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4	Correlation of antidepressant use and symptom time period in dream enactment
5	behaviors
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38 Main body:

39 It is with great interest that we read the article by Otaiku that investigated the effects
40 of dream content on future symptom exacerbation.1 In line with their study, we would like to
41 highlight three concerns.

42 First, the incidence of dream enactment behaviors (DEBs) due to antidepressant intake 43 should be considered. Antidepressants have been reported to cause DEBs.2 Considering that patients with Parkinson's disease (PD) are commonly comorbid with depression, the PD with 44 aggressive dreams group in this study may include patients with DEBs caused by 45 antidepressants, suggesting that depression comorbidity may be a confounding factor. 46 Although according to the article, "all patients were at an early stage and unmedicated at 47 48 baseline," neither the study nor the Parkinson's Progression Marker Initiative database 49 describes the rate of depression or the use of antidepressants. It would be helpful to specify the 50 antidepressants use to resolve this concern.

Second, clonazepam use may lead to cognitive decline. Otaiku reported that in patients in the PD with aggressive dreams group, cognitive function was significantly impaired. Since patients with rapid eye movement (REM) sleep behavior disorder (RBD) are often injured, it is necessary and appropriate to start medications to relieve DEBs to prevent injury. However, clonazepam, commonly used in DEB treatment, cause sedative side effects and impair cognitive function.3 The author could address the impact of medications on cognitive

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57 impairment by describing the use of DEB treatment at baseline and follow-up.

58 Third, the fluctuation in the symptoms of DEBs in PD patients was not considered. 59 DEBs in patients with idiopathic RBD or PD with RBD may diminish over time. Our previous study found that in patients with idiopathic RBD, the frequency of DEBs peaked 2-8 years 60 after RBD onset and decreased afterwards.4 Moreover, it was reported that RBD symptoms 61 62 improved after three years of follow-up in a quarter of PD patients with RBD.5 The DEBs seem to exacerbate for a while and then lessen in intensity, rather than worsen over time. 63 Therefore, when assessing the dream experience of patients with PD, there are three possible 64 situations: those who never had aggressive dreams; those currently experiencing aggressive 65 dreams; those who previously experienced aggressive dreams but are not currently 66 67 experiencing them. In the RBD screening questionnaire (RBDSQ), the period of aggressive 68 dream experience is not defined (e.g., the last six months). Therefore, patients who answered 69 "No" to item 3 of the RBDSQ, stating that "My dreams frequently have an aggressive or action-70 packed content," may include those who never experienced aggressive dreams before, and those who once experienced aggressive dreams but now no longer do. It remains to be 71 72 determined whether the group whose aggressive dreams have disappeared should be included 73 in the "without aggressive dreams" group or indicated separately. However, it is essential to clarify the time frame in the survey and obtain information on previous symptom occurrences. 74The proportion of those who have never experienced aggressive dreams before or whose 75

aggressive dreams have disappeared in the PD without aggressive dreams group should be

77 described.

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79 **Disclosures:**

80 Ethical Compliance Statement

- 81 No institutional review board or consent was obtained for this study. We have read the
- 82 Journal's position on issues involved in ethical publication and affirm that this work is
- 83 consistent with those guidelines.

84 **Funding sources and conflicts of interest**

- This study was supported by JSPS KAKENHI Grant Number 21K15745.
- 86 The authors declare that there are no conflicts of interest relevant to this work.

87 Disclosures for the previous 12 months

88 The authors declare that there are no additional disclosures to report.

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