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Relationship between the deterioration of cognitive functions in old age and adverse life events in childhood

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Summary

The aim of this study was to determine the influence of adverse life events in childhood on the rate of progression of cognitive impairment in elderly people. The study included patients who were non-demented at baseline and whose data were recorded in the site database between 1993 and 1997. 114 patients were included in the final analysis. The time between the baseline examination and the final examination one was 5 to 9 years. The comparison between the rates of progression of cognitive deterioration obtained during the five years of observation reveals a significant worsening in people who experienced adverse events in childhood. Our study seems to confirm the link between stressors experienced in childhood and the rate of progression of cognitive impairment in old age.

Key words: childhood, adverse events, cognitive functions

Introduction

The deterioration of cognitive functions in old age can be caused by many factors. These factors do not only emerge in old age but can sometimes be traced back to very remote periods of childhood. Recently, more attention was given to childhood as a decisive period during which factors affecting psychic ability in old age may develop. Adverse life events occurring early in life may alter the brain maturation and render the organism more vulnerable to psychiatric disorders [1]. Adverse life events in childhood and adolescence are often a part of the background of people with cognitive impairment [2].

The current study spans 5 years of observation and its aim is to determine the influence of stressful events in childhood and early adolescence (0 – 14 years of age) on the rate of progression of cognitive impairments in later life.

Material and Methods

Patients were selected based on data available from the database of the Department of Developmental, Psychotic, and Geriatric Psychiatry, Medical University of Gdańsk.

The database contained data on all the patients participating in research programmes carried out in the department between 1993 and 1997. Initially, 361 people were selected. During the baseline examination (between 1993 and 1997) these patients fulfilled the inclusion and exclusion criteria:

Inclusion criteria: Being over 55 years of age; first stage (no cognitive decline) or second stage (very mild cognitive decline) in the Global Deterioration Scale (GDS) developed by B. Reisberg et al. [3]; score of 24 or more in the Mini Mental State Examination (MMSE) [4]; the same standardized evaluation (including: The Mini Mental Scale Examination (MMSE) and the Alzheimer's Disease Assessment Scale (ADAS) – cognitive subscale [5] for each patient; the interview made on the basis of the AMDP Scale - (Arbeitsgemeinschaft fur Methodik und Dokumention in der Psychiatrie)[6] – Anamnesis II – events in patient's life.

The patient was examined between 1993 and 1997.

Exclusion criteria: presence of dementia (according DSM – IV criteria) regardless of the aetiology; presence or history of any of the following diseases: affective disease, schizophrenia, alcoholism, drug or narcotic dependence, epilepsy, Parkinson's disease, mental impairment or consciousness disturbances; presence of disorders of motor system, sight or hearing organs that made it significantly difficult for him/her to follow instructions and procedures included in the applied clinical scales and moreover: any form of cognitive therapy – pharmacological (including any medication of possible pro-cognitive action) and non-pharmacological in the last 2 years before the final examination.

The selected patients were contacted and it was possible to get in touch with 218 patients out of the 361 chosen (60.1%). Among those we could not reach 60 (16.6%) were already dead. Patients and caregivers were informed about the purpose of the study and 169 (46.8%) of them consented to join. At this stage, the inclusion and exclusion criteria mentioned above were considered once again and 43 subjects were excluded. The main cause of exclusion was cognitive therapy in the last 2 years before the final examination.

The patients were assessed using the Mini Mental Scale Examination (MMSE) and the Alzheimer's Disease Assessment Scale (ADAS) – cognitive subscale; to assess the severity of cognitive impairment.

Information obtained during the initial examination was verified once again by the caregiver. When there were significant discrepancies between the information obtained during the first and second examination, such patients were excluded from the study (5 patients). The interview was constructed on the basis of the AMDP Scale - (Arbeitsgemeinschaft fur Methodik und Dokumention in der Psychiatrie) – Anamnesis II – events in patient's life. The following stressful events were taken into consideration: parents' death, siblings' death, a close person's death, and separation from parents lasting more than 6 months up to the age of 14. The term "a close person" defined as a person with whom the patient had a long good emotional relationship interrupted by the person's death. Moreover, the following aspects were taken into consideration: a stay in a place of confinement, multi-week-long periods of malnutrition, necessity of taking up a paid job [6].

Their second examination was carried out at least 5 years after their initial assessment.

Patients who obtained less than 24 points in the MMSE test were subjected to further examination in order to recognize or rule out a dementia syndrome. In case dementia was recognized on the basis of the DSM-IV criteria [7], further examination including laboratory investigation, was conducted in order to determine the aetiology of the process. The following additional examinations were regarded as necessary in the diagnostic process: brain CT or MRI scans, the determination of basic blood biochemical parameters (the level of creatinine, glucose, aminotransferases and electrolytes), complete blood count, serology tests and urinalysis. Moreover, when clinical symptoms or deviation in laboratory investigation suggesting vitamin B12 deficiency or thyroid gland dysfunction were present, additional analysis was made in order to determine the levels of vitamin B12 and/or of thyroxin and triodothyronine.

7 patients were excluded from the study – because they suffered a serious physical disease or fulfilled one of the exclusion criteria specified in the preliminary selection for the examination between the first and second examinations.

Each examination was preceded by a 15-minute conversation about everyday living, in order to reduce the patient's emotional tension. The AMDP and GDS examinations were carried out by psychiatrists. A clinical psychologist conducted the ADAS Scale test. Social workers and nursing staff conducted the MMSE test.

For statistical analysis of the results, parametric tests were used (t for two independent means). The significance was set at a p level equal to or less than 5%. The rate of progression of cognitive deterioration was determined by the difference between the present examination and the baseline examination as assessed with the ADAS-cog Scale.

Results

The final analysis included 114 patients. The time between the baseline and the final examination was 5 to 9 years. The final investigation showed dementia in 15 patients, including 8 cases of the Alzheimer-type dementia, 3 cases of vascular dementia, and 4 cases of mixed dementia.

Table 1 presents mean results obtained for the study population at the beginning of the observation (baseline) and at the final examination.

The comparison between the rates of progression of disorders obtained at baseline and at final examinations reveals a significant worsening in people who experienced stressful events in childhood. Moreover this group has a higher incidence of dementia (9 cases to 6 cases). Patients who developed dementia during the period of observation were excluded from further analysis, as their dementia would have had an obvious impact on the results of the study.

Table 2 presents the results for 99 patients with no dementia recognized within the observation period.

Table 1

Mean values of age and the ADAS and MMSE scales obtained during the baseline examination and final examination in patients who experienced adverse life events in childhood and in those who were not exposed to stressors

	ABSENCE OF ADVERSE EVENTS N = 70		PRESENCE OF ADVERSE EVENTS N = 44	
	Mean	Standard deviation	Mean	Standard deviation
Age	74.6	10.9	74.5	14.0
ADAS-0	5.9	2.9	6.2	3.0
ADAS-5 *	8.2	6.3	13.6	10.4
Level of progression ADAS-5 – ADAS-0 *	2.3	5.7	7.4	9.5
MMSE-0	27.5	1.9	27.0	1.9
MMSE-5	25.9	4.3	24.4	3.9
Cases of dementia	6		9	

ADAS-0 – results of Alzheimer's Disease Assessment Scale obtained during the baseline visit and the final visit – ADAS-5

MMSE-0 – results of The Mini Mental Scale Examination obtained during the baseline visit and the final visit – ADAS-5

* – Differences statistically significant ($p < 0.05$) between two groups of subject

Table 2

Mean values of age and the ADAS and MMSE scales obtained at baseline and in the final examination in patients who experienced adverse events in childhood and in patients who were not exposed to stressors in childhood. Patients who developed dementia during the period of observation were excluded from this analysis

	ABSENCE OF ADVERSE EVENTS N = 64		PRESENCE OF ADVERSE EVENTS N = 35	
	Mean	Standard deviation	Mean	Standard deviation
Age	74.1	10.8	73.3	15.0
ADAS-0	5.5	2.8	5.5	2.9
ADAS-5 *	6.6	3.4	8.9	3.3
Level of progression ADAS-5 – ADAS-0	1.1	3.7	3.4	4.6
MMSE-0	27.8	1.8	27.4	1.8
MMSE-5 *	27.0	2.3	26.1	1.3

ADAS-0 – results of Alzheimer's Disease Assessment Scale obtained during the baseline visit and the final visit – ADAS-5

MMSE-0 – results of The Mini Mental Scale Examination obtained during the baseline visit and the final visit – ADAS-5

* – Differences statistically significant ($p < 0.05$) between two groups of subject

Discussion

Analysis of the impact of stressful factors during childhood on the level of progression of cognitive disorders at an older age showed that patients who experienced adverse life events early in life are more prone to developing intense cognitive disorders. Stress affects the brain function, through the regulation of Brain-derived neurotrophic factor (BDNF) within selected brain structures, including the hippocampus [8]. BDNF is strongly expressed in the hippocampus, where it has been associated with memory processes. Events taking place during brain maturation can induce modifications in the BDNF mRNA expression, contributing to permanent alterations in brain function [9, 10]. BDNF plays a critical role in activity-dependent neuroplasticity underlying learning and memory in the hippocampus [11]. Reduction of BDNF might be mediated by corticosterone, because corticosterone administration is known to reduce hippocampal BDNF. [12]. Moreover stress-induced elevation of glucocorticoids is accompanied by structural changes and neuronal damage in certain brain areas [13]. Subjecting children and young people to strong, long-lasting stress by prolonged glucocorticoid action can lead to the loss of temporal lobe cells. Some people are particularly susceptible to stressors. It is believed that stressful events in childhood (loss of parents in particular) contribute to the overreaction to stressors in adult life. It can be assumed that in people particularly susceptible to stressors, the process of neuron destruction in the hippocampus structures may take place quicker, thus the neurocognitive reserve will be depleted sooner, and the signs of dementia will be seen sooner as well. Our study seems to confirm the relationship between adverse life events in childhood and the rate of progression of cognitive function in late life.

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