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Risk factors across the life course and dementia in a Brazilian population: results from the Sao Paulo Ageing & Health Study (SPAH)

Marcia Scazufca,[1,2,3]* Paulo R Menezes,[2,3,4] Ricardo Araya,[2] Vanessa D Di Rienzo,[1,3] Osvaldo P Almeida,[5] David Gunnell[6] and Debbie A Lawlor[6]

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Background Several mechanisms have been suggested to explain the association between adversities across life and dementia. This study aimed to investigate the association between indicators of socioeconomic disadvantages throughout the life-course and dementia among older adults in Sao Paulo, Brazil and to explore possible causal pathways.

Methods We used baseline data from the SPAH study which involved participants aged 65 years and older ($n = 2005$). The outcome of interest was prevalent dementia. Exposures included in the analyses were socioeconomic position (SEP) indicators in childhood (place of birth and literacy) and adulthood (occupation and income), anthropometric measurements as markers of intrauterine and childhood environment (head circumference and leg length), smoking, diabetes and hypertension. Logistic regression models were used to test the hypothesized pathways and to assess whether there was an association between cumulative adversities across the life course and prevalent dementia.

Results Indicators of socioeconomic disadvantage in early life were associated with increased prevalence of dementia. This association was partially mediated through adulthood SEP. Head circumference and leg length were also clearly associated with dementia but there was no evidence that this association was mediated by early life socioeconomic disadvantage. There was an association between cumulative unfavourable conditions across the life course and dementia.

Conclusions Early life disadvantages seem to operate through biological mechanisms associated with passive brain reserve and opportunities in life representing active cognitive reserve. Prevention of dementia should start early in life and continue through life span as seen with many other chronic diseases.

Keywords Dementia, life course epidemiology, prevalence, socioeconomic position, leg length, head circumference, ageing, Brazil, LAMIC

[1] Department of Psychiatry, Faculty of Medicine, University of Sao Paulo, Sao Paulo, Brazil.
[2] Department of Community Based Medicine, Academic Unity of Psychiatry, University of Bristol, Bristol, UK.
[3] Section of Epidemiology, University Hospital, University of Sao Paulo, Sao Paulo, Brazil.
[4] Department of Preventive Medicine, Faculty of Medicine, University of Sao Paulo, Sao Paulo, Brazil.
[5] Western Australian Centre for Health and Ageing, University of Western Australia & Royal Perth Hospital, Perth, Australia.
[6] Department of Social Medicine, University of Bristol, Bristol, UK.
* Corresponding author. Institute of Psychiatry, LIM-23, R. Dr Ovídio Pires de Campos 785, CEP 05403-010, Sao Paulo, SP, Brazil. E-mail: scazufca@usp.br

Introduction

Dementia is a major cause of disability in later life and is associated with high costs for the health system and society.[1] The rapid ageing of the World's population, particularly in low- and middle-income countries (LAMIC), makes this condition a priority for the public health agenda worldwide.[2,3] There is increasing evidence suggesting that events across the life course play a role in the aetiology of cognitive decline and dementia later in life.[4,5] Adverse socioeconomic position underlies many of these risk factors, with a number of studies, largely from high income countries, showing association of dementia with measures of socioeconomic adversities, including lower educational attainment,[6–8] less complex occupational activities,[9–12] area of birth and childhood residence.[13,14] A number of possible mechanisms linking socioeconomic adversities to dementia have been proposed (Figure 1).[4] However, few studies have tested the role of mediating factors between socioeconomic deprivation across the life course and risk of dementia.

Brazil is a middle-income country with one of the fastest ageing populations in the world.[2,15] Current older adults lived through marked socioeconomic changes that rapidly transformed the country from a rural agrarian society into a diversified urban one. As a consequence, the majority of those aged 60 years or over were born in rural areas, but now live in urban centres. Life expectancy for those born between 1950 and 1955 was 51 years, but estimates for those born between 2000 and 2005 have increased to 71 years.[16] Malnutrition was endemic in large areas of Brazil during the first half of the 20th century, particularly in rural areas.[17] Many older adults now living in urban centres represent those who survived high infant mortality and endured significant socioeconomic adversity throughout their lives, with no or minimal school education and generally poorly paid unskilled occupations in adulthood.[18] Compared with wealthier older adults, they have poorer health and physical functioning, and less access to healthcare.[19] Therefore, this is an important population in which to investigate whether early life socioeconomic deprivation increases the risk of dementia later in life.

The aim of the present study is to investigate the association between indicators of socioeconomic disadvantage through the life-course and dementia among older adults of poor socioeconomic backgrounds in Sao Paulo, and to explore possible causal pathways.

Conceptual framework

A variety of mechanisms have been suggested to explain the association between socioeconomic position (SEP) across the life span and dementia.[4] One proposed pathway, the cognitive reserve hypothesis, suggests that exposure to more complex mental activities, such as challenging educational and occupational activities, throughout one's life span enhances the ability of the brain to endure stress and damage and, consequently reduces the risk of dementia.[20,21] Education may also trigger a cascade of events that reduces the risk of brain damage, such as a healthier life style (physical activity, lower alcohol consumption, non-smoking)[22] and decreased risk for cardiovascular diseases.[23–25] An alternative pathway is through the impact of early life

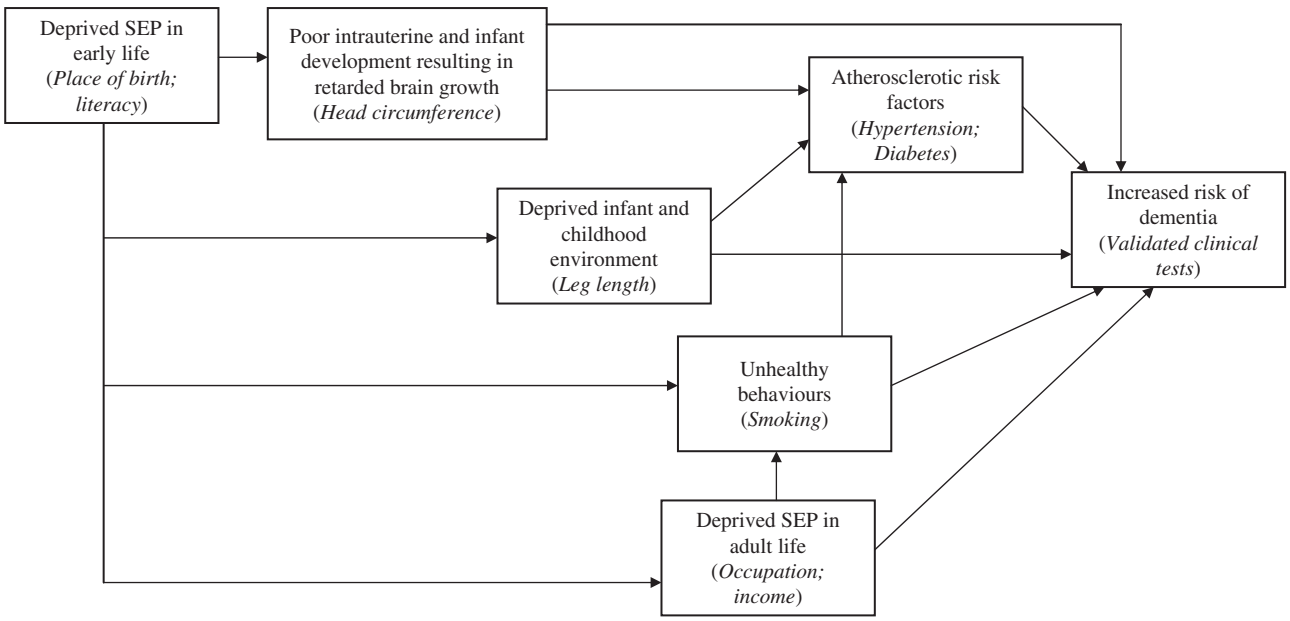

Figure 1 Hypothesized causal pathways between early life socioeconomic position and dementia, with measurements used in this study to test these pathways (these are presented in brackets in italic font)

factors that precede formal education on brain reserve, thereby increasing the vulnerability to dementia in later life.[4,20,21] The formation of neurons in most brain regions is all but confined to the intrauterine and early neonatal developmental period.[26–28] Not surprisingly, some studies have reported positive associations between birth weight and subsequent cognitive ability,[29,30] although others have questioned whether this association is driven by intrauterine factors.[31,32] These hypothesized pathways, shown in Figure 1, are related to each other and not mutually exclusive.

We have used some proxy variables to test these pathways (Figure 1). Place of birth is used as an indicator of socioeconomic circumstances during pregnancy and early childhood. In two previous studies of relatively deprived populations—African Americans[13] and Koreans[14]—rural place of residence in childhood was associated with dementia. In our study population, those born in rural areas would have experienced greater socioeconomic deprivation, with poor nutrition due to endemic and epidemic hunger in less developed areas of the country[17] and limited access to formal education,[18] compared with those born in cities. Literacy is also used as an indicator of early life SEP in our study.[33] It is the most investigated measure of SEP in dementia research, and lower educational attainment is consistently associated with increased risk of dementia.[6] Our indicators of SEP in later life (occupation attainment and current income) have also been associated with dementia.[5] Head circumference in adulthood is used as an indicator of intrauterine and infant brain development,[27,28] and previous studies have shown an association between smaller head circumference and dementia.[14,34,35] Leg length in adulthood may be a useful marker of pre-pubertal environmental influences on childhood growth,[36,37] and has also been found to be associated with dementia.[14,38] Breast feeding, high energy diets at age 2 and affluent social circumstances in early life are all specifically associated with longer leg length.[37,39,40] There is increasing evidence for the association of cardiovascular risk factors and dementia[41] and, for this reason, diabetes, hypertension and smoking habits were also included in some parts of these pathways. We hypothesized that if the association between SEP during early stages of life and prevalent dementia is mediated by indicators of SEP later in life, its association with dementia should be attenuated in models including indicators of SEP in later life. Moreover, if the association between SEP during adulthood and dementia is mediated by unhealthy behaviours, a similar attenuation of the association would be expected when testing both groups of variables in a regression model. If the mechanism behind the association between indicators of SEP early in life and dementia involves biological processes related to the brain reserve, such association should be attenuated in models where markers of these biological processes are included in the same regression model.

Methods

Study design and sample

This report is based on data from the Sao Paulo Ageing & Health Study (SPAH). Full details regarding the study population, assessments and procedures have been previously reported.[42,43] Briefly, SPAH participants were aged 65 years or older and lived in 66 pre-defined census sectors (the smallest administrative areas), of the borough of Butanta, in the city of Sao Paulo, Brazil. The selected sectors have the lowest Human Development Index in the borough,[44] and include numerous shantytowns. Participants were community-dwelling and were identified and recruited through door knocking of all households within the census sectors boundaries. Between 2003 and 2005, 2072 participants (91.4% of those invited) were interviewed and examined. The study received approval from the Brazilian National Committee for Ethics and Research (CONEP-BRAZIL).

Data collection and assessments

Assessments took place at participants' home approximately one week after recruitment. For each participant, a key informant was also identified and interviewed, usually on the same day as the participant, by another research assistant. Informants were co-residents aged 16 years or over, or a relative or friend, who were familiar with the participants' life history. Assessments with informants consisted of questions about the participant's cognitive and daily function. Informants also provided information about participants' socioeconomic and smoking history whenever cognitive impairment precluded participants from reporting this information reliably. The research team comprised mental health professionals ($n = 8$) and a research nurse. Training for the complete research protocol took ~1 month, and consisted of direct teaching and discussions about the content and administration of the various study instruments for the assessment of mental state (including cognitive function), physical and neurological assessments, and supervised application of the study protocol to older adults who did not participate in the study, by each one of the research assistants involved with such assessments. Each trainee first watched and co-rated three training video-tapes for the mental state assessment, then completed and rated two supervised training interviews in the presence of the other trainees, and finally co-rated further 8–10 training interviews performed by other trainees. Training of the neurological assessment followed a similar procedure. After the training, the research team met weekly with the project coordinators, throughout the duration of the field work, to discuss difficulties with the assessments. The research nurse performed the anthropometric assessments, measurement of blood pressure and phlebotomy at participants' home 2–15 days after the assessment interview.

Measurements

Prevalent dementia was assessed with a harmonized one-phase dementia diagnostic procedure developed by the 10/66 Dementia Research Group and validated for use in population-based studies of LAMIC.[42,45] The diagnosis of dementia followed DSM-IV criteria.[46] The procedure includes assessment of cognitive functioning with the Community Screening Instrument for Dementia (CSI-D),[47] an adapted version of the CERAD ten word list learning task with delayed recall and animal verbal fluency,[48] a structured clinical mental state interview with the Geriatric Mental State (GMS),[49,50] a structured neurological assessment of localizing signs, parkinsonism, ataxia, apraxia and primitive 'release' reflexes, assessment of participants' daily functioning and general health with the CSI-D,[47] and of functional and cognitive decline with the History and Aetiology Schedule Dementia Diagnosis and Subtype (HAS-DDS).[51] An algorithm combines data from all assessments and classifies participants as cases of dementia or not.[42,45]

Data on life course exposures were obtained through interviews, physical examination and blood tests. Participants were asked to name the place they were born (farm, town/village, city, district, state, country), and to classify that place as a city (known urban area), town (small village with reduced number of houses, shops and other amenities, and no more than a primary school) or rural area at the time of birth. Illiteracy was considered present when participants reported that they could not write or read a simple message/letter. Formal education was not mandatory in Brazil when the participants of our study were at school ages, and access to formal education was very restricted. However, many people developed writing and reading skills through informal teaching by family or community members, with those who did so increasing their possibilities of access to more complex forms of social and occupational activities throughout their life course. For the sake of describing our sample we also use number of years of formal education. We asked participants about their employment or job history, and used their highest position and the work performed to group them into three categories: professionals (such as doctors, engineers, lawyers, teachers and managers), skilled and semi-skilled occupations (such as clerical, shop keeper, skilled and semi-skilled labourer), and non-skilled occupations (non-skilled labourer and agricultural worker). Housework was classified as a non-skilled occupation. There were only 56 participants in the higher occupation group, of whom none met criteria for dementia. For this reason, we created a binary variable: skilled and semi-skilled (including professionals) and non-skilled occupations. Income was defined as the total monthly income of participants at the time of the survey (including salary, government benefits, family donations or money received from other sources), and was grouped into tertiles (the lowest tertile—none to US$85—represents an income lower than the official minimum wage in Brazil at the time of the study). Participants who, at any period of their lives, smoked at least almost every day were classified as 'ever smokers', and those who never smoked regularly as 'never smokers'.

We placed a measuring tape over the eyebrows of participants and moved it around the head over the most posterior occipital protuberance towards the eyebrows to measure head circumference. Leg length was ascertained by measuring the distance from the uppermost part of the iliac crest to the tip of the lateral malleolus of the right leg. In the rare instances when that it was not possible the left leg was measured instead. The measures of head circumference and leg length were recorded in centimetres and then each measure was standardized for age and gender. We used these standardized measures as continuous and as categorical (quartiles) variables. Diabetes mellitus was defined by a fasting blood glucose level $\geqslant 126$ mg/dl or current use of insulin or hypoglycaemic oral drug treatment.[52] Hypertension was defined as a diastolic blood pressure $\geqslant 90$ mmHg or systolic blood pressure $\geqslant 140$ mmHg or current drug treatment for hypertension.[53]

Statistical analysis

We restricted our analysis to participants born in Brazil, since the meaning of place of birth and other SEP indicators may differ for individuals born in other countries. The outcome of interest was prevalent dementia. The exposure variables were SEP indicators in childhood (place of birth, literacy) and adulthood (higher ever held occupation, current personal income), anthropometric measurements acting as markers of intrauterine and childhood environment (standardized head circumference and leg length), smoking, diabetes and hypertension. For the analyses that required binary variables, we dichotomized place of birth into rural vs. other areas (town or city), standardized head circumference as smaller size (lower quartile) vs others (three higher quartiles), standardized leg length into shorter (lower quartile) vs others (three higher quartiles), personal income into lower vs middle and higher tertiles.

We first calculated the prevalence of dementia and its association with age and gender. We used logistic regression to calculate age- and gender-adjusted associations of indicators of early life SEP with the remaining exposures, and to calculate age- and gender-adjusted odds ratios (ORs) for associations between each exposure and dementia. We then built a series of multivariable logistic regression models aimed at testing the pathways depicted in Figure 1. We first entered place of birth and literacy in the same model, adjusting for age and gender. We then extended this model with the successive inclusion of the remaining exposure variables, to examine the effect of adjusting for more proximal mediating factors, always controlling for age and gender. We also created a cumulative index with all six measures of adversity across the life course related to dementia by summing up the value of all these variables. Each exposure received a score 0 or 1, 1 indicating

more adversity (for instance, illiteracy), and 0 for the better category of exposure. Logistic regression was used to calculate age- and gender-adjusted ORs for the association between this cumulative index and prevalent dementia. *P*-values were obtained using likelihood ratio tests. When exposure variables were grouped in ordered categories, we used tests for linear trend.

Results

The mean age of the 2005 participants was 72.2 years (SD 6.3), 1221 (60.9%) were women, 1340 (66.8%) were born in rural areas and 657 (32.8%) were illiterate. The proportion of women born in rural areas was similar to that for men (67.4 vs 65.9%, respectively). The proportion of participants aged 80 or more born in rural areas was 74.0%, compared with 65.8% for those aged 65–79 years. Illiteracy among participants born in cities, towns and rural areas was 10.3, 19.7 and 40.8%, respectively. Illiteracy was higher in women (37.8%) than among men (25.0%), and increased with age, being twice as frequent amongst those aged 80 years or over (50%) compared with those aged 65–69 years (24.9%). The proportions of participants with non-skilled occupations and with up to US $85 monthly income were 47.5 and 31.2%, respectively. Women had higher proportions of non-skilled occupations (63.7 vs 22.5%) and lower income (37.8 vs 20.9%) than men. Only 176 (9%) participants had 4 or more years of formal education. The mean head circumference size was 54.4 cm (SD 3.14), and the mean leg length was 88.5 cm (SD 5.48). The Pearson correlation coefficient for head circumference and leg length was 0.19. Four hundred and thirty (22.6%) participants had diabetes, 1552 (79.0%) had hypertension and 1113 (55.5%) were ever smokers. There were 100 cases of dementia, yielding a prevalence of 5.0% (95% CI 4.0–5.9%). The prevalence of dementia was similar for males and females, and increased with age. Among the 141 participants without complete data in all exposures, 8 (5.7%) had prevalent dementia.

Table 1 shows the age- and gender-adjusted associations of place of birth and literacy with each one of the remaining exposures. Participants born in rural areas and those illiterate were more likely to have smaller head circumferences, non-skilled occupations and lower current personal income. Illiteracy was also associated with shorter leg length and smoking. Diabetes and hypertension were not associated with place of birth or literacy.

Table 2 presents the age- and gender-adjusted ORs of dementia for all exposures considered here. Prevalent dementia was more common among participants born in rural areas, those who were illiterate or had smaller head circumferences, shorter leg length, non-skilled occupations and those with current lower incomes. Smoking, diabetes and hypertension were not associated with prevalent dementia. The analysis with the 1864 (93%) participants with complete data for all exposures examined yielded similar results, with slightly lower precision for some of the associations (Table 3, model 1). Participants with complete data for all exposures did not differ from participants without complete data with respect to age, gender and dementia prevalence.

Table 3 shows the associations of SEP indicators, anthropometric measures, smoking, diabetes and hypertension with prevalent dementia for participants with complete data, with progressive adjustments for potential mediating factors. When place of birth and literacy were simultaneously entered in the model, both had their association with dementia weakened (model 2). The association of place of birth with dementia was not mediated by head circumference or leg length, whereas the association of illiteracy was slightly weakened by each one of these anthropometric

Table 1 Age- and gender-adjusted OR and 95% CI for the association of place of birth and literacy with socioeconomic position indicators, anthropometric measures, smoking, diabetes and hypertension[a]

	Rural birth OR (95% CI)	Illiteracy OR (95% CI)
Illiteracy	3.50 (2.76–4.43)[b]	-
Non-skilled occupation	2.43 (1.97–3.01)[c]	4.34 (3.46–4.43)[c]
Lower income	1.44 (1.17–1.78)[b]	2.80 (2.28–3.44)[b]
Smaller head circumference	1.39 (1.11–1.75)[d]	1.25 (1.00–1.57)[d]
Shorter leg length	1.17 (0.94–1.46)[e]	1.45 (1.16–1.81)[e]
Ever smoker	1.08 (0.89–1.32)[b]	1.84 (1.49–2.27)[b]
Diabetes (yes)	0.87 (0.70–1.09)[d]	1.00 (0.79–1.26)[d]
Hypertension (yes)	1.18 (0.93–1.48)[f]	1.03 (0.81–1.31)[f]

[a]Place of birth: rural vs town/city; Illiteracy vs literacy; Head circumference: lower quartile vs others; Leg length: lower quartile vs others; Higher occupation attained: non-skilled vs skilled and semi-skilled; Personal income: lower tertile vs others.
[b]$N = 2005$.
[c]$N = 2003$.
[d]$N = 1905$.
[e]$N = 1920$.
[f]$N = 1964$.

Table 2 Age- and gender-adjusted OR and 95% CI for the association between dementia and place of birth, higher occupation attained, current personal income, head circumference, leg length, literacy, smoking, diabetes and hypertension ($N = 2005$)

Exposure	Number of participants (%)	Number with dementia in category	Prevalence of dementia	OR (95% CI)
Place of birth				
City	223 (11.1)	6	2.7	1
Town	442 (22.0)	17	3.9	1.78 (0.68–4.66)
Rural	1340 (66.8)	77	5.8	2.22 (0.94–5.24)
P-value for linear trend*				0.04
Literacy				
Yes	1348 (67.2)	46	3.4	1
No	657 (32.8)	54	8.2	1.82 (1.19–2.79)
P-value				0.006
Occupation				
Skilled/semi-skilled	1050 (52.4)	29	2.8	1
Non-skilled	953 (47.5)	71	7.5	2.39 (1.47–3.89)
Missing	2	0		
P-value				<0.001
Income (US$)				
194 or +	679 (33.9)	12	1.8	1
86–193	700 (34.9)	35	5.0	2.05 (1.03–4.06)
None–85	626 (31.2)	53	8.5	3.96 (2.04–7.68)
P-value for linear trend				<0.001
Head circumference (quartiles)[a]				
4th	477	18	3.8	1
3rd	476	18	3.8	1.03 (0.52–2.03)
2nd	477	29	6.1	1.69 (0.91–3.12)
1st	475	29	6.1	1.64 (0.88–3.04)
Missing	100 (5.0)	6		
P-value for linear trend				0.05
Leg length (quartiles)[a]				
4th	480	14	2.9	1
3rd	480	22	4.6	1.64 (0.82–3.29)
2nd	480	26	5.4	2.19 (1.11–4.30)
1st	480	34	7.1	2.58 (1.34–4.93)
Missing	85	4		
P-value for linear trend				0.002
Smoking				
Never	892 (44.5)	48	5.4	1
Ever	1113 (55.5)	52	4.7	0.90 (0.58–1.40)
P-value				0.64
Diabetes				
No	1475 (77.4)	74	5.0	1
Yes	430 (22.6)	22	5.1	1.06 (0.64–1.75)
Missing	100	4		0.83
P-value				
Hypertension				
No	412 (21.0)	15	3.6	1
Yes	1552 (79.0)	81	5.2	1.30 (0.73–2.31)
Missing	41	4		
P-value				0.37

*All *P*-values are for Likelihood ratio statistics tests.
[a]Head circumference and leg length: 1, bigger size to 4 smaller size.

Table 3 OR with 95% CI of place of birth, literacy and possible mediating factors for dementia ($N = 1864$)*

Exposure	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)	Model 5 OR (95% CI)	Model 6 OR (95% CI)	Model 7 OR (95% CI)	Model 8 OR (95% CI)
Place of birth								
City	1	1	1	1	1	1	1	1
Town	1.52 (0.60–4.04)	1.39 (0.52–3.72)	1.43 (0.54–3.83)	1.41 (0.53–3.78)	1.14 (0.42–3.09)	1.41 (0.53–3.75)	1.41 (0.53–3.76)	1.22 (0.45–3.32)
Rural	1.96 (0.83–4.62)	1.58 (0.66–3.82)	1.57 (0.65–3.78)	1.58 (0.66–3.83)	1.21 (0.49–2.99)	1.59 (0.66–3.83)	1.60 (0.66–3.85)	1.23 (0.50–3.05)
P-value for linear trend**	0.08	0.29	0.33	0.30	0.67	0.29	0.28	0.70
Literacy								
Yes	1	1	1	1	1	1	1	1
No	1.83 (1.18–2.86)	1.71 (1.08–2.71)	1.67 (1.05–2.65)	1.64 (1.03–2.60)	1.18 (0.73–1.93)	1.76 (1.10–2.80)	1.71 (1.08–2.72)	1.18 (0.71–1.95)
P-value	0.008	0.02	0.03	0.04	0.49	0.02	0.02	0.52
Head circumference[a]	0.74 (0.59–0.93)		0.76 (0.60–0.95)					0.80 (0.63–1.01)
P-value	0.008		0.01					0.06
Leg length[a]	0.76 (0.61–0.94)			0.76 (0.62–0.97)				0.82 (0.65–1.03)
P-value	0.01			0.02				0.09
Occupation								
Skilled/semi-skilled	1				1			1
Non-skilled	2.50 (1.49–4.18)				1.73 (0.99–3.00)			1.65 (0.95–2.89)
P-value	<0.001				0.05			0.07
Personal income (US$)								
194 or more	1				1			1
86–193	1.96 (0.95–4.03)				1.69 (0.81–3.52)			1.74 (0.83–3.64)
none–85	4.30 (2.16–8.54)				3.29 (1.60–6.76)			3.38 (1.63–6.98)
P-value for linear trend	<0.001				<0.001			<0.001
Ever smoker								
No	1					1		1
Yes	0.92 (0.58–1.45)					0.83 (0.52–1.32)		0.73 (0.45–1.18)
P-value	0.72					0.45		0.20
Diabetes								
No	1						1	1
Yes	1.14 (0.69–1.89)						1.13 (0.68–1.88)	1.24 (0.74–2.09)
P-value	0.60						0.64	0.41
Hypertension								
No	1						1	1
Yes	1.25 (0.70–2.24)						1.25 (0.70–2.25)	1.39 (0.76–2.52)
P-value	0.44						0.45	0.28

*All models adjusted for age and gender; Model 1, exposure adjusted for age and gender; Model 2, place of birth + literacy; Model 3, place of birth + literacy + head circumference; Model 4, place of birth + literacy + leg length; Model 5, place of birth + literacy + occupation + income; Model 6, place of birth + literacy + smoking; Model 7, place of birth + literacy + diabetes + hypertension; Model 8, place of birth + literacy + head circumference + leg length + occupation + income + smoking + diabetes + hypertension.

**All *P*-values are for Likelihood ratio statistics tests.

[a]Head circumference and leg length: continuous variable.

measures (models 3 and 4). There were marked attenuations of the associations of place of birth and literacy with prevalent dementia with the inclusion of the two indicators of SEP in late life (model 5). None of the observed associations were mediated by smoking, diabetes and hypertension (models 6 and 7). Current income was the exposure with stronger association with prevalent dementia in the model with all exposure variables (model 8). Controlling for income led to small decreases in the associations of head circumference and leg length with dementia.

Only 10.1% of the participants had no indicator of disadvantages across the life course, whereas 7.9% had five or six such indicators (Table 4). The cumulative index of disadvantages was strongly associated with gender (there were 40% of women among those with no disadvantages, compared with 77% among those with five or six indicators), and age (there was a linear association between age and the number of indicators of disadvantage ($P < 0.001$)—mean age increased went from 71.5 years among those with no disadvantages to 75.5 years among those with five or six indicators). Table 4 shows a strongly graded association of disadvantages across the life course and prevalent dementia, controlling for gender and age. Those with five or six unfavourable indicators were more than seven times more likely to present with dementia than those with no adverse indicators. The association between the cumulative score and dementia was observed in both women (summary OR for linear trend = 1.55, 95% CI 1.26–1.91) and men (summary OR for linear trend = 1.38, 95% CI 1.07–1.78).

Eighty-eight participants (4.4% of total), 49 of whom had dementia, were unable to give information about SEP. Since for these participants information was collected from informants, we examined the possibility that information bias might have been introduced. Informants reported lower frequencies of illiteracy, non-skilled occupations and lower income for participants with dementia than when this information came from participants themselves, and reported similar frequencies of being born in rural areas, which makes information bias unlikely.

Discussion

We have examined the association of indicators of socioeconomic adversity across the life course with prevalent dementia and some possible pathways. This cohort of old adults had been exposed across their life course to a wide range of adverse risk factors previously associated with dementia. We suggested in our conceptual framework that these risk factors would be inter-related and that different mechanisms strongly influenced by SEP in childhood would be acting since birth. We found that early SEP indicators were consistently associated with indicators of adulthood SEP, body growth in childhood and smoking, but not with hypertension and diabetes. All indicators of SEP in childhood and adulthood, and measures of body growth were associated with prevalent dementia in age and gender adjusted models, but smoking, diabetes and hypertension were not. The association between indicators of SEP in childhood and dementia was attenuated by indicators of SEP in adulthood. The association between measures of body growth and dementia was independent from indicators of SEP in childhood and adulthood. The association of adversities with dementia seemed to be cumulative, that is, the risk of dementia increased steadily with the accumulation of unfavourable exposures during the life course of participants.

We hypothesized several causal pathways between early life SEP and dementia, as outlined in Figure 1. Our results suggest that early life factors operate through both biological mechanisms and opportunities in life. The association of disadvantaged early life SEP with dementia was mediated through adulthood SEP, as shown by the marked decreases in the ORs for place of birth and literacy when adulthood SEP indicators were simultaneously included in the logistic regression model. This suggests a pathway of socioeconomic adversities on

Table 4 OR and 95% CI for the association between prevalent dementia and the cumulative index of disadvantages across the life-course (place of birth, literacy, leg length, head circumference, higher occupation attained, current personal income; $N = 1864$)[a]

Indicator profile	Number (%)	Number with dementia	Prevalence of dementia (%)	OR (95% CI)[b]
0 unfavourable	188 (10.1)	3	1.6	1
1 unfavourable	443 (23.8)	8	1.8	1.21 (0.32–4.66)
2 unfavourable	449 (24.1)	19	4.2	2.73 (0.79–9.44)
3 unfavourable	368 (19.7)	21	5.7	3.77 (1.09–13.01)
4 unfavourable	268 (14.4)	19	7.1	4.22 (1.20–14.84)
5 and 6 unfavourable[c]	148 (7.9)	22	14.9	7.45 (2.12–26.20)
P-value for linear trend[d]				<0.001

[a]Participants with complete data for all exposures included in Table 3.
[b]Age and gender adjusted odds ratios (95% confidence interval).
[c]Only 25 (1.3%) participants had 6 unfavourable indicators and were merged with those with 5 unfavourable indicators.
[d]*P*-value for Likelihood ratio statistics test.

dementia probably related to the active cognitive reserve. Illiteracy, largely determined by rural area of birth and low parental SES, leads to non-skilled, poorly paid occupations, low income and possibly lack of access to leisure activities, all of which are associated with lower cognitive reserve.[5,54] The other proposed causal pathways from childhood SEP to dementia (retarded brain growth, deprived childhood environment, atherosclerotic risk factors and unhealthy behaviours) were not supported by our data. However, the independent associations of head circumference and leg length with prevalent dementia are consistent with a pathway related to brain development, which contributes to establish the individual's passive cognitive reserve and once established cannot be easily changed.[4,20] Leg length may also be representing a third pathway related to cardiovascular risk and disease, which influences negatively the passive cognitive reserve later in life.[41,55] We found that different unfavourable conditions across the life course increase the risk of dementia in a cumulative fashion, which strengthens our hypothesis that several pathways that are not mutually exclusive and are related to socioeconomic deprivation increase the risk of dementia across the life span.

Other studies from LAMIC populations support our findings,[13,14] but some appear to contradict our conclusions. A study from Nigeria[56] and one from India[57] found low prevalence of dementia, which does not fit with our suggestion that occurrence of dementia is higher amongst poorer populations. It is possible that unknown protective factors and mechanisms operate in these populations to compensate for the impact of high prevalence of socioeconomic adversities early in life on the risk of dementia. Furthermore, in both these studies, education was not associated with dementia,[56,57] which is consistent with a very large body of literature.[6] However, this may be explained by low statistical power due to the small number of cases, with just 28 cases in the study from Nigeria[56] and 37 in the study from India[57]. Empirical data from LAMIC studies in general, that could allow a better understanding of the contextual and biological factors operating in different LAMIC are still scarce, as shown in the revision of studies on the prevalence of dementia worldwide by Ferri *et al*.[3] Our work demonstrates that collecting such data is possible and we would argue that in an ageing population it is important to do so across all countries of the world.

Strengths and limitations

We used a one-phase design and had a response rate of 91.4%, which is very high compared to other large epidemiological studies with older populations.[14,58] The assessment of participants in their own homes makes it less likely that non-response was associated with morbidity. The profile of the present sample is similar to that shown by the census data for heads of households aged 60 years or over in Brazil.[15] Moreover, there is no reason to suppose that the observed associations would be different for the Brazilian population of older adults with low SES. Sample size was calculated on the basis of the precision of the prevalence estimate, and the number of cases in our study is larger than those found in most previous studies in LAMIC and several studies in high income countries. Nonetheless, we had limited statistical power for some of the associations tested, for example, this might, in part explain the lack of associations of smoking, hypertension and diabetes with dementia in our study. As in most large epidemiological studies, all measures of socioeconomic indicators and smoking were based on self-report. In general, the information we collected was simple and objective. For those who could not communicate adequately, which in most cases was due to cognitive impairment, such information was obtained from close informants, and this might have introduced information bias, if informants tended to systematically give lower status for those with dementia. Our analysis showed that this was not the case, since informants tended to give higher status instead. We acknowledge that the association of income with dementia could be due to reverse causality, as dementia might prevent the individual from having current extra sources of income. However, the main source of income in later life is retirement benefits, which are normally achieved before reaching the age of higher risk for dementia in Brazil.[15] In addition, when analysing only participants who did not have a current occupation, the association of income with dementia was very similar (data not shown). Our protocol for identification of cases of dementia was specially developed to perform equally well across people of different cultures and education levels. Nevertheless, as in all other epidemiological studies of dementia, there may have been some misclassification of cases. We cannot see any reason why this measurement error would be related to our key exposures and therefore the expectation would be that this non-differential misclassification could bias our results towards the null. Thus, such misclassification might, in part, explain the lack of association of dementia with smoking, hypertension and diabetes. Such lack of association may also be due to the cross-sectional design.[59–62] If cases of dementia with these cardiovascular risk factors were more likely to die faster than cases without such risk factors, then the association would be weakened.

Conclusion

Current predictions for dementia in LAMIC, which are based mostly on demographic changes and a limited number of prevalence studies from such countries,[3] are likely to be underestimated, since those who are now reaching old age have been exposed to a wide range of adverse factors during their lives.[2] There is no current effective treatment for dementia, and emphasis should be placed on prevention. Our results show an association between cumulative adversities across the life course and dementia, similar to that observed for

adverse socioeconomic circumstances in life and risk of several other chronic diseases in adult life.[63,64] Such adversities cluster cross-sectionally and over time and are the consequence of social processes and inequalities. Prevention of dementia should start early in life, 'at conception', and continue through the life span. Social policies are the key element for reducing socioeconomic adversities, and consequently, may have an impact on the projected burden of dementia in LAMIC, burden that is still high even in societies with relatively low social deprivation. Further research is needed to better clarify the mechanisms underlying the complex pathways to dementia throughout the life course and to establish the effectiveness of specific interventions that can be implemented at all stages of life.

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Conflict of interest: None declared.

KEY MESSAGES

- In a cohort of elderly individuals from Sao Paulo, Brazil, indicators of socioeconomic disadvantage in early life are associated with increased prevalence of dementia, with this association partially mediated via socioeconomic disadvantage in adulthood.
- Indicators of early life brain development and nutrition deprivation in childhood up to adolescence were also associated with dementia, but these do not seem to mediate the association of early life socioeconomic disadvantage with dementia.
- Old adults exposed to five or six unfavourable risk factors across their life course were over seven times more likely to develop dementia than those with no such exposures. This finding suggests a cumulative effect of adversity on the risk of dementia.
- Based on these findings current predictions for dementia in low- and middle-income countries, which are based mostly on demographic changes and prevalence studies, may be underestimated, since those who are now reaching old age have been exposed to a wide range of adverse factors during their lives.

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