

# Experimental Gerontology

Experimental Gerontology 36 (2001) 1599-1607

www.elsevier.com/locate/expgero

## Aging Research Worldwide

# Research on aging in Portugal

## Catarina Resende Oliveira\*

Department of Biochemistry and Centre for Neurosciences, Faculty of Medicine, University of Coimbra, Rua Larga, 3004 504 Coimbra, Portugal

Received 2 May 2001; received in revised form 26 June 2001; accepted 10 July 2001

#### **Abstract**

This review presents an analysis of the current state of gerontological and geriatric research in Portugal, and highlights the need for a national consensus and funding for age-related research projects. Such efforts must be multidisciplinary, since the process of aging encompasses biological, psychological, social, economic and cultural aspects.

Demographic studies reveal a growing population of elderly in Portugal as a result of a healthier population in general. This increased life expectancy, however, is accompanied by a parallel increase in degenerative pathologies and care costs among the elderly.

Preventive medicine is an important tool to reduce health care costs and avoid or abbreviate suffering from age-related syndromes, but such projects on a national basis neither exists, nor does gerontology or geriatrics receive funding to perform needed research. Consequently, research on aging depends on the initiative of individual investigators who, without funding or cohesive programs, can do little to improve the low scientific output in this area.

The implementation of a national program, that can establish health care policy and priorities as well as fund the necessary research, will permit organized cooperation among the different scientific disciplines related to aging. This is a crucial step toward improving present knowledge, ensuring application of experimental and statistical results to the clinical care of the aging population, and attract young investigators to this field. © 2001 Elsevier Science Inc. All rights reserved.

#### 1. Introduction

A commitment to aging research has not yet emerged in Portugal. Studies on the population structure and evolution by gender and age, as well as the demographic aging (Santana, 2000) and data from the decennial population census established by the Portuguese National Institute of Statistics, show that Portugal is fifth among European nations in a low percentage of aged people relative to the total population (Fig. 1). The proportion of

0531-5565/01/\$ - see front matter @ 2001 Elsevier Science Inc. All rights reserved.

PII: S0531-5565(01)00152-8

<sup>\*</sup> Corresponding author. Tel.: +351-239-82-01-90; fax: +351-239-82-27-76. E-mail address: catarina@cnc.cj.uc.pt (C. Resende Oliveira).

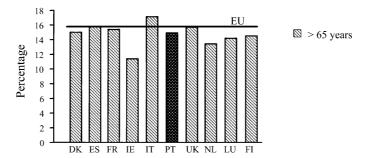


Fig. 1. Percentage of people over 65 years-old in European Union Countries. Individuals over 65 years old are represented as a percentage of the total population according to data from Eurostat collected in 1996 and published in 1998 (Instituto Nacional de Estatística, 1999). EU — European Union; DK — Denmark; ES — Spain; FR — France; IE — Ireland; IT — Italy; PT — Portugal; UK — United Kingdom; NL — The Netherlands; LU — Luxemburg; FI — Finland.

elderly citizens in Portugal was lower (86 elderly to 100 young persons) than the mean estimated for the European Community (90 elderly to 100 young persons). A decline in the number of births sustained for one or more decades, as has been observed in the last years in Portugal, reduces the proportional significance of the young, and, conversely, increases that for the elderly (Fig. 2). Such an alteration in the demographic age structure favours the increased proportion of older versus younger individuals, leads to the aging of the population and is probably related to the increasing interest in gerontological/geriatric research that has been observed recently.

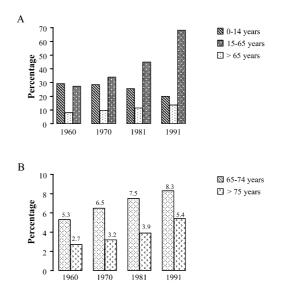


Fig. 2. Distribution of the Portuguese population according to age from 1960 to 1991. (A) Comparison of the different age groups; (B) analysis of the over 65 years old. Values are calculated as a percentage of the total population; both genders are included (Livro Branco da Segurança Social, 1998).

Old age is a multifactorial process encompassing physiological and pathological phenomena as well as environmental and socioeconomic influences. As a life stage, aging can be defined on the basis of alterations occurring at the cellular and sub-cellular levels, as well as on tissues, organs and systems. Accordingly, the aging process is beginning to be understood on a molecular basis, clarifying the means by which genetic manipulation may affect the rate of age.

Although pharmacological and genetic research is currently attracting increasing support both in the field of gerontology (the study of aging processes) and geriatrics (the treatment of diseases associated with aging), the psychological and social components should not be ignored. Research on aging must include such areas as statistics, demography, nutrition and social policy. Research programs in this area have defined two main goals: To prolong human life, and to enhance the quality of life.

Aging is not yet a unified field, and research on aging requires the engagement not only of biomedical researchers, but also of economists, social scientists and various health care professionals. This review examines the main fields of interest of the major scientifically active Institutions in aging research in Portugal.

### 2. Scientific activity in research on aging in Portugal

Most age-related research, focused on biomedicine, has been developed at the Schools of Medicine at the Universities of Lisbon, Porto and Coimbra. Institutes dealing exclusively with age-related research do not exist, gerontology is not a discipline in Medical School Curricula and, Advanced Courses on aging have not yet been organized. Accordingly, research on the medical aspects of aging is unorganized and distributed among various clinical entities in general hospitals, since only recently have specialized geriatric wards dealing with the 'heavier' and difficult elderly cases been created (Hospital Magalhães de Lemos, Porto).

Although there is not a general funding program for aging research in Portugal, several research initiatives have focused on health and social care for the elderly; new technologies and designs to help the elderly remain autonomous; studies of the causes and influences of age-related diseases and disability; prevention, treatment and rehabilitation strategies; and the molecular and cellular changes associated with cell death and senescence. It is important to note that much of the relevant research is conducted within the confines of individual diseases and technologies focused on the health and well-being of aged people rather than under aging per se.

A few aging research programs, disseminated over several areas, including neurosciences, immunology, molecular and cell biology and pathology, have been developed by individual researchers and have benefited from broad involvement in international networks (i.e. SENECA Study Nutrition and the Elderly in Europe, 1993; MEDOS, Mediterranean Osteoporosis Study, 1999).

From a policy standpoint, the independence of the elderly is an important issue. Studies directed towards specific aging-related topics, such as poverty, loneliness and the social aspects of aging, have emerged as initiatives from the Ministries of Health, Work and Social Solidarity, and the Centre for Social Intervention (CESIS).

In contrast to other European Member States, Portugal reported a relatively large number of technology and design projects in the area of housing and telematics. The Technological University of Lisbon (Taipale and Moniz Pereira, 1995; Espadinha et al., 1998; Moniz Pereira et al., 1999) and the University of Aveiro (Figueiredo and Sousa, 2001; Sousa and Figueiredo, 2001) have participated in multinational research programs focused on the development of technology concepts to ensure good health, full social participation and independent living to the elderly. Through the implementation of the programs 'Distance Education and Tutoring in Heterogeneous Telematics Environments' (DEMOS), 'Integration Broadbond Communication on Broadcast Networks' (IBCoBN), 'Development and Testing of Telecommunication Systems designed for older people and their care-givers, including the health and social care system' (RACE II) and 'The Elderly Assessment System' (EASY care), it was possible to improve social integration of the elderly, providing leisure activities and therapeutic programs at distance. The main objective of these programs was to supply the elderly with the technological options allowing them to remain integrated in the modern society, an effort primarily driven by Information and Communication Technologies.

The analysis of how and why functional capacities change with increasing age is very important for the development of gerontological research and for practical applications. Multidisciplinary projects on the evaluation of the functional capacities of the elderly and the development, feasibility and validation of a multidimensional assessment of aged people living in the community have been supported by the Ministries of Science and Technology and of Health (Almeida et al., 1995; Botelho and Rendas, 1997; Botelho, 1999; Mateus et al., 1995; Broeiro et al., 1995).

Several institutions, including governmental agencies and university hospitals (Lisbon, Porto and Coimbra), have been involved in clinical research in different areas related to aging, primarily neurological and cardiovascular diseases. This research is multidisciplinary and involves both scientists and clinicians, since a close link between the hospitals and university research centres has been maintained over the years (Marinho et al., 1997; Neves, 1995; de Sousa, 1998; Rocha et al., 1997b; Fernandes et al., 1996a,b, 1999a,b,c).

Multidisciplinary projects on Alzheimer's disease and related dementias involving molecular genetics, clinical and neuropsychological aspects have been developed at the University Hospitals of Lisbon and Coimbra (Rocha et al., 1997a; Fernandes et al., 1999a,b,c). Stroke in the elderly and cognitive decline related to several vascular diseases have also contributed significantly to aging research (Ferro and Madureira, 1997; European Carotid Surgery, a cooperative intervention trial).

Another important field is vision research, in which scientific assessment is particularly active at the Oftalmological Clinic, University Hospital and Faculty of Medicine of Coimbra (Cunha-Vaz, 1997, 2000a,b,c; Cunha-Vaz et al., 1998). Lens fluorescence measurements, the role of cholesterol oxidation on cataract pathogenesis, the involvement of blood—retinal barrier and choroidal circulatory changes on age-related macular degeneration are among the main points of interest (Alfaiate et al., 1996; Fernandes et al., 1996a,b; Mota et al., 1996; Pereira et al., 1996; Ramalho et al., 1996; Lobo et al., 1999; Girão et al., 1998, 1999).

Clinical research has also focused on nutritional habits of aged people, and selected centres have been involved in European multinational research programs such as the

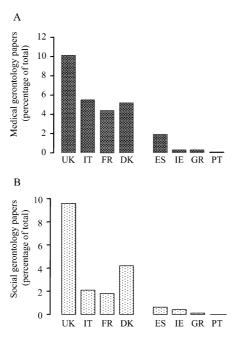


Fig. 3. Gerontology papers published by European Union Member States. (A) Medical gerontology papers; (B) social gerontology papers. The values are the percentages of world total of medical/social gerontology papers *per* year, according to the Science Citation Index/Social Science Citation Index, respectively. DK — Denmark; ES — Spain; FR — France; IE — Ireland; IT — Italy; PT — Portugal; UK — United Kingdom; GR — Greece.

SENECA Study on Nutrition and the Elderly (Ugert and de Groot, 1996; Moreiras et al., 1996; de Groot et al., 1996).

There are a number of basic research groups, namely Paula-Barbosa and colleagues (Faculty of Medicine, University of Porto) with established records in the field of neurobiology who have developed important morphometric studies on age-related changes of different brain areas and the role of stress and sexual hormones (Sousa et al., 1998a,b; Leal et al., 1998; Monteiro et al., 1998; Lukoyanov et al., 1999). Biochemical and pharmacological research related to aging, cerebral ischemia and Alzheimer's disease, specifically the studies of the modulating effect of adenosine on synaptic plasticity (Pereira et al., 2000a,b; Lopes et al., 1999a,b; de Mendonça and Ribeiro, 1996; de Mendonça et al., 1997), the role of oxidative stress and excitotoxicity in neuronal cell death in cerebral ischemia and chronic neurodegenerative disorders (Pereira and Oliveira, 1997; Agostinho et al., 1996, 1997; Rego and Oliveira, 1998; Rego et al., 1997, 1999a,b), the molecular mechanisms of β-amyloid peptides toxicity (Pereira et al., 1998, 1999, 2000a,b; Moreira et al., 2000) and the characterization of amyloid precursor protein (APP) biological function (Cruz e Silva et al., 1993, 1995) are strong points of interest in aging research. Strong research groups at the Centers for Neurosciences of Lisbon and Coimbra have been performing relevant studies on synaptic plasticity and the role of mitochondrial dysfunction on neuronal cell death occurring in neurodegenerative disorders. Obviously, Portugal possesses the expertise required to conduct significant basic and clinical research.

The scientific output of research on aging was evaluated by analysis of relevant clinical and basic research publications in peer-reviewed journals, and showed significant variations among European countries. The analysis employed the science citation index and the social science citation index, and included gerontology, age-related diseases such as Alzheimer's, Parkinson's and osteoporosis. As shown in Fig. 3A and B, the differences in scientific output among the 10 major developed countries are minor, except for the United Kingdom, which presents a large output of research on dementia. Portuguese publication rates are low, even when compared to economically and scientifically similar countries. This low output of biomedical scientific literature on aging probably reflects the low priority this field of research has had for the Portuguese government. The English language bias is another factor to be considered in the analysis of the research scientific output; this bias is less significant in basic research, which is addressed to an international scientific community, but is significant in clinical and social sciences intended for a local readership. Most gerontology research focusses on socio- and psychogerontology research and is published in national scientific journals.

#### 3. Conclusions

Research on aging, namely clinical and health care research, is a multidisciplinary and complex undertaking. Therefore, the opportunities for multidisciplinary research based upon longitudinal aging studies should be encouraged. Longitudinal studies should promote cross national comparative research and an integral understanding of the aging process. Coordinated multidisciplinary programs, including biomedical, epidemiological, clinical and social research, as well as intervention (engineering and information facilities) will be the driving force for the future of aging research in Portugal, provided that funds are made available.

The approval of a national project on aging focused on a longitudinal study of the aging process should be considered a priority and is crucial to the development of research in this field in Portugal. Under the auspices of a national effort to address the problems of aging, fresh funds could be devoted and groups of scientists with expertise in related fields (biochemistry, physiology, immunology, internal medicine and neurology) could be coordinated in a cohesive research program.

#### References

Agostinho, P., Duarte, C.B., Oliveira, C.R., 1996. Activity of ionotropic glutamate receptors in retinal cells: effect of ascorbate/Fe<sup>2+</sup>-induced oxidative stress. J. Neurochem. 67 (3), 1153–1163.

Agostinho, P., Duarte, C.B., Oliveira, C.R., 1997. Impairment of excitatory amino acid transporters activity by oxidative stress conditions in retinal cells: effect of antioxidants. FASEB J. 11, 154–163.

Alfaiate, M., Leite, E., Mira, J., Cunha-Vaz, J.G., 1996. Prevalence and surgical complications of pseudoexfoliation syndrome in Portuguese patients with senile cataract. J. Cataract Refract Surg. 22 (7), 972–976.

Almeida, M.M., Almeida, P.A.P., Dias, J.A.A., 1995. Estudo da Qualidade de Vida do Idoso. Aplicação de um Instrumento de Avaliação. Relatório da Direcção-Geral de Saúde, pp. 35

Botelho, M.A.S., 1999. Autonomia Funcional em Idosos. Caracterização multidimensional em idosos utentes de um centro de saúde urbano. PhD Thesis, Universidade Nova de Lisboa.

- Botelho, M.A., Rendas, A.B., 1997. Avaliação multidimensional de idosos: estudo piloto no ambulatório. Arquivos Med. 11 (3), 167–172.
- Broeiro, P., Ramos, V., Tavares, I., Cunha, E., Amorim, J., 1995. Avaliação de estados funcionais no idoso. Exercício de aplicação de uma versão portuguesa da escala COOP/WONCA Charts. Acta Med. Port. 8, 279–288
- Cruz e Silva, O.A.B., Iverfeldt, K., Oltersdorf, T., Sinha, S., Lieberburg, I., Ramabhadran, T.V., Sisodia, S.S., Gandy, S., Greengard, P., 1993. Regulated cleavage of Alzheimer β-amyloid precursor protein in the absence of the cytoplasmic tail. Neuroscience 57, 873–874.
- Cruz e Silva, E.F., Cruz e Silva, O.A.B., Zaia, C.T.B.V., Greengard, P., 1995. Inhibition of protein phosphatase 1 stimulates secretion of Alzheimer amyloid precursor protein. Mol. Med. 1, 535.
- Cunha-Vaz, J.G., 1997. Optical sensors for clinical ocular fluorometry. Prog. Ret. Eye Res. 16, 243-270.
- Cunha-Vaz, J.G., 2000. Blood-Retinal Barrier in Diabetes. In: van Bijsterveld, P., Dunitz, M. (Eds.). Diabetic Retinopathy., pp. 155–168.
- Cunha-Vaz, J.G., 2000. Diabetic retinopathy. surrogate outcomes for drug development for diabetic retinopathy. Ophthalmologica 214, 377–380.
- Cunha-Vaz, J.G., 2000. Ophthalmology in Portugal. Arch. Ophthal. 118, 1435-1436.
- Cunha-Vaz, J.G., Lobo, C., Castro Sousa, J., Leite, E., Faria de Abreu, J.R., 1998. Progression of reinopathy and alteration of the blood-retinal barrier in patients with type 2 diabetes. A seven-year prospective follow-up study. Graefe's Arch. Clin. Exp. Ophthal. 236, 264–268.
- Espadinha, C., Moniz Pereira, L., Martins, J., Pinto, J., Zagalo, H., 1998. Potencialidades do Hipermédia na elaboração de Situações Ludico-Pedagógicas em. Geriatria: Ano IX XI (110), 18–22.
- Fernandes, M.A.S., Santana, I., Oliveira, C.R., 1996. Studies of the aluminium effect on superoxide dismutase activity of healthy human erythrocytes and osmotic fragility or erythrocytes in Alzheimer's disease. Alzh. Res. 2, 73–78.
- Fernandes, R., Pereira, P., Ramalho, J.S., Mota, M.C., Oliveira, C.R., 1996. An experimental model for the evaluation of lipid peroxidation in lens membranes. Curr. Eye Res. 15, 395–402.
- Fernandes, M.A., Oliveira, C.R., Oliveira, L.M., Nogueira, A.J., Santiago, B., Santana, I., 1999. Apolipoprotein E epsilon4 allele is a risk factor for Alzheimer's disease: the central region of Portugal (Coimbra) as a case study. Eur. Neurol. 42, 183–184.
- Fernandes, M.A., Proença, M.T., Nogueira, A.J., Oliveira, L.M., Santiago, B., Santana, I., Oliveira, C.R., 1999. Effects of apolipoprotein E genotype on blood lipid composition and membrane platelet fluidity in Alzheimer's disease. Biochem. Biophys. Acta 1454, 89–96.
- Fernandes, M.A.S., Proença, M.T., Nogueira, A.J.A., Oliveira, L.M.V., Santiago, B., Santana, I., Oliveira, C.R., 1999. Apolipoprotein E genotype has no effect on the free intracellular Ca<sup>2+</sup> concentration of platelets from Alzheimer's disease patients. Int. J. Mol. Med. 3, 431–434.
- Ferro, J.M., Madureira, S., 1997. Aphasia type, age and cerebral infarct localisation. J. Neurol. 244, 505–559.
  Figueiredo, D., Sousa, L., 2001. EASYcare- Um instrumento de avaliação da qualidade de vida e bem-estar do idoso. Geriatria.
- Girão, H., Mota, M.C., Ramalho, J.R., Pereira, P.C., 1998. Cholesterol oxides accumulate in human cataracts. Exp. Eye Res. 66, 645–652.
- Girão, H., Mota, M.C., Pereira, P., 1999. Cholesterol may act as an antioxidant in lens membranes. Curr. Eye Res. 18, 448–454.
- de Groot, C.P., Perdigao, A.L., Deurenberg, P., 1996. Longitudinal changes in anthropometric characteristics of elderly Europeans. SENECA investigators. Eur. J. Clin. Nutr. 50 (Suppl. 2), S9–S15.
- Instituto Nacional de Estatística, 1999, 1999. As Gerações Mais Idosas. Série de Estudos 83.
- Leal, S., Andrade, J.P., Paula-Barbosa, M.M., Madeira, M.D., 1998. Arcuate nucleus of the hypothalamus: effects of age and sex. J. Comp. Neurol. 401, 65–88.
- Livro Branco da Segurança Social, 1998. Comissão do Livro Branco da Segurança Social. pp. 28-49.
- Lobo, C., Bernardes, R., Cunha-Vaz, J.G., 1999. Mapping retinal fluorescein leakage with confocal scanning laser fluorometry of the human vitreous. Arch. Ophthal. 117, 631–637.
- Lopes, L.V., Cunha, R.A., Ribeiro, J.A., 1999. Cross talk between A(1) and A(2A) adenosine receptors in the hippocampus and cortex of young adult and old rats. J. Neurophys. 82, 3196–3203.
- Lopes, L.V., Cunha, R.A., Ribeiro, J.A., 1999. Increase in the number, G protein coupling, and efficiency of

- facilitatory adenosine A2A receptors in the limbic cortex, but not striatum, of aged rats. J. Neurochem. 73, 1733–1738.
- Lukoyanov, N.V., Andrade, J.P., Dulce Madeira, M., Paula-Barbosa, M.M., 1999. Effects of age and sex on the water maze performance and hippocampal cholinergic fibers in rats. Neurosci. Lett. 269, 141–144.
- Marinho, C.F.M., Costa-Maia, J., Barros, J.P., Oliveira, C.R., 1997. Correlation between human platelet cytoplasmic membrane fluidity, Na<sup>+</sup>/H<sup>+</sup> exchanger activity and aging. Eur. Arch. Psych. Clin. Neurosci. 247, 275–277.
- Mateus, A.L., Cortez, A.I., Lourenço, I., Rocha, O., 1995. O que sabemos dos nossos idosos Um estudo sobre avaliação funcional. Rev. Port. Clin. Ger. 12, 92–99.
- de Mendonça, A., Ribeiro, J.A., 1996. Adenosine and neuronal plasticity. Life Sci. 60, 245-251.
- de Mendonça, A., Almeida, T., Bashir, Z.I., Ribeiro, J.A., 1997. Endogenous adenosine attenuates long-term depression and depotentiation in CA1 region of the rat hippocampus. Neuropharmacology 36, 161–167.
- Moniz Pereira, L., Cunha, S., Espadinha, C., Rocha, N., Martins, J., 1999. Distance support and elderly people: overview on three projects. Proceedings of the Fifth European Conference on Assistive Technology (AAATE). Dusseldorf, Germany, pp. 388–390.
- Monteiro, R.A., Henrique, R.M., Rocha, E., Marini-Abreu, M.M., Oliveira, M.H., Silva, M.W., 1998. Age-related changes in the volume of somata and organelles of cerebellar granule cells. Neurobiol. Aging 19, 325–332.
- Moreira, P., Pereira, C., Santos, M.S., Oliveira, C.R., 2000. Effect of zinc ions on the cytotoxicity induced by the amyloid β-peptide. Antioxidants Redox Signal. 2, 317–325.
- Moreiras, O., van Staveren, W.A., Amorim Cruz, J.A., Carbajal, A., de Henauw, S., Grunenberger, F., Roszkowski, W., 1996. Longitudinal changes in the intake of energy and macronutrients of elderly Europeans. SENECA investigators. Eur. J. Clin. Nutr. 50 (Suppl. 2), S67–S76.
- Mota, M.C., Ramalho, J.S., Pereira, P.C., Matos, A., 1996. Lens Fluorescence Measurements. In: Docchio, F. (Ed.). Introduction to Ocular Fluorometry. Euroeye European Concerted Action on Ocular Fluorometry, pp. 123–138.
- Neves, P.L., 1995. Chronic haemodialysis in elderly patients. Nephrol. Dial. Transp. 10 (Suppl. 6), 69-71.
- Pereira, C.M.F., Oliveira, C.R., 1997. Glutamate toxicity on a PC12 cell line involves glutathione (GSH) depletion and oxidative stress. Free Radical Biol. Med. 23, 637–647.
- Pereira, P., Fernandes, R., Ramalho, J.S., Mota, M.C., Oliveira, C.R., 1996. A technical approach to the evaluation of glucose oxidation: implications on diabetic cataract. Ophthalmic Res. 28, 275–283.
- Pereira, C., Santos, M.S., Oliveira, C.R., 1998. Mitochondrial function impairment induced by amyloid β-peptide on PC12 cells. NeuroReport 9, 1749–1755.
- Pereira, C., Santos, M.S., Oliveira, C.R., 1999. Involvement of oxidative stress on the impairment of energy metabolism induced by AB peptides on PC12 cells: protection by antioxidants. Neurobiol. Dis. 6, 209–219.
- Pereira, M.F., Cunha, R.A., Ribeiro, J.A., 2000. Tonic adenosine neuromodulation is preserved in motor nerve endings of aged rats. Neurochem. Int. 36, 563–566.
- Pereira, C., Moreira, P., Seiça, R., Santos, M.S., Oliveira, C.R., 2000. Susceptibility to β-amyloid-induced toxicity is decreased in Goto-Kakizaki diabetic rats: involvement of oxidative stress. Exp. Neurol. 161, 383–391.
- Ramalho, J.S., Marques, C., Pereira, P.C., Mota, M.C., 1996. Role of glycation in lens protein structure change. Eur. J. Ophthal. 6, 155–161.
- Rego, A.C., Oliveira, C.R., 1998. Alteration of nitric oxide synthase activity upon oxidative stress in cultured retinal cells. J. Neurosci. Res. 51, 627–635.
- Rego, A.C., Santos, M.S., Oliveira, C.R., 1997. Adenosine triphosphate degradation products after oxidative stress and metabolic dysfunction in cultured retinal cells. J. Neurochem. 69, 1228–1235.
- Rego, A.C., Areias, F.M., Santos, M.S., Oliveira, C.R., 1999. Distinct glycolysis inhibitors determine retinal cell sensitivity to glutamate-mediated injury. Neurochem. Res. 24, 351–358.
- Rego, A.C., Santos, M.S., Oliveira, C.R., 1999. Influence of the antioxidants vitamine E and idebenone on retinal cell injury mediated by chemical ischemia, hypoglycemia or oxidative stress. Free Radical Biol. Med. 26, 1405–1407.
- Rocha, L., Mendonça, A., Garcia, C., Lechner, M.C., 1997. Apolipoprotein E genotype of a Portuguese control population and Alzheimer's disease patients. Eur. J. Neurol. 4, 448–452.
- Rocha, M., Pereira, S., Barros, H., Seabra, J., 1997. Does pulmonary tuberculosis change with ageing?. Int. J. Tuberc. Lung Dis. 1, 147–151.

- Santana, P., 2000. Ageing in Portugal: regional iniquities in health and health care. Soc. Sci. Med. 50, 1025–1036.
- de Sousa, G., 1998. International views on universal leucodepletion: the perspective in Portugal. Transfus. Sci. 19 (4), 351–352.
- Sousa, L., Figueiredo, D., 2001. Qualidade de vida e bem-estar do idoso- um estudo exploratorio no Concelho de
- Sousa, N., Almeida, O.F., Holsboer, F., Paula-Barbosa, M.M., Madeira, M.D., 1998. Maintenance of hippocampal cell numbers in young and aged rats submitted to chronic unpredictable stress. Comparison with the effects of corticosterone treatment. Stress 2, 237–249.
- Sousa, N., Madeira, M.D., Paula-Barbosa, M.M., 1998. Effects of corticosterone treatment and rehabilitation on the hippocampal formation of neonatal and adult rats. Na unbiased stereological study. Brain Res. 794, 199–
- Taipale, V., Moniz Pereira, L., 1995. Social aspects of telematics concerning disabled and elderly people and the future challenges. In: Roe, P. (Ed.). Telecommunications for All, 219. EC-COST, Luxembourg, pp. 110–118.
- Urgert, R., de Groot, C.P., 1996. Consumption of unfiltered coffee brews in elderly Europeans. SENECA investigators. Eur. J. Clin. Nutr. 50 (Suppl. 2), S101–S104.