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Trauma, posttraumatic stress disorder and psychosis: Etiopathogenic and nosological implications

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ABSTRACT – Background and Objectives: The relationship between trauma, post-traumatic stress disorder (PTSD), and psychosis has promoted heterogeneous research lines, in both etiopathogenic and nosological areas. The main aim of this review is to provide a systematic framework that encompasses this theoretical gap in the literature.

Methods: A literature research was carried out through PubMed and PsycINFO between 1980 and May 2013. One hundred and thirteen articles were recruited. A first part of this review describes the role of trauma in the development of psychosis. The second part focuses on research about PTSD and psychosis.

Results: Longitudinal and cross-sectional studies with clinical and community samples confirm that childhood trauma (CT) is a vulnerability factor for schizophrenia and psychotic-like symptoms in adulthood. More empirical research is needed in order to assess the role of trauma as precipitant of acute psychosis. There is also preliminary evidence with cross-sectional samples that suggests that PTSD and psychosis are a risk factor for each other, with studies about post-psychotic PTSD (PP-PTSD) being outstanding. Finally, results from different comparative research studies postulate a subtype of PTSD with psychotic features (PTSD-SP).

Conclusions: The role of trauma in psychosis is more conclusive as predispositional rather than as trigger factor. Nosological status of acute psychoses remains a focus of controversy unresolved. The association between PTSD and psychosis is complex, requiring more prospective research in order to determine causal relationships between these pathologies. Also, research in nosological status of PTSD-SP must encourage more comparative studies not limited to neurobiological variables.

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Introduction

The presence of trauma and post-traumatic stress disorder (PTSD) in subjects with psychotic symptoms has produced a considerable amount of research, both heterogeneous and unconnected in terms of approaches and areas of development, mainly conditioned by the prevailing psychiatric paradigm in every historical period. In this sense, literature specialised in this topic has promoted different etiopathogenic and nosological models in this issue.

Over the two first thirds of twentieth century, research in this issue was solely focused in the role of trauma as a trigger factor for acute psychoses, traditionally called hysterical psychosis (HP) or psychogenic psychosis (PP)¹. However, in the last decade other research lines have been promoted alien to traditional assumptions, with an inclusion of theoretical-clinical aspects not considered before. On the one hand, from an etiopathogenic perspective, many empirical studies have been carried out in relation to the role of childhood trauma (CT) as a predispositional factor for schizophrenia or psychotic-like symptoms in adulthood². On the other hand, concerning the relationship between PTSD and psychosis, the existence of a subgroup of subjects with PTSD with secondary psychotic features (PTSD-SP) has been considered³, as well as other patients with post-psychotic PTSD (PP-PTSD)⁴.

Objectives and method

In this general framework, this theoretical review has the main aim of offering a systematic analysis of the main research lines and empiric evidence available about trauma and

PTSD in subjects with psychosis. With this purpose, a literature research was carried out through PubMed and PsycINFO between 1980 and May 2013. The descriptors used were “*hysterical psychosis*”, “*psychogenic psychosis*”, “*post-traumatic psychosis*”, “*reactive psychosis*”, “*trauma*”, “*childhood trauma*”, “*psychosis*”, “*schizophrenia*” and “*post-traumatic stress disorder*”. One hundred and thirteen articles were recruited, including theoretical, quasi-experimental, and descriptive studies. Studies that included adolescent patients were excluded because of exceeding the scope and main goals of this review. Findings were grouped into two thematic blocks. A first part describes the role of trauma in the development of psychosis, whether as 1) predisposing factor for schizophrenia or positive symptoms in adulthood, or as 2) triggering variable for acute psychosis. On the other hand, the second part focuses on research about PTSD and psychosis, with results being regrouped by considering 1) prevalence data, 2) theories explaining this relationship, and finally 3) nosological status of PTSD-SP.

Role of trauma in the etiopathogenesis of psychoses

– *CT as predisposing factor for schizophrenia or positive symptoms in adulthood*

With regard to the role of CT as a vulnerability factor for psychosis, many cross-sectional and prospective studies agreed in considering that the risk of having schizophrenia or positive symptoms (psychotic-like symptoms) in adulthood is over two-fold to four-fold if the subject has been the victim of some traumatic event in both childhood and adolescence periods^{5,6}. These findings emerged in research studies with 1) clinical samples of chronic psychotic patients, “first episodes”

and ultra-high-risk (UHR) for psychosis⁷⁻¹², 2) general adult population^{13,14}, and 3) cohorts of women that had been sexually assaulted¹⁵. At a comparative level, no more history of CT was found in patients with psychosis when the control group were subjects with another psychiatric pathology (e.g., major depression)². From a dimensional perspective, different community studies obtained a specific association between CT and presence of hallucinations in adulthood¹⁶⁻²¹, particularly if the traumatic events involved sexual abuse²²⁻²⁴.

Additionally, different variables were proposed as possible modifiers in the relationship between CT and psychosis: characteristics of the trauma (frequency and nature), genetic predisposition, gender, and cannabis abuse. As for the traumatic event, many research studies with clinical and community samples claimed that the relationship between these two variables is “dose-dependent”, that is, the relative risk of having a psychosis increases as the frequency of traumatic events is higher in childhood²⁵⁻³¹. Concerning the nature of the traumatic event, there is no consistent data to confirm a higher risk of having psychosis among people that have been victims of a specific type of CT⁶. In this sense, many research studies with community or UHR for psychosis population observed that the relative risk increases in those subjects that had been victims of either sexual abuse^{7,11} or physical abuse^{29,32,33}. With regard to biological predisposition, a study with a sample of twins observed that the probability of having psychotic-like symptoms connected to CT is modulated by a genetic predisposition for depression³⁴. As for the subjects’ gender, a research study with a community sample with control group found higher CT frequency in women (versus men) with first psychotic episodes³³. Finally, concerning substance abuse, there is agreement in point-

ing that people with childhood trauma events are at higher risk for psychosis in adulthood if they use cannabis in their early and/or mid adolescence^{6,35,36}.

With regard to variables mediating the association between CT and psychosis, different explanatory factors have been proposed: dysfunctional cognitive schemas, dissociative mechanisms, high levels of anxiety, and traumagenic neurodevelopment. From cognitive-behavioural models, many studies with community samples found that the presence of a history of CT contributes to the development of negative cognitive schemas about the Self and the others, which predispose to psychotic-like symptoms in adulthood, mainly paranoid delusions^{15,26,28,37,38}. On the other hand, a series of research studies with samples of psychotic patients claimed that the presence of dissociative processes following CT accounts for the emergence of psychotic-like symptoms in adulthood, particularly hallucinations^{15,23,39-41}. Likewise, other studies with clinical and community samples considered that high anxiety partially results in psychotic-like symptoms in subjects with traumatic events in their childhood or adolescence phases^{22,42-44}. Finally, from a biological perspective, a “traumagenic neurodevelopmental model” was proposed, which states that the stress created by CT would cause early impairments in the hypothalamic-pituitary-adrenal (HPA) axis and dopamine regulation, increasing the possibility of having a psychosis⁴⁵⁻⁴⁷. Additionally, a cross-sectional research with neuroimaging highlighted a positive relationship between CT and hippocampal and amygdalar volumes in a sample of first psychotic episodes⁴⁸.

In sum, childhood traumatic events are an unspecific risk factor for psychosis in adulthood, particularly hallucinations. Cannabis abuse and accumulation of traumas increase this probability. At a dimensional level, the

development of negative cognitive schemas and dissociative processes has been associated to the presence of paranoid delusions and hallucinations, respectively.

– *Trauma as a triggering factor for acute psychosis*

With regard to the role of trauma as triggering acute psychosis, there are scarce empirical studies that have assessed this issue in the last fifteen years. Over this period, most of these studies have focused in elucidating the general role of life events rather than traumatic ones as a trigger factor for psychosis. Concerning to this topic, there are preliminary evidences suggesting that psychotic patients have a 3-fold greater risk of life events prior to their onset compared with control groups⁴⁹. Likewise, amongst the few studies aimed to establish the specific role of trauma in the outset of acute psychosis not classified as schizophrenia, one study found that the presence of a intrusive event (e.g., physical assault) was more likely to be associated with an increased risk of psychosis, most commonly in the 3 months pre-onset (34% cases vs 3% controls)⁵⁰.

Overall, this current deficit of studies is due to a lack of agreement in relation to the nosological status of acute psychoses triggered by serious stressors, a fact that is reflected in the relevance given to these clinical entities in current psychiatric nosology. On the one hand, the ICD-10⁵¹ describes a series of “acute and transient psychotic disorders”, which can be or not secondary to stressful situations. As for the DSM-IV-TR⁵², it recognises the existence of the “brief psychotic disorder”, which may be preceded or not by a severe triggering factor, with its presence being equivalent to the “brief reactive psychosis” already defined in the DSM-III-TR⁵³. Both manuals classify this kind of psychotic conditions in the same cluster that

other acute psychoses of a more endogenous nature (e.g., cycloid psychosis), focusing on time or evolutionary criteria for their grouping. This explains that research studies carried out in the last two decades have been mainly aimed at distinguishing this heterogeneous group of acute psychoses from schizophrenia⁵⁴⁻⁵⁶.

In contrast to this current nosological framework, there is some historical background that illustrates and delimits these psychotic disorders triggered by trauma. On the one hand, French psychiatry coined the term HP⁵⁷ in the second half of the nineteenth century, with this pathology being conceptualized as a dissociative phenomenon⁵⁸. On the other hand, the Scandinavian school developed, in the first third of the twentieth century, a similar concept called PP¹. Both approaches converged when observing that this kind of psychotic disorder has 1) an abrupt onset after a traumatizing event, 2) a self-limited duration of a few weeks, 3) positive symptomatology, 4) mood lability, and 5) recovery ad integrum⁵⁹⁻⁶¹. Despite this remarkable clinical agreement, both nosological constructs fell into disuse in the decades following their formulation. With regard to HP, many patients were diagnosed with schizophrenia once this term had been introduced in psychiatric nosology. Concerning PP, its dissemination was limited from the very beginning due to the use of a minority language^{62,63}. In the case of HP, some authors tried to apply this construct later⁶⁴, with no conclusive data about its nosological validity, particularly concerning its brief or transient nature⁶⁵⁻⁶⁸.

In summary, current psychiatric nosology recognises post-traumatic psychoses in a residual manner. Despite having relative clinical validity⁶⁹, there is no agreement when defining their distinctive characteristics from an empirical perspective.

PTSD and psychosis in traumatized subjects

– Prevalence

With regard to prevalence data between PTSD and psychosis, two types of studies have been carried out. On the one hand, research studies with psychotic patients aimed at determining comorbidity with PTSD. On the other hand, studies in subjects with PTSD, which assessed the presence of psychotic-like symptoms associated with this condition, a clinical phenotype called PTSD-SP⁷⁰.

As for the comorbidity between PTSD and schizophrenia, prevalence data are in a range between 11% and 53%⁷¹⁻⁷⁴. These findings in samples of psychotic patients are significantly higher to the percentage of subjects with PTSD in general adult population, with an estimated range from 3% to 5%⁷⁵. With regard to the prevalence of PTSD-SP, available data in samples of former combatants show that 17-20% of these subjects with PTSD have secondary positive symptoms associated with trauma (e.g., paranoid delusions)⁷⁶⁻⁷⁸. Two factors have been pointed as responsible for possibly overestimating this association. On the one hand, comorbid mental disorders that would really account for the presence of psychotic-like symptoms in PTSD samples (e.g., psychotic depression). On the other hand, potential biases when distinguishing re-experiencing symptoms (e.g., intrusive images) from psychotic ones (e.g., visual hallucinations). As for the first issue, a study that excluded those patients with major depression reduced PTSD-SP prevalence in 2.5% in samples of traumatized patients⁷⁶.

In sum, there are epidemiological findings in clinical samples suggesting that the association between PTSD and psychosis happens with higher probability than in general population.

– Theories explaining the association between PTSD and psychosis

From these results on prevalence, different hypotheses have been proposed as possible etiopathogenic mechanisms of the relationship between PTSD and psychosis (schizophrenia or psychotic-like symptoms). On the one hand, one of the two disorders would emerge as predisposing for the other (unidirectional theory). On the other hand, third variables would justify this co-occurrence (theory of common risk factors).

With regard to the first approach, there is empirical evidence to claim that both pathologies are a vulnerability variable for the other disorder. In the case of subjects with PTSD, different cross-sectional research studies with community samples showed that the risk of having psychotic-like symptoms is at least twice as higher as the one observed in general population (odds ratio = 1.8-3.5), with a higher predisposition to delusional symptomatology being outstanding^{28,38,76,79,80}. Concerning this hypothesis, a model of continuity between PTSD and psychosis has been proposed, in such a way that the psychotic condition would indeed be an exacerbation of the former condition^{79,81}.

On the other hand, within this unidirectional theory, a series of mainly cross-sectional studies have aimed at determining the risk of having PTSD as a result of psychosis onset, a fact called PP-PTSD⁴. On this issue, many studies with clinical samples of subjects with first psychotic episodes showed that the prevalence of PTSD ranges from 11% to 67%, being diagnosed in a third of patients assessed on average^{4,82-88}. Two variables have been identified as potential precursors of this post-traumatic condition: positive symptoms and the type of psychiatric admission (e.g., voluntary vs. involuntary). Concerning the first factor, there are partially

consistent findings to establish a positive relationship between presence or severity of positive symptoms and PTSD^{82,85,87,88}. As for the kind of admission and/or treatment, the association is less conclusive^{82,84,85,87}. Together, these data have posed the question of what variables could be modulating the relationship between these variables and PTSD. In this sense, current findings suggest that the presence of PTSD in subjects with first psychotic episodes is higher if 1) they have a previous history of trauma, 2) use dysfunctional assessment and coping strategies in front of stress (e.g., experience of uncontrollability), and 3) show comorbid depressive symptoms^{4,82-84,88-90}.

Finally, regarding the existence of common factors in PTSD and psychosis, only two proposals have been carried out from divergent approaches. On the one hand, a “model of cognitive integration” has been proposed, which considers that both disorders would be pathologies in the post-traumatic spectrum with similar explanatory mechanisms at the level of cognitive schemas, attributional styles and dissociative processes⁹¹. On the other hand, from a neurobiological perspective, it is considered that both disorders imply a dysfunction in the HPA axis, thus causing a dysregulation in the release of cortisol in response to stress⁴⁵.

In summary, there is empirical evidence to suggest a possible reciprocal influence between both types of psychopathology. As for the presence of third variables, there is scarce research comparing PTSD and schizophrenia to determine this approach.

– *Nosological status of PTSD-SP*

The high prevalence of subjects with PTSD and co-occurring positive symptoms has encouraged a last line of research aimed at determining the nosological status of those patients with PTSD-SP^{3,92,93}.

At a methodological level, most of these research studies have been conducted with war veteran samples diagnosed with PTSD “with” versus “without” psychotic-like symptoms, with different neurobiological markers being used as dependent variables. The main results of these studies show that subjects with PTSD-SP have 1) a higher concentration of platelet serotonin, 2) higher levels of corticotropin-releasing factor in the cerebrospinal fluid, 3) a higher concentration of plasma dopamine beta-hydroxylase, 4) specific deficits in smooth pursuit eye movement, and 5) a higher presence of Met alleles in the BDNF Val66Met polymorphism⁹⁴⁻⁹⁸. Likewise, different open clinical trials found that the administration of neuroleptics as a monotherapy for 6-8 weeks reduces symptoms in those subjects with PTSD-SP resistant to conventional antidepressant treatment⁹⁹⁻¹⁰¹. On the other hand, at a psychopathological level, subjects with PTSD-SP have a more severe posttraumatic condition⁸⁰. Finally, from statistical techniques such as latent class analysis, evidence has been found in favour of this nosological approach¹⁰².

In summary, there is preliminary evidence, particularly at a neurobiological level, to advocate a subtype of PTSD-SP^{103,104}.

Discussion and conclusions

– *Summary*

In this theoretical review, we have presented the main findings and research studies about trauma and PTSD in subjects with psychosis. With regard to the role of CT, there is conclusive evidence about its influence as an unspecific risk factor, both for schizophrenia and positive symptoms (psychotic-like symptoms) in adulthood. Concerning the relevance of trauma as a triggering factor of

acute psychotic conditions, there is scarce empirical research that assesses this etiopathogenic approach, with these psychoses being residually integrated into current psychiatric nosology. On the other hand, concerning the theories explaining the relationship between PTSD and psychosis (schizophrenia or positive symptoms), there is preliminary evidence to establish a two-directional causality between both pathologies. Finally, consistent results have been obtained that would confirm a subtype of PTSD-SP.

– *Methodological limitations*

With regard to the limitations of studies on trauma and psychosis, there is a lack of empirical research aimed at clarifying the nosological status and clinical characteristics of acute psychoses triggered by a trauma or serious stressor, particularly in view of distinguishing them from other more endogenous acute psychoses. In this sense, studies that determine the role of trauma in the pathoplasty of psychosis have to be encouraged, particularly in relation to the content of delusions or hallucinations. In this issue, there are some research studies that show a relationship between history of sexual abuse and nature of psychotic symptoms^{24,105,106}. As for the theories explaining the association between PTSD and psychosis, prospective research has to be promoted to reliably determine the relationships of causality between both types of psychopathology. Likewise, there are scarce studies comparing PTSD versus psychosis with the aim of assessing potential common factors at the neurobiological, neuropsychological and/or cognitive level. With regard to the nosological status of PTSD-SP, more comparative research studies have to be encouraged to determine this question, with the inclusion of other external criteria apart from neurobiological variables (e.g., degree

of psychosocial dysfunctionality, neurocognitive profile). Likewise, controlled clinical trials have to be conducted with long-term follow-up in order to assess the efficiency of neuroleptics in this subgroup of patients. Finally, there are not comparative studies regarding clinical and functional differences between PP-PTSD and PTSD-SP. Thus, further research is warranted in this last issue.

– *Clinical implications*

- In the field of primary prevention, it is required to develop psychotherapy in those subjects with CT and UHR for psychosis, thus focusing the intervention on negative cognitive schemas and dissociative mechanisms involved.
- At a nosological level, false positive diagnosis of chronic psychosis has to be avoided in those subjects that develop psychotic experiences after a serious stressful event. It is necessary to assess the evolutionary course in order to carry out the appropriate differential diagnosis.
- In subjects with a primary diagnosis of schizophrenia, the possible occurrence of PTSD has to be assessed and treated with conventional psychotherapy¹⁰⁷⁻¹¹¹, especially considering that co-morbidity is an indicator of higher suicidal risk^{71,74}. Specifically, the potential post-traumatic symptoms in subjects with first psychotic episodes (PP-PTSD) has to be assessed, with the optimization of coping strategies in front of stress and the integration of the psychotic experience being a priority in these cases^{85,86,112,113}.
- In subjects with a primary diagnosis of PTSD, it is necessary to assess associated psychotic-like symptoms (PTSD-SP), in which case treatment with neuroleptics should be implemented.

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