2 and 3, i.e. the $Var[N(\Delta t)]$ for $\mathbf{S}_{+3}$ and $\mathbf{S}_{-1}$ (insert) are plotted on a log-log scale versus the counting

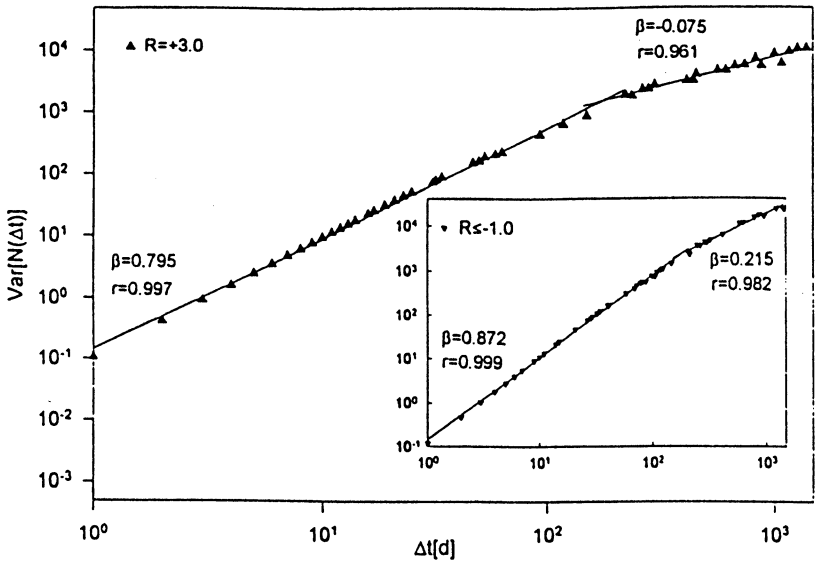

Figure 4 The variance-time curves $Var[N(\Delta t)]$ for the severe manias (main plot; $R(t_i) = +3$; cf. Figure 2) and for the mild to severe depressions (insert; $R(t_i) \leq -1$; cf. Figure 3) plotted on a log-log scale versus the counting window Δt. The variance-time curves scale as $(\Delta t)^{1+\beta}$ for $1d \leq \Delta t \leq 200d$ with indicated values of β and the corresponding correlation coefficients r.

windows Δt. From the straight lines fitted to the data points it is demonstrated that the variance-time curves follow the power laws

$$Var[N(\Delta t)] \propto (\Delta t)^{1+0.80} \text{ for } S_{+3} \tag{8}$$

and

$$Var[N(\Delta t)] \propto (\Delta t)^{1+0.87} \text{ for } S_{-1} \tag{9}$$

within the first scaling region $1d \leq \Delta t \leq 200d$ and thus the low frequency part of the spectrum scales as

$$S(f) \propto f^{-0.80} \text{ for } S_{+3} \tag{10}$$

and

$$S(f) \propto f^{-0.87} \text{ for } S_{-1}. \tag{11}$$

For $\Delta t > 200d$ a second scaling region was observed showing for S_{+3} $\beta = -0.08$ and for S_{-1} $\beta = 0.22$.

Similar results, i.e. similar scaling behavior for the variance-time curve and for the spectrum were obtained for other discriminating levels r and s of the data of the other patients.

4 DISCUSSION

Recently, also due to the introduction of the concept of self-organized criticality by Bak, Tang and Wiesenfeld (Bak, 1987), attention has been drawn to the characterization of temporal fluctuations in a number of physical and biological systems. This discussion will focus on the fluctuations of endogenous biological rhythms in the physiological and pathophysiological range.

The human heart rate, even in the healthy resting subject, displays considerable fluctuations, which have been characterized as $1/f$-fluctuations (Kobayashi, 1982), (Saul, 1987), (Zbilut, 1989), (Kleiger, 1991), (Bigger, 1992), (Meesmann, 1993), (Meesmann, 1993).

In animal experiments it has been demonstrated that the fluctuations in respiratory intervals also exhibited $1/f$-fluctuations, but these characteristic types of fluctuation disappeared into white noise fluctuations when the end-tidal p_{CO_2} was raised to 50 or 60 mmHg (Kawahara, 1989).

The fluctuating insulin requirements of an unstable diabetic over an eight-year period have been subjected to spectral analysis and it was demonstrated that the low frequency part of the spectrum also exhibit $1/f$ characteristics (Campbell, 1972).

Spectral analysis of the discharge of neurones located in the mesencephalic reticular formation of the cat has revealed that during paradoxical sleep $1/f$-fluctuations of the neuronal discharge exist there, too. However, the low frequency spectral profile became flat, i.e. white noise was found during slow-wave sleep (Yamamoto, 1986), (Grüneis, 1990). So far, also the thalamic neuronal discharge exhibited $1/f$-fluctuations in the absence of intentional stimulation, but we have not seen the transition into white noise fluctuations (Kniffki, 1992), (Mengel, 1992). Earlier, $1/f$ characeristics have also been reported for primary afferent fibres in the auditory nerve (Teich, 1989).

It is tempting to speculate that the basic mechanisms which underlie the neuronal and humoral activity in the central nervous system responsible for the state of mental order/disorder in the absence of intentional stimulation are expressions of a self-organized critical state, the notion introduced by Bak, Tang and Wiesenfeld (Bak, 1987) for physical systems. Self-organized criticality (SOC) describes the tendency of dissipative systems with many degrees of freedom to drive themselves to a critical state with a wide range of length and time scales without any fine-tuning of external fields. The idea complements the concept of chaos, wherein simple systems with a small number of degrees of freedom can display quite complex behavior (Christensen, 1992).

Currently, it is hard to give a rigorous definition for SOC, however, usually one gives this name to those systems which do not need fine-tuning by external fields to give power-law characteristics for the parameters describing the system. The canonical example of SOC is the cellular automaton model called 'sand-pile model' introduced by Bak, Tang and Wiesenfeld (Bak, 1987). The critical state is characterized by 'avalanches' (activity) with power-law spatial and temporal distribution functions limited only by the size of the system.

We assume that the endogenic dynamics of mental disorder can be described as a self-

organized critical process and characterize the temporal fluctuations by its low frequency part of the power spectrum. The method that we have used reliably discriminates $1/f^{\beta}$-fluctuations with $\beta = 0.80$ for S_{+3} and $\beta = 0.87$ for S_{-1} in our case in the first scaling region (cf. Figures 4) from a random point process, which would result in $\beta = 0.0$ as approximated in the second scaling region $\Delta t > 200d$ for S_{+3}. Similar exponents and scaling regions were obtained for all other data sets.

If the neuronal/humoral system responsible for the endogenic dynamics of mental order/disorder indeed operates at a self-organized critical state, an external perturbation could create either a small effect or a large one. There is, in principle, no limit on how long the effect may last. The degree of unpredictability is actually less severe than for chaotic systems; *SOC* systems operate at the 'border of chaos' (Bak, 1990). In *SOC* systems, owing to an external perturbation the maximum predictability decays as a power law, $t^{-\alpha}$, where α is some constant (Bak, 1990). Fluctuations due to external stimulation are much stronger in *SOC* systems than those which occur in an equilibrium system and can not be prevented. In the case of bipolar affective illness, this would mean that a transition from the 'manic' state to the 'depressive' state induced by a severe external perturbation is inevitable for the individual.

The most important result of the present study is the finding of a scaling region $1d \leq \Delta t \leq 200d$ for various discriminating levels describing the 'manias' and 'depressions' when $S(f)$ is decaying as $f^{-\beta}$ with $\beta \approx 0.8$ for patients with bipolar affective illness. Therefore, based on the monitored ratings of the intensity of the affective disorder, for a given time period (Wehr, 1984) it should be possible to predict future episodes with a certain probability by applying methods of nonlinear time series analysis (Takens, 1993) or modified feed-forward neural networks learning with the backpropagation algorithm. The predictions could be used to improve the treatment of patients.

As described by S.H. Barondes (Barondes, 1993), all of us are personally familiar with good moods. At times, we are content, optimistic, even expansive; we like to be with people, and they like to be with us. Such states of happiness may be transient conditions for some and virtually perpetual for others.

All of us also know what it means to be sad. In such a state we tend to be suspicious and pessimistic. We think poorly not only of our prospects but also of ourselves. We tend to stay away from people, and they, sensing our discomfort, tend to stay away from us. Even when good things happen, we derive little pleasure from them. Like states of happiness, states of sadness may be either transient or sustained.

All of us also have some knowledge of more extreme moods. We have felt or observed grief at the loss of a loved one; we know about the elation that accompanies some great good fortune. It is also likely that we have encountered someone in a sustained and serious depression or maybe even witnessed an ebullient and irresponsible manic episode.

But rarely, if ever, do we ask ourselves why mood exists in the first place. What is the biological function and the evolutionary advantage of this dimension in our behavior ? Might our species not be better off if we take both good and bad in stride, without any change in mood?

Moods are useful only in moderation. When they exceed a certain intensity they become destructive. But where is the boundary between normal mood and mental illness (Barondes, 1993)?

If we assume that the basic mechanisms underlying the neuronal and humoral activity in the nervous system responsible for the state of mood are expressions of a self-organized

critical state (Kniffki, 1994), it is quite natural that this state is characterized by the occurrence of avalanches of different 'energy', i.e. intensity of mood. Normal mood and mental illness will just be fluctuating episodes with different intensities like the occurrence of earthquakes with different energies released.

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