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Migraine and Cognitive Decline in the Population-Based EVA Study

Pamela M. Rist, MSc, **Carole Dufouil, PhD**, **M. Maria Glymour, ScD**, **Christophe Tzourio, MD, PhD**, and **Tobias Kurth, MD, ScD**
Division of Preventive Medicine (P.M.R., T.K.), Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; the Departments of Epidemiology (P.M.R., T.K.) and Society, Health, and Human Development (M.M.G.), Harvard School of Public Health, Boston, MA; INSERM Unit 708-Neuroepidemiology (C.D., C.T., T.K.), Paris, France, and University Pierre et Marie Curie (C.D., C.T., T.K.), Paris France

Abstract

Background—Previous studies on migraine and cognition have shown mixed results. However, many could not assess the relationship between migraine and change in cognitive function or only used a limited number of cognitive tests.

Methods—Prospective cohort study among 1170 participants of the Epidemiology of Vascular Aging Study who provided information about migraine status and completed cognitive testing. Participants were classified as having no severe headache, non-migraine headache and migraine. Cognitive functioning was measured at up to four time points using nine different cognitive

Address of Correspondence: Tobias Kurth, MD, ScD, INSERM Unit 708—Neuroepidemiology, Hôpital de la Pitié-Salpêtrière, 47 boulevard de l'Hôpital, 75651 Paris Cedex 13, France, Tel: +33 (0) 1 42 16 25 40, Fax: +33 (0) 1 42 16 25 41, tobias.kurth@univ-bordeaux.fr.

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functioning tests. Linear mixed effects models were used to evaluate the relationship between migraine status and change in cognitive function.

Results—Of the 1170 participants, 938 had no severe headache, 167 had migraine, and 65 had non-migraine headache. After adjusting for age, gender, education, and smoking status, people with migraine or non-migraine headache did not experience a greater rate of cognitive decline than those without headache or migraine in any domain (for the MMSE, p-values were 0.68 for the non-migraine headache and time interaction and 0.85 for the migraine and time interaction) during 4-5 years of follow-up. For the Wechsler, those with migraine declined less over time (p-value=. 02).

Conclusion—Migraine was not associated with faster cognitive decline over time.

Keywords

Migraine; cognitive function; epidemiology

Approximately 20% of the female population and 6% of the male population suffer from migraine (1). Migraine has been associated with increased risk of vascular events, specifically stroke (2-5). This risk appears to be the highest among people who experience transient neurological symptoms that usually manifest as visual disturbances called migraine aura. Up to one-third of migraineurs experience migraine with aura on the population level. In addition to increasing the risk of cardiovascular events, migraine has been linked to an increased risk of silent brain lesions (6-8). These associations have led to speculation that migraine may be a progressive brain disorder (9). If this theory were correct, we would expect migraine to be associated with cognitive decline over time. Given the high prevalence of migraine in the general population, determining whether migraine is associated with cognitive decline has important public health implications. However, many uncertainties exist with regard to functional consequences of migraine on the brain.

Several cross-sectional studies have looked at the association between migraine and cognitive functioning, but the results of these studies have been mixed. Some studies found no differences (10-15) while others found evidence of worse cognitive performance among migraineurs compared to migraine free controls (16-21). A more recent prospective study that examined migraine status and cognitive decline over time found that among those who were 50 years of age or older at baseline, there was less decline across time among migraineurs overall and especially among migraineurs with aura (22).

The Epidemiology of Vascular Ageing (EVA) Study provides a unique opportunity to study potential long-term consequences of migraine on cognitive function during up to five years of follow-up.

Methods

The EVA Study is a longitudinal study of vascular and cognitive aging in a population-based cohort from Nantes in France. Subjects born between 1922 and 1932 and were selected based on the city's electoral rolls. Additionally, the spouses of enrolled subjects were asked to participate if they met the age requirements. A total of 1,389 subjects completed the baseline assessment between June 1991 and June 1993. Since baseline, five additional follow-ups have been performed, the last in 2000. A standardized face-to-face interview was used to collect data on demographic background, occupation, medical history, medication use and personal habits at all visits. The study protocol was approved by the Comité d'Ethique du Centre Hospitalier Universitaire de Kremlin-Bicêtre (Kremlin-Bicêtre, France) and written consent was obtained from all participants.

Migraine Assessment

Migraine was assessed during the third wave of the study (1995-1996), when 1188 subjects (92%) participated. Of the 242 participants who reported a lifetime history of severe headache, 233 had a telephone interview with a neurologist (four died before the date of the interview, one was deaf and four could not be contacted). We used the "probable migraine" criteria from the second International Classification of Headache Disorders (ICHD-II) to define migraine to be consistent with previous population-based studies (3, 7). Individuals who did not have a lifetime history of migraine were divided into two categories: "no history of severe headache" and "non-migraine headache" a group of patients likely to have tension-type headache because other headache types are rare in the general population (23). We also collected information on whether the participant experienced migraine aura.

Cognitive Functioning

Since migraine/headache was assessed in the third wave of the study, we used cognitive assessments from the third wave of the study as our baseline measurements. Subjects completed a battery of nine neuropsychological tests administered by trained psychologists. The tests were designed to cover a large range of cognitive functions including global cognitive function, reasoning, processing speed and psychomotor speed. The battery included the Mini Mental State Examination (MMSE), the Digit Symbol Subsitution test from the Weschler Adult Intelligence Scale-Revised, the Trail Making Test Part A and B, the Rey 15-word Memory Test, the Raven Progressive Matrics, the Benton Visual Retention and Facial Recognition Tests, the Finger Tapping Test and the Word Fluency Test 1 minute. For the Trail Making Test, we assessed time to completion, thus a high value indicates worse performance. For the other tests participants received a score based on their performance on that test. The neuropsychological battery took between 60 to 90 minutes to complete. Three cognitive follow-up assessments were performed in 1998, 1999 and 2000. For the Rey 15-word Memory Test and the Raven Progressive Matrices, we only have follow-up in 1998. For the Benton Visual Retention Test and Benton Facial Recognition Test, follow-up is only available in 1999 and 2000. All other tests were offered at all follow-up times.

Statistical Methods

We excluded the nine people with missing headache information and additional nine for whom no cognitive test data were available, leaving 1170 for this study. We used linear regression adjusting for age, sex, education, and smoking status (never, past and current) to obtain mean scores for each cognitive test according to headache status (no severe headache, non-migraine headache and migraine) at baseline and at each follow-up. Analysis of covariance, adjusting for age, gender, education, and smoking status was used to test for differences in mean levels of cognitive functioning between the headache groups at baseline and at the follow-up time points.

In exploratory analyses, we further evaluated the role of migraine aura status. We used ANCOVA to examine whether there were differences in baseline cognitive functioning between those with no severe headache, non-migraine headache, migraine with aura and migraine without aura.

To examine whether change in cognitive functioning over time differed based on migraine and headache status, we used linear mixed effect models. We treated time (defined as interview wave) as a linear variable and allowed random slopes and intercepts for individuals. We also ran a separate set of models in which we treated time (defined as interview wave) as an indicator variable to account for any non-linearity in the change in scores over time and allowed random intercepts for individuals. We used these models to

test whether migraine status modified the rate of change in scores over time. Our first model adjusted for age at baseline (continuous), gender, education (continuous), and smoking status (never, past and current), variables that we believed could be confounders based on biological mechanisms. Our second model adjusted additionally for other potential confounders including systolic blood pressure (continuous), diastolic blood pressure (continuous), total cholesterol (continuous), body mass index (continuous), daily alcohol consumption (continuous), and diabetes (yes/no). Since the directionality of the association between migraine and depression is unclear, we adjusted for high depressive symptoms (yes/no) as assessed by the CES-D in a third model that additionally included all the variables in model two. Finally, to control for the impact of the APOE ε4 allele, we constructed a fourth model that controlled for age, gender, education, smoking status and ε4 carrier status (yes/no).

In a series of exploratory analyses, we tested for effect measure modification of the association between migraine status and rate of change in cognitive functioning over time by age (<69 years (the median age) or ≥69 years), gender, APOE ε4 allele carrier status (yes/no), and *MTHFR* genotype (TT genotype versus non-TT genotype). We tested for effect modification by APOE ε4 allele carrier status because it has been linked to an increased risk of Alzheimer's disease (24) and by MTHFR genotype because it has been linked to an increased risk of migraine (25). To increase power to detect effect modification, we treated time as a linear variable.

In a subgroup of participants for whom we had a brain MRI, we evaluated whether the association between migraine and cognitive decline depended on the prevalence of structural brain lesions since white matter hyperintensities have been associated with both migraine (6, 7) and cognitive decline (26). The presence of any brain infarct and total white matter hyperintensity volume was measured in 775 participants as described previously (7, 27). We then tested for effect modification of the association between migraine and cognitive decline by the presence of any brain infarct (yes versus no) and also by total white matter hyperintensity (highest tertile versus two lowest tertiles) among these participants.

Finally, we examined the association between migraine status and substantial cognitive decline in any cognitive test. For each individual we calculated the average change per year for each test by dividing the change in score between their last and first assessment by the number of years between assessments. Participants were classified as having "substantial decline" if they were in the bottom ten percent of the distribution of average yearly change in score for that cognitive test. Logistic regression was used to determine the relative risk of experiencing "substantial decline" among people with migraine and non-migraine headache versus those with no severe headache.

Less than 50 people were missing information on education, systolic and diastolic blood pressure, total cholesterol, body mass index, and presence of depressive symptoms as assessed by the CES-D. These people were assigned to the mean levels of the missing variable. Imputing missing data versus deleting the people missing covariate data did not substantially affect our results. No information was missing for the other covariates used in our analyses.

All models were fit using in SAS 9.1. All probability values were two-tailed and $p<0.05$ was considered statistically significant.

Results

Of the 1170 participants included in this analysis, 938 had no severe headache, 65 had non-migraine headache and 167 had migraine (24 had migraine with aura). The baseline

characteristics of the cohort by headache and migraine status are shown in Table 1. Those with migraine were more likely to be female and never smokers. Additionally, daily alcohol consumption was lower among those with migraine than those with no severe headache or non-migraine headache. People with migraine or non-migraine headache were more likely to have depressive symptoms than those without headache.

Table 2 shows the mean scores at baseline and all available follow-ups by migraine status for each of the cognitive tests adjusted for age, gender, education and smoking status. Average test scores declined from first to last assessment, with the exception of the MMSE and Word Fluency Test 1 minute for all groups, the Trail Making Test B for no severe headache and non-migraine headache groups and the Trail Making Test A for the no severe headache and non-migraine headache groups.

Table 2 also shows p-values from the ANCOVAs used to test for differences in mean scores comparing those with no severe headache, non-migraine headache and migraine for each cognitive test at each available time point. The majority of the tests did not show any significant difference in mean score between the groups. While a few of the p-values did reach significance, the p-values for those tests at future time points did not. Additionally, from examining the adjusted means in Table 2, we observe that some of the significant p-values were due to the higher scores among the non-migraine headache or migraine groups. Sensitivity analyses in which migraine with aura and migraine without aura were treated as separate groups showed a similar pattern (results not shown).

Table 3 shows the results from linear mixed effect models examining mean difference in rate of change in cognitive functions over time by migraine status adjusting for age, gender, education and smoking status when time was treated as a linear variable. Results were similar when time was treated as an indicator variable (results not shown). Except for the Wechsler test, all of the p-values for the migraine and time or non-migraine headache and time interactions were not significant, indicating that people with migraine or non-migraine headache do not experience a greater rate of cognitive decline than those without any headache. For the Wechsler test, we do see a significant difference in the rate of change over time when comparing those with migraine to those no severe headache. The average rate of change is −1.34 points per year among the no severe headache group. Among migraineurs the average rate of change is only −0.84 (−1.34 + 0.50 [migraine time interaction]) points per year, indicating that migraineurs decline less over time than those without headache.

Additional adjustment for blood pressure, total cholesterol, body mass index, daily alcohol consumption and diabetes did not impact our results (results not shown). Adjusting for depressive symptoms or APOE ε4 carrier status also did not change our results (results not shown).

We did not find any evidence of effect modification by age, *MTHFR* genotype, or APOE ε4 carrier status (all p-interactions >0.08). For most cognitive tests, we did not find effect modification by the presence of brain infarctions, total white matter hyperintensities or gender. For the Wechsler test, the interaction between migraine, presence of brain infarctions and time was of borderline significance (p-interaction=0.06). Among those without brain infarctions, the annual rate of change for migraineurs was −0.82, compared to −1.35 among non-migraineurs. In contrast, among those with brain infarctions, the annual rate of change for migraineurs was −1.80, compared to −1.08 among non-migraineurs, indicating that among those with brain infarcts, the rate of decline was greater for migraineurs. For the Raven test, the rate of cognitive decline appears to be in opposite directions for migraineurs with low versus high total white matter hyperintensity load (the annual rate of change is −0.34 for those with low load versus −0.09 for those with high

load) indicating that migraineurs with low total white matter hyperintensity load may experience more decline (p-interaction=0.06). Finally, there was a suggestion that gender modified the association between severe headache and cognitive decline as measured by the Raven test, indicating that males declined somewhat less than women (0.03 vs. −0.31; p-interaction=0.06).

Table 4 shows the results from analyses examining risk of substantial decline in each cognitive test by migraine and headache status. Again, there were no meaningful differences between the groups.

Discussion

Data from this population-based prospective cohort study of elderly men and women did not show a strong relationship between migraine and cognitive decline as measured by several different cognitive functioning tests. For Wechsler measure of cognitive function, we found evidence that migraineurs experienced slower decline than individuals without headache. In general, we found no evidence that the association between migraine and cognitive change was modified by presence of white matter hyperintensities or brain infarctions, although there was a suggestion of stronger decline among migraineurs with brain lesions for one test.

Several cross-sectional studies have shown no relationship between migraine status and level of cognitive functioning (10-15). Although other cross-sectional studies have found evidence of worse cognitive performance among migraineurs compared to non-migraineurs (16-20), these studies cannot evaluate change in cognitive functioning over time. Determining if there is an association between migraine and cognitive decline and not just cognitive functioning is important because cognitive decline is a strong predictor of dementia onset and intervening early in the cognitive decline process may be the most effective way of preventing dementia.

A few prospective follow-up studies have assessed the relationship between migraine and change in cognitive function over time. The Dunedin Multidisciplinary Health and Development Study assessed cognitive and neuropsychological function every few years throughout childhood and then interviewed participants at age 26 to determine if they had migraine or tension-type headache (TTH) (28). Migraineurs had slightly lower scores on tests of verbal ability (particularly verbal comprehension) from ages 3 to 13 than those with TTH or those without TTH or migraine. The difference in scores did reach significance. In contrast, migraineurs had normal scores on tests of reading, verbal expression and math skills.

A larger prospective follow-up study on migraine and cognitive decline used data from 1,448 individuals participating in Wave III and IV of the Baltimore cohort of the NIH Mental Health Epidemiologic Catchment Area study (22). Cognitive functioning was assessed by the modified version of Rey Verbal Learning Test and the MMSE. They found that although migraineurs overall and migraineurs with aura showed significantly lower scores on baseline tests of delayed and immediate recall, migraineurs overall and especially migraineurs with aura showed significantly less decline in delayed and immediate recall over time. Age-stratified analyses using results from the MMSE showed that among participants who were less than 50 years of age at baseline, there was no significant effect of migraine status on cognitive decline. Among those who were 50 years of age or older at baseline, there was less mean decline across time among migraineurs overall and especially among migraineurs with aura.

A more recent study using participants enrolled in the Maastricht Aging Study (21) assessed cognitive function at baseline and six years later using the MMSE, immediate and delayed

recall tests and other tests for simple and complex speed. No association between migraine and cognitive decline was found. Additionally, the study assessed specific and non-specific migraine medication use and found that neither were related to cognitive score.

Similar to other studies (21, 22), we also did not observe greater rates of decline among migraineurs and were able to expand upon the findings of previous studies. One of the key differences between our study and some previous studies in the age of the cohorts. By using an elderly population and asking about lifetime history of migraine, our study is able to assess the long-term consequences of migraine on cognitive functioning and expand upon the findings from younger cohorts. Additionally, we used a wider variety of cognitive tests than previous studies. This permitted us to assess the impact of migraine over a wide range of cognitive domains and to assess the impact of migraine on change in cognitive function and makes our overall lack of association more compelling. Finally the availability of MRI data allowed us to assess the impact of white matter hyperintensities and brain infarcts on the association between migraine and cognitive decline which previous studies were not able to do.

While previous studies have linked migraine, particularly migraine with aura, to increased prevalence of infarct-like lesions, subclincial cerebellar posterior circulation territory infarcts and deep white matter hyperintensities, our results suggest that they do not lead to greater cognitive decline among patients with migraine or other severe headaches.

Some limitations should be noted. First, due to low case counts, we were not able to separately examine migraine with and without aura and change in cognitive functioning over time. Sensitivity analyses did not show significant differences in mean cognitive scores, but confidence intervals were wide due to the small sample size. Additionally, a previous study has shown that migraineurs with aura tend to exhibit even less decline over time than migraineurs overall (22). Second, we did experience loss to follow-up over time which may limit the comparison of average test scores from baseline to follow-up times. However, being in the migraine or headache group did not predict being lost to follow-up or being in the MRI cohort (7). Third, while we did see a decrease in most cognitive scores over time, the follow-up time of four years limits our ability to observe larger changes in cognitive function over a longer period of time. Fourth, since participants were asked to recall lifetime history of migraine, there is potential for some misclassification of our exposure. If those with migraine were more cognitively impaired at baseline and therefore inaccurately report their history of migraine, our results may be attenuated. While this study is larger than many previous studies, we may still have limited power to detect true differences in cognitive decline between migraineurs and those who do not experience migraine or headache. Finally the generalizability of these results may be limited because EVA participants are of higher socio-economic status and are healthier compared to other people of the same age in France (29).

In conclusion, migraine and non-migraine headache do not seem to be associated with cognitive decline in the elderly and this lack of association is not substantially modified by presence or absence of several factors, including structural brain lesions. Given the high prevalence of migraine in the population, this lack of association may be reassuring for patients with migraine and their treating physicians. Future studies should examine whether the effect of migraine on cognitive functioning and cognitive decline varies by migraine specifics, such as attack frequency and severity. Additionally, future studies should assess whether chronification of migraine or other headache forms relate to cognitive decline.

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Table 1

Baseline characteristics of EVA Study participants for whom migraine status and at least one cognitive functioning test were available.

Characteristic	No history of severe headache (N=938)	Non-migraine headache (N=65)	Migraine (N=167)
Mean age (yrs) (SD)	68.9 (3.0)	69.3 (3.1)	69.0 (2.9)
Sex (% male)	45.7	49.2	15.0
Smoking status (%)			
Never	56.5	53.9	72.5
Past	34.5	33.9	22.8
Current	9.0	12.3	4.8
Age at which schooling ended (yrs) (SD)	16.9 (3.9)	16.6 (4.0)	16.8 (3.2)
Mean systolic blood pressure (mmHg) (SD)	135.9 (20.6)	135.2 (20.9)	131.5 (20.9)
Mean diastolic blood pressure (mmHg) (SD)	77.4 (12.3)	76.4 (11.9)	75.5 (13.2)
Mean total cholesterol (mmol) (SD)	6.1 (1.0)	6.1 (0.8)	6.3 (1.0)
Mean body mass index (kg/m^2) (SD)	26.0 (3.8)	25.7 (3.8)	25.6 (4.1)
Mean daily alcohol consumption (ml) (SD)	15.5 (17.9)	15.9 (20.5)	8.2 (11.9)
Diabetes (%)	6.6	4.6	5.4
Depressive symptoms (%)	9.5	14.1	12.8
MTHFR (% TT genotype)	14.4	6.6	13.9
APOE (% ε4 carrier)	23.1	22.0	24.0

Table 2

Multivariate adjusted* mean cognitive scores and standard errors (SE) at each time point by migraine status.

	No history of severe headache		Migraine		Non-migraine headache		
	No. of participants	**Adjusted mean* (SE)**	**No. of participants**	**Adjusted mean* (SE)**	**No. of participants**	**Adjusted mean* (SE)**	**Overall p-value from ANCOVA***
MMSE							
Baseline	928	27.43 (0.09)	167	27.69 (0.17)	63	27.57 (0.26)	0.32
Year 2	562	27.86 (0.10)	97	28.13 (0.20)	43	28.43 (0.27)	0.06
Year 3	625	28.11 (0.10)	118	28.36 (0.19)	41	28.30 (0.28)	0.38
Year 4	530	28.22 (0.12)	101	28.34 (0.22)	41	28.39 (0.32)	0.75
Wechsler							
Baseline	924	47.15 (0.49)	166	48.56 (0.94)	63	45.92 (1.43)	0.21
Year 2	558	44.25 (0.62)	96	46.28 (1.20)	43	45.45 (1.65)	0.21
Year 3	586	45.01 (0.60)	113	47.36 (1.14)	48	44.34 (1.63)	0.11
Year 4	506	43.28 (0.62)	96	45.28 (1.18)	39	43.91 (1.75)	0.24
Trail Making A							
Baseline	921	24.86 (0.06)	166	24.89 (0.12)	63	24.94 (0.19)	0.90
Year 2	558	24.92 (0.03)	96	24.98 (0.06)	43	24.99 (0.08)	0.39
Year 3	591	24.88 (0.06)	113	25.01 (0.12)	49	25.00 (0.17)	0.52
Year 4	504	24.86 (0.12)	96	25.02 (0.23)	40	24.93 (0.33)	0.78
Trail Making B							
Baseline	912	24.22 (0.09)	166	23.46 (0.17)	63	24.36 (0.26)	0.35
Year 2	557	24.17 (0.09)	96	24.42 (0.18)	43	24.48 (0.24)	0.21
Year 3	590	24.21 (0.10)	112	24.55 (0.19)	49	24.10 (0.27)	0.17
Year 4	502	24.02 (0.15)	96	24.23 (0.29)	40	23.98 (0.42)	0.76
Rey							
Baseline	868	52.34 (0.40)	154	55.20 (0.77)	57	54.29 (1.20)	<0.01
Year 2	544	48.17 (0.56)	94	50.01 (1.09)	42	48.61 (1.50)	0.24

	No history of severe headache		Migraine		Non-migraine headache		
	No. of participants	Adjusted mean* (SE)	No. of participants	Adjusted mean* (SE)	No. of participants	Adjusted mean* (SE)	Overall p-value from ANCOVA*
Raven							
Baseline	925	13.67 (0.11)	165	13.95 (0.22)	63	13.90 (0.34)	0.39
Year 2	588	13.52 (0.14)	96	13.74 (0.28)	43	13.36 (0.38)	0.66
Benton							
Baseline	869	21.14 (0.10)	155	21.01 (0.19)	60	20.62 (0.29)	0.18
Year 3	603	11.33 (0.10)	115	11.65 (0.20)	49	10.76 (0.29)	0.03
Year 4	502	11.60 (0.10)	95	11.64 (0.19)	40	12.01 (0.27)	0.03
Finger Tapping							
Baseline	922	138.78 (0.83)	166	140.78 (1.61)	63	139.00 (2.44)	0.47
Year 2	557	141.71 (1.06)	97	147.14 (2.04)	43	141.81 (2.82)	0.03
Year 3	589	136.64 (1.02)	111	136.44 (1.95)	49	139.27 (2.83)	0.65
Year 4	496	127.60 (1.12)	92	129.28 (2.12)	36	128.41 (3.12)	0.73
Word Fluency							
Baseline	924	25.32 (0.58)	167	25.64 (1.13)	63	25.79 (1.55)	0.93
Year 2	561	24.55 (0.43)	97	26.83 (0.83)	43	25.47 (1.15)	0.02
Year 3	615	25.78 (0.43)	119	26.26 (0.81)	49	26.93 (1.18)	0.55
Year 4	418	26.06 (0.52)	75	28.20 (1.00)	36	25.89 (1.37)	0.10

P-values from ANCOVAs comparing no history of severe headache, non-migraine headache and migraine.

*Adjusted for age (continuous), gender, education (age at which education was completed) and smoking status (never, past and current).

Table 3

Multivariate-adjusted* associations between rate of change in cognitive function by migraine and non-migraine headache status.

Cognitive Test	Coefficient (SE)	p-value
MMSE		
Time	0.24 (0.03)	<0.01
Migraine	0.28 (0.21)	0.18
Migraine*Time	−0.01 (0.07)	0.85
Headache	0.33 (0.32)	0.30
Headache*Time	−0.04 (0.10)	0.68
Wechsler		
Time	−1.34 (0.09)	<0.01
Migraine	1.09 (1.02)	0.28
Migraine*Time	0.50 (0.22)	0.02
Headache	−1.32 (1.53)	0.39
Headache*Time	0.25 (0.33)	0.44
Trail Making A		
Time	0.01 (0.05)	0.79
Migraine	−0.03 (0.24)	0.92
Migraine*Time	0.04 (0.13)	0.76
Headache	0.11 (0.37)	0.76
Headache*Time	−0.04 (0.20)	0.84
Trail Making B		
Time	−0.07 (0.04)	0.05
Migraine	0.22 (0.21)	0.29
Migraine*Time	0.02 (0.09)	0.83
Headache	0.38 (0.32)	0.24
Headache*Time	−0.13 (0.14)	0.34
Rey		
Time	−1.39 (0.10)	<0.01
Migraine	3.19 (0.82)	<0.01
Migraine*Time	−0.41 (0.27)	0.12
Headache	1.66 (1.24)	0.18
Headache*Time	−0.35 (0.39)	0.36
Raven		
Time	−0.11 (0.03)	<0.01
Migraine	0.36 (0.24)	0.14
Migraine*Time	−0.07 (0.08)	0.42

Cognitive Test	Coefficient (SE)	p-value
Headache	0.26 (0.36)	0.48
Headache*Time	−0.14 (0.12)	0.22
Benton		
Time	−3.78 (0.05)	<0.01
Migraine	−0.13 (0.38)	0.73
Migraine*Time	0.05 (0.13)	0.67
Headache	−1.06 (0.58)	0.07
Headache*Time	0.29 (0.19)	0.14
Finger Tapping		
Time	−3.49 (0.21)	<0.01
Migraine	2.53 (1.89)	0.18
Migraine*Time	−0.42 (0.54)	0.43
Headache	1.18 (2.86)	0.68
Headache*Time	0.15 (0.81)	0.85
Word Fluency		
Time	0.33 (0.11)	<0.01
Migraine	1.00 (0.93)	0.28
Migraine*Time	0.24 (0.27)	0.36
Headache	1.05 (1.32)	0.42
Headache*Time	−0.19 (0.37)	0.60

Reference group are those with no history of severe headache.

*Adjusted for age (continuous), gender, education (age at which education was completed) and smoking status (never, past and current).

Table 4

Multivariate adjusted* odds ratios of severe decline in each cognitive test comparing those with migraine or headache to those with no history of severe headache.

	No history of severe headache		Migraine			Non-migraine headache		
	No. of participants with severe decline	OR	No. of participants with severe decline	OR (95% CI)	p-value	No. of participants with severe decline	OR (95% CI)	p-value
MMSE	105	1.00	15	0.76 (0.42, 1.37)	0.55	7	0.88 (0.39, 2.01)	0.98
Wechsler	82	1.00	12	0.77 (0.40, 1.46)	0.53	6	0.95 (0.40, 2.28)	0.86
Trail Making A	32	1.00	4	0.57 (0.19, 1.65)	0.16	4	1.68 (0.57, 4.98)	0.18
Trail Making B	67	1.00	12	0.90 (0.47, 1.75)	0.26	9	1.87 (0.86, 4.04)	0.10
Rey	53	1.00	11	1.20 (0.59, 2.44)	0.47	3	0.75 (0.22, 2.54)	0.55
Raven	55	1.00	11	1.02 (0.50, 2.05)	0.31	8	2.30 (1.00, 5.31)	0.06
Benton	73	1.00	10	0.66 (0.33, 1.33)	0.09	9	1.65 (0.77, 3.56)	0.09
Finger Tapping	77	1.00	15	1.19 (0.65, 2.18)	0.31	4	0.64 (0.23, 1.83)	0.33
Word Fluency	55	1.00	11	1.13 (0.56, 2.28)	0.63	7	1.86 (0.78, 4.44)	0.22

*Adjusted for age (continuous), gender, education (age at which education was completed) and smoking status (never, past and current).