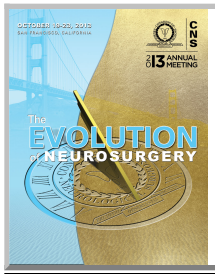

Evidence that Ly6Clow Macrophages Contribute to Spontaneous Recovery after Stroke

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Introduction

Understanding the mechanisms of post-stroke inflammation is essential to develop therapeutics that would promote recovery. Macrophages are known to promote both injury and repair in various pathologies, and these divergent properties may be due to different macrophage subtypes. Here, we investigated whether the brain macrophage subtypes alter the post-stroke outcome.

Methods

C57BL/6 mice (11-14 weeks old) were subjected to transient middle cerebral artery occlusion (tMCAo). Flow cytometry was used to analyze the immune cells in brain, blood. To deplete blood monocytes, clodronate filled liposomes (CL) were used. Phosphate-buffered saline (PBS)-filled liposomes (PL) served as controls. Lesion size was assessed by TTC at 2d post-stroke and silver staining at 7d post-stroke.

Results

A time-course analysis of immune cells after stroke identified two macrophage subpopulations in the brain with different temporal profiles: Ly6Chigh macrophages were the dominant cell population early after stroke, reaching a peak by 3d, and then decreasing in number by 5d. Conversely, the number of Ly6Clow macrophages were initially low and peaked by 5d. To investigate the effects of these cells, we used clodronate depletion of monocytes with different injection paradigms. Injecting clodronate 10 min plus 2d after stroke had no significant effect on infarct size at 2d and 7d post-stroke, or on functional deficit, compared to the PL group. However, when the injections were given every other day after stroke, from day 0 to day 6, CL-treated mice had significantly larger infarct sizes at 7d post-stroke (48.9±4.3 vs 35.6±5.8, % of contralateral hemisphere, n=10; $p<0.01$), and worse neurological scores (11.1±1.1 vs 6.2±1.1, n=10; $p<0.01$) than PL-treated mice. Furthermore, this injection paradigm resulted in significantly fewer Ly6Clow macrophages in the CL-treated group, suggesting a protective role for these cells.

Conclusions

Macrophage subtypes may have distinct roles in promoting brain damage and recovery after stroke.

Learning Objectives

By the conclusion of this session, participants should be able to understand the importance of macrophage subtypes for stroke.

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