different early stage dementias. Being a clearly insufficient function in frontal patients and possibly accounting for their early symptoms of social inappropriateness, prior evidence of medial prefrontal structures subserving Theory of Mind is supported. In patients with Alzheimer’s disease and mild cognitive impairment, it is possible that Theory of Mind deficits are secondary to their primary memory impairment, as suggested by previous research.

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Is the Chaotic Nature of Parkinson’s Disease Prone to Simulation?

To the Editor: Walking is regulated through a complex motor control system which produces a complex stride interval time series that is characterized by fractal and multifractal properties. On the other hand, studies on Parkinson’s disease show that although the chaotic nature of stride interval time is maintained, its chaotic properties change and approach more or less to a stochastic state. Some studies, as our own previous study, ignore this chaotic behavior and focus on the stochastic properties of the disease state. The disadvantage of such models is that they do not pay attention to global features of the disease and any minute change in the biological system would not be tracked by the model.

Since the last decade, the development of nonlinear dynamics and chaos theories has created new approaches to the understanding of complex biological systems, especially the nervous system. Several theories have been developed in different topics of neurobiology and psychiatry. Different research represents the main properties of nonlinear systems in different parts of the nervous system: dependency sensitive to initial conditions, self-organization, and similarity at different scales.

However, one problem remains unsolved: how such complex systems can be modeled based on experimental data? Physiological systems are so complicated that it is impossible to use the exact and detailed relations of system compartments to implement the complete model. Moreover, in chaotic states, we cannot construct our model exactly on the basis of recorded data, because each time we record the data, different quantities are achieved. It is worth noting that any minute error or noise in experimental conditions leads to a great change in chaotic system results, because chaotic systems are very sensitive to initial and environmental conditions. Hence, some global features of data are needed to simulate the biological behavior. We believe that simulations in chaotic systems must not be based on the error between recorded data and simulation results.

We propose to use some global features of chaotic systems like Lyapunov exponent, attractor properties, and Poincare map in order to present a proper model. A fitness function may be defined based on the difference of these three features between recorded and simulated data. Then, a chaotic artificial neural network can be designed, and weights which lead to better results (minimum of fitness function) must be chosen. We believe that a proper search method could be “genetic algorithm.”

If the chaotic neural network is trained properly, the model will simulate the chaotic biological system in an excellent manner; then, several benefits will be obtained. In Parkinson’s disease, the symptoms like gait disorders are seen when nearly 80% of substantia nigra neurons are destroyed; before this amount of destruction, no sign or

References

Successful Smoking Cessation and Improvement of Negative Symptoms With Varenicline in a Stable Schizophrenia Patient

To the Editor: The selective nicotinic partial agonist varenicline is approved for smoking cessation in more than 30 countries. Freedman has reported a case of a patient with a schizophrenic exacerbation after initiation of varenicline for smoking cessation. Here we present a case of successful smoking cessation and substantial improvement of negative symptoms in a clinically stable patient with schizophrenia.

Case Report
Mr. A is a 27-year-old former student with the diagnosis of schizophrenia, paranoid subtype for 4 years. His last admission as an inpatient took place 2 years ago and was due to delusions, visual and tactile hallucinations, and ideas of reference. He had no insight into his disorder and ideas of grandiosity (“the creator and guardian of the light”). By then he had also been a cannabis user (on average 0.5 g per day). No somatic disorders had been reported. He was then put on depot medication which he received every 14 days (risperidone, 37.5 mg). He smoked cigarettes for 5 years, increasing to 30 cigarettes a day over the last 6 months. His Positive and Negative Syndrome Scale (PANSS) negative symptoms score fluctuated between 42 and 45 over this period of time, with a PANSS positive symptoms score of only 8 points. Quitting smoking strategies like group counseling and nicotine replacement therapy via patch were altogether unsuccessful. Therefore, a trial with varenicline added to risperidone was started. The drug was titrated to 2 mg per day over a period of 1 week. It was tolerated well, and he experienced no nausea. After 2 weeks, complete abstinence was achieved (that was confirmed via CO measurement in the expiration air) and maintained for 6 months. Moreover, his PANSS negative score decreased from the second week on varenicline to 22 points. Risperidone and 9-hydroxy-risperidone concentrations remained unchanged.

Discussion
We report for the first time a successful trial of smoking cessation in a patient with very mild positive but marked negative symptoms which substantially improved during the treatment with varenicline without exacerbation of psychotic symptoms. We interpret this clinical observation by the indirect dopamine releasing properties of varenicline. Schizophrenia patients seem to have altered nicotinic acetylcholine receptors and stimulation by nicotine has a positive effect on cognition and other symptoms of schizophrenia, which is thought a transient effect. Nicotine as a full agonist on nicotinic acetylcholine receptors has a very high affinity for these receptors and a tolerance inducing effect that has not been described for varenicline yet. Since the patient still received risperidone he was probably sufficiently protected from the development of new positive symptoms.

Systematic controlled studies of schizophrenia patients with different predominant symptoms treated with varenicline seem warranted to evaluate its possible risks and advantages in this population.

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