Depersonalization: from disorder to the symptom

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Despersonalización: del trastorno al síntoma

Summary

In contrast with the growing interest in dissociative disorders over the last few years, depersonalization continues to be very scarcely approached. There is no agreement among clinicians regarding the concept of depersonalization, and little is known about its etiology, epidemiology and treatment. This paper has two main aims: 1) *Review the literature on this pathology focusing on nosological, historical, psychophysiological and treatment aspects, and* 2) *Explore the incidence of the depersonalization symptom in other psychiatric conditions, in particular in panic disorder. The Medline database over the last 5 years has been used for these purposes, and lack of studies on this subject has been found, especially regarding therapeutic issues. Some of the most relevant findings suggest that depersonalization, when associated to panic disorder, could correspond to the most severe forms of this disorder.*

Key words: *Depersonalization. Derealization. Panic disorder. Biological treatment. Psychological treatment.*

Resumen

En contraste con el reciente interés que han suscitado los trastornos disociativos, el trastorno de despersonalización continúa siendo uno de los menos investigados. No existe acuerdo entre los clínicos en cuanto al concepto de despersonalización y poco se sabe sobre su etiología, epidemiología y tratamiento. El propósito de los autores es: 1) *hacer una revisión de la literatura existente sobre esta patología, centrándose en los aspectos nosológicos, históricos, clínicos, mecanismos psicofisiológicos implicados y de tratamiento, y* 2) *estudiar como el síntoma de la despersonalización incide en otras patologías, especialmente en el trastorno de angustia. Para ello se utilizan las bases de datos del Medline de los últimos 5 años, con lo que se constata la necesidad de investigar el trastorno en cuestión dada la escasez de datos especialmente en el ámbito terapéutico. Algunos hallazgos sugieren que la despersonalización asociada al trastorno de angustia se podría corresponder con las formas más severas de esta patología.*

Palabras clave: *Despersonalización. Desrealización. Trastorno de angustia. Tratamiento biológico. Tratamiento psicológico.*

INTRODUCTION

Depersonalization disorder is a disorder having great interest but is still quite unknown by the clinicians. In spite of the rediscovery of the dissociation in the last decade, the depersonalization disorder continues to be one of the dissociative conditions that has been investigated and diagnosed the least and on which the least has been published. There is no agreement between the clinicians in regards to the depersonalization concept and little is known about its etiology, prevalence and incidence, but above all, the most unknown aspect is its treatment. We still lack clear lines on both biological as well as psychotherapeutical treatment, so that depersonalization becomes a condition refractary to these treatments in many cases and, thus, chronic[1].

This paper has two objectives. On the one hand, we propose to review the existing literature on the depersonalization disorder, considering historic, nosologic, clinic aspects, psychophysiological mechanism involved and treatment. On the other hand, we propose to study how the depersonalization symptom affects other psychiatric and neurological diseases, focusing, above all, on depersonalization in the anxiety disorder since this symptom seems to bestow distinctive characteristics and greater severity to this disorder[2-4].

When we speak of depersonalization, it is unavoidable to refer to derealization. These are two phenomena that often coexist and that are difficult to distinguish on many occasions. In fact, many authors indicate that there is no evidence in favor of whether they are two independent phenomena. In this review, the term depersonalization disorder will be used generically, according to the DSM-IV-TR (diagnostic and statistical manual of mental disorders) terminology, including both phenomena.

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HISTORY AND NOSOLOGICAL QUESTIONS

After the initial descriptions of Reil and Esquirol, the interest in depersonalization was initiated in the last quarter of the XIX century by Taine, Krishaber and Ribot[5]. In 1873, the clinician Maurice Krishaber presented the medical setting with the monography *De le névropathie cérébro-cardiaque*, a study based on the observation of 38 patients who suffered anxiety, fatigue and depression symptoms, creating the concept of cerebrocardiac neurosis, this being the background of the present panic attack. One third of these patients presented an unpleasant alteration of the perception of themselves and of the setting together with the sensation of living in a dream. After, Dugas, in 1911, coined the term depersonalization. In spite of the interest given by some clinicians for the experiences of depersonalization, it was not until after the First World War when the psychiatrists began to pay attention to them. Even so, the possibility that this phenomenon would be a specific syndrome was not considered until the Second World War. More recently, depersonalization has had a site in the European and American psychiatric taxonomy[6].

It appeared as a differentiated syndrome for the first time in the DSM-III-R7. The DSM-IV-TR[8], as the two previous versions, includes depersonalization within the dissociative disorders. The DSM-IV-TR8 considers derealization as an associated symptom while the ICD-10 (*International Classification of Diseases*) has a single category, the depersonalization-derealization syndrome, to include all clinical presentation characterized by depersonalization or derealization symptoms, placing them within the neurotic disorders secondary to stress situations. Given that depersonalization may manifest as a symptom in the psychiatric and neurologic population and as an isolated and transitory experience in the general population[10], the syndromic diagnosis can only be applied when the depersonalization episodes occur persistently, causing a clinically significant malaise and not appearing exclusively in the passage of time of other mental disorders[8]. Another aspect to stress is that the depersonalization disorder does not have positive traits, thus considering it a diagnosis by exclusion[11].

Even though the depersonalization disorder is considered a nosological entity by itself, there are many authors who believe that there is little proof to define depersonalization as a differentiated disorder and who consider it as a symptom. The argument used by these authors is that we generally find it as a symptom associated to different diseases, its syndromic diagnosis being rare[12].

CLINICAL ASPECTS

Concept

In the clinical practice, many patients do not manifest depersonalization symptoms because it is difficult to explain them and also because they fear that these experiences mean that they are «crazy»[13]. Surely, the phenomenon of depersonalization is difficult to define, not only by the patients but also by the clinicians[14]. Although the concept of depersonalization has been present in the medical literature since one hundred years ago, the controversy and inconsistency in regards to the specific symptoms and associated characteristics have not yet been solved[15].

In spite of the conceptual limitations, there is agreement that the essential characteristic of depersonalization is the experience of estrangement or distancing in regards to oneself. The person feels like an external observer of his mental processes, of his own body or of part of it, which is described as the sensation of being dead, empty, like living in a dream or in a picture or being a robot. Thus it is an egodystonic experience. Different types of sensorial anesthesia, absence of affective response and sensation of loss of control of one's own body and own acts, including speech, also appear[8]. A key element is that the sense of reality or insight remains intact, as the patient is aware that it deals with a sensation that is never lived as something foreign or imposed[16,17]. The expression «as if» is frequently used and helps to distinguish depersonalization from other disorders such as schizophrenia[18]. As indicated by López Íbor[19], it deals with an experience in which the essential is that the person himself is strange (table 1).

As associated symptoms, the DSM-IV-TR[8] mentions derealization, that is, the sensation that the external world is strange or unreal. The person may perceive a rare alteration of the form and size of objects and the other persons may seem to be unfamiliar or inanimate. In addition, the person may have the sensation that his limbs are larger or smaller than they really are. Other associated traits are the symptoms of anxiety, depression, obsessive-like thoughts, rituals, somatic concerns, autoscopic experiences and subjective alteration of space and passage of time[20,6].

TABLE 1. Diagnostic criteria of depersonalization disorder according to the DSM-IV-TR[8]

Persistent or recurrent experiences of distancing or of being an external observer of one's own mental processes or of the body (i.e., sitting as if one is in a dream
During the depersonalization episode, the sense of reality remains intact
Depersonalization causes clinically significant malaise or social, labor deterioration of deterioration of other important areas of the individual's activity
The depersonalization episode does not exclusively appear in the time period of other mental disorders such as schizophrenia, anxiety disorders, acute stress disorder or other disorder or other dissociative disorder, and is not due to the direct psysiological effects of another substance (i.e., drugs or medicines) or to a disease (i.e., temporal lobe epilepsy

Incidence and prevalence

Lack of agreement on the concept of depersonalization and the consequent difficulty to measure it in a valid and reliable way[15,21] explains the lack of knowledge that we have on the incidence and prevalence of the depersonalization disorder both in the general population as well as in the clinical one[1,8,10]. In any event, the usual belief that depersonalization is a rare disorder must be questioned given the lack of data, lack of information that the patients provide on this phenomenon and given that it is frequently underdiagnosed by the clinicians[1]. In fact, some authors indicate that depersonalization could make up the third most frequent psychiatric symptoms after anxiety and depression[22]. It is calculated that about two thirds of the persons subjected to life-threatening dangers present transient depersonalization phenomena[23]. In many series of hospitalized psychiatric patients, Brauer et al.[24] found that 80 % had depersonalization experiences and 12 % had them in a severe and persistent way, these never having been detected.

Course

Although childhood cases may be observed, the depersonalization disorder as such generally appears in adolescence or in the beginning of the adult age and rarely begins after 40 years of age[12]. The onset may be acute or insidious and the course is usually chronic, and normally continuous but also in form of episodes that are almost always related with stressing factors[1,8]. Some studies indicate that it is more frequent among women while others do not find significant differences in this sense[12].

Comorbidity

Although we have few investigations that make a study that is systematic and according to DSM criteria of the comorbidity between the depersonalization disorder and other psychopathologies, it has been seen that anxiety disorders (social phobia, panic attack, generalized anxiety disorder and obsessive-compulsive disorder) and of the mood state (major depression and dysthymia) are the axis I disorders that most frequently accompany depersonalization[1,25]. Some studies add bulimia, somatomorphic disorders such as body dysmorphic disorder or hypochondria and disorders related with substances to the previous diseases[8,26] (table 2).

In regards to axis II disorders, it has been found that those that present most frequently are avoidant, borderline and obsessive-compulsive disorders, the first one being associated with greater severity of the depersonalization disorder[1,26]. Although these are the most usual disorders, the diversity of personality disorders that are associated with depersonalization can be stressed, which suggests that this disorder could be understood as a character disease to some authors[1,27]. Although the obsessive-compulsive disorder has not appeared as the most frequent in these studies, there are numerous references in the old literature on the association of depersonalization with this disorder[28]. Specifically, an incidence between 75 % and 88 % of obsessive premorbid traits is described in patients with depersonalization[29-31] although the obsessive-compulsive traits are not measured systematically in these studies[32] (table 3).

TABLE 2. Prevalence over the lifetime and present comorbodity with the axis I conditions according to the DSM-III-R, of the 30 subjects of the Simeon et al.[1] study

Disorder	*Life prev.*		*Present prev.*	
	N	*%*	*N*	*%*
Bipolar disorder	1	3	1	3
Major depression	16	53	1	3
Dysthymia	10	33	9	30
Panic disorder	11	37	4	13
Social phopia	16	53	14	47
Generalized anxiety disorder	6	20	6	20
Obsessive-compulsive disorder	5	17	3	10
Simple phobia	2	7	2	7
Bulimia nervosa	4	13	0	0
Anorexia nervosa	3	10	0	0
Alcohol dependence	4	13	0	0
Alcohol abuse	0	0	0	0
Substance dependence	5	17	1	3
Substance abuse	1	3	0	0
Somatomorph disorder			1	3

Depersonalization in the general population

Up to now, we have spoken of depersonalization as a pathological phenomenon, but as an isolated and brief experience in the life of many persons, depersonalization is relatively frequent and not necessarily pathologi-

TABLE 3. Comorbidity with the axis II disorders, according to the DSM-III-R, of the 30 subjects of the study of Simeon et al.[1]

Personality disorder	*N*	*%*
Avoidance	9	30
Borderline	8	27
Obsessive-compulsive	7	23
Schizotypal	5	17
Paranoid	5	17
Dependent	4	13
Schizoid	3	10
Histrionic	2	7
Narcissistic	2	7
Passive-aggressive	1	3
Antisocial	1	3
Autodestructive	3	10

cal[10]. Some studies indicate that it may appear in 70% of the general population, without finding differences between men and women. It can also appear in children and adolescents as they develop consciousness of their self[10,16]. Several situations have been described that may favor the appearance of depersonalization in the general population: states of fatigue, prolonged sleep deprivation, certain drugs (anesthesics, antihistaminics), toxic consumptions (enol, LSD or marihuana) emotional shock, situations of life risk, etc.[10,23,33-35]. In some occasions, depersonalization is voluntarily included through meditation and transitory practices[36].

PSYCHOPHYSIOLOGICAL MECHANISMS OF DEPERSONALIZATION

In this section, we will present the data supplied by the most recent studies in regards to psychophysiological mechanisms of depersonalization.

The neurobiological model of depersonalization

From a biological point of view, it has been suggested that depersonalization is a biological mechanism of «software.» Two arguments support this statement. The first one is the appearance of experiences such as depersonalization in epilepsy of the temporal lobe and, on the other part, the evolutive point of view that considers depersonalization as a rudimentary and vestigial response of the pain to life-threatening dangerous situations[37].

According to this last argument, Sierra and Berrios[37] designed a neurobiological model of depersonalization from the experiences reported by the patients who suffer this phenomenon, from the neurobiological literature and from the findings of the neurocognitive sciences. The basic premise is that it causes a bilateral corticolimbic disconnection with a prefrontal activation and limbic inhibition, all this resulting in attentional difficulties and in hypoemotionality. This model has not been subjected to empiric studies of the frontal cortex and limbic system in the depersonalization disorder[38]. Some later studies support this model in regards to prefrontal activation and inhibition of the amygdala[39] while the findings on the frontal activation contradict the model[39,40].

Neuroimaging studies

In a functional neuroimaging study (positron emission tomography), Simeon et al.[38] found that the patients with depersonalization disorder presented metabolic abnormalities, mainly in the posterior cortex. This datum does not support the primacy of the temporal lobe described on many occassions[41,42], involving a more extensive association of cerebral networks, given the involvement of the parietal and occipital lobes. The depersonalization phenomenon is associated to functional abnormalities over different hierarchialized, unimodal and transmodal sequential areas of the sensorial cortex (visual, auditory and somatosensorial) and of the areas responsible for the integration of the body scheme.

Phillips et al.[43], using the functional magnetic resonance, indicated that patients with depersonalization show a reduction of the neural response of the regions involved in emotions (insula, and occipital-temporal cortex) and an increased response of those that are involved in emotional regulation (right ventral prefrontal cortex) when faced with the presentation of aversive stimulation.

Neurophysiological studies

Papageorgiou et al.[44] studied the characteristics of the P300 potential in patients with depersonalization, finding that its amplitude is significantly inferior in posterior areas of the brain, which indicates alterations in the information processing. These posterior areas are probably related with alterations in the gray matter as well as with changes in the cholinergic and gabaergic systems.

Neuroendocrine studies

Simeon et al.[45] studied the functioning of the HPA axis (hypothalamic-pituitary-adrenal) administering dexamethazone to patients with depersonalization and to healthy subjects. The former presented normal or elevated baseline levels of cortisol and a significant hyposuppression of the HPA axis with the administration of low doses of dexamethazone.

Stanton et al.[46] found that the patients with depersonalization show lower salivary cortisol baseline levels than patients with major depressive disorder. No differences were observed between these patients and the healthy controls.

Cognitive studies

Guralnik et al.[47] indicate that patients with depersonalization present a significantly inferior performance regards the controls in attentional measurements, short term memory (verbal and visual) and spatial reasoning but within a context of comparable intellectual skills. A pattern of general or diffuse deterioration was not detected in any case. The authors concluded that depersonalization is marked by a particular perceptive and attentional vulnerability. In this way, deficits in short term memory could be secondary to difficulties to focalize and perceive new information. These findings faithfully reflect the subjective difficulties of attention, concentration, perception and memory explained by these patients.

Neurochemical studies

Although we know very little on the neurochemistry of this disorder, it seems that dysfunction of the seroto-

ninergic pathways could be involved. Some authors suggest that there could be elevated serotoninergic tone and down regulation of the post-synaptic receptors in depersonalization[48]. There are several sources that support this statement: *1)* high inductor capacity of depersonalization of marihuana, even more than toxic consumption[35,49]; *2)* coexistence of depersonalization with the migraine[50]; 3) capacity of a potent serotoninergic agonist (meta-chlorophenylpiperzaine) to induce depersonalization experiences in patients with different psychiatric disorders[51]; *4)* correlation between the decrease in the tryptophan ratio regarding other amino acids and depersonalization in a sample of depressed patients[52], and *5)* good response of some patients to SSRI (selective serotonin reuptake inhibitors) and to clomipramine[25,53,54,55].

Organic factors related with depersonalization symptom

There must be no organic disease that can explain the phenomenon in order to diagnose the depersonalization disorder. However, depersonalization as a symptom has been associated to different diseases that justify its existence: neurological disorders (epilepsy, especially of the temporal lobe, migraine, brain tumors or cranioencephalic traumatism), endocrinal (alterations of the thyroid hor-mones or hypoglycemia), metabolic (hyperventilation and intoxication due to carbon monoxide), cardiovascular as well as consumption or intoxication with some substances (barbiturics, benzodiazepines, marihuana and practically all the substances having a similar action to phencyclidine and to hallucinogens)[10,11,56].

Psychological and environmental factors

From the psychodynamic setting, depersonalization is considered as a primitive and highly pathological defense mechanism linked to negation that appears when the most usual mechanism of repression fails to control unacceptable impulses[13]. Authors of other settings interpret depersonalization as a defensive experiential reaction to depressive humor states and anxiety and to traumatic circumstances that threaten the physical integrity of the person[23,35,57]. In this sense, recent studies warn about the importance of traumatic situations during childhood, especially emotional abuse, as factors that may play a role in the pathogenesis of depersonalization[1,26].

DEPERSONALIZATION AND THE SPECTRUM OF OBSESSIVE-COMPULSIVE DISORDERS

Recently, several authors have conceptualized depersonalization as a obsessive-compulsive spectrum disorder according to the similarities that it presents with obsessive-compulsive disorder in regards to phenomenology, comorbidity, neurochemistry and response to treatment[48]. Regarding the phenomenological coincidences, both disorders share the onset age, typically adolescence, chronicity of the course and the fact of being focused on a fixed point (contamination, aggression or sex in the obsessive-compulsive disorder and perceptive distortion of oneself in depersonalization). In regards to comorbidity, we have already commented in other sections on the frequent concomitance between depersonalization and obsessive-compulsive disorder. Both disorders share the possible alteration of the serotoninergic pathways and the good response of some patients to SRI (serotonin reuptake inhibitors)[25,35,49,51,53-55].

FROM DISORDER TO SYMPTOM

Up to the present, we have been speaking of depersonalization as a disorder but depersonalization often constitutes an important and relatively frequent symptom in other psychiatric and neurological diseases[11,52]. Some of the conditions to which depersonalization has been associated as a symptom are anxiety[2] and affective disorders[58], schizophrenia[59], other dissociative disorders[57], personality disorders such as borderline or anankastic[60-62] disorders due to substance abuse and neurological diseases such as epilepsy, especially of the temporal lobe, migraine and brain tumors. We could also find depersonalization experiences in cardiovascular, endocrine and metabolic diseases, although with less frequency[11].

DEPERSONALIZATION IN THE PANIC DISORDER

Although it has been described in many conditions, depersonalization is related, above all, with anxiety disorder and specifically with panic attack[5]. In 1959, Roth[30] described the phobic-anxiety depersonalization syndrome, that would be a presentation of the panic disorder in which the symptoms and signs of depersonalization-derealization (D-D) would predominate and that would lead to the appearance of avoidant behaviors equivalent to agoraphobic ones. In recent years, several authors have become interested in how the experiences of (D-D) affect panic disorder. Given that these experiences seem to bestow distinctive characteristics and greater severity to this disorder, some authors believe that the patients who present D-D during the panic attack could form a specific subgroup of patients with this disorder[2,3,63]. In the following, we present the most significant findings that have been described for this patient subgroup.

Clinical characteristics

Cassano et al.[2] indicated that the symptoms of patients with D-D correspond to the most severe forms of

panic disorder, presenting more avoidant behaviors, being more depressed, with earlier onset of the disorder and with greater comorbidity with other psychiatric disorders as obsessive-compulsive disorder (OCD) and generalized anxiety disorder (GAD). Along the same line, Segui et al.[3] found that this subgroup of patients is younger, with an earlier age at onset of the disorder, who present a greater clinical severity evaluated through the frequency of the panic attacks in the month prior to the study, of the measurements of anxiety, depression, phobia of blood, agoraphobia and anticipatory anxiety. The symptoms that are most associated to depersonalization are fear of becoming crazy, hot flashes, tremors and sweating, data that are consistent with those of the factorial studies[64-67]. On the other hand, the authors found an elevated comorbidity with the specific phobia. In a later study, Márquez et al.[4] corroborated the previous data and verified a greater functional deterioration in this subgroup of patients with D-D, which agrees with the findings of Hidalgo et al.[68], although these authors did not find distinctive clinical characteristics in the patients with D-D. Miller et al.[69] indicated that this subgroup is younger, with a shorter duration of the anxiety disorder and with higher scores on the measurements of stress/tension, depression, anxiety and fearfulness for the panic sensations. McWilliams et al.[70] found a greater frequency of traumatic history during childhood of these patients (neglect, rape and humiliation) on the contrary to the Marshall et al. study[71] in which no differences were found in this sense between patients with D-D and without D-D during the panic attack. Ball et al.[72] indicated that patients with D-D do not present differential characteristics in regards to onset age and duration of the disease, in the measurements of anxiety, depression, agoraphobia or in the personality traits.

Frequency of depersonalization-derealization symptom

The frequency of the D-D experiences during the panic attack varies substantially, ranging from 7.7 % and 69 % of the patients with panic disorder. According to Shiori et al.[73], this variability may be attributed to transcultural differences. Depersonalization appears in 50 % of the Anglo-Saxon[72,74-76] and Dutch patients[77], between 25 % and 30 % in the patients of Mediterranean samples[2,78] and in 10 % of the Japanese patients[73,79].

Neurobiological and etiological factors

The involvement of the temporal lobe in the etiopathogeny of the panic disorder was already suggested by Roth and his team when they found some similarities with complex partial epilepsy[80]. The ECA study (Epidemiologic Catchment Area Study)[81] shows an important association between the panic disorder and the epileptic episodes. In spite of the lack of efficacy of carbamazepine in this disorder[82], the data that are obtained from the clinical, neurophysiological and neuroimaging studies suggest that the panic disorder could be caused by alterations in the temporolimbic system[74,80,83-88]. This hypothesis that could be applied to all the forms of panic disorder seems to be especially valid for the D-D patient subgroup. In this sense, the study of Ontiveros et al.[89], done with MRI (magnetic nuclear resonance), stands out. It detects a subgroup of patients with panic disorder who have structural abnormalities in the temporal lobe and who are characterized by having an earlier onset of the disorder and a greater number of panic attacks in the month prior to the study, characteristics that agree with those of the patients with D-D from the Seguí et al. study[3]. Thus, the latter authors indicate that the temporolimbic dysfunction could be more important in the subgroup of patients with D-D, although this hypothesis must be proven with future neuroimaging studies.

TREATMENT OF DEPERSONALIZATION

In the previous sections, we have already commented that the depersonalization disorder is one of the least investigated dissociative conditions and that this is especially valid in the case of treatment[1]. The lack of investigation in this area explains why we do not have clear lines of biological and psychological treatment, so that depersonalization frequently becomes a condition that is refractory to these treatments and, thus, chronic[1,25]. In this section, we review the studies existing on the treatment of depersonalization and, to finish, we will make a brief commentary on the treatment of depersonalization as symptom.

Biological treatments

Pharmacological treatment

Although the resistance to pharmacotherapy is a widely recognized aspect by the clinicians, it seems that some patients may benefit from certain drugs. In the following, we present the results of the most recent studies that have been performed in this area, although it should be stressed that there are few controlled studies and the results are contradictory.

Given the relationship between depersonalization and the obsessive-compulsive disorder, several authors have been interested in the effect of SRI on the disorder in question in recent years. Hollander et al.[53] corroborates that the chronic experiences of depersonalization resolves in six of eigth patients treated with fluoxetine (5-80 mg/day) or fluvoamine (300 mg/day), clomipramine (400 mg/day) having little effectiveness. After, other authors re-verified the efficacy of the SSRI (selective serotonin reuptake inhibitors), in this case fluoxetine (20-60 mg/day) alone or combined with alprazolam (0.25 mg/day) or with buspirone (20 mg/day)[54,55,90]. Simeon et al.[25] indicated the

efficacy of clomipramine in two of seven patients with depersonalization. The authors established the follow-up of one of these patients for four years, verifying an almost complete remission of the picture, with relapses when an attempt was made to substitute paroxetine or fluoxetine in place of clomipramine.

Sierra et al.[91] have verified the efficacy of lamotrigine (200-250 mg/day) alone or combined with other drugs (SSRI and LITHIUM) in six of 11 patients with depersonalization (table 4).

Some authors have retrospectively studied the efficacy of the pharmacological treatment in patients with depersonalization. Simeon et al.[1] indicated that only the SSRI (fluoxetine and sertraline) and benzodiazepines had supplied some benefit to the patients in a group of 30 patients. In the Lambert et al. study[92], clomipramine (200 mg/day), imipramine (400 mg/day) and risperidone appeared as useful drugs, although the most effective ones were sertraline (100-200 mg/day) and clonazepam (1-8 mg/day), administered either combined or separately.

Electroconvulsive therapy and neurosurgery

Electroconvulsive therapy (ECT) is another modality of treatment that some authors have suggested[18,29,93], although the studies on its efficacy are contradictory. In the cases of severe and intractable depersonalization, neurosurgery has been recommended, specifically prefrontal leucotomy, although it is a rare practice[94,95].

Psychological treatment

Psychological treatment of the depersonalization disorder has been even less studied that the biological one. Although the controlled studies are limited, it can be concluded from most of them that this disorder also shows resistance to psychological treatment.

Sookman and Solyom[96] indicated the benefit of the behavior techniques (flooding in vivo/imagination, paradoxical intention, exposure with response prevention and thought stopping) especially when the anticipatory anxiety, phobic avoidance and obsessive symptoms worsen the depersonalization picture. Blue[97] verified the benefit of behavioral therapy (basically, paradoxical intention) in a patient with depersonalization.

Other therapeutic strategies that have been used from the behavioral area are progressive muscle relaxation, biofeedback and systematic desensitization[98].

Some authors state that depersonalization may respond to the self-hypnosis in patients with high hypnotizability[12].

In regards to psychodynamic therapy, Catell and Catell[22] indicate that the use of the couch is contraindicated in this type of patients. The sensation of unreality towards them and towards the surrounding is so great that the lack of visual contact with the therapists may increase these sensations to the point of panic. When depersonalization is clearly associated with psychological trauma, recovery of unconscious traumatic memory and cathartic release of associated emotions may be therapeutical.

Regarding support therapy, although the minor forms of the disorder may show a positive response, this type of therapy is generally ineffective in severe cases[99]. In any event, it is useful to reduce the stress caused by this disease[100].

Simeon et al.[1] retrospectively studied the efficacy of psychological treatment in 30 patients with depersonalization. A total of 28.83% had received psychotherapy having different duration and orientation (cognitive-behavior, hypnosis and acupuncture). The patients reported an improvement in their coping and introspection capacity and only one of them indicated a significant decrease of these experiences during the treatment (table 5).

Treatment of depersonalization as symptoms

When depersonalization is a symptom secondary to other psychiatric diseases, the effective treatment of the primary disorder generally resolves this symptom. We do not have studies that describe a specific treatment for

TABLE 4. Studies on the pharmacological treatment of the patients with despersonalization disorder

Study	*N*	*Treatment*	*Results*
Hollander et al.[53]	8	FLUOX, FLUV and CLOMI	FLUOX and FLUVO are effective and superior to CLOMI
Fitchner et al.[54]	1	FLUOX	Improvement of the anxiety and depersonalization but not total remission
Ratliff y Kerski[55]	1	FLUOX + ALPR	Total remission of the depersonalization
Abbas et al.[90]	1	FLUOX + BUSP	Total remission of the depersonalization
Simeon et al.[25]	8	Placebo (n = 8) (1 week) (blind)	The two drugs are superior to the placebo
		CLOMI (n = 8) (8 week) vs	CLOMI: 2 of 7 patients improve
		DESI (n = 8) (8 week)	DESI: 1 of 6 patients improve
		(randomized double blind)	
Sierra et al.[91]	11	LAM+SSRI + lithium or	
		LAM alone	6 of 11 patients show a clinically significant improvement

FLUOX: fluoxetine; FLUV: flovoxamine; ALPR: alprazolam; BUSP: buspirone; CLOMI: clomipramine; DESI: desipramine; LAM: lamotrigine; SSRI: selective serotonin reuptake inhibitors: citalopram, sertraline, fluoxetine and paroxetine.

TABLE 5. Therapeutic modalities used in the psychological treatment of depersonalization

Study	*Therapeutic modality*	*Comments*
Sookman and Solyom.[96]	Case 1: flooding in imagination	Case 1: almost complete remission
	Case 2: flooding in vivo + paradoxical intention + exposure of response prevention + thought stopping	Case 2: unimportant improvement
Blue[97]	Paradoxical intention + other behavior prescriptions	Almost complete remission
Talbot, Hales and Yudofski[12]	Self-hypnosis	It can be useful in patients with elevate hyponotizability
Talbot, Hales and Yudofski[98]	Progressive muscle relaxation Biofeedback Systematic desensitization	
Catell and Catell[22]	Psychodynamic therapy	The use of the couch is contraindicated
Kaplan and Sadock[100]		Useful if the depersonalization is associated to a psychological trauma
Shilder[99]	Support psychotherapy	Effective in the minor forms of the disorder
Kaplan and Sadock[100]		It reduces the stress caused by the disorder
Simeon et al.[1]	Cognitive-behavior therapy	One case improves and one case worsens
	Hypnosis	No changes are detected
	Acupuncture	No changes are detected

depersonalization associated to other diseases except one study that establishes a possible treatment for depersonalization association to panic disorder. This is the work of Miller et al.[69] who proposes including depersonalization induction tasks in interoceptive exposure in the treatment of patients who present depersonalization during panic attacks.

CONCLUSIONS

Depersonalization is a disorder that has received little attention in the research scope. In fact, the controversy and inconsistency in regards to the specific symptoms and characteristics associated have not yet been resolved. Some authors even question its validity as a diagnostic category.

The lack of epidemiological studies as well as studies in the clinical context and the difficulty to validly and reliably measure depersonalization explain the lack of knowledge that we have in regards to its incidence and prevalence.

The disease as such usually appears during adolescence or at the beginning of adulthood, following a usually chronic course. It presents a high comorbidity with personality disorders, especially with avoidance, borderline and obsessive-compulsive ones, the first one being associated with a greater severity of the picture.

In regards to the psychophysiological mechanisms of depersonalization, it seems that a dysfunction of the serotoninergic pathways could be involved. Neurophysiological and functional neuroimaging studies show abnormalities in the parieto-occipital lobes, which do not support the primacy of the temporal lobe described on many occasions or the neurobiological model proposed by Sierra and Berrios.

Neuroendocrine studies indicate a HPA axis deregulation in the sense that the activity of this axis is reduced.

On the cognitive level, depersonalization is marked by a particular perceptive and attentional vulnerability.

An association has been observed between depersonalization disorder and interpersonal trauma in childhood. Some authors suggest that emotional abuse may have a role in the pathogenesis of depersonalization.

Similarities with the obsessive-compulsive disorder in regards to phenomenology, comorbidity, neurochemistry and response to treatment suggest that depersonalization could make up an obsessive-compulsive spectrum disorder.

Depersonalization as symptom has been described in many psychiatric and organic conditions but above all it is related with the panic attack. Some authors indicate that patients with D-D during these attacks could form a specific subgroup within the panic disorder given the greater clinical severity (they score higher on the measurements of anxiety, depression and agoraphobia), greater comorbidity with other anxiety disorders, greater sociolaboral deterioration, earlier onset age and, thus, a more unfavorable prognosis. On the other hand, the temporolimbic dysfunction proposed by all the forms of panic disorder could be especially valid for this subgroup of patients.

On the therapeutic level, an elevated refractivity to the biological and psychological treatments that we have stands out, since although certain patients may benefit from the drugs with serotoninergic action and from the benzodiazepines, we cannot forget that many patients do not totally or partially respond to any type of medication. Thus the treatment of this disease is far from being satisfactory. In regards to psychotherapy, the present therapeutic strategies are scarce and of little utility.

Regarding depersonalization associated to panic disorder, some authors have proposed the inclusion of depersonalization-derealization induction experiments in the interoceptive exposure that could increase the efficacy of this technique and improve the therapeutic response of the patients.

FUTURE LINES OF INVESTIGATION

Given that depersonalization is a disorder that has been studied little, multiple research lines exist. The most important include epidemiological and clinical investigation that make it possible to study phenomenology, prevalence, incidence, psychophysiological mechanisms, morbidity and comorbidity of depersonalization, the design of the controlled studies on the efficacy of the pharmacological treatment and the design of the specific psychological intervention programs for this disorder.

In regards to depersonalization associated to panic disorder, prospective and follow-up studies must be performed to determine if the presence of depersonalization in the panic disorder is predictive of poorer results to the treatment. In this sense, the greater clinical severity and sociolaboral deterioration of this subgroup of patients that has been found in some studies must be considered. On the other hand, it would be interesting to study if the inclusion of induction experiments of depersonalization experiences in the interoceptive exposure increases the therapeutic efficacy of the technique in these patients.

One consideration, that is not really a future line of investigation, is that it is essential to unify criteria in regards to the concept of depersonalization in this area. Specific measurement instruments, validated with a population with depersonalization disorder and having satisfactory psychometric properties, must be used and investigation with larger samples must be carried out.

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