

# MORPHOLOGY OF THE HUMAN PINEAL GLAND IN RELATION TO AGE AND SEX

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## ABSTRACT

Plasma concentration of melatonin - the hormone secreted by the human pineal gland is highest in children between 1 and 3 years of age. In the next age groups its levels decrease and in adults they are by approximately 80% lower. These drastic age differences in the function of the pineal gland made us hypothesize that some structural differences in it related to age and sex can be expected. The aim of this study was to investigate the macroscopic and microscopic characteristics of the pineal gland in relation to age and sex. Some 126 pineal glands were observed and histologically studied. Of them, 87 were taken from men and 37 from women with mean age of 52,65 (from 20 to 95) years. Slices of 5  $\mu$  were cut from paraffin blocks, stained with hematoxylin and eosin and microscopically examined. Data was analysed with standard statistical procedures. No gender-related differences in the macroscopic characteristics and the histologic structure of the pineal gland were identified. Age was not related to the macroscopic characteristics of the pineal gland, too. However, some differences in the histologic structure of the gland in relation to age were observed. Partially defined pseudolobes prevailed in the glands of younger people, while with increasing age glands with well-defined pseudolobes were more common.

**Key words:** pineal gland, age, sex, histology

There are no daily fluctuations in the levels of plasma melatonin after birth. Secretion of the hormone is gradually increased around the third month after birth. Highest levels of plasma melatonin are observed in children between 1 and 3 years. In the next age groups its levels decrease and in adults they are by approximately 80% lower (13). In the senile period, melatonin secretion continues to decrease which is discussed as one of the possible factors contributing to degenerative changes in the elderly. According to some theories for aging, this process is a result of free radicals (11) or nitrogen oxyde (9) accumulated in the body in parallel to the decreasing plasma melatonin levels. According to other theories, melatonin has a protective effect for diseases that are more common at old age such as ischemic heart disease, malignant neoplasms, Alzheimer disease, etc. Decreasing melatonin secretion is discussed as a cause for the above diseases by some authors (3). Besides the functional changes and some morphological changes have been described in the innervation of the pineal gland (6) such as accumulation of phosphorylated neurofilaments (10), lipofuscin and microacervulus in the pinealocytes (2). It remains not clarified if there are changes in the structural characteristics of the pineal gland in relation to age and sex.

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The present study is undertaken with the aim to answer the following questions:

1. Is there a difference in the macroscopic characteristics of pineal glands between males and females?
2. Is there a difference in the presence of the main histological structures of the gland between men and women?
3. Are there changes in the macroscopic characteristics of the pineal glands related to age?
4. Are there changes in the histological structure of the pineal glands related to age?

## MATERIALS AND METHODS

A total of 126 pineal glands was observed and histologically studied. The glands were obtained from people who died as a result of violence or disease and to whom autopsy was done in the Department of General and Clinical Pathology or in the Department of Forensic Medicine and Deontology at Prof. Paraskev Stoyanov Medical University of Varna during the period from September 2002 till March 2003. Of them, 87 were taken from men and 37 from women at a mean age of 52,65 (from 20 to 95) years. Before fixation of the material, size, volume, weight and density of the glands were measured. After fixation with 10% neutral formaldehyde solution, slices of 5  $\mu$  were cut from paraffin blocks, stained with hematoxylin and eosin

and microscopically examined. Data was analysed by using standard statistical procedures.

## RESULTS AND DISCUSSION

The five main structural components of the pineal glands are equally represented in men and women (Table 1).

Table 1. Structural components of the pineal glands in relation to gender

No	Characteristics	Men		Women			
		n	P	n	P	t	P
1	Capsule						
	Gentle	75	58.33	28	57.14	0.10	n.s
	Thick	75	41.66	28	42.85	0.10	n.s
2	Acervulus	75	65.67	28	74.34	0.86	n.s
3	Pseudolobs						
	Not defined	75	37.50	28	57.14	1.79	n.s
	Partially defined	75	30.55	28	17.85	1.38	n.s
	Well defined	75	31.94	28	25.00	0.70	n.s
4	Gliososis	75	50.00	28	50.00	0.00	n.s
5	Cysts	75	17.80	28	21.42	0.40	n.s

Same results were obtained for the four main macroscopic parameters (Table 2).

Table 2. Main macroscopic parameters of the pineal glands in relation to gender

Characteristics	men		women		P
	n	X±	n	X±	
Length (mm)	72	8.22±0.88	28	8.98±1.42	n.s
Width (mm)	72	6.25±0.65	28	5.88±1.04	n.s
Weight (mg)	67	124.67±25.45	26	154.66±41.77	n.s
Density (kg/m <sup>3</sup> )	67	3.74±1.33	26	2.33±1.82	n.s

The material was separated in two groups according to age: glands taken from people who died in the age of 20-39 years and those who died at 40 and above. Thick capsule, acervulus, gliosis and non-tumour cysts were equally represented in the glands of both groups. Formation of pseudolobs appeared to be more interesting. The percentage of glands with partially defined pseudolobs was approximately two times bigger in the age group 20-39 years, while the percentage of glands with well-defined pseudolobs was by about three times bigger in the age

group over 40 (Table 3). The percentage of pineal glands without pseudolobs was equal in both age groups. There was a clear tendency of increasing frequency of glands with well-defined pseudolobs with age and decreasing frequency of glands with partially defined pseudolobs. This fact deserves special attention in future.

Table 3. Structural characteristics of the pineal glands according to age

Characteristics	20-39 years		> 40 years				
	n	P	n	P	t	P	
1. Thick capsule	19	36.84	101	45.54	0.71	n.s	
2. Acervulus	19	89.47	101	78.21	1.38	n.s	
3. Pseudolobs							
	Not defined	19	42.10	101	38.6	0.20	n.s
	Partially defined	19	47.36	101	23.76	1.96	<0.05
	Well defined	19	10.52	101	36.63	3.07	<0.05
4. Gliosis	19	42.10	101	52.48	0.84	n.s	
5. Cysts	19	15.79	101	27.72	1.26	n.s	

Macroscopic characteristics are equally represented in the glands of both age groups (Table 4).

Some authors report significant changes in the structure of acervulus in a small number of cases with increasing age. The concentration of phosphorus decreases while that of calcium increases. Some changes in the brain sand with increasing age are observed by metalography (12).

A large study of 2700 human pineal glands (4) reports a lack of atrophic changes and of changes in the number of pinealocytes, the frequency of acervulus, gliosis and cysts with increasing age, while they find some sex related differences. No changes in the weight of the gland have been reported after the age of 10 years. In an other study of 167 pineal glands no difference in the weight of pineal glands in relation to age and gender was found. The same authors report a statistically significant correlation between the weight of the glands and the availability of acervulus as well as lack of correlation between the level of calcification and availability of cysts and lack of involution related to age (5). Age-related accumulation of acervulus in combination with lipofuscin in the histochemical and ultrastructural study of pineal glands could not be proved (2). In an experimental material age-related thickening and fibrotic changes of the pineal capsule and gliosis were observed (7) along with increasing number of myelin filaments of the capsule (8).

The results of our study agree with those of other authors (2,4,5) and do not match with the conclusions of other authors (7,8). We can suggest that the influence of the species specificity on morphology is the cause of this mismatch.

Table 4. Macroscopic characteristics of the pineal gland in the age groups 20-39 and 40 and above

Characteristics	20-39 years		> 40 years			
	n	X ± Δ	n	X ± Δ	t	P
Length (mm)	19	9,39 ± 1,68	107	8,88 ± 0,71	0,78	n.s
Width (mm)	19	6,94 ± 1,19	107	6,44 ± 0,49	1,08	n.s
Weight (mg)	18	184,83 ± 54,61	98	146,03 ± 23,37	1,83	n.s
Density (kg/m <sup>3</sup> )	18	2,81 ± 2,21	98	2,96 ± 0,92	0,18	n.s

## CONCLUSIONS

1. There are no gender-related differences in the macroscopic characteristics and the histologic structure of the pineal glands.
2. Age is not related to the macroscopic characteristics of the pineal glands.
3. In the glands of younger people partially defined pseudolobes prevail while with increasing age glands with well-defined pseudolobes are more common. The other characteristics are equally represented in the gland of both age groups.

## REFERENCES

1. Ferrari, E., A. Arcaini, R. Gornati, L. Pelanconi, L. Cravello, M. Fioravanti, S. B. Solerte, F. Magri. Pineal and pituitary-adrenocortical function in physiological aging and in senile dementia.- *Exp. Gerontol.*, **35**, 2000, No 9-10, 1239-1250.
2. Galliani, I., F. Frank, P. Gobbi, F. Giangaspero, E. Falcieri. Histochemical and ultrastructural study of the human pineal gland in the course of aging.- *J. Submicrosc. Cytol. Pathol.*, **21**, 1989, No 3, 571-578.
3. Grad, B. R., R. Rozenzweig. The role of melatonin and serotonin in aging: update.- *Psychoneuroendocrinology*, **18**, 1993, No 4, 283-295.
4. Gusek, W. Histology of the pineal gland in the elderly human.- *Aktuelle Gerontol.*, **13**, 1983, No 3, 111-114.
5. Hasegawa, A., K. Ohtsubo, W. Mori. Pineal gland in old age: quantitative and qualitative morphological study of 167 human autopsy cases.- *Brain Res.*, **409**, 1987, 343-349.
6. Jengeleski, C. A., R. E. Powers, D. T. O'Connor, D. L. Price. Noradrenergic innervation of human pineal gland: abnormalities in aging and Alzheimer's disease.- *Brain Res.*, **481**, 1989, No 2, 378-382.
7. Johnson, J. E., Jr. Fine structural alterations in the aging rat pineal gland.- *Exp. Aging Res.*, **6**, 1980, No 2, 189-211.
8. Kawai, Y. Light microscopic observations on intrapineal neurons and myelinated fibers distributed in the pineal gland and its capsule in cotton rats (*Sigmodon hispidus*) at various postnatal ages.- *Hokkaido Igaku Zasshi*, **65**, 1990, No 5, 517-528.
9. McCann, S. M., J. Licinio, M. L. Wong, W. H. Yu, S. Karanth, V. Rettorri. The nitric oxide hypothesis of aging.- *Exp. Gerontol.*, **33**, 1998, No 7-8, 813-826.
10. Pardo, C. A., L. J. Martin, J. C. Troncoso, D. L. Price. The human pineal gland in aging and Alzheimer's disease: patterns of cytoskeletal antigen immunoreactivity.- *Acta Neuropathol. (Berlin)*, **80**, 1990, No 5, 535-540.
11. Reiter, R. J., D-X. Tan, B. Poeggeler, A. Menendez-Pelaez, L-D. Chen, S. Saarela. Melatonin as a free radical scavenger: implications for aging and age-related diseases.- *Ann. N. Y. Acad. Sci.*, **719**, 1994, 1-12.
12. Schmid, H. A., G. Raykhtsaum. Age-related differences in the structure of human pineal calcium deposits: results of transmission electron microscopy and mineralographic microanalysis.- *J. Pineal Res.*, **18**, 1995, No 1, 12-20.
13. Waldhauser, F., B. Ehrhart, E. Forster. Clinical aspects of the melatonin action: impact of development, aging, and puberty, involvement of melatonin in psychiatric disease and importance of neuroimmunoendocrine interactions.- *Experientia*, **49**, 1993, 671-681.