An in vitro microfluidic model of microglia migration after stroke

S. White[1,2], R. Plevin[1], M. Zagnoni[2] and H. Carswell[1]

[1]University of Strathclyde, Strathclyde Institute of Pharmacy and Biomedical Sciences, Glasgow, United Kingdom

[2]University of Strathclyde, Electronic and Electrical Engineering, Glasgow, United Kingdom

Abstract

Objectives: Microglia migrate to the site of ischemic insult in response to mediators such as glutamate and ADP being released from damaged or stressed cells and can exert both protective and detrimental effects[1]. Our present objective is to characterise microglia migration in vitro using a microfluidic model which allows precise chemical concentration gradients to be established over time, mimicking the release of mediators after stroke in vivo.

Methods: Microglial cell line, SIM-A9, were seeded in microfluidic culture chambers at 2.5×106 cells/ml for 24 hrs prior to exposure to concentration gradients of glutamate (100 µM) or vehicle (DMEM, control), with and without direct LPS (1µg/ml). Real time time-lapse imaging and cell tracking software were used to quantify cell migration velocity, and accumulated and Euclidean distance. Preliminary experiments analysed an average of 24 cell tracks per group (mean ± SD).

Results: Microglia were observed to migrate towards increasing chemical concentration gradients compared to control. This directionality effect was supported by an increased average number of cells entering the microchannels and an increased Euclidean distance towards the glutamate gradient versus control (170.36 ± 108.19 µM vs 35.5 ± 36.9 µm, respectively). Interestingly, the addition of direct LPS dampened down the increased Euclidean distance to 75.26 ± 53.5 µm. Compared to vehicle, a concentration gradient of glutamate induced a substantial increase in velocity which was further increased by the additional direct application of LPS (0.33 ± 0.18 µm/min vs 0.58 ± 0.15 µm/min vs 0.65 ± 0.18 µm/min, respectively). A similar pattern was observed for accumulated distance (372.8 ± 203.12 µm vs 651.02 ± 169.4 µm vs 730.4 ± 205.47 µm, respectively).

Conclusions: These results suggest that a pro-inflammatory environment limits glutamate-induced directionality and provide novel insight into dynamics of microglia responses after stroke.

References

[1]Patel et al., Int J Physiol Pathophysiol Pharmacol, 2013; 5, 73–90

This project is funded by BBSRC DTP.

Presented at the 28th International Symposium on Cerebral Blood Flow, Metabolism and Function / 13th International Conference on Quantification of Brain. Published as: White, S., Plevin, R., Zagnoni, M., & Carswell, H. (2017). An in vitro microfluidic model of microglia migration after stroke. *Journal of Cerebral Blood Flow and Metabolism*, *37*(1 (Suppl)). DOI: 10.1177/0271678X17695986