

ESF Exploratory Workshop on

**THE ADOLESCENT BRAIN.
NEW INSIGHTS FROM CLINICAL
AND ANIMAL MODELS**

Rome (Italy), 22-24 October 2009

Convened by:
Giovanni Laviola

SCIENTIFIC REPORT

Co-sponsored by



EXECUTIVE SUMMARY

Adolescence is usually considered as the period of physical, psychological and social transition between childhood and adulthood. This period is characterized by psychological changes that affect individual's sense of identity, their self-consciousness and their relationships with others. During the last decades, significant advances have been made from different fields of research in the study of adolescence. Unfortunately, scarce crosstalk between the different disciplines of research is nowadays available. The present ESF exploratory workshop has brought together leading European experts from distant scientific fields in order to gain a deeper knowledge on the natural variations of adolescent traits in humans. The main goal of the workshop was to forge new links between clinical studies and basic neurosciences in order to establish the most promising scientific opportunities for improving the understanding of the genetic and psychobiological determinants at the basis of so-called deviant behaviours during adolescence. Discussion on scientific tools and technologies presently available has been considered. Given the relevance of interdisciplinary research approaches together with the necessity of further infrastructure investments, potential partnerships aimed to support and conduct adolescence research at the cutting edge of neurosciences has been explored.

Adolescence, the transitional period between childhood and adulthood, is often characterized by extreme-oriented behaviours, possibly mediated by discontinuities in brain development. Compared with adults, adolescents are more sociable, and display a propensity to sensation seeking and risk taking behaviours. Asynchronous trajectories of neural development during adolescence may account for such behavioural peculiarities. Research on animal models has been an essential tool in behavioural neuroscience and still provides scientists new insights into the understanding of adolescence, given that adolescent rodents and non-human primates display a behavioural repertoire similar to that described for humans. A prominent inner drive for sensation seeking behaviour at adolescence may have adaptive benefits with regard to the development of independence and survival without parental protection. In this line, an adaptive role during hominid evolution has been proposed. Along evolution, increments in lifespan were accompanied by an extension of the adolescent phase, allowing an increased room for the exploration of new environments that would facilitate the emergence of innovative behaviours. On the other hand, these higher levels of exploration may lead to risk taking behaviours, including experiences with psychotropic drugs. Moreover, research into the neurobiological mechanisms underlying normative and deviant adolescent behaviour will bring to light neural and genetic factors relevant for the increased vulnerability of adolescents to psychopathology. In summary, adolescence cannot be solely considered as a critical window of vulnerability for psychopathology and drug abuse, but also as a significant window of opportunity because of the increased brain plasticity occurring at that time.

This Workshop was then conceived as explorative in its very nature: in that we sought to have scholars taking the risk of crossing the boundaries of their disciplines and putting their boldest ideas, hypotheses and expertise at the service of fellow researchers in other, related fields. Starting from a critical point of view towards their specific field of expertise, and openly addressing the points that are most needful for new vistas, they were called to evoke suggestions from fellow scientists from neighbouring areas.

One innovative aspect of the Workshop was that of having also clinician scientists in the panel of presenters and discussants, to address the distance currently separating animal models, genetic epidemiological studies and clinical practice. As such, this Workshop provided a rather unique and innovative occasion for a small group of researchers within the EU to freely interact on what are the difficulties in connecting human studies to animal research and vice-versa, on how they can reciprocally improve their work, and on how to expand on practical implications in mental health-related problems.

Discussion of recent evidence from humans and animal models has contributed to develop a common road map for the interdisciplinary research of adolescence not only as a critical window of vulnerability, but also as a favourable window of opportunity provided by a still available degree of brain plasticity. Emphasis has been paid to reach a consensus on the main areas of research critical for 1) the development of more effective strategies limiting adolescent risk behaviour, including drug abuse, and for 2) the identification of a personality profile at risk for psychopathologies, as soon as adolescent, in order to elaborate directories and prevention programs for specific treatment approaches.

The Workshop was thus aimed at supporting a cultural and technical effort which can be sustained only through European scale collaboration, as suggested by the variegated panel of international experts. It is in fact unrealistic that a single nation or even a small consortium of few nations can effectively address these issues successfully. Beyond cultural advancements, the Workshop added potential for heralding collaborative efforts between participants which have already been primed, for initiating follow-up research activities and/or developing future collaborative actions among participants and within the EU.

SCIENTIFIC CONTENTS

The workshop was organized in four main sections aimed to cover the various aspects of adolescence. During these general sections invited speakers presented an overview of their research field, and, at the end of each section, a general discussion was allowed and participants encouraged to actively intervening. Abstracts of the Workshop presentations will be provided, although they might be treated in confidence by the relevant Committee (and not published).

On the first day, following the welcome from the convenor, **Giovanni Laviola**, who briefly presented the ESF Workshop on the adolescent brain, the ESF representative, **Emmanuelle Wollman** provided a general overview of the ESF organization and a resume of the several initiatives currently being undertaken by the ESF. In particular, information from the Medical Research Council was emphasized and useful information about forthcoming granting initiatives relevant for researchers in biomedicine was provided.

Session I was programmed to provide a general background on human adolescence. The concept of adolescence in the history of hominid evolution was updated by the anthropologist **Jacopo Moggi-Cecchi**, who, by the study of tooth development in fossil hominins was able to provide information about the origin of adolescence. In the human lineage, it is only in our species (*Homo sapiens*) that a prolonged childhood started to occur. Afterwards, the sociologist **Carles Feixa** presented adolescence from a socio-cultural point of view. The concept of adolescence mostly in occidental cultures was analysed, emphasizing the critical relevance of the *passage* from childhood to adulthood in the different societies. A more recent update of the concept of adolescence and youth in our modern society was possible by the presentation of three very well known characters from literature and cinema (Tarzan, Peter Pan and Blade Runner) that might represent the main features of youngsters during the last three centuries. Thereafter, Prof. **Massimo Ammaniti** presented a more psychophysiological vision of human adolescence, providing a link between the anthropologic and socio-cultural concept of adolescence and the physiological bases of this developmental period. Investigation of correlations between structure/physiology and behavior during development might be of great value for the study of adolescence and great advances have been made thanks to magnetic resonance techniques. At this regard, **Stephanie Burnett** in the final intervention discussed on the discontinuities of brain development during adolescence by using magnetic resonance techniques. In particular, her research has been focused in social cognition given the critical importance of social competence in adolescent life.

During **Session II** the possibility of forging links between clinics and animal models was emphasized. Research on animal models provides scientists new insights into the understanding of adolescence, given that adolescent rodents and non-human primates display a behavioural repertoire similar to that described for humans. **Susan Andersen**

introduced such topic by presenting parallel data from both animal studies and human adolescent populations. Along her talk, adolescence was described as a critical period particularly sensitive to environment. Despite early life events might have altered brain maturational endpoints (e.g. cortico-limbic circuitry), the adolescent brain might be still malleable, thus providing a critical age window for both vulnerability and/or opportunity for intervention. Thereafter, **Giovanni Laviola** presented data from animal studies demonstrating that the dopaminergic system might be in the basis of sensation seeking and impulsive behaviour. During adolescence, an immature dopaminergic system might probably account for the decreased inhibitory control over impulsive that is feature of that age. **Bauke Buwalda** discussed animal data on age-related differences on stress vulnerability. Adolescent rats seemed much more sensitive to chronic social stress than adults, although they are also responsive to the appeasing influence of congeners. Finally, **Maria Paz Viveros** presented behavioural and neuroendocrine sexual dimorphisms on adolescent rodents in studies of drug abuse. The evidence provided critically highlights the importance of considering both sexes in the research of adolescence both in animal and human studies. This session provided further indications for the valuable application of animal models in the study of adolescence and opened new avenues for the putative collaborative pathways between basic and clinical neuroscience.

The **Session III** covered the genetic bases of personality traits as studied in the adolescent population. **Zsofia Nemoda** described a genetic association between human temperament (i.e. novelty seeking) and a polymorphism of the dopamine D4 receptor (DRD4) gene among adolescents. Other polymorphisms in the monoamine receptors and transporter genes were evaluated as well as possible genetic variants of the enzymes catalyzing rate-limiting steps in the synthesis and breakdown of monoamines [i.e. tyrosine and tryptophan hydroxylase, catechol-O-methyltransferase (COMT), and monoamine oxidases (MAO-A, MAO-B)]. The importance of such polymorphisms in personality traits mainly present during adolescence and in psychiatric disorders (e.g. ADHD, Attention Deficit Hyperactivity Disorder and/or anxiety disorders) was also in depth discussed. The relevance of genetic polymorphisms on drug addiction and dependence was then discussed by **Gilberto Gerra**, who also emphasised the importance of gene x environment interactions. Moreover, early life developmental events arised as a critical factor in adolescent and adult neuro-behavioural outcomes. Gene x environmental interaction was also investigated by **Robin M. Murray** in relation to the altered risk of psychoses and/or schizophrenia observed among heavy consumers of cannabis during adolescence, and also assessed possible association with the genetic variability of COMT.

Session IV was devoted to the discussion of representative ongoing research projects on adolescence within Europe. On the one hand, **Tineke Oldelinkel** reported some results from the TRAILS ('TRacking Adolescents' Individual Lives Survey') study, a prospective cohort study of Dutch adolescents. She focused on mood disorder and depression that emerge during adolescence with a higher prevalence among females. The gender-specific increased sensitivity to stressful life events observed for females might critically account for this observation. On the other hand, **Corinna Petersen-Ewert** described her contribution to European projects aimed at assessing mental health and well-being in children and adolescents in Germany. In particular, she described the importance of using a standardised screening instrument for the implementation in representative national and European health surveys (i.e. KIDSCREEN and DISABKIDS projects). By this last session we aimed to better understand the major European biomedical needs in relation to youth, and the principles aspects that should be covered in future competitive proposals.

Sessions were followed by a final roundtable that allowed a more detailed discussion of the data presented. At this point, a global vision of adolescence was already available, but a lively debate on the definition of adolescence and of its limits arised. Some basic and clinical researchers participating to this ESF Workshop were already engaged in exploring adolescence; their contribution to the discussion was highly stimulating for the audience and facilitated the fluent and constructive bidirectional dialogue established between basic and clinic neuroscientists.

ASSESSMENTS OF RESULTS

Overall, the aim of promoting the interaction between researchers in human psychology, sociology and epidemiology and researchers in the field of animal models has been fulfilled. During the discussions and interactions we witnessed a growing interest of researchers in one field for what people in the other field were doing, and what perhaps counts more, acknowledgment of several oversimplifications proper of each sub-field. In the endeavour to understand how genetic and environmental factors influence vulnerability to emotional disorders and deviant behaviour, with special attention to the adolescent phase of life, this workshop has had the merit of putting together persons who otherwise would have had limited possibility to interact.

Pluridisciplinarity and integration of adolescence research at the European level is critical and of great concern for future advances in this field. Although some of the participants are already engaged in exploring adolescence, one of the first steps following this ESF Workshop will be the establishment of a network at the EU level, that may also possibly include the participation of non-EU countries. In general, participants were enthusiastic of such an initiative, and positive and enriching comments were done at this regard. Part of the general discussion was also aimed at finding common interests of great public concern that may urgently need coordinated action at the European level, and that might allow the conjunct proposal at the EU level (e.g., EUROCOREs programme). Although some more brainstorming needs to be done at this respect, this “adolescent network” may serve to assemble forces on specific issues such as deviant behaviours during adolescence that might account for future mental health problems, including addictive behaviours. Gender differences and stressful life events during (pre and postnatal) development will be considered as critical factors throughout.

A proposal for publishing a Special Issue on *Neuroscience and Biobehavioral Reviews* based on the discussion that followed this ESF-EMRC Exploratory Workshop has been submitted, and delightfully accepted in the recent days. Our proposal for a Special Issue might be entitled “Running the blades of adolescence: brain pruning and adjusting developmental trajectories” and might be published by the last trimester of next year, 2010.

FINAL PROGRAMME

Friday 23 October 2009

- 09.20-09.40 **Welcome by Convenor**
Giovanni Laviola (Istituto Superiore di Sanità, Rome, Italy)
- 09.40-10.00 **Presentation of the European Science Foundation (ESF)**
Emmanuelle Wollman, ESF Standing Committee for the European Medical Research Councils (EMRC)
- 10.00-13.00** **Session I: Human Adolescence. State of the Art**
- 10.00-10.30 **“Growth and development in human evolution”**
Jacopo Moggi-Checchi (Florence University, Florence, Italy)
- 10.30-11.00 **“Past and present of youth in society”**
Carles Feixa (Lleida University, Lleida, Spain)
- 11.00-11.30 *Coffee / Tea Break*
- 11.30-12.00 **“New Frontiers in the clinical research of adolescents”**
Massimo Ammaniti (Sapienza University, Rome, Italy)
- 12.00-12.30 **“The social brain in adolescence: Evidence from brain imaging”**
Stephanie Burnett (Institute of Cognitive Neuroscience, London, UK)
- 12.30-13.00 **Discussion**
- 13.00-14.00 *Lunch*
- 14.00-18.00** **Session II: Forging Links between clinics and animal models**
- 14.00-14.30 **“Brain developmental trajectories in human adolescents and animal models”**
Susan L. Andersen (McLean Hospital, Belmont, MA, US)
- 14.30-15.00 **“Investigating peculiarities in behaviour, including drug response, in the adolescent rodent model”**
Giovanni Laviola (Istituto Superiore di Sanità, Rome, Italy)
- 15.00-15.30 **“Framework for gender differences in adolescent neuroscience”**
Maria Paz Viveros (Universidad Complutense, Madrid, Spain)
- 15.30-16.00 **“Lasting effects of stress during adolescence in rats”**
Bauke Buwalda (University Groningen, Groningen, The Netherlands)
- 16.00-16.30 *Coffee / Tea break*
- 16.30-18.00 **Discussion**
- 20.00 *Social dinner*

Saturday 24 October 2009

- 09.00-11.00** **Session III: Genetic bases of personality traits as studied in adolescence**
- 09.00-09.30 **“Genetic analyses of dopaminergic and serotonergic polymorphisms in child psychiatric disorders and personality traits among healthy children and young adults”**
Zsafia Nemoda (Institute of Medical Chemistry, Budapest, Hungary)

09.30-10.00	<p>“Adverse child experiences and genetic polymorphisms in experimentation with psychotropic drugs among adolescents” Gilberto Gerra (UNODC, Vienna)</p>
10.00-10.30	<p>“Adolescent cannabis use; the risk for mental health” Robin M. Murray (Institute of Psychiatry, London, UK)</p>
10.30-11.00	<i>Coffee / Tea Break</i>
11.00-13.00	Session IV: European ongoing research on adolescence
11.00-11.30	<p>“Stressful events, stress responses, and mental health in adolescent boys and girls” A.J. (Tineke) Oldehinkel (University Medical Center, Groningen, The Netherlands)</p>
11.30-12.00	<p>“Assessing Mental Health and Quality of Life in European Children and Adolescents” Corinna Petersen-Ewert (Hamburg University of Applied Sciences, Hamburg, Germany)</p>
12.00-13.00	Roundtable: Adolescence as a window of vulnerability and opportunity
13.00-14.00	<i>Lunch</i>
14.00-16.00	Discussion on follow-up activities and networking
16.00	<i>End of Workshop and departure</i>

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STATISTICAL INFORMATION ON PARTICIPANTS

Finally, a total of 24 persons participated in this present ESF Exploratory Workshop. There were two missing participants (Drs. Viviana Trezza and Anna Szekely) that because of personal problems could not assist and communicated such eventuality on the very last days prior to the Workshop.

Participation was perfectly sex-balanced, being half of the participants from the male sex and the other half females. Participation across EU nations was also assured, and speakers came from Germany, Italy, Hungary, Spain, The Netherlands and United Kingdom. There was also one speaker representing the United Nations (from the United Nations Office on Drugs and Crime, UNODC), and another speaker coming from the United States. Discussants came from a diversity of EU nations, including Belgium, France, Italy, Spain, The Netherlands and United Kingdom. Participants and speakers covered a wide age range, from PhD students to senior researchers and University professors. In our opinion, this ESF Exploratory Workshop managed to put together a notable group of experts in the adolescence field that might perfectly represent the actual panorama of the EU research community on adolescent studies.

	Sex	Nation	Age range
1 Etienne QUERTEMONT	male	Belgium	Senior
2 Ezio TIRELLI	male	Belgium	Senior
3 Gilberto GERRA	male	EU	Senior
4 Marcello SOLINAS	male	France	Junior
5 Giovanni LAVIOLA	male	Italy	Senior
6 Massimo AMMANITI	male	Italy	Senior
7 Jacopo Moggi-Cecchi	male	Italy	Senior
8 Walter ADRIANI	male	Italy	Junior
9 Carles FEIXA PAMPOLS	male	Spain	Senior
10 Alvaro LLORENTE BERZAL	male	Spain	PhD Student
11 Bauke BUWALDA	male	The Netherlands	Senior
12 Robin M MURRAY	male	UK	Senior
13 Emmanuelle WOLLMAN	female	France	Senior
14 Corinna PETERSEN-EWERT	female	Germany	Junior
15 Zsófia NEMODA	female	Hungary	Junior
16 Eva M. MARCO	female	Italy	Junior
17 M. Gabriela CHOTRO	female	Spain	Senior
18 M Paz VIVEROS	female	Spain	Senior
19 A.J. (Tineke) OLDEHINKEL	female	The Netherlands	Senior
20 O. M. (Odilia) LACEULLE	female	The Netherlands	PhD Student
21 Esther Nederhof	female	The Netherlands	Junior
22 Stephanie Burnett	female	UK	PhD Student
23 Gilian BROWN	female	UK	Junior
24 Susan L. ANDERSEN	female	US	Senior