

Hormonal relationship in the chronic development of schizophrenia spectrum and other psychotic disorders in adolescent patients: Literature update

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Relación hormonal en el desarrollo crónico del espectro esquizofrénico y otros trastornos psicóticos en pacientes adolescentes: Actualización de la literatura

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Abstract

Adolescence is established as an important stage in the human being, we try to show how positive or negative this stage can be in the development of an adequate environment, elucidating the benefits or consequences that can affect the psychomotor development of a person. Adolescence is the time when the personality of an individual is defined, influenced by various factors that can help the subject to develop adequately in society, as well as factors that can affect the subject conditioning him/her to an environment that is not favorable for his/her development. Both physical and psychological changes are mentioned, as well as hormonal factors which play an important role in development. It is intended to demonstrate the hormonal mechanisms that condition the changes in the development of the human being.

KEY WORDS

Adolescence, Hormones, Estradiol, Gonads.

Resumen

Se establece la adolescencia como una etapa importante en el ser humano, se intenta dar a conocer lo positivo o negativo que puede ser esta etapa en el desarrollo de un entorno adecuado, dando a dilucidar los beneficios o consecuencias que pueden afectar el desarrollo psicomotor en una persona. En la adolescencia es donde se define la personalidad de un individuo, influyen diversos factores que pueden ayudar a que el sujeto se desarrolle adecuadamente en la sociedad, así como factores que pueden afectar al sujeto condicionándolo a un entorno no favorable para el desarrollo de este. Se mencionan los cambios tanto físicos como psicológicos, así como factores hormonales los cuales juegan un papel importante en el desarrollo. Se pretende evidenciar los mecanismos hormonales que condicionan los cambios en el desarrollo del ser humano.

PALABRAS CLAVE

Adolescente, Hormonas, Estradiol, Gónadas.

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Introducción

Adolescence is a time of significant hormonal, physical and social changes and a major risk factor for the development of psychopathology, especially in females.¹ It is substantiated that adolescence is characterized by dramatic changes in behavior and emotional disturbances; increasing support has been obtained from empirical research showing that the peripubertal and postpubertal stages of development are associated with an increase in the rate of psychiatric symptoms and syndromes, which confer an important characteristic of severity and gradual weakness, where schizophrenia stands out along with other disorders (e.g., schizoaffective disorders and schizoaffective disorders), schizoaffective disorders and mood disorders with psychotic features).² The adolescent, in striving for autonomy and individuation, demonstrates an increase in neuroendocrine and cardiovascular reactivity to stressful stimuli from the extrinsic environment, causing an excitation of the subcortical region constantly in the face of social stress.³ A review of the literature was carried out, with the aim of filtering and analyzing the information concerning the hormonal relationship in the chronic development of schizophrenia spectrum and other psychotic disorders in adolescence.

Adolescence

Adolescent age is a decisive factor in human development, represented by the age of 10 to 19 years, which, according to research, is characterized by a stage of high neuroplasticity, positive maturation of the emotional areas of the brain and maturity in social reorientation.⁴ Because of this it is not surprising that the networks that bind adolescents together are purely of similarities in different aspects such as behavior, culture, values, beliefs and introspective thoughts.⁵ Thus, they will be challenged to develop a range of psychosocial skills that is complex for their age, that being regulating the range of their emotions and behaviors, interacting with and caring for others.⁶ For adolescents, learning to balance being themselves and at the same time, managing to fit in with a social group in their environment, is challenging and at the time, necessary, given that it is at this stage where a unique identity is established that coincides with the human desire to belong to a group and form a bond with it.⁷

By the year 2050, the total number of adolescents with mental health problems is expected to increase to 45 million, which is why an application of recognition of the factors that can contribute to improving health outcomes in this age group is needed. It is important to note that this growing number of adolescents with psychotic disorders represents an economic and social burden. The annual cost of treating childhood mental health disorders is estimated at \$237 billion.⁸ Suicide as a risk factor is interpreted as one of the leading causes of deaths in patients under the age of 14 years. This tells us that there is a problem for public health in Mexico, since the suicidal urge is predisposed to increase at an age between 11 and 17 years in males and between 15 and 16 years in females.⁹

Theories of adolescence and psychotic disorders

Adolescence is the target of examination in the psychiatric field, since it is during this phase that several of these disorders tend to be exacerbated. The exacerbation can take place ethologically in different ways, as it is known, this is a stage of great vulnerability to stressful stimuli and this makes it easier for the psychotic disorder to unmask itself and thus be able to perform a valuable early detection and intervention.¹⁰

As important factors in the development of psychotic disorders, heavy internet use is recognized, since it can induce social isolation, depression, and suicidal ideation.¹¹ Currently, depressive symptoms become a threat to the mental

health of adolescents, where emotional regulation is a process of modifying emotional reactions.¹²

Sleep disorders often accompany depression, since 75% of adolescents suffering from depression also suffer from this conditioning circadian cycle disturbance, and it is during adolescence that the first changes in sleep patterns are likely to emerge.¹³ Borderline personality disorder is considered a spectrum in which the personality resides as a pathology and which can manifest itself in a heightened form during the period of adolescence, since it is from here that a “borderline” can happen resulting from the detonation of the personality, orbiting the adolescent to be a risk target for his or her educational, social or work life.¹⁴ On the other hand, it is estimated that “perfectionism” leads to 25-30% of adolescents being negatively affected, which is a risk factor for the consequent development of anxiety, depression and suicidal ideation, given that it is based on the aspiration for success in early areas of life.¹⁵

The adolescent goes through a period of storm and stress, whose physicochemical changes occur at the encephalic level from the early stage, thus resulting in a hormonal and neuronal imbalance where emotionality is the starting point that will cause a hyper-response to all those stressful stimuli, whether real or superficially perceived, since the emotional self-regulation system will have its participation adequately until entering the first stage of adulthood. The sum of increased interpersonal stress, poor self-regulation and emotional hyperreactivity, serve as risk factors in the development of psychopathology.¹⁶

The musculoskeletal, reproductive and neurodevelopmental systems begin to transform into those of an adult, and the changes reflected physically will also be reflected hormonally in behavior.¹⁷

Psychotic disorders

Psychotic disorders are a spectral range constituted by a set of other psychotic disorders, such as schizophrenia and schizotypal disorder, manifesting in abnormalities in one or more of the following five items: delirium, hallucination, disorganized thinking, motor behavior and negative symptom, originating in turn, different subtypes that unfold in the form of a single entity.¹⁸ The incidence of non-affective psychotic disorders is altered according to certain factors such as sociodemographic, geographic and type of neighborhood where the person interacts. In addition, it is estimated that neighborhoods with increasing levels of social disorganization have higher levels of schizophrenia.¹⁹

Delusions consist of false beliefs that are irrevocably maintained in spite of possessing credible evidence contradictory to what was initially stated, thus keeping the belief firm. Within delusions there will be two characteristics that will be determinant: high subjective certainty and rigidity of beliefs.²⁰

Hallucinations, on the other hand, are constituents of 60-80% of those patients who are diagnosed with a schizophrenia spectrum disorder. It is characterized by hearing different sounds during this period in which the hallucination occurs, causing irritability, increased anxiety levels, leading to depression and/or social isolation.²¹

Disorganized thoughts are usually inferred from the speech given by an individual, characterized by jumping from one topic to another, somehow derailing the associations, where the answers may be related to the initial question or not related at all.²²

Negative symptoms are those that result from the expression of deficiencies in the interpretation of reality as it is known, being an inclusive complex of cognitive dysfunctions. Negative symptoms harbor aspects such as abulia, psychomotor disorder, dulled affect and, in addition, are persistent and have a poor prognosis.²³

This makes it clear that education and knowledge on the subject would help in early detection during adolescence and thus have a better prognosis for patients.²⁴

The influence of hormones on the spectrum of schizophrenia and other psychotic disorders in adolescence

Adolescence is a well-established risk factor for major depressive disorder in females. Increases in hormones produced by the Hypothalamic-Pituitary-Adrenal Axis (HPA) and the Hypothalamic-Pituitary-Gonadal (HPG) Axis have been identified as drivers of the physical, emotional, and cognitive changes associated with the adolescent stage.¹

Estradiol

Estradiol acts on the neural circuits of the Limbic System and prefrontal cortexes of the adolescent brain, driving most of the physical, cognitive, and emotional changes typical of this stage. In one study, estradiol was associated with externalizing psychopathology, but only when Cortisol levels were low and personality traits of emotional unpleasantness and instability were high, suggesting an important dual hormonal regulation of the Estradiol-Psychopathology association. These dual hormonal associations are derived from the rationale proposed by the dual hormone hypothesis, which demonstrated that Testosterone promotes status seeking, but only in the presence of low Cortisol levels.¹

Based on these ideas, we propose that the association between Estradiol and mental health among females during adolescence is, in part, moderated by the adolescent's perception of her pubertal timing, such that an adolescent who believes herself to be puberally "outdated" relative to her peers will be at elevated risk for mood disorders when Estradiol levels that have been associated with increased social awareness are high.

Hormones of the gonads

The basolateral amygdala is intimately involved in the progression of psychiatric disorders. These disorders sustain notable sexual commitments, being the female gender the most subject to form an anxiety disorder. As for the pituitary gland, it controls a variety of functions of the human body, such as growth, maturation, coping and daily rhythm, therefore, it is considered, the most important endocrine gland.²⁵

Hormonal changes may play an important role in the "acute risk of daily suicidal ideation, planning, and intent" in individuals with sensitivity to hormonal changes. Research has reported that an increased risk of suicide attempts and more severe suicidal thoughts and intentions are associated with relatively low levels of Estradiol and Progesterone (i.e., during the follicular/menstrual or early premenstrual phases).²⁶

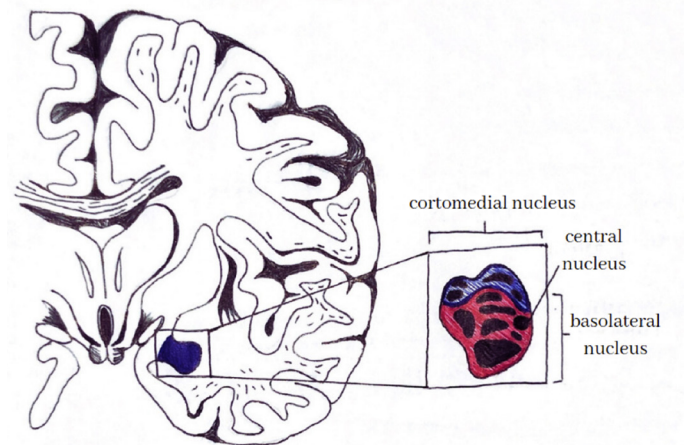
Thyroid hormones

Mental symptoms such as anxiety, dysphoria, irritability, emotional lability, sleep disorders, intellectual dysfunction, mania or depression are some of the manifestations of hyperthyroidism. Anxiety is the main symptom and requires further study. The prevalence of anxiety in patients with hyperthyroidism is suggestively more frequent compared to euthyroid patients.²⁷

Tetrahydrodeoxycorticosterone is a neuroactive steroid that regulates the action of the Central Nervous System by means of rapid activities, of which it has become visible that there is an increase in its level in Major Depressive Disorder.²⁸

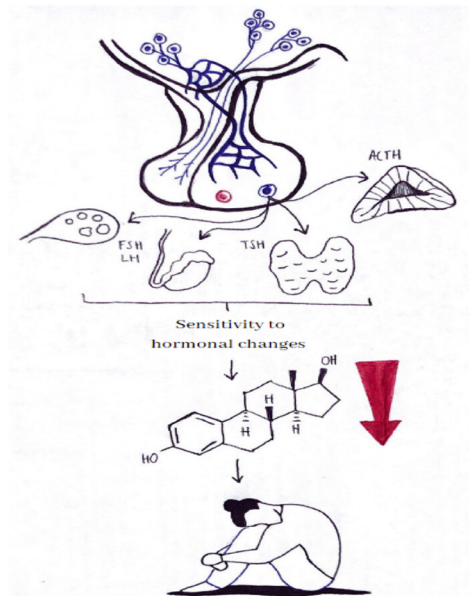
Proven studies have been published in researches that speak about the Hypothalamic-Pituitary-Thyroid Axis, which is the protagonist in the regulation

Figure 1
Basolateral amygdala



Source: Own elaboration.

Figure 2
Gonadal Hormones



Source: Own elaboration.

of the individual's behavior.²⁹ It was hypothesized that adolescents with mood problems are predisposed and sensitive to pathological changes in thyroid tissue, even when thyroid hormone levels (T3 and T4) are within normal parameters.³⁰

Studies have shown how thyroid hormones are involved in brain developmental events, such as neurogenesis, axon and dendrite growth, and astrocyte proliferation and differentiation.³¹ Thyroid hormones are important for the modulation of Dopaminergic, Serotonergic, Glutamatergic and GABAergic networks. It has been documented that clinically significant hyperthyroidism may manifest in patients with psychotic symptoms, whereas, hypothyroidism does so by referring to mood symptoms resembling the negative symptoms of schizophrenia. The development of implausible endocrine abnormalities is associated with individual-level risk factors. However, some of them, such as hyperprolactinemia and insulin resistance, may appear in early psychosis and may be related to intrinsic pathophysiological mechanisms.³²

Adrenal Hormones

In addition to cardiovascular disease, people with schizophrenia tend to develop various endocrine abnormalities related to Hypothalamic-Pituitary-Adrenal Axis (HPA) dysfunction, release of neurosteroids and appetite-regulating hormones, as well as hyperprolactinemia.³² Studies have shown that, when exposed to a traumatic event in childhood, there may be an increased disposition to psychotic disorders. In fact, if a person has a history of stressful episodes, it may stimulate an increase in the hypothalamic-pituitary-adrenal axis.³³ Even though studies with the correlation of adrenal hormones and mental health were not conducted in the past, they are now beginning to play a prominent role in conceptualizations of adolescent brain development, as well as the onset of psychiatric symptoms during this period.²

Discussion

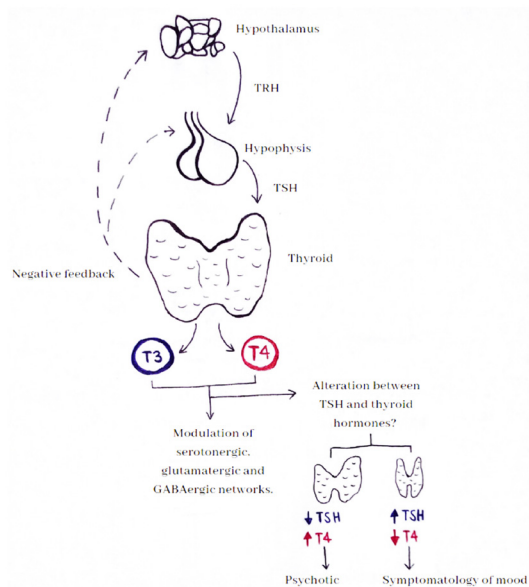
The development of emotions has predominance in adolescence, in which hormonal, physical and social changes interact; being able to be altered, a risk factor for exacerbating psychopathologies would be obtained since adolescence is a stage of great vulnerability to stress stimuli and this favors suffering from a psychotic disorder.

At present, the knowledge we have regarding the relationship of hormones in schizophrenia and psychosis disorders in adolescence is limited and more studies are required to demonstrate the propitious effect of the aforementioned influence in order to mitigate them at an early stage of life and to benefit them with an optimal treatment.

Conclusion

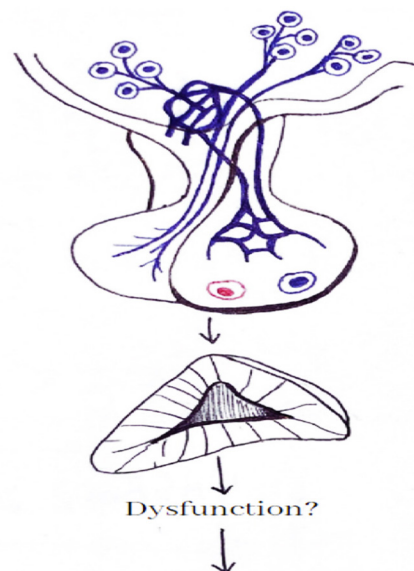
Adolescence is a substantial period of transition in the life of the human being, it is a stage of the growth cycle that marks the end of childhood and the beginning of adulthood, which can become a stage of perplexity and even despair when it is involved in specific health problems; as in this case, in the progression of psychotic disorders such as schizophrenia. It is recognized that in such disorders the interaction of different hormones in the human body interferes. It is necessary to continue with this archetype of research that investigates this interaction and to extend the knowledge of this argument.

Figure 3
Thyroid hormones



Source: Own elaboration.

Figure 4
Adrenal hormones



Alteration in: release of neurosteroids and appetite regulating hormones.

Source: Own elaboration.

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Conflicts of interest

The authors declare no conflicts of interest.

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