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MINI-SYMPOSIUM: Astroglia in Neurodegenerative Diseases

Introduction

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INTRODUCTION

The progress in our understanding of neurodegenerative diseases is imperative for developing novel therapeutic strategies. Neurodegenerative diseases are defined by dysfunction of neurons as an early feature and neuronal loss as a consecutive step leading to complex neurological symptoms in particular presenting with, or converging to, cognitive disturbance. This definition emphasizes that neurons must be the primary target in the handling of these devastating disorders; therefore much of the research efforts have been directed, without breakthrough success, toward developing neuroprotective therapies. However, neurons are not alone: the central nervous system consists of a variety cells including astroglia, oligodendroglia, and microglia. Initial studies using silver staining demonstrated that oligodendroglia, similarly to neurons, can be affected by inclusion body pathology as exemplified by the α-synucleinopathy multiple system atrophy (7). Subsequently, protein depositions have been reported by immunohistochemical methods in astroglial cells. In particular, protein pathology is now regarded as central to the pathogenesis of most of the adult-onset neurodegenerative conditions (2); therefore protein deposits in oligodendroglia and astroglia have been considered relevant for the pathophysiology. In addition, description of tau pathology in astrocytes in chronic traumatic encephalopathy or in aging, known as aging-related tau astrogliopathy (ARTAG), as well as the discovery of astroglial tau accumulation as an early event in the pathogenesis of a primary tauopathy, corticobasal degeneration, prioritized the need for an update on this topic (3, 6).

This mini-symposium highlights three active areas of investigation in astroglia pathophysiology. The first is a publication by *Alexei Verkhratsky*, *Robert Zorec*, and *Vladimir Parpura*, which focuses on the "Stratification of astrocytes in healthy and diseased brain" (8). Classification of astrocytes is presented with the emphasis on evolutionary traits, morphological appearance and numerical preponderance. Beginning with the ancient forms of neuroglia, characterized in round worms and in the Acoela worms, authors provide a systemic overview expanding the complexity of astroglial cells in the human brain that can be identified and visualized based on morphological criteria and expression of specific markers. The paper discusses the numbers of astrocytes, their role in cognitive capacity, provides an overview of glioma models, and finally proposes a classification of astrogliopathies, including astrodegeneration, pathological remodeling and reactive astrogliosis. This is followed by the review article by *Isidro Ferrer* entitled "Diversity of astroglial responses across human neurodegenerative disorders and brain aging," which provides a captivating summary of observations and the reader will not question anymore the importance of these homeostatic cells in the physiology and pathophysiology of the CNS (1). This paper provides a list of major physiological functions of astrocytes, defines astrogliopathy as a seminal concept of gliodegeneration, categorized as reactive gliosis and astrocytopathy. An exhaustive overview of functional disturbances and deficits in different neurodegenerative diseases follows this classification. Isidro Ferrer concludes that a role of astrocytes in the seeding and transfer of abnormal proteins, and in the progression of neurodegenerative diseases ought to be considered. This thought leads to the third paper of the Mini-Symposium by *Gabor G. Kovacs, Virginia M. Lee,* and *John Q. Trojanowski*. Authors introduce the term protein-astrogliopathy (PAG) and collect literature data and personal observations showing that astroglial deposition of amyloid-β, prion protein, tau, α-synuclein, and very rarely transactive response DNA-binding protein 43 (TDP-43) is not unprecedented in neurodegenerative diseases (4). They discuss the relevance of PAG for the classification of neurodegenerative diseases and focus on tau pathologies involving astrocytes in a wide range of disorders, in particular the aging brain. It is tempting to speculate on a conceptual link of tau immunoreactive astroglial morphologies (5). Finally, overlapping features of astroglial protein depositions are highlighted.

In summary, this mini-symposium presents the recent progress that has been made in our understanding of the heterogeneity of

astrocytes in the mammalian and human brain, their role in neurodegenerative conditions and the spectrum of various astrocytic protein depositions. These aspects reveal that considerable progress has been made in spite the fact that this research area still falls behind neuron-centric approaches to understand neurodegenerative conditions. The summary of recent advances offer the potential to consider novel targets for therapies that preserve neuronal function by providing support to the supporters of neurons or alternatively result in the protraction of the spreading of pathological proteins associated with neurodegenerative diseases.

CONFLICT OF INTEREST

Author reports no conflict of interest.

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