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The effect of vascular risk factors on Cross Cultural Dementia screening

Masterthesis

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Abstract

This study was an attempt to find out whether carrying vascular risk factors had effect on the capacity of executive functioning. 976 cognitively healthy participants, out of which 600 carried indeed vascular risk factors, were gathered and tested through subtests of the CCD, which measured the inhibition and cognitive flexibility of the participant.

People carrying vascular risk factors perform worse on executive functions such as inhibition and cognitive flexibility, compared to people without vascular risk factors. In addition, the more risk factors one carries, the worse the performance is for up to two risk factors. Correcting for differences in demographic characteristics between the groups, on inhibition scores carrying vascular risk factors is leading to worse inhibition scores only at 2 vascular risk factors. On a cognitive flexibility task, carrying vascular risk factors leads to worse performance, with no further effects of the amount of existing vascular risk factors.

Furthermore, males had better scores than females, younger people better than elder and people with higher level of education scored better than less educated people. Dutch participants scored the best on both inhibition and cognitive flexibility, Moroccan Berber the worst on inhibition and Moroccan Arabic participants the worst on cognitive flexibility. For future research, expanding the five heart and vessel diseases and analyze whether the effect of hypertension and heart and vessel diseases are embedded in the proportion of influence diabetes already explains, are suggested improvements.

Introduction

It is a widespread, well-known fact that the population on earth is rapidly increasing. At the moment, there are 7 billion people living all over the world. By the year of 2050, it is estimated that this amount will climb up to 9.7 billion (United Nations, 2015).

Increased life expectancy leads to population ageing which is one of the factors causing multiple changes in the world population. Two major inducers for the remarkable shift in life expectancy are the development of health care and improved living conditions. Between 1950-1955 and 2005, the global average life expectancy at birth rose from 48 to 70 years in women, and from 45 to 65 years in men (United Nations, 2009). In 2012 there was a sequal, the estimated average life expectancy was according to the World Health Organization 81,4 and 78,4 for women and men respectively (Colin, Stevens, Boersma, White & Tobias, 2015). Due to better health care and modern civilization there is an incline in birth rates. Together with the increased life expectancy, this is nowadays leading to an unwanted increase of the proportion of older persons (United Nations, 2015). Population ageing will be very significant in the next several decades, it is estimated that by 2050 34% of the population of Europe will be over 60 years old ("World population," 2015).

Moreover, the migration of humankind all over the world is contributing too to a natural change in composition of society. An illustrative example for this change is the migration of non-EU *Gastarbeiters,* for which the literal translation is guest workers, to different countries, which nowadays make part out of the European Union (Sonmez, 2008). By exceeding the amount of 2.3 million in the year of 2011, citizens of Turkey take the first place together with Romania when it comes to numbers of foreigners in the EU Member States (Vasileva, 2012). Morroco has the second place with approximately 1.9 million people.

Inevitably, the ageing of a population and migration bring also a change in common diseases with it and other demands of care too. An ageing population is much more likely to require care for chronic diseases like heart diseases, osteoporosis and dementia, rather than for acute illnesses (Wiener & Tilly, 2002). Furthermore, diversity in the population causes types of used intervention and relationships between patient and practitioner to vary too.

The most common health problems in the elderly are vascular and neurodegenerative diseases of the central nervous system (Owecki, Michalak, Kozubski, 2011). Especially memory loss is a key concern when it comes to older adults. The most related disease thereby is dementia. Even though this disease is seen in all population groups, when it comes to prevalence, diagnostics and further treatment, there are big differences.

Population ageing will stimulate the prevalence of dementia in the Netherlands. Estimations are made for an increase of 17% by the year of 2012, and 61% by the year of 2030 (Alzheimer Nederland, 2014). In 2020 there will be a growth of 34%, and in 2030 109% in the immigrant subpopulations. Compared to the local citizens, in non-western immigrant groups some risk factors as low level of education are more frequent. While 10% of autochthonous people has the risk factor diabetes for dementia, these number is 28% among the Turkish inhabitants and 31% when in comes the Moroccan population. Conclusively, the amount of immigrants with dementia will increase twice as fast as autochthonous.

§ 1.1 Dementia

Alongside of memorial problems, the most central concept of dysfunctions of people with dementia is cognitive impairment (Ford, 2015). Cognitive dysfunctions include disturbed perception, mood and/or thought content (Cankurtaran, 2014), categorised as following: aphasia (inability of understanding or expressing language), apraxia (inability to acting target consciously), agnosia (inability to recognize objects, sounds and people for example) and/or disturbed executive functions (the inability of organizing, planning and deducing). Effects on the behavior can be seen in forms of physical/verbal aggression, disinhibition in general and in sexual terms and culturally inappropriate behaviors. Anxiety, depressive mood, hallucinations and misidentification syndrome are some examples of emotional effects.

There are multiple forms of dementia, with a variety of etiologies and clinical manifestations. The two most common sorts of dementia as categorised in the *Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM V)* are Dementia of the Alzheimer's Type and Vascular Dementia (American Psychiatric Association, 2013). While Alzheimer's disease makes half out of all cases, vascular dementia is the second most common type of dementia, yielding 25 to 30% of all dementia cases (O'Brien et al., 2003).

Vascular cognitive impairment is characterised by a specific cognitive profile and involves not only preserved memory but impairments in attentional and executive functioning too (O'Brien et al., 2003). Besides, a slowing in motor performance and information processing can also be seen. During an international workshop there are valid, reliable and applicable criteria determined for probable, possible and definite vascular dementia (Roman et al., 1993). While having dementia and cerebrovascular disease which are interrelated is enough to meet the criteria for probable dementia, definite vascular dementia needs additionally histopathologic evidence, absence of exceeding neurofibrillary tangles and neurotic plaques and the absence of other disorders capable of producing dementia.

Since we know that some factors have a large impact on the level of cognition, there are some vascular risk factors to name such as diabetes, hypertension, smoking and heart complaints. These all can be predictors for vascular dementia *or Mild Cognitive Impairment*, which is a term for the stage between normal ageing and dementia.

§ 1.2 Diagnostic assessment of dementia

In order to distinguish people without dementia from the ones with, different neuropsychological assessments and questionnaires are in use. Herewith, researchers can check whether the criteria summed up in DSM-V are met or not. Together with further clinical observations from a professional a more reliable conclusion will be achieved. It is also crucial to exclude other invalid causes of the problematic (Barnes & Raskind, 1981). Evidence from physical exam, laboratory tests or other specific organic factors is very useful.

§ 1.3 Diagnostic shortcomings

When it comes to illiterate people or foreigners, these instruments have some shortcomings. The questions and tasks asked cannot be answered adequately by these populations and therefore the obtained scores are not valid for the actual capacity of these tested people. In addition, the variety in language and culture in the targeted population makes standardization of these instruments even more difficult.

Reading and writing skills influence the performance on cognitive and language tests (Kim, Yoon, Kim & Kim, 2014). Especially performal subtests of assessments are more difficult to succeed in for illiterate people. Performal tests are, after spoken instructions, less complex for this population to perform at. Tasks like completing sentences by writing, detecting unmatching words or pairing cohesive words make it almost impossible to measure the level of cognitive functioning, since the very fundamental abilities required for the tasks are not met. Illiteracy is mostly associated with socio-economic level, low educational background and can therefore be associated with dementia. In order to approach the actual level of capacity it is important to identify the level of impact of both illiteracy and education.

Some cognitive instruments include pictures of well-known food or daily used accessories. These choices withhold the test from providing equal opportunities to the participants too, because cultural aspects could influence the knowledge and recognition among tested people. For an immigrant, an avocado that is well known and widely used in the local cuisine, could be meaningless. In the same way, the picture of the current king of the country of living could be unmeaning. The reason holding this person back from recognition in these cases is nothing but renewed circumstances which is not supposed to be measured.

Current instruments have to be revised in order to generate culture and language neutral assessment. Main core adjustments for an applicable culture neutral test are giving more examples, making use of vocal instruction instead of written ones, increasing the use of pictures and avoiding culture sensitive factual knowledge (Baan, 2011). To include elderly migrants in the testable population through providing them a culture neutral test, researchers of the University of Amsterdam, the Medical Centre Slotervaart, the Amsterdam Medical Centre have developed the Cross-Cultural Dementia Screening, the *CCD* (Goudsmit, 2005). This introduced screening test consists of multiple components, which help measuring the level on some cognitive domains like memory, visuoconstruction and executive functioning.

§ 1.4 Previous studies

There is some research conducted in earlier stadium of the development of this screening test. At the beginning the CCD consisted of the four subtests Object Test, Sun-Moon Test, Dots Test and Card Sorting Tasks. When analysis showed the Card Sorting Task to be insufficiently contributing to the predictive value of the CCD, this fourth subtest was removed from the test (Goudsmit, Parlevliet, Van Campen & Schmand, 2014, p. 30).

Goudsmit developed the CCD and conducted a first validation study on the CCD, and concluded that the overall test could not significantly discriminate between elderly who suffer from dementia and elderly who do not (2005). As possible explanations she considered the small size of her sample (n= 43) with just three dementia patients, the non-standardized instructions of researchers and the required level of verbal capacity. In order to lower these last two, Vleeschouwer adjusted and when necessary even replaced subtests with alternatives (2007). Using a homogeneous native Dutch sample (n=50), she concluded the test to be significantly discriminating people with and without dementia. Insight in leading this test, made her notice that even for native Dutch people it was hard to complete the test without proper verbal instructions. The set was adjusting once again, by adding standardized vocal instructions in multiple ethnic languages, which could be used by any researcher.

In the research of De Hen in 2009, there was also no significant difference found between the overall performance of Moroccan and Turkish participants too (n=58). Therefore there was concluded that the CCD is culture neutral. Research on a subgroup showed demographic factors as level of education and age to be underlying and explanatory to the differences found between the scores of ethnical groups when they were tested in larger amounts (n=1587) (Goudsmit, Parlevliet, Van Campen & Schmand, 2014, pp. 49-54). By matching comparable participants (n=180), there was no significant difference anymore. The developers concluded the CCD to be cross culturally applicable.

§ 1.5 Research goals and hypotheses

The purpose of this research is to find out whether carrying vascular risk factors means lower scores on subtests, which require executive function, and if the amount of risk factors makes differences too. Out of the complete CCD, part B of the Sun-Moon Test and part B of the Dots Test are tests of executive functioning (and mental speed).

The research question of this study is: does a subpopulation of cognitively healthy elderly carrying vascular risk factors perform worse on the executive subtests Sun-Moon part B and Dots Test part B compared to the cognitively healthy elderly who do not have any vascular risk factor? Furthermore, is carrying multiple risk factors associates with lower scores on these subtests?

We expect a difference between the scores of participants with and without vascular risk factors on parts B of the Sun-Moon and the Dots Test. Since we know that vascular risk factors increase the risk of vascular injury very early in life, possibly leading to attentional and executive dysfunctions, tasks which require processes of working memory, reasoning and task flexibility will be more difficult to complete accurately (O'Brien et al., 2003). We also expect that the more risk factors one carries, the lower the score on executive tasks will be. The effect of vascular risk factors on dementia risk is cumulative (Maillard, Carmichael, Reed, Mungas & DeCarli, 2015) and the risk for dementia increases for having multiple vascular risk factors (Whitmer, Sidney, Selby, Caliborne Johnston & Yaffe, 2005).

§ 1.6 Practical relevance

Worldwide, stroke is as a (result of) vascular risk factor the second leading cause of death and a third of patients develop post-stroke dementia within a year (Sahathevan, 2012) (O'Brien, 2003). This shows that vascular dementia is a crucial health issue to consider since it is estimated that the prevalence of neuropsychiatric symptoms associated with dementia will increase as the population ages (Ford, 2015). Over the next 30 years it is expected for the prevalence to double, making cognitive disorders a priority for health and social-care services.

Not only screening on dementia, but also finding specific profiles on obtained scores is essential. Vascular injury happens very early in life, but is in early stages clinically silent (O'Brein, 2003). Low scores on the specific subtests could break silence and be a sign for the eventual presence of vascular risk factors or even disruptions of frontosubcortical circuits.

Even though a large amount of research has been done on health issues concerning vascular dementia, more research is needed when it comes to interpret and diagnose it through applicable and befitting assessment, which will help circumvent a language barrier and oppress culture sensitivity. After all, the European Union calls health a human right.

Methods

§ 2.1 Sample

The cognitively healthy participants were recruited from different general practitioners in areas with low socio-economic status. Information about the psychopathological history was gained from the data provided by the practitioners or the participants themselves. We selected the four largest cities of the Netherlands. In these cities the target populations are twice as dense as compared to other towns. The minimum age for inclusion was 55 years, since this is the standard used in comparable previous study (Goudsmit, 2005). Further criteria for inclusion were to be born in Turkey, Morocco, Suriname or the Netherlands and the ability to speak and understand either Dutch or one of the languages of the country of origin (Parlevliet, Uysal-Bozkir, Goudsmit, Van Campen, Schmand & De Rooij, 2014).

The sample of cognitively healthy elderly for this investigation includes a total of 1022 participants, of six different ethnicities (Dutch, Moroccan-Arabic, Moroccan-Berber, Surinamese-Creole, Surinamese-Hindi and Turkish). Out of this total sample we selected participants without missing values (n=976). We compare a subgroup with vascular risk factors (n=600) to those without any vascular risk factor (n=376). Relevant risk factors are diabetes, hypertension, cardiovascular diseases including peripheral vascular disease, ischemic heart disease, heart failure, renal failure and stroke, collected from participants and patient records of the general practitioner. The group carrying vascular risk factors consisted of 294 men and 306 women and the group without vascular risk factors includes 176 men and 200 women.

§ 2.2 Materials

All participants were administered the Cross-Cultural Dementia Screening test, the *CCD* (Goudsmit, 2005). The CCD provides the opportunity to test the participant in the mother language through recorded instructions for each subtest. Responses were saved in the computer program and simultaneously on a paper sheet. These tasks were led by a trained test leader. Each CCD-take consisted of 3 subtests, which are the following: (I) Object Test to test the memory, the (II) Sun-Moon Test to test the interference sensitivity and the (III) Dots Test to determine the cognitive flexibility. The result of the total of these tests was presented the test leader at the end of the registration of the responses on the computer, in traffic lights, of which the colour is an indication for the degree of possible dementia. A score lower than the 5^{th} percentile was considered as a deviating score. If required so, the result was sent as feedback to the general practitioner.

§ 2.2.1 Objects Test

The Objects Test consists of two parts, presenting the imprinting (part A) and the recognition (part B). It exists of 214 pictures of vegetables, fruits, tools and other commonly used everyday objects. In part A, the participant is shown 1, 2 or 3 objects to take time on inculcating with the purpose to recognize these target items on the next page between other objects, which were not shown before (distractors). There are two examples given before the test items, and the level of difficulty increases gradually. After an interval of 20 minutes, part B is presented. At part B, the participant was asked to point out the target items remembered from part A, again surrounded by other distracting daily used items. During the interval, participants were taking the other subtests of the CCD.

This test measures memory. Part A stands for the capacity of recognition and direct imprinting while part B gives an insight into the ability of delayed recognition. Both parts included 30 target items and 92 distractors which make a maximum score of 122 for each.

§ 2.2.2 Sun-Moon Test

The Sun-Moon Test consists of two parts as well. In part A, participants get to see five rows of eight symbols. These symbols are suns and moons in random frequency and order. Participants are asked to name out loud what they see from left to right as fast as possible in their mother tongue. The administration sheet contains the right answers in different languages to facilitate the test leader to code, manage and evaluate the given responses even though not comprehending the language of the participant. In order to make clear that the participant understands the purpose of the test, there are two examples given before the test items. In part B, the participants get similar testing material, but this time they are asked to call all the symbols vice versa. Thus, when they saw a *sun* they had to say *moon,* and vice versa, which evokes a *Stroop-effect* (Stroop, 1935).

The Sun-Moon Test is testing the ability of mental speed and inhibition. In both parts there are 40 words used. The time needed for completing the tests and the amounts of uncorrected errors and self-corrections are noted. The score is the completion time in seconds plus the corrected time for mistakes, both accuracy and speed are taken into account. For part B a score exceeding 71 seconds will be considered as deviating.

§ 2.2.3 Dots Test

As well as the previous two subtests, the Dots Test consists of two parts. In part A, participants had to connect nine white domino stones printed on a paper sheet. The stones had black dots on them, ranging from 1 to 9 pieces. Participants were given the instruction to connect these domino stones in the right ascending order and do this as fast as possible.

Moving on to part B where the task gets more difficult, participants had to connect 18 domino pieces. Nine out of them were again white and had black dots, while the other nine pieces were black with white dots on them. The aim was to make lines between these domino pieces again in ascending order, meanwhile alternating between the black and white stones. For both parts there were practice items before the testing items. This test is derived from the well-known *Trail Making Test* (Reitan, 1955). Instead of numbers and letters, graphics are used to reduce the effect of illiteracy.

In part A, the psychomotor speed is measured. The score on part B represents the divided attention and cognitive flexibility. As well as made errors, which were corrected immediately by the test leader, and the amount of given hints were registered. The test is interrupted when 3 errors are made in a row or in case of lack of understanding. The total score includes the time in seconds in both part A and B. The self-corrections are meant for qualitative interpretation of performance. For part B a score exceeding 216 seconds is considered as deviating.

§ 2.2.5 Questionnaire

In addition to these cognitive tests, administrators made also use of a questionnaire, which is taken on the same appointment date as the CCD. This questionnaire is based on the Minimal Dataset, the *MDS,* of the National Program of Elderly Care (Kring Ouderenzorg AMC, 2010). Incorporated questionnaires in the MDS are the EuroQol 5D, and the Katz Index of independence in activities of Daily Living (ADL). Participants were asked some questions about their health, their use of health care, social and daily activities and further factors affecting the quality of life. Moreover, there were questions included which made it possible to investigate whether vascular risk factors were existent or not. The vascular risk factors relevant to this research were diabetes, hypertension, depression and heart and vascular diseases. All questions were asked in the native language of the participants in order to facilitate the communication.

§ 2.3 Design

This study is conducted with an observational design. There is a control group embedded in the research design, but there is no manipulation of a factor. The design is approved by the Medical Ethical Testing Committee of the Amsterdam Medical Centre (METC).

§ 2.4 Procedure

Potential participants were sent a letter in their native language to their home addresses as an invitation to participate in the study, called the *SYMBOL*-study. After two weeks, these potential participants were contacted by telephone by one of the bilingual interviewers. During this first conversation they got an introduction to the research and the aim of the research. They were asked if they had time to read the letter sent and if they were willing to participate. Participation could be at their own houses, in a social centre or at the office of their own general practitioner. All agreements resulted in an appointment. Test leaders were trained in conducting the assessment consisting of providing information about the conducted research, taking the CCD and the questionnaire. The duration of the appointment was one and a half hour. In advance, the participant was asked to sign the informed consent and was told to have the right to quit the research anytime they want without giving any reason for quitting. With permission of the participant the result could be transmitted to the general practitioner.

§ 2.5 Analysis

All analyses are performed by SPSS version 22 with a confidence interval of 95%. Outliers based on performance scores, are excluded of the sample used for further analysis. Furthermore, a Power test is done, in order to test the strength of the design.

We expected the subpopulation carrying vascular risk factors to score lower on the Sun-Moon Test part B and Dots Test part B compared to the other tested healthy elderly, which do not have any form of vascular risk factor. In case of normally distributed variables, we analyse this by comparing the two groups with an unpaired t-test. If there is not a normal distribution, we will choose to analyse by a MannWhittney U test.

We also expect the effect of the vascular risk factors to be cumulative, thus the more risk factors one carries, the lower the score on the subtests of executive functioning is expected to be. In order to test this hypothesis, we will compare groups with 1, 2, 3 or 4 risk factors with each other through a one-way ANOVA. Prior to the analysis, we have to compare the subgroups of our research on some factors as level of education, socio-economic status, age, gender and culture in order to detect possible confounders. The categorical variables gender, culture, depression and level of education were assessed with Chi-Square Tests. The remaining variables age and socio-economic status were assessed with Kruskal-Wallis Tests. If some factors are influential, we have to correct the results by adding them as covariates to the analysis.

Results

§ 3.1 Effect of existence vascular risk factors on performance scores

The performance on parts B both of the Sun-Moon and the Dots tests of 436 participants without vascular risk factors and 538 participants with vascular risk factors was compared.

		Without vascular risk factors (n=436)	Range	With vascular risk factors (n=538)	Range
Age	M(SD)	64.09 (6.701)	55 – 91	67.03 (7.730)	47–95
Gender	N_{male}(%)	202 (46.3%)		267 (49.6%)	
Culture	$N_{Turkish}$(%)	57 (13.1%)		112 (20.9%)	
	$N_{Moroccan\text{-}Arabic}$(%)	46 (10.6%)		55 (10.2%)	
	$N_{Moroccan\text{-}Berber}$(%)	7 (1.6%)		18 (3.4%)	
	$N_{Surinamese\text{-}Creole}$(%)	37 (8.5%)		105 (19.6%)	
	$N_{Surinamese\text{-}Hindu}$(%)	12 (2.8%)		41 (7.6%)	
	N_{Dutch}(%)	250 (57.3%)		163 (30.4%)	
Depression	$N_{depressed}$(%)	61 (14%)	0 – 1	87 (16%)	0 – 1
Socio-economic status	M(SD)	-1.3281 (1.172)	-5.08 –1.54	-1.6296 (1.096)	-4.73 – 1.84
Level of education	Mdn	5	0 – 7	4.0	0 – 7

Their demographic characteristics are described in Table 1.

Table 1 – Demographic characteristics of participants

The variables age, gender, culture, depression, socio-economic status and level of education were possible predictors for differences in performance scores between the groups with and without vascular risk factors. Since there was not a normal distribution for the variable age, as assessed by a Shapiro-Wilk's test ($p < .05$), we could not conduct a Univariate Analysis of Covariance, ANOVA for this ratio scale.

There was no statistically significant difference between the groups with and without vascular risk factors on gender ($\chi^2(1) = 1.049$, $p = .169$) and depression ($\chi^2(1) = .888$, $p = .197$). For culture ($\chi^2(6) = 83.731$, $p < .001$), level of education ($\chi^2(7) = 40.552$, $p < .001$), age ($\chi^2(1) = 37.289$, $p < .001$) and socio-economic status ($\chi^2(1) = 32.151$, $p < .001$) there was a statistically significant difference comparing the groups with and without vascular risk factors.

The variable Sun-Moon Test part B was not normally distributed ($D(958)=.141$, $p < .005$), with a skewness of 2.381 (SE=.078) and kurtosis of 9.684 (SE=0.157). Furthermore, the variable Dots Test part B was not normally distributed ($D(958)=.145$, $p < .005$), with a skewness of 2.351(SE=.079) and kurtosis of 8.009(SE=.158). For both variables, the Q-Q-plots and histograms were confirming the non-normality of distribution.

In order to determine if there were differences in performance scores on the subtests between participants with and without vascular risk factors, the Mann-Whitney Test was run. We used the presence of vascular risk factors as independent variable and the score on the subtests as dependent variable. The higher the score, the worse the performance since it represented the completion time corrected for the mistakes made.

Distribution of the scores (range: 11.0-157.1) on part B of the Sun-Moon Test, were similar for participants with and without vascular risk factors, assessed by visual inspection of boxplots and histograms. Time score was significantly higher in the group with vascular risk factors (*Median* = 34.5) than in the group without any vascular risk factor (*Median* = 29.0), U = 87039, z = -6.931, p < .001. On the Dots Test part B the scores (range: 2.0-518.0), were significantly higher for the group with vascular risk factors (*Mdn* = 84.0) than for the participants without vascular risk factors (*Mdn* = 56.0), U = 79889.5, z = -7.942, p < .001. For the Sun-Moon Test part B there was a small effect (r = .222), while for the Dots Test part B there was a nearly medium effect (r = .257). Squaring *Cohen's r*, for both of the Sun Moon Test (η^2 =.049) and Dots Test (η^2 =.066) there was a small effect .

§ 3.2 Effect of the amount of vascular risk factors

Amount of risk factors	Sun-Moon Test				Dots Test			
	Frequency (N)	M(SD) *	Estimated marginal mean	Mdn	Frequency (N)	M(SD) *	Estimated marginal mean	Mdn
0	436	32.5 (15.0)	34.5 (.7)	29.0	435	71.3 (51.0)	80.7 (2.7)	56.0
1	333	36.9 (16.8)	35.7 (.8)	33.0	323	96.4 (72.5)	92.8 (3.1)	79.0
2	172	41.9 (18.6)	40.0 (1.2)	38.0	168	109 (78.1)	96.2 (4.3)	88.0
3	33	44.2 (19.3)	36.2 (2.7)	40.5	32	127 (77.8)	90.8 (10.1)	108.5
Total	974	36.1 (16.8)			958	88.3 (67.0)		

Table 2 – Means and estimated marginal means of the four groups corrected for age, culture, socio-economic status and level of education
** Note that a higher score represents a worse performance*

The frequencies and mean scores of the formed four groups based on the amount of vascular risk factors, are presented in Table 2. On the Dots Test there was a different sample size due to missing values. There was no normality of distribution, therefore we conducted the non-parametric Kruskal-Wallis H Test twice for both subtests. The assumptions were met. As test variable we filled in the score on the subtest, and the presence/amount of vascular risk factors was the grouping variable.

There were differences in Sun-Moon part B scores between groups that differed in the amount of vascular risk factors, $\chi^2(3) = 64.112$, $p < .001$. Distributions of subtest scores were similar for all groups, as assessed by visual inspection of boxplots and histograms. Performance scores were higher for group 3, than for group 2, than for group 1, than for group 0.

Scores on the Dots Test part B were different for the groups differing in the amount of present vascular risk factors, $\chi^2(3) = 75.064$, $p < .001$. Scores were higher for group 3, than for group 2, than for group 1, than for group 0. Distributions of scores were similar for all groups, as assessed by visual inspection of boxplots.

We conducted a set of six Mann-Whitney U Tests for both subtests to study the contrasts. As presented in Table 3, the comparisons of groups showed significant differences between 0vs1, 0vs2, 0vs3, 1vs2 and 1vs3. Between the groups carrying 2 and 3 vascular risk factors, there was no significant difference between scores on the Sun-Moon Test part B and the Dots Test part B.

Comparison between groups	Sun-Moon Test				Dots Test			
	U	z	p	η^2	U	z	p	η^2
0 – 1	59317	- 4.352	*<.001**		53552	- 5.602	*<.001**	
0 – 2	24039	- 6.901	*<.001**		23180.50	- 6.966	*<.001**	
0 – 3	3683	- 4.680	*<.001**		3157	- 5.162	*<.001**	
1 – 2	23467	- 3.329	*.001**		23788.50	- 2.242	*.025**	
1 – 3	3860.50	- 2.820	*.005**		3503.50	- 3.006	*.003**	
2 – 3	2588.50	- .800	.424		2125	- 1.876	.061	

Table 3 – Post Hoc Tests between the groups after the Kruskal-Wallis Test

A Univariate Analysis of Covariance, ANCOVA was conducted to study potential differences in performance scores of the four groups on the concerned subtests. Performance scores on the subtests were the dependent variables and the amount of vascular risk factors the independent variable. Besides, the possible confounders age, culture, socio-economic status and level of education were added to the analysis as covariates.

Corrected for the confounders, the groups differed significantly on the Sun-Moon test part B, $F(7)=37.537$, $\eta_p^2 = .218$, $p < .001$. The confounders had the following results: age, $F(1)=14.542$, $\eta^2 = .015$; $p < .001$, culture, $F(1)=21.772$, $\eta^2 = .023$, $p < .001$; level of education, $F(1)=53.787$, $\eta^2 =.054$, $p < .001$; socio-economic status, $F(1)=1.345$, $\eta^2 = .001$, $p = .247$. Post hoc analysis was performed with a Bonferroni adjustment, showing only significant differences in scores between group 0vs2 and 1vs2 as presented in Table 4.

On the Dots Test part B the groups differed significantly too when controlling for confounders, $F(7)=68.450$, $\eta_p^2= .341$, $p < .001$. The confounders had the following results: age, $F(1)=24.970$, $\eta^2 = .026$, $p<.001$; culture, $F(1)=41.159$, $\eta^2 = .043$, $p < .001$; level of education, $F(1)=105.087$, $\eta^2 =.102$, $p < .001$; socio-economic status, $F(1)=3.648$, $\eta^2 = .004$, $p = .056$. Post hoc analysis was performed with a Bonferroni adjustment, showing significant differences in scores between 0vs1 and 0vs2 as presented in Table 4.

Comparison between groups	Sun-Moon Test	Dots Test
	p	p
0 – 1	1.000	*.022**
0 – 2	*.001**	*.018**
0 – 3	1.000	1.000
1 – 2	*.017**	1.000
1 – 3	1.000	1.000
2 – 3	1.000	1.000

Table 4 – Group comparisons by amount of risk factors after ANCOVA

§ 3.3 Effect of risk factors

In order to investigate which vascular risk factors are explaining more variance, we conducted a Multiple Regression Analysis. The dependent variable was the score on Sun-Moon Test part B. As independent variables we selected all risk factors named before and the possible confounders which were all together listed as heart- & vessel diseases, diabetes, hypertension, age, gender, socio-economic status, culture, depression and level of education. In the second analysis the dependent variable was the Dots Test part B with the same variables on de independent dimension.

The multiple regression model predicted a statistically significant portion of the variance for the Sun-Moon Test part B, $F(9) = 30.317$, $p < .001$, adj. $R^2 = .225$. The variables diabetes, gender, age, culture, socio-economic status and depression added statistically significantly to the prediction (see Table 5), other variables did not. The multiple regression model predicted statistically significantly for the Dots Test part B, $F(9) = 54.495$, $p < .001$, adj. $R^2 = .347$. The variables diabetes, gender, age, culture, socio-economic status and level of education added statistically significantly to the prediction, as presented in Table 5. Other variables were not statistically significant. Regression coefficients and standard errors are presented in Table 5.

Variable	Sun-Moon Test			Dots Test		
	B	SE	p	B	SE	p
Heart & vessel diseases	.948	1.373	.490	1.600	5.135	.755
Diabetes Non-diabetic	2.731	1.091	*.012**	9.640	4.082	*.018**
Gender Men	3.002	.977	*.002**	9.815	3.652	*.007**
Age 45-65	.262	.068	*.000**	1.396	.255	*.000**
Culture Dutch	-1.555	.310	*.000**	-7.582	1.159	*.000**
Socio-economic status	-.516	.443	.244	-3.219	1.659	.053
Level of education High	-2.047	.292	*.000**	-10.787	1.091	*.000**
Depression	-2.432	1.354	.073	4.539	5.044	.368
Hypertension	1.874	1.373	.490	7.635	4.029	.058

Table 5 – Coefficients of the Multiple Regression Analysis

In order to establish the directions of the associations, we made use of visual inspection of partial plots. Compared to men, females scored higher on the subtests. Divided into three categories, participants aged 76 years or more scored higher than people who fall in the age interval 66-75 years and this group scored higher than the younger age range 45-65 years. For both subtests, the height of the scores is correlated adversely with the categories of education Verhage suggested. Thus, the higher level of education one possesses, the lower the time score on the test.

On the variable culture, there were different directions of differences in scores for both subtests. Considering the Sun-Moon Test the descending order of scores based on culture is as following: Moroccan Berber, Moroccan Arabic, Turkish, Surinamese Creole, Surinamese Hindu followed by Dutch. In contrast, for the Dots Test the order is Moroccan Arabic followed by Moroccan Berber, Turkish, Surinamese Creole, Surinamese Hindu, Dutch.

Discussion

This study was an attempt to find out whether carrying vascular risk factors had effect on the capacity of executive functioning. 976 cognitively healthy participants, out of which 600 carried indeed vascular risk factors, were gathered and tested through subtests of the CCD, which measured the inhibition and cognitive flexibility of the participant.

Comparing the scores of the two groups on inhibition, participants with vascular risk factors responded slower than the participants without vascular risk factors. The significance had a small effect size. On cognitive flexibility too, people with vascular risk factors performed worse, with a nearly medium effect size.

Comparing the groups based on the amount of carried vascular risk factors, on inhibition as well as on cognitive flexibility, groups with 1, 2 or 3 vascular risk factors scored significantly worse than the group without any vascular risk factor. The group with 2 vascular risk factors scored worse compared to the group with just one vascular risk factor. Carrying 3 risk factors compared to just 1 meant a worse score too. In addition, there was no significant difference between the groups with 2 and 3 vascular risk factors.

On other demographic factors the groups with and without vascular risk factors differed significantly too. When corrected for age, culture, level of education and socio-economic status, significant differences in inhibition still remained between the group without and with 2 risk factors, and participants with 1 and 2 vascular risk factors. For the Dots Test part B, after correction there were significant differences between the people without and with 1 risk factor, and participants without and with 2 vascular risk factors.

Out of all vascular risk factors and possible confounders, the variables diabetes, gender, age, culture, socio-economic status added significantly to the prediction of scores on both domains. Specifically for inhibition depression, cognitive flexibility and level of education were further significant predictors. For both concepts, diabetic participants without organ damage scored better compared to diabetic participants with organ damage. Males had better scores than females, younger participants better than elder and people with higher level of education scored better than less educated people. On inhibition, Dutch participants scored the best and Moroccan Berber the worst. On cognitive flexibility, again the Dutch had the best scores while the worst scores were for Moroccan Arabic participants.

§ 4.1 Interpretation and place in literature

Cognitively healthy participants carrying vascular risk factors perform worse on tasks for inhibition and cognitive flexibility, compared to those without vascular risk factors. Besides, the more vascular risk factors one carries, the worse the performance on these executive functioning tasks. However, this does not apply for carrying more than an amount of two vascular risk factors. The inverse relationship between carrying vascular risk factors and the capacity on executive functioning confirms our hypothesis and is in line with the study of O'Brien et al. (2003), which concludes vascular risk factors increase attentional and executive dysfunctions, making it more difficult to complete the two subtests of the CCD accurately.

Conversely to the study of Maillard and colleagues suggesting the effect of vascular risk factors on dementia risk to be cumulative, this study shows that exceeding the amount of 2 risk factors, this difference extinguishes while it seems to be present for up to 2 vascular risk factors (Maillard et al., 2015). This also is in contract to the finding that the risk for dementia increases for having multiple vascular risk factors (Whitmer et al., 2005). A possible explanation could be the fact that the group with 3 vascular risk factors in this study was too small to proof evidence for a correlation.

After correcting for differences in age, culture, level of education and socio-economic status which could be causes of found differences, the effects remained. For inhibition the difference between no vascular risk factors and just 1 risk factor disappeared. The group with 2 vascular risk factors remained different from the group without and the group with just 1 risk factor. A possible explanation is that the scores of participants without and people with 1 risk factor are too close to each other, excluding a significant difference between no risk factor and just one vascular risk factor.

For cognitive flexibility there remained the differences between the group with no vascular risk factor and the group with 1 or 2 risk factors. The fact that there is no significant difference anymore between the group with 1 and the group with 2 vascular risk factors means that the amount of risk factors was not correlated with cognitive flexibility in this sample.

In addition to the variables explaining for both psychometrical domains, for inhibition, depression was important, which is in line with the fact that depressed people have problems with executive functions as inhibition regulation, which depend on the working memory (Harvey et al., 2004). Furthermore, the disrupted selective attention is another indication.

Since scholastic skills lead to experience of practising different tasks and alternating between them, they could improve the cognitive flexibility. Therefore, it is understandable that level of education is correlated with the cognitive flexibility task.

Interestingly, while diabetes is a predictor for the test score, heart and vessel diseases and hypertension were not. Possibly, diabetes already explains a proportion of influence, which is overlapping with the effect of the other two vascular risk factors. In addition, the high amount of coexistence of risk factors in one participant could also be explaining. A bas performance of participant with a heart disease and diabetes for example, could unfairly totally be ascribed to diabetes.

§ 4.2 Strengths and weaknesses

The amount of participants in this study is very large. The analyses have a high power, therefore the results are reliable and should be considered carefully for further implications in clinical practice. As stated before, this study analysed cognitively healthy participants and still found significant differences in performances on executive functioning tasks, depending on amount of vascular impairment. Vascular impairment seems to be a significant risk factor for lower scores on cognitive tests and could be one of the first signs for mild cognitive impairment or dementia. Neuropsychological testing or screening could be a good way to screen for these impairments in an early stage. Early detection could mean better treatment of vascular disease and possibly, as a result, prevent further cognitive impairment.

The developers of the CCD made the test as applicable as possible for participants from multiple ethnicities. This means that the results are adequate and valid measurements representing the level of capacity. Moreover, the CCD is improved after being tested multiple times on the validity and reliability with good results (Goudsmit, 2005). These aspects are very useful to maintain doing further research on the CCD.

We grouped five different components in the term heart and vessel diseases. This study did not take into account the potential differences between carrying specific heart or vessel disease, such as peripheral vascular disease, ischemic heart disease, heart failure, renal failure and stroke. Forming multiple groups for this variable, each representing one specific disease, is a recommendation for future research. This could provide more information about differences specific for each disease.

The fact that hypertension and heart and vessel diseases do not seem to be very explaining for the worse capacity of executive functioning of people with vascular risk factors, should be taken into account formulating further research questions and hypothesis. There should be checked whether there is an overlap in proportion of explained variance by each variable.

§ 4.3 Conclusion

This study shows that people carrying vascular risk factors perform worse on executive functions such as inhibition and cognitive flexibility, compared to people without vascular risk factors. In addition, the more risk factors one carries, the worse the performance is for up to two risk factors. Correcting for differences in demographic characteristics between the groups, on inhibition scores carrying vascular risk factors is leading to worse inhibition scores only at 2 vascular risk factors. On a cognitive flexibility task, carrying vascular risk factors leads to worse performance, with no further effects of the amount of existing vascular risk factors.

Important to take into account conducting future research is that differences in scores could be explained simply based on gender, age and level of education. These factors do not cause the totality of differences between performances of participants with and without vascular risk factors. Another crucial factor to consider is depression. The study shows depressed people to perform worse since their level of executive functioning and selective attention is not as high as before the depression. Future research has to include an instrument to measure the level of depression in order to avoid unfair conclusions about the source of executive functioning and therefore about the presence of dementia.

Out of the vascular risk factors included in this study, diabetes seems to be the biggest predictor, possibly including the effect of heart and vessel diseases and hypertension. Analyzing whether the effect of hypertension and heart and vessel diseases are embedded in the proportion of influence diabetes already explains, will be a qualitative addition to the results of this study. Moreover, for future research, expanding the five heart and vessel diseases would be an improvement in order to analyse the effect of each disease individually. Conclusively, the effects of heart and vessel diseases have to be separated from the effect of diabetes.

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I am glad this masterthesis is here to read and at the same time I am convinced that it can place a piece of information in the current literature. Therefore, I am highly satisfied.

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Attachments