

Emotional and Environmental Factors Aggravating Dream Enactment Behaviors in Patients with Isolated REM Sleep Behavior Disorder

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Objective: To identify emotional and environmental factors that aggravate dream enactment behaviors (DEBs) in isolated rapid eye movement (REM) sleep behavior disorder (iRBD).

Methods: In this cross-sectional study, a total of 96 polysomnography-confirmed iRBD patients (mean age, 68.5 years; men, 68%) and their caregivers completed questionnaires regarding potential aggravating factors related to DEBs, including emotion/feelings (stress, anger, anxiety, depressive mood, fatigue, pain), food (alcohol, caffeine, overeating in the evening, fasting/hunger), activities and sleep patterns (strenuous exercise, sex before bed, conflict/fighting, sleep deprivation, oversleeping, sleeping away from home, watching TV before bed), weather/environmental factors (cloudy or rainy weather, heat, cold, noise) and medication (skipping medication, taking hypnotics).

Results: The patients reported that stress (61%) was the most aggravating factor for DEBs, followed by anxiety (56%), anger (51%), fatigue (49%), and watching TV before bed (46%). Similarly, the caregivers reported that these factors were most relevant to the aggravation of DEBs in the patients, although some factors were ranked differently. In the subgroup analyses, aggravating factors for DEBs did not differ by RBD symptom severity. Interestingly, the proportion of patients experiencing DEB aggravation by stress, anxiety and depressive mood was significantly higher in women than in men. Furthermore, depressed patients reported that stress and cloudy or rainy weather made DEBs worse than nondepressed patients.

Conclusion: Our results suggest that DEBs in iRBD patients may be mainly aggravated by emotional factors. These negative effects appeared to be more prominent in female and depressed patients.

Keywords: REM sleep behavior disorder, dream enactment behavior, precipitating factors

Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by dream enactment behaviors (DEBs) due to a loss of muscle atonia during REM sleep.¹ A growing body of evidence suggests that patients with isolated RBD (iRBD) eventually develop a neurodegenerative disease, including Parkinson's disease (PD), dementia with Lewy bodies, and, less frequently, multiple system atrophy, with a conversion risk of over 80% in a decade or more.²

DEBs in patients with RBD range from simple motions such as limb jerking and sleep talking to complex and violent movements such as punching and kicking.^{3,4} Previous studies have shown that DEBs can result in sleep disruption and

life-threatening injuries for both patients and their bed partners.⁵ Accordingly, appropriate treatment should be considered depending on the symptoms in patients with RBD. The current treatment guidelines for DEBs in RBD include pharmacological agents, mainly clonazepam and melatonin.^{6,7} However, definitive conclusions cannot be drawn from recent randomized controlled trials, in which both drugs failed to show effectiveness in patients with iRBD and PD patients with RBD.^{8–10}

Bedroom environmental modifications are also recommended to prevent injurious behaviors for all patients with RBD. Recommended measures include removing dangerous objects from the bedroom, placing a mattress on the floor, and sleeping in separate bedrooms. However, these recommendations focus only on modifying the bedroom environment. In our experience, some patients with RBD complained of aggravation of DEBs after emotional stress or alcohol consumption. Furthermore, it has been reported that the worsening of DEBs was related to traumatic stress following a disturbing event^{1,11,12} or chocolate ingestion.¹³ These observations suggest that it is necessary for patients with RBD to avoid DEB precipitating factors, but there have been no studies to comprehensively explore such factors. Therefore, in this study, we aimed to identify the emotional and environmental factors that potentially aggravate DEBs in iRBD patients.

Methods

Study Design and Participants

We prospectively recruited consecutive patients with iRBD from the Department of Neurology at Seoul National University Hospital between 1 March 2020 and 31 August 2021. All participants underwent overnight video-polysomnography (PSG), and a diagnosis of RBD was confirmed based on the third edition of the International Classification of Sleep Disorders.¹⁴ The participants were excluded if they had any sign suggestive of neurodegenerative disease, such as parkinsonism and dementia, confirmed by a neurologist. This study was approved by the Review Board of the Seoul National University Hospital and written informed consent for research was obtained from all individuals who participated in the study (IRB No. 2007-189-1144). The study followed the principles of the Declaration of Helsinki.

Variables

Twenty-three potential precipitating factors related to DEBs were selected by seven RBD experts based on their clinical experience, including emotion/feelings (stress, anger, anxiety, depressive mood, fatigue, pain), food (alcohol, caffeine, overeating in the evening, fasting/hunger), activities and sleep patterns (strenuous exercise, sex before bed, conflict/fighting, sleep deprivation, oversleeping, sleeping away from home, watching TV before bed), weather/environmental factors (cloudy or rainy weather, heat, cold, noise) and medication (skipping medication, taking hypnotics). Patients and their caregivers were independently asked to respond either “yes” or “no” to the questions about whether the above factors aggravated DEBs in the past.

In addition, the clinical severity of RBD was assessed using the Korean version of the RBD Questionnaire-Hong Kong (RBDQ-KR).^{15,16} Depression was assessed using the Korean version of the Geriatric Depression Scale (GDS-K),¹⁷ and the cutoff value for the presence of depression was defined as ≥ 18 . Cognitive function was assessed using the Korean version of the Montreal Cognitive Assessment (MoCA-K).¹⁸

Statistical Analysis

All data are presented as the mean \pm standard deviation. Data distribution and normality were assessed using the Shapiro–Wilk test. Demographic and clinical characteristics were compared using the chi-square test for categorical variables and Student’s *t*-test or the Mann–Whitney *U*-test for continuous variables, as appropriate. We investigated the relationship between aggravation of DEBs by emotional and environmental factors and clinical variables, including age, RBD duration, and scores on the RBDQ-KR, GDS-K, and MoCA-K using point-biserial correlations for binary outcomes (aggravation yes/no). Furthermore, subgroup analyses were performed using the chi-square test or Fisher’s exact test to explore whether the association between DEB aggravation and emotional and environmental factors differs by sex, RBD symptom severity, the presence of depression, or severity of obstructive sleep apnea (OSA). Because this is an

exploratory study, no adjustments were made to control type I error. All *P* values were two-sided, and a *P* value of less than 0.05 was considered statistically significant. Calculations were performed with SPSS (IBM) version 27.

Results

A total of 96 iRBD patients and 84 caregivers were included in this study. The demographic and clinical characteristics of all patients are shown in [Table 1](#). The mean age of the iRBD patients was 68.5±6.7 years, and 65 (67.7%) were men. The patients had a mean RBD symptom duration of 7.0±5.4 years. The male group had a higher education level than the female group (*P*=0.006). The scores on the GDS-K, MoCA-K and RBDQ-KR did not significantly differ between men and women. All patients were receiving clonazepam and/or melatonin for RBD at the time of the study.

The results for potential DEB aggravating factors are shown in [Figure 1](#). Fifty-five patients (61%) and 56 (67%) caregivers answered that stress was the primary factor that aggravated DEBs. The other top 5 precipitating factors for DEBs were anxiety (56%), anger (51%), fatigue (49%) and watching TV before going to bed (46%) ([Figure 1A](#)). According to caregivers, the top 5 precipitating factors for DEBs were fatigue (62%), watching TV before going to bed (57%), anxiety (56%), and anger (50%), which was roughly similar to the responses according to the patients ([Figure 1B](#)). The results for potential DEB aggravating factors were not significantly different between the patients and their caregivers ([Supplementary Table 1](#)). Next, we examined which clinical parameters were associated with the top 5 precipitating factors for DEBs, and these results are summarized in [Supplementary Table 2](#). We found that the aggravation of DEBs by stress was correlated with higher GDS-K scores (*r*=0.230, *P*=0.024), whereas there were no significant correlations with the other clinical variables.

Table 1 Demographic and Clinical Characteristics

Variables	Total (n=96)	Men (n=65)	Women (n=31)	P value
Age, years	68.5 (6.7)	68.3 (6.7)	69.0 (6.9)	0.610
RBD duration, years	7.0 (5.4)	7.7 (6.0)	5.6 (3.6)	0.086
Male sex, %	65 (67.7%)	–	–	–
Educational level, years	12.4 (4.0)	13.3 (3.5)	10.7 (4.4)	0.006
GDS-K	6.7 (4.0)	9.2 (7.2)	10.7 (6.0)	0.323
MoCA-K score	25.9 (2.8)	25.7 (3.2)	25.4 (2.6)	0.657
RBDQ-KR score	46.3 (19.3)	44.6 (20.9)	50.0 (18.7)	0.222
Medication				
Clonazepam only, %	50 (52.1%)	33 (50.8%)	17 (54.8%)	–
Melatonin only, %	49 (51.0%)	28 (43.1%)	21 (67.7%)	–
Antidepressant, %	2 (2.1%)	1 (1.5%)	1 (3.2%)	–
Polysomnographic variables				
Time in bed, min	450.9 (54.9)	450.6 (60.0)	451.7 (49.2)	0.927
Total sleep time, min	345.9 (77.8)	340.2 (85.8)	354.2 (62.9)	0.426
Wake after sleep onset, min	86.7 (61.7)	90.3 (60.0)	84.3 (68.8)	0.665
Sleep efficiency, %	77.6 (13.7)	76.6 (13.8)	79.0 (14.6)	0.425
Sleep latency, min	16.0 (23.0)	14.0 (18.2)	20.2 (28.0)	0.276
REM sleep latency, min	112.7 (60.4)	111.2 (58.0)	127.6 (72.5)	0.244
N1 sleep, %	23.0 (15.8)	28.0 (15.3)	15.2 (12.1)	<0.001
N2 sleep, %	49.8 (14.2)	45.5 (12.0)	57.4 (14.2)	<0.001
N3 sleep, %	5.6 (7.0)	5.5 (6.3)	7.1 (9.4)	0.390
REM sleep, %	21.1 (6.9)	21.1 (6.6)	21.0 (6.7)	0.975
AHI, events/hour	14.6 (14.6)	16.8 (15.7)	9.1 (8.3)	0.003
Arousal index, events/hour	16.7 (18.5)	18.7 (19.2)	14.1 (16.6)	0.263

Notes: Data are n (%) and the mean (standard deviation). Bold values denote statistical significance at the *P* < 0.05 level.

Abbreviations: AHI, apnea-hypopnea index; GDS-K, Korean version of the Geriatric depression scale; MoCA-K, Korean version of the Montreal Cognitive Assessment; N1, non-REM sleep stage 1; N2, non-REM sleep stage 2; N3, non-REM sleep stage 3; RBDQ-KR, Korean version of the REM Sleep Behavior Disorder Questionnaire-Hong Kong.

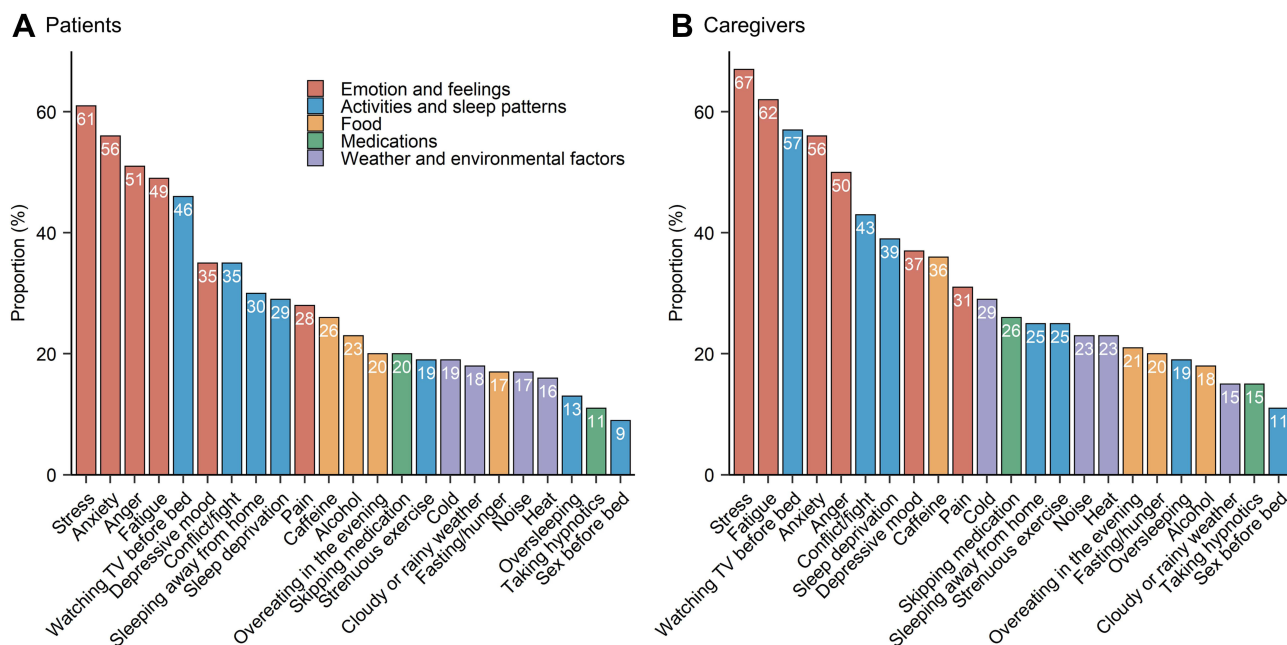


Figure 1 Dream enactment behavior aggravating factors, colored by category, according to isolated REM sleep behavior disorder patients (A) and their caregivers (B).

In the subgroup analyses, the female group had a higher proportion of DEB aggravation by stress ($P=0.026$), anxiety ($P=0.045$), and depressive mood ($P=0.022$) than the male group (Table 2). The proportion of DEB aggravation by alcohol was significantly higher in men than in women ($P=0.002$). A comparison between depressed and nondepressed patients, depressed

Table 2 Comparison of Precipitating Factors on Dream Enactment Behaviors Between Men and Women

Variables	Men (n=65)	Women (n=31)	P value
Emotion and feelings			
Stress	35 (53.8%)	24 (77.4%)	0.026
Anger	29 (44.6%)	20 (64.5%)	0.068
Anxiety	32 (49.2%)	22 (71.0%)	0.045
Depressive mood	18 (27.7%)	16 (51.6%)	0.022
Fatigue	29 (44.6%)	18 (58.1%)	0.218
Pain	15 (23.1%)	12 (38.7%)	0.111
Food			
Alcohol	21 (32.3%)	1 (3.2%)	0.002
Caffeine	17 (26.2%)	8 (25.8)	0.971
Overeating in the evening	14 (21.5%)	5 (16.1%)	0.534
Fasting/Hunger	10 (15.4%)	6 (19.4%)	0.625
Activities and sleep patterns			
Strenuous exercise	13 (20.0%)	5 (16.1%)	0.650
Sex before bed	8 (12.3%)	1 (3.2%)	0.153
Conflict/fight	20 (30.8%)	14 (45.2%)	0.168
Sleep deprivation	17 (26.2%)	11 (35.5%)	0.347
Overleeping	8 (12.3%)	4 (12.9%)	0.934
Sleeping away from home	19 (29.2%)	10 (32.3%)	0.763
Watching TV before bed	29 (44.6%)	15 (48.4%)	0.729

(Continued)

Table 2 (Continued).

Variables	Men (n=65)	Women (n=31)	P value
Weather or environmental factors			
Cloudy or rainy weather	12 (18.5%)	5 (16.1%)	0.780
Heat	11 (16.9%)	4 (12.9%)	0.612
Cold	10 (15.4%)	8 (25.8%)	0.221
Noise	13 (20.0%)	3 (9.7%)	0.204
Medication			
Skipping medication	12 (18.5%)	7 (22.6%)	0.636
Taking hypnotics	6 (9.2%)	5 (16.1%)	0.321

Note: Bold values denote statistical significance at the $P < 0.05$ level.

patients reported that stress ($P=0.026$) and cloudy or rainy weather ($P=0.05$) made DEBs worse than nondepressed patients (Table 3). Aggravating factors did not differ by RBD symptom severity or OSA severity (Supplementary Tables 3 and 4).

Table 3 Comparison of Precipitating Factors on Dream Enactment Behaviors Between Depressed and Nondepressed Groups

Variables	Depressed Group (n=13)	Nondepressed Group (n=83)	P value
Emotion and feelings			
Stress	12 (92.3%)	47 (56.6%)	0.026
Anger	10 (76.9%)	39 (47.0%)	0.071
Anxiety	10 (76.9%)	44 (53.0%)	0.138
Depressive mood	7 (53.8%)	27 (32.5%)	0.211
Fatigue	8 (61.5%)	39 (47.0%)	0.382
Pain	4 (30.8%)	23 (27.7%)	1.000
Food			
Alcohol	2 (15.4%)	20 (24.1%)	0.726
Caffeine	5 (38.5%)	20 (24.1%)	0.313
Overeating in the evening	5 (38.5%)	14 (16.9%)	0.126
Fasting/Hunger	3 (23.1%)	13 (15.7%)	0.450
Activities and sleep patterns			
Strenuous exercise	2 (15.4%)	16 (19.3%)	1.000
Sex before bed	1 (7.7%)	8 (9.6%)	1.000
Conflict/fight	8 (61.5%)	26 (31.3%)	0.058
Sleep deprivation	5 (38.5%)	23 (27.7%)	0.514
Oversleeping	2 (15.4%)	10 (12.0%)	0.664
Sleeping away from home	4 (30.8%)	25 (30.1%)	1.000
Watching TV before bed	6 (46.2%)	38 (45.8%)	1.000
Weather or environmental factor			
Cloudy or rainy weather	5 (38.5%)	12 (14.5%)	0.050
Heat	4 (30.8%)	11 (13.3%)	0.117
Cold	4 (30.8%)	14 (16.9%)	0.257
Noise	2 (15.4%)	14 (16.9%)	1.000
Medication			
Skipping medication	1 (7.7%)	18 (21.7%)	0.454
Taking hypnotics	3 (23.1%)	8 (9.6%)	0.168

Note: Bold values denote statistical significance at the $P < 0.05$ level.

Discussion

In this study, we investigated which emotional and environmental factors aggravate DEBs in iRBD patients. Our results showed that iRBD patients reported that emotional factors such as stress, anxiety, and anger were the factors that aggravated DEBs most frequently, which is roughly consistent with the results reported by their caregivers. In the subgroup analyses, the proportion of patients experiencing DEB aggravation by stress, anxiety and depressive mood was significantly higher in women than in men. Furthermore, depressed patients reported that stress and cloudy or rainy weather made DEBs worse than nondepressed patients. To the best of our knowledge, this is the first study to systematically investigate precipitating factors for DEBs in iRBD patients.

Previous studies found that post-traumatic stress disease (PTSD) is related to DEBs in patients with RBD as well as those with non-REM parasomnias,^{11,12} which is in line with our findings. While the precise mechanism of RBD in patients with PTSD remains largely unknown, it is suggested that the increased turnover of noradrenaline by PTSD results in its depletion in the peri-locus coeruleus, which causes dysfunction in the regulation of REM sleep atonia.¹⁹ Furthermore, there is also evidence showing that psychological stress itself, regardless of PTSD, provokes disturbances of noradrenergic function in various brain regions.²⁰ Given the potential role of noradrenaline in the occurrence of RBD,²¹ one can postulate that noradrenergic pathway alterations due to emotional stress contribute to the aggravation of DEBs in iRBD patients. Although stress has also been reported to increase serotonin turnover in the brain,²² it remains debatable whether the serotonergic system is directly involved in RBD pathogenesis.^{21,23} Alternatively, a recent animal study revealed that chronic stress provokes enhanced REM sleep,²⁴ which may partially explain our findings.

On the other hand, stressful events can result in highly traumatic or violent dreams.^{25,26} Considering the fact that verbal or motor components of dreaming are enacted behaviorally in iRBD patients,¹ changes in dream contents by stressful events may not only increase the occurrence of DEBs per se but also provoke more aggressive DEBs. In support of this hypothesis, a recent study showed that aggressiveness was more frequent in dreams related to DEBs in iRBD patients, although the frequency of aggressive dream contents did not differ between the patients and healthy controls.²⁷

Our results showed that the proportion of patients experiencing DEB aggravation by emotional factors was significantly higher in females than males, indicating sex-specific effects of precipitating factors for DEBs in iRBD patients. In general, females tend to have a higher prevalence and greater severity of mental disorders, including PTSD, panic disorder, and major depressive disorder.²⁸ Accordingly, it is plausible that the absolute proportion of patients experiencing emotional factors is higher in females, which may contribute to disparities between the sexes in factors aggravating DEBs. However, this possibility cannot be explained by our finding that there was no significant difference in depressive symptoms between men and women. On the other hand, sex differences in responses to the stress neuropeptide, which is a corticotropin-releasing factor, are thought to increase female vulnerability to stress in mental disorders.²⁹ In this context, increased stress sensitivity in females may be linked to sex differences in the emotional factors aggravating DEBs in iRBD patients.

Similarly, the impact of stress on DEB aggravation was more prominent in depressed patients than in nondepressed patients, which may be associated with emotion dysregulation.³⁰ Emotion regulation is a complex process that involves adjusting emotional responses to cope with difficult situations, and its impairment is regarded as a potential mechanism in the development of depression.³¹ Accordingly, we speculate that depressed patients have more severe emotion dysregulation, increasing vulnerability to stress.

In addition to emotional factors, “watching TV before bed” was one of the major factors aggravating DEBs in iRBD patients. It is well known that watching TV at night is associated with sleep problems, mainly due to exposure to bright light.³² However, considering the current finding of a potential association between emotional factors and DEBs, TV content may be more important than the act of watching TV itself in determining the extent of aggravation by watching TV. One patient had repetitively experienced DEBs more frequently and violently when he watched action movies or martial sports before going to bed. Unfortunately, our study did not include an analysis of the contents or duration of watching TV before bed, which needs to be performed in future studies.

A recent review suggests that patients with RBD should avoid alcohol consumption, as this factor can aggravate RBD-related symptoms.³³ Based on our experience, we also hypothesized that alcohol intake would be associated with

the worsening of DEBs in iRBD patients. However, only approximately one-quarter of our patients answered that alcohol intake aggravated DEBs, and alcohol intake was ranked 12th among 23 potential precipitating factors. This weak relationship may be due to the low frequency of alcohol consumption in this study sample. In the current study, the proportion of patients who consumed alcohol more than 2 times per week was just less than 10%. Consistent with this assumption, our results showed that the negative impact of alcohol intake on DEBs seemed prominent only in men, and not surprisingly, men (68%) were more likely to drink alcohol than women (10%).

The present study has several limitations. First, the assessment of DEBs or its aggravating factors was based on self-report and therefore may have the risk of introducing recall bias. However, given the night-to-night variability in DEBs, patient-reported outcome measures may be more reliable than objective outcome measures using PSG. Moreover, to minimize bias, we also included each caregiver's assessment, and the results were similar to those of patients. Second, because this study focused on the frequency of DEBs as an outcome measure, it still remains unclear whether exposure to emotional and environmental factors affect the severity of DEBs. Third, the sample size in subgroup analyses was modest in some cases, which may hamper the detection of significant associations. Additionally, our sample size was limited to the power to determine differences according to sex or the presence of depression in precipitating factors for DEBs. Fourth, the proportion of patients consuming alcohol in our dataset was relatively small. Furthermore, we did not obtain data on the quantity of alcohol consumption. For these reasons, a reliable conclusion about the association between alcohol intake and DEBs cannot be drawn from our results. Further studies with a larger sample size of regular alcohol-drinkers and detailed information on alcohol consumption, such as the frequency and intensity of alcohol consumption and the type of alcohol consumed, should be considered to clarify this issue. Fifth, although dream content changes may be one of the plausible mechanisms by which emotional factors were associated with DEB aggravation in our findings, we could not perform a dream content analysis due to lack of data. Last, the cross-sectional design of the current study prevented us from drawing conclusions about causality.

In summary, our results suggest that DEBs in iRBD patients may be mainly aggravated by emotional factors such as stress, anxiety, and anger. These effects were more prominent in females and depressed patients. Our results may emphasize the potential importance of emotional control as well as lifestyle modification to manage DEBs in iRBD patients. However, because this study design has potential biases from self-reported subjective data, further studies using objective measures of emotional factors and DEBs should be performed to clarify this issue.

Funding

This study was supported by a research grant of National Research Foundation funded by the Ministry of Science and ICT (MSIT) in Korea (NRF-2020R1C1C1013382), the Brain Research Program through the National Research Foundation of Korea funded by the Ministry of Science, ICT & Future Planning (2017M3C7A1029688) and the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIP) (2017R1A2B2012280).

Disclosure

Dr Carlos H Schenck reports personal fees from Eisai, Inc., outside the submitted work. The authors report no other conflicts of interest in this work.

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