

Neuroweb project

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Integrated biomedical information for better health



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Introduction

The aim of the NEUROWEB project is to design and develop an intelligent web-based system that allows integration, easy access and sharing of clinical data and biomedical knowledge, with a prototypical application in neurology and neurosciences: the system will support scientists and doctors in their every day work by allowing them to define workflows that can be stored, shared and executed any time.

NEUROWEB project represents one of the first applied research financed by EU e-Health programme, in the field of neurovascular diseases that might systematically generalise the exploitation of genomic information into the daily clinical practice, facilitating significant quality improvements in diagnosis and therapy.

The Neuroweb project is focused on the cerebrovascular diseases defined by the WHO in diagnostic categories 433, 434 and 435.

These diagnostic categories of cerebrovascular diseases established by WHO (ICD-9CM) stay for:

- 433 Occlusion and stenosis of precerebral arteries (the following fifth-digit subclassification is for use with category 433: 0 without mention of cerebral infarction, 1 with cerebral infarction):
 - o 433.0 Basilar artery
 - o 433.1 Carotid artery
 - o 433.2 Vertebral artery
 - o 433.3 Multiple and bilateral

- o 433.8 Other specified precerebral artery
- o 433.9 Unspecified precerebral artery
- 434 Occlusion of cerebral arteries (the following fifth-digit subclassification is for use with category 434: 0 without mention of cerebral infarction; 1 with cerebral infarction):
 - o 434.0 Cerebral thrombosis
 - o 434.1 Cerebral embolism
 - o 434.9 Cerebral artery occlusion, unspecified
- 435 Transient cerebral ischemia:
 - o 435.0 Basilar artery syndrome
 - o 435.1 Vertebral artery syndrome
 - o 435.2 Subclavian steal syndrome
 - o 435.3 Vertebrobasilar artery syndrome
 - o 435.8 Other specified transient cerebral ischemias
 - o 435.9 Unspecified transient cerebral ischemia

Ischemic stroke is a major health problem in developed countries: it is the most common cause of permanent disability, the second most common cause of dementia and the third most common cause of death. Since it is most common in the elderly, the public health impact of stroke will increase in the next decades with growing life expectancy.

Ischemic stroke is a complex phenotype caused by obstruction of blood flow through extra or intracranial vessels. Complexity regards the diversity of its pathophysiology (large-vessels occlusive disease, small vessel occlusive disease, cardiogenic, rare or undetermined data), clinical presentation (depending on the affected brain area), and medical care (requires multidisciplinary

nary approach with neurologist, cardiologist, haematologist, psychiatrist and so on). The predominant risk factor for all type of stroke is hypertension. Hypertension in itself is a complex disease, as are the other known risk factor, diabetes and hyperlipidemia. In addition there are environmental risk factors, such as smoking.

Stroke results therefore from a group of heterogeneous disorders with multiple risk factors. The genetic factors contributing to stroke may act not only directly (several genes of rare stroke syndromes have been identify, such as Notch3 in cerebral autosomal dominant arteriopathy with subcortical infarctions and leukoencephalopathy CADASIL) but also indirectly, by increasing the risk of some predisposing conditions, such as diabetes, hyperlipidemia and hypertension. Moreover epidemiological studies have suggested that there could be also unknown genetic factors for stroke that do not influence susceptibilities to the known risk factors.

Individualized therapies and alternative strategies for prevention require new instruments that are able to expand knowledge in stroke pathophysiology, identifying new risk factors and means to modulate their impact on clinical outcome (death, relapse, disability). Since ischemic stroke is one of the most complex diseases, a large number of clinical, cellular, molecular (including genomic) data have to be integrated and analyzed to have significant improvements.

It is generally accepted that Europe has been leading in brain research until approximately 10 or 20 years ago. After that time this role has been taken over by the United States and the gap between European brain research and United States' brain research is ever widening. NEUROWEB will contribute to ameliorated treatments for brain diseases and to increase European competitiveness in this field, by building partnerships between advanced laboratories, medical institutions and software and service providers.

Methods

The project aims at designing and developing a software tool to allow to integrate into a single virtual database the clinical and genetic databases

of the participating clinical centres, which are different for structure, language, territorial area and pathologies of interest.

The software will be able to query the databanks present on the web containing human polymorphism profiles in normal and pathological populations.

The neuroweb project wants to generate "new knowledge" in order to ameliorate healthcare delivery achieving personalized health care in prevention, diagnosis and therapy. The project involves different research centres and hospitals: Istituto Nazionale Neurologico Carlo Besta Milano Italy, Erasmus Universitair Medisch Centrum Rotterdam Netherlands, University of Patras Greece, National Stroke Centre, National Institute of Psychiatry and Neurology Hungary, University of Veszprem Hungary, Consiglio Nazionale delle Ricerche Italy.

This collaboration can find in the Internet technology its practical mean. Neuroweb will create a network, based on Internet technology among the medical institutions involved in the project. In this way doctors and researchers will have an access to clinical information and knowledge from a networked computer regardless of regional or national boundaries.

Since diseases arise from complex interaction between genetic factors and environment it's important to enhance the value of the genomic research through the associations with key patient clinical data.

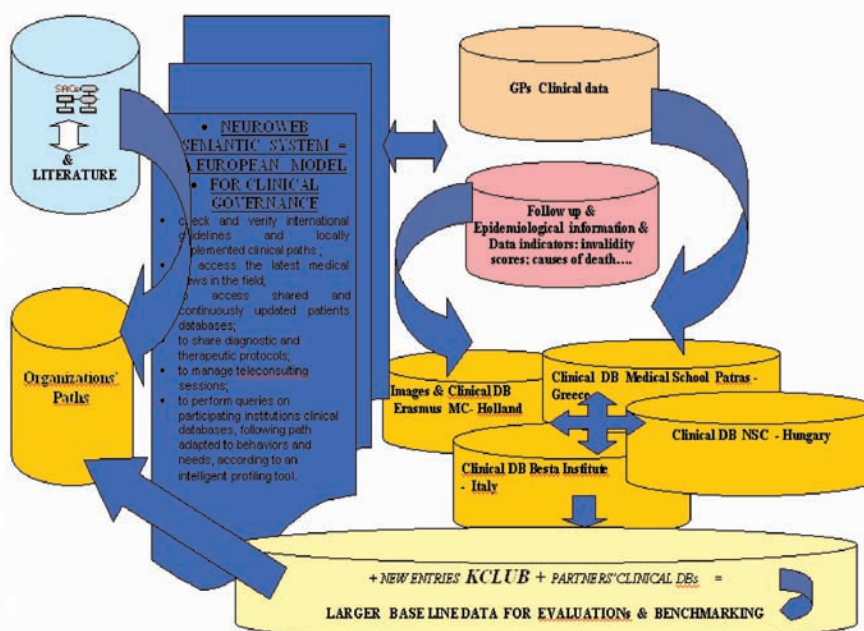
The project aim is that of designing and developing a software tool to allow the integration of clinical and genetic databases of the participating centres which are different for structure, language, territorial area and pathologies of interest, into a single virtual database. Moreover Neuroweb will query the databanks present on the web containing human polymorphism profiles in normal and pathological populations.

The Neuroweb hospitals will make available their genetic, biological, clinical, imaging data that will constitute the kernel of the project. Based on semantic web technology and on web services, neuroweb will perform tasks such as retrieving (throughout the web), integrating and delivering clinical information, medical images, as well as



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Integration and sharing of information and knowledge in neurology and neurosciences



molecular and genomic profiles. The genetic database will be based on innovative technologies such as cDNA-microarray-based method for single nucleotide polymorphisms (SNPs) genotyping (gene-chip).

The exploitation of Neuroweb results envisages the adhesion of other institutions which could improve the NEUROWEB with their data and could enhance the completeness and the quality of their own offered services.

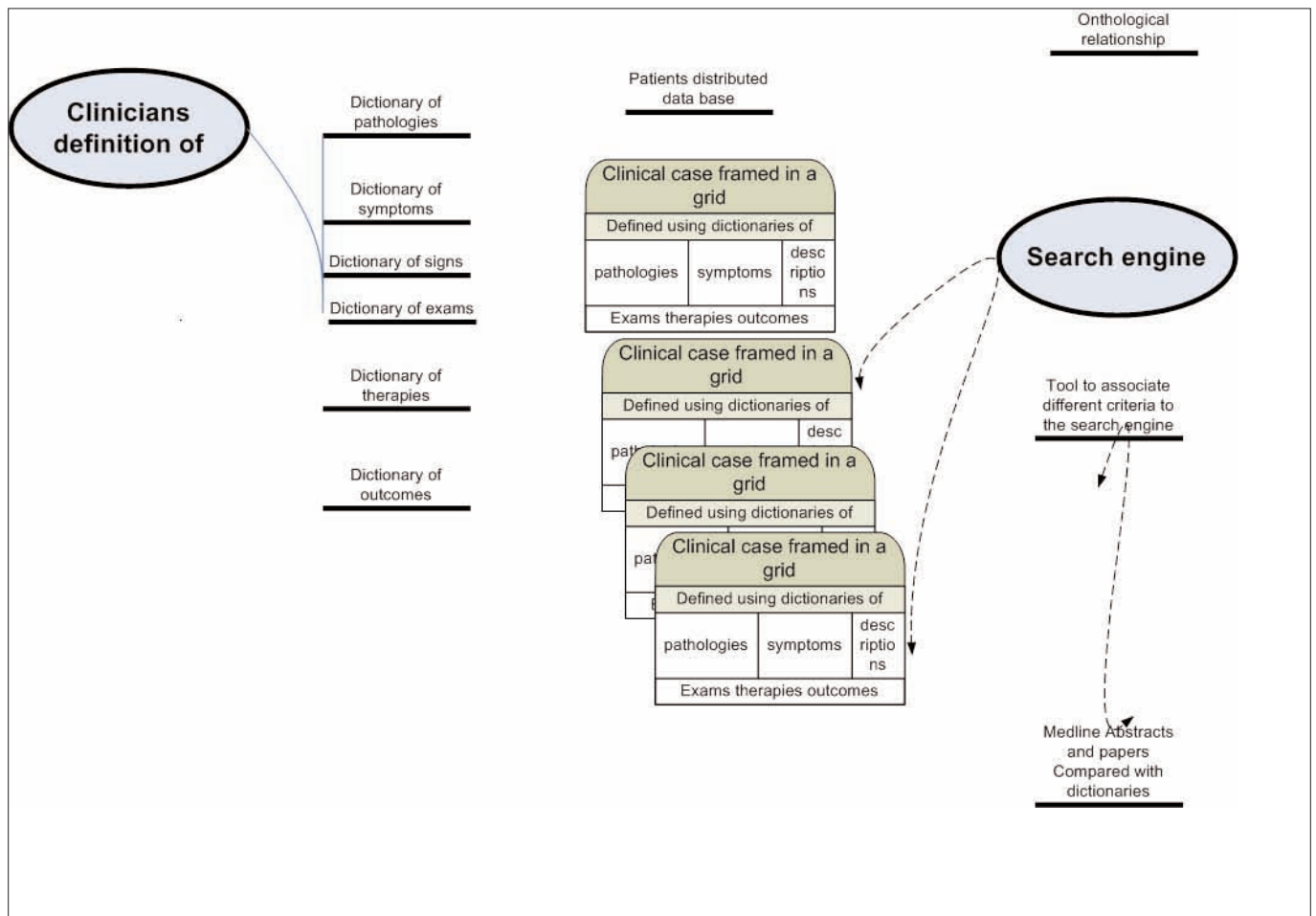
Clinical partners, Scientific Association, University will exchange and share experience, researches and studies from the academic world. Exploitation of the project results will develop both on clinical and technological sides.

On the clinical side clinical partners are committed to setup a "Knowledge Club" where other clinical institutions with own databases or not may ask to enter to get the advantages of NEUROWEB system and to offer their own data for a better verification of existing clinical paths.

On the technological side, the developed engine may be customised to serve other pathologies which may be approached with the same logic of a common shared knowledge base organised around existing standardized clinical paths.

The natural beneficiaries of the project outcomes will be the community of users actually involved in the consortium. The dissemination activities will be thus primarily addressed to these targeted users such as Hospitals and Clinical associations. Once engineered, NEUROWEB will offer to professionals within health organisations the possibility to evaluate and benchmarking - at any time needed - their diagnostic clinical cases and clinical protocols. By discussing and reviewing cases, when needed, with the excellence clinical centres belonging to NEUROWEB Knowledge Club - characterized also for their systematic use of genomic information in daily practice - in the long term they might modify their own adopted profile.

As much as the knowledge Club will increase in



partners number, analysed cases will directly increase enlarging the available data base for more accurate statistical inferences.

Results

The system will provide suggestions on the techniques currently used worldwide to solve similar cases. In case, the users would be able to organise a tele-consult with other specialists.

Given the recorded incidence of neurological disorders, the project has an impact for society at European level in terms of improvement in the safety of patients through a more personalised implementation of treatments and a reduction in medical errors. The generation of a critical mass of information from a vast number and range of disciplines will facilitate accurate clinical applications. This is a prerequisite in order to benefit in future from an improvement in the accuracy of diagnosis and treatment effectiveness achieved through proper intervention for a specific patient via optimised processing of general and patient-specific information. The increased efficiency

generated by the application of the project results and the productivity gained in health information management and improvements in access, speed and quality of care will predictably lead to significant health sector savings and increased revenues.

Discussion

NEUROWEB currently involves 12 partners including universities, clinical and research centres, companies, scientific organisations and local governments from 4 European countries (I, NL, EL, HU). This international co-operation would primarily contribute to offer a systemic example of how genomic knowledge could contribute to the amelioration of daily medical practice in one specific medical field but potentially exportable to other pathologies: after the experimental phase, the NEUROWEB system could be transferred to other clinical fields, by adapting it to the needs of different contexts, other than the neurological field, in order to assist health professionals in all field of clinical research. Furthermore it would contribute to a reduction of fragmentation

among existing databases in the field. In fact the proposed study will investigate how to best exploit the maximum information from a wide basis of data, thus addressing a well defined need of the scientific community. The Community support will have as major outcome an ambitious and unique new facility of Pan-European interest, with a crucial impact on the development of the neuroscience field in Europe. Its impact will go across and beyond national boundaries, representing a permanent facility with the capacity to generate all the relevant data for consultation, exchanging and reporting potentially open to any European researcher in the neuroscience field.

By using this system, the health professionals will be able to understand the state of the art of the medical knowledge on a specific problem in the field of the neurosciences.

NEUROWEB purpose is not to create a new data warehouse gathering together different data sets, but to create a new environment where the information related to data is extrapolated and mined to obtain enhanced knowledge on the patient.

The consortium network of health professionals, specialists and researchers will enhance the actual health knowledge leading to a new generation of eHealth systems assisting in the individualization

of disease prevention, diagnosis and treatment. Moreover NEUROWEB project pursues the Europe Action Plan 2005 specific objective of Stimulating services, applications and content that create new markets and reduce costs and eventually increase productivity throughout the economy.

Of course, the interface will be user-friendly. The system interface will be built browser-like so that only basic skills will be necessary in order to use the system.

NEUROWEB will ensure the respect of the security procedures taking into account all the issues related to privacy and sensitivity of health care data. All data will be anonymous.

Bibliografia

- Garcia-Donaire JA, Nunez AG, Segura J, Ruilope LM, Cerebrovascular Protection and Anthypertensive Therapy *Curr Opin Nephrol Hypertens.* 2004 Sep; 13(5):507
- Rashiol P, Leonardi-Bee J, Bath P
Blood pressare reduction and secondary prevention of stroke and other vascular events: a systematic review *Stroke* 2003 Nov; 34 (11): 2741-8
- Straus SE, Majumdar SR, McAlister FA
New Evidence for Stroke prevention:scientific review *JAMA* 2002 Sep 18;288(11):1388-95
- Ahamad Hassan and Hugh S. Markus
Genetic and Ischaemic Stroke
Brain, Vol 123, No 9, 1784-1812, September 2000

Participants to the Neuroweb Project

Participant name	Country
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Consiglio Nazionale delle Ricerche	Italy
Università degli Studi di Milano-Bicocca	Italy
Regione Lombardia	Italy
Erasmus Universitair Medisch Centrum Rotterdam	Netherlands
University of Patras	Greece
Országos Pszichiatriai es Neurologiai Intezet	Hungary
Pannon University	Hungary
Sirse-Net Spa	Italy
Microsystems S.r.l.	Italy
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