



Neurobiology of Schizophrenia: an Integrative Review

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Abstract

Psychological diseases are gaining more and more space in the medical field, being considered by some studios the evil of the century, as more and more people are affected worldwide. Among these diseases we have schizophrenia, which consists of a mental condition that modifies the perception of reality of the individual, impairing his memory and development of basic activities that require concentration and memorization. Because it develops mainly between adolescence and adulthood, without a defined cause, many studies and tests have been conducted for decades in order to find out the precise causes of such disorders, since only with an accurate diagnosis

can effective treatment be determined. From this perspective, this article aims to conduct a survey and discussion of the theoretical material already existing regarding the neurobiology of a schizophrenic in order to understand its mental disorders. Although research indicates which region of the brain, when affected, can cause disturbances there is no accuracy as to how the process occurs, it was also possible to notice little evolution in studies, and lack of accuracy of the causes of the changes neurobiologicals which result in disorders.

INTRODUCTION

Studies on psychiatric diseases and their possible neurotransmitters began in the 1950s. However, only at the end of the century there were considerable advances, since the emergence of neuroimaging techniques allowed the evaluation of neurostructural, chemical and functional alterations, being of fundamental importance not only for the diagnosis of schizophrenia, but also in the monitoring and identification of patients at high risk of developing schizophre-

nia (ARARIPE NETO, BRESSAN and BUSATTO FILHO, 2007).

Schizophrenia and the so-called schizophrenic disorders constitute a group of severe mental disorders characterized by distortions of thought and perception, inadequacy and blunting of affect without impairing intellectual capacity (BRASIL, 2013).

Until then, it is not possible to know the exact cause of such disorders, however, genetic, environmental factors, brain and biochemical alterations seem to influence the appearance and/or evolution of the disease in a variable way. Recent studies show that the brain of schizophrenic patients has structural and physiological abnormalities; however, the disease commonly manifests itself during adolescence, making it difficult to find the cause of these changes (ALVES and SILVA, 2001).

Schizophrenic patients have difficulty in activities that require attention, memorization and / or long durability, and are unable to solve problems easily, even with the normal intelligence quotient. These are the main reasons why they cannot interact with the en-

vironment in which they live naturally (COSTA and MACHADO, 2012).

Schizophrenics present generalized cognitive deficit, which consists in impairment in the performance of activities that requires, for example, concentration, logical reasoning, among others; at lower levels than those of healthy people. Schizophrenia sufferers “have multiple neuropsychological deficits in tests of complex conceptual thinking, psychomotor speed, new and incidental learning memory, and motor, sensory, and perceptual skills” (SILVA, 2006, p. 266).

Although many studies addressing psychological disorders are found, especially on schizophrenia, the specific causes of these disorders are still largely unknown. Aiming to contribute to the existing collection, systematizing the information and comparing works of different researchers, this article aims to conduct a survey and discussion of existing theoretical material about the neurobiology of a schizophrenic, in order to understand the causes of your mental disorders.

METODOLOGY

As a methodological framework, it was decided to develop an integrative review, based on the survey of scientific articles available in the literature, which consists of a careful research and analysis of studies on the neurobiology of schizophrenia. To facilitate understanding of the relevance of this strategy as a facilitating practice in the training process, sought to guide the research through the following problem: how is neurobiology different in a schizophrenic patient? The possible factors that cause these structural abnormalities were also considered.

“Integrative review is a method that provides the synthesis of knowledge and incorporation of the applicability of results of significant studies in practice” (SOUZA, SILVA and CARVALHO, 2010). Thus, it is possible to make a selection of studies relevant to the research area, comparing them and discussing critically.

The execution plan, to select the bibliographic survey, was made through research of scientific articles, by consulting the following

databases: Scientific Electronic Library Online (SCIELO), Web of Science and Medical Publications (PUBMED). Used as search criteria the articles published in the last twelve years, using as descriptors the English terms: “Neurobiology” and “Schizophrenia” with the use of the boolean operator “AND”. The terms were searched in quotation marks so that the results retrieved the terms in the exact expressions.

After reading the articles, those who did not have access to the free full text were excluded, as well as articles with serious flaws in the methodological description that compromised the understanding and use of the data. Were also disregarded the productions presented in the form of letter to the editor, communication, abstract, monograph, dissertation or thesis.

As inclusion criteria, were considered only articles in the health area that addressed the possible neurobiological causes of schizophrenia, published in the English language and produced in the period from 2007 to 2019. Thus, after analyzing the data, were selected for the present research, among the

22 (twenty-two) found, 09 (nine) scientific articles, which were widely discussed.

RESULTS AND DISCUSSION

The following table (Table 01) shows the works selected for discussion of this article, including author, year of publication and title.

Author (s)	Year of publication	Title
Anticevic, Repovc e Barch	2011	Working Memory Encoding and Maintenance Deficits in Schizophrenia: Neural Evidence for Activation and Deactivation Abnormalities
Datta e Arnsten	2018	Unique Molecular Regulation of Higher-Order Prefrontal Cortical Circuits: Insights into the Neurobiology of Schizophrenia
Ruby et al.	2014	Pathways Associating Childhood Trauma to the Neurobiology of Schizophrenia
Lee et al.	2008	Origins of Spatial Working Memory Deficits in Schizophrenia: An Event-Related fMRI and Near-Infrared Spectroscopy Study
Howes, McCutcheon e Stone	2015	Glutamate and dopamine in schizophrenia: an update for the 21 st century
Kimoto, Makinodan e Kishimoto	2019	Neurobiology and treatment of social cognition in schizophrenia: Bridging thebed-benchgap
Nucifora Jr.	2019	Treatment resistant schizophrenia: Clinical, biological, and therapeutic perspectives
Dienel e Lewis	2019	Alterations in cortical interneurons and cognitive function in schizophrenia
Woo	2014	Neurobiology of Schizophrenia Onset

Table 01: Articles pertinent to the research/ Source: Research data.

Kimoto, Makinodan and Kishimoto (2019) state that impaired social cognition of schizophrenics remains unknown in neurobiology and, therefore, treatments are limited and inefficient in most cases. Social cognition consists of the psychological processes of perception,

codification, storage, retrieval and regulation of information about oneself and others, being essential for survival in the social environment.

Nucifora Jr. (2019) notes that patients with schizophrenia respond differently to various types of treatment, such as drug combinations, electroconvulsive therapy, repetitive transcranial magnetic stimulation, deep brain stimulation and psychotherapies; this is because the clinical, neuroimaging and neurobiological characteristics are wide and variable.

Working memory is a central deficit in schizophrenic patients. Anticevic, Repovs and Barch (2011) attested that these abnormalities come from prefrontal recruitment during the development of daily activities common to healthy individuals. The authors also found deactivation abnormalities, possibly due to inefficient prefrontal recruitment. Lee et. al (2008), years earlier, claimed that “abnormal prefrontal functioning plays a central role in working memory deficits of schizophrenic pa-

tients, but the nature of the relationship between working memory and prefrontal activation remains undetermined.”

In their researches, Lee et. al (2008) found that while healthy individuals recruit right frontal regions during spatial maintenance of working memory, schizophrenic individuals recruit a broader network in both hemispheres of the brain to achieve the same level of memory performance, being able to generate false memories.

In full agreement with the other authors cited, Dienel and Lewis (2019) state that working memory disorders in schizophrenic patients seem to emerge more specifically from altered gamma oscillatory activity in the prefrontal cortex; in view of the essential role of GABA neurotransmission in both memory working memory and gamma oscillations.

More specifically, Datta and Arnsten (2018) state that schizophrenia is associated with selective atrophy of pyramidal cell microcircuits in the deep layer of the newly evolved dor-

solateral prefrontal and compensatory weakening of related GABAergic interneurons. Given that glutamate actions are dependent on cholinergic stimulation and there are inherent mechanisms to weaken connectivity, such as cyclic adenosine monophosphate signaling and neuronal firing, which open nearby potassium channels, impairing the functioning of the cortex of the newly evolved prefrontal and causing central deficits in cognitive skills.

Considering that “the clinical symptoms and cognitive and functional deficits of schizophrenia usually begin to emerge gradually during late adolescence and early adulthood” (WOO, 2014, p. 267), stress is identified as a potential cause of the neurobiological disorders that result in mental disorders such as schizophrenia. Ruby et. al. (2014) state that traumatic experiences during childhood are risk factors for the development of psychotic disorders, including schizophrenia.

For Woo (2014) stress may contribute to the functio-

nal impairment of photovoltaic neurons, leading to inadequate development of pyramidal cell circuits during adolescence in the prefrontal cortex, which directly leads to excessive synapse loss contributing to the onset of schizophrenia.

Howes, McCutcheon and Stone (2015) point out that there are still many gaps in existing knowledge about the possible causes of mental disorders such as schizophrenia, requiring not only neurobiological knowledge, but knowing the cause of these changes also contributes to an accurate diagnosis which is of paramount importance for applying effective treatment.

In summary, all the authors presented in Table 01 argue in their respective works that patients with schizophrenia suffer mainly from memory disorders, which may alter reality, provoke false memories, impair coexistence in society, as well as the ability to perceive of reality, attention, among others, and that these are caused abnormalities in the frontal hemisphere of the brain. Woo (2014) and Ruby

(2014) go further, questioning the cause of these abnormalities, which, according to them, may be reflections of the environment.

Although there is evolution in the studies, when considering the dates of the publications, it is possible to realize that some productions occur independently, without consulting the existing collection. For even with the publications of Antevic, Repovs, and Barch; Datta Arnsten; and Dienel and Lewis in 2011, 2018 and 2019 respectively, who researched, more specifically, what occurs in the prefrontal region that causes the symptoms; Kimoto (2019) claims that there are few neurobiological studies related to schizophrenia.

It is noteworthy that the in-depth search for existing studies on the subject, allows the researcher to continue a study or research, on top of what has already been discovered. Thus, it is noted the importance of bibliographic survey before the development of tests. Considering that all the authors agree with the region where the symptoms of the

disease develop and the possible causes of these abnormalities, it is extremely important that the next researches pay attention to the fact of how the psychoses occur.

CONCLUSIONS

From what has been presented, it is noted that existing studies and research show that mental disorders in schizophrenic patients are caused abnormalities in the frontal globule of the brain; however, most authors are unable to specify exactly what these abnormalities are and why the disorders occur at different degrees of intensity between patients.

In addition, was also noted that the treatments are not yet effective. Thus, the importance of developing studies and research aimed at understanding the causes of the disorders is emphasized, in order to improve the diagnosis and consequently contribute to obtain more effective treatments.

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