

EADC OVERVIEW

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Bruno Vellas:

The European Alzheimer's Disease Consortium is a European funded network of centres of excellence, working in the field of Alzheimer's disease. It was launched in 2001, ten years after the ADCS. The EADC exists to provide a setting in which to increase basic scientific understanding and to develop a way to prevent, slow, and improve the primary and secondary symptoms of AD. The EADC objectives were to establish and now maintain a functional network of AD centres. That has been difficult because we are 48 centres, from different European countries, with different languages, and diverse cultures. But we have been successful. Within the setting of the EADC we aimed to standardise nomenclature, assessment tools and diagnostic criteria. In addition we have set up a system for qualitative analysis of data and have developed and tested a website for remote data entry. Two European funded studies, ICTUS and DESCRIPA, are underway.

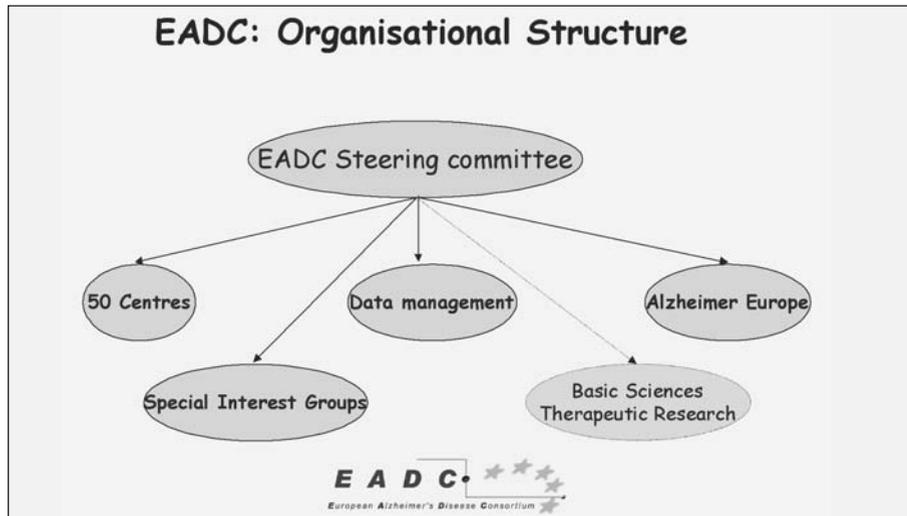
The EADC organisation now includes now 50 centres of excellence (see appendix 1). The directors of the centres are members of the EADC Steering Committee. Moreover, the EADC network includes 7 special interest subgroups, a data management system in Toulouse, and links with the family association, Alzheimer Europe.

EADC-ADCS

| EADC European Alzheimer's Disease Consortium | | EADC: Members | |
|---|---|---|---|
| Dr. Frolich Lutz Pr. Kurz Alexander Dr. Werner Hans Jorg Dr. Stoppe Gabriela Pr. Kornhuber Johannes Pr. Hampel Harald | Mannheim-Germany Munchen-Germany Darmstadt-Germany Goettingen-Germany Erlangen-Germany Munchen-Germany | Pr. Winblad Bengt Dr. Sjögren, Magnus | Huddinge-Sweden Malmö-Sweden |
| Pr. Burns Alistair Pr. McKeith Ian Pr. Sinclair Allan Pr. Whalley Lawrence Pr. Roy Jones Pr. Wilcock Gordon Pr. Bullock Roger Pr. Lovestone Simon Pr. Wilkinson David | Manchester-UK Newcastle-UK Birmingham-UK Aberdeen-UK Bath-UK Bristol-UK Swindon-UK London-UK Southampton-UK | Pr. Salmon Eric Pr. De Deyn Peter Paul Pr. Vanderbelghe Rick | Liège-Belgium Antwerp, Belgium Leuven - Belgium |
| Pr. Scheltens Philip Pr. Olde Rikkert MGM | Amsterdam-Netherlands Nijmegen- Netherlands | Dr. Blesa Rafael Dr. Boada Merce Dr. Salva Antonio Pr. Ribera Casado J-M Pr. Masdeu Josef Pr. Lopez Fernando | Barcelona-Spain Barcelona-Spain Barcelona-Spain Madrid-Spain Pampelona-Spain Cordoba-Spain |
| Dr. Bianchetti Angelo Dr. Frisonni Giovanni Pr. Senin Umberto Pr. Rodriguez Guido Pr. Bernabei Roberto | Cremona-Italy Brescia-Italy Perugia-Italy Genoa-Italy Roma-Italy | Pr. Erkinjuntti Timo Dr. Soininen Hilikka | Helsinki-Finland Kuopio-Finland |
| Dr. Hock Christopher Pr. Michel Jean-Pierre Pr. Staehelin Hannes-B | Zurich-Switzerland Geneva-Switzerland Basel-Switzerland | Pr. Orgogozzo J-Marc Pr. Pasquier Florence Pr. Touchon Jacques Pr. Robert Philippe Pr. Forette Françoise Pr. Dubois Bruno Pr. Vellas Bruno Dr. Camus Vincent | Bordeaux-France Lille-France Montpellier-France Nice-France Paris-France Paris-France Toulouse-France Tours-France |
| | | Dr. Spiru Luiza | Bucharest-Romania |
| | | Dr. Costa-Tsolaki Magda Pr. Waldemar Gunhild Pr. Barcikowska Maria | Thessaloniki-Greece Copenhagen-Denmark Warsaw-Poland |

The aims of the special interest groups are to:

- summarise current practice and identify areas of special expertise in the EADC centres
- standardise nomenclature, diagnostic criteria and assessment tools, decide minimum data set, organise preliminary trials
- provide up to date "state of the art" information to the members of the consortium regarding research issues as they become apparent
- identify interesting areas for future research.



The behavioural problems group, as part of the initial feasibility study of remote data entry, has produced some data on frequency of BPSD in Alzheimer patients in Europe (see table below).

EADC- BPSD Observational study: Behavioral and Psychological Symptoms in Dementia: Clinical and biological aspects

P.H Robert, F.Verhey, J.Byrne, C.Hurt, P.De Deyn, F.Nobili, R.Riello,
G.Rodriguez, G.Frisoni, M.Tsolaki, N.Kyriazopoulou, R.Bullock, A.Burns,
B.Vellas. *European Psychiatry Journal*: Submitted.

- **Frequency of BPSD in 836 AD patients in EU**
- - Delusions : 22% Hallucinations: 8.5%
- - Agitation: 35% Depression : 44.9%
- - Anxiety : 42% Apathy : 55%
- - Irritability : 30% Aberrant Motor: 24%
- - Sleep : 14% Appetite : 21%



EADC-ADCS

The EADC recently published or submitted some EADC consensus papers on different topics including neuro-imaging (J Neurol Neurosurg Psychiatry), BPSD (Eur J Psychiatry), continuing education, cognitive assessment tools, informal caregiver burden assessment in therapeutic trials, and a survey on national differences in the process of obtaining ethical approval (Eur J Neurology). There are some very important differences in the way that ethical approval is granted in Europe.

Ongoing EADC projects include 2 studies currently financed by the European Commission. The first is the impact of cholinesterase treatment on the natural history of AD in Europe, or the ICTUS study. It is no longer ethical to perform long-term placebo controlled studies, however we need more documentation on the impact of long-term treatment in clinical practice (Cochrane Review). Only a small percentage of patients are likely to be included in placebo double-blind studies. For these reasons, observational studies seem to be a means of providing reliable information in the field of the impact of drugs in real clinical practice. The aims of the Ictus study are to describe the patterns of use and the impact of treatment used in AD (cholinergic drugs, memantine and others) in clinical practice, with a European comparative approach.

The population will include 1400 AD patients (MMSE: 12-26, at home at entry, with a caregiver), recruited from 30 Alzheimer's Centers in the EU from different specialities: geriatric, neurological or psychiatric. Nearly 1100 Alzheimer's patients have been already included in the Ictus study. Inclusions will be completed before the end of 2005. All these patients will have a 2-year follow up, with a complete 6 monthly evaluation : ADAS-COG, IADL-ADL, NPI, Zarit, RUD (Resource Utilisation in Dementia).

A web data entry system has been developed with direct access for all Ictus centres.

The second EU-funded study is DESCRIPA, or the development of screening guidelines and clinical criteria for predementia Alzheimer's disease in Europe. The aims of the DESCRIPA study are to develop diagnostic criteria for predementia AD in a clinical setting and to develop screening guidelines for predementia AD in the general population. These aims will be achieved by a longitudinal multi-centre follow-up study of 800 non-demented subjects with cognitive complaints. Variables tested as markers for predementia AD will be: demographics, cognitive tests performance, rating scale scores, medial temporal lobe atrophy, white matter lesions, ApoE genotype, with also in some subset centers: tau/amyloid in CSF, EEG measures, Specit.

In addition the first preventive study on Alzheimer's disease in Europe is now under way in French EADC centres evaluating the impact of Ginkgo biloba treatment on the progression of memory complaints to dementia. The

GuidAge study is a double-blind 5-year follow-up study of 2800 elderly persons making cognitive complaints to their general practitioner. Half are on 240 mg of EGb 761, a purified Ginkgo biloba extract, and half on placebo.

These studies are now ongoing. We do therefore have the possibility to add studies to their basic protocols and this may be a way to carry out some collaborative studies with the North American Consortium, such as imaging and biological studies (plasma and DNA banking are underdevelopment).

In the same way, the EADC and ADCS will coordinate the 3-year follow-up of patients who received the Elan Vaccine to observe its long-term outcome.

With the Ictus study, the PHRC studies (French National Network), the Descripa study and the GuidAge study, we have access to very large cohorts:

- 3000 Alzheimer's patients, with 6-monthly comprehensive neuropsychological and geriatric assessment
- 800 MCI patients
- and 2800 elderly patients with cognitive complaints.

Some plasma, DNA and neuro-imaging banking projects are planned.

EADC : Ongoing Projects

- **ICTUS Study:**
Impact of Cholinergic Treatment on the Natural History of AD:
B.Vellas (France)
- **DESCRIPA Study:**
Development of Screening guidelines and clinical Criteria for
Predementia Alzheimer's disease
F.Verhey, P.J.Visser (Netherlands)
- **Joint EADC-ADCS AN1792(QS-21)-201 Follow up Study Proposal:**
Rationale Post Vaccine follow-up: EADC-ADCS study
- *Alzhemed™ : A Potential Disease-Modifying Treatment for
Alzheimer's Disease*



Emma Reynish:

So what does the future hold for the European Alzheimer's Disease Consortium? Unfortunately, we're all bound by the restrictions of funding. European Union funding is based in framework programmes and we're currently beginning the sixth framework programme. Within this there are possibilities for funding collaborative basic research within the division of the molecular mechanisms of neuronal degeneration. This would be in the setting of a network of excellence on neuro-degenerative diseases and, of course, Alzheimer's disease is just one of these clinical entities. Also within the fixed framework programme of the European Commission, Magda Tsolaki from Greece has submitted a grant application for a continuing education programme on Alzheimer's disease in Europe.

The work of the special interest groups seems to have gone very well. Without funding they seem to have developed their own motivation and their own ways of working within each group, and they are continuing to work together to harmonise European research in the field of Alzheimer's disease. As we know, there are ongoing projects that are funded until 2006: the ICTUS Project and the DESCRIPA Project. Beyond this we will be looking for further European Commission funding within the sixth framework for a grant support, but also look at externally funded projects, perhaps in the form of the Gaudi study, which is going to be started in Northern Spain, and future clinical trials.

EADC; Future

- Continuing work (European harmonisation) within special interest groups
- Completion of ongoing projects plus "add -on" studies
- European commission FP6 funding (basic research and education)
- Externally funded projects (Gaudi study, other future clinical trials)
- Extension of EADC into Eastern European Countries
- Intercontinental collaboration?



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The advantage of an international meeting of this type is that we can all benefit from exchange of ideas and exchange of experiences that we've had in the past, and hopefully this will lead to further international collaboration.

