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DOI

[10.1016/S0344-0338\(86\)80149-2](https://doi.org/10.1016/S0344-0338(86)80149-2)

Publication date

1986

Published in

Pathology, Research and Practice

[Link to publication](#)

Citation for published version (APA):

Stam, F. C., Wigboldus, J. M., & Smeulders, A. W. M. (1986). Age incidence of senile brain amyloidosis. *Pathology, Research and Practice*, 181, 558-562. [https://doi.org/10.1016/S0344-0338\(86\)80149-2](https://doi.org/10.1016/S0344-0338(86)80149-2)

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Age Incidence of Senile Brain Amyloidosis

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SUMMARY

Neuropathological examination of 1400 successive autopsies in general and mental hospitals revealed that senile plaques and congophilic angiopathy are age related phenomena. There is, however, a remarkable difference between the two types of manifestation of senile amyloidosis. There was a significantly higher incidence of senile plaques in females. Moreover the increase of the incidence with age was also significantly higher in females. Congophilic angiopathy showed no predominance in females. In total 59% of males and 55% of females with senile plaques suffered from Senile Dementia of the Alzheimer Type (SDAT). SDAT appeared to be also an age related phenomenon characterized by a linear increase with age and a predominance in females.

Introduction

In the senile human brain amyloid occurs in the central core of senile plaques² and in the walls of leptomeningeal and cortical arteries and arterioles^{2,6} (Fig. 1). The presence of senile plaques is an inconstant feature in the cortex of the elderly brain.

Fischer³ found plaques only in patients suffering from senile dementia. Simchowicz⁸ (1911), however, found them also in the brain of non demented elderly people. In his opinion senile dementia is the expression of an accelerated normal aging of the brain. This statement is still an actual problem. Terry¹⁰ (1978) pointed out that it is quite possible that there is a continuous spectrum between normalcy and dementia. In his opinion senile dementia of the Alzheimer type is a threshold phenomenon. When a particular concentration of lesions is reached, a particular degree of transmitter loss is attained, or there is a sufficient loss of dendritic arbor, then functional loss becomes increasingly apparent. Most members of the population, however, never reach these negative thresholds. It is plausible that a number of elderly people nearly reach the negative thresholds. These people form a risk group. It is a well known clinical fact that the clinical manifestation of senile dementia can be provoked by head injury, narcosis

Fig. 1. Amyloid cores in senile plaques. Thioflavine-S $\times$ 125.

and psychotraumatata. It is plausible that in these cases senile degeneration of the brain had already nearly reached the thresholds. The vascular amyloidosis or congophilic angiopathy is a disorder characterized by deposits of amyloid in the media and intima of the arteries and arterioles of the brain and meninges. Some authors supposed a possible relationship between the amyloid in senile plaques and in cerebral vessels. Schwartz⁷ was of the opinion that the amyloid in senile plaques originates by seepage through cortical arteries. This hypothesis seems to be supported by the presence of plasma proteins in the amyloid core of senile plaques⁶.

However, senile plaques can be found without demonstrable vascular amyloidosis and congophilic angiopathy can occur without plaque formation⁴. Consequently the relationship between congophilic vessels and plaque formation is still an open question. In this study we will analyse the incidence of senile plaques and congophilic angiopathy in the 6th to 10th decades of life. The results of this analysis will be compared with a study of the clinical records of the patients in order to obtain an impression of the relationship between senile brain amyloidosis and senile dementia of the Alzheimer type.

Material and methods

In order to obtain data about the age incidence of senile amyloid we examined 1400 successive autopsies from different types of hospitals. The autopsies in the different hospitals were divided into autopsies of patients under and over age 50 (Table I). The highest percentage of autopsies of patients over age 50 was found in the mental hospital, as could be expected. The total number of 1400 autopsies included 714 males and 686 females. Table II illustrates the distribution over the decades of life. In all 1400

autopsies the brain was examined. Tissue was taken from frontal, parietal and temporal lobes. 4–5 μ thick sections of the paraffin embedded material were made and stained with hematoxylineosin, congo-red, copper phthalocyanin (Klüver) and Bielschowsky's silver technique. In the stained sections the presence or absence of senile plaques with amyloid cores and of congophilic vessels was studied. A quantitative approach was deliberately omitted. We were only interested in the presence or absence of senile brain amyloidosis. Using the linear regression analysis it was tested whether the incidence in this dataset increases linearly with age or not.

Results

In our study we did not find senile plaques or congophilic angiopathy under the age of 50 years. Senile plaques were found in 41% of 1216 autopsies of people aged over 50 years and congophilic angiopathy was found in 13.5%. We did not find congophilic angiopathy in cases without senile plaques. The specification of the results per decade is rendered in Table III and IV and illustrated in Fig. 2. This figure strongly suggests that the incidence of senile amyloidosis increases with age. The data of the linear regression analysis are summarized in Table V. From the figures in the first column we may conclude that the incidence of senile plaques and congophilic angiopathy indeed increases linearly with age. This means that in each decade approximately the same percentage, given in the second column, is added to the percentage of the incidence in the preceeding decade. By extrapolation it is possible to estimate the age in which no incidence of senile amyloidosis could be expected. From the third column we may deduce that in our dataset no manifestation of senile amyloidosis could be expected before the age of 52 years. In

Table 1. 1400 autopsies in different types of hospitals

	under age 50	over age 50	total	percentages of autopsies over age 50
University hospital	96	454	550	82.5%
Neuropsychiatric clinic	59	241	300	80.3%
Mental hospital	29	521	550	94.7%
Total	184	1216	1400	84%

Table 2. Distribution of autopsies over the decades of life in different types of hospitals

Decades	University hospital		Neuropsychiatric clinic		Mental hospital		total	
	♂ ♂	♀ ♀	♂ ♂	♀ ♀	♂ ♂	♀ ♀	♂ ♂	♀ ♀
0–6	55	41	37	22	18	11	110	74
6	44	36	26	14	31	25	101	75
7	107	62	45	42	44	61	196	165
8	75	62	44	31	90	121	209	214
9	30	35	16	21	42	90	88	146
10	1	2	1	1	8	9	10	12
1400 autopsies	312	238	169	131	233	317	714	686

Table 3. Percentage of cases with senile plaques in 1216 autopsies of patients aged over 50 years

Decades	Number of autopsies			Number of cases with senile plaques			Percentage		
	♂♂	♀♀	total	♂♂	♀♀	total	♂♂	♀♀	total
6	101	75	176	8	4	12	7.9	5.3	6.8
7	196	165	361	33	41	74	16.8	24.8	20.4
8	209	214	423	93	129	222	44.4	60.2	52.4
9	88	146	234	56	115	71	63.6	78.7	73
10	10	12	22	8	12	20	80	100	90.9
Total	604	612	1216	198	301	499	32.7	49.2	41

Table 4. Incidence of congophilic angiopathy

Decades	Number of cases			Percentage		
	♂♂	♀♀	total	♂♂	♀♀	total
6	5	3	8	4.9	4	4.5
7	10	12	22	5.1	7.3	6.1
8	34	37	71	16.3	17.3	16.8
9	21	33	54	23.9	22.6	23.1
10	6	4	10	60	33.3	45.5
	76	89	165	12.6	14.5	13.6

Table V, between brackets, 95% confidence margins are indicated. Due to the number of observations these margins are very small.

Another important result of this study is the evidence of a significantly higher incidence of senile plaques in females. Moreover the increase of the incidence with age is significantly higher in females ($p > 0.99$).

The incidence of congophilic angiopathy, as may be increase in females is $26.0 \pm 0.3\%$.

The incidence of congophilic angiopathy, as may deduced from linear regression analysis, is significantly higher in males than in females ($p > 0.99$). This difference between males and females is predominantly due to the

Fig. 2. Occurrence of senile plaques and congophilic angiopathy in 1216 autopsies.

observations in the 10th decade. Removing these data from the set, the sex difference nearly vanishes ($7.3 \pm 0.2\%$ in males and $6.9 \pm 0.1\%$ in females). As has already been mentioned before, congophilic angiopathy was never found in the absence of senile plaques. This implies that 42% of males and 27% of females with senile plaques also had congophilic angiopathy.

Table 5. Statistical linear regression analysis of the data displayed in Figure 1 and 2. The numbers in brackets indicate the 95% confidence region

	Goodness of fit	Increase of incidence per decade	Estimated zero incidence (years of age)
♀♀ Senile plaques	0.99	26.0% (25.7%–26.3%)	54.1 (53.9–54.4)
♀♀ Congophilic angiopathy	0.98	7.1% (6.9%– 7.2%)	53.1 (52.7–53.4)
♀♀ SDAT	0.97	14.4% (14.1%–14.8%)	56.1 (55.7–56.4)
♂♂ Senile plaques	0.98	20.2% (19.9%–20.5%)	54.6 (54.3–54.9)
♂♂ Congophilic angiopathy	0.89	8.5% (8.2%– 8.9%)	59.0 (58.3–59.6)
♂♂ SDAT	0.92	11.9% (11.4%–12.2%)	58.0 (57.5–58.6)

Fig. 3. Occurrence of senile dementia (SDAT) in patients showing senile plaques.

Table 6.

Percentage SDAT in patients with senile plaques without congophilic angiopathy			Percentage SDAT in patients with plaques and congophilic angiopathy		
Decades	♂ ♂	♀ ♀	Decades	♂ ♂	♀ ♀
6	33.3%	100%	6	60%	100%
7	21.7%	27.6%	7	60%	66.6%
8	52.5%	40.2%	8	79.4%	78.4%
9	31.4%	46.3%	9	76.2%	72.7%
10	50%	75%	10	83.3%	75%

A very important social aspect of senile amyloidosis is the relationship with a clinical manifestation of senile dementia of the Alzheimer type (SDAT).

In Figure 3 the incidence of SDAT is illustrated together with the graph illustrating the incidence of senile plaques. Linear regression analysis (Table V) revealed that the incidence of SDAT and the increase of the incidence per decade is higher in females than in males ($14.4 \pm 0.4\%$ in females, $11.9 \pm 0.5\%$ in males). This difference was significant ($p > 0.99$). As in our dataset no cases of SDAT were found in the absence of senile plaques, it may be concluded that 59% of males and 55% of females with senile plaques suffered from SDAT. These percentages were approximately the same in the various decades.

Table VI illustrates that the highest percentages of SDAT were found in cases showing senile plaques and congophilic angiopathy.

Discussion

The results of this study are only valid for people who died in general and mental hospitals of the Netherlands and can not be used as the reflection of the incidence of senile amyloidosis in the general population. Post mortem examination, however, is until now the only possibility to get information about the incidence of senile amyloidosis.

From our dataset we may conclude that senile plaques and congophilic angiopathy are age related phenomena.

From the linear regression analysis we may conclude that both phenomena become manifest at about the same age.

This common start and the linear increase with age do not mean that both phenomena are the expression of the same process. There is a remarkable difference in sex distribution suggesting that the origin of the amyloid in senile plaques is different from that in congophilic vessels. This statement is supported by immunopathological studies^{9,11}.

The relationship between senile amyloidosis and SDAT is an intriguing item. From this study it may be concluded that SDAT is also an age related phenomenon characterized by a linear increase with age and a predominance in females. The linear regression analysis has demonstrated that senile plaques and SDAT become manifest at the same age and reveal a rather constant relation to one another in the different decades of life. From this fact we may conclude that SDAT is not a delayed clinical expression of senile amyloidosis. The rather constant percentage of SDAT in the different decades rises a very important question: which factors determine the clinical manifestation of SDAT in people with age related amyloidosis? In the literature it is suggested that this manifestation is dependent on the intensity of senile amyloidosis^{1,8}. Terry¹⁰ has pointed out that the difference between normal elderly people with senile plaques and SDAT-patients is clearly a quantitative one. In his opinion SDAT seems to be a threshold phenomenon. Our study revealed that the clinical manifestation of SDAT is not a simple threshold phenomenon. The presence or absence of congophilic angiopathy has an important influence on the percentage of SDAT manifested in people with senile plaques (Table VI). It seems to be very important to look for other factors that can influence this percentage. Based on our study we came to the conclusion that senile amyloidosis must be divided into two distinct types: an age related formation of senile plaques showing a predominance in females and a congophilic angiopathy, which is also age related but which has no sex preference or which is perhaps predominant in males.

Acknowledgment

We like to thank the medical directors of the mental hospitals Bloemendaal, Ermelo-Veldwijk and the Valerius Kliniek for their permission to study the clinical records.

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Received February 18, 1986 · Accepted in revised form March 13, 1986

Key words: Amyloidosis – Brain – Age – Senile Amyloidosis – Senile plaques

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