Clin Schizophr Relat Psychoses
Volume 18:S1, 2024
DOI: 10.3371/CSRP.AMOS.100004

Clinical Schizophrenia & Related Psychoses

Mini-Review Open Access

Cortisol and High-Risk People for Schizophrenia: A Mini Review

Brofman-Epelbaum Jacobo Jose*

School of Pedagogy and Psychology, Pan American University. Alvaro del Portillo, Zapopan, Jalisco, 45010, Mexico.

Abstract

Schizophrenia is a psychiatric disorder characterized by neurocognitive symptoms and a generalized sensitivity to stress due to a neurodevelopment predisposition to this condition. We review some difficulties studying the relationship between subjacent vulnerability and stress response. These are mainly delimited to the selection of the samples and the scientific community's different conceptions of the clinical symptoms. With some of our work, we hold that the neurocognitive performance interacts positively with the allostatic load, mainly in the genetic high-risk group.

Keywords: Genetic high-risk • Schizophrenia • Cortisol levels • Stress • Vulnerability

Introduction

According to the Diagnostic and Statistical Manual of Mental Disorders in its 5th revisited edition (DSM-5-TR, 2022) of the American Psychiatric Association (APA), schizophrenia is considered a heterogeneous mental disorder. This is because professionals in the field assume that this disease "involves a range of cognitive, behavioural and emotional dysfunctions, but no single symptom is pathognomonic of the disorder. Thus, individuals with the disorder will vary substantially on most features". Adding up, criterion B for schizophrenia states: "For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved before the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning" (DSM-5-TR, 2022).

This means, on the one hand that patient's symptoms could be very different from each other and, on the other, that at some level, the patient behaves, feels and thinks differently than expected before the appearance of the first psychotic episode. This is considered the prodromal phase and its duration differs from person to person.

As it´s understood, there is no explicit consent of what schizophrenia is and its main symptoms or core clinical manifestations. Going further, we also have to consider if there is a fundamental difference between the other disorders that belong in the chapter of schizophrenia spectrum and other psychotic disorders of the DSM-V-TR in biological terms, so we can be sure they are different entities or their diagnosis depends on symptom severity, time of duration and to the domain of psychopathology as it is conceived today, making the differential diagnosis blur.

Its marked etiological heterogeneity indicates that schizophrenia is a disease with numerous and varied primary pathophysiological mechanisms that ultimately affect brain function. In the absence of focal anatomical lesions or well-defined hypotheses, the biological mechanisms of schizophrenia have been challenging to define.

Literature Review

In the pursuit to understand the etiology of schizophrenia, many studies found several familial genetic risks and various specific environmental factors during the antenatal and perinatal periods, early and late childhood, adolescence and early adulthood that have been implicated in the onset of the disorder [1]. However, since the proposal of the "Diathesis-Stress" for schizophrenia as an etiological model, which conceives schizophrenia as the result of brain abnormalities in neurodevelopment and the effects of stressors on this diathesis, studies have focused on trying to identify if whether these factors act together with genetic susceptibility independently (addition) or interactively (synergy) in which the effect of one factor is conditional on the other. The importance of studying this relationship is because it has been stated that the atypical stress response or the Hypothalamic-Pituitary-Adrenal (HPA) axis malfunction in these patients, mainly measured by cortisol levels, has been implicated in the presentation and exacerbation of the schizophrenic symptoms, the cognitive deficits and the neurotransmission failure [2].

Various studies have shown that it is likely that a person will suffer from schizophrenia if other members of his or her family are affected and that the probability of suffering from this disorder correlates with the proximity of these family relationships [3]. However, even today, it is not known how genetic predisposition is transmitted and it cannot be predicted whether or not a particular person will develop the disease. Highlighting the importance of studying high-risk groups for schizophrenia before the onset of the disease.

Hence, another problem emerged: Do clinical high-risk (people who manifest clinical symptoms but don't necessarily have a relative with the illness) and genetic high-risk (people who necessarily have at least one relative with the disease) for schizophrenia be considered similar or perhaps they belong to different clinical entities? Recently, we published an article showing some sampling biases based on empirical evidence that result from the indiscriminate inclusion of individuals at risk, both clinical and genetic and of related disorders-schizotypal or schizoid personalities and bipolar or schizoaffective disorders- in one investigation [4].

***Corresponding Author:** Brofman-Epelbaum Jacobo Jose, School of Pedagogy and Psychology, Pan American University. Alvaro del Portillo, Zapopan, Jalisco, 45010, Mexico. E-mail: jbrofman@up.edu.mx*

***Copyright:** © 2024 Jose BEJ. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.*

Received: 03-Sep-2024, Manuscript No. CSRP-24-147161; **Editor assigned:** 05-Sep-2024, PreQC No. CSRP-24-147161 (PQ); **Reviewed:** 20-Sep-2024, QC No CSRP-24-147161; **Revised:** 27-Sep-2024, Manuscript No. CSRP-24-147161 (R); **Published:** 04-Oct-2024, DOI: 10.3371/CSRP.AMOS.100004

Some of these biases are seen in studies concerning cortisol levels in high-risk populations. Many studies have found higher Cortisol Awakening Response (CAR) or basal dairy cortisol levels and blunted cortisol response to stress events in patients with schizophrenia and high-risk populations compared to healthy controls [5]. However, other authors have found no such difference, suggesting that cortisol response is heterogeneous among the schizophrenia spectrum [6]. On the other hand, some authors state that this may not be the case and the lack of sample standardization and various methodological procedures influencing the interpretation and generalization of this relationship [7]

To better understand the relationship between cortisol response during a stressful event and high risk of schizophrenia, avoiding this bias, we conducted a study considering only people with no psychiatric diagnosis being a first-degree relative (sibling) of a family member diagnosed with schizophrenia with another family member having a psychiatric diagnosis belonging to the schizophrenic spectrum, to guarantee high familial loading. We recruited a total of 36 participants divided into two groups. The first group consisted of 18 male individuals at genetic risk for schizophrenia and the second group involved 18 male individuals with no familiar history of psychiatric diagnosis.

Participants were evaluated in two different circumstances during two morning sessions:

- An induced mild hypoglycaemia condition, which consisted of an 18-hours fasting period beginning at 16:00 hours the previous day.
- After regular breakfast. During each session, all the participants performed three N-back tasks.

The experimental pattern consisted of three working memory tasks with varying cognitive load: 0-back, 1-back and 2-back. Each task consisted of 200 trials of pseudo-randomly presented male and female faces containing different emotional expressions on a black background. 30% of the total stimuli were targets (n=60) and 70% non-targets (n=140). Visual stimuli were presented during 500 ms, with an Interstimulus Interval (ISI) of 1500 ms. Eighteen colour photographs (16 cm × 13 cm) of young model faces, 6 with a neutral expression (3 males), 6 with a happy expression (3 males) and six angry faces (3 males) were used as visual stimuli. The cognitive load was also counter balanced between the participants (Figure 1).

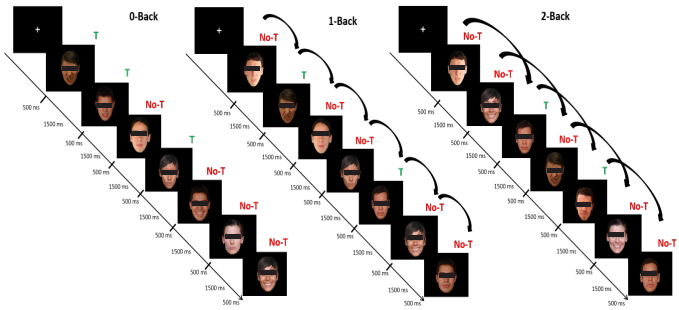

Figure 1. Schematic representation of the N-back tasks.

We measured blood glucose in the fasting and non-fasting conditions. We also took salivary cortisol samples in three moments: one after breakfast intake, one under the hypoglycaemic condition and one after performing the 2-back task. They all signed informed, voluntary participation consent before the experimental sessions.

Our results showed that a metabolic stressful event affects people with a high genetic risk of schizophrenia mediated by cortisol functioning, supporting the notion that the allostatic load contributes to cognitive impairments in this population [8,9].

Discussion

From our perspective, our study represents a further step in understanding how physiological stress and cognitive demands may act interactively (synergistically) in the preclinical context of individuals at genetic risk for schizophrenia, probably influencing the subsequent appearance and worsening of the schizophrenic symptoms when they appear. As the allostatic load increases, we may expect worse cognitive functioning, especially in tasks that require working memory capacity. However, we still need to study how and why these processes manifest the way they do, but now we have a delimited phenotypic expression and we can focus on determining the genotypic trait. Results need to be clearly and directly stated in the clinical high-risk population, as shown in the existing literature.

Conclusion

We acknowledge that achieving big homogeneous samples requires a lot of effort and sometimes, it could take a long time to gather. In our study, we managed to recruit 18 participants and we may need a bigger sample to gain statistical power, but from a clinical and epistemological point of view, the inclusion criteria of the population to be studied will determine to a large extent, the generalization of the results.

Acknowledgement

I would like to express my deepest appreciation and gratitude to professor Andres Antonio Gonzalez Garrido and professor Fabiola Reveca Gomez Velazquez from the Institute of Neuroscience, University of Guadalajara, Mexico, for their support and guidance in making of this investigation.

Conflict of Interest

All authors disclose no actual or potential conflicts of interest, including any financial, personal or other relationships with other people or organizations that could inappropriately influence (bias) their work.

References

1. Walker, F Elaine and Donald Diforio. “Schizophrenia: A Neural Diathesis-Stress Model”. *Psychol Rev* (1997): 667-685
2. Pruessner, Marita, Alexis Cullen, Monica Aas and Elaine Walker. “The Neural Diathesis-Stress Model of Schizophrenia Revisited: An Update on Recent Findings Considering Illness Stage and Neurobiological and Methodological Complexities”. *Neurosci Biobehav Rev* (2017): 191–218.
3. Chou, Jun I, Chang-Fu Kuo, Yu-Shu Huang and Matthew Grainge et al. “Familial Aggregation and Heritability of Schizophrenia and Co-Aggregation of Psychiatric Illnesses in Affected Families”. *Schizophrenia Bulletin* (2017): 1070–1078.
4. Jose, Brofman-Epelbaum Jacobo, Andres Antonio Gonzalez-Garrido and Fabiola Reveca Gomez-Velazquez. “Sampling Bias and its Implications in the Evaluation of the Population with Genetic Risk for Schizophrenia”. *Psiquiatria Biologica* (2020): 34-39.
5. Coulon, Nathalie, Sylvie Brailly-Tabard, Michel Walter and Sylvie Tordjman. “Altered Circadian Patterns of Salivary Cortisol in Individuals with Schizophrenia: A Critical Literature Review”. *J Physiol Paris* (2016): 439–447.
6. Lange, Claudia, Lorenz Deutschenbaur, Stefan Borgwardt and Undine Lang. “Experimentally Induced Psychosocial Stress in Schizophrenia Spectrum Disorders: A Systematic Review”. *In Schizophrenia Research* (2017): 4–12.
7. Dauvermann, Maria and Gary Donohoe. “Cortisol Stress Response in Psychosis from the High-Risk to the Chronic Stage: A Systematic Review”. *Ir J Psychol Med* (2019): 305–315.
8. Jose, Brofman-Epelbaum Jacobo, Andres Antonio Gonzalez-Garrido and

Fabiola Reveca Gomez-Velazquez. "Cortisol Response in Individuals with Genetic Risk of Schizophrenia. Some Considerations". *Schizophr Res* (2024): 56–57

9. Cullen, Alexis, Patricia Zunszain, Hannah Dickson and Ruth E Roberts. "Cortisol Awakening Response and Diurnal Cortisol among Children at Elevated Risk for Schizophrenia: Relationship to Psychosocial Stress and Cognition". *Psychoneuroendocrinology* (2014): 1–13.

How to cite this article: Jose, Brofman-Epelbaum Jacobo,"Cortisol and High-Risk People for Schizophrenia: A Mini Review." *Clin Schizophr Relat Psychoses* 18 (2024). DOI: 10.3371/CSRP.AMOS.100004