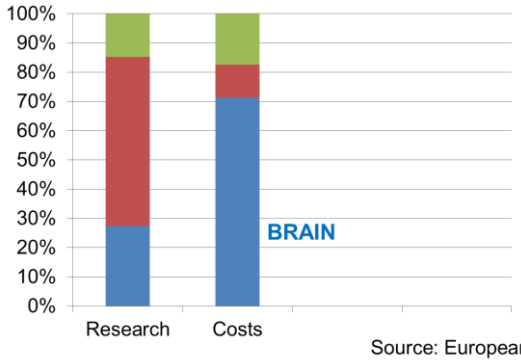
NEWSLETTER 2016-2017

VISIT OUR WEBSITE WWW.ALAMAYA.NET

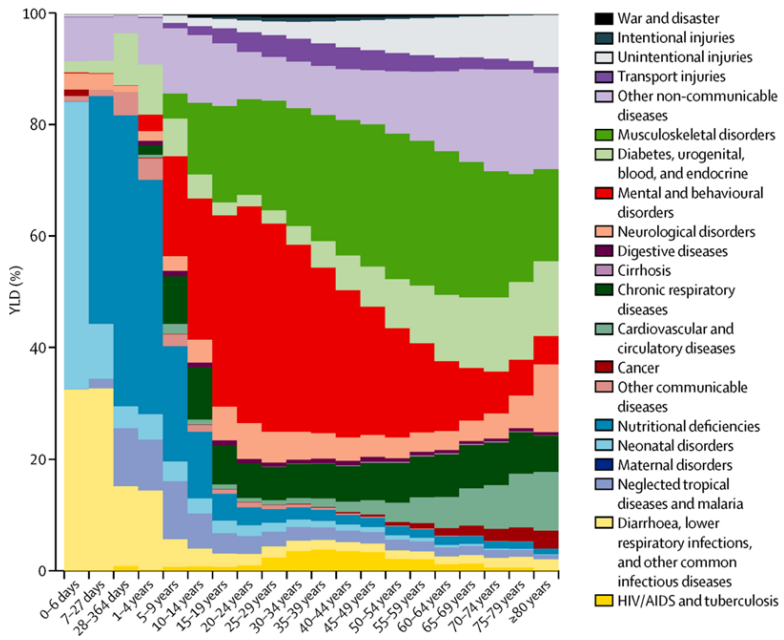
The mission of the Alamaya Foundation, which consists in raising the private funds needed to advance the studies conducted at the Unit for Research in Schizophrenia (URS, Center for Psychiatric Neuroscience, Lausanne University Hospital), remains a significant challenge given the erratic economic environment on one hand, and, on the other hand, the still widespread lack of knowledge concerning the extent and impact of psychiatric disorders on a great number of people.

	Research (millions €)		Costs (billions €)	
BRAIN	431	27%	798	71%
CANCER	914	58%	126	11%
CARDIO-VASCULAR	232	15%	196	18%



Source: European Brain Council

The graph above illustrates the striking **IMBALANCE** between investments granted for diseases affecting the brain (among which psychiatric disorders) and the costs they occasion for society (treatments, hospitalizations, rehabilitation, disablement allowances, etc.) in comparison with a disease such as cancer. The figures published by the *European Brain Council* show that **investments in research targeting brain diseases correspond to 27% whereas their costs amount to 71%**. Investments in cancer add up to 58% whereas its costs are equivalent to only 11%.



Furthermore, in terms of Years Lived with Disabilities (YLD), **psychiatric disorders in young adults represent approximately 50% of all pathologies** (figures published by the WHO, in red in the opposite graph).

The Alamaya Foundation strives to highlight these facts, which the general public and potential sponsors are widely unaware of; they represent a strong case to emphasize the importance and necessity of the studies conducted by the URS.

NEWS FROM RESEARCH

The location of the URS on the site of the psychiatric hospital of Cery allows **close collaboration with the clinicians of the Service of General Psychiatry** (Department of Psychiatry, Lausanne University Hospital), directed by Prof. Philippe Conus. Given the complex issues at stake, the URS team consists of specialists in neuroscience (neurobiology, genetic and molecular biology, neurochemistry, neuroanatomy, neurophysiology, study of behavior, etc.) and professionals in direct contact with patients (psychiatrists, psychologists, radiologists specialized in brain imaging, etc.). This collaboration is crucial to achieve significant progress, and facilitates the essential **participation of patients** in the research process.

The present evolution of clinical psychiatry in the field of schizophrenia is aimed at an **early detection of individuals at risk of developing the disease** since experience has shown that the prognosis is all the more favourable if the treatment begins as early as possible. It is therefore crucial to identify **neurobiological markers**, which are currently missing and required for:

- The early detection of potential patients;
- The definition of the different stages of the disease;
- The evaluation of the progression of the pathology;
- The development of new therapeutical means;
- The development of preventive measures.

It is also essential to discover **molecules likely to inhibit the progression of the pathological process (prevention) or to avoid its damaging evolution once the disease is clinically manifest (treatment)**. These are the goals of the Unit for Research in Schizophrenia (URS), which endeavours to bridge clinical and fundamental research, and works along the following lines:

- The collection of biological and psychological observations in patients;
- The investigation of the disease mechanisms in experimental models;
- The exploration of biological markers and of new, potentially preventive treatments.

The studies supported by Alamaya now focus on three main occurrences, whose combination plays a prominent role in the causes and mechanisms of schizophrenia and other psychiatric disorders: **oxidative stress** (deregulation of the balance between free radicals and antioxidants in cells), **inflammatory reactions** (immune responses) as well as dysfunctions linked to the **NMDA receptor** (one of the most important excitatory receptors of the brain, who plays an essential role in all learning and memory processes).

Indeed, the excess of oxidations in the brain induces an inflammatory response and, conversely, an inflammatory surge increases oxidative stress. These two phenomena therefore tend to amplify each other, thus aggravating their damaging consequences. The same damaging interaction can be observed between oxidative stress and the NMDA receptor: oxidation causes a reduced activity of the receptor and this reduction leads to a lack of stimulation of antioxidant mechanisms.

In summary, these three factors, oxidation, inflammation and hypofunction of the NMDA receptor, which are all involved in the disease, converge to amplify each other's negative effects.

It is likely that future preventive treatments will consist in attempting to counter these three factors during the development of the brain by combining antioxidants, anti-inflammatory agents and activators of the NMDA receptor. The URS works towards the development of novel redox modulators which are suited to act on these three mechanisms.

Clinical Trial with N-acetyl-cysteine (NAC) in First Episode Patients

The clinical trial with N-acetyl-cysteine (NAC) in young patients during their first psychotic episode has been closed and the results have been analysed; they have been published in *Schizophrenia Bulletin*, a major scientific journal in the field of biological psychiatry.

A trial with the same antioxidant substance had been conducted between 2002 and 2005 in chronic patients. Its results turned out to be very positive in particular on the level of negative symptoms (language, communication, emotional and social deficiencies), which were improved with NAC and which are not treated by presently available medication.

These results have prompted a trial with NAC in young patients in the hope that the effects might be even better given the fact that young patients do not (yet) show the damages due to the chronicity of the disease. Researchers from Harvard University (USA) have asked to collaborate in this second study.

Results concerning patients treated with NAC, as compared to those who took a placebo, revealed **two important findings**:

- **Patients treated with NAC** showed an **improvement of their cognitive symptoms**, in particular the speed of information processing, which is of crucial importance for cognitive functions (attention, abstraction, communication, memory, etc.).
- Patients in whom a **"redox" blood marker**, which allows to evaluate the state of oxidation in cells, has a **high level of activity** (synonymous with a state of high oxidation) also showed an **improvement of their positive symptoms** (hallucinations, confusion, incoherent behaviour) following treatment with NAC.

For the first time, the latter observation paves the way for a "biomarker-guided treatment" in psychiatry, in other words for a **personalized treatment** whose efficiency can be determined on the basis of a biological marker; the **URS** team thus becomes a **world leader and pioneer** in this field.

Trauma in Young Psychotic Patients

Investigations conducted by a clinician-scientist of the URS group in young patients showed that those among them who experienced abuse or trauma during their childhood (physical / sexual violence) are much less responsive to treatment (their condition does not improve) than those who were not subjected to such violence.

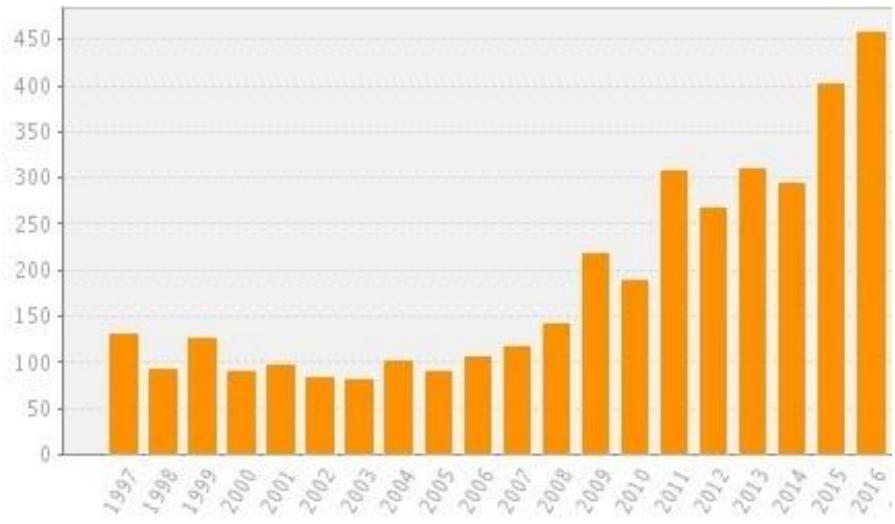
These investigations, in parallel to those conducted in the animal model, revealed that the **experience of stress/trauma, which occurs during the development of the brain, causes irreversible damages/lesions on certain neurons – and that these damages lead to the breakout of the disease at the beginning of adulthood.**

Why is this evolution irreversible? The recent achievements of the URS showed that two major phenomena are involved in this process: oxidative stress and inflammation. These two factors amplify each other and create a vicious circle, which has to be interrupted at an early stage to prevent the damages/lesions mentioned above. Now the investigations in the animal model showed that if NAC is administered immediately after a stress, the damages on neurons are avoided. This leads to the following perspective: **if an antioxidant substance is given to children at risk who experienced abuse/trauma, it should be possible to prevent the disease from breaking out at a later stage**. This perspective obviously needs to be considered in the long term but it represents an extremely promising road to the **prevention of psychosis**.

In addition to the above, several other studies are under way at the URS focusing in particular on:

- The development of **novel molecules for the regulation of the redox system** (balance between reductions and oxidations) targeted at treatment and prevention;
- The identification of **peripheral markers of the brain redox state**;
- The role of **brain glutamate** (neurotransmitter which activates the NMDA receptor);
- Interactions between the **redox system** and **immune reactions**;
- Interactions between the **redox system** and the **formation of myelin** (protecting envelope of nervous fibres).

In summary, **the Unit for Research in Schizophrenia**, in collaboration with several other research centers, **continues to advance by leaps and bounds towards a better understanding of the disease, more efficient treatments and possible measures allowing to prevent psychosis**. The number of citations regarding articles published by the URS group are constantly on the rise (see graph) and Prof. Kim Do Cuénod is invited to present her work at major national and international meetings, as well as to participate as a consultant in important clinical trials in Germany, the United Kingdom and the Netherlands.



Number of citations - 1997-2016

THE ALAMAYA FOUNDATION IS A REGISTERED NOT-FOR-PROFIT ORGANIZATION
DONATIONS ARE TAX DEDUCTIBLE – THANK YOU FOR YOUR SUPPORT!

For any information or to receive postal payment slips (for Switzerland only), please contact our secretariat:
Ms Cristina Marich – Le Grand Chemin 63, CH – 1066 Epalinges – Phone: +41 21 341 41 03 – Email: **cmarich@alamaya.net**
Registered Office: Chemin de la Becque 42, CH – 1814 La Tour-de-Peilz
Bank Details: Banque Julius Baer & Cie SA, Avenue de la Gare 39, CH – 1001 Lausanne
IBAN: CH 65 0851 5026 0026 6200 3 – BIC: BAERCHZZ – CLEARING: 8515