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Distressing dreams in childhood and risk of cognitive impairment or Parkinson's disease in adulthood: a national birth cohort study

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Summary

Background Distressing dreams in middle-aged and older adults have been associated with an increased risk of developing cognitive impairment (including dementia) and Parkinson's disease (PD). Whether distressing dreams in younger people might be associated with an increased risk of developing these conditions is unknown. This study investigated the association between distressing dreams in childhood and the risk of developing cognitive impairment or PD by age 50.

Methods Data from the 1958 British Birth Cohort Study - a prospective birth cohort which included all people born in Britain during a single week in 1958, were used in this longitudinal analysis. Information on distressing dreams were obtained prospectively from the children's mothers at ages 7 (1965) and 11 (1969). Cognitive impairment and PD at age 50 (2008) were determined by cognitive assessment and doctor-diagnosis respectively. The association between distressing dreams at ages 7 and 11 (no time point, 1 time point, 2 time points) and cognitive impairment or PD at age 50, was evaluated using multivariable Firth logistic regression, with adjustment for potential confounders.

Findings Among 6991 children (50.6% female) with follow-up available at age 50, 267 (3.8%) developed cognitive impairment or PD. After adjustment for all covariates, having more regular distressing dreams during childhood was linearly and statistically significantly associated with higher risk of developing cognitive impairment or PD by age 50 (P for trend = 0.037). Compared with children who never had distressing dreams (no time point), children who had persistent distressing dreams (2 time points) had an 85% increased risk of developing cognitive impairment or PD by age 50 (adjusted odds ratio = 1.85; 95% CI: 1.10, 3.11).

Interpretation Having persistent distressing dreams during childhood may be associated with an increased risk of developing cognitive impairment or PD in adulthood. Future studies are needed to confirm these findings and to determine whether treating distressing dreams during early life may lower the risk of dementia and PD.

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Keywords: Dreaming; Cognitive impairment; Parkinson's disease; Ageing; Nightmares

Introduction

The number of people living with dementia is projected to triple from 50 million to 150 million globally within the next three decades,¹ and the number living with Parkinson's disease (PD) is set to reach 14 million by 2040.² Both dementia and PD cause distress for those affected, and the economic costs of the two conditions combined exceeds \$1 trillion annually.^{1,3} Given that there is currently no cure for either condition,

identifying risk factors and early signs for their development is now a major public health priority.

Recent studies have identified that having frequent distressing dreams (bad dreams and nightmares) during adulthood, may be an early sign or potentially modifiable risk factor for developing both dementia and PD.^{4,5} These studies have demonstrated that older adults in the general population who experience weekly distressing dreams, have a greater than 2-fold risk of developing

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Research in context

Evidence before this study

A PubMed search was conducted using the search string (('nightmares' OR 'bad dreams' OR 'dream content')) AND (('cognitive impairment' OR 'dementia' OR 'Alzheimer's disease' OR 'Parkinson's disease')). Primary research studies published in any language up until December 17, 2022 were identified. Previous population-based studies have shown that having frequent distressing dreams (bad dreams and nightmares) during middle and older adulthood, is associated with an increased risk of developing cognitive impairment or Parkinson's disease (PD) later in life. However, no study has evaluated whether having distressing dreams during childhood might also be associated with increased risk of developing cognitive impairment and PD.

Added value of this study

This prospective, longitudinal study in the 1958 British Birth Cohort, has shown for the first time that having distressing

dreams during childhood, may be associated with an increased risk of developing cognitive impairment or PD in adulthood. Among 6991 children included in this study, 262 had developed cognitive impairment by age 50, and 5 had been diagnosed with PD by age 50. Compared with children who never had distressing dreams during middle childhood (ages 7 and 11), those who had persistent distressing dreams were 76% more likely to develop cognitive impairment, and were nearly seven times more likely to develop PD.

Implications of all the available evidence

Having persistent distressing dreams during childhood may be associated with an increased risk of developing cognitive impairment or PD in adulthood. If these findings are replicated in future studies, and the association is shown to be causal, it is possible that early treatment of distressing dreams could become a primary prevention strategy for dementia and PD.

dementia or PD, compared to older adults who rarely experience distressing dreams.^{4,5} Additionally, there is evidence that having regular distressing dreams during middle adulthood, may be associated with an increased risk of developing cognitive impairment or PD several decades later.^{4,6}

Given that distressing dream frequency is a relatively stable trait from early childhood to middle adulthood,⁷⁻⁹ this raises the possibility that having regular distressing dreams as a child, may be a very early indicator of dementia and PD risk.

If shown to be true, this would have substantial public health implications, and would suggest that interventions to delay or prevent cognitive impairment and PD should begin during childhood.

This study used 50 years of prospectively collected data from the 1958 British Birth Cohort Study,¹⁰ to investigate whether having distressing dreams during childhood (reported by the children's mothers at ages 7 and 11), would be associated with an increased risk of developing cognitive impairment or PD by age 50.

Methods

Study design and participants

The 1958 British Birth Cohort Study includes 17,416 (99%) of 17,634 births in England, Scotland and Wales during the week of March 3–9, 1958.¹⁰ Data were obtained from cohort members, as well as their parents, schools, and medical officers, at ages 7, 11, 16, 23, 33, 42, 45, 50, and 55 years of age. Immigrants to Britain born during the same week in 1958 were added to the cohort at ages 7, 11, and 16. The respondents in middle adulthood were broadly representative of the surviving cohort.¹¹

The base population for the present study included 11,721 participants who were enrolled at birth (1958), and had information on distressing dreams at ages 7 (1965) and 11 (1969). Participants who did not take part in the follow-up at age 50 (2008; n = 4457), or had missing data for incident cognitive impairment or incident PD (n = 273, 3.8%), were excluded. This left a final analytic sample comprising 6991 children with follow-up at age 50.

Distressing dreams

Distressing dreams were assessed when the children were 7 and 11 years of age. Mothers were asked to report whether their child had experienced "bad dreams or night terrors" in the previous three months (yes/no). No definition was provided to the mothers.

In this analysis, the participants were categorised into three groups based on the presence of distressing dreams at ages 7 and 11: "no time point", "1 time point (at 7 or 11)", or "2 time points (at 7 and 11)." This categorisation has been used in previous studies to determine the impact of persistent distressing dreams.^{12,13}

Incident cognitive impairment

When participants were 50 years old, trained interviewers administered a battery of three cognitive tests,¹⁴ a 10-item word recall test, which assesses verbal episodic memory (the delayed recall score was used); the Animal Naming Test, which assesses verbal fluency; and the Letter Cancellation Test, which assesses processing speed.¹⁵ For each test, higher scores are indicative of better cognitive performance. Incident cognitive impairment was defined as scoring ≥ 2 SD below the population mean on ≥ 1 test.¹⁶

Incident PD

At age 50, participants were asked to report whether a doctor had ever diagnosed them with a chronic medical condition. Furthermore, they were asked to specify which conditions they had been diagnosed with. Incident PD was defined as doctor-diagnosed PD at age 50.

Covariates

Potential confounders were chosen based on *a priori* knowledge of early-life factors associated with distressing dreams, cognitive impairment, and PD; as well as relevant publications.^{7,17–19} Variables collected at birth included: sex (male, female), country of birth (England, Scotland, Wales), low birthweight (yes/no), mothers age at birth (continuous), and childhood socioeconomic position (Class I, II, III, IV, V). Variables collected at age 7 included: ever breastfed (yes/no), handedness (left, right, ambidextrous), number of siblings (continuous), cognitive ability (continuous), height (continuous), overweight (yes/no), special educational needs (yes/no), childhood neglect (continuous), head trauma (yes/no), previous infections (continuous), chronic health conditions (yes/no), depression (continuous), anxiety (continuous), and difficulty falling asleep (yes/no). Information on race (white, non-white) was collected at age 11.

Sex, country of birth, mother's age at birth, and birth weight, were derived from medical records. Birth weight was recorded in pounds and ounces and converted into kilograms (low birthweight was defined as <2.5 kg). Childhood socioeconomic position was based on the father's occupation at birth, classified according to the registrar general's scale, ranging from class I (professional) to V (unskilled manual). Households with no male head of household were included with class V. Difficulty falling asleep and history of head trauma (concussion or head injury with unconsciousness) were reported by the children's mothers at age 7. The mothers also reported whether they had ever breastfed their child; whether they believed their child was right-handed, left-handed, or ambidextrous; and the number of children in their household. Height (in metres) and weight (in kilograms) were measured by the medical officers according to standardised protocols. BMI was calculated as weight/height² (overweight was defined as ≥ 17.92 kg/m² for boys and ≥ 17.75 kg/m² for girls).²⁰ Special education needs was defined by special school attendance and/or intellectual disability documented by the medical officers. Chronic health conditions (diabetes, asthma, eczema, epilepsy, cerebral palsy, and heart conditions) were documented by the medical officers. Previous infections (measles, German measles, whooping cough, chickenpox, mumps, and scarlet fever) were reported by the children's mothers. A continuous score was created by summing the total number of previous infections reported. Depression and anxiety were evaluated by schoolteachers using the Bristol

Social Adjustment Guide (BSAG) of behavioural problems.²¹ Childhood cognitive ability was measured using four age-appropriate tests (Southgate reading test, 20-item Problem Arithmetic Test, Copy Design Test, and Draw-a-man test).²² The four test scores were z-scored and then averaged to yield a single score for overall cognitive ability. A score for childhood neglect was derived from information obtained from parental interviews and the child's teacher, using structured questionnaires.²³ Race was documented by the medical officers at age 11. The proportion of missing data for these covariates ranged from 0% to 8.7%. Indicator variables were used for missing information for categorical covariates, and median imputation was used for missing continuous covariates.

Statistical analysis

Demographic characteristics of the participants, stratified by distressing dreams status at ages 7 and 11, were compared using χ^2 tests for categorical variables, ANOVA for normally distributed continuous variables, and Kruskal–Wallis tests for nonnormally distributed continuous variables. Normality was assessed using the Shapiro–Wilk test. Multivariable Firth logistic regression was used to obtain odds ratios (ORs) and 95% confidence intervals (CIs) to determine the association between distressing dreams at ages 7 and 11 and risk of cognitive impairment or PD at age 50. In all analyses, distressing dreams status was modelled as both a categorical variable (referent group “no time point”) and as a continuous variable (to obtain a P value for linear trend).

All analyses were adjusted for potential confounders. Model 1 was adjusted for sex. Model 2 further adjusted for race, country of birth, mothers age at birth, low birthweight, childhood socioeconomic position, number of siblings, ever breastfed, handedness, cognitive ability, height, overweight, special educational needs, childhood neglect, head trauma, previous infections, chronic health conditions, depression, anxiety, and difficulty falling asleep. Potential effect modification by sex was tested by adding an interaction term to the model. Multiple imputation by chained equations (with five imputed datasets) was performed to impute missing covariate data as a sensitivity analysis, under the assumption that data were missing at random.

As an exploratory analysis, the regression models were repeated using incident cognitive impairment and incident PD as two separate outcomes.

Statistical testing was performed two-sided at $P < 0.05$. All analyses were performed using Stata version 17 (StataCorp., College Station, TX).

Ethical considerations

Ethical approval for the 1958 British Birth Cohort Study was obtained from the London Multi-centre Research Ethics Committee, and informed consent was obtained from all participants. The present study received

approval from the University of Birmingham (Ref No ERN_21–1463).

Role of the funding source

There was no funding source for this study. AIO had full access to the dataset and had final responsibility for the decision to submit for publication.

Results

Demographic characteristics of the participants ($n = 6991$; 50.6% female; 0.7% non-white) stratified by distressing dream status at ages 7 and 11, are presented in [Table 1](#). Of the participants, 78.2% never had distressing dreams (no time point); 17.9% had transient distressing dreams (1 time point); and 3.8% had persistent distressing dreams (2 time points). The participants who experienced distressing dreams had younger mothers, were less likely to have been breastfed, were more likely to have been born in England, and at age 7 were more depressed, more anxious, had more difficulty sleeping, and had more previous infections.

At age 50, 267 (3.8%) participants had developed cognitive impairment or PD (262 cognitive impairment; 5 PD). In the fully adjusted model ([Table 2](#)), having more regular distressing dreams during childhood was linearly and statistically significantly associated with higher risk of developing cognitive impairment or PD by age 50 (P for trend = 0.037). Compared with children who never had distressing dreams, children who had persistent distressing dreams were 85% more likely to develop cognitive impairment or PD by age 50 (adjusted odds ratio [aOR] = 1.85; 95% CI: 1.10, 3.11; $P = 0.019$).

There was no significant interaction between distressing dreams and sex on risk of incident cognitive impairment/PD (P 's for interaction >0.05).

In the sensitivity analysis which used multiple imputation to impute missing data for covariates, the association between distressing dreams and incident cognitive impairment/PD was similar and remained significant ([Table 2](#)).

The associations were present when analysing incident cognitive impairment and incident PD as two separate outcomes ([Tables 3 and 4](#)). Compared with children who never had distressing dreams, children who had persistent distressing dreams were 76% more likely to develop cognitive impairment by age 50 (aOR = 1.76; 95% CI: 1.03, 2.99; $P = 0.037$), and were nearly seven times more likely to be diagnosed with PD by age 50 (aOR = 7.35; 95% CI: 1.03, 52.73; $P = 0.047$). The linear association was statistically significant for PD (P for trend = 0.050), and had a trend towards statistical significance for cognitive impairment (P for trend = 0.074).

Discussion

In this prospective UK birth cohort, having persistent distressing dreams during childhood was associated

with an increased risk of developing cognitive impairment or PD during adulthood, even after accounting for a wide range of potential confounders. The association was especially strong for PD, although this finding should be interpreted with caution given the small number of PD cases in the analysis. Given that there was no evidence of effect modification by sex, this indicates that distressing dreams were associated with an increased risk of developing cognitive impairment or PD in both male and female children.

This is the first study to investigate the association between distressing dreams in childhood and the risk of developing cognitive impairment or PD in adulthood. Although, two population-based cohort studies in the USA had evaluated the association between distressing dreams in middle-aged and older aged adults, and the risk of developing cognitive decline, dementia, and PD later in life.^{4,5} These studies consistently found distressing dreams during both stages of adulthood, to be associated with an increased risk of developing all three outcomes in the future. Therefore, the present study is consistent with, but also extends these prior findings, by demonstrating that distressing dreams which occur during childhood, may also be associated with future dementia and PD.

There are at least three possible explanations for this association. First, as suggested in previous studies,^{4,5} it is possible that distressing dreams in some individuals, are an early manifestation of age-related neurodegenerative diseases such as PD, dementia with Lewy bodies (DLB), or Alzheimer's disease (AD) – which occur as a result of neurodegeneration in right frontal brain regions that are required for downregulating negative emotions during rapid eye movement (REM) sleep dreaming.²⁴ This hypothesis would be consistent with a recent study which demonstrated that the frequency of distressing dreams in adults with PD, was positively correlated with atrophy of grey and white matter in their right frontal lobes.²⁵ In addition, previous studies have shown that REM sleep behaviour disorder (RBD) – a sleep disorder with a high prevalence of distressing dreams - can precede a diagnosis of PD or DLB by up to half a century.²⁶ However, given that the present study identified an association in children as young as age 7, whose brains are still developing, and the fact that no study to date has shown that RBD beginning in childhood is linked with an increased risk of developing DLB or PD,^{26,27} it therefore seems highly unlikely that an underlying neurodegenerative process could explain the present association.

Second, there may be genetic factors that predispose individuals to distressing dreams and to dementia and PD. Indeed, previous studies have identified that nightmare frequency is a highly heritable trait,⁸ and one of the two genes that were shown to confer increased risk for developing nightmares in a recent preprint (*PTPR*),²⁸ is also known to confer increased risk for

| Characteristic | No time point | 1 time point (at 7 or 11) | 2 time points (at 7 and 11) | P value |
|-----------------------------------------|---------------|---------------------------|-----------------------------|---------|
| N | 5470 | 1253 | 268 | |
| Birth | | | | |
| Sex, n (%) | | | | 0.77 |
| Male | 2689 (49.2) | 630 (50.3) | 132 (49.3) | |
| Female | 2781 (50.8) | 623 (49.7) | 136 (50.7) | |
| Country of birth, n (%) | | | | 0.001 |
| England | 4477 (81.8) | 1085 (86.6) | 225 (84.0) | |
| Scotland | 341 (6.2) | 62 (4.9) | 19 (7.1) | |
| Wales | 652 (11.9) | 106 (8.5) | 24 (9.0) | |
| Low birthweight, n (%) | | | | 0.45 |
| Yes | 293 (5.4) | 61 (4.9) | 18 (6.7) | |
| No | 5001 (91.4) | 1152 (91.9) | 240 (89.6) | |
| Missing | 176 (3.2) | 40 (3.2) | 10 (3.7) | |
| Socioeconomic Position, n (%) | | | | 0.71 |
| Class I | 235 (4.3) | 59 (4.7) | 13 (4.9) | |
| Class II | 786 (14.4) | 177 (14.1) | 31 (11.6) | |
| Class III | 3186 (58.2) | 724 (57.8) | 159 (59.3) | |
| Class IV | 638 (11.7) | 133 (10.6) | 29 (10.8) | |
| Class V | 624 (11.4) | 160 (12.8) | 36 (13.4) | |
| Missing | 1 (0.0) | 0 (0.0) | 0 (0.0) | |
| Mother's age at birth, yrs ^a | 27.74 ± 5.6 | 27.18 ± 5.5 | 27.67 ± 5.9 | 0.02 |
| Age 7 | | | | |
| Ever breastfed, n (%) | | | | 0.050 |
| Yes | 3778 (69.1) | 899 (71.7) | 174 (64.9) | |
| No | 1659 (30.3) | 345 (27.5) | 91 (34.0) | |
| Missing | 33 (0.6) | 9 (0.7) | 3 (1.1) | |
| Handedness, n (%) | | | | 0.085 |
| Right | 4557 (83.3) | 1028 (82.0) | 222 (82.8) | |
| Left | 547 (10.0) | 118 (9.4) | 24 (9.0) | |
| Ambidextrous | 330 (6.0) | 102 (8.1) | 20 (7.5) | |
| Missing | 36 (0.7) | 5 (0.4) | 2 (0.7) | |
| Number of siblings ^b | 2.02 ± 1.5 | 1.94 ± 1.5 | 1.94 ± 1.6 | 0.12 |
| Cognitive ability, z-score ^c | 0.01 ± 0.7 | -0.03 ± 0.7 | -0.04 ± 0.7 | 0.13 |
| Height, metres ^d | 1.23 ± 0.1 | 1.23 ± 0.1 | 1.23 ± 0.1 | 0.87 |
| Overweight, n (%) | | | | 0.35 |
| Yes | 490 (9.0) | 114 (9.1) | 31 (11.6) | |
| No | 4550 (83.2) | 1043 (83.2) | 216 (80.6) | |
| Missing | 430 (7.9) | 96 (7.7) | 21 (7.8) | |
| Childhood neglect ^e | 0.75 ± 1.1 | 0.68 ± 1.1 | 0.76 ± 1.2 | 0.14 |
| Anxiety ^f | 1.13 ± 1.9 | 1.30 ± 2.1 | 1.18 ± 1.9 | 0.02 |
| Depression ^g | 0.87 ± 1.5 | 0.93 ± 1.4 | 0.93 ± 1.4 | 0.03 |
| Difficulty falling asleep, n (%) | | | | <0.001 |
| Yes | 911 (16.7) | 351 (28.0) | 76 (28.4) | |
| No | 4537 (82.9) | 899 (71.7) | 191 (71.3) | |
| Missing | 22 (0.4) | 3 (0.2) | 1 (0.4) | |
| Special educational needs, n (%) | | | | 0.50 |
| Yes | 92 (1.7) | 22 (1.8) | 7 (2.6) | |
| No | 5172 (94.6) | 1178 (94.0) | 247 (92.2) | |
| Missing | 206 (3.8) | 53 (4.2) | 14 (5.2) | |
| Head trauma, n (%) | | | | 0.61 |
| Yes | 155 (2.8) | 42 (3.4) | 8 (3.0) | |
| No | 5284 (96.6) | 1201 (95.8) | 259 (96.6) | |
| Missing | 31 (0.6) | 10 (0.8) | 1 (0.4) | |

(Table 1 continues on next page)

| Characteristic | No time point | 1 time point (at 7 or 11) | 2 time points (at 7 and 11) | P value |
|----------------------------------|---------------|---------------------------|-----------------------------|---------|
| (Continued from previous page) | | | | |
| Previous infections ^h | 2.45 ± 1.1 | 2.56 ± 1.1 | 2.45 ± 1.1 | 0.02 |
| Chronic health conditions, n (%) | | | | 0.064 |
| Yes | 314 (5.7) | 84 (6.7) | 23 (8.6) | |
| No | 4895 (89.5) | 1101 (87.9) | 225 (84.3) | |
| Missing | 261 (4.8) | 68 (5.4) | 19 (7.1) | |
| Age 11 | | | | |
| Race, n (%) | | | | 0.47 |
| White | 5109 (93.4) | 1174 (93.7) | 246 (91.8) | |
| Non-white | 33 (0.6) | 10 (0.8) | 3 (1.1) | |
| Missing | 328 (6.0) | 69 (5.5) | 19 (7.1) | |

Plus-minus values are means ± SD. ^aData was missing for 5 participants. ^bData was missing for 15 participants. ^cData was missing for 390 participants. ^dData was missing for 404 participants. ^eScore ranged from 0 to 7, with higher scores indicating greater childhood neglect. Data was missing for 203 participants. ^fScore ranged from 0 to 17, with higher scores indicating more severe anxiety. Data was missing for 185 participants. ^gScore ranged from 0 to 10, with higher scores indicating more severe depression. Data was missing for 185 participants. ^hScore ranged from 0 to 6, with higher scores indicating a higher number of previous infections. Data was missing for 605 participants.

Table 1: Demographic characteristics by distressing dreams status at ages 7 and 11.

developing late-onset AD.²⁹ However, no shared genetic factors have been identified with regards to nightmares and PD.^{28,30}

Third, it is possible that distressing dreams are causal risk factors for cognitive impairment and PD. A causal association would be consistent with a recent population-based study in the USA which identified a dose–response relationship between distressing dream frequency and rates of cognitive decline and dementia development, in both middle-aged and older adults.⁴ Moreover, there are several plausible mechanisms by which distressing dreams could increase dementia and PD risk. For example, distressing dreams are known to cause disturbed sleep (including repeated awakenings during the night), which could in turn lead to impaired glymphatic clearance during sleep,³¹ and thus greater accumulation of pathological proteins in the brain - such as amyloid-β and α-Synuclein.³¹ Alternatively, it is also possible that having regular distressing dreams during childhood and early life might increase dementia and

PD risk by negatively affecting the building of brain and cognitive reserve capacity.^{32,33} Interestingly, if either of these causal hypotheses were to be confirmed, it would suggest that treating distressing dreams during childhood^{34,35} - or preventing them,³⁶ could become a primary prevention strategy for dementia and PD.

This study has several strengths, including the prospective design, long follow-up period, assessment of distressing dreams at two different time periods in childhood, inclusion of a wide range of potential confounders, and the novelty of the approach (few studies have investigated childhood risk factors for cognitive impairment or PD in a nationally representative birth cohort). The study also has some limitations. First, as with all observational studies, it is possible that there was unmeasured confounding. However, to evaluate the robustness of the results to potential unmeasured confounding, E-values can be calculated.^{37,38} The E-value calculated using the aOR for persistent distressing dreams in the primary analysis (1.85) was 3.11,

| Analysis | No time point | 1 time point (at 7 or 11) | 2 time points (at 7 and 11) | P for linear trend |
|-----------------------------------|---------------|---------------------------|-----------------------------|--------------------|
| Cognitive impairment/PD [n (%)] | 199 (3.6) | 51 (4.1) | 17 (6.3) | |
| N | 5470 | 1253 | 268 | |
| Main Analysis | | | | |
| Sex-Adjusted Model | 1 [reference] | 1.13 (0.82, 1.54) | 1.84 (1.11, 3.05)* | 0.041* |
| Fully adjusted Model ^a | 1 [reference] | 1.15 (0.83, 1.58) | 1.85 (1.10, 3.11)* | 0.037* |
| Sensitivity Analysis ^b | 1 [reference] | 1.14 (0.83, 1.58) | 1.84 (1.10, 3.09)* | 0.040* |

OR, odds ratio; CI, confidence interval; PD, Parkinson's disease. *P < 0.05. ^aAdjusted for sex, race, country of birth, low birthweight, mothers age at birth, socioeconomic position, ever breastfed, handedness, number of siblings, cognitive ability, special education needs, height, overweight, childhood neglect, head trauma, chronic health conditions, previous infections, depression, anxiety, and difficulty getting to sleep. ^bSensitivity analysis which used multiple imputation to impute missing covariate data. This analysis was adjusted for covariates in the full model.

Table 2: Risk of cognitive impairment or PD at age 50 by distressing dreams status at ages 7 and 11 (OR and 95% CI).

| Analysis | No time point | 1 time point (at 7 or 11) | 2 time points (at 7 and 11) | P for linear trend |
|-----------------------------------|---------------|---------------------------|-----------------------------|--------------------|
| Cognitive impairment [n (%)] | 197 (3.6) | 49 (3.9) | 16 (6.0) | |
| N | 5470 | 1253 | 268 | |
| Sex-Adjusted Model | 1 [reference] | 1.09 (0.80, 1.50) | 1.75 (1.04, 2.93)* | 0.083 |
| Fully adjusted Model ^a | 1 [reference] | 1.11 (0.80, 1.54) | 1.76 (1.03, 2.99)* | 0.074 |

OR, odds ratio; CI, confidence interval. *P < 0.05. ^aAdjusted for sex, race, country of birth, low birthweight, mothers age at birth, socioeconomic position, ever breastfed, handedness, number of siblings, cognitive ability, special education needs, height, overweight, childhood neglect, head trauma, chronic health conditions, previous infections, depression, anxiety, and difficulty getting to sleep.

Table 3: Risk of cognitive impairment at age 50 by distressing dreams status at ages 7 and 11 (OR and 95% CI).

indicating that an unmeasured confounder would have to be more than three times as prevalent among children with persistent distressing dreams as it was among children with no distressing dreams, and would have to increase the risk of cognitive impairment/PD by more than threefold, in order to fully explain the observed association. As such, the E-value provides evidence for this study's robustness. Second, the children's distressing dreams status was determined by maternal report rather than self-report. Although maternal report is routinely used in birth cohort studies to determine children's distressing dream status,^{12,13} and has previously been shown to have a fairly high correlation with children's self-reports,³⁹ it can however lead to an underestimation of the prevalence of distressing dreams.³⁹ Consequently, this could have led to an underestimation of the association between distressing dreams and incident cognitive impairment/PD in this study. Third, the questionnaire item used to assess distressing dreams asked about night terrors (sleep terrors) as well as bad dreams, and thus it is possible that some children in the distressing dreams groups were misclassified (i.e., they had night terrors, but not bad dreams or nightmares). However, given that parents frequently describe their children's nightmares using the term "night terrors",⁴⁰ and the fact that a significant proportion of people with night terrors also experience nightmares and bad dreams,⁴¹ it is probable that only a small proportion of participants in the distressing dreams groups were misclassified - if any. Fourth, this study relied on self-reported doctor-diagnosis to determine

incident PD, and therefore may have missed or misclassified some cases. Fifth, although cognitive impairment and PD can emerge during midlife,^{16,42} they most often develop after the age of 65, which means that assessing these outcomes at age 50 is relatively early (which would explain why the number of incident PD cases in this study was small and the fact that only few participants [n = 21] were impaired in more than one cognitive domain). Continued follow-up of this cohort will allow for more PD cases to be diagnosed over time and will enable more precise estimates for the association between distressing dreams and incident PD (Table 4). In addition, longer follow-up will allow for clinical dementia to be assessed as an outcome - which may be preferable to cognitive impairment - given the fact that some individuals classified as cognitively impaired may not have an underlying neurodegenerative dementia. Sixth, it is possible that including covariates with missing data might have introduced some bias. However, the results were similar and remained significant when using multiple imputation to impute missing covariate data (Table 2). Finally, given that distressing dreams were only assessed during middle childhood, it is possible that the findings might not be generalisable to younger and older children.

In summary, this study provides evidence for the first time that having distressing dreams during childhood, may be associated with an increased risk of developing cognitive impairment or PD during adulthood. Furthermore, these findings raise the possibility that distressing dreams may be an independent risk

| Analysis | No time point | 1 time point (at 7 or 11) | 2 time points (at 7 and 11) | P for linear trend |
|-----------------------------------|---------------|---------------------------|-----------------------------|--------------------|
| PD [n (%)] | 2 (0.04) | 2 (0.2) | 1 (0.4) | |
| N | 5470 | 1253 | 268 | |
| Sex-Adjusted Model | 1 [reference] | 4.35 (0.75, 25.13) | 12.25 (1.61, 93.03)* | 0.018* |
| Fully adjusted Model ^a | 1 [reference] | 3.12 (0.57, 17.11) | 7.35 (1.03, 52.73)* | 0.050* |

OR, odds ratio; CI, confidence interval; PD, Parkinson's disease. *P < 0.05. ^aAdjusted for sex, race, country of birth, low birthweight, mothers age at birth, socioeconomic position, ever breastfed, handedness, number of siblings, cognitive ability, special education needs, height, overweight, childhood neglect, head trauma, chronic health conditions, previous infections, depression, anxiety, and difficulty getting to sleep.

Table 4: Risk of PD at age 50 by distressing dreams status at ages 7 and 11 (OR and 95% CI).

factor for neurodegeneration. If these findings are replicated in future studies, and the association is confirmed to be causal, it is possible that early treatment of distressing dreams could become a primary prevention strategy for dementia and PD.

Contributors

AIO was responsible for conception, organisation, and execution of the research project; design and execution of the statistical analysis; verification of the underlying data; and manuscript preparation. AIO had full access to all the data in the study and accepts responsibility for the decision to submit for publication.

Data sharing statement

Data from the 1958 British Birth Cohort Study are available by application through the UK Data Service: <https://beta.ukdataservice.ac.uk/datacatalogue/series/series?id=2000032>.

Declaration of interests

The author declares no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.eclinm.2023.101872>.

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