Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 4 (2016) 56-66

Cognitive & Behavioral Assessment

The association between pulse pressure change and cognition in late life: Age and where you start matters

Eric McDade[a,*], Zhaowen Sun[b], Ching-Wen Lee[b], Beth Snitz[b], Tiffany Hughes[c], Chung-Chou H. Chang[d,e], Mary Ganguli[b,f]

[a]Department of Neurology, School of Medicine, Washington University at St. Louis, St. Louis, MO, USA
[b]Department of Psychiatry, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA
[c]Department of Sociology, Anthropology, and Gerontology, Youngstown State University, Youngstown, OH, USA
[d]Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA
[e]Department of Biostatistics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA
[f]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA

Abstract

Introduction: Variations across studies in the association between blood pressure (BP) and cognition might be explained partly by duration of exposure to hypertension and partly by nonrandom attrition over time. Pulse pressure (PP) reflects arterial stiffness which may better reflect chronicity of hypertension.

Methods: Over six annual cycles, 1954 individuals aged 65+ years from a prospective population-based cohort underwent BP measurements and cognitive evaluations. We examined the relationship of change in five cognitive domains to longitudinal PP patterns across the late-life age spectrum, before and after stratifying by baseline systolic blood pressure (SBP) and adjusting for attrition.

Results: There were four longitudinal PP patterns: stable normal, stable high, increasing, and decreasing. Those with lower baseline SBP and an increasing or stable high PP had less decline in cognition, an effect that was attenuated with aging. Among those with higher baseline SBP, there were no differences across PP groups, but increasing age was consistently associated with greater cognitive decline.

Discussion: The effect of PP on cognitive decline depends on age, baseline SBP, and the trajectory of PP change. Cardiovascular mechanisms underlying cognitive aging should be recognized as nuanced and dynamic processes when exploring prevention and treatment targets in the elderly, so that the optimal timing and type of intervention can be identified.

Keywords: Pulse pressure; Cognitive decline; Heterogeneity

1. Introduction

Despite strong evidence for a positive association between midlife hypertension and late-life cognitive impairment [1–5], the relationship between late-life hypertension and cognitive function remains unclear [1,4,6–8]. Observed inconsistencies between studies partly reflect variations in study design and populations. Another likely factor is unmeasured heterogeneity, within populations, as regard the timing and duration of exposure to hypertension, which in turn could influence its effects and potential modifiability [9]. Such investigations would benefit from a proxy measure representing the duration of exposure to hypertension.

The authors report no conflict of interest.

*Corresponding author.
E-mail address: mcdadee@neuro.wustl.edu

http://dx.doi.org/10.1016/j.dadm.2016.03.008

A potential proxy or surrogate measure is pulse pressure (PP), partly reflecting arterial stiffness, measured as the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP). PP is potentially a better measure of the chronic effects of hypertension than blood pressure itself [1,10–13]. PP increases with age and is associated with a number of cardiovascular risk factors and outcomes [14,15]. Arterial stiffness appears related to Alzheimer disease (AD) pathology, providing a potential vascular marker that is more closely related to AD [13,16–18] than other cardiovascular measures. However, evidence remains conflicted as to the association of cognitive performance with arterial stiffness, whether measured as PP or through ultrasound determined pulse wave velocity [19–24].

Here, we explored the relationships between longitudinal change in PP and cognitive performance in multiple cognitive domains over 5 years and how these relationships were influenced by initial (baseline) blood pressure (BP). We identified subgroups of individuals with distinct PP trajectories over time and compared their relationships with change in cognition over the same period. As an increase in PP typically reflects significant vascular remodeling and stiffening, we hypothesized that those with increasing PP over time would have a greater decline in cognition. Further, because the impact of arterial health on brain health likely varies across the age spectrum of late life, we assessed whether the relationship between change in PP and cognition differed in the young-old and old-old. Finally, we accounted for the potential effects of participant loss over time, which is inevitable and likely nonrandom in longitudinal studies.

2. Methods

2.1. Subjects

The Monongahela–Youghiogheny Healthy Aging Team is an epidemiologic study of cognitive decline and dementia in an age-stratified, random sample drawn from the voter registration list of small town communities in Southwestern Pennsylvania [25]. Details of sampling, recruitment, and cohort characteristics have been previously reported [25]. Inclusion criteria were age 65 or older, not residing in a long-term care facility at study entry, no substantial sensory impairment, and no decisional incapacity. Initial screening was performed on 2036 participants, of whom 54 were excluded from the full evaluation based on substantial baseline cognitive impairment (<21 on age and education-adjusted mini-mental state examination [MMSE]) [26,27]. The full evaluation was conducted on the remaining 1982 participants who had a mean (SD) age of 77.6 (7.4) years; were 61.1% women and 94.8% of mixed European descent; and had a median educational level of high school graduate. For the present analyses, we further excluded another 32 individuals whose full evaluation revealed severe cognitive impairment at study entry, leaving 1954 total participants for the analyses reported here. All procedures were approved by the University of Pittsburgh Institutional Review Board and all participants provided written informed consent.

2.2. Clinical evaluation

At study entry and each follow-up visit, trained research staff performed comprehensive in-home evaluations including medical history (self-report of diagnosis by health care professional), current and past alcohol and tobacco use, current medications, a brief physical examination, neurologic evaluation, and cognitive testing (see below). At each study visit, blood pressure was measured approximately 90 minutes after the start of the visit by a trained interviewer according to protocol. After the appropriate cuff size was determined, the participant's blood pressure was measured using an aneroid sphygmomanometer and stethoscope. Before the BP reading was taken, the participant was in a seated position for at least 5 minutes with feet flat on the floor. A second reading was taken after having the participant stand for at least 3 minutes. If SBP was >175 mm Hg or DBP was >100 mm Hg in either position, a repeat measurement was performed later in the physical examination. The BP variable used here represents an average of the total measurements taken at each visit.

PP was calculated as SBP-DBP. Participants were classified as hypertensive if they had SBP >140 or DBP >90 or if taking antihypertensive medications. The vascular-related factors included a self-report of physician-diagnosed myocardial infarction, hypertension, congestive heart failure, cardiac related procedures, transient ischemic attack, stroke, diabetes, and elevated cholesterol.

2.3. Cognitive evaluation

The cognitive evaluation consisted of multiple tests in the domains of attention/processing speed, executive function, language, learning and memory, and a single test for visuospatial function. For each domain, a composite Z-score was estimated as the mean of individual Z-scores by test, standardized to raw score means and SDs of the cohort at baseline [25]. Slope of cognitive change in each domain for each individual over time was estimated from a linear mixed model with random intercept and random slope of time.

2.4. Diagnostic category

Using the Clinical Dementia Rating scale (CDR) [28], participants were rated as having no dementia (CDR = 0), possible/very mild dementia (equivalent to mild cognitive impairment; CDR = 0.5), and dementia (CDR ≥1). We restricted the analytic sample at baseline to individuals with CDR <1.

2.5. Statistical methods

See detailed statistical methods in the Supplementary Material.