International Journal of Neurorehabilitation

Cai et al., Int J Neurorehabilitation 2019, 6:2
DOI: 10.4172/2376-0281.1000348

Commentary Open Access

New Insights on the Role of Neutrophils in Ischemic Stroke

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Received date: April 05, 2019; **Accepted date:** April 22, 2019; **Published date:** April 29, 2019

Commentary

Recent study entitled with "functional dynamics of neutrophils after ischemic stroke" by Cai et al. has documented the important impact of neutrophil functions on stroke outcomes [1]. The authors demonstrated that neutrophil counts in the peripheral blood could be an early indicator of stroke outcomes. Neutrophil phenotypic shift, its self-clearance by microglia/macrophage, formation of neutrophil extra cellular traps (NETs) could all affect neuronal survival in stroke lesion. This work presents a dynamic and functional role of neutrophils in ischemic stroke.

Firstly, neutrophil, as forerunner in stroke lesion, reaches the first-hand danger-associated signals and infiltrates into stroke lesion in large scale, plays a vital role in the pathophysiological process of ischemic stroke [2-4]. Nevertheless, due to the sensitivity and short half-life of neutrophil, study on biological characteristics of neutrophils is difficult. As a result, advance of work on neutrophil functions is slow and our knowledge on the neutrophil behavior in stroke lesion is limited. The authors have performed a set of thorough investigation on the temporal and spatial dynamics of neutrophil after stroke, which has provided detailed and valuable information of the time courses of neutrophil behavior. Nevertheless, with the mentioned difficulty, the work by Cai et al., was mostly descriptive. Mechanical study in depth on neutrophil functions, including phenotypic shift, cross-talk with cells within stroke lesion, formation of NETs, etc., deserves a further investigation.

Secondly, the authors depicted time courses of neutrophil phenotypic shift after stroke. Phenotype of macrophage is controlled by multiple cell signaling, such as PPARγ pathway and STATs family [5-9]. Since previous studies have demonstrated that type II neutrophils (N2) was correlated with improved stroke outcomes [10,11], transcriptional factors that drive neutrophil phenotypic shift are worth studying in depth. It will be interesting to compare the similarity and difference between neutrophils and neutrophil/IL-17+ cells since the latter also involves in organ damage [12]. Additionally, regulatory T cells can target immune cells and non-immune cells [13-18], it will be very interesting to learn if regulatory T cells affect the phenotypic shift and function of neutrophils and then affect the outcome of stroke in the future. As far as we know, the benefits of N2 lies mainly on that the population facilitates self-clearance by microglia/macrophage. Therefore, alteration in metabolism, cell structure and cytoplasmic movement during neutrophil phenotypic shift and its crosstalk with microglia/macrophage are worth exploring. Dynamics of neutrophil phenotypic shift and its clearance by microglia/macrophage described by the authors should have afforded the basis.

Thirdly, formation of NETs is a process that combats invading microbes [19]. Surprisingly, NETs formation has been discovered in lesion of aseptic inflammation recently [20,21]. In the current study, the authors have documented the presence of NETs in stroke lesion, and further confirmed the detrimental role of NETs to neuronal survival. However, what triggers the formation of NETs, whether and how NETs contributes to progression of post-stroke neural inflammation, what is the impact of NETs to its self-clearance by microglia/macrophage, and so on still remain elusive. It has been reported that bio-markers of NETs pointed to worse stroke outcomes [22]. Thus, inhibiting NETs formation or accelerating clearance of NETs should be a promising therapeutic strategy for ischemic stroke. Exploring the mechanisms of NETs formation in stroke lesion is of vital significance.

In conclusion, neutrophil could be a key therapeutic target for stroke although our current knowledge on biological activities and features of this cell population is still insufficient. The current study has offered a basic information of neutrophil functions and behaviors alteration in stroke lesion. Nevertheless, many questions remain to be answered so as to better understand the irritable cell roles and to break a new pathway for stroke treatment.

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