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MRI of experimental focal cerebral ischaemia in sheep

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Purpose

A new model of experimental focal cerebral ischaemia by permanent middle cerebral artery (MCA) occlusion in sheep was developed to study therapy for stroke with autologous stem cells from umbilical cord blood. Regarding the specific characteristic of rete mirabile epidurale rostrale in sheep we aimed to investigate the utility of time of flight (TOF) magnetic resonance angiography (MRA) to observe the vascular anatomy and to validate the MCA occlusion. Furthermore we intended to assess the extent and natural time course of ischaemic focal brain injury in sheep using functional and morphological magnetic resonance imaging (MRI).

Materials and Methods

13 Merino sheep were randomly assigned to one of

group		number of animals
1	occlusion of all branches of the MCA	4
2	sparing of 1 to 2 branches of the MCA	5
3	sham operation (no vessel occlusion)	1
4	controls (no operation)	3

Fig. 1: Subgroups were build depending on the degree of MCA occlusion

Following exposure of the MCA branches, the vessels were occluded or touched (sham) by bipolar forceps. Controls did not undergo any surgical procedure. In 10 sheep 23 MRI sessions before and 2 to 46 days after onset of stroke (fig. 2) were performed using a 1,5T clinical MR scanner (fig. 3). Corrosion casts of the cerebral arteries of 3 sheep were prepared and compared to MRA.

Results

MRA visualised vessel anatomy (fig. 4) or occlusion distal to the rete mirabile. Anatomical variants concerning variant origin of the MCA and inconstant Arteria choroidea rostralis and communicans rostralis were revealed (fig. 5). Depending on the number of preserved MCA branches (0; 1; 2) significant ($p<0,001$) differences in lesion size (21±5,7; 13; 1,7±1,3 ml) could be found (fig. 6). In the sham operated animal no indications of ischaemia but a small contusion damage could be observed. Sheep with occluded left MCA showed space occupying lesions with drop of ADC values. From day 7 ADC values recovered and edema decreases (fig. 7).

Conclusion

In our study for the first time focal cerebral ischaemia was generated in sheep and examined using MRI. Depending on the occlusion type the model produced reproducible lesion size. TOF-MRA proves to be able to clearly depict the anatomy, variants and occlusion type of the cerebral arteries in sheep comparable to the corrosion casts despite of the upstream rete mirabile. MRI with MRA is a useful tool to assess the extent of brain injury and the type of MCA occlusion and therefore is suitable for non-invasive monitoring of lesion development in stem cell therapy of stroke.

MRI Timetable and Parameters (Fig. 2 and 3)

group	4			3	2				1			
preoperative	x			x	x		x	x				
MRI day 3±1				x	x	x	x	x	x	x		
MRI day 7±1				x			x		x	x		
MRI day 10					x						x	
MRI day 15/16					x	x		x				
MRI day 46										x		
corrosion cast		x	x									x

Fig. 2: Timetable of the MRI sessions after the operation for each animal divided into groups.

sequence	T2-TSE	T2*-GRE	DWI SE-EPI	3D-TOF MRA	T1-TSE
TE / TR (ms)	3600/ 100	629/ 18	4179/ 80	25/ 6,9	550/ 10
matrix	256 x 256	192 x 192	128 x 128	400 x 400	288 x 288
FOV (mm)	120	120	120	150	160
slices	22	22	22	96	20
orientation	transverse	transverse	transverse	transverse	coronal
thickness (mm)	4/ Gap 0	4/ Gap 0	4/ Gap 0	0,4/ Gap –0,2	2/ Gap 0,3
sense factor	1,5	0	1,5	1,3	0

Fig 3: MRI parameters

Vessel Anatomy and Variants (Fig. 4 and 5)

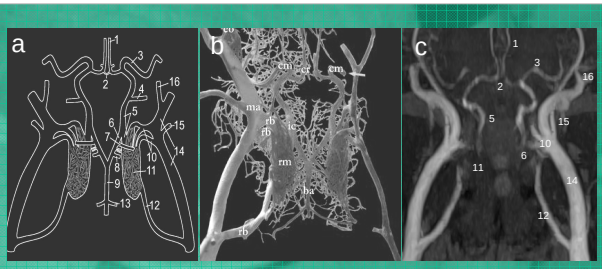

Fig. 4: Anatomy of the cerebral vessels in sheep (view from dorsal).
(a) circumcision, (b) corrosion cast and (c) MR angiography: 1) A. cerebri rostralis, 2) A. communicans rostralis (inconstant), 3) A. cerebri media (MCA), 4) A. choroidea rostralis, 5) A. carotis interna (ICA, arising from 11), 6) A. communicans caudalis, 7) A. cerebri caudalis, 8) A. cerebelli rostralis, 9) A. basilaris, 10) Rami rostrales ad rete mirabile epidurale rostrale, 11) Rete mirabile epidurale rostrale, 12) Ramus caudalis ad rete mirabile epidurale rostrale, 13) A. cerebelli caudalis , 14) A. maxillaris, 15) A. buccalis, 16) A. ophthalmica externa.

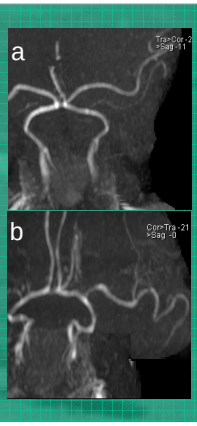

Fig. 5: MRA (MIP) of the rostral part of the circle of Willis displaying variant vessel anatomy:
In **variant (a)** the middle cerebral artery arises from the distal part of the ICA. A clearly visible A. choroidea rostralis branches off proximally, running approximately parallel to the MCA.
In **variant (b)** the MCA shows a more proximal origin. No second vessel can be identified.

MRI of Cerebral Ischaemia in Sheep (Fig. 6 and 7)

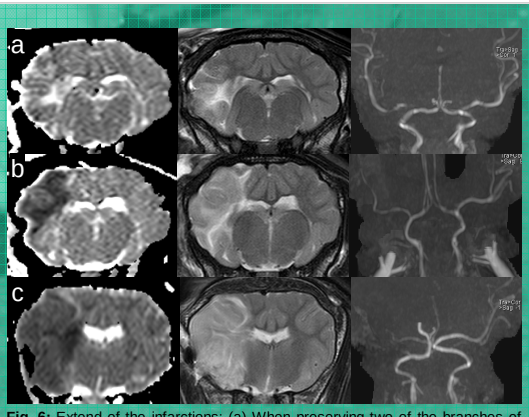

Fig. 6: Extend of the infarctions: (a) When preserving two of the branches of the MCA MRI shows only a small ischaemic lesion. (b) Focal ischaemia can be found, when one branch of the MCA remains in the MRA. (c) Complete middle cerebral artery occlusion with widespread infarction of the right hemisphere.

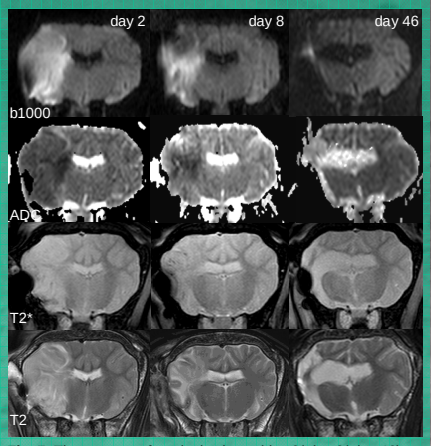

Fig. 7: Time course of stroke in sheep (day 2/ day 8/ day 46).

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