Journal of Parkinson's Disease xx (2022) x–xx
DOI 10.3233/JPD-223315
IOS Press

Short Communication

Gender Distribution in Deep Brain Stimulation for Parkinson's Disease: The Effect of Awake versus Asleep Surgery

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Accepted 30 May 2022
Pre-press 18 June 2022

Abstract. There is evidence that men are more likely to undergo deep brain stimulation (DBS) for Parkinson's disease (PD), suggesting that women are relatively undertreated. 121 consecutive PD patients undergoing awake with microelectrode recording and intraoperative clinical testing (30 patients, 5 women) or asleep MRI-guided and CT-verified (91 patients, 38 women) bilateral subthalamic nucleus DBS were included in this study. The results showed an increase of the proportion of female patients from 16.7% to 41.8% after changing our operative technique (OR = 5.61; 95%CI: 1.52–20.78; $p = 0.010$) from awake to asleep, suggesting that women are more likely to undergo DBS when operated asleep.

Keywords: Deep brain stimulation, gender, asleep, awake, MRI-guided, microelectrode recording

INTRODUCTION

Parkinson's disease (PD) affects men and women differently in various ways. For example, PD is more common in men [1, 2], and the disease presentation and healthcare behavior show considerable differences between genders. A recent review showed that men are more likely than women to undergo deep brain stimulation (DBS) of the subthalamic nucleus (STN), and this difference is greater than what can be expected based on prevalence alone [3]. It could therefore be that women with PD are relatively undertreated. After we changed the operative method at our center from an awake surgical procedure with microelectrode recording (MER) and intraoperative clinical testing (ICT) to an asleep MRI-guided and CT-verified approach, we noticed a change in gender distribution.

METHODS

121 consecutive patients, who underwent awake (30 patients, 5 women) or asleep (91 patients, 38 women) bilateral STN-DBS between 20 March 2018

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Table 1
Multinomial logistic regression with gender as factor, type of surgery as dependent variable and covariates listed in the table below. The means and standard deviations (SD) of the mean, as well as the odds ratio, the lower and upper boundary of the 95% confidence interval (CI) and the *p*-value are given. UPDRS, Unified Parkinson's Disease Rating Scale; PDQ-39, Parkinson's DiseaseQuestionnaire 39; PAS, Parkinson Anxiety Scale; BDI, Beck Depression Inventory;MoCA, Montreal Cognitive Assessment; QUIP, Questionnaire for Impulse Control Disorders in PD; ZCL, Disease Cognition List; ESS, Epworth Sleepiness Scale

Gender	Type of surgery	Mean	SD	Odds Ratio	95% CI Lower Boundary	95% CI Upper Boundary	*p*
Age				1.005	0.944	1.071	0.871
Women	Asleep	62.42	1.16				
	Awake	64.80	1.69				
Men	Asleep	62.04	1.37				
	Awake	61.00	3.78				
Disease duration				1.073	0.933	1.234	0.321
Women	Asleep	9.32	3.07				
	Awake	10.06	2.61				
Men	Asleep	9.21	3.48				
	Awake	9.71	4.15				
UPDRS I				0.943	0.929	1.072	0.369
Women	Asleep	12.26	5.31				
	Awake	11.20	2.39				
Men	Asleep	10.38	4.32				
	Awake	9.20	5.32				
UPDRS II				0.976	0.829	1.072	0.592
Women	Asleep	15.39	6.41				
	Awake	17.20	4.15				
Men	Asleep	16.25	8.37				
	Awake	14.40	6.08				
UPDRS III OFF				0.990	0.938	1.045	0.725
Women	Asleep	49.53	12.56				
	Awake	50.40	11.44				
Men	Asleep	51.79	13.19				
	Awake	49.60	13.48				
UPDRS III ON				0.968	0.903	1.038	0.361
Women	Asleep	19.79	8.49				
	Awake	20.40	12.10				
Men	Asleep	20.94	10.75				
	Awake	19.24	9.98				
UPDRS IV				0.861	0.737	1.005	0.058
Women	Asleep	11.37	3.12				
	Awake	11.00	1.41				
Men	Asleep	10.26	3.62				
	Awake	9.40	3.74				
PDQ-39				0.610	1.006	0.984	1.028
Women	Asleep	57.18	16.64				
	Awake	62.80	20.39				
Men	Asleep	44.64	20.82				
	Awake	45.88	19.19				
PAS Total				0.973	0.887	1.069	0.570
Women	Asleep	13.95	6.17				
	Awake	16.00	7.18				
Men	Asleep	10.45	5.76				
	Awake	9.52	7.04				
BDI				1.011	0.911	1.120	0.845
Women	Asleep	11.47	5.73				
	Awake	13.20	3.42				
Men	Asleep	11.17	6.69				
	Awake	10.39	5.20				
MoCA				1.079	0.925	1.258	0.334
Women	Asleep	25.89	3.11				
	Awake	25.60	2.88				

(*Continued*)

Table 1
(*Continued*)

Gender	Type of surgery	Mean	SD	Odds Ratio	95% CI Lower Boundary	95% CI Upper Boundary	*p*
Men	Asleep	25.36	4.52				
	Awake	25.95	1.88				
QUIP				0.955	0.824	1.107	0.541
Women	Asleep	25.89	2.22				
	Awake	25.60	0.00				
Men	Asleep	25.36	4.03				
	Awake	25.95	3.68				
DCL Total				0.992	0.909	1.081	0.848
Women	Asleep	42.63	6.84				
	Awake	40.60	2.51				
Men	Asleep	44.42	6.16				
	Awake	44.08	5.15				
ESS				0.802	0.661	0.973	0.072
Women	Asleep	5.84	3.85				
	Awake	3.80	2.68				
Men	Asleep	5.50	3.32				
	Awake	4.16	2.39				

and 21 September 2021, were included. Baseline data included age, gender, disease duration, Unified Parkinson's Disease Rating Scale part I-IV (part III ON and OFF medication), PDQ-39, Parkinson Anxiety Scale total score, Beck Depression Inventory, Montreal Cognitive Assessment, Questionnaire for Impulse Control Disorders in PD, Disease Cognition List total score, and Epworth Sleepiness Scale. On 1 July 2019 we changed our operative technique from awake MER-guided surgery to asleep MRI-guided and CT-verified surgery. There was no change in the way patients were recruited, screened, or considered suitable for surgery. All personnel and all preoperative procedures remained identical. Multinomial logistic regression was used to assess the relationship between type of surgery (asleep vs. awake, dependent variable) and gender (male vs. female, factor), with the other studied measures as covariates (Table 1). Statistical significance was set at $p < 0.05$.

RESULTS

The difference in gender distribution for both types of surgery is shown in Fig. 1. The proportion of female patients increased significantly from 16.7% to 41.8% after the change in operative method (OR = 5.61; 95%CI: 1.52–20.78; $p = 0.010$). The other investigated factors did not reach statistical significance (Table 1). Nevertheless, there was a trend towards statistical significance for UPDRS part IV in favor of female (OR = 0.861; 95%CI: 0.737–1.005; $p = 0.058$). There was a similar trend

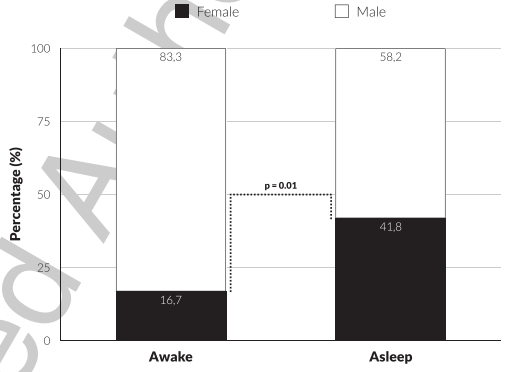

Fig. 1. Difference in distribution gender x type of surgery (awake vs. asleep).

for the Epworth Sleepiness Scale (ESS) (OR = 0.802; 95%CI: 0.661–0.973; $p = 0.072$).

DISCUSSION

Our findings provide a first indication that women are more likely to undergo STN-DBS when an asleep MRI-guided and CT-verified operative method was used. In fact, this change normalized the female-male ratio to closely the ratio as expected in the general population of PD. Similar findings have been reported for other neurosurgical treatment options for PD, such as pallidotomy and thalamotomy [4]. Furthermore, differences in gender distribution have been reported for surgery other than neurosurgery [5]. Prior to this switch, the gender distribution at our center resembled the international experience,

with a predominance of men opting for surgery at the time when this was still performed awake. The reason why men were previously more likely to undergo an awake surgical procedure is unclear. A possible explanation is gender referral bias [3]. However, this is unlikely since preoperative recruitment and screening were not changed. Furthermore, women with PD tend to be more anxious than men [1, 6], which might lead to women avoiding surgery [7]. However, our analysis showed no gender differences in anxiety. We also believe that our results were not influenced by any cultural differences, as all except for four (1 female) out of 121 patients had the same cultural background. We cannot rule out that some differences were missed, because of the unequal sample sizes resulting in a wide 95% CI. There was a trend towards statistical significance for UPDRS part IV in favor of female. This would be consistent with the existing literature that women are more likely to develop dyskinesias [1]. Regarding the similar trend in the ESS, both means would classify as normal based on the scale-specific cutoff criteria [8]. Therefore, this trend is not clinically relevant. Further prospective studies should confirm this finding, which may help to alleviate undesirable gender differences in Parkinson's care.

CONFLICT OF INTEREST

RSV acts as an independent consultant for Boston Scientific. The other authors have nothing to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

[1] Georgiev D, Hamberg K, Hariz M, Forsgren L, Hariz GM (2017) Gender differences in Parkinson's disease: A clinical perspective. *Acta Neurol Scand* **136**, 570-584.

[2] Savica R, Grossardt BR, Bower JH, Ahlskog JE, Rocca WA (2016) Time trends in the incidence of Parkinson disease. *JAMA Neurol* **73**, 981-989.

[3] Hariz GM, Nakajima T, Limousin P, Foltynie T, Zrinzo L, Jahanshahi M, Hamberg K (2011) Gender distribution of patients with Parkinson's disease treated with subthalamic deep brain stimulation; a review of the 2000-2009 literature. *Parkinsonism Relat Disord* **17**, 146-149.

[4] Hariz GM, Lindberg M, Hariz MI, Bergenheim AT (2003) Gender differences in disability and health-related quality of life in patients with Parkinson's disease treated with stereotactic surgery. *Acta Neurol Scand* **108**, 28-37.

[5] Rucker D, Warkentin LM, Huynh H, Khadaroo RG (2019) Sex differences in the treatment and outcome of emergency general surgery. *PLoS One* **14**, e0224278.

[6] Picillo M, Amboni M, Erro R, Longo K, Vitale C, Moccia M, Pierro A, Santangelo G, De Rosa A, De Michele G, Santoro L, Orefice G, Barone P, Pellecchia MT (2013) Gender differences in non-motor symptoms in early, drug naive Parkinson's disease. *J Neurol* **260**, 2849-2855.

[7] Hamberg K, Hariz GM (2014) The decision-making process leading to deep brain stimulation in men and women with parkinson's disease - an interview study. *BMC Neurol* **14**, 89.

[8] Johns MW (1991) A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep* **14**, 540-545.