

## The test of Random Rhythm Generation and neuropsychological performance in schizophrenic patients

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### Summary

The objective of this study was the assessment of neuropsychological performance in a sample of schizophrenic patients using a new computer-administered instrument, the Test of Random Rhythm Generation (ARG). The test was applied to a group of 20 DSM-IV schizophrenic patients (SG) and 20 sex- and age-matched controls (CG). The Positive and Negative Syndrome Scale (PANSS) and Frankfurt Complaint Questionnaire (*Frankfurter Beschwerdefragebogen*, FBF) were used to study patients' psychopathology. The neuroleptic treatment received by each patient during the last month was converted into daily equivalents of chlorpromazine. In the ARG, the subject is asked to press the space key of the computer at a rhythm as irregular as possible. The test aims at assessing the individual's ability to create random rhythms by means of sequences of blows, which is hypothetically associated with a high neuropsychological performance. The data were analyzed by means of three different mathematical techniques. Results showed that schizophrenic patients generated more regular and rhythmic sequences than controls (correlation dimension in SG =  $2.78 \pm 0.81$ , in CG =  $3.69 \pm 0.64$ ,  $p < 0.01$ ). This suggests that neuropsychological performance measured by the ARG was worse in patients compared to controls.

ARG is proposed as a new technique to evaluate neuropsychological performance with the following advantages: (1) its short-time application (it usually takes no more than 10 minutes), (2) personnel only require a short training to learn how to apply it, and (3) different analyses of the data are quickly carried out by the computer program.

### Introduction

Schizophrenia is a brain disease that disrupts the normal functioning of many cognitive abilities. Patients usually show bilateral frontal and temporal lobe dysfunction, including impairments on attention, retention time and problem solving ability. Therefore, the study of neuropsychological performance in schizophrenic patients must use a wide range of tools, including general tests and batteries, tests for attention, executive functions, fluency, motor function or verbal, as well as visual, short-term and long-term memory. In the last years, some computer-administered tests have been developed. Their advantages include that measures are more accurate, correction of the data is simplified, and interpretations are more quickly and easily obtained. Our research group has developed a new computer-administered instrument, the Test of Random Rhythm Generation (ARG), which was presented elsewhere [Jimeno et al. 1996a; Hornero et al. 1999] and has been registered at the University of Valladolid.

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**Key words:** neuropsychological performance, schizophrenia

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A random rhythm of blows is an irregular sequence lacking of an evident rule for its generation; there is much variation along



time. This hypothetically requires a certain level of mental ability. Consequently, generation of random rhythms must be understood as a „normal“ performance. On the contrary, a stable rhythm will be formed by a regular sequence of blows where a rule for its generation is easily found; variation along time is now small. This sort of sequences is associated with a loss of mental ability and therefore must be considered as a „pathological“ performance. In order to prove that individual's ability to create random sequences is associated with a high neuropsychological performance, we have assessed this ability in schizophrenic patients by means of the ARG.

## Methods

### Test of Random Rhythm Generation (ARG)

If possible, the test is performed in an ordinary examination room, being the computer placed at a side of the table (or on an additional one). A dim natural light projected on the computer is preferred. Interruptions during the exploration or pressure of time must be avoided. The doctor in charge holds a short interview with the patient in order to check his/her present mental state –acute positive symptoms should obviously be avoided– as well as the level of motivation and cooperation to perform the test. If the interviewer judges them satisfactory, the patient must sit in front of the computer and see perfectly the screen. The interviewer first asks which hand he/she uses normally and checks that the patient is able to press comfortably the space key with his/her dominant hand. Then the following instruction is given: „This is a simple test with a computer. You must press this key –and shows the space key– with a finger at a rhythm as irregular as possible during some time, until the screen indicates the end of the task. First, you are going to see an example“. The computer shows an example, consisting of a square of 4 by 4 cm which appears and disappears in the screen at an irregular rhythm. The presence of the square in the screen is accompanied by a beep. In this way, the patient may follow the example of the required task. The interviewer repeats now that this was only an example and that he/she must try to do it as irregular as possible. The subject performs now a sequence consisting of a sequence of blows. Once the patient has completed 64 blows, the program stops and asks about a second sequence. The interviewer inquires the patient how difficult he/she found the task and checks that the subject understands the task to perform. If necessary, the examiner may explain that the task does not consist in going only too fast or too slow, but in changing the rhythm. Usually only one trial is necessary, then a second and a third sequence are proposed.

Data of all the sequences are collected, but the first one(s) is(are) considered as a trial and only the last two sequences will be analyzed. In a previous study with the ARG [Hornero et al. 1999], we noticed that sequences of 128 points –or blows– are optimal to analyze data: results might be wrong both if the sequence is too long, because generating long random sequences is a very hard and tiring task, or if it is too short, because mathematical procedures might not be properly applied.

Once the data acquisition is finished, the program carries out automatically the following analyses: (1) a histogram of interval frequencies between blows, (2) a plot of the chaotic dynamic attractor of the generated sequences expressed in the phase space, and (3) the correlation dimension, applying the technique

of Grassberger and Procaccia (1983). The statistical analysis was done by means of the ANOVA test. Further details about this methodology are provided elsewhere [Hornero et al. 1999].

## Subjects

A sample of 20 patients diagnosed of schizophrenia according to DSM-IV criteria were recruited from the Department of Psychiatry of the University Hospital of Valladolid, Spain. Inclusion criteria were (1) age between 16 and 55 years, (2) history of prior hospital admission(s), (3) no psychotic episodes during the last year, and (4) no mental retardation or other cerebral disorders. Their main sociodemographic and clinical variables are shown in Table 1. All patients of the schizophrenic group (SG) were living at home and on ambulatory treatment, 15 were receiving neuroleptics, mainly middle doses of haloperidol or risperidone. Neuroleptic treatment during the last month was converted into equivalents of chlorpromazine; the mean daily dosis was  $192.5 \pm 205.7$  mg/day. In addition, a control group of 20 sex- and age-matched subjects lacking of past or present psychiatric history was tested. There were 15 men (75%) and 5 women (25%) in both groups. Mean age was  $30.8 \pm 7.4$  years in the schizophrenic group (SG) and  $30.9 \pm 7.4$  in the control group (CG). All the patients and control subjects had right-hand dominance.

	SG	CG
Sex		
Male	15 (75)	15 (75)
Female	5 (25)	5 (25)
Mean age	$30.8 \pm 7.4$	$30.9 \pm 7.4$
Age at onset	$19.7 \pm 4.6$	
Duration of the illness (years)	$11.3 \pm 6.7$	
Diagnosis of patients with schizophrenia		
Paranoid type	12 (60)	
Catatonic type	0 (0)	
Disorganized type	0 (0)	
Undifferential type	2 (10)	
Residual	6 (30)	

Figures in parantheses indicate percentages

**Table 1.** Sociodemographic and clinical data of the sample (abbreviations see text).

In the SG group, psychopathology assessment was carried out by means of the Positive and Negative Syndrome Scale (PANSS) [Kay et al. 1990] and the Frankfurt Complaint Questionnaire (*Frankfurter Beschwerdefragebogen*, FBF) in its third version [Süllwold and Huber 1986], both in their Spanish language



adaptation [Peralta and Cuesta 1994; Jimeno et al. 1996b]. All the clinical assessments were carried out by the same experienced psychiatrist (N.J.). While the PANSS objectively collects positive and negative symptoms, the FBF aims at subjectively-perceived deficiency symptoms, also called "basic symptoms". A certain degree of patient's cooperation is necessary to fulfil the FBF and perform the ARG, what is usually achieved after some days of hospitalization. Psychopathologic symptoms at this time point were assessed by means of the PANSS.

**Results**

The main results of this study are presented in Table 2. Since in analyses 1 and 2, already described in the methods section, it is not possible to show global results but only individual cases, data of the 'type subject' of each group -or subjects who had the most similar performance to the group's average- are displayed: patient number 16 in the SG (pat-16) and control number 19 (con-19) in the CG.

The first analysis focuses on the histogram of interval frequencies between blows. The X-axis contains the different time intervals (or time between one blow and the next), measured in miliseconds, and the Y-axis shows the number of cases - or occurrences - corresponding to each interval. A blow corresponding to the interval 0-20 has been produced immediately after the previous blow. On the contrary, if another blow is represented in the interval 240-260, this means that it has taken a long time to occur. This also explains that, if the sequence is rather fast, the columns of the histogram are mostly placed on the left, and if it is rather slow, columns tend to be on the right. However, the fact that the sequence is rather fast or slow, which might be fixed by the time needed to accomplish the task (the computer program stops once the necessary blows have been carried out), is not the essential point of this test, which aims at assessing the individual's ability to create random sequences of blows.

Fig. 1 shows the histogram of the type-subject of the SG (pat-16), which contains a few number of intervals. The time between

SG											CG	
No.	Sex	Age	Age at onset	Duration	Diagnosis	PANSS-P	PANSS-N	PANSS-C	PANSS-G	FBF	CD	CD
1	F	33	16	17	295.60	10	18	-8	35	23	2.5	5.0
2	F	36	30	6	295.30	26	24	2	39	91	4.3	3.1
3	M	31	20	11	295.30	19	12	7	27	65	1.9	2.9
4	F	54	29	25	295.60	23	23	0	42	58	2.2	2.7
5	M	32	17	15	295.30	13	28	-15	30	17	3.2	4.4
6	M	16	13	3	295.30	23	27	-4	52	25	2.9	3.9
7	M	35	16	19	295.30	31	11	20	43	49	3.4	3.9
8	M	28	22	6	295.60	10	28	18	41	17	2.6	4.1
9	M	28	15	13	295.60	16	16	0	32	28	2.1	4.4
10	M	23	22	1	295.30	15	22	-7	37	56	3.1	3.9
11	M	27	19	8	295.90	18	16	2	41	83	2.8	3.0
12	M	39	19	20	295.60	10	18	-8	35	84	3.4	3.2
13	M	23	22	1	295.30	13	16	-3	33	90	2.7	3.4
14	M	26	20	6	295.30	19	19	0	34	65	1.2	4.1
15	M	34	21	13	295.60	28	25	3	46	59	3.2	4.2
16	F	32	25	7	295.30	9	16	-7	31	31	2.7	3.6
17	F	31	18	13	295.90	16	27	-11	33	n.v. <sup>1</sup>	4.5	2.5
18	M	34	16	18	295.30	9	20	-11	36	50	2.9	4.0
19	M	27	15	12	295.30	10	17	-7	33	56	2.3	3.6
20	M	26	21	5	295.30	17	20	-3	37	53	1.6	3.8
Mean						16.7±6.8 (15) <sup>2</sup>	20.2±5.3 (30) <sup>2</sup>	-3±8.5 (40) <sup>2</sup>	36.8±6.1 (20) <sup>2</sup>	52.6±24.8 (75.8) <sup>3</sup>	2.78±0.81	3.69±0.64*

<sup>1</sup> Not valuable.

<sup>2</sup> Percentile compared with a sample of 100 schizophrenic patients [Peralta and Cuesta 1994].

<sup>3</sup> Percentile compared to a sample of 293 assessments of psychotic patients [Jimeno et al. 1996b].

\* p < 0.01.

**Table 2.** Results obtained in the psychopathological scales and in the correlation dimension of the ARG.



one blow and the next tends to be very similar, and there are few changes of rhythm. The subject always repeats the same sequence. In a few words, the presence of a small number of columns suggests that the sequence is quite regular and rhythmic. With the same number of columns in the histogram, the sequence would be even more regular and rhythmic if the columns had a similar height. This would mean that several intervals between blows are repeated with the same frequency. The most regular and rhythmic sequence would be represented by a single column (only one interval would appear).

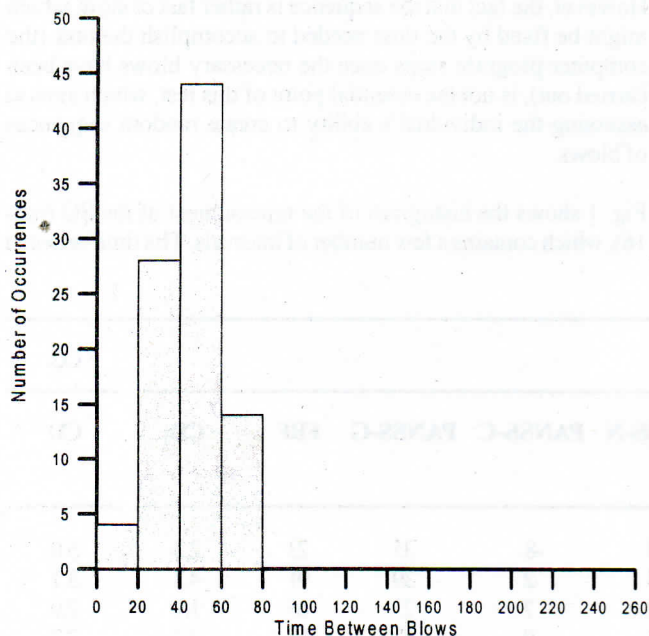


Figure 1. Histogram of the time series generated by the type-subject of the SG (pat-16).

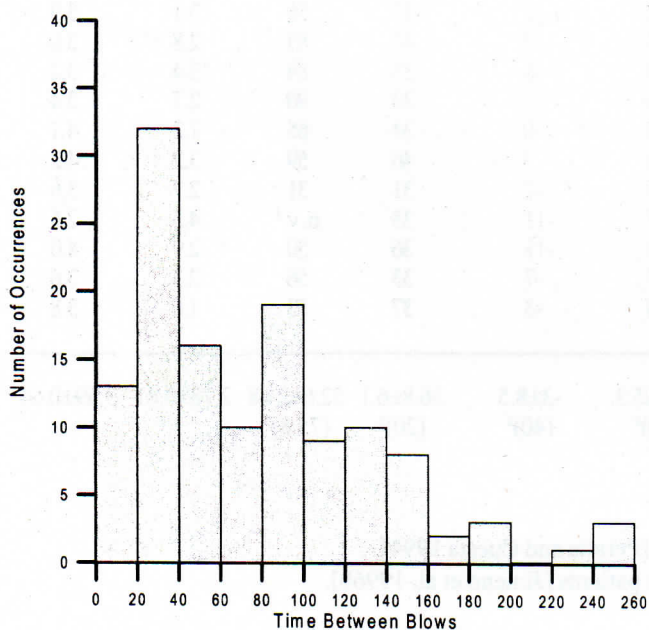


Figure 2. Histogram of the time series generated by the type-subject of the CG (con-19).

Fig. 2 displays the histogram of the type-subject of the CG (con-19). It contains a significantly higher number of intervals, again with different heights. Then, it can be deduced that the sequence here is more variable or irregular, and less rhythmic. This fact was verified in 17 of the 20 patient-control comparisons (with the exception of numbers 2, 12 and 17), what suggests that sequences generated by the schizophrenic patients were more regular and rhythmic than those of control subjects.

The second analysis plots the chaotic dynamic attractor. This analysis requires that values of certain parameters –time delay, embedding dimension- are previously fixed [see more details in Homero et al. 1999]. By means of a complex mathematical procedure [Grassberger and Procaccia 1983], the blow sequence is converted into a figure called attractor which in fact contains 8 dimensions, although only 3 can be represented on a paper sheet. However, if in this plot there is a dominant shape -or, in other words, a regularity pattern- to recognize, we can affirm that the sequence is rather rhythmic. This is the case of a few-side polygon (i.e., triangle, rectangle..) or a curve. The most regular and rhythmic sequence would be represented by a single point. On the contrary, a plot lacking of any dominant shape is related to an irregular and random sequence. No information about this point can be deduced from the attractor's size, since this variable depends more on the mathematical procedures than on the degree of randomness. In spite of their limitations, both the histogram and the attractor can provide a preliminary idea of the kind of generated sequence.

Fig. 3 shows the reconstructed attractor of the time sequences generated by the type-subject of the SG (pat-16), whose histogram was drawn in Fig. 1. The dominant shape is approximately a 6-side polygon. Similarly, the reconstructed attractor of the time sequences generated by the type-subject of the CG (con-19), whose histogram was displayed in Fig. 2, is shown in Fig. 4. No dominant shape is here easily recognized. We calculated all the subjects' attractors in both groups, which are not shown in this paper because of space reasons. However, we observed that in the same mentioned 17 of the 20 comparisons, attractors of the CG subjects have a more complex tangle than the patients' ones.

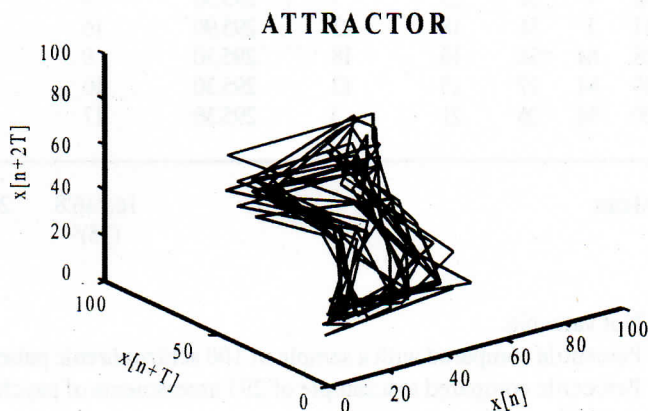
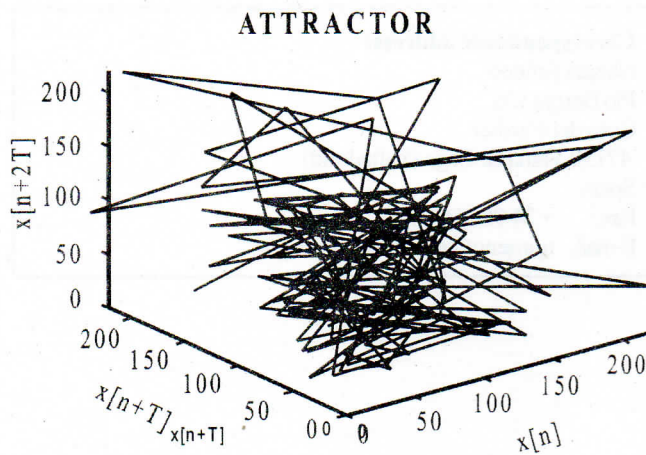


Figure 3. Reconstructed attractor of the time series generated by the type-subject of the SG (pat-16).





**Figure 4.** Reconstructed attractor of the time series generated by the type-subject of the CG (con-19).

Finally, the third analysis is a quantitative value called correlation dimension (CD). Indeed, only an estimation of the correlation dimension can be obtained by means of this procedure [Hornero et al. 1999]. The bigger the correlation dimension is, the more irregular and arrhythmic the sequence is. Table 2 also summarizes results of correlation dimensions for the two groups of subjects, once matched by sex and age. The mean value of the correlation dimension in the schizophrenic group was lower than in the control group ( $SG = 2.78 \pm 0.81$ ,  $CG = 3.69 \pm 0.64$ ;  $p < 0.01$ ). In the same 17 (85.0%) of the 20 patient-control comparisons, correlation dimensions of time sequences generated by schizophrenic patients were lower than their respective controls. In other words, in only three comparisons correlation dimension was higher in schizophrenic patients than in their controls. In summary, this third analysis of data shows that schizophrenic patients generated more regular and rhythmic sequences than controls (correlation dimension in  $SG = 2.78 \pm 0.81$ , in  $CG = 3.69 \pm 0.64$ ;  $p < 0.01$ ).

With regard to the PANSS, schizophrenic patients obtained a score of  $16.7 \pm 6.8$  in the positive scale (PANSS-P),  $20.2 \pm 5.3$  in the negative (PANSS-N) and  $36.8 \pm 6.1$  in the scale of general psychopathology (PANSS-G). In the FBF, the group of patients obtained a mean total score of  $52.6 \pm 24.8$ .

## Discussion

The first two analyses of results in the ARG -histograms of interval frequencies and reconstruction of the attractor- provide a visual interpretation of the generated sequence of blows. In our study, schizophrenic patients tend to have a small number of columns in their histogram and their chaotic dynamic attractor usually shows a dominant shape or regularity pattern. Both analysis suggest that patients generate more regular and rhythmic, i.e. more rigid sequences, than control subjects. In other words, schizophrenic patients seem to show a reduction of complexity compared to controls when performing the ARG. This idea is confirmed by the third analysis, correlation dimension, which consists in a numerical value and therefore always provides a more accurate information. Values obtained

in the two groups are:  $SG = 2.78 \pm 0.81$ ,  $CG = 3.69 \pm 0.64$ ;  $p < 0.01$ .

Assessment of repetition of rhythms is included in some neuropsychological batteries, e.g. the Luria battery and the Neurological Evaluation Scale [Buchanan and Heinrichs 1989]. Indeed, the „Rhythm Tapping Test“ of this last scale consists in asking the subject to reproduce exactly the series of taps heard while keeping the eyes closed. However, to our knowledge, the ARG is the only test developed to measure the ability of generating random rhythms.

Several objections can be raised against the ARG: First, whether the patient correctly understands the instruction „press this key with a finger at a rhythm as irregular as possible“. To assure this, an example is given by the computer; also, the subject has the possibility of making several trials, and the interviewer must check that the subject understands the task to perform. However, the moment of assessment should be carefully selected; the doctor in charge of the patient should check his/her present mental state. Second, whether the patient is motivated to perform the test. This question arises when applying most of cognitive tests, symptom questionnaires and psychosocial therapies in schizophrenic patients. It is again the doctor in charge who must check the degree of motivation and cooperation. The interviewer also tries to enhance them by presenting the test in an attractive way. Our experience shows that the test is generally very well accepted by the patient, and that the instruction „This is a simple test with a computer“ helps to minimize any possible patient's fear or mistrust at the beginning. The third objection which might be discussed is the influence of neuroleptic medication in the performance of the ARG. Once the neuroleptic treatment was converted into equivalents of chlorpromazine, we obtained that patients of this study were receiving  $192.5 \pm 205.7$  mg/day of chlorpromazine. Therefore, neuroleptic treatment could effectively account for at least some part of the results. We certainly believe that the task to perform -generate random sequences- is not only of a motor nature, but also includes a high component of executive functions, particularly cognitive flexibility: to get the best results, the subject has to use different strategies and plan exactly when he/she is pressing the key. However, this interesting point about the possible influence of medication requires further investigation and is one of the research lines we are dealing with.

The main interpretation of our results is that the group of schizophrenic patients generate more regular and rhythmic sequences than the group of control subjects or, in other words, that patients show a reduction of complexity when performing the ARG. This fact agrees with findings showing that schizophrenic patients are characterized by less complex neurobehavioral and neurophysiological measurements than control subjects: (1) in a test of random number generation, consisting in choosing several times a number between 1 and 10 without any generative rule, schizophrenics tended more to repetition and therefore performed worse than normal subjects [Rosenberg et al. 1990]; (2) when performing a listening task they showed a high degree of semantic recurrence in hallucinated „voices“ [Hoffman et al. 1994], and (3) when predicting 500 random right or left appearances of a stimulus, they generated more predictable or interdependent sequences [Paulus et al. 1996].



We have hypothesized that the generation of random rhythms, that is, irregular sequences lacking an evident rule for its generation, requires a certain level of mental ability and must be understood as a „normal“ performance. On the contrary, regular and rhythmic sequences are hypothetically associated with a loss of mental ability and consequently must be considered as a „pathological“ performance.

In addition, some data can be derived from the psychopathological scales, the PANSS and the FBF. Values obtained in the PANSS were compared with those corresponding to a sample of 100 schizophrenic patients [Peralta and Cuesta 1994]. The score of  $16.74 \pm 6.83$  in the positive scale (PANSS-P) is comprised between the percentiles 10 and 15, the score of  $20.16 \pm 5.30$  in the negative scale (PANSS-N) corresponds to the interval between percentiles 30 and 35, and the score of  $36.8 \pm 6.1$  in the scale of general psychopathology (PANSS-G) to percentiles 20 and 25. In the FBF, the group of patients obtained a mean total score of  $52.6 \pm 24.8$ , which corresponds to the percentile 75.8 when compared with a sample of 293 psychotic patients [Jimeno et al. 1996b]. According to these results, our patients show a very small degree of positive symptoms (percentile 10-15 in the PANSS-P), certain general symptoms (percentiles 20 and 25 in the PANSS-G), a little higher degree of negative symptoms (percentile 30-35 in the PANSS-N), and particularly marked self-experienced symptoms (percentile 75.8 in the FBF). Therefore, they could be considered moderate chronic schizophrenic patients.

The fact that the group of moderate chronic schizophrenic patients show poorer performance in the ARG than sex- and age-matched normal controls might indicate, according to our hypothesis, that this neurocognitive measurement is a new indicator of vulnerability to schizophrenia. This possibility should be tested in several ways to fulfill the required criteria [Green and Nuechterlein 1999]: Firstly, the neurocognitive measurement should reveal a deficit in a sample of schizophrenic patients compared to the general population. Secondly, the deficit should be present during periods of symptomatic remission as well as in the psychotic episode. Thirdly, the deficit should be disproportionately present in first-degree relatives of the patient, even if the relatives do not have the illness. Further research with the ARG is needed. Performance in more groups of patients both during periods of relapse and symptomatic remission, as well as in controls and first-degree relatives, should be carefully assessed. In addition, associations with neuropsychological and clinical variables, including drug therapy, must be studied.

## Conclusion

Using a new computer-administered instrument, the Test of Random Rhythm Generation (ARG), it was observed that a group of 20 schizophrenic patients generated more regular and rhythmic sequences than sex- and age-matched controls (correlation dimension in SG =  $2.78 \pm 0.81$ , in CG =  $3.69 \pm 0.64$ ,  $p < 0.01$ ).

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## References

1. Buchanan RW, Heinrichs DW (1989) The Neurological Evaluation Scale (NES): A structured instrument for the assessment of neurological signs in schizophrenia. *Psychiatry Res* 27:335-350
2. Grassberger P, Procaccia I (1983) Characterization of strange attractors. *Phys Rev Letters* 50: 346-349
3. Green MF, Nuechterlein KH (1999) Backward masking performance as an indicator of vulnerability to schizophrenia. *Acta Psychiatr Scand* 99:34-40
4. Hoffman RE, Oates E, Hafner, RJ, Hustig HH, McGlashan TH (1994) Semantic organization of hallucinated "voices" in schizophrenia. *Am J Psychiatry* 151:1229-1230
5. Homero R, Alonso A, Jimeno N, Jimeno A, López M (1999) Estimation of correlation dimension to evaluate cognitive performance in schizophrenic patients using a new computer technique. *Nonlinear Dynamics Psychol Life Sci* 3:49-63
6. Jimeno N, Jimeno A, Alonso A, Segovia E, Vargas ML (1996a) Basic symptoms and cognitive dynamic disorders in schizophrenic patients. *Neurol Psychiatry Brain Res* 4:171-178
7. Jimeno N, Jimeno A, Vargas ML (1996b) El síndrome psicótico y el Inventario de Frankfurt: Conceptos y resultados. Springer, Barcelona
8. Kay SR, Fiszbein A, Vital-Herne M, Silva L (1990) The Positive and Negative Syndrome Scale - Spanish Adaptation. *J Nerv Ment Dis* 178:510-517
9. Paulus MP, Geyer MA, Braff DL (1996) Use of methods from chaos theory to quantify a fundamental dysfunction in the behavioral organization of schizophrenic patients. *Am J Psychiatry* 153:714-717
10. Peralta V, Cuesta MJ (1994) Validación de la Escala de los Síndromes Positivo y Negativo (PANSS) en una muestra de esquizofrénicos españoles. *Actas Luso-Españolas Neurol Psiquiatr* 22:171-177
11. Rosenberg S, Weber N, Crocq MA, Duval F, Macher JP (1990) Random number generation by normal, alcoholic and schizophrenic subjects. *Psychol Med* 20:953-960
12. Stillwold L, Huber G (1986) *Schizophrenie Basisstörungen*. Springer, Berlin Heidelberg