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NUTRITIONAL STATUS AND COGNITIVE IMPAIRMENT AMONG THE VERY OLD IN A COMMUNITY SAMPLE FROM SOUTHERN BRAZIL

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Abstract: *Objective:* To determine which factors, especially those related to nutrition, are associated with cognitive function in the oldest old, here considered those at least 80 years of age. *Design:* A cross-sectional, population-based study. *Setting:* Veranópolis, Rio Grande do Sul, Brazil, and surrounding rural areas. *Participants:* Individuals aged 80 years and older. *Measurements:* The Mini Nutritional Assessment, anthropometric measurements, and serum levels of albumin and vitamin B12 were associated with cognitive function according to the Mini Mental State Examination (MMSE) and the Clock Drawing Test (CDT). Socio-demographic data were obtained through a structured questionnaire. Multivariate analysis was used to determine the associations. *Results:* According to the MMSE and the CDT, the prevalence of cognitive impairment was 47.7% [95%CI 39.7–55.7] and 58.2% [95%CI 50.3–66.1], respectively. In the adjusted analysis, the only positive linear association with MMSE scores indicating cognitive impairment was age. However, CDT scores indicating cognitive impairment were five times higher among those with low serum vitamin B12 concentrations. For the other variables, there was a positive association between age, being widowed, a low educational level and central nervous system drugs. Being single, living with children and living alone were protective factors for cognitive impairment. *Conclusions:* Although cognitive impairment was positively associated with old age, being widowed and low educational level in this population, the only nutritional variable positively associated with cognitive impairment was a low vitamin B12 concentration.

Key words: Cognitive aging, older adults, nutritional status, vitamin B12.

Introduction

According to data from the World Health Organization, there are now approximately 841 million people aged 60 years or older. This number is expected to double by 2025 and reach two billion by 2050, and 80% of these people will be living in low- and middle-income countries (1). According to 2010 census data, the current population of adults over 60 years of age in Brazil is approximately 20 million, and this number is projected to surpass 64 million by 2050, with adults over 80 years of age being the fastest growing demographic (2). Accompanying this population shift will be an epidemiological transition involving increased risk of infectious, chronic, neurodegenerative, and cardiovascular diseases among these individuals. Dementia is among the most frequent neurodegenerative alterations, leading to cognitive impairment, which is a devastating complication for older adults and their families (3, 4).

Although it is estimated that approximately 66% of the world's dementia cases occur in developing countries, less than 10% of the population surveys on neurodegenerative diseases, cognitive deficits, and dementia are performed in these countries (5, 6). Worldwide, the prevalence and incidence of dementia increase exponentially with age, doubling every 5 years after 60 years of age. After the age of 75, these rates are 15-20% and 2-4%, respectively (7).

Nutritional deficiency, particularly vitamin B12 deficiency and protein-calorie malnutrition, are associated with lower cognitive performance, even in individuals without dementia (8-10). Changes in nutritional status are predictors of cognitive impairment severity and progression (11). One study showed that low concentrations of vitamin B12 and increased homocysteine are related to accelerated cognitive function impairment (12). A lack of nutrients in the diet can lead to changes in the brain, which can lead to cognitive impairment. In other words, malnutrition, which leads to physical frailty, also leads to cognitive changes, leading to what has been called "cognitive frailty" (13, 14).

Since an association of these factors (malnutrition, frailty and cognitive impairment) is frequently found among the oldest old, which is the fastest growing population worldwide, study of these nosological entities is of vital importance. Despite the impact of neurodegenerative diseases on older adults, Brazilian studies on the subject are rare. Therefore, the objective of this study was to determine which factors, especially those related to nutrition, are associated with cognitive function in the oldest old, here considered those at least 80 years of age.

Methods

Study design and participants

This cross-sectional, population-based study, conducted in 2015, included very old residents of Veranópolis, Rio Grande do Sul, Brazil, and surrounding rural areas. Veranópolis is a city in the northeast region of the state of Rio Grande do Sul, 170 km from the state capital Porto Alegre. Its altitude is 705

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m and its climate is subtropical. Life expectancy in Veranópolis is approximately 77.9 years for women and 73.2 years for men, and among cities nationwide with over 17,000 inhabitants, it is ranked among the top twenty in life expectancy. Population estimates include 1010 individuals over 80 years old (357 men and 653 women) (15).

Ethics

This study adhered to the ethical principles involved in studies of this nature and was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments (16) as well as with Resolution 466/12 of the National Health Council. Prior to data collection, ethical approval was obtained from the Institutional Review Board of the Universidade do Vale dos Sinos (São Leopoldo, Rio Grande do Sul, Brazil). All participants gave informed consent prior to participation, and all information about the participants was kept strictly confidential.

Sample size

The sample size was calculated to estimate the prevalence of cognitive impairment based on a study by Herrera et al. (17) conducted in Catanduva, São Paulo, Brazil, which found a cognitive deficit prevalence of 23.5% in individuals aged 80 years and over. Considering a margin of error of 6 percentage points, a 95% confidence interval (CI) and adding 10% for eventual losses, 177 subjects were necessary.

To associate the above findings with malnutrition, the sample size was calculated based on the following assumptions: 95% CI, 80% power, 3:1 unexposed/exposed ratio, a 23.5% outcome prevalence among the non-exposed (17) and a prevalence ratio of 2, adding 10% for eventual losses, a total of 212 subjects were necessary.

Sample selection

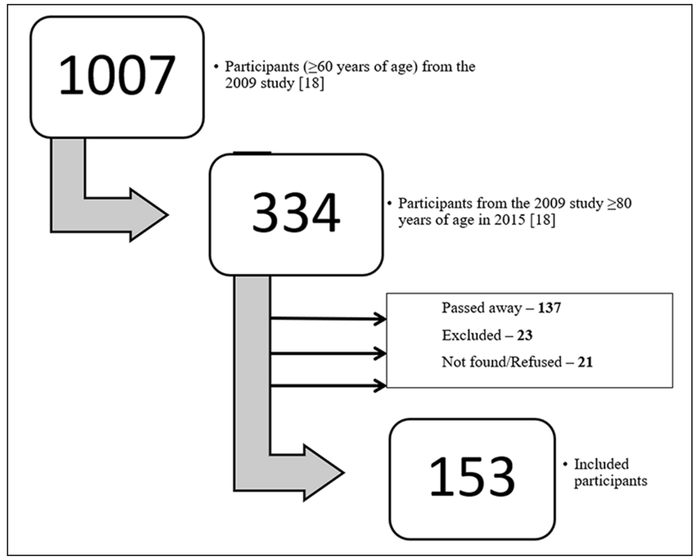
Participants were recruited from an older adult population that had participated in a 2009 study that characterized older adults in relation to an influenza vaccination campaign. By 2015, 334 of these participants would have been at least 80 years old. A systematic randomization process, described in Quatrin et al. (18), was used for this study. Of the 334 participants in the 2009 study, 153 were included in this study. The sample selection process is depicted in Figure 1.

Procedures and outcome measures

A structured, standardized and pre-tested questionnaire that included the demographic, socioeconomic, nutritional, cognitive, neurological and biochemical variables (serum vitamin B12 and albumin) was used for data collection. Data was collected at the city hospital in the participants' homes.

The study outcome was cognitive impairment, which was assessed with two neuropsychological tests: the Mini Mental State Examination (MMSE) and the Clock Drawing Test (CDT). The MMSE is a cognitive assessment scale that helps investigate and monitor the evolution of cognitive decline in individuals at risk of dementia, such as the oldest old. This scale has been widely used internationally since its initial publication by Folstein et al. (19).

Figure 1
Sample selection diagram for the 2009 and 2015 studies



The MMSE was adapted for Brazilian populations by Bertolucci et al. (20) and was modified by Brucki et al. (21) with the following cutoffs for normality according to years of education:
- Illiterate: ≥20 points
- ≤ 4 years: ≥25 points
- 5-8 years: ≥26 points
- 9-11 years: ≥28 points
- ≥12 years: ≥29 points

This version of the MMSE presented a sensitivity of 84% and a specificity of 60% with a cutoff point of 23/24 in a population of older adults treated at a mental health outpatient clinic (21).

The CDT is a simple and easily applied neuropsychiatric instrument for evaluating several cognitive functions (22). Over the past 20 years, the CDT has attracted considerable interest for its role in early screening for cognitive decline, especially in older adults, since it can detect changes more quickly than the MMSE due to greater sensitivity to early executive function. Three types of CDT scales have been developed, presenting similar results, although the Schulman scale had the best sensitivity (74.2-84.8%) and specificity (66.7-89.9%) (22).

Demographic variables included age group (80-84, 85-89, and ≥90 years), sex (male or female), marital status (married or living with a partner; single or widowed), and residence (urban or rural). The socioeconomic variable was completed years of education, which was distributed as follows: <4 years, 4 years, or ≥5 years.

Table 1
Distribution of altered Clock Drawing Test and Mini-Mental State Examination results according to independent variables among older residents of Veranópolis, Rio Grande do Sul, Brazil (n=153)

Variables	n	n%	%altered CDT	P-value*	%altered MMSE	P-value*
Age category						0.001
80 – 84 years	79	51.6	49.4	0.004	35.4	
85 – 89 years	48	31.4	62.5		47.9	
≥90 years	26	17	80.4		84.6	
Sex						0.311
Female	105	68.6	61.0	0.429	50.5	
Male	48	31.4	54.2		41.7	
Marital status						0.001
Married	59	38.6	59.3	0.047	32.2	
Widowed/single	94	61.4	58.5			
Living status						0.001
With partner	67	43.8	59.7	0.133	32.8	
With son/daughter	58	37.9	65.5		67.2	
Alone	28	18.3	42.9		42.9	
Living area						0.634
Urban	119	77.8	58.0	0.930	48.7	
Rural	34	22.2	58.8		44.1	
Educational level						0.125
≥5 years	31	20.3	45.2	0.017	38.7	
4 years	62	40.5	54.8		45.0	
<4 years	60	39.2	70.0		55.0	
Nutritional category						0.723
Eutrophic	51	33.3	60.8	0.599	47.1	
Overweight	67	43.8	61.2		46.3	
Obese	35	22.9	51.4		51.4	
Waist circumference						0.702
Normal	59	38.6	61.0	0.662	48.9	
Abdominal obesity (F ≥88 cm, M ≥102 cm)	94	61.4	57.4		45.8	
Mini Nutritional Assessment						
Normal (>13.5)	143	93.5	58.7	0.938	46.9	0.421
Light malnutrition (17–23.5)	10	6.5	60.0		60.0	
Daily medications						
0–3	55	35.9	61.8	0.887	56.4	0.349
4–6	52	34.0	53.8		38.5	
≥7	46	30.1	60.9		47.8	
CNS drugs						
None	73	47.7	52.1	0.104	45.2	0.553
≥1 type	80	52.3	65.0		50	
Vitamin B12						
>200 pg/mL	133	86.9	56.4	0.115	46.6	0.484
≤200 pg/mL	20	13.1	75.0		55.5	
Serum albumin						0.039
> 3.5 g/dL	146	95.4	56.8	0.023	45.9	
≤3.5 g/dL	7	4.6	100.0		85.6	

*Fischer's Exact Test Chi-Square for Linear Trend; CDT, clock drawing test; MMSE, Mini Mental State Examination; CNS, central nervous system; MNA, Mini Nutritional Assessment; n, absolute frequency; n%, relative frequency; F, female; M, male; P, statistical significance; Significance set at 5% for all analyses; Bold font indicates statistical significance.

Table 2
Odds ratio for altered Clock Drawing Test results according to independent variables among older residents of Veranópolis, Rio Grande do Sul, Brazil (n=153)

Variables	Unadjusted OR [95%CI]	P-value*	Adjusted OR [95%CI]	P-value*
Age category				
80 – 84 years	1		1	
85 – 89 years	1.71[0.82–3.55]	0.005	2.95[1.21–7.18]	0.001
≥90 years	4.31[1.48–12.6]		6.35[1.85–21.78]	
Marital status				
Married	1		1	
Widower	1.12[0.57–2.21]	0.117	8.73[1.22–62.50]	0.035
Single	0.11[0.01–1.01]		0.33[0.03–3.92]	
Living status				
With partner	1		1	
With son/daughter	1.28[0.62–2.66]	0.140	0.10[0.01–0.79]	0.036
Alone	0.51[0.21–1.24]		0.07[0.01–0.53]	
Educational level				
≥5 years				
4 years	1.47[0.62–3.51]	0.018	1.92[0.68–5.44]	0.005
<4 years	2.83[1.16–6.95]		4.96[1.54–15.96]	
CNS drugs				
None	1		1	
≥1 type	1.71[0.89–3.28]	0.105	2.48[1.11–5.56]	0.025
Vitamin B12				
>200 pg/mL	1		1	
≤200 pg/mL	2.32[0.80–6.75]	0.123	5.37[1.44–19.97]	0.012
Serum albumin				
> 3.5g/dL	1		1	
≤3.5g/dL	4.55[0.53–38.79]	0.165	2.88[0.30–27.39]	0.353

*Wald test (heterogeneity and linear trend); OR, Odds Ratio; CDT, clock drawing test; CNS, central nervous system; n, absolute frequency; 95%CI, 95% confidence interval [superior–inferior limits]; P, statistical significance; Significance set at 5% for all analyses; Bold font indicates statistical significance.

The participants' nutritional status was assessed through anthropometric and body composition measurements (e.g., body weight, height, body mass index [BMI], and waist circumference), as well as through the Mini Nutritional Assessment (MNA) (11) and biochemical markers (serum vitamin B12 and albumin). Based on the weight and height measurements, BMI was calculated using World Health Organization cut-off points: eutrophic (from 18.5 to 24.9kg/m2), overweight (25 to 29.9 kg/m2), and obese (≥30 kg/m2). Waist circumference was used to assess abdominal obesity: ≥88 cm for women and ≥9 cm for men (23).

The MNA was developed to detect malnutrition in older adults (11). It consists of simple anthropometric measurements, such as BMI, abdominal circumference, arm circumference, leg circumference, wrist circumference, and weight loss percentage in the last year. Among the oldest old, fat tends to be redistributed to the central region, which compromises the value of abdominal circumference measurements. The MNA also includes a global patient assessment (six questions related to lifestyle, drug use and functional capacity), subjective assessment (self-perception of health and nutrition), and a dietary questionnaire (eight questions related to the number of meals, food and liquid intake, and autonomy with respect to meals) (11). The validated MNA scores anthropometric measurements (wrist circumference and BMI), food intake, motility, psychological problems or acute diseases and global assessment (arm circumference, leg circumference, medication, skin lesions, eating habits, and self-reported health status) as separate stages. A score >12 points for the anthropometric measurements classifies the individual as eutrophic and the survey is interrupted, whereas scores ≤11 points require application of the global assessment. Final scores >24 points indicate well-nourished/normal individuals, scores between 17-23 points represent a risk of malnutrition/borderline, and scores <17 represent malnutrition (24).

Serum albumin measurement was performed because it is the most abundant plasma protein (up to 50% of total human serum proteins) (25). Blood albumin levels were determined with the calorimetric method (26). Serum albumin concentrations ≥3.5 g/L were considered normal (27, 28). Vitamin B12 was measured with the immunoassay technique (PerkinElmer, Wallac Oy, Turku, Finland). Vitamin B12 serum concentrations ≥200 pg/mL (148 pmol/L) were considered normal (8, 29).

Medication use was assessed by counting the number of daily medications reported by the participants, including the number of general purpose (0-3, 4-6, and ≥7) and central nervous system drugs (none or ≥ 1).

Data organization and analysis

EPIDATA version 3.1 was used for data processing, double entry in the database and review. Using Fisher's exact test and the chi-square test for linear trend, absolute (n) and relative (n%) frequencies of the independent variables were described in relation to the outcome. Due to the dichotomous outcome and the relatively small sample size, logistic regression was used to assess crude and adjusted odds ratios. The adjusted analysis only included variables whose statistical significance reached P ≤0.2. A significance level of P ≤0.05 was used to detect associations. All analyses were conducted in STATA version 12.1.

Results

Of the 334 elderly participants in the 2009 study who would have been 80 years or older in 2015, 137 had passed away, 23 were excluded, and 21 could not be located or refused to participate. Thus, 153 elderly subjects aged 80 years or older were included in the analysis (Figure 1).

The mean age of the participants was 86 years (standard deviation ±4). Most were female (69%), widowed or single (62%), and lived in urban areas (78%), with up to 4 years of education (80%). Of the total sample, 102 participants (67%) were overweight or obese (BMI ≥25), 61% of whom had abdominal obesity. Only 6.5% of the participants were classified as having mild malnutrition according to MNA criteria, and no one met the BMI, waist circumference, arm circumference, and leg circumference malnutrition criteria. A total of 64% of the participants reported taking at least four or more medications, and 52.3% reported taking a central nervous system drug. The biochemical measurements indicated that 13% had serum vitamin B12 levels ≤200 pg/mL and only 5% had serum albumin levels ≤3.5 g/dL (Table 1).

The prevalence of cognitive impairment was 58.2% (95% CI 50.3–66.1) and 47.7% (95% CI 39.7– 55.7), according to the CDT and MMSE (data not shown), respectively. A higher prevalence of cognitive impairment was found among the following groups: individuals ≥90 years, widows/widowers, those with low education, and those with low serum albumin levels (Table 1).

Table 2 shows the adjusted analysis for cognitive impairment according to the CDT. The odds of cognitive impairment increased linearly with age (the odds of an altered CDT was six times higher for individuals ≥90 years than for those aged 80–84 years), and there was a ninefold increase among widows/widowers and singles. Cognitive impairment was linearly and inversely correlated with educational level (the odds were five times higher among those with ≤4 years of education than for those with ≥5 years) and was 2.5 times higher among those who used central nervous system drugs. In general, being single and living with children or alone were protective factors for cognitive impairment. The chance of cognitive impairment was also five times higher among those with low serum vitamin B12 concentrations.

In the adjusted analysis, the odds of having altered MMSE results were 7 times greater among participants ≥90 years old than among those between 80–84 years. Although not significant, participants with low serum albumin were 6 times more likely to have altered MMSE results than those with normal albumin levels (Table 3).

Discussion

The main objective of this study was to evaluate the relationship between nutritional status and cognitive function among very old community-dwellers (over 80 years of age). Herrera et al. (17) reported a cognitive impairment prevalence of 23.5% among individuals aged over 80 years in Catanduva, São Paulo, Brazil. We found a much higher prevalence: 58.2% and 47.7% according the CDT and MMSE, respectively. This may be due to the high frequency of central nervous system drugs used in our population (51% of our participants used central nervous system drugs).

The prevalence of cognitive impairment, which was assessed with the MMSE and CDT, was higher at older ages, among widows/widowers, and among those with a lower educational level. Participants who reported using central nervous system drugs also had greater cognitive impairment according to the CDT. Inouye et al. (30) reported that older Americans whose cognitive screening performance was in the highest tertile had a higher educational level, higher family income, better health conditions, no depressive symptoms (reporting fewer central nervous system drugs) and greater participation in social and physical activities than those whose performance was intermediate or low. Similarly, in a study by Ylikosk et al. (31), groups who performed better on cognitive screening tests participated more frequently in social activities and had a higher educational level. Our findings agree with these studies, since participants with a higher educational level and lower consumption of central nervous system drugs showed less cognitive impairment.

In the adjusted analysis, living alone or with a child reduced the chance of cognitive impairment in the CDT results, which seems contradictory. Our interpretation is that those who reported living alone may be more independent due to better health, while those who live with their children would have more cognitive stimuli due to being surrounded with other

Table 3
Odds ratio for altered Mini Mental State Examination results according to independent variables among older residents of Veranópolis, Rio Grande do Sul, Brazil (n=153)

Variables	Unadjusted OR [95%CI]	P-value*	Adjusted OR [95%CI]	P-value*
Age category				
80 – 84 years	1		1	
85 – 89 years	1.66[0.81–3.48]	0.001	1.75[0.77–4.01]	0.001
≥90 years	10.02[3.13–1.98]		7.11[2.10–24.08]	
Marital status				
Married	1		1	
Widower	3.28[1.64–6.58]	0.001	2.77[0.58–13.23]	0.257
Single	0.35[0.04–3.12]		0.58[0.06–5.98]	
Living status				
With partner				
With son/daughter	4.20[1.99–8.88]	0.001	0.18[0.22–6.09]	0.433
Alone	1.53[0.62–3.79]		0.61[0.12–3.01]	
Educational level				
≥5 years	1		1	
4 years	1.30[0.54–3.14]	0.123	1.14[0.41–3.20]	0.334
<4 years	1.94[0.80–4.68]		1.40[0.45–4.32]	
Serum albumin				
> 3.5 g/dL	1		1	
≤3.5 g/dL	7.07[0.83–6.24]	0.073	6.16[0.61–62.50]	0.104

*Wald test (heterogeneity and linear trend); OR, Odds Ratio; MMSE, Mini Mental State Examination; CNS, central nervous system; n, absolute frequency; 95%CI, 95% confidence interval [upper–lower limits]; P, statistical significance; Significance set at 5% for all analyses; Bold font indicates statistical significance.

people.

Regarding the nutritional status and cognitive impairment according to the CDT, participants with low vitamin B12 levels had a fivefold higher chance of scoring lower on the CDT than those with normal levels of this vitamin, which is considered fundamental for neuronal function. Vitamin B12 deficiency is common among older adults, reaching 2–4% (10) due to atrophic gastritis, which increases with aging and leads to absorption difficulties (32). Vitamin B12 deficiency may be associated with neurological deterioration and cognitive impairment (33), which corroborates the results of our study. In clinical practice, it is accepted that dementia due to vitamin B12 deficiency is considered a potentially reversible form: once the deficiency is corrected, there is often a reversal of cognitive impairment (34).

While cross-sectional studies have shown an association between low plasma vitamin B12 levels and low MMSE scores, the results from prospective studies been controversial (35). It should be considered that our sample had a very low percentage of altered serum vitamin B12 and albumin levels. Although not significantly associated, effect measures were found for these biochemical markers for both cognitive impairment assessment tools in the crude and adjusted analyses. However, this was a relatively well-nourished population, with only 20 participants having altered vitamin B12 levels and 9 having altered albumin levels. Therefore, the existence of type II statistical errors cannot be dismissed.

Regarding other nutritional status assessments (e.g., BMI, abdominal circumference, arm circumference, MNA), only the MNA identified mild malnutrition (6.5%) among the participants. No significant association was found between these variables and cognitive impairment. Data from the literature show a positive association between BMI and lower morbidity and mortality after 70 years (36, 37).

Although our study failed to demonstrate this relationship, it is reported that abdominal obesity increases the risk of cognitive impairment (38) by indirect mechanisms such as hyperinsulinemia and increased cytokines, as well as by direct mechanisms, such as vascular (mainly cerebrovascular) diseases (39). Despite the prevalence of altered CDT and MMSE results in participants with mild but non- significant nutrition deficits according to the MNA, the literature reports that cognitive impairment may lead to malnutrition, inducing increased or decreased weight or nutritional deficit. Apathy, lack of initiative, and a reduced sense of smell contribute to reduced food intake, which is mediated by less motivation to prepare meals, a higher likelihood of missing meals, and a decreased interest in food. Another possible explanation for weight loss in cognitively impaired individuals could be decreased appetite due to limbic system dysfunction and changes in the hypothalamus (40). These mechanisms could explain the controversial results of previous studies (41).

Our findings corroborate the idea that cognitive performance in older adults is a process and the result of different factors associated with lifestyle and socioeconomic and health conditions (e.g., an absence of chronic degenerative and psychiatric diseases) (31, 33, 42). The sample loss was important limitation of our study, and selection bias cannot be dismissed.

The prevalence of cognitive impairment according to the MMSE and CDT was higher among the oldest age group, widows/widowers, and those with less education. A significant association was found between low serum vitamin B12 concentration and cognitive impairment according to the CDT. Since this population had a low prevalence of albumin deficiency and malnutrition according to the MNA and anthropometric measures, the sample may not have had enough power to detect an association between cognitive impairment and the proposed nutritional aspects.

Compliance with Ethical Standards: This study adhered to the ethical principles involved in studies of this nature and was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments as well as with Resolution 466/12 of the National Health Council. Prior to data collection, ethical approval was obtained from the Institutional Review Board of the Universidade do Vale dos Sinos (São Leopoldo, Rio Grande do Sul, Brazil). All participants gave informed consent prior to participation, and all information about the participants was kept strictly confidential.

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