Social Activity

Brain Volume, White Matter Lesions and Cognitive Function

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Are low levels of Social Activity associated with brain abnormalities observed on MRI and with poor cognitive function?

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Abstract

Contrary to the number of research reporting the effects of Social Activity on cognitive decline and dementia, there is not much known about the influence of Social Activity on the neuropathology. Therefore, the present study will explore the association between Social Activity and brain volume and WML, and will verify the association between Social Activity and cognitive function. The data of the SMART-study is used. Three questions about the frequency of social contact of the participants with neighbors, family and friends formed the factor Social Activity. WML and brain volume was measured and normalized for intracranial volume. Cognition is measured with the 15-word learning test. Linear regression analysis is used for the statistical analyses. The findings show that people with low levels of Social Activity with neighbors have larger brain volume (B=.642; 95% CI= .132 to 1.151 %; p=.014). People with low levels of Social Activity with neighbors (B=.256; 95% CI= .004 to .507 %; p=.046) and family (B=.270; 95% CI= .022 to .519 %; p=.033) have more WML. People who have low levels of Social Activity (B=.2.439; 95% CI= .418 to 4.460 %; p=.018) or moderate (B=.1.995; 95% CI= .488 to 3.501 %; p=.010) levels of Social Activity with friends have better Cognitive function. These results are compared to people with high levels of Social Activity. The mixed results indicate that social ties influence the relation between Social Activity and brain volume and cognition. It indicate an effect of the frequency of Social Activity on WML. Finally, the results indicate that low levels of Social Activity is associated with more WML and is therefore probably a risk factor.

Introduction

According to the prediction of the World Health Organization (WHO) it is expected that the amount of patients with dementia in 2030 will be 65.7 million, this number will double every twenty years (WHO, 2012). This increase of the population with dementia can become an enormous problem for health systems and health organizations. In particular, the expensive care associated with dementia will be a challenge for health systems to deal with the expected increase. Beside the increase of patients with dementia, the extension of life expectancy will result in an increase of patients with Mild Cognitive Impairment (MCI). The epidemiological study of Wada-Isoe, Uemura and Nakashita and colleagues (2012) demonstrated the prevalence of MCI in Japan to be 23.4%. Comparable results are found by Ritchie (2004); in this meta-analysis of experiments with a western population, it is suggested that the prevalence of MCI is between 5% and 29%. Furthermore, 39% of the patients diagnosed with MCI advance to dementia, while even less than 1% of healthy elderly develop dementia (Mitchell, Shiri-

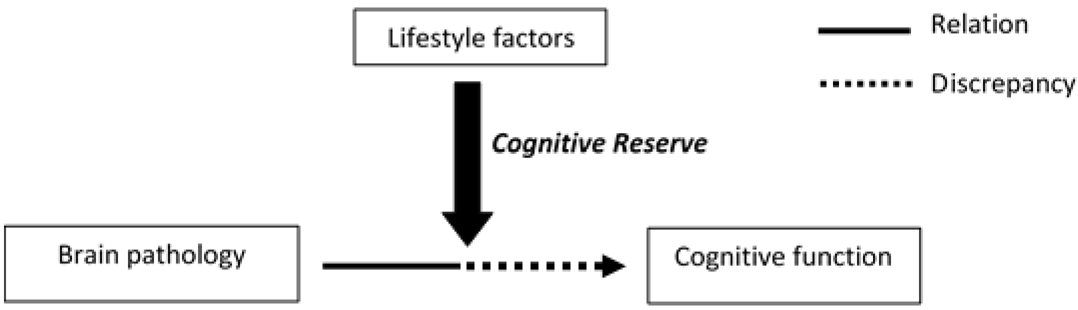
Feski, 2009). With this increasing incidence of dementia and MCI, it is important to establish factors that can prevent the development of MCI and dementia in the elderly.

Prior to discussing the factors that aid in the prevention of dementia, the etiology of dementia will be described. As noted by Imtiaz, Tolppanen, Kivipelto and Soininen (2014) in their review, although in the past dementia has been seen as a disease associated with old age, recent research centers on the life course of people with dementia. As a result, recent studies are focused on the development of dementia. The outcomes of these studies suggest a complex and multifactorial etiology of dementia (Imtiaz, 2014; Gardner, Valcour and Yaffe, 2013). The four different groups of risk factors mentioned by Imtiaz and colleagues (2014) are vascular, psychological, genetic and lifestyle factors. Some of these groups are confirmed by Gardner and colleagues (2013), who summarize risk factors for dementia in the oldest old. They mention that low level of education, poor mid-life general health, low level of physical activity, depression and delirium are risk factors for dementia in this population (Gardner et al., 2013). Because of the research that investigates modifiable factors, the once untreatable aspect of aging, dementia, is transformed into a potentially preventable disease (Imtiaz, 2014).

Regarding the current study, the focus will be on lifestyle factors, and more specifically on psychosocial factors. There are different factors considered to reduce the risk of dementia. According to the meta-analyses of Bennett, Arnold, Valenzuela, Brayne and Schneider (2014) education and years of education was one of the first psychosocial variables associated with the prevalence of dementia. In studies with higher cohort incidence rates in the cohort, it is illustrated that more education corresponds with a lower incidence of dementia (Bennett, 2014). Meng and D'Arcy (2012), also summarized that people with lower education are at a higher risk for dementia than those with higher education. In addition to these factors, leisure activities are also associated with a lower risk of dementia (Wang, Xu, & Pei, 2012). Wang and colleagues (2012) illustrated that compared to the elderly who did not participate in mental, social or productive activity; those who did, had a lower incidence of dementia. Furthermore, participation in cognitive activities was associated with delayed onset of memory decline (Hall, Lipton, Sliwinsky, Katz, Derby & Verghese, 2009). All these factors can reduce the cognitive decline and the risk of developing dementia or MCI.

Regarding the previous factors, the Cognitive Reserve model summarizes the influence of these factors on cognitive decline and on the risk of developing MCI and dementia. In addition to the cognitive decline that is common in aging, the process of brain deterioration is also part of the aging process. Symptoms like a reduced brain volume, brain atrophy and accumulation of amyloid protein are part of normal aging and often seen in people 60 years or older (Walhovd, Fjell, Espeseth, 2014). Although there is a decline in both cognition and brain structures in healthy aging people (Walhovd, 2014), a direct relation between brain volume or brain atrophy and cognitive function is not found

(Stern, 2002). According to Stern (2009), the concept Reserve is responsible for the differences in cognitive function in people with the same brain volume, brain atrophy or brain damage. The concept Reserve can be differentiated in two models, a passive model: Brain Reserve and an active model: Cognitive Reserve (Stern, 2002). The Brain Reserve model summarizes that factors of the brain are responsible for the different cognitive consequences in people with the same brain volume, brain atrophy or brain damage (Barulli & Stern, 2013). The Cognitive Reserve model states that cognitive processes influence the cognitive outcome and, depending on the differences in cognitive processes between people, these processes are considered to be responsible for the different cognitive function in people with the equal brain volume, brain atrophy or the same brain damage (Barulli & Stern, 2013). This model is shown in Figure 1. Furthermore, Barulli and Stern (2013) give attention to the associations between life exposures, such as education and participation in leisure activities, and a decreased risk of developing dementia. They refer to these associations as evidence for the existence of Cognitive Reserve. Moreover, the active Cognitive Reserve model is in line with the suggestion of Imtiaz and colleagues (2014) who claimed that because of the growing knowledge of the modifiable factors, dementia can be influenced and become a preventable disease.



Figuur 1 Illustration of Cognitive Reserve

In addition to the factors mentioned previously, there are more factors that help prevent dementia. However, not every protective factor is known as providing Cognitive Reserve. For instance, in many studies the factor Social Activity is proven to reduce the risk of dementia and cognitive decline, the results of these studies are summarized in Table 1. It is proven that the association between dementia and Social Activity is significant (Sörman, Sudström, Rönnlund, Adolfsson & Nilsson, 2013). In fact, spending time with family, relatives and friends was considered the most common Social Activity of the leisure activities, 74% of the participants were engaged in this, sometime per week or every day (Sörman et al., 2013). Furthermore, the study of Wang, Karp, Winblad, and Fratiglioni (2002) presented that frequent participation in Social Activity is associated with lower risk of dementia. Additionally, it has been shown that Social Activity can postpone the age of onset of dementia (Paillard-Borg, Fratiglioni, Xu, Winblad, & Wang, 2012). In the study of Paillard-Borg and colleagues (2012) it

Table 1. research that explores the association between social activity, social engagement, social network and social interaction with cognitive function, cognitive decline, risk of dementia, Alzheimer Disease (AD) pathology and brain volume.

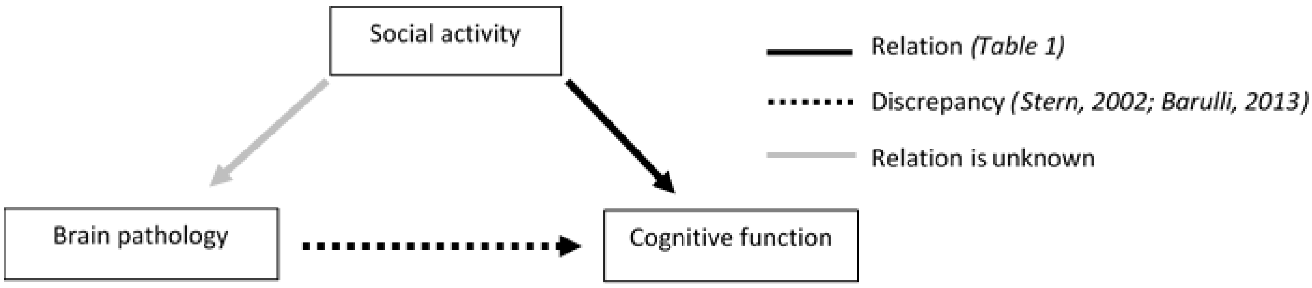
Author	Year	Design	Study population	N	Age	Determinant	Social Activity measure	Outcome	Covariates	Results
Bennett	2006	longitudinal/ repeated measures	non-demented elderly	89	81	SN	quantitative	AD pathology and cognitive function	cognitive, physical, and social activities, depressive symptoms, and chronic medical conditions	The interaction between tangles and social networks was significant (*p*=.001; R^2 increased to 0.454) Social networks modified the relation of global Alzheimer's disease pathology with semantic memory. (R^2 increased from 0.210 to 0.318)
Conroy	2010	cross-sectional	elderly 65+	802	74.2	social engagement	quantitative	cognitive function	age, presence of depression and physical disability	Low social engagement is associated with significantly higher prevalence of cognitive impairment (OR= 1.6; p=0.222)
James	2011	longitudinal	non-demented elderly	1138	79.6	SA	quantitative	cognitive decline	age, sex, education, race, social network size, depression, chronic conditions, disability, neuroticism, extraversion, cognitive activity, and physical activity	More socially active persons had higher levels of global cognition at baseline (r=50.30; p<.001)
Krueger	2009	cross-sectional	non-demented elderly	838	80.2	SE	quantitative	cognitive function	age, sex, education, depressive symptoms, personality, cognitive, physical activity, chronic illness and disability	More social engagement is associated with better cognitive function (B=0.173, SE=0.029, p<.001)

Mortimer	2012	repeated-measures/ mixed modelling	elderly 60+	120	67.7	Social interaction	quantitative	Brian volume & cognitive function	Age, gender, education,	More social interaction is associated with increase in brain volume (t=2.03; *p*<.05) and an improvement in verbal fluency (*t*=2.49; *p*=.01) and Trials A en recall (*p*<.10)
Paillard-Borg	2012	longitudinal	elderly 75+ and good cognition	388	81.6	SA	quantitative	age onset dementia	Age, gender, education, cognitive functioning, comorbidity, social network, depressive symptoms, and physical dependence	Moderate social activity (β=0.87; SD=0.32; *p*=.006) significant different age onset than High social activity (β=1.24; SD= 0.29; *p*<.001)
Sörman	2013	repeated measures	non-demented elderly 65+	1475	74	SA	quantitative	risk dementia	age, gender, and years of education, diseases, smoking, alcohol use, marital status, general stress, feelings of depression, APOE ε4 status (carrier/non-carrier)	More Social activity is associated with a lower risk of dementia (HR=0.94, 95% CI=0.88–1.00)
Wang	2002	longitudinal	non-demented elderly 75+	1375	81.1	SA	quantitative	risk dementia	age, sex, education, baseline Mini-Mental State Examination score, comorbidity, depressive symptoms, and physical functioning.	More social activity is associated with a lower risk of dementia (RR=0.70; 95 % CI=0.49 – 1.01)
Zunzunegui	2003	longitudinal	community-dwelling people over 65	1540	-	social networks, social integration, and social engagement	qualitative	Cognitive function	Age, baseline cognitive function, level of education, sex, integration index, engagement with relatives, friends, and children, depression, systolic and diastolic blood pressure, and functional limitations	Social engagement with friends was associated with cognitive function in women (coefficient=0.53; SD= 0.16; *p*=.09)

was presented that the no Social Activity group and the moderate or high Social Activity group were significantly different.

In addition to the findings about the influence of Social Activity on dementia, there is also a positive effect of Social Activity on cognitive function. For instance, Social Activity and social engagement is suggested to aid in the prevention of cognitive decline (Conroy, Golden, Jeffares, O'Neill, & McGee, 2010). Other findings indicated that a one-point increase in Social Activity is associated with a 0.034 unit reduction in rate of cognitive decline per year. For a person who is socially active, this can lead to a reduction of 70% of the cognitive decline, when compared with an infrequent socially active person (James, Wilson, Barnes, & Bennett, 2011). Furthermore, there is a positive association between Social Activity and global cognition, this significance remains when physical and cognitive activity are added (Krueger, Wilson, Kamenetsky, Barnes, Bienias & Bennett, 2009). Mortimer and colleagues (2012) investigated the influence of social interaction on cognition, whereby social interaction was an intervention. They presented an improvement of the social interaction group for the verbal fluency test as well as for the Trials A and recall after the third learning of the auditory verbal learning test.

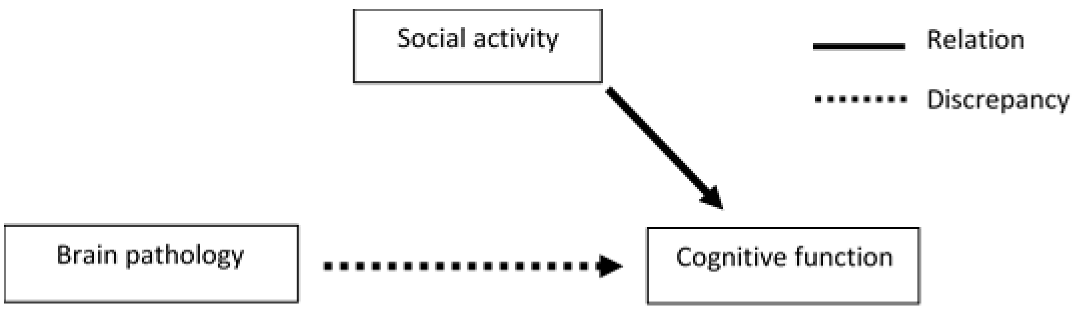
Despite several different studies reporting the effects of Social Activity that reduces the risk of cognitive decline and dementia, little is known about the influence of Social Activity on the neuropathology underlying these associations. The same is mentioned by Bennett, Schneider, Tang, Arnold, & Wilson (2006). In their research on the effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in seniors, they described that they were unaware of any study that examined the relation between social networks and neuropathology underlying the association of social networks and cognitive function. There are different measures of neuropathology, one of them is brain volume. The only study that explores the association of Social Activity and brain volume is done by Mortimer and colleagues (2012). They used social interaction as an intervention and explored the association between social interaction and normalized whole brain volume. They discovered a significant increase in brain volume in the social interaction group when compared with the control group. Another measure of neuropathology is white matter lesions (WML). There are no studies that studied the association between Social Activity and WML. However, the review article of Fratiglioni, Paillard-Borg and Winblad (2004) makes a relevant suggestion. They assert that the social lifestyle component, including Social Activity, is related to the vascular hypothesis. This hypothesis states that vascular disorders and vascular risk factors are involved in the pathological process and progression of Alzheimer's disease. Furthermore, Fratiglioni and colleagues (2004) mention the possibility of an association of the effect of Social stimulation on cognition and the vascular hypothesis, although they do not explain this association. However, it is conceivable that Social Activity reduces the vascular risk through the social support that can be experienced. This support can give a reduction of the stress level, which is a risk factor for vascular diseases (Katsarou, Triposkiadis & Panagiotakos, 2012). Without Social Activity there is a lack of social support, consequently there could be a greater stress experience which can lead to an increased risk of vascular diseases. Furthermore it has been confirmed that vascular diseases increases the possibility for WML (Shrestha et al., 2009). Therefore, it is relevant to examine a population with vascular problems the SMART-population.



Figuur 2 Illustration of the knowledge about the influence of social activity on brain pathology and cognitive function

As a result of the lack of knowledge about the influence of Social Activity on neuropathology, it is not possible to make any statements about the possibility of Social Activity providing Cognitive Reserve. It is necessary to have knowledge of the effect of social activity on the brain, because compensation or transformation of the brain by social activity have to be excluded (Stern, 2002). As mentioned before, the influence of social activity on the brain is not studied. A summary of the knowledge according social activity and brain pathology and cognitive function is shown in Figure 2. If the relation between social activity and the brain does not exist, then it can be stated that the improved and better cognitive function is not due to changes in the brain. In that case it can be reasoned that the discrepancy between brain pathology and cognitive function can be explained by the influence of social activity on cognitive function, that is what we call cognitive reserve. A model of this reasoning is shown in Figure 3. The fact is that there does not exist a research that report about the influence of social activity on brain pathology. In other words, it is necessary to explore the influence of Social Activity on neuropathology, before the engagement of Social Activity in Cognitive reserve can be examined.

For this reason, the present study will explore the association between Social Activity and brain volume and WML. In particular it will be investigated whether low levels of Social Activity is associated with Smaller Brain Volume, and whether low levels of Social Activity is associated with more WML. Furthermore, this research will verify if there is any support in the population of the SMART-study for the findings of previous studies about the association between Social Activity and cognitive function. Based on the findings of Mortimer and colleagues (2012) that indicated an increase in brain volume for the social interactive group, it is hypothesized that Low Social Activity is associated with Smaller Brain Volume. As a result of the suggestions of Fratiglioni and colleagues (2004) it is expected that Low Social Activity is associated with WML. Lastly, it is expected that studying the SMART-population will reveal an association between Social Activity and cognition, whereby Low Social Activity causes lower cognitive function. In other words, it is hypothesized that this study will find support for the protective role of Social Activity against cognitive decline. To summarize, in accordance with previous studies and hypotheses it is hypothesized that Low Social Activity is associated with Smaller Brain Volume, more White Matter Lesions and lower cognitive function.



Figuur 3 Illutration of the relation between Social Activity and cognitive function and the discrepancy between brain pathology and cognitive function, when Cognitive Reserve can be suggested

Methods

Data from the Second Manifestations of ARTerial Disease-Magnetic Resonance (SMART-MR) study will be used. This study collected data from 1309 independently living patients with symptomatic atherosclerotic disease. During a one-day visit to the University Medical Center Utrecht, different examinations were performed. In short, these examinations included MRI of the brain, physical examination, ultrasonography of the carotid arteries, and blood and urine sampling. Risk factors, medical history, and functioning were assessed with questionnaires that the patients completed prior to their visit to the medical center. The study started in May 2001, in 2003 neuropsychological tests were added to the procedure, these tests were also performed during the one-day visit. These tests included the MMSE, the Dutch Adult Reading Test, the 15-word learning test, the Rey complex figure and the Digit Symbol substitution. From 2006 until 2009, the follow up started among patients who were still alive. Just as during baseline, the procedure included MRI of the brain, neuropsychological testing, a physical examination, blood and urine sampling, risk factors, medical history, functioning and a depression interview. A questionnaire with questions about social activity was added. The follow-up is called the SMART-Medea (Memory, Depression, and Aging) study. It is aimed at investigation of the association between brain changes and psychosocial vulnerability and stress factors. For the present study we used this study sample. (Geerlings, Appelman, Vincken, Mali & Van Der Graaf, 2009)

Social Activity

For the present study, the Stress Questionnaire, conducted by the SMART study, is used to compose the factor Social Activity. Three questions are used to compute a score of Social Activity: 'Hoe vaak heeft u in het algemeen contact met buren (inclusief telefonisch of per brief)?' ('In general, how often do you have contact with neighbors (including telephone calls or letters)?'), 'Hoe vaak heeft u in het algemeen contact met familieleden (inclusief telefonisch of per brief)?' ('In general, how often do you have contact with your family members (including telephone calls or letters)?'), 'Hoe vaak heeft u in het algemeen contact met vrienden of echt goede kennissen (inclusief telefonisch of per brief)?' ('In general, how often do you have contact with your friends or well-known acquaintances (including telephone calls or letters)?'). There were eight answer options: 'daily'; 'several times a week'; 'about once a week'; '2 or 3 times a month'; 'about once a month'; 'less than once a month'; 'never'; 'Non Applicable, I do not have neighbors/family/friends'. These options are clustered in three different levels of Social Activity, high, moderate and low levels of Social Activity. First, high levels of Social Activity consist of the answering options 'daily' and 'several times a week'. Moderate levels of Social Activity includes the options 'about once a week' and '2 or 3 times a month'. Lastly, low levels of Social Activity consist of the answers 'less than once a month', 'never' and 'non applicable, I do not have neighbors/family/friends'.

Brain volume

MRI measures were performed on a 1.5-Tesla wholebody system (Gyroscan ACSNT, Philips Medical Systems, Best, the Netherlands). The protocol consisted of transversal T1-weighted gradient-echo (repetition time [TR]/echo time [TE] 235/2 ms), transversal T2-weighted turbospin-echo (TR/TE2200/11 and 2200/100ms, turbo factor 12), fluid-attenuated inversion recovery (FLAIR) (TR/TE/inversion time 6000/100/2000 ms), and transversal IR (TR/TE/inversion time 2900/22/410ms) sequences (field of view230 × 230mm,matrix size 180 × 256, slice thickness 4 mm, no slice gap 38 slices).

For brain segmentation, the T1-weighted gradient-echo, IR, and FLAIR sequences were used. The segmentation was done with k-nearest neighbor classification, which is a probabilistic segmentation technique, as described by Anbeek, Vincken, Van Bochove, Van Osch and Van Der Grond (2005). The segmentation program distinguishes cortical gray matter, white matter, sulcal and ventricular cerebrospinal fluid, and WMLs. The automatic segmentation was visually checked, and a further distinction was made between WML and infarct volumes by manually assigning the lesion volumes to one of these two categories. Total brain volume was calculated by summing the volumes of gray and white matter and, if present, the volumes of WMLs and infarcts. All volumes cranial to the foramen magnum were included. As a result, the total brain volume includes the cerebrum, brain stem, and cerebellum. Total intracranial volume (ICV) was calculated by summing the total brain volume and the volumes of sulcal and ventricular cerebrospinal fluid.

The factor Total Brain Volume was calculated by the ratio of total brain volume (sum of the volumes of gray and white matter, WML and infarcts) and intracranial volume. (Geerlings, 2009)

White Matter Lesions

In addition, for the factor White Matter Lesions (WML), the volumes of WML obtained with the segmentation program were summed to obtain the total volume of WML. A difference between deep and periventricular WML was not distinguished because it has been shown that deep, periventricular, and total WML are highly correlated with each other, and it has been suggested that categorical distinctions between periventricular and deep WML are arbitrary. The WML volumes are normalized for intracranial volume to correct for differences in head size by dividing total WML volume by intracranial volume and multiplying this value by the average intracranial volume of the study population. (Geerlings, 2009)

Cognition

Another variable is Cognition, which is composed of measures of different neuropsychological tests. Global cognitive functioning was measured by using the Mini-Mental State Examination (MMSE), which consist of 30 questions. The 15-word learning test was performed for the assessment of verbal memory. This test consists of 5 consecutive trials of a row of 15 words, immediate recall (range, 0–15) and delayed recall (range, 0–15) are assessed. A retention score was calculated by dividing the number of words recalled after 25 minutes by the maximum number of words recalled during the immediate recall. A composite score for memory performance was calculated by averaging the z scores (individual test score minus mean test score divided by the standard deviation of that score) for the mean score of the 5 trials of the immediate recall, the z score for the delayed recall, and the z score for the retention score.

Covariates

This study was controlled for (model 1) age, sex and education; (model 2) physical activity, depression score and social support; and (model 3) brain volume or WML. Education was divided into 7 categories, graded from primary school to academic degree, according to the Dutch educational system. Physical activity and also the social support is measured by a questionnaire. To compose the depression score, the PHQ-9 questionnaire was used.

Statistical Analysis

Firstly, the demographical description were assessed. For the data analysis, the linear regression analysis will be used to investigate the association of the independent variable Social Activity and the dependent variables Brain Volume, White Matter Lesions and cognitive function. Consequently, the linear regression analysis will be performed three times, for every outcome variable once. Because the independent variable is an ordinal variable, dummy variables of the variable Social Activity will be created prior to the assessment.

Study sample

Of the 754 participants who were examined between 2006 and 2009, 745 participants answered the social questions about neighbors. In order to the other social questions about family and friends 743 participants answered these. A MRI scan and a calculation of brain volume was made of 691 participant.

Results

The characteristics of the 745 participants are summarized in Table 2. The participants had a mean age of 61.7 (SD=9.5) years, 82.1% of them were male. The mean Brain Volume in percentage was 78.34 (SD=2.94) and the participants had a mean of -2.20 (SD=1.21) for the Log of White Matter Lesions. In regards to cognitive function, the score for the 15-Words Learning Test ranged from 0-75 and the mean score for this test was 38.6 (SD=10.5). In Table 3, the frequencies and the percentage of the different levels of social activities with neighbors, family and friends are shown. This table presents that the majority of the participants have high levels of Social Activity with neighbors, family and friends.

Brain Volume

Regarding the analysis of the dependent variable Brain Volume, it was hypothesized that low levels of Social Activity would be related to smaller Brain Volume. The results, summarized in Table 4, showed an influence of Social Activity with neighbors on Brain Volume. A significant bigger Brain Volume was found for people with low levels of Social Activity with neighbors when compared to the people with high levels of Social Activity with neighbors (B=.642; 95% CI= .132 to 1.151 %; *p*=.014). This finding was independent of age, sex and education. There was no change of effect after adding the variables depression, social support and physical activity (B=.640; 95% CI= .126 to 1.155; *p*=.015). Even after controlling for WML the result was significant (*p*=.009) with a B-value of .682 and 95% Confidence Interval that ranged from .167 to 1.196 % intracranial volume. Contrary to the expectations, these results suggest that people with low levels of Social Activity with neighbors have bigger Brain Volume than people who have high levels of Social Activity with neighbors. Lastly, no significant association was found between Social Activity and Brain Volume for the Social Activity with family or friends (Table 4).

Table 2. Baseline characteristics of participants of the

	N	Frequency	Minimum	Maximum	Mean	SD
Age	754	.	31	83	61.7	9.5
Sex	754	.	.	.	.	.
Male	.	619	.	.	.	.
Female	.	135	.	.	.	.
Level of education	744	.	1	8	4,1	2,2
15-Words learning Test- Total Correct (0-75)	734	.	5	63	38,6	10,5
Sumscore social support	741	.	0	14	11,5	2,8
Sumscore depression	743	.	0	24	2,8	3,6
Physical Summary Scale score	725	.	16,67	63,30	48,21	9,2
Brain volume (%)	691	.	68,26	85,11	78,34	2,94
WML (natural log transformed total wml/icv,)	691	.	-5,58	1,67	-2,20	1,21

Table 3. Frequency and percentage of the different levels of Social Activity with neighbors, family and friends

	N	Frequency	%
Contact with neighbors	745	.	
High level	.	437	58,66
Moderate level	.	222	29,80
Low level	.	86	11,54
Contact with family	743	.	
High level	.	433	58,28
Moderate level	.	208	27,99
Low level	.	102	13,73
Contact with friends	743	.	
High level	.	337	45,36
Moderate level	.	291	39,17
Low level	.	115	15,48

Table 2. Dummy variables Social Activity with neighbors, family and friends and the dependent variable Brain volume

			Brain Volume (%)			
			N	B	CI (95 %)	*p*
SA neighbors	Model 1	High	397	*Ref.*	-	-
		Moderate	205	.115	-.254 *to* .484	.540
		Low	84	.642	.132 *to* 1.151	*.014**
	Model 2	High	397	*Ref.*	-	-
		Moderate	205	.092	-.275 *to* .459	.622
		Low	84	.640	.126 *to* 1.155	*.015**
	Model 3	High	397	*Ref.*	-	-
		Moderate	205	.075	-.291 *to* .441	.668
		Low	84	.682	.167 *to* 1.196	*.009**
SA family	Model 1	High	397	*Ref.*	-	-
		Moderate	196	.230	-.147 *to* .607	.232
		Low	91	-.060	-.565 *to* .444	.814
	Model 2	High	397	*Ref.*	-	-
		Moderate	196	.150	-.235 *to* .535	.444
		Low	91	-.050	-.571 *to* .470	.849
	Model 3	High	397	*Ref.*	-	-
		Moderate	196	.145	-.239 *to* .529	.460
		Low	91	-.011	-.532 *to* .510	.967
SA friends	Model 1	High	311	*Ref.*	-	-
		Moderate	266	-.115	-.474 *to* .244	.529
		Low	107	-.049	-.530 *to* .431	.840
	Model 2	High	311	*Ref.*	-	-
		Moderate	266	-.119	-.476 *to* .238	.512
		Low	107	-.035	-.520 *to* .449	.886
	Model 3	High	311	*Ref.*	-	-
		Moderate	266	-.132	-.488 *to* .255	.468
		Low	107	-.025	-.509 *to* .458	.918

Model 1: age, sex and education; Model 2: physical activity, depression score and social support; Model 3: WML

Table 3. Dummy variables Social Activity with neighbors, family and friends and the dependent variable WML

			WML (%)			
			N	B	CI (95 %)	*p*
SA neighbors	Model 1	High	397	*Ref*	-	-
		Moderate	205	-.111	-.292 *to* .071	.233
		Low	84	.256	.004 *to* .507	*.046**
	Model 2	High	397	*Ref*	-	-
		Moderate	205	-.106	-.289 *to* .077	.255
		Low	84	.257	.000 *to* .513	*.050**
	Model 3	High	397	*Ref.*	-	-
		Moderate	205	-.102	-.285 *to* .080	.271
		Low	84	.282	.025 *to* .539	*.031**
SA family	Model 1	High	397	*Ref*	-	-
		Moderate	196	-.058	-.244 *to* .127	.538
		Low	91	.270	.022 *to* .519	.033*
	Model 2	High	397	*Ref*	-	-
		Moderate	196	-.038	-.230 *to* .153	.695
		Low	91	.281	.022 *to* .540	.033*
	Model 3	High	397	*Ref.*	-	-
		Moderate	196	-.033	-.224 *to* .158	.735
		Low	91	.279	.021 *to* .538	*.034**
SA friends	Model 1	High	311	*Ref*	-	-
		Moderate	266	-.088	-.264 *to* .089	.331
		Low	107	.072	-.164 *to* .309	.549
	Model 2	High	311	*Ref*	-	-
		Moderate	266	-.087	-.264 *to* .091	.339
		Low	107	.069	-.172 *to* .310	.575
	Model 3	High	311	*Ref.*	-	-
		Moderate	266	-.091	-.168 *to* .086	.314
		Low	107	.068	-.173 *to* .308	.582

Model 1: age, sex and education; Model 2: physical activity, depression score and social support; Model 3: brain volume

Table 4. Dummy variables Social Activity with neighbors, family and friends and the dependent variable Cognition

			Cognition (15 word learning task)			
			N	B	CI (95 %)	*p*
SA neighbors	Model 1	High	424	*Ref*	-	-
		Moderate	216	.780	-.786 *to* 2.346	.328
		Low	84	.010	-2.197 *to* 2.217	.993
	Model 2	High	424	*Ref*	-	-
		Moderate	216	.692	-.867 *to* 2.252	.384
		Low	84	-.074	-2.299 *to* 2.151	.948
SA family	Model 1	High	422	*Ref*	-	-
		Moderate	203	1.425	-.175 *to* 3.026	.081
		Low	96	-.076	-2.169 *to* 2.017	.943
	Model 2	High	422	*Ref*	-	-
		Moderate	203	1.289	-.337 *to* 2.916	.120
		Low	96	.223	-1.934 *to* 2.381	.839
SA friends	Model 1	High	328	*Ref*	-	-
		Moderate	282	1.995	.488 *to* 3.501	.010*
		Low	111	2.439	.418 *to* 4.460	.018*
	Model 2	High	328	*Ref*	-	-
		Moderate	282	2.098	.603 *to* 3.593	.006*
		Low	111	2.755	.715 *to* 4.796	.008*

Model 1: age, sex and education; Model 2: physical activity, depression score and social support

WML

As shown in Table 5, the analysis for the dependent variable WML revealed a significant relation between low levels of Social Activity with neighbors and WML (B=.256; 95% CI= .004 to .507 %; *p*=.046). This association was not changed after adding depression score, social support and physical activity (Table 5). The difference of the amount of WML between people with high levels of Social Activity and people with low levels of Social Activity was even bigger after controlling for Brain Volume (B=.282; 95% CI= .025 to .539 %; *p*=.031). These results indicated that the group with low levels of Social Activity with neighbors has more WML than the group with high levels of Social Activity with neighbors. In addition, significant more WML was found in people with low levels of Social Activity with family than the reference group (B=.270; 95% CI= .022 to .519 %; *p*=.033). This difference remained significant in models 2 and 3 (Table 5). These findings confirm the hypothesis that states that low levels of Social Activity is associated with more WML. The association between Social Activity and WML is not mediated by the factor social support, this is due to the absence of significant association between social support and WML (β=-.041; *p*=.288). However, Social Activity with friends was not significantly associated with WML (Table 5). Neither were any significant results found for the groups with moderate levels of Social Activity (Table 5).

Cognition

Finally, it was expected that low Social Activity would be associated with lower Cognitive function. After the analysis, an association was found between Social Activity with friends and Cognitive function. However, these findings did not confirm the hypothesis. The results of this analysis are presented in Table 6. A significant better cognitive function was found for people with moderate levels of Social Activity with friends when compared with the group with high levels of Social Activity (B=.1.995; 95% CI= .488 to 3.501 %; *p*=.010). The difference between the cognitive function of people with high levels of Social Activity and people with moderate levels of Social Activity was bigger after adding the covariates depression score, social support and physical activity (B=.2.098; 95% CI= .603 to 3.593 %; *p*=.006). A significantly better cognitive function was found for people with low levels of social Activity when compared to people with high levels of Social Activity (B=.2.439; 95% CI= .418 to 4.460 %; *p*=.018). The same result was found after controlling for the covariates of model 2 (Table 6).

Discussion

The purpose of this study was to explore the influence of low Social Activity on brain volume, WML and on cognition. We found that people with low levels of Social Activity with neighbors have larger brain volume, when compared to people with high levels of Social Activity with neighbors. Furthermore, the analysis for WML showed that people with low levels of Social Activity with neighbors and family have more WML than people with high levels of Social Activity with neighbors and family. Finally, it was found that people who have low or moderate levels of Social Activity with friends have better Cognitive function, when compared to people who have high levels of Social Activity.

The results of many studies indicated the positive influence of social factors on cognitive decline (Conroy et al., 2010; James et al., 2011; Krueger et al., 2009; Mortimer et al., 2012) or on developing mci or dementia (Wang et al., 2002; Sörman et al., 2013; Paillard-Borg et al., 2012), we were interested in the possibility of establishing cognitive reserve by social activities. However, there were no studies that explored the effect of Social Activity on neuropathology. Therefore, it was not possible to make any suggestions if social activities are able to influence the relation between cognition and neuropathology. Neither it was possible to answer the question that questioned if Social Activity can provide cognitive reserve. Because of these reasons and because of the lack of knowledge about the relation between Social Activity and neuropathology, we wanted to explore the association between Social Activity and brain volume and wml. We also checked the influence of Social Activity on cognition.

It was expected that low levels of Social Activity would be associated with smaller brain volume. As mentioned above, the findings of the present research did not confirm this expectation. The significant results indicated the opposite, low levels of Social Activity with neighbors are associated with a larger brain volume than in people with high levels of Social Activity. Differences in brain volume were not found for people with Social Activity with family or friends. The results of the analysis of people with Social Activity with neighbors were not in accordance with a previous study that had explored the same relationship: the findings of Mortimer and colleagues (2012) showed an increase of the brain volume in people who had more Social Activity. The social Interaction groups of this study showed increases in total brain volume when compared to the control group.

Regarding WML, it was hypothesized that low levels of Social Activity were to be associated with more WML. This is confirmed by the findings of the present study, as these shows that low levels of Social Activity with neighbors or family are associated with more WML. Comparable effects were not found in people with Social Activity with friends. The outcomes of the analysis confirmed the expectation that was based on the suggestion of Fratiglioni and colleagues (2004), stating that social stimulation influences the vascular hypothesis. Specifically, it was expected that the effect of Social Activity on WML would be mediated by social support, which could lower the stress levels and by consequence lower the vascular risk (Katsarou, 2012). However, an effect of social support on WML was not found. This indicates that Social Activity in itself is an important factor that influences WML.

Lastly, the influence of Social Activity on cognition was explored. It was expected that low levels of Social Activity was associated with lower cognitive function. Surprisingly, the results of Social Activity with friends showed a different relation. People with moderate or low levels of Social Activity had a better cognitive function when compared to the people with high levels of Social Activity. Differences in cognitive function between people with high levels of Social Activity and moderate or low levels of Social Activity with neighbors and family were not found. The result of the effect of Social Activity with friends on cognition differs from the findings of Mortimer and colleagues (2012). They found that intervention with social interaction improves the performance on the verbal fluency test and on the recall after the auditory verbal learning test. However the findings of the present study show the opposite: people with low levels of Social Activity had a better performance on the verbal learning test.

Only the hypothesis of the association between Social Activity and wml is confirmed. The other analyses found different results than expected. Explanations of these findings can be the amount of leisure time, the daytime activities and the priority of people to contact neighbors, family or friends. Regarding the amount of leisure time, this influences the levels of Social Activity with neighbors, family and friends. When people have a lot of daytime activities, they have not much time to contact other people. These daytime activities potentially also influence the brain volume, the amount of wml and cognitive function besides the social activities we measured. In addition, the priority of people influences choices of filling in the leisure time and the choices to contact neighbors, family or friends.

When we evaluate the results of the analysis of Social Activity and brain volume, only Social Activity with neighbors was significant. As mentioned before, these results showed a positive difference between high levels of Social Activity and low levels of Social Activity. An explanation for the not confirmed hypothesis can be the fact that this social tie is more sensitive for the amount of leisure time, because people possibly do not have a high priority for contacting their neighbors, what results in low levels of Social Activity. Nevertheless, other leisure activities like physical activities also can influence brain volume. This is proved by the research of Braskie and colleagues (2014), they found that lower physical activity intensity is associated with lower total brain volume 9 years later. This illustrates that other daytime and leisure time activities can explain the larger brain volume in people with low levels of Social Activity.

In regards of the results of the analysis of Social Activity and cognitive function, it is difficult to explain why people with low levels of Social Activity with friends have better performance on the 15-words learning test. Possibly, this is also influenced by the type of daytime activities, the amount of leisure time and the priority to contact friends. The priorities of the participants with low levels of social activities with friends are different than the priorities of people with high levels of Social Activity with friends. Other interests and hobbies could be a reason for having less or no contact with friends. These interests, hobbies and daytime activities are just like Social Activity also influencing cognitive function. The influence of employment is proved by Wickrama and O'Neal (2013). They found that older people who work full-time have better immediate memory than retired, non-working or partially retired older people. Further, Leist, Glymour, Mackenbach, van Lenthe and Avendano (2013) concluded that unemployment is associated with cognitive decline and that the direction of this association depends on the performance of activities. They found that the activities that people did during this employment gap have a positive influence on the cognitive function, whereas sickness and unemployment are associated with a higher risk of cognitive decline. These reasons can explain the result of better cognitive function in people with low levels of social activities with friends.

A limitation of this study regarding the measure of Social Activity is that a questionnaire of only three questions was used. Furthermore, this was the first study that used the data of these questions, so these questions could not be checked for validity and reliability. It would be advisable for future research to evaluate the questions for these factors. In addition, there are confounders that are not measured and checked in this study. As already mentioned, the amount of leisure time, daytime activities and priority of people to contact neighbors, family or friends are factors that potentially are important for the reason why people have high of low levels of Social Activity and influence both the level of Social Activity and the dependent factors brain volume, WML and cognition. Following studies should collect more information of the participants and their daily and leisure time activities and control for these factors. Furthermore, the present study measured not only the frequency of social activities, but it also measured the type of the social contact. We measured whether the social contact is accomplished with their neighbors, family or friends. The measure of Social Activity in previous studies was more focused on the frequency of Social Activity. This difference makes it hard to compare the results of the present study with the results of previous studies. This presents a limitation, because the purpose of this study was to expand the knowledge of Social Activity and the pathological factors like brain volume and WML. On the other hand, this is the strength of this study, as it breaks ground on the exploration of the effect of Social Activity with different social ties on brain volume and WML.

It is noteworthy to mention the different effects of Social Activity on brain volume, WML and cognition for the social contact with neighbors, family and friend. The current findings suggest that the specific social ties do influence the effect of Social Activity on different outcome variables. However, as the present study is the first to explore the effect of Social Activity with different social ties on brain volume and WML, it is not possible to compare these findings with previous results.

Although there are no previous studies that have explored the influence of Social Activity with specific social ties on brain volume and WML, earlier research does indicate that a dissociation between different social ties is of absolute importance. Glass, Mendes de Leon, Seeman, & Berkman (1997) discussed two different models of the social network: the structural model, and the role-specificity model. The structural model is more focused on the size of the social network and the frequency of contact. The other way of characterizing the social network is according to the role-specificity model, which emphasizes the nature of the social tie. For this model the kind of social ties included in the social network are of importance. Glass and colleagues (1997) point to the research of Croog, Lipson and Levine (1972) which suggests that the type of relationship influences the availability of support. Furthermore, as a result of their own findings and the conclusions of previous research, Glass and colleagues (1997) presented the multidimensionality of the social network. They hypothesized that the social network can be divided in four subnetworks that corresponds to four primary social roles, specifically the roles of children, relatives, friends and confidant (defined as 'a special person you feel close and intimate with'). After testing their theory, they concluded that the social network comprised of four uncorrelated subnetworks which are clustered according to the four social role categories (Glass et al., 1997). The measurement of Social Activity by using the different social ties of the present study corresponds with the theory of the multidimensionality of the social network presented by Glass and colleagues (1997).

In previous research there is already explored the influence of Social Activity with specific social ties on cognitive function and cognitive decline. Zunzunegui, Alvarado, Del Ser and Otero (2003) examined the influence of social networks and social engagement on cognitive decline. Based on the findings of Glass and colleagues (1997), Zunzunegui and colleagues (2003) argued that besides the function of the social network, the nature of the ties would also have important effects on cognitive decline. Therefore, they divided the social network in subnetworks according to the nature of the tie. As it was demonstrated by Glass and colleagues (1997), four subnetworks were distinguished in this case consisting of friends, relatives, children and couple. The results of this study showed that engagement with friends seemed to be protective against cognitive decline, however, this was only found in woman.

It is remarkable that the research of Zunzunegui and colleagues (2003) only found a preventive role of social engagement with friends. The same social tie is responsible for an effect of Social Activity or on cognitive function in the present study. However, the results are not in sync. The results we found indicated that people with moderate or low levels of Social Activity have better cognitive function than people with high levels of Social Activity, this is opposes the findings of Zunzunegui and colleagues (2003). There are more differences between the studies. The questions posed by Zunzunegui and colleagues (2003) are focused on the social engagement of the participant. An example of a question is: ‘How often do you feel you help your children (family/friends)?’. While the questions that are used in the present study are focused on social activities (‘In general, how often do you have contact with neighbors (including telephone calls or letters)?’). Furthermore, Zunzunegui and colleagues (2003) also explored the differences in results between men and woman. Consequently, direct comparisons between the two sets of research cannot be made. However, it can be concluded from both studies that social ties are important for the effect of Social Activity on cognition.

Although we did not found clear results of the influence of Social Activity on brain volume and on cognition, an association was found between low levels of Social Activity and more WML. Because previous research did present a positive effect of Social Activity on cognitive function (Mortimer et al., 2012; Krueger et al., 2009), addition of our exploration about WML suggests a potential involvement of Social Activity in cognitive reserve. With this new consideration, it would be interesting for future research to explore the influence of Social Activity in cognitive reserve further.

To summarize, there are three different findings. Firstly, regarding the influence of Social Activity on brain volume and on cognition, there are no clear results. The mixed results do indicate that the social ties influence the relation between Social Activity and brain volume and cognition, and the Social Activity with different social ties gives different results. This could account for the differences between our findings and those of previous studies. It also explains why the hypotheses cannot be confirmed. This conclusion supports previous research that proved that the nature of the social tie is important in the research of social influences (Glass et al., 1997; Zunzunegui et al., 2003). However, more studies are needed to enlarge the knowledge about the influence of different social ties on cognition and neuropathology. Therefore, future studies of Social Activity should not only focus on the frequency of Social Activity, but also explore the effect of social ties. Secondly, the results also indicate an effect of the frequency of Social Activity on WML. Due to these results, it would be interesting for future studies to pay more attention to the effect of Social Activity on WML and other neuropathological factors. Finally, the results of the analysis of the effect of Social Activity on WML indicate that low levels of Social Activity is associated with more WML and is therefore probably a risk factor. To validate these suggestions more research is needed. In addition, the results of WML in combination with the results of previous studies about the influence of Social Activity on cognitive function give an indication of the possibility that Social Activity can provide cognitive reserve. However, future research is needed to show if Social Activity is definitely a protective factor and involved in cognitive reserve.

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