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Effects of Basal Heart Rate on Memory with Interference among 832 Unselected Hypertensive Subjects from General Population

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Abstract

High resting heart rate (HR) is independently associated with cardiovascular disease risk. Few studies took into consideration the possible effects of HR on memory. Therefore, memory with interference (MI) at 10 (MI10) and at 30 (MI30) seconds was chosen to test this hypothesis and the role of resting HR on an MI in hypertensive subjects was analysed. MI was chosen because it's strictly connected with everyday life. Among 832 hypertensive subjects aged 18 - 88 years living in North East Italy recruited in the frame of the Growing Old with Less Disease Enhancing Neurofunctions (GOLDEN) study, we performed an association analysis, accounting for potential confounders, to identify the possible determinants of MI. Both in univariate and multivariate regression analysis, MI10 and MI30 were indirectly associated to basal HR: the higher the HR, the lower the MI. Years of schooling were associated directly and age inversely to both MI10 and MI30. A progressive trend towards reduction of the score was particularly evident for MI30, with two evident cut-off values (equal to 65 and to 73 bpm, respectively). In the case of MI10, 60 bpm was the upper limit of the best performance. Furthermore, being in the first three quartiles rather than in the fourth quartile of MI30 was significantly lower. High HR should be counted among the risk factors or indicators of low memory. The inverse association between high HR and low memory is not ineluctable as it can be prevented by education.

Keywords

Heart Rate, Hypertension, Cognition, Memory

*These three authors contributed to the manuscript equally.

1. Introduction

Many papers from different research groups have shown that high heart rate (HR) is independently associated with cardiovascular disease risk. Research on this field is centred on the cardiovascular system, high HR leading to worse mortality and morbidity (Palatini, 2017; Palatini & Julius, 2014; Palatini et al., 1999, 2013, 2016, 2017, 2018) and being also associated to metabolic risk (Palatini, 2013; Palatini et al., 1997).

To our knowledge, the question of whether HR influences cognition has been scarcely investigated in hypertensive subjects. A limited number of papers in this field took into account HR variability but not HR *per se* (Liu et al., 2013). In different analyses, higher resting HR variability predicted enhanced memory inhibition (Gillie et al., 2014), and lower HR variability was associated with higher risk of future functional decline in older adults (Ogliari et al., 2015).

In the present epidemiological analysis, we took into consideration the possible effect of basal (resting) HR on memory. Memory with interference (MI) was chosen to test this hypothesis. The tests of MI at 10 and 30 seconds (MI10 and MI30) (Mondini et al., 2003) are of special relevance because they reproduce in laboratory the conditions of everyday life, where important inputs have to be understood and durably remembered while interfering stimuli not directly correlated with the main information arrive from usual interfering activities. MI is how much more similar, in laboratory and in epidemiology, to this natural situation. Stable memorization of information despite undercurrent distractions is of paramount importance because it contributes to build the autobiographic memory which is the basis of the egoic (subjective) consciousness and of the feeling of self. Many factors influence MI (mainly age and education), but basal HR has never been considered one of its determinants.

2. Methods

2.1. Cohort

Eight hundred and thirty-two hypertensive subjects (427 men and 405 women) aged 18 - 88 years (57.4 ± 12.2 years), living in North East Italy in a semi-rural area of about 504 km^2 in the Leogra and Illasi valleys and sharing a homogeneous lifestyle, were studied in 2012-2018 in the frame of the Growing Old with Less Disease Enhancing Neurofunctions (GOLDEN) study. The protocol of the study was extensively described elsewhere (Casiglia et al., 2005, 2012, 2013a, 2013b) and is here briefly summarized.

All subjects aged ≥ 18 years living in that area were contacted by letter and then, when necessary, by phone from the registry office lists. The attendance rate was 73% and the subjects analyzed in the present paper represent the first 832 hypertensive recruited. No significant social or demographic differences were detected between the subjects included in the study and the other subjects belonging to the same population object of the ongoing study (data not shown).

The investigation conformed to the Declaration of Helsinki and was approved

by the local Ethics Committees of the University of Padua and Verona (Italy). Each subject was previously and personally informed about the aim and the meaning of the study, and was free to ask all the questions they felt necessary to have a full comprehension of it. All the participants gave a valid written informed consent and signed a form approved by the Ethics Committee according to Italian law 675/1996 and to the law of the Veneto Region 34/2007.

2.2. General Items

At a clinical visit, all subjects underwent a detailed Rose's questionnaire concerning lifestyle, smoking and drinking habits, physical activity, quality of life, medication, and personal and familial medical history.

Education was defined as number of years of schooling based on the highest educational qualification achieved.

Height (in m) and weight (in kg) were recorded without shoes with the subjects wearing light indoor clothing. Body mass index was calculated in (kg/m^2) as body weight divided by squared height.

HR was taken from basal electrocardiographic RR intervals in a range of 15-min rest. Systolic and diastolic (Korotkoff phase 5) blood pressure was taken in triplicate at 10-min intervals in the supine position by trained doctors using an Omron 705 IT device (Omron Europe, Hoofddorp, Netheralnds). To minimize white-coat effects, the average of the last two measurements (in mmHg) was taken into consideration. The label of arterial hypertension (Mancia et al., 2013) required systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or history of hypertension or appropriate antihypertensive treatment or hospital discharge with diagnosis-related group (DRG) 401 - 404 or 40,200 - 40,290 or 40,300 - 40,391. Treatment of hypertension was ascertained by hospital discharge files, general practitioners' files and asking subjects and double-checked.

A 138-item food frequency detailed questionnaire previously validated for the Mediterranean diet was administered at the initial screening. The reported frequencies of food intake per week were converted to number of intakes per day and multiplied by the weight of the portion size indicated. Each food was then resolved into its chemical components according to composition tables conceived for Italian food, where data were expressed as percent of food actually consumed after eliminating the scrap. We therefore calculated fish, lipidic and glucidic intake (g/day). This method was already used and validated by our group. Daily caffeine intake (Casiglia et al., 1992, 2018; Stolarz et al., 2004) was calculated from the formula: $\text{caffeine}_{\text{mmol/day}} = [\text{coffee}_{\text{cups/day}} \times 0.412 + \text{tea}_{\text{cups/day}} \times 0.214 + \text{cola}_{\text{drinks/day}} \times 0.082 + \text{chocolate}_{\text{portions/day}} \times 0.081]$ and ethanol intake from: $\text{ethanol}_{\text{g/day}} = [(\text{wine}_{\text{ml/day}} \times 0.12 + \text{beer}_{\text{ml/day}} \times 0.05 + \text{aperitifs}_{\text{ml/day}} \times 0.11 + \text{liquors}_{\text{ml/day}} \times 0.40) \times 0.80]$ (Casiglia et al., 2018).

Blood glucose, serum uric acid and low-density-lipoprotein (LDL) cholesterol were measured at fast by automated standard methods.

2.3. MI10 and MI30

Participants were seen by a neuropsychologist at an *ad hoc* hospital unit. They were requested to recall a consonant trigram after an interval delay during which they had to count backward starting from a random number suggested by the examiner immediately after the trigram (Mondini et al., 2003). More in details, each subject was individually invited to observe three cardboards with 3 alphabetic letters each (**Figure 1**). Subject had to read the letter aloud and try to memorize them. Then the cardboards were covered and the subject was asked to count by twos for 10 seconds (MI10) starting from a number randomly chosen by the researcher. After these 10 seconds, subject had to repeat the trigrams, and the number of correct letters was recorded and used as score. If this test was completed with a score > 0, it was repeated with different trigrams asking the participant to count by twos for 30 seconds (MI30) and to repeat the trigrams, recording the number of letters correctly repeated. The aim of those two tests is to ascertain the ability of subjects to remember short-term information while they were distracted immediately after the memorization by external events of different duration, as it happens in everyday life (Mondini et al., 2003).

2.4. Statistical Analysis

For database management and statistical analysis, the Statistical Analysis System (SAS) software version 9.3 (SAS Institute, Cary, USA) was used. The null hypothesis was always rejected when p value was <0.05. *A priori* power analysis showed that 200 subjects per cell were sufficient to show effects (power 0.90, test level 0.10 for β error and 0.05 for α error), assuming a putative difference of 1 point score in MI10 or MI30 between the highest and lowest HR (**Table 1**). This difference was chosen a priori based on preliminary tests of our laboratory, as no data on the effects of HR on MI in the general population exist. Our 832 subjects also appeared adequate after stratification into quartiles.

Continuous variables were expressed as mean and standard deviation and compared with analysis of variance and the *post hoc* Bonferroni's correction.

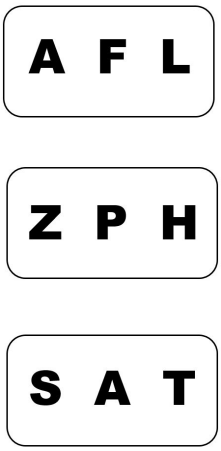

Figure 1. The trigrams used to study the memory with interference.

Table 1. Power analysis for power estimates for sample size concerning memory with interference at 10 and at 30 seconds. I Q, II Q, III Q, IV Q: first, second, third and fourth quartiles.

Test	Type 1 Error (α)	Power (β)	Mean HR (I Q)	Mean HR (II 2)	Mean HR (III 3)	Mean HR (IV 4)	Sample size
MI10	0.05	80%	5.7 ± 2.7	5.3 ± 2.8	5.5 ± 2.7	5.2 ± 2.9	832
MI30	0.05	80%	4.0 ± 3.3	4.0 ± 3.3	4.0 ± 3.3	3.5 ± 3.1	832

Categorical variables were expressed as percent rates and compared with the Pearson's χ^2 test.

Two multivariate regression analysis (REGLIN), having MI10 and MI30 respectively as dependent variables, were used to identify the possible determinants of MI. Sex, age, schooling, systolic and diastolic blood pressure, resting HR, ethanol and caffeine intake, cigarettes, blood glucose, serum LDL cholesterol and uric acid, fish, lipids and glucose intake, and treatment of hypertension, logarithmized when proper, were considered as possible confounders.

Increasing quartiles of HR were created. Analysis of covariance adjusted for the above mentioned confounders was first used to check for differences in continuous variables between quartiles of HR. To this purpose, p for trend was shown.

The first three quartile of HR were also cumulated together and played in a multiple regression having MI10 and MI30 respectively as dependent variable adjusted for the same confounders, in order to calculate the hazard ratio to be in the fourth quartile.

In sensitivity analysis, to explore the reverse causality, HR was used in REGLIN as dependent variable and MI10 e MI30, respectively as independent covariables adjusted for the same confounders.

3. Results

3.1. Descriptive Statistics

The general characteristics of the cohort are summarized in Table 2, also showing stratification by quartiles of HR. Across quartile of HR, there is a progressive increase of systolic and diastolic blood pressure and serum blood glucose. MI10 score was in average 5.43 ± 2.79 (range 0 - 9, 95% CI 5.24 - 6.62) and MI30 score 3.85 ± 3.25 (range 0 - 9, 95% CI 3.63 - 4.07).

3.2. Multivariate Analysis of MI as Continuous Variable

Multivariate REGLIN showed that both MI10 and MI30 were inversely associated to HR (Table 3): the lower the HR, the greater the MI.

Years of schooling were associated directly and age inversely to both MI10 and MI30 (Table 3), although unable to nullify the HR ↔ MI relationship. No other determinants or confounders were identified.

In sensitivity analysis, inversing the REGLIN model (i.e. using MI10 or MI30

Table 2. General characteristics of the study population (n = 832), also showing stratification by quartiles of resting heart rate.

		Quartiles of resting heart rate				
	Whole cohort (n = 832)	**I quartile (n = 208)**	**II quartile (n = 208)**	**III quartile (n = 208)**	**IV quartile (n = 208)**	***p*-value for trend**
Continuous variables						
Resting heart rate (bpm)	67.1 ± 10.6	55.1 ± 4.4	62.6 ± 1.8	69.8 ± 2.2	81.0 ± 7.6	<0.0001
Age (years)	57.4 ± 12.3	62.4 ± 15.2	61.6 ± 13.0	61.9 ± 15.8	62.1 ± 15.5	0.96
Schooling (years)	8.3 ± 3.5	8.5 ± 3.9	7.9 ± 3.3	8.3 ± 3.3	7.9 ± 3.2	0.18
Systolic BP (mmHg)[§]	153.6 ± 19.9	151.5 ± 17.8	151.3 ± 20.1	153.8 ± 20.5	157.7 ± 20.5	<0.01
Diastolic BP (mmHg)[§]	89.7 ± 9.2	87.4 ± 8.2	88.9 ± 9.5	91.1 ± 9.2	91.3 ± 9.3	<0.0001
Body mass index (kg/m^2)*	27.3 ± 4.4	27.0 ± 4.0	27.5 ± 4.7	27.6 ± 4.9	26.8 ± 3.8	0.16
Cigarettes/day in smokers	12.3 [10.3 - 13.6]	11.6 [8.6 - 14.5]	10.5 [7.0 - 14.2]	13.6 [10.4 - 16.8]	12.2 [8.4 - 16.0]	0.58
Ethanol intake (g/day)	47.2 [44.2 - 50.3]	47.9 [41.7 - 54.1]	47.4 [41.9 - 53.0]	45.6 [39.8 - 51.4]	47.9 [41.0 - 54.7]	0.95
Caffeine intake (mmol/day)[Δ]	1.00 ± 0.68	1.02 ± 0.70	1.04 ± 0.66	0.90 ± 0.63	1.03 ± 0.70	0.11
Serum glucose (mmol/l)	5.41 ± 1.03	5.23 ± 0.78	5.40 ± 1.07	5.44 ± 1.03	5.58 ± 1.17	<0.01
Serum uric acid (μmol/l)	305.2 ± 78.0	304.4 ± 72.8	307.6 ± 79.9	297.7 ± 81.3	311.2 ± 80.7	0.33
LDL serum cholesterol (mmol/l)	3.71 ± 0.93	3.67 ± 0.90	3.79 ± 0.92	3.68 ± 0.93	3.72 ± 0.97	0.57
Fish intake (g/week)	100.4 ± 115.3	105.3 ± 109.2	109.0 ± 122.4	98.5 ± 132.0	89.0 ± 94.8	0.31
Glucose intake (g/week)	906.7 ± 380.7	914.1 ± 393.5	897.0 ± 408.0	905.4 ± 368.1	910.3 ± 354.6	0.99
Lipid intake (g/week)	548.1 ± 256.2	575.7 ± 261.3	554.8 ± 246.7	525.5 ± 252.5	536.5 ± 263.0	0.26
Categorical variables						
Males, n (%)	427 (51.3)	125 (60.1)	116 (56.0)	98 (47.1)	88 (42.3)	<0.0001
Treatment of HT, n (%)	367 (44.2)	84 (40.4)	91 (44.0)	97 (46.6)	95 (45.7)	0.59
Smokers, n (%)	98 (11.2)	26 (12.5)	26 (12.5)	26 (12.5)	20 (9.6)	0.73
Drinkers, n (%)	525 (63.2)	140 (67.3)	143 (69.1)	120 (57.7)	122 (58.7)	0.03
Diabetics, n (%)	50 (6.0)	6 (2.9)	11 (5.3)	15 (7.2)	18 (8.7)	0.08

Number of subjects in brackets. Differences between groups analyzed by analysis of variance followed by Bonferroni's tests. [§]Average of two blood pressure readings obtained at clinic. *The body mass index is weight in kilograms divided by the square of the height in meters. [Δ]To convert values for caffeine intake to milligrams per day, multiple by 194.21. Abbreviations: BP, arterial blood pressure; LDL, low-density-lipoprotein; HT, arterial hypertension.

Table 3. Determinants of the tests of memory with interference at 10 seconds and at 30 seconds.

Variables	**Coefficient (standard error)**	**Standard coefficient**	***p*-value**
Test of memory with interference at 10 seconds			
		Determinants	
Resting heart rate (bpm)	−1.7517 (0.6651)	−0.0949	<0.01
Age (years)	−2.9522 (0.5713)	−2.2640	<0.0001
Schooling (years)	2.2595 (0.3204)	0.3213	<0.0001
		Possible confounders	
Sex (0 = women, 1 = men)	−0.4055 (0.2590)	−0.0697	0.12

Continued

Systolic BP (mmHg)	−1.7567 (0.9799)	−0.0820	0.07
Diastolic BP (mmHg)	1.6205 (1.1245)	0.0605	0.15
Serum LDL-cholesterol (mmol/l)	−0.2014 (0.4403)	−0.0171	0.65
Blood glucose (mmol/l)	−0.3455 (0.6655)	−0.0203	0.61
Serum uric acid (μmol/l)	0.3535 (0.4585)	0.0310	0.44
Caffeine intake (mmol/day)	0.0011 (0.0008)	0.0471	0.19
Ethanol intake (g/day)	0.0010 (0.0030)	0.0131	0.74
Fish intake (g/week)	−0.0005 (0.0008)	−0.0215	0.55
Lipid intake (g/week)	0.0002 (0.0004)	0.0144	0.70
Glucose intake (g/week)	0.0005 (0.0003)	0.0612	0.12
Treatment HT (0 = no, 1 = yes)	−0.1987 (0.2305)	−0.0341	0.39
Smoking (cigarettes/day)	0.0084 (0.0225)	0.0134	0.71
Test of memory with interference at 30 seconds			
	Determinants		
Resting heart rate (bpm)	−1.7241 (0.6880)	−0.0819	0.012
Age (years)	−4.7657 (0.5824)	−0.3798	<0.0001
Schooling (years)	2.4628 (0.3372)	0.3104	<0.0001
	Possible confounders		
Sex (0 = women, 1 = men)	−0.0890 (0.2702)	−0.0135	−0.74
Systolic BP (mmHg)	−1.8652 (1.0155)	−0.0764	0.07
Diastolic BP (mmHg)	0.6606 (1.1664)	0.0215	0.57
Serum LDL-cholesterol (mmol/l)	−0.5182 (0.4473)	−0.0391	0.25
Blood glucose (mmol/l)	−0.7352 (0.6778)	−0.0383	0.28
Serum uric acid (μmol/l)	−0.0692 (0.4746	−0.0054	0.28
Caffeine intake (mmol/day)	0.0004 (0.0008)	0.0144	0.66
Ethanol intake (g/day)	−0.0018 (0.0031)	−0.0211	0.56
Fish intake (g/week)	−0.0002 (0.0008)	−0.0057	0.86
Lipid intake (g/week)	0.0003 (0.0004)	0.0268	0.43
Glucose intake (g/week)	−0.0003 (0.0003)	−0.0324	0.38
Treatment of HT (0 = no, 1 = yes)	0.0892 (0.2351)	0.0134	0.70
Smoking (cigarettes/day)	−0.0004 (0.0008)	−0.0539	0.10

MI30 and MI30, respectively, are the dependent variables. Multivariate regression analysis adjusted for plausible biological confounders. Abbreviations as in Table 2.

as dependent variables and HR as an independent covariable), memory did not result to be a determinant of HR: in fact, HR was only determined by sex (coefficient −0.050, standard error, SE, 0.017, standard coefficient 0.588, $p = 0.003$), by diastolic blood pressure (coefficient 0.295, SE 0.073, standard coefficient 0.693 $p < 0.001$) and by serum blood glucose (coefficient 0.110, SE 0.043, standard coef-

ficient 0.786, $p < 0.01$), while MI30 and MI10 were rejected from the model.

3.3. Univariate and Multivariate Analysis of Quartiles of MI

After dividing HR into 4 quartiles of 208 subjects each and comparing them with analysis of covariance adjusted for schooling and age, both MI10 and MI30 were significantly greater in the first quartile than in the fourth (Figure 2).

MI30 was also greater in the first two quartiles cumulated together than in the forth, while the difference between the first three quartiles cumulated together and the forth was near to statistical significance although not sufficient to exclude the null hypothesis ($p = 0.053$) (Figure 2).

For MI30, the between-quartile boundaries were 60 bpm from the I and the II, 65 bpm from the II and the III, and 73 bpm from the III and the IV. It appeared that 60 bpm was a clear cut-off value associated to significant change in MI10 (Figure 2): when this cut-off was used as a factor in analysis of covariance, it

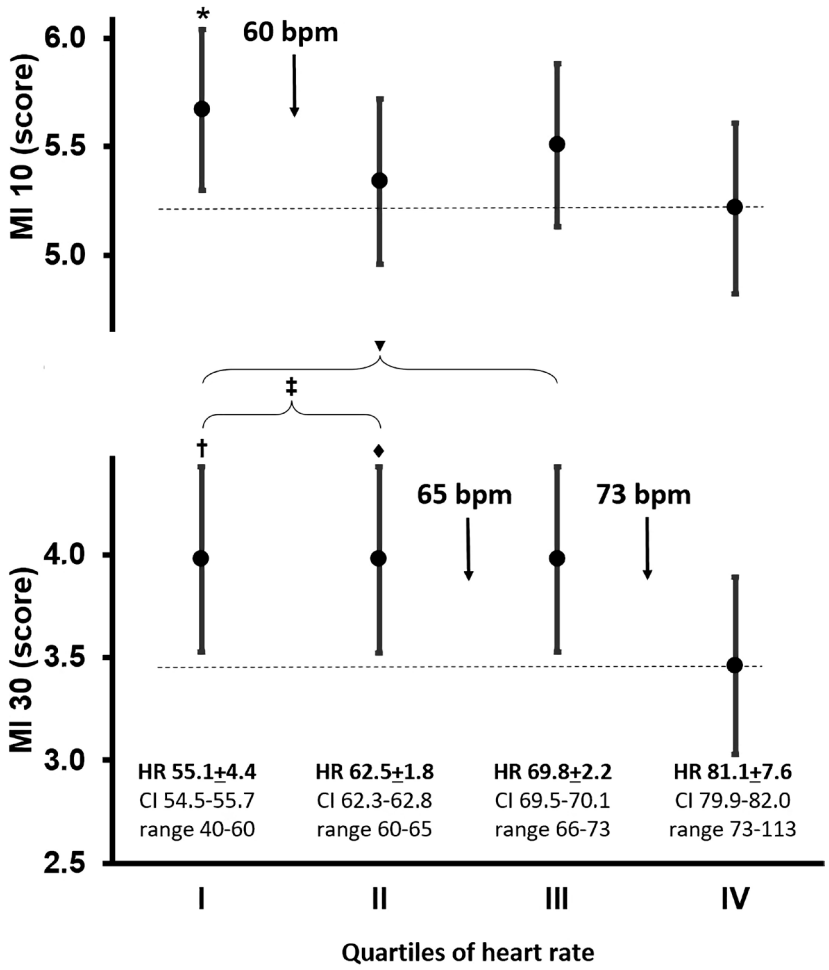

Figure 2. Scores of memory with interference at 10 seconds (MI10) and at 30 seconds (MI30) in Y-axis, by quartiles of heart rate (n = 208 each) in X-asis. ANCOVA vs. IV quartile. The analysis was adjusted for age and schooling, being therefore independent of these items. Explanations of symbols: $^{*}p = 0.03$ (F = 4.71), $^{\dagger}p = 0.005$ (F = 3.73), $^{\ddagger}p = 0.022$ (F = 5.28), $^{\blacktriangledown}p = 0.0053$ (F = 3.75).

definitely divided lower and higher values of MI10 scores (F = 5.79, $p = 0.016$). Analogously, 73 bpm clearly divided lower and higher values of MI30 scores (F = 4.17, $p = 0.041$).

When the fourth quartile was used as independent variable in adjusted multivariate REGLIN, the hazard ratio of being in the first three quartiles rather than in the IV was 0.560 (95% confidence intervals 0.996 - 0.358; $p = 0.047$) for MI30, while the results for MI10 were not significant (hazard ratio 0.748, 95% confidence intervals 0.485 - 1.542, $p = 0.2$).

4. Discussion

4.1. HR as an Inverse Determinant of Cognition

Both the univariate and multivariate analyses demonstrate that MI is indirectly associated to basal HR: the higher the HR, the lower the MI. A progressive trend towards reduction of the score was particularly evident for MI30, with values of HR equal to 65 and 73 bpm as cutoff values between quartiles. In the case of MI10, 60 bpm was the upper limit of the best performance. Furthermore, at multivariate REGLIN, the risk of being in the first three rather than in the IV quartile of MI30 was significantly lower. The symmetrical hypothesis that MI inversely determines HR was excluded by the fact that no significant association was found between these two items when HR was used as dependent variable.

4.2. An Attempt to Explain the Association

The data showed herein simply indicate that, as regards everyday memory, it is better to have lower than higher HR values. The reasons for this evidence go beyond the instruments available to epidemiologists and can only be an object of speculation. High blood pressure (a factor that notoriously tends to decrease the cognitive abilities) was not accepted in the multivariate models and therefore cannot be singled out to explain the phenomenon. A link between HR and memory in the frame of an echogenetic context (Stolarz et al., 2004) cannot be excluded but is far to be demonstrated. The hypothesis that high-HR subjects are sympathetically hyperstimulated and therefore less able to focus attention on stimuli and concepts precluding optimal memorization must be rejected, as it is known that arousal experienced during the exposure to an event able to enhance the release of norephinephrine and epinephrine (two agonists influencing the amygdala and the hippocampus during encoding and consolidation) leads to improved memory (Rimmele et al., 2016). Activation of β-adrenergic receptors during consolidation even helps memory formation and later remembering (Barsegyan et al., 2014; Roozendaal et al., 2008) and norepinephrine is necessary for reconsolidation of certain types of the degraded memory (Little et al., 2017). Finally, at a population level, overweight subjects with hyper-stimulated sympathetic drive have shown enhanced cognitive performance (Tikhonoff et al., 2015). On the contrary, what leads to low HR, such as isotonic exercise (Most et al., 2017; McNerney & Radvansky, 2015) and sleep (Bolinger et al., 2018; Wagner

et al., 2002; Werner et al., 2015), tends to favour memory, while sleep deprivation reduces cognitive abilities (Patrick et al., 2017). Experimental studies are mandatory in order to clarify the mechanism underlying the HR ↔ cognition relationship put in evidence in the present pilot epidemiological analysis.

4.3. Consequences of Results and Significance of the Research

One consequence of the results of the present study is that high HR should be counted among the risk factors or indicators of low memory. This circumstance could be of particular importance, for instance, in hiring workers, for whom memory can play an important role. Ideally, it could probably be better, when possible, to choose, for these works, subjects having low HR.

Another consideration is that the inverse, unwanted association between high HR and low memory is not ineluctable, as it can be prevented by education. In fact, years of schooling potently enter directly and independently the models having MI10 and MI30 as dependent variables, strongly reducing the negative effect of high HR. Schooling persisted for years is therefore the best way to counteract the negative effect of tachycardia on memory and the deleterious effects of age in increasing this association.

4.4. Is an Intervention Plausible?

HR deceleration is triggered and controlled by subcortical structures (amygdala and brainstem) (Öhman et al., 2000). Having low HR is convenient from a cognitive point of view, but the question on whether reducing pharmacologically HR leads to best memory is of course unanswered. If so, for the reasons exposed above, β-blockers (reducing the sympathetic drive) would not be a good choice (Rimmele et al., 2016). No information at all is available in this respect as regards non-adrenergic reduction of HR *via* ivabradine. Non-pharmacological ways to reduce HR are to reduce stress (which increases HR) (Delgado-Moreno et al., 2017) and practicing endurance isotonic exercise, which actually improves cognitive functions and memory in particular (Most et al., 2017; McNerney & Radvansky, 2015; Barry et al., 2018; Mahinard et al., 2016; Lin et al., 2017). Another way is sleep, which notoriously reduces HR and, as demonstrated, consolidates immediate emotional meaning by enhancing automatic responses and promotes top-down control of emotional responses by strengthening respective neocortical representations and increases or preserves the emotional tone associated with memories (Bolinger at al., 2018; Wagner et al., 2002; Werner et al., 2015). A simple nap after a learning session can improve assimilation of information and memory (Bolinger et al., 2018). The road to build the complete map of the risk factors and their consequences is still incompletely known. Studies involving more items and the echo-genetic context are mandatory (Casiglia & Palatini, 1998; Mazza et al., 2001; Tikhonoff et al., 2003).

4.5. Strength and Limitations of the Study

The strength of the study is that it is, to our knowledge, the first taking into con-

sideration the importance of HR in determining memory, and that it took into considerations subjects from general population directly generalizable to the community. It should be considered a pilot study.

Limitations of the study are that it is confined to hypertensive subjects only, and that other aspects of cognition have not been considered. It would be to the good that the study was repeated in normotensive subjects from general population and that other cognitive tests apart from memory were taken into account.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

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