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Literature reviews

Little-known neurons of the medial wall: a literature review of pyramidal cells of the cingulate gyrus

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Abstract

Objective: The purpose of this article is to provide an overview of the current state of knowledge of poorly understood and underresearched neuroanatomy of selected pyramidal cells of the medial wall of the cingulate gyrus.

Methods: A literature review was performed; and separate computerized literature searches of PubMed, Science Direct, Cochrane Library, Science Citation Index, SCOPUS, CINAHL, and the World Wide Web were used for each cell type using individual set time scales for the discovery of each cell. A narrative overview of the literature was developed using information from searches of computerized databases and authoritative texts.

Discussion: The medial walls of the cerebral hemispheres, notably the cingulate gyri, contain species-specific neuron fields that to date are not well known within the scientific community and yet have been implicated as the underlying cause of such varying conditions as dysgraphia and autism in children and obsessive-compulsive disorder and Alzheimer disease in adults. As these neurons are late to develop both phylogenetically and ontogenetically, it has been suggested that they may be particularly vulnerable to stressors that potentially could be an underlying factor in a wide range of neurodevelopmental and neuropsychiatric disorders.

Conclusion: It is considered that knowledge of these little-known pyramidal fields of the medial wall of the human brain is essential to the understanding of how the brain functions both in sickness and in health.

Introduction

The cingulate gyri of the medial wall of the cerebral hemispheres contain neuron fields that are limited to certain species and that vary in numbers present and in both their structure and columnar arrangement. They

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are also unevenly distributed between the hemispheres, with a greater dominance of von Economo neurons (VENs) having been described in the right hemisphere of the human brain and those of certain great apes.[1-6] Only 15% of the total adult population of VENs are present at birth, the remaining 85% developing in a window between 4 months and 4 years postnatally. This puts them among a unique group of neurons known to develop postnatally.[7] The presence of these neuron fields within the cingulate gyrus also lends weight to the argument that the cingulate gyrus should be considered as being isocortex as opposed to proisocortex.[4,8] The gigantopyramidal field buried in the depth of the cingulate sulcus has been shown to be involved in the planning and execution of the fine motor control of the fingers, and the delayed development of these fields may explain why some children struggle to learn to write and use a fist grip.[4,9] Calcium-binding calretinin neurons of the anterior cingulate like VENs have been found to be species specific, to date only having been found in the anterior cingulate of the human brain and that of the great apes.[10] Furthermore, in common with VENs, their numbers increase stepwise, the lowest numbers being found in the orangutan, followed by the gorilla, then the chimpanzee, with the highest numbers being found in the human brain. Little is known concerning the precise function of the calcium-binding calretinin neurons of the anterior cingulate; but it has been suggested that they may be discrete projection neurons to specific motor centers involved with the control of vocalization, facial expression, and autonomic function.[10]

Although some of these cells were described as early as 1881, they have remained in relative obscurity until 1995; since then, interest in them has increased, leading to further research that potentially has far-reaching possibilities in terms of treatment of many neurodevelopmental/neuropsychiatric disorders. The purpose of this literature review is to provide a summary of the current literature that described these neurons.

Methods

Information was collected using a selective sampling strategy from the following sources using the Boolean operators (*von Economo cells* OR *spindle cells*) AND *anterior cingulate*; *von Economo neurons* AND *infraorbital area* OR *frontal pole*) AND *gigantopyramidal cells* AND *cingulate gyrus* AND *calcium-binding calretinin cells* AND *handedness* and was fully reported. Separate computerized literature searches of PubMed, Science Direct, Cochrane Library, Science Citation Index, SCOPUS, CINAHL and the World Wide Web were used for each cell type using individual set time scales for the discovery of each cell. The temporal fields were 1925-2009 for VENs, 1976-2009 for gigantopyramidal cells, and 2001-2009 for Ca-binding calretinin cells. Articles chosen were limited to those concerning human studies, the great apes, cetaceans, dolphins, and the African and Indian elephants. Only articles published or translated into English were included. Hand searches of the references of retrieved literature were carried out by the authors. Texts and articles on second-generation neuron by the authors were also reviewed.

Results

von Economo neurons

History

von Economo neurons were first described by Betz[11] but were later described in detail by von Economo et al.[1] However, they remained in relative obscurity until 1995, when an article by Nimchinsky et al led to renewed interest in these cells that in turn led to numerous articles being published concerning their location,[2,3,12,13] species in which they had been found,[3,6,12,14] their structure,[15,16] possible functions, and their role in various neuropsychiatric conditions.[2,7,17,18] They were known as *spindle cells* until 2005, when Allman renamed them as *von Economo neurons* in honor of von Economo's work and to avoid confusion with the accepted use of the term in the field of oncology. In 2008, they were also reported to be present in the dorsolateral prefrontal cortex of humans.[13]

Phylogeny

Originally, spindle cells were described by Betz[11]; but a more detailed description was provided by von Economo, particularly in terms of their location in limited areas of the cortex, namely, the anterior cingulate gyrus and the anterior region of the insula of the human brain.[1] It was not until 1995 that spindle cells were studied using modern neuroanatomical methods, namely, computer-assisted mapping and immunocytochemical techniques.[2] In 1999, it was reported that spindle cells had been found in layer Vb of the anterior cingulate cortex of pongids and hominids.[12] It was also