REVISTA NEUROCIÊNCIAS



# Comportamento Hipersexual e Esclerose Múltipla

## *Hypersexual Behavior and Multiple Sclerosis*

## *Comportamiento Hipersexual y Esclerosis Múltiple*

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## Resumo

**Introdução.** A esclerose múltipla (EM) está associada a uma ampla gama de distúrbios comportamentais. Embora a disfunção sexual seja comum, o comportamento hipersexual é raramente relatado e tem sido frequentemente associado a comorbidades psiquiátricas. **Objetivo**. Realizar uma revisão sistemática dos relatos dos séculos XX e XXI sobre o comportamento hipersexual na EM. **Método**. Realizou-se uma revisão sistemática dos relatos de casos nos séculos XX e XXI sobre comportamento hipersexual na EM. Foram analisadas referências da era da pré-neuroimagem e da literatura mais recente com neuroimagem. A pesquisa inicial no PubMed incluiu as palavras hipersexualidade, hiperlibidinismo, parafilias, distúrbios sexuais e esclerose múltipla. **Resultados**. Foram encontrados sete casos relatados na literatura pré-neuroimagem e dez na era da neuroimagem, e identificadas três categorias distintas de distúrbios de acordo com a predominância dos sintomas: aumento primário da libido, desinibição e doença generalizada. A análise das lesões a partir dos estudos de neuroimagem e autópsia revelou doença do lobo frontal, periventricular e generalizada na maioria dos casos. Casos de doença disseminada apresentaram mudança abrupta do comportamento sexual e menor idade de início do acometimento. **Conclusão**. Em resumo, comportamento hipersexual em pacientes com EM podem ser categorizados em grupos dependendo dos sintomas e local anatômico das placas. A revisão da literatura revelou frequentemente casos com manifestações neurocomportamentais graves. O espectro leve a moderado de mudanças comportamentais pode ser subnotificado devido ao estigma social.
**Unitermos.** Exibicionismo; Transtorno do Comportamento Sexual Compulsivo; Esclerose múltipla; Neuroimagem

## Abstract

**Introduction**. Multiple sclerosis (MS) is associated with a wide range of behavioral disorders. Although sexual dysfunction is common, hypersexual behavior is rarely reported and has often been associated with psychiatric comorbidities. **Objective**. To perform a systematic review of 20th and 21st-century reports of hypersexual behavior in MS. **Method**. A systematic review

of 20th and 21st-century case reports of hypersexual behavior in MS was performed. References from the pre-neuroimaging era and more recent neuroimaging literature were analyzed. The initial PubMed search included the words hypersexuality, hyperlibidinism, paraphilias, sexual disorders, and multiple sclerosis. **Results**. Seven cases reported in the pre-neuroimaging literature and ten in the neuroimaging era were found, and three distinct pathological categories were identified according to the predominance of symptoms: primary increase in libido, disinhibition, and generalized disease. Analysis of lesions from neuroimaging studies and autopsy revealed frontal lobe, periventricular, and generalized disease in the majority of cases. Cases of disseminated disease showed abrupt change in sexual behavior and younger age of onset. **Conclusion**. In summary, hypersexual behavior in patients with MS can be categorized into groups depending on symptoms and anatomical location of plaques. This literature review revealed frequent cases with severe neurobehavioral manifestations. The mild to moderate spectrum of behavioral changes may be underreported due to social stigma**.**
**Keywords.** Exhibitionism; Compulsive Sexual Behavior Disorder; Multiple Sclerosis; Neuroimaging

## Resumen

**Introducción**. La esclerosis múltiple (EM) se asocia con una amplia gama de trastornos del comportamiento. Aunque la disfunción sexual es común, el comportamiento hipersexual rara vez se informa y a menudo se ha asociado con comorbilidades psiquiátricas. **Objetivo**. Realizar una revisión sistemática de informes de los siglos XX y XXI sobre el comportamiento hipersexual en la EM. **Método.** Se realizó una revisión sistemática de reportes de casos de los siglos XX y XXI sobre conducta hipersexual en EM. Se analizaron referencias de la era anterior a la neuroimagen y literatura más reciente sobre neuroimagen. La búsqueda inicial en PubMed incluyó las palabras hipersexualidad, hiperlibidinismo, parafilias, trastornos sexuales y esclerosis múltiple. **Resultados**. Se encontraron siete casos reportados en la literatura preneuroimagen y diez en la era de la neuroimagen, y se identificaron tres categorías distintas según el predominio de los síntomas: aumento de la libido, desinhibición y enfermedad generalizada. El análisis de las lesiones mediante estudios de neuroimagen y autopsia reveló enfermedad del lóbulo frontal, periventricular y generalizada en la mayoría de los casos. Los casos de enfermedad diseminada aparecieron con un cambio abrupto en el comportamiento sexual y una edad de inicio más temprana. **Conclusión.** En resumen, el comportamiento hipersexual en pacientes con EM se puede clasificar en grupos según los síntomas y la ubicación anatómica de las placas. La revisión de la literatura reveló con frecuencia casos con manifestaciones neuroconductuales graves. Es posible que el espectro de cambios de comportamiento de leves a moderados no se notifique debido al estigma social.
**Palabras clave.** Exhibicionismo; Trastorno de Conducta Sexual Compulsivo; Esclerosis múltiple; Neuroimagen

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# INTRODUCTION

Psychiatric comorbidities are common in Multiple Sclerosis (MS). There is a high prevalence of anxiety (21.9%), depression (23.7%), bipolar disorder (5.8%) and psychosis (4.3%)[1]. The incidence of neurocognitive

impairment, such as dementia, is also higher in MS than in the general population (1.7% vs 0.7%)[2]. Factors including functional disability and lack of social support may be a significant component for mood disturbances in MS[3].

Sexual dysfunction (SD) is a common behavioral disturbance in MS, especially in association with depression, spinal cord lesions, and autonomic impairment, significantly affecting quality of life[4]. In most instances, there is no pathognomonic correlation between the topography of brain or spinal cord lesions and sexual dysfunction, although spinal cord disease is highly associated with impairment of sexual function, especially in men. Recent findings suggest an association between lesions in the occipital lobe, hippocampus, and left insula and sexual arousal impairment, and in the pons, left temporal periventricular, and right occipital areas to orgasmic dysfunction[5].

Neurological diseases associated with executive dysfunction, impulsivity and obsessive-compulsive disorder may also be associated with hypersexuality and alteration of internal sexual drive, such as increased libido (hyperlibidinism)[6]. In the extreme scenario, neurological dysfunction can lead to behaviors including acquired pedophilia and paraphilias[7]. The full spectrum of those abnormalities and anatomical localization has not been fully evaluated[7].

In MS, increased or inappropriate sexual behavior in patients without dementia or significant psychiatric impairment is rare. There is a single case series of

exacerbated sexuality in 4 out of 108 MS patients[8]. However, this investigation addressed hypersexuality as a secondary finding[8].

To our knowledge, there are no literature review studies evaluating the topic of hypersexuality in MS patients. No previous study conducted lesion analysis attempting to correlate hypersexual manifestations and the location of MS plaques. Thus, the aim of this review is to analyze all XX and XXI-century medical literature about hypersexual behavior in patients with MS. Part of our present study has been reported in abstract form elsewhere[9].

## METHOD

We reviewed the XX and XXI-century medical literature, comparing views about this topic from a pre- and recent neuroimaging era. Initially, we searched PubMed for all articles written in any language, using the terms multiple sclerosis and hypersexuality (nine papers), hyperlibidinism (one paper), pedophilia (one paper), paraphilias (five papers), and sexuality (751 papers).

After this initial step and reviewing all abstracts, we selected seven articles. Subsequently, we reviewed all references cited in those articles. We found six additional papers before the widespread use of head Computed Tomography (CT) or brain Magnetic Resonance Imaging (MRI) and four additional papers from the neuroimaging era.

Since the diagnostic criteria for MS evolved, from Charcot's triad to the modern diagnostic criteria evaluating

neuroimaging and cerebrospinal fluid studies, our analysis of the diagnosed MS patients throughout the centuries focused on the type of symptoms, change of behavior, neurological examination and lesion analysis based on neuroimaging and autopsy.

Thereafter, we categorized the cases according to pathways of sexual desire[6]. The first group consisted of hyperfunctional sexual excitation or increased libido. The second group is characterized by disinhibition (generally by frontal lobe disease), leading to abandonment of socially acceptable rules for sexuality. A third group was characterized by a mix of the two previous groups, usually associated with significant cognitive compromise and widespread disease.

Finally, reports from patients with MS with co-morbid psychiatric disorders were analyzed. In such cases, the conditions were classified according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) available at the time and assessed by psychiatrists.

## RESULTS

We found sixteen articles reporting hypersexual behavior in MS patients. We analyzed the literature prior to the Neuroimaging era (Table 1) and from the Neuroimaging era (Table 2), and we classified behavioral manifestations into three distinct categories according to the predominance of symptoms: increased libido (n=4), disinhibition (n=4), and widespread disease (n=5). Finally, we identified a group

of patients with a pre-existing psychiatric diagnosis (n=3). One patient was reported to have isolated transvestism, which was considered at that time as pathological.

Table 1. Case Reports and Case Series from the Pre-Neuroimagging Era.

| Paper | Sex | Age/Disease Duration/ hypersexuality | Group | Hypersexual Behavior | Other Psychiatric Mnifestations | Previous Psychiatric Disorders | Neurological Examination | Anatomical Studies | Therapeutic approach |
|---|---|---|---|---|---|---|---|---|---|
| Valentiner 1856[10] | M | 55/0/46 | Increased libido | Increased sexual desire and masturbation | Chronically depressed mood | None | Dysarthria, dizziness, unstable movement of the eyes, violent tremors, left body paralysis, lower limb paresthesias, ataxia, urinary retention and severe headaches | Autopsy: Periventricular, cerebral peduncle, pons and medulla oblongata lesions | No specific treatment for hypersexual symptoms |
| Lannois 1903[11] | M | 27/5/27 | Increased libido | Excessive masturbation, eroticism | Visual hallucinations and delusions | None | Nystagmus, intention tremor and ataxia | Autopsy: Lesions in extensive plaques in the frontal region evidenced by histological sections after autopsy | No specific treatment for hypersexual symptoms |
| Howes 1927[15] | F | 19/2/19 | Disihinbition | Sudden-onset risky sexual behavior | Drastic personality change, becoming easily irritable, defiant and emotionally labile | None | Scanning speech, nystagmus, amblyopia, intention tremors, paraparesis, absent abdominal reflex and pseudobulbar affect (uncontrollable laugher and crying) | No autopsy | No specific treatment for hypersexual symptoms |

Table 1 (cont.). Case Reports and Case Series from the Pre-Neuroimagging Era.

| Paper | Sex | Age/Disease Duration/ hypersexuality | Group | Hypersexual Behavior | Other Psychiatric Mnifestations | Previous Psychiatric Disorders | Neurological Examination | Anatomical Studies | Therapeutic approach |
|---|---|---|---|---|---|---|---|---|---|
| Langworthy 1941[13] | M | 27/0/27 | Disihinbition | Public masturbation | Drastic personality change, becoming combative, threatening, and euphoric | None | Left eye central scotoma, nystagmus, scanning speech, "signs of injury of the cortico-efferent and cerebellar pathways bilaterally", lower limbs ataxia | No autopsy | No specific treatment for hypersexual symptoms |
| | F | 52/25/37 | Disihinbition | Exhibitionism | Persecutory delusion, mild cognitive deterioration and memory deficit | Possibly major depression | Pallor of both optic discs, intention tremors, left lower and upper limb paresis, asymmetrical upper extremities paresthesias, sensory ataxia, ataxia of limb, and absent abdominal reflexes | No autopsy | No specific treatment for hypersexual symptoms |
| Ungerleider 1962[32] | M | 32/0/32 | - | None | Transvestic disorder | Possibly decreased libido | Optic disk pallor, diplopia, Ptosis, nystagmus, tetraparesis, asymmetric deep tendon reflexes and bilateral Babinski sign, upper and lower limbs paresthesias, ataxia of all extremities | No autopsy | - |
| Salguero 1969[12] | F | 11/3/10 | Widespread disease | Public masturbation | Manipulative and seductive behavior, visual and auditory hallucinations, lack of impulse control, severe cognitive impairment, and coprophagia | None | Optic atrophy, left exotropia, bilateral horizontal nystagmus, scanning speech, dysphagia, left terminal tremor of the hand, rigidity in all extremities, grasp reflex on the left hand, Babinski sign bilaterally, ataxia | Autopsy: Widespread presence of plaques, with particular limbic involvement in the orbitofrontal lobe, putamen, dorsal thalamus, substantia nigra, and red nucleus | Diphenhydramine, thioridazine and ascorbic acid did not achieve success. Methylprednisolone, 24 mg once daily due to suspected demyelinating disorder. The patient died at 11 years old. |

M = Masculine, F = Feminine. Age and disease duration represented in years.

Table 2. Case Reports from the Neuroimagging Era.

| Paper | Sex | Age/Disease Duration/ hypersexuality | Group | Hypersexual Behavior | Other Psychiatric Manifestations | Previous Psychiatric Disorders | Neurological Examination | Anatomical Studies | Therapeutic approach |
|---|---|---|---|---|---|---|---|---|---|
| Testa 1987[16] | M | 20/0/20 | Widespread disease | Compulsive masturbation and erotic delusion | Visual and auditory hallucinations | None | No signs of focal neurological disease or impairment of cranial nerves | MRI: widespread disease | No specific treatment for hypersexual symptoms |
| Huws 1991[14] | M | 28/4/24 | Widespread disease | Hypersexuality, disinhibition and assault at 26. Foot fetishism at 28 | Manipulative behavior and outbursts of temper | None | Bilateral optic atrophy, bilateral extensor plantars and a broad-based ataxic gait | MRI: Diffuse periventricular and frontal damage | Counseling, behavioral therapy, cyproterone acetate, and carbamazepine with slight improvement but never sustained |
| Ortego 1993[21] | F | 39/13/39 | Disihinbition | Incest, hypersexuality, zoophilia, exhibitionism, scoptophilia, ephebophilia. | None | Possibly major depression | Paraplegia and urinary incontinence | MRI: Extensive subfrontal, subtemporal, subparietal white matter and dorsomedial thalamus and right midbrain lesions. Autopsy: extensive plaques on centrum semiovale white matter, primarily periventricular and frontal lobes. Dorsal lateral geniculate nucleus of the thalamus. | No specific treatment for hypersexual symptoms |
| Gondim 2001[20] | F | 65/20/63 | Increased libido | Increased libido, excessive masturbation, and hyperexcitation | None | Anxiety (not specified) | Horizontal nystagmus, left lower limb paresis, lef upper and lower limbs paresthesia, diminished propioception and vibration in lower limbs, left upper and lower extremities dysdiadochokinesia, gait ataxia (EDSS: 6.0). | MRI: Bilateral deep white matter, periventricular, and internal capsule lesions in frontals parietal and occipital lobes | No specific treatment for hypersexual symptoms |
| Frohman 2002[18] | M | 36/11/27 | Widespread disease | Frequent masturbation, and inappropiate sexual contact with strangers | Cognitive decline, poor judgment, impulsivity. New onset substance-use disorder | None | Optic disk pallor, dysarthria, nystagmus, tetraparesis, paresthesias upper and lower limbs | MRI: Severe lesions in the hypothalamus and septal region | Fluvoxamine maleate and medroxyprogesterone acetate with improvement in behavioral control |
| Dubisar 2002[23] | M | 21/3/18 | Possibly related to primary psychiatric illness | Inappropriate sexual behaviors, pedophilia | Lack of awareness of his environment, and failure to develop appropriate peer relationships | Tourette's syndrome, pedophilia, and Asperger's syndrome | Not reported | MRI at the diagnosis showed white matter lesions (no specific location reported) | Guanfacine and risperidone with no new episodes of hypersexual behavior after the treatment |
| Yang 2004[19] | F | 51/9/51 | Increased libido | Increased libido and excessive masturbation | Ten days of new-onset impulsiveness, gambling | Major depression | Left lower limb paresis, hypoalgesia in the left cheek, lower limbs ataxia, constipation | MRI: Periventricular white matter lesions with no changes to previous studies before sexual exacerbation | The patient received Methylprednisolone 1g IV for five days followed by oral prednisone with immediate reduction of symptoms |

Table 2 (cont.). Case Reports from the Neuroimagging Era.

| Paper | Sex | Age/Disease Duration/ hypersexuality | Group | Hypersexual Behavior | Other Psychiatric Manifestations | Previous Psychiatric Disorders | Neurological Examination | Anatomical Studies | Therapeutic approach |
|---|---|---|---|---|---|---|---|---|---|
| Lopez 2005[17] | F | 11/0/11 | Widespread disease | Sexual disinhibition, excessive masturbation | New-onset substance use disorder, and multiple suicide attempts. Expansive affect, dysphoria, and abrupt mood changes | None | The general neurological exam revealed no significant signs of motor, sensitive or autonomic disturbance | MRI: Multiple supratentorial white matter lesions and frontal and temporal lobe atrophy, at 20<br>MRI: New onset multiple white matter lesions involving frontal lobes, periventricular region, corpus callosum and temporal lobes at 21 | Steroids led to some response at disease onset, but Clozapine and valproic acid-controlled impulsivity better |
| Smith 2009[24] | F | 41/0/41 | Psychiatric comorbidity | Paranoid delusions centered on sexual themes | Mood fluctuations, anhedonia, fatigue, weight gain, feelings of worthlessness, poor concentration, ideas of reference | 5-year visual hallucinations | Perseveration, decreased sensation to pinprick, joint position and temperature on feet bilaterally in the arch and on the toes on the right | MRI: Multiple periventricular lesions extending into deep white matter and corpus callosum | Aripiprazole with decreases in delusions, while interferon B-1a was prescribed when the patient was discharged. Later, the patient self-discontinued the antipsychotic, but no further episodes of hallucinations or delusions happened |
| Smith 2018[22] | M | 32/0/32 | Psychiatric comorbidity | New onset hypersexuality (not detailed) | Visual hallucinations, persecutory delusions | Bipolar disorder type 1, borderline personality disorder, and substance use disorder | Decreased peripheral vision, eye pain and urinary incontinence | MRI: Multiple cortical and cervical cord lesions | Carbamazepine and, lately, steroids, improved symptoms of hypersexuality and mood lability |

M = Male, F = Female. Age and disease duration represented in years.

There were seven cases from the pre-neuroimaging era (four case reports and two case series) and 10 from the neuroimaging era (ten case reports), comprising 17 cases (nine women and eight men). The mean age of hypersexual behavior onset was 31.8±13.7 years [28.3±10.9 years in older literature vs. 32.6±15.2 years in the neuroimaging literature (p=0.27)]. There was no significant difference in

the age of hypersexual behavior onset or in the interval between the reported onset of MS and the reported onset of hypersexual behavior among the old versus new literature. The frequency of clinical presentation characteristics - according to the symptom group - was similar between men and women. The group of patients with widespread disease (18.4±6.8) had a significantly lower age of hypersexual symptoms appearance when compared to increased libido (46.7±13.0) or disinhibition groups (30.5±8.0, $p<0.01$).

In the pre-neuroimaging literature, the spectrum of disorders was broad, but details about neuropsychological or psychiatric evaluation are scarce. A significant percentage had compulsive masturbation[10,11], public masturbation[12,13] and disinhibition[14]. A few cases were associated with drastic personality changes[13,15], and psychosis[11,12]. The Neuroimaging era literature revealed compulsive behavior[16], disinhibition[14,17], impulsivity[17-19], marked sexual arousal[14,20-22], fetishistic[14], and pedophilic disorder[23]. In several cases, behavioral changes occurred in association with MS exacerbation, sometimes at the time of diagnosis[16,17,22,24].

In the pre-imaging literature, the neurological exam was consistent in most cases with advanced MS, including significant cognitive impairment, involvement of the pyramidal and cerebellar systems, and in several instances also parkinsonism and optic neuritis (Table 1). In the current literature, neuroimaging studies showed a broad spectrum of structures affected, but most papers reported damage to periventricular white matter (Table 2). In most cases,

neurological examination was consistent with advanced disease, but isolated hypersexuality was found in two reports[16,17]. In the four autopsy cases, there were periventricular, frontal lobe lesions or widespread presence of plaques (Tables 1 and 2).

## DISCUSSION

Both in the pre-neuroimaging and neuroimaging era, MS-associated hypersexual behavior manifested in different patterns of symptoms. We identified three distinct groups: the first characterized by primary increase in libido, sexual appetite and increased sexual behavior; the second characterized by impaired inhibition of sexual behavior, more commonly due to frontal lobe lesions; and the third group, severe cognitive impairment, widespread disease and mix of the other two groups.

For the first group (primary increase in libido), significant changes were found involving increased sexual arousal, binge masturbation[19,20], in some cases, in association with gambling[19], or even visual hallucinations and delusions[11]. Despite the limited number of available imaging studies, periventricular white matter lesions were usually present[19, 20]. The second subgroup had frontal release and disinhibition. Hypersexual behavior secondary to frontal lobe lesions has been reported with other pathologies and is markedly linked to sexual disinhibition, compulsive masturbation, and exhibitionism[25]. In this review, we found patients with drastic changes in behavior, including sexual

disinhibition[13,15] and compulsive masturbation[13]. MRI revealed a new onset of multiple white matter lesions involving the frontal lobes, periventricular region[17,24], corpus callosum, and bilateral temporal lobes[17]. Steroids[17] and antipsychotics improved symptoms[17,24].

A third subgroup of patients showed a rapid progression depicted by the cases suggesting a widespread disease[12]. Severe behavioral changes occurred early in life and were present, including criminal behavior such as sexual assault[14,18], sudden paraphilia, impulsivity, poor judgment[16], and ephebophilia[21] during MS exacerbations. Some were refractory to several psychopharmacological approaches before the diagnosis of MS[17,24]. Diffuse brain damage occurred in such cases in the subfrontal, subtemporal, hypothalamus, and septal regions[14,18,21].

In two cases, isolated hypersexual behavior was found, even before significant findings on neurological examination[16,17]. A few MS patients had previously been diagnosed with psychiatric conditions, such as Tourette's syndrome, Asperger's syndrome[23], and borderline personality features, with[19] and without previous suicide attempts[17]. Regarding the differential diagnosis, the development of abrupt, unprecedented, bizarre behaviors in a patient with no previous history may suggest a new brain injury rather than a primary psychiatric condition.

As instances of hypersexuality or paraphilic sexual behavior occur in the general population[26], patients with MS may also be affected. While some reports in this review with

insidious presentations may represent a primary psychiatric condition, cases that occur with established MS or in the setting of an exacerbation or respond well to steroids are probably secondary to this condition. In terms of clinical management, no specific therapy was available in the pre-neuroimaging era, and psychiatric hospitalization was the only intervention. Other approaches included potassium iodine, herbal medicine, hyoscine injections, diphenhydramine, thioridazine, and ascorbic acid. In one report, the patient received steroids but died at age 11[12]. Steroids were used on a larger scale in the neuroimaging era, along with antipsychotics.

Risk-taking activity, impulsivity, and poor judgment may constitute a maniac/hypomanic episode secondary to a psychiatric condition[27]. A case of sudden occurrence of gambling, increased libido, and insatiable sex appetite in a married elementary teacher affected by MS for nine years exemplifies the importance of the differential diagnosis[19]. The patient received Methylprednisolone 1g IV for five days, followed by oral prednisone with immediate reduction of symptoms, most likely linking her condition to MS rather than a psychiatric manifestation[19]. MRI showed white matter, periventricular, and internal capsule lesions in the frontal, parietal, and occipital lobes[20] and the hypothalamus and septal region in the more severe case[18]. Structures involved in dopaminergic pathways, hypothalamus, septal nuclei, temporal-limbic area, and amygdala can cause disturbances

in pleasurable responses, perception of sexual behavior, and sexual preoccupation[28].

In parallel, patients with autonomic dysreflexia due to spinal cord lesions suffer sensory deficits and difficulties in sexual arousal or triggering of ejaculation. Women may experience a lack of vaginal lubrification and orgasm[29]. Patients with a blunted sexual expression may have an aberrant episode of sexual arousal or socially inappropriate sexual expression.

Although hypersexual symptoms mostly occurred at or several years after the diagnosis of MS, in some cases, they were observed long before the diagnosis of the disease. In many instances, it was the result of the lack of follow-up of the patient or due to limitations of the neurological evaluation from that time.

The evolution of MS & psychiatric diagnostic criteria limits the conclusions of this review. Only with the advances in neuroimaging could McDonald's criteria be proposed, leading to sensitivity in diagnosis[30]. However, due to the rarity of cases with hypersexual symptoms in MS, this review cannot disregard the broad approach to historical papers and the use of pre-neuroimaging diagnostic tools.

Another crucial point is that the definitions for pathological conditions evolved from a historical perspective. Medical literature in the XX century and the first DSM considered masturbation (onanism) pathological. The current understanding does consider hypersexuality an illness *per se* but requires its combination with other

impairments to characterize morbidity[31]. Therefore, for some patients presented in the reports with isolated increased frequency for and urges of sexual activity, the pathological meaning is clinically relevant only when significant distress is present. Ungerleider reported in 1962 a case of transvestism simultaneous with the beginning of symptoms with MS[32]. While previously considered a disease, a diagnosis of transvestic disorder does not apply to all individuals who dress in opposite-sex clothes but requires sexual excitement and suffering in this activity[33].

Hypersexual behavior and related disorders are rare in MS patients, usually presenting as increased sexual arousal, disinhibition or widespread disease. Still, a mild to moderate spectrum of behavioral changes may be more prevalent but underreported due to social stigma. In many studies, especially in pre-neuroimaging literature, there was no investigation for organic conditions nor a complete description of the psychiatric condition or comorbidities.

## CONCLUSION

In summary, MS patients commonly exhibit sexual dysfunction. Most develop hyposexuality, especially MS patients with spinal cord disease. However, our literature review discloses at least 3 types of hypersexual disorders: primary increase in libido (hyperlibidinism), disinhibition with loss of sexual control due to frontal lobe disease and widespread disease associated with cognitive impairment. The last group commonly is associated with rapid disease

progression, lower age of onset, abrupt change in behavior, refractoriness to psychotropic drugs and widespread neuroimaging findings. To our knowledge, this review provides the single and most comprehensive review on this subject. MS, being a central nervous system disease with a wide range of lesion sites, may serve as a model for understanding the neuroanatomy linked to hypersexual behavior.

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