DYNAMICAL SYSTEMS AND DEPRESSION: A FRAMEWORK FOR THEORETICAL PERSPECTIVES

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ABSTRACT

The theory of dynamical systems allows one to describe the change in a system's macroscopic behavior as a bifurcation in the underlying dynamics. We show here, from the example of depressive syndrome, the existence of a correspondence between clinical and electro-physiological dimensions and the association between clinical remission and brain dynamics reorganization (i.e. bifurcation). On the basis of this experimental study, we discuss the interest of such results concerning the question of normality versus pathology in psychiatry and the relationship between mind and brain.

Key words: Dynamical systems; depressive syndrome; normal/pathologic; mind/ brain; electroencephalogram.

1. INTRODUCTION

Despite physiological and psychological studies having shown that thought, emotion and action arise from brain activity, the relationships between neurobiological and psychological aspects of mental activities are still difficult to model and explain. Nevertheless, it is usually assumed that changes in mental states are related, in one way or another, to changes in cerebral processes (Widlöcher, 1986; Horowitz, 1987; Searle, 1992). The domain of psychopathology, where passages from normal to pathological thinking and reverse are of major interest, constitutes a natural field for the investigation of those transitions. The study of the brain correlates with such mental states modifications and so may thus offer valuable insights into the articulation between brain activity and mental states and further into the status of the opposition between normal and pathologic.

A first step into the study of biological correlates of mental trouble can focus on cerebral cortex which is the major part of the brain one can study in a non-invasive manner. Anatomical studies of cerebral cortex have pointed out its high level of recurrence and connectivity (Braitenberg and Schüz, 1991). These observations led to considering it as a recurrent neural network of which the dynamical properties give

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rise to cognitive, affective or action processes. In this sense, a macroscopic structure emerges from the microscopic organisation of the network, but cannot be totally reduced to the elements' properties (Petitot-Cocorda, 1992; Varela *et al.*, 1991). In such a model, one considers mental states as macro-structures emerging from dynamical properties of cortical neuronal networks (Hopfield, 1982; Hoffmann, 1987). The articulation between normal and pathological mental states would thus refer to changes in the dynamics of underlying cerebral networks (Globus and Arpaïa, 1994; Sabelli and Carlson-Sabelli, 1993).

The dynamical systems theory offers an appropriate framework to study the dynamics of complex systems, such as the brain. This theoretical point of view has previously been applied in human physiology and gave first results comparing pathological and healthy states (Milton and Black, 1995). The transition between those states was related to a modification in physiological system rhythms leading to a change in behaviour (Mackey and Glass, 1977; Glass and Mackey, 1979; Carlson-Sabelli *et al.*, 1994). Besides the application of dynamical systems concepts and mathematical tools to the physiological domain, studies of cerebral states have been developed on the basis of electroencephalogram (EEG) signals analysis (Babloyantz and Destexhe, 1986; Rapp *et al.*, 1989). As a consequence, the study of the relationship between cerebral and mental states and of the passage between normal and pathological mental state can be undertaken within this framework.

Our research aims to reveal, in the depressive syndrome, the existence of a bifurcation (i.e. clear change in dynamical properties) in neuronal activity which might be the process underlying this pathological state. Indeed, this trouble presents physiological (Wehr and Goodwin, 1979; Hollister *et al.*, 1980; Claustrat *et al.*, 1992) and electrophysiological rhythms modifications (Nandrino *et al.*, 1994; Pezard *et al.*, 1996a) which have been considered as landmarks of a dynamical disease (Glass and Mackey, 1977; Mackey and Milton, 1987; Milton and Black, 1995). Nevertheless, it should be shown that these changes appear simultaneously with depressive mental states. For that purpose, longitudinal studies only are able to reveal the process of the trouble appearance.

Since it is not possible to observe transition from a healthy state to a depressive one, we observed the reverse phenomenon: the clinical improvement of a depressed patient during her treatment at the hospital. We have thus proceeded, during the entire treatment, to the follow-up of brain dynamics characteristics associated with depressive mood assessment and tried to observe if brain dynamics' bifurcation is concomitant with mental states modifications. In the case where concomitant changes are observed, this result points into the direction that depressive clinical productions are macroscopic manifestations emerging from brain dynamics.

Of course, we do not believe to solve here the whole complexity of these problems but propose experimental schemes which could help the foundations of a dynamical approach of the problem of normality/pathology in psychiatry.

2. MENTAL TROUBLE AS BIFURCATION IN BRAIN DYNAMICS

Brain dynamics characterization

The experimental study is based on the hypothesis that the system giving rise to EEG signal is governed by a differential dynamical system. In other words, the state of activity $\xi(t)$ of the 10^5 cortical macro-columns (Nunez, 1990) can be described as $d\xi/dt = F_\mu(\xi)$ where F_μ denotes the form of the dynamical system with parameters μ. Such a system has certain dynamical behavior which depends upon the values of the set of parameters μ. Our hypothesis is that the depressive syndrome corresponds to a dynamical change due to parameters modifications.

In order to observe the characteristics of the system's dynamics without access to its equation, it is necessary to characterize the dynamics on the sole basis of a set of m measurements ($\mathbf{X}(t) = \{x_j(t)\}$; j=1, ..., m) of the system's state $\xi(t)$. $\mathbf{X}(t)$ is related to $\xi(t)$ through a measurement function H. Thus, for a system's state $\xi(t)$ defined in a k-dimensional space $\mathbf{R}^k$, H is an application from $\mathbf{R}^k$ to $\mathbf{R}^m$ and $\mathbf{X}(t) = H(\xi(t))$. For EEG, $\mathbf{X}(t)$ corresponds to m potentials values (recorded over m electrodes), which depend on $\mathbf{X}(t)$ *i.e.* the activities of all the k macro-columns of the brain.

Under the assumption that the time evolution of $\xi(t)$ is governed by a differential system, a three-step procedure allows one to infer on the dynamics (i.e. the ξ-trajectory in the state space $\mathbf{R}^k$) from the measurements $\mathbf{X}(t)$.

First step:

A trajectory, topologically equivalent to the ξ-trajectory, is reconstructed from the measurements **X**. This "embedding procedure" can use several methods (successive derivatives, time-delay, spatial and spatio-temporal embeddings) to build an observation matrix **V**. We used here the technique called *spatial embedding* (or multichannel method).

EEG signals (recorded on 31 electrodes equidistributed on the scalp and referred to the ears) were digitized on 12 bits using a 1 kHz sampling rate. For each recording session, ten 8192-milliseconds multi-channel EEG-segments free of artifacts were selected. For each of the 70 EEG-segments used in this study, the observation matrix **V** was built as:

$$\mathbf{V} = \{ v(t) \} \text{ and } v(t) = \{ x_1(t); x_2(t); ...; x_{31}(t) \}$$

where $x_j(t)$ corresponds to the potential value recorded at time t on electrode j and $t = i.\tau$ (τ = 1 ms) for i = 1, ..., 8192. The observation matrix **V** thus corresponds to the trajectory of 8192 successive vectors in a 31-dimensional space.

Second step

Topological invariants (dimensions, Lyapunov exponents, Kolmogorov entropy ...) of the reconstructed trajectory which are closely related to the dynamics, are then computed (for reviews see Abarbanel *et al.*, 1993; Grassberger *et al.*, 1991; Kantz and Schreiber, 1997; Ott *et al.*, 1994). In the present study, each EEG-segment was analyzed using a numerical method based on non-linear forecasting (Pezard *et al.*, 1994, 1996b). It permits one to estimate Kolmogorov entropy (K) which quantifies the loss of predictability for the global brain electrical activity. In turn, an increase of entropy corresponds to less predictable signals and thus to a more complex dynamics.

Third step

In addition, since it has been recognized that correlated noise can depict similar characteristics as truly non-linear dynamics (Osborne and Provenzale, 1989; Rapp *et al.*, 1993), surrogate data testing has been introduced to validate the non-linear indices obtained with the first two steps (e.g. Pijn *et al.*, 1991; Prichard and Theiler, 1994; Theiler *et al.*, 1992). It is ensured by testing the significance of the difference between K obtained for raw data and K obtained for a set of 39 multi-channel surrogate data. We accepted the dynamics to be non-linear when the entropy (K) for the surrogate data was significantly higher than that for the raw data as revealed by a non parametric test (one-tailed level of significance: 2.5%). 2,800 multi-channel segments were thus characterized in this study (70 raw data + 39×70 surrogate data).

Experimental investigation: depressive episode remission

A patient treated by convulsive therapy, has been selected according to DSM-IV criteria for major recurrent depressive episode. Every two days during two weeks, she was submitted both to EEG recording sessions and to mood self-assessment questionnaire (von Zersen, 1970). Seven EEG recordings were obtained in eyes closed resting condition. For each experimental session, mood score was obtained and EEG-segments were analyzed by using the method described above. For each day of recording, the subject was characterized by an entropy value averaged over the ten EEG-segments.

The presence of non-linear dynamics in EEG signals is confirmed by the surrogate data test (the linear hypothesis was rejected in 30% of the analyzed EEG-segments). This result justifies the use of the non-linear method to quantify EEG.

During the two weeks of clinical and electrophysiological follow-up, we observed a decrease in the mood assessment scores in accordance with the evolution of the entropy values (see Figure 1a). For close mood scores, similar entropy values are obtained (D.0 to D.4 and D.9 to D.14). The correlation coefficient computed between entropy measurements and mood assessment scores of seven sessions is of 0.88 (significant threshold $p<0.05$; see Figure 1b). In the light of this result, we have shown a strong correlation between clinical state and the underlying brain dynamics' characteristics. In other words, we bear out that a macroscopic level of observation, such as clinical productions, may refer to a microscopic level, such as neuronal dynamics.

Moreover, the clear drop in mood assessment scores, as observed between day 4 and day 9, is traduced by a decrease in the entropy values. This rupture indicates important changes in brain dynamical characteristics and denotes a bifurcation. It suggests a drastic re-organization in brain dynamics when the patient's state is clinically improved (Figure 1c). Moreover, we have shown that remission of a depressive episode (i.e. clear decrease of mood assessment score) is subtended by a modification of the brain dynamics characteristics (i.e. decrease of the system's entropy). Such bifurcation appearing in accordance with clinical remission of depressive syndrome could be the connection between pathologic and normal states. In extension, the passage from normal to pathological state could be related to a similar physiological phenomenon.

Conclusion

We have assumed that the understanding of the passage between normal and pathologic state could remain in the bifurcation of brain dynamics. The simultaneous characterization of brain dynamics and depressive mood level has allowed us to associate mental state and the neuronal level of organization. Consequently, abnormal

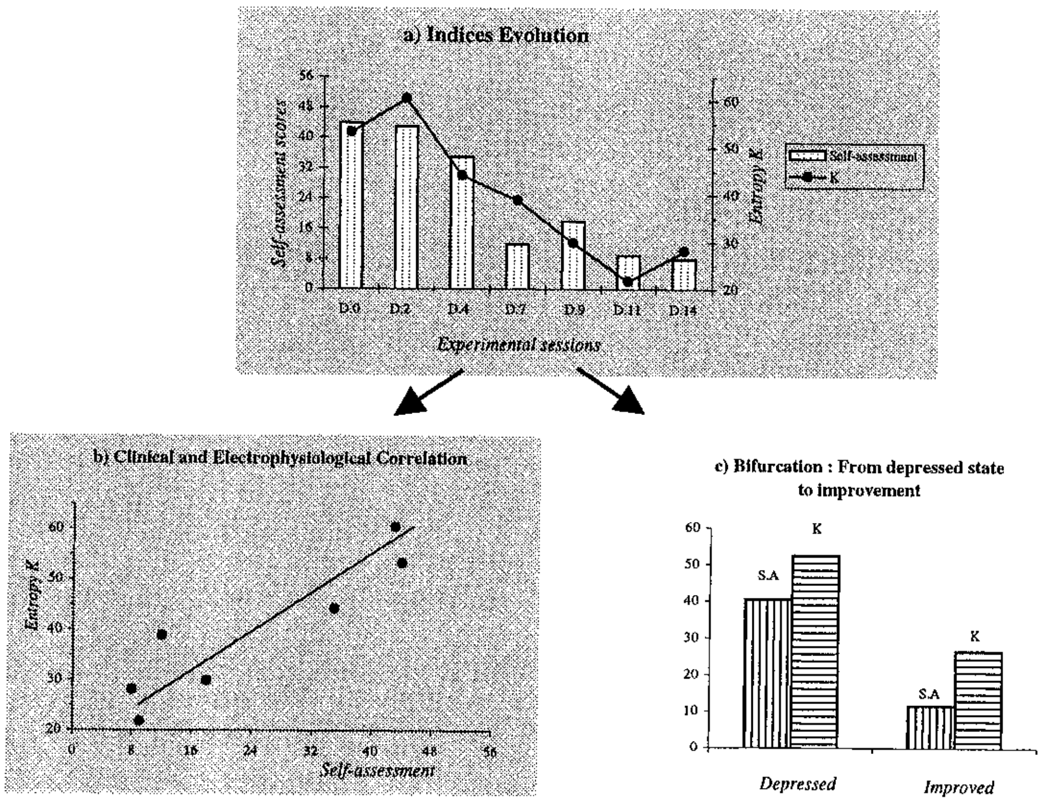

Figure 1. Results of the simultaneous follow-up of mood self-assessment scores (S.A.) and of brain dynamics' entropy (K, in sec^{-1}) during the treatment of a depressive episode. (a) Evolution of both indices along treatment. (b) Significant correlation between these indices. (c) Averaged characterization of the two states observed: depressed (first three recording sessions) and improved (last three recording sessions).

mental activity can be considered to emerge from specific brain dynamics which bifurcation may be concomitant to clinical remission.

These experimental findings lead to theoretical implications on, firstly, the relationships between mind and brain and, secondly, on the normal/pathologic question (Canguilhem, 1966).

3. THEORETICAL PERSPECTIVES

Biological representation of mind

As a biological investigation of mental troubles refers to the brain, it has to take position concerning the mind/brain problem. Our results favor a discussion of this problem in the sense of emergence. In fact, the "emergentist" conception considers the mental reality as emerging from the underlying neuronal organizational processes. In other words, mental processes emerge from neurons interactions as the quality of liquidity emerges from molecules dynamics for water: liquidity depends upon the dynamics of the water molecules but no molecule is itself liquid. Furthermore, mind is a function of brain and their relationship is a neuroscience problem (Searle, 1992). From a neurophysiological point of view, this perspective emphasizes the dynamical properties of the nervous tissue and can be retraced from physiological works of Köhler (1940) to more theoretical propositions of Thom (1977, 1988) and Zeeman (1976). Nowadays, the recurrent neurons networks models (e.g.: Hopfield, 1982; Amit, 1989) and the development of dynamical system theory (e.g.: Guckenheimer and Holmes, 1986) allow one to investigate the brain functioning in dynamical terms more precisely. The correspondence between a mental state and a cerebral one as illustrated in experimental results could reinforce this position.

In fact, within the perspective of psychopathology, some other positions concerning the mind/brain problem seem difficult to hold on to. On the one hand, for physical reductionism, cerebral functioning is identified to the mental activities and thus mental activities are denied. Applied to the field of psychopathology, this strict physical reductionism would imply, in a certain sense, the rejection of the domain of psychodynamics and psychoanalysis, which have proved some efficiency in its century of existence. On the other hand, for a functionalist perspective, the relationships between physical and mental activities are based on their functional properties (this point of view has led to the computer metaphor). This now dominating metaphor implies that the physical basis of mind is irrelevant to the question of mental processes, and thus excludes clear biological investigation (Clark, 1989). Moreover, this model hardly takes into account the possible reorganizations of both mental and nervous processes that permit fitting in with the fluctuations in the environment. Its incapacity to describe mental and nervous processes as interdependent dynamical phenomena constitutes its major limitation in the domain of psychopathology.

The normal/pathologic problem

In psychiatry, the frontier between mental "normality" and "abnormality" is not as easily drawn as in somatic medical science and this articulation between health and pathology remains the key-question in this medical field (Devereux, 1977; Rechtman and Raveau, 1993). The modifications in perceptive, affective and action domains encountered in mental pathology lead thus to question their connection with anterior normal state. The ontological position proposes the existence of a fundamental difference between health and pathology whereas a dynamical one favors a continuum between them. From an empirical reality, healthy individuals are commonly characterized by classic ways of being. They exhibit integrated purposeful behavior; they can direct their attention in meaningful ways and have a rich sense of inner life. At the same time, they are flexible and adjustable and can be sensitive to the events of their environment. By contrast, psychiatric patients are characterized by a paucity and rigidity of response, by repetitive behavior and inappropriate action. They may have a general lack of meaning, an interior blankness and a loss of sensation. The normal sense of integration, of openness and appropriate response to the inner and outside worlds has been compromised and changed (Foucault, 1954; 1972). The modifications present in mental pathology ask for a reflection on their relations with anterior "normality".

In this article, we have proposed an attempt to deal with this massive behavioral and mental change in a biological and dynamical perspective. The depressive syndrome example tends to attest that if the individual's adaptation to environment takes a different form from what we call "normality", this new way of being is the expression of an original organization and not a remnant of a normal anterior organization (Goldstein, 1933). Indeed, the depressed brain dynamics is different from a healthy one and has its own characteristics (Pezard *et al.*, 1996a) but this state belongs to a same individual's dynamics. This change frequently denotes patient's incapacity to answer to the exigency of the anterior environment; it is one side of his way to be.

Moreover, such a change in individual mental states would come from a continuous transition inside its brain dynamics. Normal and pathological states are not two different entities but rather two different expressions of the same dynamics. The occurrence of a pathological state expresses that the relationship between organism and environment has been modified by a strong organism perturbation.

Conclusion

We have proposed, in this paper, a framework which permits one to associate, both theoretically and experimentally, the proposition of emergence with the connection between normal and pathological states. In fact, it provides us with a natural description of two interdependent levels such as brain physiology and mental processes and takes into account the evolution of structures: it thus fulfils a strong support to conceive normal/pathologic problem. In this way, the dynamical systems theory succeeds in the description of the phenomena and their transformation processes. Moreover, macroscopic levels are thus considered as stable organization of microscopic phenomena.

As mental troubles refer to a specific mental functioning, we have illustrated their correspondence at the brain level with the development of a new cerebral dynamics. Clinical productions, even if they cannot be reduced to biology, would be the emergent product of a microscopic level: the neuronal organization. This organization is generally in accordance with physiological norm but remains different in its macroscopic realization. Such a consideration of mental trouble as a specific mental activity emerging from microscopic dynamics of brain activity encourages the nondissociation between mental and cerebral state, between psychology and neurophysiology.

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