Marie Schaer, could you kindly tell us about your training and career so far?
M.S: I completed my medical studies in 2005 in Geneva. I was interested in doing research in neuroscience and, thanks to the MD-PhD SNF-Fellowship, I had the opportunity to start a PhD directly after my medical diploma. My thesis project was anchored in the research unit from Prof. Stephan Eliez (Child Psychiatry), where I learnt the use of structural neuroimaging techniques to quantify brain development in patients with psychiatric diseases. Aside from the application of these methods, I could benefit from the co-supervision of Prof. Jean-Philippe Thiran at the Signal Processing Laboratory at the EPFL to develop new methods for brain image analysis. Hence, I developed the necessary technical skills to be able to adapt the algorithms to answer specific clinical questions. When I finished my PhD in September 2008, I had to leave the lab to start the clinical training. I remember that I found very difficult to leave the research work at the point when I started to be really productive. With the goal to specialize in child psychiatry, I first completed one year in of adult psychiatry in Geneva, and then one year in Neurology at the University Hospital of Zürich. Since October 2010, I am back in Geneva. Thanks to the NCCR Fellowship, I am able to pursue my research along with a part-time clinical work in child psychiatry.

You are an MD, how did you become interested in psychiatry?
M.S: I have always been interested in understanding how the brain works. How do these 1300 grams of cells acquire the ability to produce complex cognitive functions? How come that the fine-tuned cascade of brain development sometimes goes awry, with the emergence of abnormal mental functioning? With the help of neuroscience, we increasingly get the tools to approach these fundamental questions. I am willing to bet that the field of psychiatry will dramatically evolve over the next decades, with the ability to increasingly understand mental disorders, and hopefully to prevent part of them. I feel that we are very lucky to be able to contribute to this revolution.

What is your motivation in research?
M.S: I want to learn; research provides me the time to read, think, and develop ideas. I love solving small questions, like puzzle pieces that will fill in the gaps between neuroscience and psychiatry. In particular, I like the technical aspects of image analysis: neuroimaging is half way between medicine and engineering and I really enjoy playing with the MRI and the algorithms. To answer specific clinically-relevant issues, one must sometimes be able to question the methods. For that purpose, I

learnt enough programming to be independent in almost all the research questions that I may have.

What are the characteristics of the disorder you are studying and how can imaging techniques help to better understand the disease?
M.S: Within the lab of Prof. Stephan Eliez, we are studying a neurogenetic disorder: 22q11 deletion syndrome (22q11DS). About one third of the patients affected with this syndrome will develop schizophrenia during adolescence and young adulthood, so that 22q11DS has been increasingly recognized as a model to study this devastating psychiatric disease. More specifically, 22q11DS represents a unique opportunity to learn about the interplay between genetic, cerebral, behavioral, environmental and psychiatric factors in the context of schizophrenia.

Prof. Eliez's laboratory comprises a multidisciplinary team, where I am carrying out the structural neuroimaging aspects. The precise delineation of the cerebral morphology brought by the evolution of image analysis technique increasingly permits to point the mechanisms responsible for the emergence of mental diseases. Indeed, the first neuroimaging methods aimed at identifying the structures that were morphologically impaired in specific psychiatric condition. For instance, a reduction in the frontal gray matter volume has been consistently observed in schizophrenia and has been related to the executive difficulties in patients. Nowadays, we are able to produce accurate three-dimensional reconstruction of the cortex, which are in turn allowing new insights on the pathogenesis of the disease. The question of where cerebral structures alterations arise has progressively shifted into a new query about why these changes occur. For instance, cortical thickness analysis makes it possible to follow in vivo the maturation-associated refinement of the neural circuitry (pruning) with an exquisite spatial resolution. Thanks to this powerful technique, we could suggest that a delayed cortical maturation was characterizing 22q11 deletion syndrome, whereas the onset of schizophrenia was tightly preceded by a collapse of the cortical architecture.

You developed a specific method in that field, could you describe it?
M.S: A fascinating feature of the brain structure is the high folding of the cortex (gyrification), which permits to pack an impressive amount of gray matter into the restricted skull space. As cortical folding develops very early and is thereafter barely modified, gyrification has been proposed as a window into the early brain development. In other words, the cerebral folds of grown-up individuals may carry the signature of early abnormal insults that are predisposing them to develop certain psychiatric diseases. When I was doing my PhD, several methods existed for measuring cortical folding (gyrification), but I was relatively unsatisfied either by their ability to measure a meaningful marker of folding or by their technical implementations. For this reason, I developed a new method that has the advantage of being technically satisfying while measuring an easy to interpret and biologically relevant process. Probably due to its elegance, this method received a large interest and I had the opportunity to integrate it within one of the most used neuroimaging software: FreeSurfer (Harvard University). As a result, my method was made freely

available for the worldwide scientific community. A few groups already published results using this method in recognized journals, and I hope that its success will continue.

What is in your eyes the benefit of the NCCR Excellence Fellowship?
M.S: Most of all, the NCCR Fellowship allows me to dedicate a consequent time for research. Being otherwise constrained with the clinical work, this grant permits to secure time for the production of scientific work. As such, it represents an inestimable support to help me building my career.

Another advantage of this Fellowship is to benefit from the stimulating setting provided by the NCCR Core, with the opportunity of many fruitful discussions. More specifically, having worked on 22q11 deletion syndrome since a few years, I find the close collaboration with new groups very profitable and the translational approach from mouse models to humans particularly exciting.

What is your long term goal?
M.S: I would like to get a position balanced between research and clinical work. Ideally, I would keep a small percentage of time devoted to the clinical work, to stay in contact with patients, and a sufficient time for research, to further contribute to psychiatric neurosciences. Hence, an academic carrier is probably the best way to satisfy this ideal in my everyday work. On the short-term, I plan to go abroad for a few years to acquire other visions of research and reinforce existing collaborations.

Marie Schaer's advices to young clinicians interested in research

ADVICE N° 1
Start relatively early.

For instance, interested medical students should take advantage of their elective (e.g. during the last year) to experiment the everyday work in a research laboratory. And if they like research, just head down for a PhD! Research is highly competitive, and it's probably much easier to start with research and come back later to clinical work than the other way around… And even without the goal of an academic carrier, a PhD is always a constructive experience, to get a better sense of where medical knowledge comes from, and to build a structured thought.

ADVICE N° 2
Carefully select your advisor.

My second advice would be to carefully select your advisor. Take a place where you can learn, where you can express yourself while being supported, where you can publish and progressively become independent. German-speaking colleagues use to name their advisor "Doktorvater", which nicely reflects how much an advisor will influence your research career.