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Effect of age on neocortical brain cells in 90+ year old human females—a cell counting study

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Abstract

An increasing number of people are living past the age of 100 years, but little is known about what differentiates centenarians from the rest of the population. In this study, brains from female subjects in 3 different age groups, 65–75 years ($n = 8$), 76–85 years ($n = 8$), and 94–105 years ($n = 7$), were examined to estimate the total number of neocortical neurons, astrocytes, oligodendrocytes, and microglia. There was no statistically significant difference in the mean number of neocortical neurons between the 3 groups: 17.9×10^9 (CV = SD/mean = 0.15) in the youngest group, 18.1×10^9 (CV = 0.22) in the second group, and 16.32×10^9 (CV = 0.24) in the oldest group. However, there was a significant difference in the total number of neocortical glial cells between the youngest (41.0×10^9) and oldest (29.0×10^9) age groups ($p = 0.013$). The significance was probably driven by a significant difference in the total number of neocortical oligodendrocytes that differed significantly between the youngest (27.5×10^9) and oldest ($18.1. \times 10^9$, $p = 0.006$) age groups. In conclusion, very old individuals have brain neuron numbers comparable with younger individuals, which may be encouraging for those who live into the "fourth age" and may contribute to the longevity of this exceptional group of people.

Keywords: Cell count; Human; Stereology; Normal aging; Neocortex

1. Introduction

Human beings are among the longer-lived species of animals, with an average life expectancy of up to 85 years in certain countries. Some individuals in the population, however, have exceptionally long life spans exceeding 100 years. This phenomenon of people living past 100 appears to be fairly recent. For example, the first verified centenarians lived in the 18th century, while supercentenarians, who exceed 110 years of age, have not been documented prior to 1950. The oldest known individual in the world to date, Jeanne Calment of France, died in 1997 at the age of 122 years (Jeune and Andersen-Ranberg, 1999). The factors contributing to human longevity are not known, but such drastic changes in lifespan over such a short period of time are most likely environmental rather than genetic.

Although the aged brain retains some capacity for plasticity, it is subject to degeneration and atrophy. Longitudinal magnetic resonance imaging studies have reported a 0.2%–0.5% annual decrease in gross brain volume (Ezekiel et al., 2004; Scahill et al., 2003). Stereological postmortem studies of the brain show an even higher rate of brain volume loss, with decreases of 12.3% for neocortical volume, 12.2% for total brain weight, and 28% for white matter volume between age 20 and 90 years (Pakkenberg and Gundersen, 1997). Though volume reduction does not necessarily imply neuronal loss, it is estimated that total neocortical neuronal number is reduced by 9.5% from age 20 to 90 years (Pakkenberg and Gundersen, 1997). In subcortical regions such as the hippocampus, specific regions show age-related neuronal loss of up to 67% (Simic et al., 1997; West and Gundersen, 1990). Furthermore, the length of subcortical myelinated fibers decreases by 45% between the ages of 20 and 80 years (Marner et al., 2003). However, no

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studies have compared neocortical neuronal number between old and very old individuals.

Most basic research on the mechanisms of aging have studied species that are short-lived and therefore not successful at combatting the aging process (Austad, 2009). However, focusing instead on a species, as well as individuals within that species, with long, healthy lives may shed light on the mechanisms that distinguish them from their shorter-lived relatives. Here, we compared the total number of neocortical neurons and glia in the brains of very old women and younger women.

2. Methods and materials

For this study, 24 brains from normal female Danes were selected from a large Danish brain bank formed for the purpose of stereological research. All brains were collected in accordance with Danish laws governing the use of postmortem tissue in research. One sample had to be excluded for technical reasons, leaving 23 samples divided into the following 3 age groups: Group 1: average age 71.5 years, range 65–75 years ($n = 8$); group 2: average age 81.4 years, range 76–85 years ($n = 8$); and group 3: average age 98.0 years, range 94 to 105 years ($n = 7$). Samples were excluded from the study if the individual suffered from diseases that might affect the central nervous system, such as dementia or neurodegenerative illnesses, cerebrovascular diseases, metastatic cancer, diabetes, hypertension, or abuse of alcohol or drugs (Table 1). The health of the individuals was assessed by examination of donors' hospital and general practitioner files as well as autopsy reports. Although

Table 1
Personal data for tissue donors in the present study

Age (y)	Origin	Body height (cm)	Body weight (kg)	Total weight of brain (g)	Cause of death or other diagnosis at time of death	Postmortem evaluations
65	NL	—	—	1200	Respiratory insufficient	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD for all individuals between 65 to 75 y.
70	DK	139	55	1150	Bronchopneumonia, cor pulmonale	
71	DK	167	95	1600	Rupture of aorta, aneurism, atherosclerosis	
72	DK	156	53	1160	AMI	
72	DK	183	81	1400	Pulmonary embolism, pancreatitis	
73	DK	177	51	1230	AMI	
74	NL	—	—	1200	AMI	
75	DK	159	60	1150	AMI, aorta stenosis	
77	DK	162	55	1330	AMI, myocardial rupture	Few scattered tangles in neocortex; art. sclerosis replace with: arteriosclerosisart. sclerosis cerebri
78	DK	154	59	1195	Pneumonia	Multiple plaques and tangles in neocortex
80	DK	162	47	1170	Mitral insufficiens, morbus cordis	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
81	DK	157	51	1090	AMI	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
83	DK	146	46	1100	Congestive heart failure	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
83	DK	160	71	1080	AMI	Few scattered tangles. No AD, no LBD, no multi-infarct; normal pathology for that age
84	DK	155	67	1265	AMI	Sequela after cortical microinfarct in insula
85	DK	159	39	1180	AMI	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
94	DK	151	73	1112	Bronchopneumonia, morbus cordis	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
95	DK	—	—	940	Coronary occlusion	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
95	DK	151	69	1180	AMI	Widespread plaques and tangles in neocortex
97	DK	153	36	1000	Pneumonia, morbus cordis	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
98	NL	—	—	1170	Congestive heart failure	The neocortex contains no classical plaques and no sign of neurofibrillary degeneration. The substantia nigra contains normally pigmented cells. There is no Lewy degeneration
102	DK	—	—	—	Congestive heart failure	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD
105	DK	150	44	1129	Congestive heart failure	No plaques or neurofibrillary tangles in neocortex. Negative for AD, vascular disease, and PD

Key: AD, Alzheimer's disease; AMI, acute myocardial infarction; DK, Denmark; LBD, Lewy body disease; NL, The Netherlands; PD, Parkinson's disease.