Habitual blood pressure and cognitive performance

Chapter 11

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ABSTRACT

In all MAAS panel studies, special attention has been paid to the identification of vascular risk factors as potential determinants of cognitive aging. In the first panel study A_1, (N=463), laboratory blood pressure status was used as a predictor of cognitive performance. After correction for age, sex, general intelligence, and prevalent cardiovascular morbidity, no systematic effects of systolic or diastolic blood pressure were found on cognitive test performance. However, pulse pressure (difference in systolic and diastolic blood pressure) was negatively associated with several measures that reflect the speed of information processing. It is suggested that an increased pulse pressure is associated with a generalized deterioration of the arterial vascular system, including that of the cerebral region, which compromises the integrity of cognitive functions.

INTRODUCTION

Hypertension is regarded as the most important risk factor in the pathogenesis of cerebral vascular disease. Since 1980, the results of a series of well-designed case-control studies and cross-sectional studies have strongly suggested that hypertensive status is related to decrements in performance in several cognitive domains, including abstract reasoning, and memory and attentional processes (e.g., Elias, Robbins, Schultz, & Pierce, 1990; Farmer, White, Abbott, Kittner, Kaplan, Wolz, et al., 1990; Waldstein, Manuck, Ryan, & Muldoon, 1991).

The mechanism underlying hypertension mediated cognitive decline is still open to debate. It has been suggested that cerebral ischaemia is the key factor in the underlying pathophysiological mechanism. This so-called 'silent infarction' appears to be caused primarily by hypertension, but other concomitant conditions (e.g., age, hyperlipidaemia, diabetes, smoking, genetic factors) may also be involved (Desmond, Tatemichi,

Paik, & Stern, 1993; Starr, Whalley, Inch, & Shering, 1993). There is evidence that the areas in which reduced blood flow is observed in hypertensive patients, namely the temporal and frontal cortices, are also relevant to the neuropsychological domains affected in primary aging (Rodriguez, Arvigo, Marenco, Nobili, Sandini, & Rosandini, 1987).

The present project aims at substantiating the hypotheses about the relationship between mild to moderate hypertension and accelerated cognitive decline in adult subjects. The main questions addressed in this study are: (1) can effects of blood pressure (BP) and other cardiovascular risk factors on cognitive performance be identified in a normal aging population, (2) which cognitive domains are most sensitive to the main components of BP status (systolic, diastolic, and pulse pressure), when background variables known to act on cognition (calendar age, sex, and intelligence) are controlled for, (3) are BP-related decrements in cognitive performance age-dependent, and (4) do more sophisticated techniques for measuring BP (Ambulatory Blood Pressure Monitoring, ABPM) add to the explained variance compared to more conventional techniques? BP in all MAAS panels is assessed in several ways, using sophisticated automated recording techniques (van Boxtel, Gaillard, van Es, Jolles, & de Leeuw, submitted), along with determination of other vascular risk factors (body mass index, waist-to-hip ratio, smoking habits, diabetes) as potential predictors of cognitive performance deficits.

In this chapter, the first results from the MAAS–A_1 data set are presented on the relationship between laboratory BP status and measures of cognitive outcome.

METHOD

Subject characteristics and medical background

All participants in the A_1 test programme (N=469) were included in the analysis, except for six subjects with incomplete data. Extensive medical background information on all MAAS participants was obtained from several sources, including postal survey, a morbidity checklist, and medical problem-oriented status notes from the general practitioner. For this analysis the participants were subdivided into groups with and without self-reported evidence of cardiovascular events (CVE) in the medical history. These included reported evidence of angina pectoris, cardiac arrhythmia, cardiac insufficiency, myocardial infarction, valvular lesions, heart surgery, peripheral arteriosclerosis, a history of cardiac reanimation or antihypertensive drug use. Reported hypertension was considered insufficient to classify a subject in the CVE group, unless it was supported by the patient taking antihypertensive drugs. The CVE were identified in order to be able to study the total group and the CVE-free group separately.

Blood pressure measurement

BP was recorded five times on the left arm of seated subjects during a 25 minute break in a three-hour neuropsychological test session (see Section 4.3.1). A Dinamap® 8100 blood pressure monitor was programmed to record BP at fixed intervals of 5 minutes, under standard resting conditions. The average of BP values measured at 15 and 20 minutes was used to control for adaptation in the first 15 minutes of measurement (van Boxtel et al., 1995). Pulse pressure (systolic/diastolic BP difference) was calculated as an index of pressure variability. BP values by age group and sex are shown in Table 11.1.

Cognitive performance tests

The cognitive tests that were used are described in detail in Section 4.3. In short, general intelligence was assessed with the abridged Groningen Intelligence Test (GIT). Tests taken from the Short Cognitive Screening Battery (SCSB) were used to assess performance in several cognitive domains. Five outcome measures were derived from the SCSB; memory, cognitive flexibility, sensorimotor speed, word fluency, and letter copying. The first three measures are compound scores that were calculated from *Z*-transformed raw scores of the SCSB, using the formulae:
Memory (MEMORY) = $(Z_{VLTTOT} + Z_{VLTMAX} + Z_{VLTDEL}) / 3$
Cognitive flexibility (FLEX) = $-(Z_{CST\text{-}C} + Z_{SCWT\text{-}III}) / 2$
Sensorimotor speed (SPEED-S) = $-(Z_{CST\text{-}0} + Z_{CST\text{-}A} + Z_{CST\text{-}B} - Z_{TAP} + Z_{SCWT\text{-}I}) / 5$
Total, maximal, and delayed recall scores on the Verbal Learning Task (VLT) made up the memory score. The letter-digit version of the Concept Shifting Task (CST) and Stroop interference were combined to give the cognitive flexibility score (reflecting information processing speed), and the null, digit, and letter versions of the CST, continuous tapping, and Stroop Color Word Test yielded an index of sensorimotor speed (van Boxtel, Langerak, Houx, & Jolles, in press). Symbol copying (Letter Digit Substitution Test, LDST) and fluency (animal naming) were treated as separate variables, as performance in these tests draws on virtually every aspect of cognitive function.

RESULTS

Table 11.1 summarizes the BP values and cognitive outcome measures by aggregated age group and sex. All cognitive outcome measures were sensitive to age, and increasing age was consistently associated with a poorer cognitive performance. Women outperformed men on memory and letter copying, but had a slightly lower sensorimotor speed. No age by sex interaction effects were present.

Table 11.1.
Number of CVE-affected subjects, mean BP values, and mean cognitive outcome measures (+*SD*) by age and sex. Significance levels of main effects for age and sex on cognitive outcome measures (using ANOVA) are indicated.

	Age				Sex	
	25-35y	40-50y	55-65y	70-80y	M	F
Total (*N*)	120	122	120	101	235	228
CVE in history (*n*)	2	13	39	55	63	46
Blood pressure						
DBP (mmHg)	68.5 (8.9)	72.8 (10.4)	74.0 (10.8)	73.7 (14.0)	74.4 (9.7)	69.9 (12.2)
SBP (mmHg)	118.0 (11.5)	121.1 (12.6)	130.2 (18.8)	139.8 (21.9)	128.4 (15.1)	125.1 (21.2)
Pulse pressure (mmHg)	49.5 (8.5)	48.3 (8.3)	56.2 (14.2)	66.1 (20.1)	54.0 (12.0)	55.1 (17.4)
Cognitive outcome measures						
Memory	.57 (.74)	.19 (.83)	−.09 (.85)	−.75*** (.91)	−.23 (.98)	.25*** (.85)
Cognitive flexibility (FLEX)	.56 (.35)	.34 (.48)	−.09 (.54)	−.81*** (.91)	.01 (.77)	.07 (.77)
Sensorimotor speed (SPEED-S)	.62 (.41)	.29 (.52)	−.15 (.60)	−.88*** (.72)	.05 (.76)	−.04* (.81)
Verbal fluency (#)	25.8 (5.7)	23.6 (5.0)	22.0 (6.1)	19.5*** (5.0)	22.7 (5.8)	22.9 (6.0)
Letter copying (LDST)	58.0 (9.0)	51.7 (9.8)	44.3 (8.8)	35.7*** (9.7)	46.6 (12.3)	49.0* (12.4)

Note. CVE = cardiovascular event; DBP = diastolic blood pressure; SBP = systolic blood pressure; Pulse pressure = SBP minus DBP. Note that the compound scores Memory, FLEX, and SPEED-S are derived from population based *Z*-scores.
* $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Table 11.2.
Partial correlations between BP values and cognitive outcome scores after correction for age, IQ, and sex, for the total group (N=463) and for the CVE-free group (n=354).

		Memory	FLEX	SPEED-S	Fluency	LDST
SBP	all	−.03	−.03	−.09	−.11	−.09
	no CVE	−.04	−.10	−.09	−.07	−.16**
DBP	all	.01	.09*	.05	−.09	−.03
	no CVE	−.03	.06	.06	−.04	−.10
Pulse Pressure	all	−.05	−.12*	−.14**	−.06	−.09
	no CVE	−.03	−.18***	−.17**	−.06	−.12*

Note. CVE = cardiovascular event; DBP = diastolic blood pressure; SBP = systolic blood pressure; Pulse pressure = SBP minus DBP; LDST = letter digit symbol test.
* $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Next, partial correlations were computed between pressure values and cognitive scores, corrected for the effects of chronological age, GIT intelligence, and sex (Table 11.2). Except for a small negative correlation between systolic pressure and LDST (CVE-free subjects), and a positive correlation between diastolic pressure and the cognitive flexibility score (all subjects), no systematic effects of diastolic and systolic pressure were observed. However, pulse pressure was negatively associated with cognitive flexibility and sensorimotor speed in the total group. The same pattern of effects was evident in the CVE-free group. In addition, LDST was also negatively correlated with pulse pressure. When the age by BP interaction term was also controlled for (results not shown here) these partial correlations tended to increase slightly.

DISCUSSION

The first findings with this MAAS–A_1 panel indicate that the difference between systolic and diastolic BP (pulse pressure) in this normal aging population was predictive of several aspects of basic and information processing speed. Although the effects were small in terms of additional explained variance (1.4% in LDST performance, up to 3.2% in the cognitive flexibility score), the pattern of effects on the performance speed was systematic and more outspoken in the subgroup free of cardiovascular events than in the subgroup with one more of these events in the medical history.

Pulse pressure increases with age as progressive atherosclerosis decreases the elasticity of the arterial walls of the larger blood vessels, which results in a reduced damping of the systolic pressure wave. Results from studies in animal models have drawn attention to the fact that pulse pressure may be more important in the development of hypertrophy in cerebral arterioles than the mean pressure (Baumbach & Heistal, 1992). In recent epidemiological research, signs of peripheral atherosclerosis (ankle-brachial index, plaque formation in carotid arteries) were negatively related to a cognitive performance index, the MMSE (Breteler, Claus, Grobbee, & Hofman, 1994). Our results should be interpreted with caution, as the age range of our subject was large and birth cohort differences may confound the BP–cognition relationship. Still, these results are to be confirmed in the MAAS panel studies A_2 to A_4. Furthermore, an age stratified analysis should be performed on the pooled MAAS population to control more rigorously for potential cohort effects.

Because the subjects were stratified by age (and thus there was a relative over-representation of older subjects compared to the general population), the prevalence of isolated systolic hypertension in this group was relatively high (13.2%) (van Boxtel et al., submitted). Typically, isolated systolic hypertension is associated with an increased pulse pressure. It is not clear if this category of hypertensive subject is 'at risk' of developing cognitive impairment. However, if the effect of pulse pressure on information processing speed proves to be robust, this finding may contribute to the discussion on if and how systolic hypertension in elderly subjects should be treated (Forette, Amery, Staessen, Strasser, Thijs, Beevers, et al., 1991).

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