Female sexual dysfunction in multiple system atrophy: does it matter?

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Sexual activity is a complex process requiring a coordinated functioning of the person's mental, autonomic, sensory, and motor systems and relies on the proper function of the neurological, vascular, and endocrine system as well as a healthy emotional state [1]. Indeed, chronic diseases have an impact on sexual function through both direct and indirect mechanisms [1]. Urogenital dysfunction is a cardinal diagnostic feature of multiple system atrophy (MSA) [2]. Nonetheless, while erectile dysfunction is a well-known feature of men with MSA, sexual function in women with MSA has been poorly investigated so far. Women are less prone to discuss sexual and genital issues at the doctor's office and, conversely, physicians frequently omit specific questions on sexual health if the patients are women.

In this issue of *Clinical Autonomic Research*, Raccagni and colleagues investigated sexual function using the standardized questionnaire Female Sexual Function Index (FSFI), in 25 women with MSA and 42 age-matched healthy controls [7]. Raccagni and colleagues are to be commended for performing the most comprehensive investigation of the pattern of sexual dysfunction in women with MSA by means of a female-specific instrument to date. The results unequivocally show severe sexual dysfunction in women with MSA. Namely, FSFI scores were significantly lower in sexually active women with MSA compared to control women, with greater involvement of the desire, arousal and lubrication domains. Moreover, the authors confirmed a high prevalence (56%) of genital hyposensitivity in women with MSA, previously described by Oertel and colleagues [4]. Sexual inactivity was much more prevalent in women with MSA (60%) than control women (12%), but the authors

did not investigate the potential underlying causes of this, either physical limitations or psychological factors. Among the areas of greater impairment in women with MSA, cognitive and behavioral components, such as sexual desire, are strongly influenced by central pathways mediating mood, while other domains, like arousal and lubrication, more probably reflect disturbances in lower autonomic pathways, specifically the degeneration of Onuf's nucleus that is involved in genital arousal in both sexes [8].

The study has some limitations, such as its relatively small sample size and the lack of a control group with MSA-like neurodegenerative disorders (e.g., Parkinson disease or adult-onset sporadic ataxias). It is well described that, in men, erectile dysfunction is a feature of prodromal MSA, predating the onset of parkinsonian or cerebellar motor dysfunction by several years [9]. A better understanding of sexual dysfunction in women with MSA is required to better characterize the phenotype of prodromal MSA in women and help early differential diagnosis. Raccagni and colleagues interviewed patients and controls about the onset of genital hyposensitivity. Only four women with MSA were able to describe the onset of symptoms. Anorgasmia and genital hyposensitivity were present at the onset of the disease in two of them, appeared within 2 years from the onset of motor dysfunction in a third woman, and developed after 9 years in a fourth. Further studies on larger cohorts of women affected by MSA and MSA-related disorders are needed to assess if symptoms of sexual dysfunction may be included in the criteria for possible prodromal MSA, opening a window for early diagnosis and intervention.

In the European MSA registry, including 437 consecutive patients, erectile dysfunction, known to severely impair quality of life, was reported in 84% of male patients, but only 2.5% received pharmacological treatment, which may indicate that sexual problems require additional medical attention [3]. Because effective pharmacological therapies for sexual dysfunction are available, sex life should be

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proactively investigated in MSA. Sexual dysfunction is also frequent in other neurodegenerative disorders. In patients with early Parkinson's disease, sexual problems are more frequently reported by male patients compared to women [5]. In a large prospective longitudinal study of patients with Parkinson's disease, higher levels of sexual activity were associated with better quality of life and lower depression scores in men, while no such association was found in women [6]. Both psychosocial and biological factors likely contribute to this difference, which is common also in the general population, and probably reflects a different proportion of sexually active people between the two sexes in this age range, cultural factors, and women having a greater difficulty reporting sexual problems. Further studies must evaluate the impact of the presence and treatment of different symptoms of sexual dysfunction on quality of life in patients with MSA. Such studies must ideally evaluate patterns of sexual dysfunction by comparing men and women with MSA, taking into consideration the biological differences between men and women affected by the same pathology.

In conclusion, clinicians caring for patients with MSA should pay attention to sexual issues, as discussing and treating sexual problems is not a small part of a holistic patient-centered approach. Characterizing all aspects of sexual dysfunction in women with MSA could unveil new insights to improve treatment and accelerate the early diagnosis of patients with possible prodromal MSA.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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