both in humans and models. Reference to these studies are given in Giannattasio's editorial. Calibration by cuff sphygmomanometer provides its greatest inaccuracy in measuring aortic pressure as it does for measuring upper limb pressure. The article by Davies *et al.* [1] would have been more accurately titled 'Peripheral blood pressure measurement is as *bad as . . .*'.

Acknowledgement

Michael O'Rourke is a Director of Atcor Medical Pty Ltd, manufacturer of systems for pulse wave analysis and measurement of arterial stiffness.

References

- 1 Davies JI, Band MM, Pringle S, Ogston S, Struthers AD. Peripheral blood pressure measurement is as good as applanation tonometry at predicting ascending aortic blood pressure. *J Hypertens* 2003; **21**:571–576.
- 2 Giannattasio C. How to assess central arterial blood pressure? *J Hypertens* 2003; **21**:495–496.
- 3 Pauca AL, Wallenhaupt SL, Kon ND, Tucker WY. Does radial artery pressure accurately reflect aortic pressure? *Chest* 1992; **102**: 1193–1198.
- 4 White WB, Berson AS, Robbins C, Jamieson MJ, Prisant LM, Roccella E, Sheps SG. National standard for measurement of resting and ambulatory blood pressures with automated sphygmomanometers. *Hypertension* 1993; **21**:504–509.
- 5 O'Brien E. Blood pressure measuring devices, recommendations for the ESH. *BMJ* 2001; **322**:531–536.
- 6 Borow KM, Newburger JW. Noninvasive estimation of central aortic pressure using the oscillometric method for analyzing systemic artery pulsatile blood flow: comparing study of indirect systolic, diastolic, a mean brachial artery pressure with simultaneous direct ascending aortic pressure measurements. *Am Heart J* 1982; **103**:879–886.
- 7 Breit SN, O'Rourke MF. Comparison of direct and indirect arterial pressure measurements in hospitalised patients. *Aust NZ J Med* 1974; **4**:485–491.
- 8 Cohn JN, Finkelstein S, McVeigh G, Morgan D, Lemay L, Robinson J, *et al.* Noninvasive pulse wave analysis for the early detection of vascular disease. *Hypertension* 1995; **26**:503–508.
- 9 Watson S, Wenzel RR, di Matteo C, Meier B, Lüscher TF. Accuracy of a new wrist cuff oscillometric blood pressure device: comparisons with intraarterial and mercury manometer measurements. *Am J Hypertens* 1998; **11**:1469–1474.
- 10 Lane D, Beevers M, Barnes N, Bourne J, John A, Malins S, Beevers DG. Inter-arm differences in blood pressure: when are they clinically significant? *J Hypertens* 2002; **20**:1089–1095.
- 11 Pauca AL, O'Rourke MF, Kon ND. Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform. *Hypertension* 2001; **38**:932–937.
- 12 Davies JI, Struthers AD. Pulse wave analysis and pulse wave velocity: a critical review of their strengths and weaknesses. *J Hypertens* 2003; **21**:463–472.
- 13 O'Rourke MF. Target organ damage: use of pulse wave analysis as a manifestation of aortic degeneration in assessment of hypertension. *Vasc Med* 2002; **7**:83–86.

Assessment of central arterial pressure?

Authors' reply

Justine Davies and Allan Struthers

Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee, UK.

Correspondence and requests for reprints to Justine Davies, Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee, UK. E-mail: j.i.davies@dundee.ac.uk

We thank doctors O'Rourke and Avolio for their correspondence regarding our article. Although we are aware that peripheral blood pressure measurements are

associated with a degree of inaccuracy, this does not challenge our findings. In our study, we compared standard peripheral blood pressure measurements with the SphygmoCor system as calibrated with the same peripheral blood pressure measurement. Therefore, the inaccuracies encountered with the peripheral blood pressure measurement applied equally to the two techniques under comparison. We found that the SphygmoCor system actually augmented this inaccuracy. We accept that, when applied to invasive data, the transfer system of the SphygmoCor system is accurate; however, invasive blood pressure monitoring is clearly not acceptable in a clinical setting, which is one of the situations in which this system is promoted for use. We have clearly shown that, in a clinical setting, a simple peripheral oscillometric blood pressure measurement is better than the SphygmoCor system at estimating ascending aortic blood pressure. Perhaps if we were to change our title, as doctors O'Rourke and Avolio suggest, it should be to 'the SphygmoCor and peripheral blood pressure measurements are both bad at estimating ascending aortic pressure, but the SphygmoCor system is worse'.

Is angiogenesis a plausible hypothesis in Alzheimer's disease?

Willem H. Birkenhäger^a and Jan A. Staessen^b

^aErasmus University, Rotterdam, The Netherlands and

^bStudiecoördinatiecentrum, Hypertensie en Cardiovasculaire Revalidatie Eenheid, Departement Moleculair en Cardiovasculair Onderzoek, Katholieke Universiteit Leuven, Leuven, Belgium.

Correspondence and requests for reprint to Jan A. Staessen, Studiecoördinatiecentrum, Hypertensie en Cardiovasculaire Revalidatie Eenheid, Departement Moleculair en Cardiovasculair Onderzoek, Katholieke Universiteit Leuven, Leuven, Belgium. E-mail: jan.staessen@med.kuleuven.ac.be

The evocative hypothesis on angiogenesis as a major contributing factor in the pathogenesis of Alzheimer's disease by Vagnucci and Li [1] raises a variety of comments.

First, their hypothesis does not account for the substantial role of hypertension in the pathogenesis of both vascular and degenerative dementias [2], although hypertension notably coincides with microvascular rarefaction rather than proliferation.

Second, the list of various drugs with attributed preventive effects on Alzheimer's disease (their Table 1) is based on the evidence that all drugs, with the exception of nitrendipine, merely contain at best an educated guess at their potential. The latter investigations basically comprise uncontrolled retrospective observational data sources, and are devoid of ruling out a host of confounding factors pervading such *post-hoc* evaluations [3].

Of course such crude trends may harbour the potential for generating attractive hypotheses [1], but a sound and viable hypothesis should rather rest on infallible evidence. The latter can only be obtained through well-controlled, randomized, comparative prospective trials, of which the authors list one (!) example in their Table 1, referring to the preventive role of the calcium-antagonist nitrendipine used in the Systolic Hypertension in Europe (Syst-Eur) trial. Its first report [4] was followed by a second one 4 years later [5], doubling the median observation period, as well as the further incidence of Alzheimer's disease, and maintaining a reduction by 50% through active treatment based on nitrendipine as the main stay of drug therapy. Such dramatic effects have not been observed in other prospective trials using several other anti-hypertensive regimes versus their control arms [6–9]. Apparently blood pressure reduction *per se* lacks the potential of preventing hypertension-related (degenerative) dementia, at least past a certain stage. This seems to justify invoking dihydropyridine-induced calcium-channel blockade as a specific preventive mechanism in this regard, although this remains to be tested by direct comparison between a dihydropyridine calcium antagonist and any other current antihypertensive drug(s). For such a trial, we are urgently seeking the necessary funding to confirm the above, together with the results of one convincing experimental study [10].

This brings us to our third exception regarding the hypothesis by Drs Vagnucci and Li. It ignores the accumulative evidence regarding the dysregulation of cerebrocellular calcium homeostasis as a core factor in the pathogenesis of Alzheimer's disease [11,12]. This is not to negate the presence of angiogenesis, although the latter may well rate as a secondary epiphenomenon.

References

- 1 Vagnucci AH, Li WW. Alzheimer's disease and angiogenesis. *Lancet* 2003; **361**:605–608.
- 2 Birkenhäger WH, Forette F, Seux M-L, Wang J-G, Staessen JA. Blood pressure, cognitive functions, and prevention of dementia in older patients with hypertension. *Arch Intern Med* 2001; **161**:152–156.
- 3 Birkenhäger WH, Wang J-G, Staessen JA. Dementia and statins [Letter]. *Lancet* 2001; **357**:880.
- 4 Forette F, Seux M-L, Staessen JA, Thijs L, Birkenhäger WH, Babarskiene MR, *et al.* Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. *Lancet* 1998; **352**:1347–1352.
- 5 Forette F, Seux M-L, Staessen JA, Thijs L, Babarskiene MR, Babeanu S, *et al.* The prevention of dementia with antihypertensive treatment. New evidence from the Systolic Hypertension in Europe (Syst-Eur) study. *Arch Intern Med* 2002; **162**:2046–2052.
- 6 Prince MJ, Bird AS, Blizzard RA, Mann AH. Is the cognitive function of older patients affected by antihypertensive treatment? Results from 54 months of the Medical Research Council's treatment trial of hypertension in older adults. *BMJ* 1996; **312**:801–805.
- 7 SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 1991; **265**:3255–3264.
- 8 PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood pressure lowering regimen among 6105 individuals with prior stroke or transient ischaemic attack. *Lancet* 2001; **358**:1033–1041.
- 9 Lithell H, Hansson L, Skoog I, Elmfeldt D, Hofman A, Olofsson B, *et al.*, for the SCOPE Study Group. The study on cognition and prognosis in the elderly (SCOPE). Principal results of a randomised double-blind intervention trial. *J Hypertens* 2003; **21**:875–886.
- 10 Amenta F, Strocchi P, Sabbattini M. Vascular and neuronal brain damage: protective effect of treatment with nicardipine. *J Hypertens* 1996; **14** (suppl 3):S29–S36.
- 11 Thibault O, Porter NM, Chen K-C, Blalock EM, Kaminker PG, Clodfelter GV, *et al.* Calcium dysregulation in neuronal aging and Alzheimer's disease: history and new direction. *Cell Calcium* 1998; **24**:417–433.
- 12 Pascale A, Etcheberrigaray R. Calcium alterations in Alzheimer's disease: pathophysiology, models and opportunities. *Pharmacol Res* 1999; **39**:81–88.