alamaya
foundation for research in schizophrenia

NEWSLETTER 2012

IN ANDEAN INDIAN, ALAMAYA MEANS HOPE FOR A MIRACLE

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NEWS FROM THE FOUNDATION

Alamaya constantly endeavours to increase its visibility and raise awareness about its mission in order to advance fundraising, and to help de-stigmatizing schizophrenia as well as other psychiatric disorders.

The Foundation was thus present at the **Brain Week** (**Semaine du Cerveau**) in March 2011 and 2012, via an information stand located in the main building of the Lausanne University Hospital (CHUV) during public forums. Interaction with the general public often allows to uncover a great number of misconceptions about schizophrenia, and to answer the manifold questions people have with respect to psychiatric diseases.

In December 2011, Alamaya was chosen as the beneficiary of an initiative conducted by the service clubs of the Riviera during the **Montreux Christmas Market** (**Marché de Noël de Montreux**). During one week, members of the various clubs took turns daily from 11 am to 11 pm to serve drinks at the "Cabane des Bûcherons"; the profit of this operation, generously "rounded up" by the service clubs, was allotted to the Foundation. This action, which was echoed in the media (24heures, Le Régional, Radio Chablais), was achieved thanks to the wonderful commitment of many club members and has made it possible for Alamaya to be brought to the attention of a large and diversified public.

Kim Do Cuénod, Director of the Unit for Research in Schizophrenia, receives the cheque donated by the service clubs of the Riviera from Mr Pierre-André Roduit, interclub coordinator

The number of potential **beneficiaries** of the research programme supported by Alamaya is constantly **on the rise**. As a matter of fact, scientific studies conducted by Professor Kim Do Cuénod are also leading to relevant progress in the understanding and treatment of other psychiatric disorders – in particular **autism** and **bipolar (manic-depressive) disorders**; the Unit for Research in Schizophrenia (URS) has thus included these disorders in its work programme.

On average, **schizophrenia** affects **1 out of 100 individuals,** approximately 80'000 persons in Switzerland, **autism** affects **1 out of 110 children** and **bipolar disorders** between **1% and 2% of the population**; bipolar disorders, as schizophrenia, generally appear during **adolescence** or in **young adults**. These numbers clearly indicate the crucial issues at stake in the fight against those diseases, which seriously and persistently threaten the future prospects of so many young people.

NEWS FROM RESEARCH

The research programme conducted by the URS is centred on the concept that a deficient regulation of the balance between reductions and oxidations ("redox") in the body leads to **oxidative stress**, which is highly damaging for the central nervous system. **Glutathione** is the main protective agent of nerve cells against these aggressions, induced by the respiration of oxygen, which generates toxic substances. Insufficient synthesis (production) of glutathione impedes the normal functioning of **contacts** between nerve cells, and, during the development of the brain, causes **anomalies** of some of these **cells** as well as of the **nerve fibres** that ensure their connections. These disturbances are presently considered to be an important **risk factor** that is likely to explain the disorders affecting patients.

CLINICAL RESEARCH (IN PATIENTS)

The study involving **young psychotic patients** and aimed at **analyzing the evolution of their symptoms in the long term** is being pursued. Patients participating in the study are evaluated when they join the study and every 6 months once they have been included. Each evaluation consists of:

- Interviews to assess their situation
- Tests to assess their memory, concentration, attention
- A biomedical analysis (blood or skin sample)
- An examination of the brain through magnetic resonance imaging (Scanner)
- An electroencephalogram (EEG) of the brain

The trial with a **new medication** in young patients is also being pursued. The drug, called **N-acetyl-cysteine (NAC)**, helps to **reduce oxidative stress** and to **improve the synthesis of glutathione**. It is a randomized, double-blind and placebo-controlled trial – which means: half of the patients participating in the trial receives NAC, the other half takes a placebo (neutral substance); the distribution is carried out randomly. The study is conducted simultaneously in both groups; neither the patients nor the team responsible for the study know who receives NAC and who receives the placebo. NAC and the placebo are absorbed in addition to the standard medical treatment.

Data concerning patients and the substance they receive (NAC or placebo) are coded during the whole duration of the trial in order

to guarantee a fully objective evaluation; consequently, the potential effectiveness of NAC can only be assessed at the end of the study, once all data will have been decoded.

Patients receive NAC or the placebo during a period of 24 weeks. A thorough evaluation of each patient is carried out at the start of the trial and every 4 weeks thereafter until the end of the 24 week period; an additional evaluation is conducted 28 weeks after the beginning of the trial in order to assess the effects of interrupting the treatment. These evaluations all include biochemical analyses, assessments on the cognitive and functional level as well as examinations by means of brain imaging and electroencephalography.

The recruitment of patients for both these studies will be stopped at the end of 2012 / beginning of 2013. The collected data will then be examined and **final results will be available at the end of 2013**.

Basic Research (Laboratory)

Studies involving our animal model (mice), in which a **glutathione deficiency similar to the one affecting patients** has been replicated, are being pursued at several levels.

The URS demonstrated that two areas of the brain involved in schizophrenia, the hippocampus and the anterior cingular cortex (medial part of the frontal lobe), are the site of alterations of a particular type of cells, i.e. **fast spiking inhibitory interneurons**. These alterations cause a deficit of synchronized neuronal oscillations, which are essential for the normal functioning of cognitive activities, as observed in patients.

In the young animal, but not in the adult, oxidative stress further and persistently aggravates the anomalies due to fast spiking inhibitory interneurons. These observations reveal the existence of a **"window of vulnerability",** also called **"critical period ",** in the young animal with a glutathione deficiency.
How can the vulnerability of inhibitory interneurons to oxidative stress be explained? Cells of this type are normally surrounded with a special substance, the **peri-neuronal net**, which **protects them against oxidative stress**. This net develops progressively in the young animal, and reaches maturity in the adult animal – which explains why these **neurons** are **particularly sensitive to oxidative during the early stages of the animal's life**, as long as their peri-neuronal net has not reached maturity. The URS also showed that the selective destruction of this net in the adult animal, by means of a specific enzyme, makes these neurons vulnerable again to oxidative stress.

The most remarkable result, on the level of therapeutic perspectives, lies in the administration N-acetyl-cysteine (NAC) during gestation and the life of the young animal: **NAC protects against the anomalies caused by oxidative stress.** It is precisely this substance – NAC – whose effects are presently tested in patients.

Investigations are also being undertaken in the cellular and animal models to evaluate the impact of insufficient glutathione on the cells that are responsible for the formation of myelin. **Myelin** is a substance that surrounds and protects **nervous fibres** (which show anomalies in patients), ensuring their insulation and the efficient conduction of nerve impulses.

Thanks to the internationally acknowledged relevance and interest of its research programme, the URS has developed a **great number of collaborative projects in Switzerland and abroad**, in particular with the Brain Mind Institute and the Center for Biomedical Imaging at EPFL, the Services de Radiology, Clinical Chemistry and Clinical Pharmacology of the University Hospital in Lausanne (CHUV), the EPFZ, the Psychiatric University Hospital in Basel, the University Hospitals in Oslo (N), Copenhagen (DK) and Southampton (UK), the Federal University of Minas Gerais in Belo Horizonte (Brazil) and following institutions in the USA: Rockefeller University (New York), University of Cincinnati Medical Center, Harvard Medical School (Boston), University of Maryland School of Medicine (Baltimore), Johns Hopkins University School of Medicine (Baltimore), Stanford University School of Medicine.

Private donations are essential to advance research
On behalf of patients and their families: THANK YOU for your support
The Alamaya Foundation is a registered not-for-profit organization – donations are tax deductible

Avec le soutien de la Loterie Romande

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