

# Schizophrenia: Stress and Neuroleptics: What Support?

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**Abstract:** *This work is primarily due to describe abnormalities of the HPA axis in schizophrenic patients, after the administration of dexamethasone (0, 5 mg), and secondarily to determine the action of Neuroleptics (terms of prescription) on stress. Our research included 18 male schizophrenic patients, admitted to the psychiatric Emergency Department. The result of the dexamethasone suppression test revealed a large amount of no suppression of cortisol after DST (44%), also, the neuroleptic treatment has not influenced anomalies of the test, or the decrease in the level of stress in these patients. These results support idea that schizophrenics are hyper stressed, and unfortunately they are not treated as they should be. We also affirm that the efficacy of antipsychotic treatment depends on the quality of the work does the practitioner with the patient, and its support.*

**Keywords:** schizophrenia, suppression test of dexamethasone, cortisol, neuroleptic, support, psychiatric hospital

## 1. Introduction

Schizophrenia is a disease with multifactorial determinants [1]. It is associated with an inappropriate response to stress through hyperactivity of the hypothalamic-pituitary-adrenal axis (HPA) [2-3].

A method of research studies directly the effect of stress in psychosis is the use of specific challenge of the measures of the response of the hypothalamic-pituitary-adrenal axis (HPA) using suppression to dexamethasone test (DST) [4].

In 1985, A. Baumgartner et al. observed a level of cortisol post dexamethasone (dex) in some schizophrenics higher than that found in healthy subjects. Another group of researchers found that schizophrenics had a frequency of 30% of abnormal response to dexamethasone [5-6-7-8].

Neuroleptics are psychotropic products, they serve only symptomatic treatment and in no way specific to schizophrenic psychosis [9]. Conflicting opinions on the antipsychotic relationship and the dexamethasone suppression test have been developed [10-7-2].

Join the effort of this reflection; such is the objective of this study. Indeed, we would mainly like to describe abnormalities of the HPA axis in schizophrenic patients, after the administration of dexamethasone (0, 5 mg), and secondarily to determine the action of Neuroleptics (terms of prescription) on stress.

## 2. Material and Methods

This is an etiological study at front sight and after, it included 18 male schizophrenic patients; chosen in a random manner; at the level of the inlet of the emergency psychiatric hospital Abu Bakr ER-Razi of Annaba; over a period from September 2012 to December 2013.

The pathology diagnosis by the physician psychiatrist during the first interview with the patient, and based on the diagnostic criteria of DSM - IV [11].

We have excluded from the study the outgoing schizophrenic patients, were under immunosuppression, chronic disease carrier or they did not accept this study.

### 2.1. Methods

The records of patients and gathering important information: stressors, age, type of treatment (first or second generation), number of neuroleptic command, their routes of administrations, dosage, and duration of dst. This is the delay between the taking of antipsychotic treatment (admission of the patient), and administration of dexamethasone. We also recorded the treatments that were not part of the psychiatric range, the biochemical balance admission of patients, any pathology that was not related to the psychiatric disorder. We have established an insane intensity of pathology study approach based on the BPRS items (*Brief Psychiatric Rating Scale*) [12], the items of the questionnaire were completed by one person and in the presence of the psychologist of the service. 2.1.1. Tests to the dexamethasone, blood sampling and assays:

Blood samples are taken twice before and after the test in dexamethasone (DEX - pre and Post-DEX). The blood collected in dry tubes is centrifuged at 3000 rpm for 15 minutes at 4 ° c. The resulting plasma is aliquoted in Eppendorf tubes and kept at a temperature (-20 ° c). It will be the determination of cortisol.

A first sampling is performed on the first day (pre - DEX) fasted eight o'clock in the morning. Dexamethasone (dex) is administered by oral tablets at low doses (0.5 mg) at 11 o'clock in the evening the same day [13]. The next day at the same time (eight o'clock in the morning), a second blood sample obtained (Post-DEX). Plasma cortisol is measured by

electro-chemiluminescence immunological assay by the statistical treatment XLSTAT software version (ECLIA, module Elecsys 1010, Roche).

7.5.2.

**2.1.2. Statistical analysis of the data**

The results will be represented as average more or less the standard deviation (m±s). A Pearson correlation test was performed between cortisol post dex and the qualitative variables (the route of administration, the type of treatment, dosage). The level of significance  $p=0,05$  A linear regression test was done using cortisol post dex as the dependent variable, and the age, the length of DST and the number of prescribed treatment as quantitative variables. The level of significance  $p=0,1$  These tests were conducted

**3. Results**

This study has recorded 18 male patients with a mean age of (35,33 ±9, 72 years). Dexamethasone suppression test result showed 44% of no suppression of cortisol rate after the DST. All patients in this research have lived stressful biographical events, (table I) wanted to demonstrated the impact of these events on pathology (intensity), and on the outcome of the DST (the rate of non-removal of cortisol after the DST).

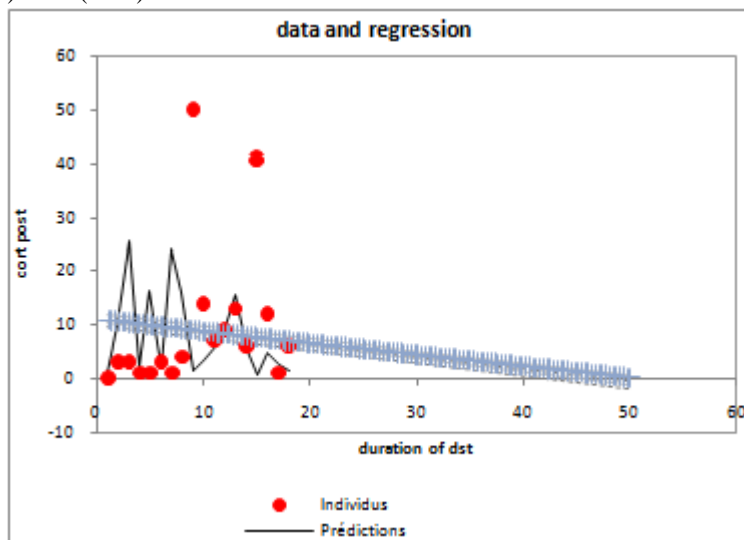
**Table 1:** distribution of stressors and their effects on the outcome of the DST, intensity of Pathology, and the number of admission

The type of problem	Family problems	unemployment	Disappointment in love	addiction
Number of patient (%)	50%	22%	25%	3%
No suppression rate	62%	33%	62%	0%
Intensity of Pathology (±)	(68±20,5)	(60±21,3)	(47±12,3)	(58)
Number of admission (±)	(7±5,05)	(4±4,5)	(4±3)	(1)

This study cannot assert that these factors are the cause of the outbreak of the disease; because records provide no information on the subject, my they play an important role in the persistence of disorder, worsening of the disease which responds to relapse.

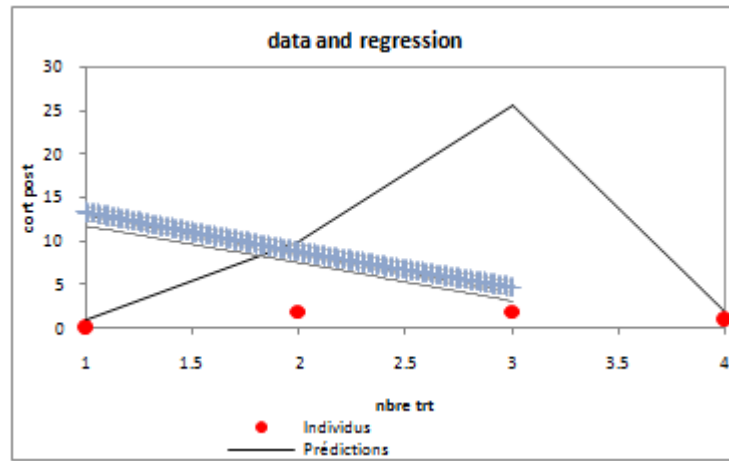
The BPRS total score indicated 78 percent of patients suffering from severe schizophrenia symptoms with intensity (57±18,34). We recorded 2 groups of patients with “values for dst” close to admission (3±2 days), and far from the admission (18±13, 11 days). (90%) of patients were under first generation antipsychotics (10%) were under 2nd generation Neuroleptics. The association of Neuroleptic most frequent was to:haldol®(halopéridol)-nozinan®(lévomépromazine)with (44%), followed by : Largactil®(chlorpromazine)-nozinan®(lévomépromazine) with (33%).

Our study has saved (50%) patients were under antipsychotic oral. The correlation test revealed no significant association between the choice of the route of administration and the intensity of pathology (r = 0. 5), or with « duration of the dst » (r = 0. 3). A Pearson correlation test was performed between the rate of cortisol post dex and the following qualitative variables: the route of administration, the type of treatment, dosage. The result is as follows: no significant association with (r = 0, 7), (r = 0, 5), (r = 0. 7) according to the order. Figures I and II presented the results of the linear regression between cortisol post dex and: the duration of the dst, number of treatment



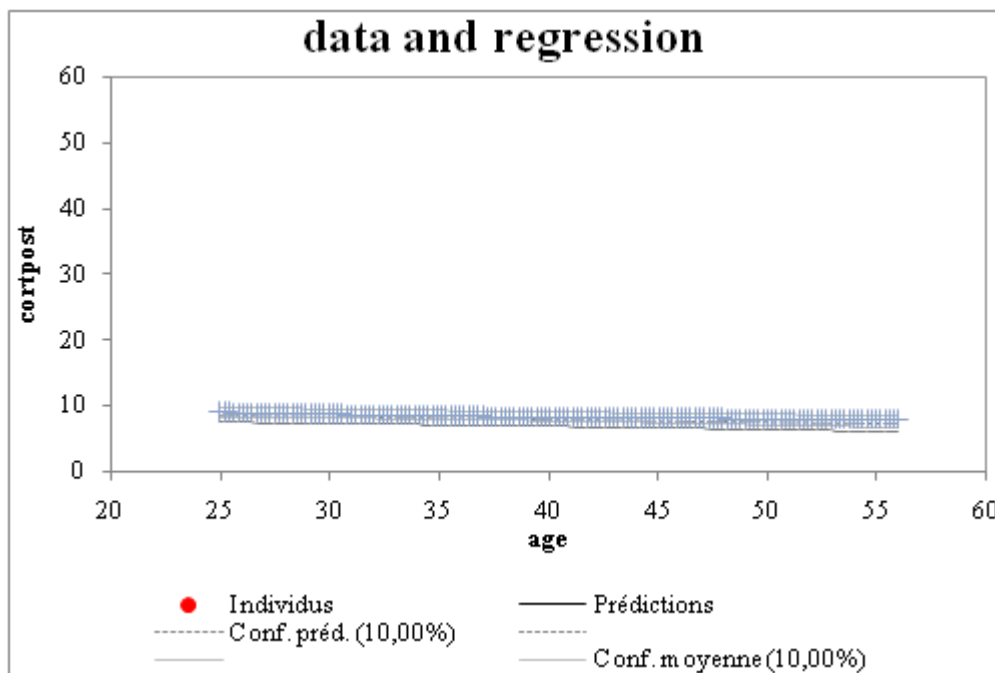
**Figure 1:** the linear regression line between cortisol post dex and the dst legend of figure I duration:cort post= cortisol post dex

Individus: invidious  
 Prédictions: prediction



**Figure 2:** the linear regression line between cortisol post dex and the number of treatment Legend of figure II: nbretrt= number of treatment

Individus: invidious  
 Prédictions: prediction



**Figure 3:** the linear regression line between cortisol post dex and age

(I, II) figures indicate that no significant correlation was identified between cortisol post dex and the duration of the  $r = 0, 4$  dst, or with the number of treatment  $r = 0, 3$ . On the other hand, Figure III indicates a significant correlation between cortisol post dex and age,  $r = 0, 05$ . We recorded no prescription of medicine which was part of the psychiatric, and which could alter the response of the DST.

#### 4. Discussion

Our results reveal an important no suppression rate (44%) which approximates values discovered by Berger and al. (1984), Dewan and al. (1982)[14-6], Herzand al (1985) [7], but also of the values estimated by various other researchers (between 11% and 55%) [6-4-5-15-16-17-18].

This observation leads us to look for factors that could influence these data, we can already rule out adrenal or pituitary gland-related defects that may influence the results of the test.

Our research recorded no association significant between quantitative variables (age, number of treatment, duration of dst) or qualitative (routes of administration, dosage, type of Neuroleptic) and rate of cortisol post dex. This means that these parameters did not influence the response of the DST.

The duration ofdst is a very important parameter, because the duration between the admission of the patient (taking treatment) and the time where the dexamethasone suppression test was performed may be indicative of the effect of antipsychotics on this test. This parameter confirms that Neuroleptics, and

some is the lifetime of decision-making, have no effect on the test result.

All these findings argue the hypothesis that stress is an important factor likely to influence non-suppression of cortisol after the DST [19, 20]. Our study found 75% of patients were suffering from a severe schizophrenic intensity; this assumption may justify no suppression of cortisol rate [19].

To prove that the type of stress played a role vital in abnormalities of the DST, we divided patients into several groups according to the type of stressful event recorded from records (table I), this operation showed that the rate of no suppression, and the intensity of the pathology and the number of admission had changes depending on the type of event.

This table also shows that 97% of patients were readmitted to the hospital more than times during the study after a symptomatic relapse, as the indicated table, these relapses were due to family problems in the first place, followed by unemployment and the emotional disappointment. These patients were young men; aged between 25 to 30 years, they have returned to hospital to escape deplorable conditions outside: absence of structure of reintegration and rehabilitation; patients were either wandering the streets where they were tap or insult by the citizens.

Therapeutic judgments due to the exaggerated drug costs were another reason for re-hospitalization. Brutal therapeutic discontinuation can result in appearances by other symptoms or amplification of old symptoms [21]. Researchers have confirmed this hypothesis through the BPRS [21].

Even in the service where they were admitted, patients were not at the shelter to meet other stressful factors: shouts and insults on the part of the paramedical body, rare visits or non-existent for some of the families, more than 90% of patients were dependent on caffeine and tobacco mainly, they received routinely on the part of nurses and security officers, and unfortunately when they were lack of time; they were restless and developed a level of stress.

Studies have noted a relationship between age and the result of the DST [22-23] this result has been confirmed in this study with non-correlation of it with post dex cortisol levels.

The significant impact of no-suppression indicates also that the treatment prescribed by doctors failed to decrease the level of stress. This study has an obligation to find the reasons of inefficiency chemo therapeutic:

- No doctor was important to discover the factors triggering the pathology, certainly the etiology of this condition remains still unknown; But researchers have developed a model stress (Middle life, toxin, stressful events) and vulnerability (congenital, genetic factors) that still makes reference to explain the occurrence of the disease

[24].Indeed, more than 90% of the sample lived the period of terrorism, lived in rural areas where poverty and illiteracy were on a daily basis. This study is aware that genetic or congenital factors cannot be controlled, but it is important that practitioners have knowledge of the high incidence of trauma or stress in patients suffering from schizophrenia and that they know that this area must be evaluated, although gradually and sensitive [25].

- This survey has discovered (44%) prescription of Halopéridol-Lévomépromazine, this high rate of prescription was not due to the therapeutic interest that brings this pathology [26] association, but this is only a requirement for all patients.
- 90% of the patients were under conventional antipsychotics (1st generation or typical), despite the therapeutic interest of medication [27], but the introduction of more of second generation antipsychotics (atypical) ca would bring better results, what has already been proven [28].
- The careful study of the records of patients of the first admission to that at the time of the study, identified a disinterest with the psychological approach to service emergency, or in the hospital service. This reflects the quality of the support which remains insufficient.

Non-correlation of the route of administration of treatment and the intensity of the pathology is another reason to consider as the right choice of the path of assimilation of the treatment can be effective against the severity of the symptoms. For example: by its speed of resorption and its bioavailability [27], the injection is most effective to decrease the intensity of the pathology degree.

## 5. Conclusion

The peculiarity that makes this investigation in addition to the result of the effect of antipsychotics on the DST, is the highlight of inadequate hospital care to these patients. Indeed, the rate of positivity of the DST (44%) which is close to that found in the literature in schizophrenia, and the lack of effect of Neuroleptics on DST, argue idea discussed in the article that schizophrenics are hyper stressed, and unfortunately they are not treated as they should be. Follow-up to the results of this study, we affirm that the efficacy of antipsychotic treatment depends on the quality of the work that makes the practitioner with the patient; by the knowledge of his level of stress, prescription of any treatments specific to the symptoms and their intensity, then place the best support.

## References

- [1] Tandon R, Keshavan MS, Nasrallah HA. Schizophrenia, "just the facts": what we know in 2008. Part II. Epidemiology and etiology. *Schizophr Res* 2008; 102(1-3):1-18.
- [2] Tandon R, Mazzara C, DeQuardo J, Craig KA, Meador-Woodruff JH, Goldman R, et al. Dexamethasone

- suppression test in schizophrenia: Relationship to symptomatology, ventricular enlargement and outcome. *Biol Psychiatry* 1991 ; 29:953–964
- [3] Lammers CH, Garcia-Borreguero D, Schmider J, Gotthard U, Dettling M, Holsboer F, and al. Combined dexamethasone/corticotropin-releasing hormone test in patients with schizophrenia and in normal controls: II. *Biol Psychiatry* 1995 ; 38:803– 807.
- [4] Yeragani VK. The incidence of abnormal dexamethasone suppression in schizophrenia: a review and a meta-analytic comparison with the incidence in normal controls. *Canadian Journal of Psychiatry* 1990;35:128–32.
- [5] Asnis GM, Eisenberg J, Lemus C, Halbreich U. The dexamethasone suppression test in schizophrenia – A study and review. *Neuropsychobiology* 1986 ; 15 : 109-113.
- [6] Dewan MJ, Pandurangi AK, Boucher ML, Levy BF, Major LF. Abnormal dexamethasone suppression test results in chronic schizophrenic patients. *Am J Psychiatry* 1982 ; 139:1501-1503.
- [7] Herz MI, Fava G, Molnar G. The dexamethasone suppression test in schizophrenia. *Psychosom Med* 1983 ; 45:79-80.
- [8] Myers ED. Serial dexamethasone suppression tests in male chronic schizophrenic patients. *Am J Psychiatry* 1994 ; 141:904-905
- [9] Zarifian E. Des paradis plein la tête : Odile Jacob, 1994, 248p.
- [10] Arana GW, Baldessarini RJ, Omsteen M. The dexamethasone suppression test for diagnosis and prognosis in psychiatry. *Arch. Gen. Psychiatry* 1985 ; 42 : 1193-1204.
- [11] Diagnostic and statistical manual of mental disorders. American Psychiatric Association. Washington. 4th Ed : DC: APA Press ; 1994.
- [12] Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep* 1962 ; 10, 799-812.
- [13] Yehuda R, Resnick H, Kahana B, Giller EL. Long-lasting hormonal alterations to extreme stress in humans: normative or maladaptive? *Psychosom Med* 1993;55 :287–97
- [14] Berger M, Pirke KM, Doerr P, Krieg JC, von Zerssen D. The limited utility of the dexamethasone suppression test for the diagnostic process in psychiatry. *Br J Psychiatry* 1984 ; 145-372.
- [15] Baumgartner A, Gräf KJ, Kürten I. Serial dexamethasone suppression tests in psychiatric illness: part I. A study in schizophrenia and mania. *Psychiatry Res* 1986 ; 18:9-23.
- [16] Holsboer F, v Bardeleben U, Wiedemann K, Müller OA, Stalla GK. Serial assessment of corticotropin-releasing hormone response after dexamethasone in depression—implications for pathophysiology of DST nonsuppression. *Biol Psychiatry* 1987 ; 22:228-234.
- [17] Coryell W, Zimmerman M. HPA axis hyperactivity and recovery from functional psychoses. *Am J Psychiatry* 1989 ; 146: 473-477.
- [18] Coryell W, Tsuang D. Hypothalamic-pituitary-adrenal axis hyperactivity and psychosis: Recovery during an 8-year follow-up. *Am J Psychiatry* 1992 ; 149:1033-1039.
- [19] Baumgartner A, Gräf KJ, Kürten I. The dexamethasone suppression test in depression, in schizophrenia, and during experimental stress. *Biol Psychiatry* 1985 ; 20:675–679.
- [20] Mück-Seler D, Pivac N, Jakovljević M, Brzović Z. Platelet serotonin, plasma cortisol, and dexamethasone suppression test in schizophrenic patients. *Biol Psychiatry* 1999;45:1433-9.
- [21] Katherine M, Putnam MA (by invitation), Philip D, Harvey Ph.D, Michael Davidson MD, Grant Ko MD, et al. neuroleptic-discontinuation variables as predictors of treatment response in chronic schizophrenic patients. *Biol Psychiatry* 1990;27:41A-179A.
- [22] Stangl D, Pfohl B, Zimmerman M, Coryell W, Corenthal C. The Relationship between Age and A Test of Three Post-Dexamethasone Cortisol: Hypotheses. *J Affect Disord* 1986; 11: 185-197
- [23] Nelson WH, Orr Jr WW, Shane SR, Stevenson JM. Hypothalamic-pituitary-adrenal axis activity and age in major depression. *J Clin Psychiatry* 1984 ;45 :120–121
- [24] Berna F. La mémoire autobiographique et le self dans la schizophrénie. PhD in science. Strasbourg : Strasbourg University, 2010, 411p.
- [25] Lysaker PH. Signification clinique et psychosociale d'une histoire de trauma chez les patients souffrant d'un trouble du spectre de la schizophrénie. 2009. [in line]. In: International Society for Psychologic Treatments of Schizophrenias and other psychoses : <http://www.google.fr/url?url=http://www.isps-ch.org/fr/archives/congres/2007/textes%2520conferences/Lysaker%2520-%2520Signification%2520clinique%2520et%2520psychosociale.pdf&rct=j&frm=1&q=&esrc=s&sa=U&ei=g5NzVKiCBtPTaKa6gKgO&ved=0CBQQFjAA&usg=AFQjCNHE51AdwaHgeY5hHMF3SS33AMbKFw>. (Page accessed on 8/11/2014)
- [26] Rector NA. La thérapie cognitivo-comportementale « Guide d'information ». Canada : Centre de toxicomanie et de santé mentale ; 2010.
- [27] Franck N, Thibaut F. Pharmacologie et mode d'action des neuroleptiques. *EMC-Psychiatrie* 2005 ; 2 : 282–299
- [28] Kahn R, Davidson M, Siever L, Sevey S, Davis K. Clozapine treatment and its effects on neuroendocrine responses induced by the serotonin agonist m-chlorophenylpiperazine. *Biol Psychiatry* 2002;26:935-8.