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Response to letter by Yao

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Response:

We thank Dr Yao for his interest and comments on our article[1]. However, we challenge the points raised as possible pitfalls. 1. MABP. For MRI scanning, SHRSP were anaesthetised (2-3% isoflurane to immobilise) and ventilated. MABP was 93 ± 4mmHg. It is inappropriate to compare this with MABP recorded under 0.5% halothane and neuromuscular blockade [2], as Yao suggests. With this regime MABP will be higher but the animal may be conscious, the stress induced contributing to hypertension. Our SHRSP and WKY rats come from an established colony (20 years) within Glasgow University. Colony integrity and hypertensive phenotype are maintained by selecting SHRSP adult breeders with conscious systolic blood pressure (SBP) between 170-190mmHg (males) and 130-150mmHg (females) measured by tail cuff (TC). 12-16 week old SHRSP progeny have conscious SBP of 187mmHg compared to 134mmHg for age-matched WKY (comparable with values for Charles River (Wilmington, MA) [3] and Medical College of Georgia, originally University of Michigan, Ann Arbor) [4]). Japanese colonies generally demonstrate much higher baseline BP’s. Divergence of BP phenotypes between distinct SHRSP colonies is not unexpected considering different husbandry regimes (including Na⁺ content of diet) and criteria for selecting breeding pairs.

2. Age of rats. We believe the age range used in our study is appropriate. Using TC and
telemetry, SHRSP start to develop hypertension from 6-8 weeks and by 12-16 weeks SBP levels out and significant differences in conscious BP are evident between SHRSP and WKY [5,6].

Yao’s point that infarct volume is higher in 5 month versus 10-12 week old SHRSP is interesting but may not be pertinent for proximal MCAO. Further, in the current study the comparison was between SHRSP and age-matched WKY.

3. We disagree with Yao’s statement that stroke-resistant SHR are a better model for this study (more stable in terms of lower mortality). Experimental stroke is known to be more severe in SHRSP compared to WKY, their normotensive control [7], but we did not experience any significant mortality issues. Increased stroke sensitivity is likely to be due not just to genetically-determined hypertension, but include additional genetic factors influencing cerebral vessels, oxidative stress levels and insulin resistance.

4. Penumbra. We concluded that SHRSP (not SHR as Yao states) had limited penumbra (based on PWI/DWI mismatch area) one hour after stroke, significantly smaller than WKY. We acknowledge the limitations of PWI/DWI mismatch for detecting penumbra since in both animal and human stroke some of the diffusion abnormality can be reversed upon early reperfusion. This could partly explain greater tissue rescue in the SHR study [8]. The stroke model used [8] may generate a greater % of penumbra: distal MCAO induces ischaemia in cortex, which has a collateral supply, while ischaemia induced by proximal MCAO [1] includes striatal end artery tissue resulting in a greater % of ischaemic core. The important point is that mismatch area in core MCA territory was significantly larger in WKY compared to SHRSP, which led us conclude that SHRSP have less potentially salvageable tissue.

References


