Published in final edited form as:

Brain Imaging Behav. 2015 June ; 9(2): 204–212. doi:10.1007/s11682-014-9297-9.

WHO WANTS A FREE BRAIN SCAN? ASSESSING AND CORRECTING FOR RECRUITMENT BIASES IN A POPULATION-BASED sMRI PILOT STUDY

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Abstract

Neuroimaging research is usually conducted in volunteers who meet *a priori* selection criteria. Selection/volunteer bias is assumed but cannot be assessed. During an ongoing population-based cohort study of 1982 older adults, we asked 1702 active participants about their interest in undergoing a research brain scan. Compared with those not interested, the 915 potentially interested individuals were significantly younger, more likely to be male, better educated, generally healthier, and more likely to be cognitively intact and dementia-free. In 48 of the interested individuals, we conducted a previously reported pilot structural magnetic resonance imaging (sMRI) study modelling mild cognitive impairment (MCI) vs. normal cognition, and Clinical Dementia Rating (CDR)=0.5 vs. CDR=0, as a function of sMRI atrophy ratings. We now compare these 48 individuals (1) with all interested participants, to assess selection bias; (2) with all who had been asked about their interest, to assess volunteer bias; and (3) with the entire study cohort, to assess attrition bias from those who had dropped out before the question was asked. Using these data in propensity score models, we generated weights which we applied to logistic regression models reanalyzing the data from the pilot sMRI study. These weighted models

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CONFLICT OF INTEREST STATEMENT

Authors Ganguli, Lee, Hughes, Jakubcak, Snitz, Chang, and Duara declare no conflicts of interest.

adjusted, in turn, for selection bias, interest/volunteer bias, and attrition bias. They show fewer regions of interest to be associated with MCI/ CDR than were in the original unweighted models. When study participants are drawn from a well-characterized population, they can be compared with non-participants, and the information used to correct study results for potential bias and thus provide more generalizable estimates.

Introduction

Neuroimaging research is typically conducted in clinical samples, where study participants have volunteered or been referred for the studies of brain structure and processes in aging and disease. The scientific value of these studies is unquestionable, but there is always a concern about how selection factors may influence study results. Their internal validity could be affected if those who do and do not participate are systematically different with regard to the characteristics under study. Even if internally valid, a study may lose generalizability (external validity) if selection criteria for study participation are too narrow (Kukull 2012). Since the characteristics of those who do not participate in a given study are typically unknown, the nature and extent of “volunteer bias” and “selection bias” are difficult to determine. Previous studies have shown that volunteers are younger, better educated, healthier, cognitively better than those randomly selected for research (Ganguli 1998; Jaramillo 2007); another study investigated personality traits of those who agreed to participate in a functional imaging study (Oswald 2013). How these factors actually influence the imaging study results is usually a matter for speculation. One potential solution is to recruit neuroimaging study participants from within a well-characterized population, so that characteristics of participants and non-participants can be compared. Any differences detected can then be duly considered when interpreting study results, and potentially adjusted for in the analyses (Jaramillo 2007).

During a large ongoing population-based cohort study of mild cognitive impairment in older adults, we asked all active participants about their potential interest in enrolling in a future brain MRI study. We compared those who were asked this question with those who had been lost to followup before the question was asked; and we compared those who expressed interest with those who did not express interest in an MRI study. We then recruited a small nonrandom subgroup of interested participants to take part in a pilot structural MRI (sMRI) study. Comparing those who originally expressed interest versus no interest, we identified characteristics associated with potential interest in MRI study participation. Using this information, we generated weights that could be used to adjust MRI study analyses, and determined how selection bias, volunteer/interest bias, and attrition bias may have influenced study results.

Methods

Study site and population

Our ongoing study cohort, the Monongahela-Youghiogheny Healthy Aging Team (MYHAT), is an age-stratified random population sample drawn from the publicly available voter registration lists for a small-town region of Pennsylvania (USA.) All study procedures

followed are in accordance with the ethical standards of the University of Pittsburgh Institutional Review Board and with the Belmont Report (Department of Health, Education, and Welfare, Belmont Report 1979). All participants provided written informed consent.

Recruitment criteria were (a) age 65 years or older, (b) living within the selected towns, (c) not already in long-term care institutions. Individuals were ineligible if they (d) were too ill to participate, (e) had severe vision or hearing impairments, (f) were decisionally incapacitated. We recruited 2036 individuals over a two-year period. Since the project was designed to study MCI, we screened out 54 who exhibited substantial impairment by scoring $<21/30$ on the age-education-corrected Mini-Mental State Evaluation (MMSE). The remaining 1982 individuals underwent a detailed assessment at study entry and were invited to be re-assessed annually (Ganguli 2009; Ganguli 2010). As each data collection wave lasted two years, annual assessments took place in overlapping waves, such that, e.g., half the cohort had their second cycle while the other half was still in its first cycle. Starting a year after the study was initiated, we asked 1702 individuals still participating in the study, as part of the annual assessment, “If you had the opportunity to participate in a brain scan research study, at the local hospital, and were offered a cash incentive for your time, would you be interested?” Response options were “Definitely, Probably, Maybe, Definitely Not.” We categorized participants as Potentially Interested (responses of “Definitely,” “Probably,” or “Maybe”) or Not Interested (response of “Definitely Not”).

Assessments

At baseline and annual visits, participants underwent a detailed assessment that has been described previously (Ganguli 2009, 2010) including but not limited to demographics, marital status, living arrangements, global cognitive screening with the Mini-Mental State Examination (MMSE) (Folstein 1975), neuropsychological assessment, subjective cognitive concerns, depression symptom screening, self-rating of health, instrumental activities of daily living (IADLs), total number of regularly taken prescription medication (as an objective measure of overall morbidity); central obesity (waist: hip ratio); history of stroke, transient ischemic attack (TIA), heart attack, and cardiac pacemaker.

Based on the neuropsychological test results, relative to norms, we classified participants as cognitively normal, mildly cognitive impaired, or severely cognitively impaired (Ganguli 2010). Using all relevant information other than the neuropsychological tests, including the trained interviewer’s observations, we rated participants on the Clinical Dementia Rating (CDR) scale as no dementia (CDR=0), possible/ very mild dementia (CDR=0.5), or dementia (CDR ≥ 1) (Morris 1993).

MRI Pilot Study

During a one-year period spanning Cycles 2–4, we conducted a pilot sMRI brain study in 48 participants to demonstrate feasibility of recruitment and approach. Selection criteria for the pilot study included having previously expressed potential interest in MRI, being within 3 months of an annual MYHAT assessment, being available for the scan during that time window, having no contraindications to MRI, and being classified as either cognitively normal or MCI, with CDR <1 . These requirements clearly precluded our conducting the

MRI pilot study in a random subsample of the MYHAT cohort. The scans were performed at the local community hospital in a 1.5T General Electric scanner on which the Alzheimer Disease Neuroimaging Initiative (<http://www.loni.ucla.edu/ADNI/ResearchCores>) image acquisition protocol had been installed. Image analysis was performed using a Visual Atrophy Rating approach (Urs 2009). Results were published, showing the expected associations between cognitive state and regional volumes (Becker 2012). Given our selection criteria, we assumed that these unweighted analyses were influenced by some degree of selection and volunteer factors, even though the study was embedded within a population-based cohort, and also age-related factors. [Duara 2013]

Statistical analyses

For the first set of analyses, we compared the Interested (n=915) and Not Interested (n=787) subgroups on a range of variables measured at the same time that they were asked about MRI interest. We used Wilcoxon two-sample rank sum tests to compare the continuous variables and chi-square tests to compare proportions of the categorical variables, and then logistic regression models for univariable and multivariable analyses. The final multivariable model was selected by stepwise selection methods with significance thresholds of 0.15 and 0.10 to enter and stay in the model, respectively. Age, gender, and education were also included in the final model.

For the second set of analyses, we first used logistic regression to examine the differences between individuals who participated in the sMRI pilot study (n=48) and (1) those who did not participate in the pilot study but had expressed potential interest in MRI (n=867=915-48); (2) those who did not participate in the pilot study but were asked about their MRI interest (n=1654=1702-48); and (3) those who did not participate in the pilot study but were in our baseline cohort (n=1934=1982-48).

We applied three propensity score models, using logistic regression described above, to generalize the results of the sMRI pilot study (n=48) to the larger samples of (1) 915 participants expressing potential interest in MRI, (2) all 1702 participants who were asked about their MRI interest, and (3) the entire baseline cohort of 1982 individuals. For each model we considered the following covariates: age, gender, education, race, marital status, employment status, living arrangements, hearing, vision, impaired (IADL), number of regularly taken prescription medications (an index of overall morbidity), self-rated health, mCES-D (modified Center for Epidemiological Studies) score reflecting number of depression symptoms, subjective memory concerns (overall self-rating of memory and of whether memory has declined over the preceding year), MMSE (general cognition), waist: hip ratio (measure of adiposity), Apolipoprotein E (*APOE*)*4 gene carrier status, and history of TIA, stroke, heart attack, and cardiac pacemaker. We used backward selection methods with a significance threshold of 0.2 to select covariates for the final models, and also included age, gender, and education. We further examined interaction effects in the final model with a significant level of 0.05 to select significant interaction terms for the final models. Missing values of the covariates in the propensity models were imputed 5 times using the multiple imputation technique. We assessed the adequacy of the propensity score

models based on the areas under the receiver operating characteristic curve (AUC) (Sturmer 2005; Gorkiewicz 2009).

Using the data from the MRI pilot study (n=48), we first fit an unweighted logistic regression model for each region of interest on the Visual Atrophy Rating Scale for the following dependent variable: CDR classification of no dementia (CDR=0) vs. possible/very mild dementia (CDR=0.5). Next, we fit an unweighted model for the following dependent variable: cognitive classification of normal cognition vs. MCI.

We then used the previously described propensity score models to sequentially weight each of the above-mentioned CDR and MCI models to generalize the results of the pilot study of 48 participants back to the 3 progressively larger samples of 915 interested participants, 1702 who were asked about interest, and the entire baseline cohort of 1982. Weights were inversely related to the probability of participating in the sMRI pilot study. As weights may adversely affect standard errors, we performed logistic regression analyses using the survey sampling technique to adjust for the impact of the weights on the standard errors while still providing the functionality of the regular logistic regression procedure (An 2002; Pfefferman 1996; Freedman and Berk 2008).

Results

MRI Interest

Of 1982 individuals assessed at baseline (Cycle 1), 1702 participants were asked about their potential interest in a future brain MRI study. Of these, 658 (38.7%) responded “Definitely,” 137 (8.0%) “Probably,” and 120 (7.0%) “Maybe,” for a total of 915 (53.8%) with potential interest, and 787 (46.2%) “Definitely Not.”

Comparing these two groups (Table 1) the Interested group were significantly younger, more likely to be men and have greater than high school education, and more likely to be married, employed, and living unsupervised. They were more likely to subjectively rate their own health as good or excellent, to report no depressive symptoms, and to have normal hearing. They had higher average scores on the Mini-Mental State Examination, were more likely to be classified as cognitively normal, to be CDR=0, and to have no IADL impairments. They took fewer prescription medications, and were less likely to report a history of stroke or heart attack. They were also more likely to be *APOE**4 carriers. The two groups were similar in race, subjective cognitive concern and cognitive decline, vision, waist: hip ratio, history of TIA, and presence of cardiac pacemaker. In the final multivariable model, the interested group were significantly younger, more likely to be men, more likely to be *APOE**4 carriers, to take fewer prescription medications, and to be classified as cognitively normal (p values < 0.05; data not shown).

Propensity Score Models

In the first propensity score model for comparing individuals who participated in the sMRI pilot study (n=48) to those who did not participate in the pilot study but were potentially interested in MRI (n=867=915-48), the variables significantly different between the two groups were marital status, number of regularly taken prescription medications, history of

heart attack, self-rated health, and mCES-D, after adjusting for age, gender, and education ($p=0.2$ to select covariates for the final models)

In the second propensity score model for comparing individuals who participated in the sMRI pilot study ($n=48$) to those who did not participate in the pilot study but were asked about their MRI interest ($n=1654=1702-48$), the significantly different variables were marital status, number of regularly taken prescription medications, waist: hip ratio, self-rated health, and mCES-D, after adjusting for age, gender, and education ($p=0.2$). The differences between this model and the first propensity score model was that waist: hip ratio was only significant in this model, while history of heart attack was only significant in the first model.

In the third propensity score model for comparing individuals who participated in the sMRI pilot study ($n=48$) to those who did not participate in the pilot study but were in our baseline cohort ($n=1934=1982-48$), all the above-mentioned variables plus subjective memory, MMSE, and an interaction term of education and MMSE were significantly different between two groups of individuals at significance level of 0.2.

The AUCs of all three propensity score models were around 0.75. Results from these three propensity score models were used to create weights for the subsequent CDR models and MCI models.

CDR Models

In the unweighted models ($n=48$) with the CDR outcome (CDR=0 vs. CDR=0.5), atrophy in the following regions of interest was significantly greater among those with CDR=0.5: left and right perirhinal cortex, left and right entorhinal cortex, left and right medial temporal cortex. When weighted back using propensity scores to the 915 participants potentially interested in MRI, only left perirhinal cortex was significant; when weighted back to the 1702 participants who were asked about potential interest, both left and right perirhinal regions were significant; and when weighted back to the entire baseline cohort of 1982 participants, both left and right perirhinal and left medial temporal regions were significant (Table 2).

MCI Models

In the unweighted models ($n=48$) with the cognitive outcome (Normal cognition vs MCI), atrophy in the following regions of interest was significantly greater among those with MCI: overall cortex, right lateral ventricle, 3rd ventricle, right hippocampus, right and left entorhinal cortex, left perirhinal cortex, left and right medial temporal cortex. When weighted back using propensity scores to the 915 participants who expressed potential interest in MRI, only overall cortical atrophy and right ventricular size were significant, along with grade of periventricular white matter hyperintensities. When weighted back to the 1702 participants who were asked about potential interest, overall cortical atrophy, right ventricular size, and third ventricular size remained significant. When weighted back to the entire baseline cohort of 1982 participants, both periventricular and subcortical white matter hyperintensities became significant; of cortical areas, only right entorhinal cortex was significant (Table 3).

With both the MCI and CDR models, we note that as the data were weighted back to larger and larger samples, the confidence intervals grew wider (whether or not they were statistically significant, i.e., whether or not they include 1.0). For both outcomes, we also noted that the effect sizes (as measured by the consistently significant odds ratios) were highest in the final weighted model.

Discussion

In the first part of this article, we report that just over half of the participants in an ongoing population-based cohort study of older adults, responded positively when asked about their potential interest in an MRI brain scan study. They were younger and better educated, more likely to be men, married, employed, and living unsupervised. They were generally healthier, with fewer IADL impairments, objective cognitive impairments, and depressive symptoms. There were no differences in race or subjective memory concerns between the groups interested and not interested in MRI research. Further, there were no differences in obesity and cardiac pacemaker implantation, which could be contraindications to MRI scanning.

We are not aware of previous studies assessing level of potential interest in neuroimaging studies, but our findings are largely consistent with those of a careful investigation (Jaramillo 2007) of over 2,000 women approached for the Women's Health Initiative Memory Study (WHIMS) -MRI study. That study obtained a 72% MRI consent rate and a 61% completion (image acquisition) rate. Lower completion rates were associated with older age, lower education, history of smoking, cardiovascular disease, diabetes, cognitive function, cognitive decline, and depression. Other population-based studies with similar findings include the Cardiovascular Health Study (Longstreth 1966), the Rotterdam Study (De Groot 2000), the Honolulu-Asia Aging Study (Havlik 2000), and the Framingham Study (DeCarli 2005). In partial contrast, the Atherosclerosis Risk in Communities study (ARIC) (Bryan 1999) found lower completion rates in younger individuals, but this study included only participants aged less than 75 years. No studies besides ours appear to have found a gender effect, although the WHIMS and HAAS studies were restricted to women and men, respectively. The Framingham and ARIC studies found lower completion rates in individuals with greater body weight; the Rotterdam and WHIMS studies showed no effect of body weight, consistent with the lack of association that we found with waist: hip ratio which is our measure of central obesity. Previous studies did not report associations with marital status and employment, as we did.

The concept of volunteerism adds another layer of complexity in studies where recruitment is not population-based. In a previous study, we investigated the characteristics of those who volunteered to participate in an observational study of aging and cognition, compared to those who were randomly selected for the same study. The volunteers were significantly more likely to be women, more educated, and less likely to have used several health and human services. They also had higher cognitive test scores, fewer IADL impairments, and, over 6–8 years of follow-up, had significantly lower mortality rates than the randomly selected participants (Ganguli 1998). Using a different conceptual paradigm to study volunteerism and self-selection bias, a recent study (Oswald 2013) recruited by

advertisement a sample of healthy young adults aged, assessed their demographic and personality characteristics, and offered them the opportunity to enroll in a positron emission tomography (PET) study involving intravenous amphetamine administration. Those who consented to this PET study were more likely to be male and to score significantly higher on sensation-seeking traits.

In the second part of this study, we addressed the possibility of using statistical methods to handle various forms of potential bias, using data collected for a small pilot study of sMRI within our cohort. Propensity scores are frequently modeled by logistic regression analysis. Individuals comprising a non-random sample are characterized and weighted so as to make the sample more representative of a larger population from which it was drawn, i.e., creates a pseudo-random population. In effect, each member of the small sample is assigned a weight which reflects the extent to which his characteristics represent the larger sample, so that all the weights sum to 100%. Analyses carried out in this weighted, pseudo-random population, using data from the smaller non-random sample, are designed to produce estimates that can be generalized to the larger population. Here, we used the variables that distinguished the small group of scanned individuals with 3 successively larger groups of participants who were not scanned, using propensity score models to create weights with which to reanalyze the original pilot data. In doing so, we found fewer significant associations between MCI /CDR stage and regions of interest, as would be expected if the MRI pilot study had been conducted on a truly random, heterogeneous, sample of the community. We judged as adequate the fit of our propensity score models based on the areas under their receiver operating characteristic curves (AUC) of approximately 0.75. These models do not address the possibility of residual confounding by covariates that might be associated with having the MRI but not with the region of interest.

In the first weighted model, which we conceptualize as adjusting for selection bias, we generalized the pilot study results from the 48 participants we selected to all 915 individuals who had expressed potential interest in a brain scan research study, whether or not they had been scanned. In the second weighted model, we additionally adjusted for interest or volunteer bias, by generalizing the results to all 1702 individuals whom we had queried about their interest, whether or not they had expressed interest. In the third weighted model, we also adjusted for attrition bias, by generalizing the results to the entire baseline cohort of 1982 individuals, whether or not they had remained in the study long enough to be asked about their interest. In our sample, it appeared that considerable weighting was required to adjust for selection bias, minimal additional weighting for interest/volunteer bias, and also substantial additional weighting for attrition bias. The end result in general was that after adjustment for these biases, the confidence intervals become wider. In most cases the significant associations between atrophy and the clinical outcome were seen in fewer regions of interest than in the unweighted sample. However, there were some examples (e.g. periventricular and subcortical white matter hyperintensities in relation to MCI, Table 3) where despite the wider confidence intervals, the size of the odds ratio was large enough to become significant. We can potentially attribute both kinds of changes to reduction of bias.

It is improbable that a truly random sample of individuals could be recruited into any neuroimaging study. Based on their findings in the WHIMS-MRI study, the authors

(Jaramillo 2007) concluded that while it was feasible to enroll older women in brain imaging studies, selection bias would limit the generalizability of the findings to the broader population. Statistical adjustment for selection bias may render study results less dramatic, but might also make them more realistic and representative of the community at large. Further, where feasible, information about the characteristics typically under-represented among neuroimaging study participants could be used to weight the sampling frame for recruitment in future studies, thus facilitating the *a priori* selection of a minimally biased sample.

Acknowledgments

Authors Ganguli, Lee, Hughes, Jakubcak, and Chang are supported by grant # R01 AG023651 from the National Institute on Aging. Dr. Ganguli is also supported by grant # K07 AG044395, Dr. Snitz is supported by grant # K23 AG08347.

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Comparison of Individuals Potentially Interested and Not Interested in MRI Research

Table 1

Variable	Not Interested in MRI		Potentially Interested in MRI		Univariable Logistic Regression Model		
	Mean or N	SD or %	Mean or N	SD or %	Odds Ratio	95% Confidence Interval	P *
Age	81.39	7.27	78.33	7.08	0.94	0.93 0.96	<.0001
Sex							
	Male	271	34.43	41.53			
Education	Female	516	65.57	58.47	0.74	0.61 0.90	0.00
	High School	477	60.61	55.74			
Marital status	> High School	310	39.39	405	1.22	1.01 1.48	0.04
	Unmarried	443	56.29	461			
Race	Married	344	43.71	454	1.27	1.05 1.54	0.02
	Non-White	44	5.59	44			
Employment	White	743	94.41	871	1.17	0.76 1.80	0.47
	Not working	719	91.48	805			
Living arrangement	Working	67	8.52	110	1.47	1.07 2.02	0.02
	Unsupervised	758	96.32	896			
Subjective Health	Supervised	29	3.68	19	0.55	0.31 1.00	0.05
	Poor/fair	150	19.06	113			
Rx Meds	Good	383	48.67	449	1.56	1.18 2.06	0.00
	Very good/excellent	254	32.27	353	1.85	1.38 2.47	<.0001
Subjective Memory	Mean/SD	5	3.38	4.36	0.94	0.91 0.97	<.0001
	Fair/poor	198	25.16	204			
Subjective Decline	Good/excellent	589	74.84	711	1.17	0.94 1.47	0.17
	No	609	77.68	708			
IADL	Yes	175	22.32	206	1.01	0.81 1.27	0.92
	No impairment	719	95.87	870			
	1 impaired IADL	31	4.13	14	0.37	0.20 0.71	0.00

Variable	Not Interested in MRI		Potentially Interested in MRI		Univariable Logistic Regression Model		
	Mean or N	SD or %	Mean or N	SD or %	Odds Ratio	95% Confidence Interval	P *
Hearing							
	Normal	570	72.52	76.72			
	Corrected	126	16.03	16.07	0.95	0.73	0.69
Vision							
	Abnormal	90	11.45	7.21	0.60	0.43	0.00
	Normal	54	6.87	7.10			
Depression symptoms (mCES-D)							
	Corrected	716	91.09	838	0.97	0.67	0.88
	Abnormal	16	2.04	1.31	0.62	0.27	0.26
MMSE							
	0	588	74.71	78.25			
	1-2	117	14.87	13.99	0.90	0.68	0.44
History of stroke							
	3	82	10.42	7.76	0.71	0.51	0.05
	Mean/SD	26.55	3.04	27.24	1.10	1.06	<.0001
History of TIA							
	No	745	94.66	888			
	Yes	42	5.34	2.95	0.54	0.33	0.01
History of heart attack							
	No	780	99.36	901			
	Yes	5	0.64	1.53	2.42	0.87	0.09
Heart pacemaker							
	No	769	97.71	906			
	Yes	18	2.29	9	0.98	0.19	0.04
Waist:Hip ratio							
	No	776	98.60	910			
	Yes	11	1.40	5	0.55	0.13	0.08
APOE*4 carrier							
	Mean/SD	0.9	0.09	0.9	1.27	0.43	0.67
	No	576	81.47	659			
Cognitive classification							
	Yes	131	18.53	199	1.33	1.04	0.02
	Normal	406	54.21	580			
Clinical Dementia Rating							
	MCI	301	40.19	279	0.65	0.53	<.0001
	Severe	42	5.61	46	0.77	0.50	0.23
CDR=0							
	CDR=0	534	67.85	676			
	CDR=0.5	230	29.22	225	0.77	0.62	0.02

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Variable	Not Interested in MRI		Potentially Interested in MRI		Univariable Logistic Regression Model		
	Mean or N	SD or %	Mean or N	SD or %	Odds Ratio	95% Confidence Interval	P *
	23	2.92	14	1.53	0.48	0.25 0.94	0.03

* ref: reference group for the other category(ies) in the logistic regression model.

Table 2

CDR=0.5 vs. CDR=0

Region of Interest (Visual Atrophy Rating)	Unweighted N=48			Weighted back to 915			Weighted back to 1702			Weighted back to 1982						
	Individuals participating in MRI pilot study			Individuals potentially interested in MRI			Individuals asked about interest in MRI scan			Entire baseline sample						
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P				
Cortical Atrophy	1.91	0.81	4.49	0.14	2.53	0.77	8.27	0.13	1.79	0.61	5.26	0.29	3.02	0.74	12.28	0.12
R. Lateral Ventricle	1.25	0.61	2.59	0.54	1.02	0.39	2.66	0.96	0.88	0.35	2.19	0.78	1.49	0.52	4.28	0.46
L. Lateral Ventricle	1.20	0.55	2.60	0.65	1.19	0.44	3.17	0.73	1.11	0.44	2.77	0.83	2.28	0.61	8.50	0.22
3 rd Ventricle	1.72	0.83	3.57	0.14	1.36	0.55	3.34	0.51	1.26	0.55	2.90	0.59	2.67	0.92	7.70	0.07
Periventricular WMH	1.68	0.81	3.49	0.17	0.99	0.37	2.65	0.98	1.03	0.42	2.53	0.95	2.12	0.63	7.17	0.23
Subcortical WMH	1.29	0.67	2.50	0.45	1.27	0.45	3.63	0.65	1.09	0.42	2.81	0.86	1.86	0.56	6.15	0.31
R. Hippocampus	1.86	0.97	3.58	0.06	1.35	0.55	3.33	0.51	1.56	0.65	3.78	0.32	1.20	0.48	3.04	0.69
L. Hippocampus	1.61	0.89	2.91	0.12	1.47	0.68	3.19	0.33	1.61	0.76	3.40	0.21	2.69	0.97	7.45	0.06
R. Entorhinal Cortex	1.91	1.10	3.31	0.02	1.70	0.78	3.70	0.18	1.92	0.88	4.20	0.10	1.81	0.86	3.79	0.12
L. Entorhinal Cortex	2.08	1.15	3.75	0.02	1.73	0.75	3.98	0.20	1.99	0.87	4.58	0.10	3.42	0.95	12.36	0.06
R. Perirhinal Cortex	1.95	1.11	3.43	0.02	1.89	0.91	3.93	0.09	2.10	1.03	4.29	0.04	2.40	1.14	5.09	0.02
L. Perirhinal Cortex	2.24	1.27	3.95	0.01	2.21	1.08	4.48	0.03	2.48	1.20	5.11	0.01	3.24	1.55	6.74	0.00
R. Medial Temporal	2.24	1.16	4.32	0.02	1.85	0.73	4.70	0.20	2.15	0.84	5.48	0.11	2.09	0.82	5.31	0.12
L. Medial Temporal	2.35	1.21	4.55	0.01	2.02	0.79	5.16	0.14	2.31	0.91	5.90	0.08	4.07	1.24	13.34	0.02

Table 3

Mild Cognitive Impairment versus Normal Cognition

Region of interest (visual atrophy rating)	Unweighted N=48			Weighted back to 915			Weighted back to 1702			Weighted back to 1982						
	Individuals participating in MRI pilot study			Individuals potentially interested in MRI			Individuals asked about interest in MRI scan			Entire baseline sample						
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P				
Cortical Atrophy	2.44	1.03	5.78	0.04	4.76	1.62	14.04	0.00	4.96	1.68	14.69	0.00	2.62	0.81	8.52	0.11
R. Lateral Ventricle	2.36	1.06	5.22	0.03	3.23	1.04	10.02	0.04	3.74	1.23	11.39	0.02	1.81	0.72	4.56	0.21
L. Lateral Ventricle	2.11	0.94	4.74	0.07	2.84	0.85	9.51	0.09	3.00	0.89	10.15	0.08	2.20	0.73	6.69	0.16
3 rd Ventricle	2.14	1.03	4.47	0.04	3.36	0.96	11.78	0.06	4.04	1.10	14.85	0.04	2.31	0.97	5.50	0.06
Periventricular WMH	1.88	0.92	3.85	0.09	2.53	1.10	5.80	0.03	1.96	0.77	5.01	0.16	2.79	1.05	7.38	0.04
Subcortical WMH	1.41	0.75	2.66	0.29	1.73	0.70	4.27	0.24	1.63	0.67	3.99	0.28	2.37	1.08	5.21	0.03
R. Hippocampus	2.28	1.15	4.53	0.02	1.65	0.79	3.46	0.18	1.58	0.77	3.27	0.21	1.65	0.72	3.75	0.24
L. Hippocampus	1.66	0.94	2.94	0.08	1.39	0.69	2.81	0.36	1.36	0.70	2.65	0.37	1.78	0.86	3.69	0.12
R. Entorhinal Cortex	1.82	1.09	3.05	0.02	1.67	0.80	3.45	0.17	1.64	0.84	3.18	0.15	2.11	1.07	4.16	0.03
L. Entorhinal Cortex	1.81	1.07	3.05	0.03	1.58	0.78	3.19	0.20	1.52	0.79	2.94	0.21	1.87	0.99	3.56	0.06
R. Perirhinal Cortex	1.54	0.92	2.58	0.10	1.59	0.81	3.15	0.18	1.39	0.73	2.63	0.32	1.76	0.80	3.88	0.16
L. Perirhinal Cortex	1.68	1.03	2.75	0.04	1.78	0.99	3.20	0.06	1.49	0.83	2.69	0.18	1.84	0.96	3.51	0.07
R. Medial Temporal	2.10	1.12	3.92	0.02	1.82	0.81	4.09	0.14	1.66	0.80	3.48	0.18	2.26	0.94	5.46	0.07
L. Medial Temporal	1.96	1.08	3.53	0.03	1.73	0.80	3.74	0.16	1.57	0.76	3.23	0.22	2.07	0.97	4.44	0.06