Supplementary materials to

Difference between Okinawa and Dutch older adults in prefrontal brain activation

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Methods

NIRS acquisition

Table S1 Source-Detector Locations and Associated Anatomical Regions

	Left hemisphere		Anatomical regions[a]	Right hemisphere	
	Optode	10/20 System		Optode	10/20 System
Sources	S1	Fp1	Superior frontal gyrus (rostral)	S5	Fp2
	S2	F7	Inferior frontal gyrus (rostral)	S6	F8
	S3	AFF5h	-	S7	AFF6h
	S4	Between AF3 and Fp1	-	S8	Between AF4 and Fp2
Detectors	D1	AF7	Middle frontal gyrus	D5	AF8
	D2	F5	Middle frontal gyrus	D6	F6
	D3	AF3	Superior frontal gyrus	D7	AF4
	D4	Between F7 and F5	-	D8	Between F8 and F6

Note. [a] Source: Koessler and associates (2009); Homan, Herman, and Purdy (1987).

Table S2. Source-Detector locations

Channel	Source	Detector	Distance [mm]
1	1	1	30.39
2	1	3	31.59
3	2	1	30.49
4	2	2	30.76
5	2	4	15.40
6	3	1	20.32
7	3	2	33.15
8	3	3	20.17
9	3	4	36.22
10	4	1	32.93
11	4	3	14.11
12	5	5	29.82
13	5	7	31.42
14	6	5	30.00
15	6	6	30.55
16	6	8	15.30
17	7	5	20.10
18	7	6	32.62
19	7	7	19.96
20	7	8	35.66
21	8	5	31.33
22	8	7	14.69

TableS2. Channels between the sources and detectors. The left column lists the channel number. The second and the third columns from the left list the source and detectors respectively. The channel refers to the measurements between the respective source and detector. The fourth column lists distances between sources and detectors in mm.

Educational level adjustment

Number of years and completed level of education were self-reported by participants. Education is an important factor that can affect cognitive functions. There are differences in Dutch and Japanese educational system. For instance, Dutch primary education (8-year period) is intended for children in the age group of 4 to 12 and is compulsory for children from the age of 5. Then, they need to spend 5 years in high school (in total 13 years) to receive a Dutch HAVO diploma or high school certificate. However, the Japanese compulsory education is comprised of primary education (6-year period) from

6 years old and lower secondary education (3-year period), lasting a total of 9 years. They need to spend another three years in high school, which sums up to twelve years of education in order to receive a Japanese High School Certificate of Graduation.

We adjusted Japanese educational system to Dutch educational system in order to match the educational level in both groups. This was done according to the different reports by Nuffic (8), a Dutch organization for the internationalization of education, and the Dutch Qualification Framework (NLQF) (Table S3). To classify the level of education system, the Dutch Verhage scale was used (9). The seven categories were merged into three ordinal categories: low educational level (Verhage 1 until 4), middle educational level (Verhage 5), and high educational level (Verhage 6 and 7; Table S3). Table S4 shows the numbers for each group per educational category.

Table S3. Description of educational levels

Level		Verhage category[a]	NLQF[b]/EQF[c]	The Netherlands	Japan
Low	1	less than primary school/primary school not finished	Entry Level	Basic Education (Primary)	Primary School
	2	Finished primary school	1	MBO1	Junior High school
	3	Completed primary school and further education less than 2 years	2	MBO 2/ vmbo kb, gl, tl	
	4	lower than MULO/MAVO level, e.g. LTS, LEAO, LHNO	3	MBO 3	Upper Secondary Vocational school
Middle	5	MULO/MAVO/MEAO diploma	4	Havo/ Vwo/ Vavo-Havo	High School certificate
High	6	HAVO/VWO/HEAO/HBS/HBO diploma	5	Associate Degree	Diploma at a professional level/Junior college/College of technology
	7	university diploma	6	Bachelor Degree	Advanced Diploma/Bachelor's degree
			7	Master Degree	Master Degree
			8	Doctorate	Doctorate

[a] Adapted from Verhage (1964). [b] Dutch Qualification Framework. [c] European Qualifications Framework

Table S4. Participants' distribution in each educational level

Tests	Total No.		Educational Level (n)					
	Groningen	Okinawa	High		Middle		Low	
			Groningen	Okinawa	Groningen	Okinawa	Groningen	Okinawa
Verbal Fluency	24	37	23	32	0	0	1	5
n-back	38	37	36	32	1	0	1	5

Conversion from optical density to Hb and HbO levels

The absorption data were converted into concentration data using the modified Beer-Lambert Law (mBLL): $OD_\lambda = \left(\varepsilon^{\lambda}_{HbO_2}[HbO_2] + \varepsilon^{\lambda}_{HbR}[HbR]\right) \cdot DPF \cdot d + G$ (Zhao et al., 2017). Here, OD denotes optical density or absorption, λ the wavelength of the light, ε denotes the extinction coefficient, the d in the formula denotes the distance between the source and the detector, while G represents loss of light intensity due to scattering. We used the absorption spectra provided by Gratzer and associates (Gratzer and Kollias, 1999) to determine the ε of HbO and Hb for each wavelength. DPF is the differential pathlength factor and the current study used the DPFs provided by Essenpreis and colleague (Essenpreis et al., 1993). Eventually, the changes of concentration values were calculated.

Additional measures

A number of tests and questionnaires were used to characterize the groups in terms of cognitive status, social functioning and physical activity. The neuropsychological tests include: (a) Digit Span is a subtest included in both the Wechsler Memory Scale-III (WSM-III) and the Wechsler Adult Intelligence Scale (WAIS) and consists of two versions (10). The Digits Forward (Forwards) is considered as a simple memory span test, while the Digits Backward (Backwards) is a more complex test with an executive component (11); (b) Symbol Digit Modalities Test (SDMT) was originally developed to identify neuropsychological impairments and may assess divided attention, visual scanning, and motor speed (12,13); (c) Trail Making Test (TMT) consists of two parts where part A (TMT-A) assesses attention and speed, while part B (TMT-B) also involves divided attention and mental flexibility ; (d) Stroop Test was initially developed by Stroop (14) and is a measure of selective attention and cognitive flexibility; and (e) Mini Mental State Examination (MMSE) was developed by Folstein, and McHugh (1975) and has been a popular measure to screen cognitive impairments especially in older adults (13,15). In addition, we administered other screening measures, including (f) Edinburgh Handedness Inventory is a 10-item questionnaire assessing handedness which was developed by Oldfield (16); (g) Social Functioning Scale (SFS) assesses seven areas that are crucial for social competence, namely social engagement/withdrawal, interpersonal behavior, prosocial activities, recreation, competence for independence, the performance of independence, and employment or occupation (17); and (h) Physical Activity Scale for the Elderly (PASE) assesses physical activities commonly engaged in by older persons and can be administered in person or via telecommunication (18).

Results

Demographics

Table S5 summarizes all the demographics and behavioral data. The two groups were matched for gender (Table S5). There was difference in age of 2.9 years which was statistically significant. However, all participant were between 64 and 80 (Groningen participants were up to 77 years old), thus belonging to the same age range. Educational level (according to the classification in Table S3) did not differ significantly between groups. In addition, The groups did not differ in psychopathological measures (i.e., MMSE and SFS) but, as expected, there was a difference in the physical activities as measured by PASE.

Regarding the screening measures, test performance was generally comparable between the two groups. Nevertheless, it is essential to note that some test performances are not comparable due to different standard versions of the screening tests used. The Groningen site utilized the forward digit span test from the WAIS-R which starts with a 3-digit number, while the Okinawan site used another version from the WAIS-III which starts with a 2-digit number. For the TMT, the Japanese version was administered on a horizontal A4 paper, while the Dutch version was presented on a vertical A4 paper. The two versions also differ in terms of the constellation pattern of numbers and letters. Additionally, the beginning and end points were pointed out to Dutch participants, while this procedure was missing in the Okinawan group. Lastly, the Japanese version of the Stroop test has only 48 items in each part, while the Dutch one has 100 items.

Performance on the verbal fluency and n-back tasks

The verbal fluency results showed that participants named different on number of words all four conditions (Table S5). The Okinawan elderly named (M=7.18, SD=3.07) words with the letter "A", while Dutch elderly named (M=11.62, SD=3.22). Similarly, in the "K" condition, the Okinawan elderly named (M=9.29, SD=3.14) words while the Dutch elderly named (M=14.58, SD=4.89). Furthermore, in the semantic condition "animals", the Okinawan elderly named (M=15.25, SD=2.97) and the Dutch elderly (M=21.79, SD=5.26),. And lastly, in the semantic condition "occupations", the Okinawan elderly named (M=10.64, SD=2.64) words which is less compared to the Dutch elderly (M=18.83, SD=5.89).

However, as explained in more detail in the Discussion, the Dutch participants had a clear "advantage" in the phonemic conditions. Because of language differences, they had a bigger pool of words to choose from compared to the Okinawan participants. Furthermore, normative data show that the mean words recalled by the Okinawan group fall within the normal age range for both the letter and category condition (19). Normative data for the Dutch population shows that the values of the categories "animals" and "occupations" fall within a normal range as well (20). Unfortunately, there is no normative data for the Dutch population for the letter conditions "A" and "K" for duration of 1 minute (the norms are given for 3 letters consecutively -total duration of 3 minutes). Thus, the performance on the VF task of both groups falls within norms.

Table S5 Verbal Fluency Task Results in Groningen and Okinawa Groups

Variable	Mean (SD)	
	Groningen (n=24)	Okinawa (n=37)
Phonemic Letter "A"	11.62 (3.22)	7.18 (3.07)
Phonemic Letter "K"	14.58 (4.89)	9.29 (3.14)
Semantic "Animals"	21.79 (5.26)	15.25 (2.97)
Semantic "Occupations"	18.83 (5.89)	10.64 (2.64)

The result of n-back tests is shown in Table S6. The two groups had same accuracy. They differed in terms of proportions of true negative (U=303.5, p-value<0.001) and false positive detection (U=303.5, p-value<0.001) with Dutch participants demonstrated better performance. Although significant, these differences only translate to roughly 2 to 3 trials which are not practically meaningful.

Further, the Dutch group also completed more trials on average than the Okinawa counterpart (t (73)=3.12, p-value<0.01).

Table S6. N-back task performance in Groningen and Okinawa groups

Variable	Median (SD)		Significance
	Groningen (n=38)	Okinawa (n=37)	Groningen vs. Okinawa
Accuracy	0.79 (0.09)	0.74 (0.14)	U= 559 (0.12)
True negative	0.91 (0.06)	0.81 (0.11)	U=303.5 (p<0.001)
False positive	0.08 (0.06)	0.18 (0.11)	U=303.5 (p<0.001)
Miss	0.2 (0.09)	0.25 (0.14)	U=559 (0.12)
Number of trials	25.15 (3.02)	22.82 (3.41)	t (73)=3.12 (0.003)

HbO levels after including handedness, age and PASE:

Supplementary Figures:

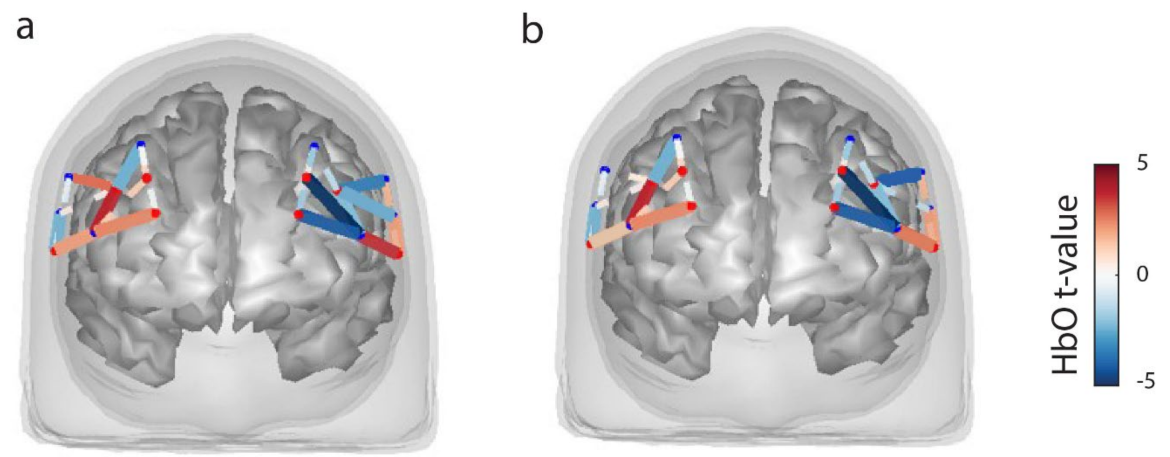

Figure S1 a. Verbal Fluency Level Contrasts for HbO after the correction for education – three left-handed participants were excluded. Only significant channels (p_{FDR}<0.05) are shown. For HbO contrasts, positive t-values (red) correspond to relatively larger activity in the

Groningen group as compared to Okinawa group, and negative t-values (blue) correspond to larger activity for the Okinawa group. **b.** Same as a. after correction for PASE and age.

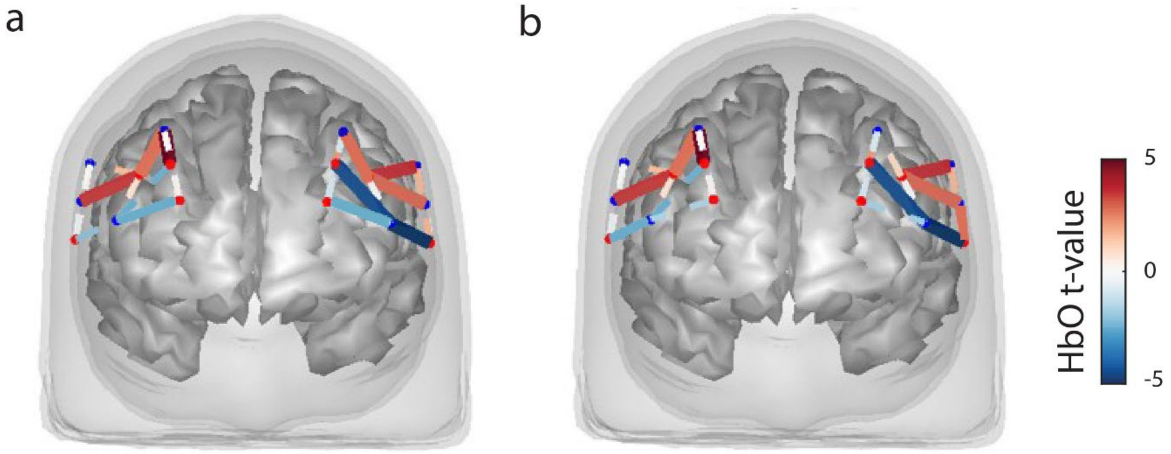

Figure S2 a. N-back level contrasts for HbO after the correction for education – three left-handed participants were excluded. Only significant channels (p_{FDR}<0.05) are shown. For HbO contrasts, positive t-values (red) correspond to relatively larger activity in the Groningen group as compared to Okinawa group, and negative t-values (blue) correspond to larger activity for the Okinawa group. **b.** Same as a. after correction for PASE and age.

Discussion

Verbal fluency is a commonly used neuropsychological task that engages not only language processing, but also executive functioning such as monitoring (to keep track of which words were named) and inhibition (to avoid repeating the same words) (7,21). Previous fMRI studies found that verbal fluency activates consistently and most robustly inferior and middle frontal gyri mainly in the left but also in the right hemisphere, in addition to the anterior cingulate, bilateral insulae and left superior frontal gyri (21-25). Additionally, fNIRS studies that measured frontal cortical HbO levels found robust activation of same brain regions (26-28).

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