## **Originals**

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# The importance of loss in the genesis of depressive disorders

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Introduction. The role of loss has been carefully examined in the investigation of depression since it constitutes a central aspect of most of the life events that lead to depression.

Methods. In the present study, a review was made of the different studies on the role of loss, focusing on its different aspects and different types, the association between loss and some mental diseases, loss and prognosis, relationship between hopelessness and loss, variations of the events of loss based on different factors, also considering loss in the childhood.

Results. Loss constitutes a central role in the appearance of many depressive disorders. It can act as a provoking agent, a vulnerability factor or an agent that can modify the form, severity and course of a depressive disorder. Different factors such as the genetic one, gender or moment of life when the loss takes place, can modulate the influence of loss events.

Key words: Loss. Depression. Life events. Hopelessness.

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# El papel de la pérdida en la génesis de los trastornos depresivos

Introducción. En la investigación de la depresión, el papel de la pérdida ha sido examinado en detalle, puesto que constituye un aspecto central de la mayoría de los acontecimientos vitales que llevan a la depresión.

Material y método. En el presente trabajo se realizó una revisión acerca de los estudios previos sobre la importancia de la pérdida centrándonos en diversos aspectos como sus diferentes tipos, la asociación con algunas enfermedades mentales, pérdida y pronóstico, relación entre desesperanza y pérdida, y variaciones de los acon-

Correspondence: Pilar Sierra San Miguel Hospital Universitario La Fe. Unidad de Psiquiatría Avda Campanar n°21 46009 Valencia (Spain) E-mail: sierra\_pil@gva.es tecimientos de pérdida en función de diversos factores, considerando también la pérdida en la infancia.

Resultados. La pérdida ejerce un papel clave en la aparición de muchos trastornos depresivos. Puede actuar como agente provocador, factor de vulnerabilidad o agente modificador de la forma, gravedad y curso de un cuadro depresivo. Diversos factores como el factor genético, el sexo o el momento de la vida en el que tiene lugar la pérdida pueden modular la influencia de los acontecimientos de pérdida.

Pérdida. Depresión. Acontecimientos vitales. Desesperanza.

#### INTRODUCTION

The concept of loss is a diffuse one that fundamentally includes interpersonal separation and decrease of self-esteem, among other situations such as discussions with close persons, loss of a person, of a certain role, of desired resources and ideas as well as deceptions due to the return of a problem apparently solved in the past. Traumatic events such as the death of a significant other, matrimonial breakup or accident or robberies, have clearly been considered as risk factors for the appearance of a psychiatric disorder.<sup>1-3</sup> Paykel points out that stressful events that precede the appearance of psychiatric disorders generally are not ones that are as traumatic as death, end-stage disease or financial crisis but rather they more frequently are domestic problems such as social discussions, marital problems, separations and difficulties at work.4

There are life events that fulfill a series of characteristics that make them a greater threat for the subject. Most of the new cases of depressive disorders are caused by particularly threatening stressful events, which generally suppose some type of loss or deception.<sup>5-9</sup> The strongest relationship appears when the events are grouped in terms of «threatening or undesirable». Important aspects in this sense are helplessness, loss of power and sensation of defeat. In fact, when samples of persons who have suffered at least one se-

vere event are studied, 79% of the patients have suffered at least one that means a loss.9

In this work, we propose to make a review of the literature on the most important aspects on the implications of loss in depressive disorders.

#### MATERIAL AND METHODS

A review of the literature was made in Medline (1965-2007). The search terms were loss, depression and life events. Additional articles were obtained through the references of the articles.

The articles with the greatest relevance were selected and the information collected was summarized in several sub-sections that are presented in the following.

#### **RESULTS**

#### Previous studies on the role of loss

Regarding the individual differences in response to loss, the works made have focused on child mourning, since most of the symptoms give great importance to the facts and answers of childhood to explain the variations in the responses of the adults. There are two different schools of thought in this controversy:

- The classical psychoanalytic school of thought that attributes pathogenic meaning to the loss of a parent or loved one, but does not relate child mourning or the tendency in childhood of the mourning processes to follow a pathological course with the origins of pathological mourning in adults and the psychiatric diseases this originates.
- The school of Klein that focuses on the idea that how a child responds to the mourning processes and depressive phases during the first year of life and related with breastfeeding and weaning determines how they will respond to losses when he/she is an adult.

The first article that associated an unmistakable role to decrease in self-esteem after an event was published by Bibring in 1953, with a psychoanalytic orientation. However, the concept of loss as a central depressogenic experience comes from Freud's work Mourning and Melancholia.

Years later, in 1978, Brown states that loss is not only related with depression but also makes a distinction, stating that loss due to death is more frequent among psychotic depressive and loss due to separation among neurotic depressive subjects.<sup>12</sup>

In 1983, in a review of the studies they considered to be methodologically more correct, Cooke and Hole conclude that three fifths of the depressive pictures can be related with losses.<sup>13</sup>

The importance of loss is also seen in a work that analyzed the effects of stress, social support and a series of personality variables in populations of control, depressive and schizophrenic subjects. According to the findings, depressed patients accumulated significantly greater levels of inevitable losses regarding the controls during the year prior to the onset of the depression. This did not occur in the schizophrenics regarding the controls.14 An epidemiological study conducted over one decade beginning in 1965 in non-depressed individuals analyzed what the predictor variables would be for them to present depressive symptoms in 1974. Within the latter group, those who had any physical disability had a three times greater likelihood of becoming depressed than those who did not. Elevated levels of distress also appeared associated to an increase of likelihood of being depressed, those of job and financial problems being those that explained a greater proportion of the variance between the different types of stress.15

Gilbert<sup>16</sup> stressed the importance of the feeling of belonging and stressed a certain number of «depressogenic» situations, such as direct attacks against the self-esteem of a person that brings them to a position of subordination, the event that decrease their attractiveness and value, and those that generate a sensation of «blockage.» These ideas go beyond the concept of loss of a person or object. While the experience of loss is generally prior to the appearance of a depressive episode, it is not necessarily associated to the experience of defeat and «entrapment» (this concept means that a person may be highly motivated to leave a certain situation, but he or she feels incapable), that they may also appear after experiences other than loss.

In a study performed in the sample of 680 twins, 17 considering different variables such as mental state, paternal warmth in childhood or loss, psychological traumas over the lifetime, neuroticism, social support, history of previous episodes of depression and stressful difficult events in the last year, the conclusion was drawn that the genetic factors exercise a direct effect on the tendency to develop a major depression, but the remaining 40% was an indirect effect mediated by stressful events, traumas over the life time, a previous history of episodes of major depression and neuroticism. Therefore, the study defended the multifactorial character of depression. Later, these same authors published one work in which the influence of the dimensions of loss, humiliation, entrapment and danger was analyzed in the prediction of the appearance of major depression and generalized anxiety. They found that in addition to loss, the events that meant humiliation were strongly bound to the risk of depressive episodes, the impact of those of loss being the most potent. Furthermore, in the month in which the event occurred, the risk for anxiety or depression syndromes was predicted by high levels of loss and humiliation, but not by the sensation of blockage or danger.18

The article published by Brown<sup>19</sup> in which two groups were studied is of key importance when analyzing the role of loss in depressive disorders. One group included women who developed depression in a sample of the general population in Islington in the north of London and the other was a series of depressed patients treated in the National Health Service of the same area. The aim of this study was to solve the question of whether loss has a fundamental importance in depression or whether it is simply a correlate of a more basic series of experiences. The experiences of loss associated to humiliation or entrapment were important as depression-causing agents in both samples, that is, in that of the patients and of the general population. However, experiences of danger were more weakly associated with its appearance. Brown provided a series of considerations in this same work when he defined the different losses that an individual may undergo:

- Dimension of loss. These are the cases in which the loss appears alone. They supply a classification of four subcategories using the Life Events and Difficulties Schedule (LEDS). These are death, experience of separation (the subject plays an active role and thus those due to infidelity or violence are excluded), other losses (such as abortion, job losses, etc.), or minor losses (for example, death of a relative that the subject had little contact with).
- Dimension of humiliation. It can appear in several forms. Either as separation, that generally concerns a close person such as a relative or a significant person. In these cases, feelings such as failure or rejection generally appear and include the separations due to an infidelity or violence. As humiliation, for example, being the target of crime acts by others or as conflicts the decrease self-esteem, for example infidelities or physical attacks by close persons. Or situations that entail shame or public humiliation.
- Dimension of entrapment. They are events that entail a difficulty maintained for at least six months and with likelihood to persist or become worse.

Table 1 shows the different dimensions of the losses.

Broadhead stated that in relationship with the highly threatening events, the rates of appearance of depressive episodes were higher after the combination of the categories of humiliation or sensation of blockage, followed by losses due to deaths, followed by another type of loss and were less after events of danger.<sup>20</sup>

Gilbert<sup>21</sup> developed a questionnaire of situations of «blockage» through which the same results were obtained in relationship to the strong association between feeling of entrapment and depression, defeat and hopelessness. Along the same line, another study published later was found. It was conducted in a sample of depressed subjects in comparison with a control sample, according to which the events

of loss and humiliation were particularly depressogenics. Thus, the depressed subjects had experienced a severe event of loss or humiliation more frequently.<sup>22</sup>

#### Association of loss and some mental diseases

In the works of Brown in women of the community, the events of «loss» were associated with depressive disorder, while those involving «dangerous» situations were associated with anxiety disorders<sup>23,24</sup> and those that combined both caused both depressive and anxious symptoms.<sup>23</sup>

Few rigorous investigations in this sense have been performed in the case of bipolar disease. Although the origin of mania is never reactive according to some classical authors, 25,26 subsequent studies have found a relationship between some stressor events and loss events with the onset of manic pictures. It has been suggested that the sleep disorders associated to said events might lead to a manic episode. It was found in a study published by Kessing consisting in a registry of cases that included more than 1,500 bipolar patients that losses such as suicide of one's mother or of a sibling were associated to a very high risk of a first time admission to a psychiatric unit due to a manic/mixed episode. Other losses such as unemployment, divorce or recent matrimonial ones showed moderate effects.

In psychotic disorders, situations that imply feeling subordinated (due to loss of states) and blocked are also highly associated to depression.<sup>29</sup> Specifically, the events associated with humiliation and entrapment situations have been shown to be depressogenic,<sup>19</sup> and are also related with depression in schizophrenia<sup>29</sup> and suicide attempts.<sup>30</sup>

#### Loss and prognosis

There is evidence that the prognosis for unipolar depressive patients who experience a previous life event to the appearance of the episode is better,<sup>31-33</sup> although some studies state the opposite.<sup>34-35</sup> The personal relevant events and those linked to self-esteem are predictive of the prognoses in a study in the three following months in unipolar depressed adults.<sup>36</sup> Fateful and disruptive events were also significant.<sup>37</sup> In addition, those that supposed humiliation and being involved in a difficult relationship were significant for the female gender in particular.<sup>19</sup> An increase in the life of vital events having a positive sign has been described in the three months prior to recovery in patients with depression and anxiety.<sup>38</sup> Losses such as breakup of a conflictive sentimental relationship have been related with the recovery in a group of non-melancholic depressive patients.<sup>39</sup>

However, the event is only partially responsible for the appearance of the disease and the causal proportion that can be attributed to it directly may not be important. The

Table 1 Brief definitions of the life events categories*	
Category	Definition
Death	Dimension of loss Close relationship with the deceased person
Separation (initiated by the subject him/herself)	The initiative of separation by the subject or by mutual agreement: it should be prolonged
Another type of loss	Other loss events scoring at least from elevated to moderate
Minor loss	Any event that scores as mild severity
	Dimension of humiliation
Separation (initiated by the other)	Separation from a spouse or significant other, discussions, etc. initiated by the other person or forced by circumstances (infidelity or violence). It should last several months
Criminal acts of others	Criminal behavior committed by someone close**
Public humiliation	Rejection or verbal or physical attack by someone close or person of authority in public, irresponsible behavior by someone close or family member.  All those situations that entail shame or personal failure
	Entrapment dimension (blockage)
Sensation of long term entrapment	Severe event that causes serious problems that worsen or are maintained with limited possibilities of solution
Entrapment with long term worsening	Event that worsens in its course, problems of at least six month's duration
Failures	Event that will become enormously worse in the next 1-2 weeks, leaving the person stagnant in as bad or worse of a situation than initially
*The dimension of danger has no categories.  **Close person is typically defined as husband/wife/signific Modified of Brown et al. 1995.	ant other, boyfriend/girlfriend, parent/paternal figure, child, confident or close friend.

loss interacts with other environmental factors that include work, social relationships, presence of small children in the home and low social class.<sup>40</sup> Vulnerability to events will also depend on the personal factors of the individual together with genetic and environmental factors. One example is obsessive personalities that confer a greater vulnerability to the events that involve change. Losses at an early age may also predispose to depression or suicide attempts after a subsequent loss event.<sup>40,41</sup> In addition, biological factors may include structural or functional abnormalities that predisposed to different psychiatric and somatic diseases.

Birtchnell<sup>42</sup> found that if the severity of the symptoms were considered separately when women had experienced a loss before 20 years of age, 38% of the more depressed women and 22% of the least depressed ones had lost one of their parents during childhood. Brown tried to explain the effect of the losses in the past in a general way.<sup>12</sup> Along these lines, he observes that the loss in the past may mean a permanent cognitive influence and modify how the subject will react to it at a later time. Loss due to death may be related with psychotic type symptoms in its irreversible sense. On the contrary, losses related with rejection may condition a less passive cognitive attitude. This means the distinction

between this psychotic sense of abandonment and the neurotic one of rejection that would have plausible agreement with the traditional ideas of the typical forms of psychotic and neurotic depression.

In the community study of Islington, 3/4 of the severe events consisted in experiences of humiliation or entrapment. Most of the other events (22%) only meant loss and the remaining 5% only danger.<sup>19</sup> The previously described findings were demonstrated in that study.<sup>43</sup> It stressed the importance of considering the provoking agents in terms of threat to a role or to a relationship as a whole. All these elements may interact in complex ways. For example, a situation of humiliation in a person may not have a depressogenic effect because at the time when it occurred, the victim perceived the change as beneficial. Thus, the experience of a loss may be a provocative agent (it increases risk and determines the moment of appearance), a vulnerability factor (it increases sensitivity of the subject to these experiences) or a factor that influences the severity, form and development of a depressive disorder. Those events that are associated in greater degree to the possibility of provoking a depression are undesired events, uncontrollable ones and independent ones.44-46

#### Hopelessness and depression

According to Melges and Bowlby, 47 hopelessness is the key factor in the genesis of clinical depression and loss is possibly the most likely cause of profound hopelessness. The implications that this loss has on our ability to find satisfactory alternatives are of special importance. That is, feelings of hopelessness are not only restricted to the provoking incidence but also may generate thoughts on the hopelessness of the life itself in general. According to Beck, this generalization is that which constitutes the central nucleus of the depressive disorder.<sup>48</sup> The theory of Beck also defends the idea that the individual's self-esteem is crucial in favoring the development of hopelessness. This explains the action of the vulnerability factors when favoring depression when there are severe events and greater difficulties (loss of the mother before 11 years of age, presence in the home of three or more children under 14 years of age, absence of a confidential relationship, especially with the husband, and lack of full time or part time work).

Therefore, when considering the relationship between environmental distress and psychiatric disease, it is important to distinguish between the stressors that can contribute to the vulnerability and those that precipitate the appearance of the disorder. The events that act as risk or vulnerability factors may be temporally distant from the appearance of the clinical symptoms. The influence of the experiences of loss in childhood in the appearance of major depression in the adult, abuse in childhood in the development of personality disorders<sup>49</sup> and abnormalities in rearing<sup>50</sup> can be considered among these.

## VARIATIONS OF LOSS EVENTS BASED ON DIFFERENT FACTORS

#### The genetic factor

Some authors have described that the patients with the greatest genetic risk of depression also have a greater risk when there are dependent events that include assaults, marital problems, divorce, job loss, financial problems and other interpersonal problems.<sup>51</sup> In a study conducted in adopted twins, the inheritance of depressive symptoms was only 16%, rearing had a significant contribution, but the greatest contribution was made by life events.<sup>52</sup>

#### Influence of gender

While women present a greater vulnerability for certain subtypes of events, for example, domestic problems, those that affect the social network such as loss of a confident or relationship problems with persons in their proximal network,<sup>53,54</sup> men are more affected by job loss, legal problems, robberies and work problems. In an analysis of the Epidemiologic Catchment Area study, men presented a greater in-

dex of new episodes of major depression related with matrimonial disruption.<sup>55</sup> The analysis of five previous population studies verified that women were more sensitive to the depressogenic effects of the social events and death of a loved one while men were more sensitive to loss of income.<sup>56</sup>

The assumption that an increase in risk of depression in the woman is largely due to environmental stressors has been supported by the findings of a study conducted in twins that found that there were no differences in gender in regards to genetic risk.<sup>57</sup> Bebbington conducted an exhaustive review in which it was stated that social and psychological inequalities seems to be the most important determining factors of the differences between both genders in regards to reactivity to live events and the greater percentage of major depression among women.<sup>58</sup>

### The influence of age

Loss in childhood

As we have indicated previously, losses in childhood have been studied in detail since there is proof that there are some situations that act in early stages, which leave the individual vulnerable to suffer a depressive disorder in the future. In fact, there is a significantly greater number of cases of early parent losses among psychiatric patients than among healthy controls.42,59 This fact is more frequent among depressive patients than among the remaining psychiatric pathologies.48 However, some works have not found the existence of associations between early parent death and a general psychiatric disorder in the adult.<sup>42</sup> After reviewing more than 20 controlled studies on this subject, it has been found that other authors 60 have concluded that «it has not been established that the death of a parent in childhood is a significant etiological factor for either depression in the adult or for any subtype of depression.» However, studies that have reviewed practically the same literature state that the death of a parent in childhood multiplies the risk of depression 2 or 3 times.<sup>61</sup> On the one hand, some studies show that subjects who suffered the death of their parents during their childhood generally have more periods of emotional sadness than those who did not suffer it in the first stage of adult age. Others have found that there is a greater proportion of losses suffered in childhood among children and adolescents referred to the child psychiatric clinics. In addition, loss of a parent during childhood influences the symptoms of any psychiatric disorder that the subject suffers afterwards.62

Te relationships between early losses (separation, death of one of the parents or mental disease of a parent), severe stressful events and depression were analyzed<sup>63</sup> in a work examining a community sample. The information was collected through an interview in which a psychiatric diagnosis was made using a standardized instrument (DIS),<sup>64</sup> a series of questions regarding the separations/deaths of the par-

ents and a questionnaire on the presence of twenty stressful events during the year prior to the interview. It was found that early negative experiences increase the vulnerability of the adult person to stressful events. Separation-divorce of the parents interacted with the stressful events of the adult period of the subjects, increasing their vulnerability for a series of psychiatric disorders. On the other hand, loss due to death of the parent in childhood did not interact with the recent severe events to provoke the appearance of a psychiatric disorder.

In the case of loss of the mother due to separation at an early age, several studies have analyzed the pathological conditions occurring subsequent to that event, 65,66 since this would generate greater needs of dependence in those subjects in the adult age.67 The earlier the loss, the more likely that the subject will have a delay in learning of management in the setting. If it occurs before 11 years of age, it may permanently reduce the sensation of capacity for selfefficacy and self-esteem and act as a vulnerability factor, interfering in how one manages losses in the adult period. Most of the studies support the hypotheses that loss of the mother in childhood or adolescence is more associated with depression than loss of the father, 68,69 although this finding has not been consistent in all of them.<sup>17,70</sup> It seems that the quality of the substitute parent care after the loss is more important than the loss of the mother itself.71-73 Two reviews on the childhood experiences of loss concluded that divorce of the parents predicts depression in the adult, however death of these do not do so.74-75

Another study conducted on a sample of 73 bipolar patients and 570 with unipolar depression did not find a significant association between adult depression and death of a parent in childhood.<sup>76</sup> However, separations, especially those that occur within the context of a family or parental quarrel, could contribute to depression in the adult age. In addition,<sup>8,77,78,75</sup> it has been described that loss events in children are associated with depression while conflictive and stressing events predict behavioral problems.<sup>79</sup> In comparison with a loss in late childhood and adolescence, that occurring in early childhood seems to have a major pathogenic significance,<sup>69,80</sup> although this has not been observed in all of the studies.<sup>17</sup>

Regarding gender, loss in women,<sup>68</sup> especially that of the mother<sup>70</sup>, may be more associated with the late development of depression than loss in men. However, many of the studies and early parental loss have only analyzed samples of women.<sup>17,81,69</sup> Studies that have analyzed masculine populations have also found an association between loss and depression.<sup>82</sup>

The influence of childhood experiences in psychosocial functioning of the adult

The fact that the early experiences in childhood may have long-lasting psychosocial repercussions has been defended by at least two mechanisms. According to the first one, they could facilitate behaviors by the individuals in the future so that they would have more likelihood of suffering adverse events since the life experience do not occur randomly but rather we somehow select them and determine the circles in which we live.83 It was observed in some studies that young antisocial subjects have greater likelihoods than the controls of suffering problems in their relationship, of matrimonial breakups, unemployment and frequent job changes. The negative experiences may act by generating disruptive character behaviors that significantly increase the incidence in the adult period of stressful situations and adversities; it being these that would predisposes them towards the appearance of psychopathological phenomena. A follow-up of 171 children who, due to the breakup of their patients, had been institutionalized, was made in a longitudinal study. The risk factors accumulated were family disagreements, which ended up in the breakup of the family and the experience of an institutionalized education. They compared this population with another nonrandomized control study made up of 83 children who had lived with their families in the same area of London. The findings showed an increase in the level of psychosocial functioning deficits, with a tendency to inadequate marriages due to psychiatric disease, toxic abuse or delinquency by the spouse, or early maternity, which would generate less emotional support and consequently greater psychiatric morbidity in the adult period, associated to the specified risk factor.78

The second mechanism defends the hypothesis that the early influences act by increasing the individual vulnerability to subsequent adversities since there are very important differences in the responses of the individuals to the environmental events and part of this variation may be a consequence of the previous experiences.<sup>84</sup>

#### Loss and adolescence

In adolescents, the possible stressful situations described have been problematic rearing, interpersonal and familial conflicts, together with physical diseases.<sup>85</sup> On the other hand, the losses that affect their parents also have a significant impact. Factors such as maternal distress<sup>86</sup> and paternal depression<sup>87</sup> acted as predictors of depression in adolescents and behavior problems in children.

#### Loss and old age

There is a term called «psychological immunization» that describes the process by which some persons develop resistance to adverse events and losses through repeated exposure.<sup>88</sup> A study of Kessing<sup>89</sup> in a sample of 13006 patients, did not find greater susceptibility to life events over the lifetime. There is only one study with an important sample according to which the impact of maternal loss on the risk of depression significantly varied with age, it being greater

in those individuals who were younger at the time of the loss. On the contrary, no interaction between age and spouse loss was found.<sup>90</sup>

#### CONCLUSIONS

Loss has a key role in the appearance of many depressive disorders. The case of its appearance in childhood has been the object of special interest in the literature by different schools. The relationships between the different types of loss and their association with some mental diseases have also been studied.

On the other hand, loss interacts with different factors of vulnerability characteristic of the subject. This confers a multifactorial character to depression and can assume different roles such as provoking agent, vulnerability factor or modifying agent of the form, severity and course of a depressive picture. In addition, the influence of loss events may be modified based on different factors such as genetic factor, gender, or the imoment of the life when the loss occurs.

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