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Communication

The carotid artery as an alternative site for dynamic autoregulation measurement: an inter-observer reproducibility study

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ABSTRACT

The internal carotid artery (ICA) has been proposed as an alternative site to the middle cerebral artery (MCA) to measure dynamic cerebral autoregulation (dCA) using transcranial Doppler ultrasound (TCD). Our aim was to test the inter-operator reproducibility of dCA assessment in the ICA and the effect of interaction amongst different variables (artery source × operator × intra-subject variability). Two operators measured blood flow velocity using TCD at the ICA and MCA simultaneously on each side in 12 healthy volunteers. The autoregulation index (ARI) was estimated by transfer function analysis. A two-way repeated measurements ANOVA with post-hoc Tukey tested the difference between ARI by different operators and interaction effects were analysed based on the generalized linear model. In this healthy population, no significant differences between operator and no interaction effects were identified amongst the different variables. This study reinforced the validity of using the ICA as an alternative site for the assessment of dCA. Further work is needed to confirm and extend our findings, particularly to disease populations.

1. Introduction

Dynamic cerebral autoregulation (dCA) is an important physiological mechanism that maintains adequate or relative constant cerebral blood flow despite changes in cerebral perfusion pressure [1]. Several pathological conditions can compromise dCA such as ischemic stroke [2,3], head trauma [4], prematurity of the newborn [5] or diabetes [6]. In critical care patients, a non-invasive and bedside method like transcranial Doppler ultrasound (TCD) is the preferred approach to measure cerebral haemodynamics, considering cerebral blood flow velocity (BFV) as a surrogate of cerebral blood flow, when assuming no or only minor change in the diameter of the probed vessel [7,8]. dCA can be assessed using non-invasive and continuous blood pressure (BP) measurement simultaneously with BFV using TCD [9]. Although different manoeuvres can be adopted to induce changes in BP, a more convenient approach is to extract dCA parameters using spontaneous fluctuations of BP and BFV and calculate the autoregulation index (ARI) with transfer function analysis [1,10].

For dCA assessment based on spontaneous fluctuations of BP, BFV needs to be measured continuously for periods of at least 5 min., usually using a probe-holding device, such as a head frame, at the middle cerebral artery (MCA) position. However, in certain patient groups, like severe brain trauma or neonates [11,12], a head frame is unlikely to be tolerated. A previous report demonstrated that hand-held probe monitoring can be used with good acceptability in healthy subjects [13]. Moreover, it has been demonstrated [14] that the internal carotid artery (ICA) can be used as an alternative site for dCA measurements in healthy volunteers with good intra-subject reproducibility, and could be applied in patients whose temporal bone window is inadequate [15], as often encountered in the elderly population [16]. However, inter-observer reproducibility has never been tested for this purpose.

Therefore, our aim was to test the following hypotheses: (1) there is no difference between ARI values extracted from both MCA and ICA, and (2) ARI values derived from baseline recordings in a healthy population are not influenced by artery source (MCA and ICA), and intra- or inter-operator factors.

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2. Materials and methods

Healthy volunteers were recruited from the Neurology Department at Hospital das Clinicas, Universidade de São Paulo, Brazil. Exclusion criteria were any neurological (including migraine), cardiovascular or chronic disease. The study was approved by the local ethics committee, and all subjects provided informed consent.

All measurements were performed in a dedicated room and each subject was instructed to rest in a supine position. Two operators (RCN and NPS) performed all measurements. Both have obtained doctoral degrees in the field of TCD ultrasound and have extensive experience of performing TCD examinations in healthy subjects and patients with different cerebrovascular conditions. Non-invasive BP was measured using an arterial volume-clamping device (Finometer™, Finapress Medical Systems BV, Netherlands) with a cuff placed on the middle finger of the right hand; end-tidal CO_2 ($EtCO_2$) was monitored using a capnograph attached to a face mask (Dixtal, DX 1265 $EtCO_2$ Capnogard, Manaus, Brazil).

Using B-mode ultrasound, the ICA was identified and examined to ensure it was free of plaque. The Doppler site of measurement was marked 1.0–1.5 cm distal to the bifurcation bulb. ICA and MCA BFV were measured simultaneously on each side using a TCD; for MCA a 2 MHz probe was used and attached to a head frame, and for ICA a 4 MHz probe was hand-held with the probe located in the centre of the mark for ICA with an angle of 60° to the artery. A 3-minute recording was performed on each side with a 2-minute rest period between recordings.

All data were edited off-line, using dedicated software (Department of Cardiovascular Sciences, University of Leicester, UK). The beginning and end of each cardiac cycle were detected, and mean, systolic and diastolic beat-to-beat values were calculated for BP, and right and left MCA and ICA channels. The ICA BFV signals were corrected for 60° angle, by multiplying the values by 2 [17]. The end tidal value of the $EtCO_2$ signal was detected for each breath. Using spline interpolation and re-sampling the data at 5 Hz, a uniform time base was achieved for all signals.

dCA was assessed using transfer function analysis to obtain the coherence, phase and gain using BP as an input and BFV as an output [9]. A low coherence (less than 0.5) within the frequency range (0.01–0.25 Hz) indicated poor signal-to-noise ratio or lack of an input–output relationship. Estimates of the impulse response were obtained with the inverse FFT of gain and phase [9], and ARI was obtained by fitting the step response profile to one of 10 possible BFV template response curves [9,10]; each corresponding to an ARI value ranging from zero (absence of autoregulation) to 9 (best observed autoregulation). Other parameters, including BFV, SBP, DBP, EtCO2 and HR, were also averaged for the entire recording.

To measure variability amongst operators, the ARI value corresponding to each operator obtained from repeated measurements was averaged for both arteries (ICA & MCA) and the coefficient of variation (CV) of each was calculated as sample standard deviation divided by sample mean.

Inter-operator agreement was assessed using the Bland and Altman approach [18] by plotting the difference between ARI measurements (bias) of the two operators against their average and calculating the limits of agreement as ±1.96 SD of the difference.

A two-way repeated measurements ANOVA with post-hoc Tukey test was applied to test the difference between the ARI values corresponding to different operators and at each location (MCA and ICA). To evaluate interaction effects and separate contributions to ARI value from the three factors, i.e. artery source (ICA and MCA), operator (NPS and RCN) and intra-subject variability (recording 1 and 2), a generalized linear model with repeated measures was used. The level of statistical significance was set at $p \leq 0.05$ for all tests.

Table 1
Subject characteristics and baseline physiological parameters as mean (SD) values averaged for both operators.

Demographics	Volunteers ($n = 12$)
Age (years)[range]	48 ± 11 [32–69]
Sex	10 (F) 2 (M)
Heart rate (bpm)	66 ± 7
Systolic BP (mmHg)	134 ± 13
Diastolic BP (mmHg)	71 ± 8
$EtCO_2$ (mmHg)	36 ± 3
ICA BFV (cm/s)	46.01 [4.68]
MCA BFV (cm/s)	71.82 [7.37]

BP, blood pressure; $ETCO_2$, end tidal CO2; BFV, cerebral blood flow velocity; MCA, middle cerebral artery; ICA, internal carotid artery.

Table 2
Mean (SD) ARI values for ICA and MCA for both operators.

ARI	Operator 1	Operator 2	*p*-value
ICA	5.0(2.0)	5.3(2.2)	0.88
MCA	5.4(1.4)	5.8(1.6)	0.41
p-value	0.17	0.2	

ARI, autoregulation index; ICA, internal carotid artery; MCA, middle cerebral artery.

3. Results

Twelve volunteers (2 male) were recruited with mean age of 48 ± 11 years (range 32–69). Each subject had 8 recordings at MCA and ICA; a total of 13 ICA/MCA recordings, distributed at random across the group, were rejected due to artifacts and/or poor data quality. Baseline values were not significantly different between operators; parameter values averaged across operators are listed in Table 1.

3.1. Extra-cranial versus intra-cranial artery measurements

The ARI estimated from the two arteries was not significantly different when evaluated by two-way ANOVA test (Table 2). A representative plot of BFV of MCA and ICA is presented in Fig. 1.

3.2. Intra- and inter-operator reproducibilities

Intra-operator variability, expressed by the coefficient of variation, was similar at both extra- and intracranial arteries; ICA (28.7%) and MCA (25.5%). The two-way ANOVA showed no significant differences between ARI values between the two operators (Table 2). Bland–Altman plots of the differences between measurements performed by the two operators against their average indicated symmetrical distributions with few outliers for either ICA or MCA (Fig. 2).

3.3. Effects of interaction from artery source, intra- and inter-operator variability

The combined analysis of the three factors (artery, operator and intra-subject variability) showed no effect of interaction in ARI estimation (Table 3). After confirming the absence of effect, the analysis of separate contributions of the three variables also showed no statistically significant difference in artery source (ICA × MCA), operator (NPS × RCN) or recording (recording 1 × recording 2) (Table 3).