MR assessment of cerebrovascular reserve in patients with symptomatic carotid artery occlusion using an acetazolomide challenge

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Introduction: It is thought that only a minority of ischaemic strokes result directly from low cerebrovascular flow, the majority being embolic in nature. Carotid artery occlusion is often clinically silent: the circle of Willis playing an important role in compensating for occluded feeding vessels. Even when there is severe compromise at the carotid bifurcation and poor collateral flow via the circle of Willis, cerebral hypoxia can be averted by the brain drawing upon its cerebrovascular reserve. This paper reports findings from an integrated MR assessment of the factors defining low-flow states, involving MRA and exogenous perfusion investigation at rest and following a challenge with a carbonic anhydrase inhibitor.

Methods: Six patients with clinically defined unilateral anterior circulation transient ischaemic attacks were studied. On conventional catheter angiography all 6 had occlusion of the internal carotid artery (NASCET criteria) ipsilateral to the symptomatic hemisphere. The MR examination was performed at 1.5T (Eclipse, Philips Medical Systems, Best) and consisted 3D time-of-flight sliding interleaved Ky (SLINKY) angiography of the carotid bifurcations (neck coil) and circle of Willis (head coil) and exogenous perfusion mapping. The perfusion assessment methodology utilised a single-shot gradient-recalled echo technique (TE=60ms) which obtained 12 anatomical transaxial slices every 1.4sec. Eighty time-points were sampled, a 10ml intravenous injection of 1.0M gadolinium (Gadovist, Schering AG, Berlin) being administered via a pump injector (5ml/sec) on the 10^{th} time-point followed by a 30ml saline flush. After the 1^{st} perfusion assessment, 1000mg acetazolamide (Diamox Sodium perenteral, Wyeth Laboratories, Maidenhead) was given intravenously over 5 minutes. Perfusion assessment was repeated 10-12 minutes after this challenge. Perfusion data was analysed using standard methods (1), including calculation of bolus first moment mean transit time (TT_{fm}). The difference in transit time, ΔTT_{fm}, between symptomatic and asymptomatic hemispheres was used as an index of abnormal cerebral haemodynamic flow. The functional status of the circle of Willis was assessed using standard, qualitative neuroradiological interpretation of maximum intensity projected datasets.

Results: MR data are summarised in the tables below. All patients showed increased gadolinium TT_{fm} in their symptomatic compared to asymptomatic contralateral territories. The TT_{fm} asymmetries became more pronounced after acetazolamide challenge in all patients. This increase in transit time asymmetry was inversely correlated with the degree of collateralisation around the circle of Willis. Four of the 6 patients demonstrated normal posterior circulation anatomy and perfusion timing data pertaining to their relevant parenchyma are included in table 2 for comparative purposes.

Table 1. Data from the worst effected anatomical position in all 6 patients (Post WS = posterior watershed territory, Cent SO = centrum semiovale, ACA = anterior cerebral artery distribution) indicating the degrees of ICA stenosis at the level of the carotid bulb and the asymmetry in first moment mean transit time (ΔTT_{fm}) between symptomatic and asymptomatic hemispheres within that anatomical position.

CASE #	*Carotid stenosis (%)*	*Region*	*ΔTT_{fm} before acetazolamide (sec)*	*ΔTT_{fm} after acetazolamide (sec)*
1	R=50; L=100	Post WS	9.9	12.1
2	R=100; L<10	Cent SO	7.6	12.4
3	R=0; L=100	Post WS	0.9	3.6
4	R=100; L=30	ACA	3.0	9.5
5	R=100; L=70	Putamen	4.3	5.7
6	R=90; L=100	Post WS	1.4	5.3

Table 2. Comparative data showing interhemispheric difference in bolus first moment mean transit time (ΔTT_{fm}) for the 4 patients who had normal appearing posterior circulation anatomy.

CASE #	*Posterior circulation*	*ΔTT_{fm} before acetazolamide (sec)*	*ΔTT_{fm} after acetazolamide (sec)*
1	Occluded basilar	-	-
2	Normal	-0.8	-0.7
3	Hypoplastic P1 segmnents	-	-
4	Normal	-1.8	-0.4
5	Normal	0.0	-0.1
6	Normal	0.5	0.0

Discussion: This study shows that routine clinical systems can be used to investigate the possible hemodynamic causes of cerebral ischaemia. As expected, reduced flow in the symptomatic hemisphere can be inferred from the interhemispheric asymmetry in TT_{fm} observed at rest. Increase in this asymmetry implies a failure in vasoreactive dilation on the affected side. Cerebrovascular reserve using an acetazolamide challenge can be performed in one imaging event and the effects are measurable using existing technique. The results highlight the importance of knowing the anatomy of the circle of Willis when interpreting cerebral perfusion data and cerebrovascular reserve, which is not possible with other techniques such as PET, SPECT or xenon-CT.

Reference:

1) Wilkinson ID *et al*. AJNR 2003; 24(8):1501-1507.