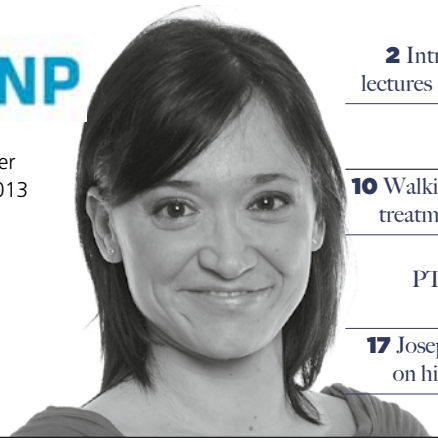
ECNP

The official newspaper of ECNP Congress 2013

Issue 1
Sunday
6 October 2013



ECNP DAILY NEWS

A warm welcome

It is always stimulating to come to Barcelona, and to walk in the footsteps of Gaudí on pavements that sparkle with inspiration. This time we come to Barcelona for a very special reason: to celebrate the 26th ECNP Congress.

Welcome, you are joining now over 6,000 participants from over 100 countries that have come to attend this meeting.

The hallmark of ECNP is its multidisciplinary approach and its gathering together of participants from across the spectrum of neuroscience disciplines, from psychiatrists, pharmacologists and psychologists, to neuroscientists, neurologists and epidemiologists.

This multidisciplinary perspective is reflected in the structure and the content of the meeting. There are five parallel sessions divided into five tracks; each is marked by different colour in the programme book and in the Smartphone apps.

The tracks are:

- Clinical treatment track (CT): evidence-based treatment
- Clinical research track (CR): clinical research issues
- Interface research track (IR): link between preclinical and clinical research
- Preclinical research track (PR): preclinical research
- Educational Update Sessions (ET)

The parallel sessions run from 9:00 to 10:40 in the morning and 14:30 to 16:10 in the afternoon. Every day there are two plenary sessions – they all take place in the Auditorium, and run from 11:00 to 11:45 in the morning and 13:30 to 14:15 in the afternoon.

The poster sessions are located at the poster area and interactions with the presenters take place every day from 11:45 to 13:30.

The educational sessions, which present cutting-edge, balanced developments in the clinics, are interactive – each attendee gets an answer pad – and are always fun. They all take place in Room M2 and run every day from 9:00 to 10:40 in the morning and from 14:30 to 16:10 in the afternoon.

The special feature are our scientific cafés, which take place every day from 16:10 to 16:40 and are aimed at semi-structured post-session information-sharing and networking.

This year we are again arranging a special place where you can meet colleagues and friends: the ECNP Plaza, which is located on level -1 at the heart of the venue.

For early birds there are brainstorming sessions that start at 7:45 in the morning and take place in Rooms M1, M3 and Y3.

You can find more about the meeting using our Smartphone app, by following our Twitter account (@ECNPtweets) and finding our Facebook page (European College of Neuropsychopharmacology).

As you can see, there is an exceptionally rich and diverse programme at this meeting. I warmly encourage you to get involved!

Thanks for joining us, enjoy our 26th annual meeting, and welcome to Barcelona.

Yossi

Joseph Zohar
President ECNP

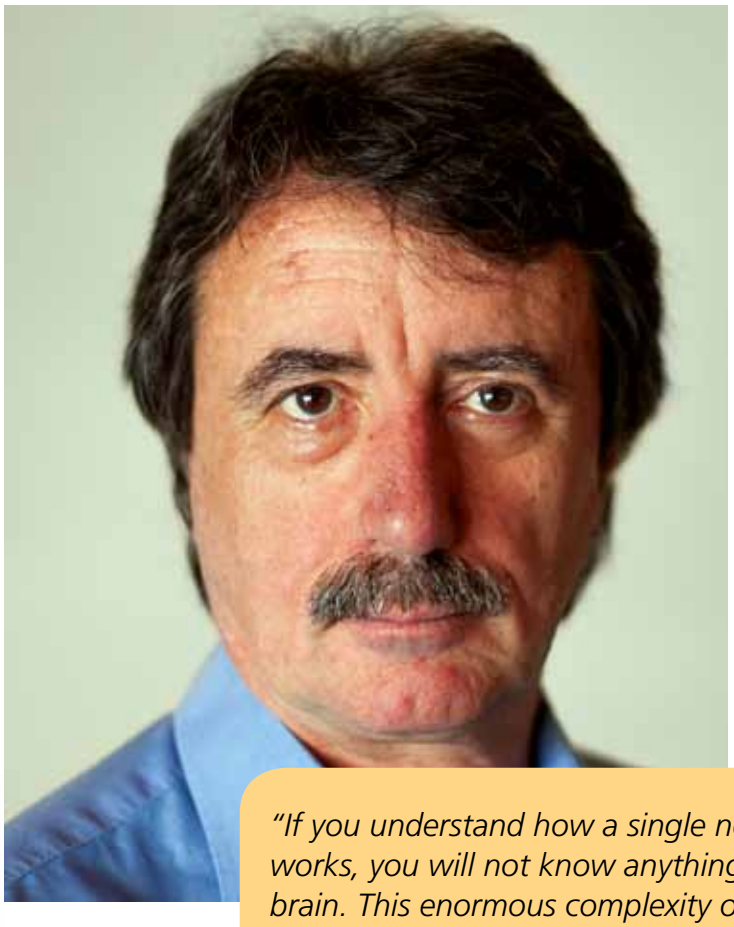
PLENARY LECTURES

Prefrontal cortex-based circuits: relevance for antidepressants and antipsychotics Sunday 6 October 11:00-11:45 **Auditorium**

Much promise for antidepressant therapy

This morning will feature the first of six plenary lectures to be hosted at this year's congress, in which Francesc Artigas (Barcelona Institute of Biomedical Research, Spain) will share his expertise within the field of antidepressants and antipsychotics in prefrontal cortical circuits.

Classical treatments for depression are widely known to require a few weeks to start taking effect, during which patients are highly vulnerable. But new discoveries have the potential to assign this period of limbo to the history books. "Everyone accepts that antidepressants are only effective in about two-thirds of patients," Professor Artigas told *ECNP Daily News*. "However, there are a couple of really exciting observations from the last decade which have really changed our views about how depression can be treated. One is the finding that ketamine, which is an NMDA [N-methyl-D-aspartate] receptor antagonist, is actually effective in a subset population of patients who are refractory to practically every pharmacological treatment.



"If you understand how a single neuron works, you will not know anything about the brain. This enormous complexity of the brain means that large research efforts need to be made, requiring larger investments than other diseases to identify new targets."

Francesc Artigas (Barcelona Institute of Biomedical Research, Spain)

"The other finding is the electrical manipulation of the ventral subdivision of the prefrontal cortex (Brodmann area 25): deep brain stimulation [DBS], as used in drug-resistant Parkinsonian patients. Actually, DBS is very effective in subsets of patients that are refractory to all kinds of treatments. These two different findings have really shaken the world of research in depression, not because these interventions can be routinely used but because they definitely show that more rapid and effective treatments can be obtained. Now, basic and clinical researchers are frantically trying to find out why these treatments are so effective. I would say that probably half of the neuropharmacology people all over the world are working in one or the other."

Even so, moving from clinical research to clinical reality takes time. New drugs, Professor Artigas estimated, will take a decade or more to arrive into the hands of patients. These drugs adopt a different mechanism to the current monoamine system targets, and include agonists of metabotropic glutamate receptors, chemical analogues of ketamine, amongst others. Hence, glutamate modulation within the prefrontal cortex, either via ionotropic or metabotropic receptor binding, could be the key to improving the efficacy of antidepressant therapy. Meanwhile, new drugs are still based on multiple monoamine targets, incorporating advances in this field. Clinical research takes money too, as much as it takes time. While the financial crisis has impacted every sector of work, Professor Artigas noted additional factors that have led to difficulties in brain research: "First, when investing in non-CNS diseases, companies get more revenue because the brain is very complicated!" he said. "The pharmacology of the brain cannot be approached in the same way as the pharmacology of, say, cancer or diabetes, because one of the most important differences between the brain and the rest of the body is the complexity of the human brain.

"So, if you understand how a cancer cell works you will understand that particular type of cancer. If you know how a hepatocyte works you will understand the liver. But if you understand how a single neuron works, you will not know anything about the brain. This enormous complexity of the brain means that large research efforts need to be made, requiring larger investments than other diseases to identify new targets. And then, there is a long way from a target to a medicine, and many potential targets at preclinical level never translate into new medicines."

He continued: "In addition to that, there is one important problem with regulatory aspects. In general, since we have treatments for virtually all psychiatric illnesses, the regulatory agencies ask for new drugs to be very safe. That probably means that, sometimes, drugs that could provide better efficacy are abandoned because of potential side effects. That is a very important problem too."

But new efforts are working to overcome these problems. Effective research is borne out of collaboration, and new EU initiatives strive to shorten the link between scientific innovation and economic growth in many fields, including drug development. Working together, the journey from basic research to new drugs ought to be less tough. "I am involved in a EU project called NEWMEDS, which is part of a new initiative from the European Un-

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ECNP Daily News

Publishing and Production
MediFore Limited

President
Joseph Zohar

Editor-in-Chief
Peter Stevenson

Editor
Ryszarda Burmicz

ECNP Office
Suzanna Tjoa

Design
Peter Williams

Press Editors
Becky McCall
Alastair McQueen

Head Office
19 Jasper Road
London SE19 1ST, UK
Telephone: +44 (0) 208 244 0583
editor@medifore.co.uk
www.medifore.co.uk

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ion, the IMI (Innovative Medicine Initiative)," said Professor Artigas. "These are projects in different fields in which drug companies and academic groups work together. This is an excellent initiative to shorten the delay of the translation of basic data to industrial products. This can improve the joint effort between academic people and industrial people in search of new targets and new medicines."

The conveyor belt of such translational efforts must pass through animal modelling before reaching the stage of human testing. While these models can never be mimics, they nevertheless serve as useful analogues of disorders, as Professor Artigas explained: "We don't have any really reliable models for depression or for schizophrenia. We attempt to make the animal behave in a certain way, in which the current drugs, antidepressants and antipsychotics, are effective to treat the alterations of any kind produced in the model. Chronically stressed animals are not really depressed animals. Animals treated with phencyclidine or ketamine are not schizophrenic animals. "But these models are useful in terms of trying to see what brain areas or circuits and what neurochemical elements are involved in the response to the drug. They are good for that, but they are not good for trying to understand the pathophysiology of the illness, because of course the rat or the mouse cannot mimic the changes in the brain of a depressed or schizophrenic person. We should know the limitations of these models, but we should work with these models because there is no other way to reliably test new drugs."

> *"We don't have any really reliable models for depression or for schizophrenia. We attempt to make the animal behave in a certain way... chronically stressed animals are not really depressed animals."*
>
> *Francesc Artigas (Barcelona Institute of Biomedical Research, Spain)*

A broad goal of new medicines is to address individual symptoms that make up complex disorders such as depression and that differ from patient to patient. Environmental and biological factors play a role, and Professor Artigas outlined his vision for genetics in future patient assessment. "The genetic factors are indeed very important for the treatment of depression," he said. "A large number of studies have defined individuals having one or another gene polymorphism that respond with higher or lower efficacy to certain drugs. These are really key issues for the future. I think we should abandon the idea of a single drug being effective in all depressed patients. Many people support that there should be genetic characterisation, to see which drugs are more effective for that particular patient. This has been shown in many different studies – there is one very classical study showing that a polymorphism of the serotonin transporter gene makes some people better than others. So it seems very clear."

'Prefrontal cortex-based circuits: relevance for antidepressant and antipsychotic drug action', 11:00–11:45, Sunday 6 October, Auditorium.

PLENARY LECTURES

Autoimmune processes in encephalopathy: a promise for treatment Monday 7 October 13:30-14:15 **Auditorium**

Autoimmunity and psychiatric disorders

A plenary lecture that will examine the association between encephalitis and antibodies to membrane proteins (namely ion channels), receptors and other associated proteins – with particular focus on the implication for treatment in psychiatric disorders – will take place tomorrow afternoon at the Congress.

"The antibodies are directed to voltage-gated potassium channel complex proteins, particularly LGI1 and CASPR2, NMDA-receptors, AMPA, GABAb and Glycine receptors," Angela Vincent (Nuffield Department of Clinical Neurosciences, Oxford University Hospitals Trust, UK) told *ECNP Daily News*.

Antibodies to the water channel aquaporin-4 (AQP4) are present in a rare but relapsing disease, neuromyelitis optica, that can be confused with multiple sclerosis. "Although originally described in neurological syndromes such as neuromyelitis optica, limbic encephalitis, NMDAR-antibody encephalitis or progressive encephalomyelitis with rigidity and myoclonus, there is little doubt that these antibodies can cause partial forms of disease without clear evidence of an encephalopathy. For instance, NMDAR and VGKC-complex antibodies have been identified in certain forms of epilepsy, rare cases of dementia and in a few case reports of patients who present with psychosis."

She continued: "The most important aspect of these newly described conditions is that the patients respond well to immunotherapies, particularly plasma exchange, steroids and intravenous immunoglobulins; in some it is necessary to use the CD20 targeting monoclonal antibody Rituximab and/or cylcophosphamide or other second-line therapies.

> *"Antibodies have been identified in certain forms of epilepsy, rare cases of dementia and in a few case reports of patients who present with psychosis."*
>
> *Angela Vincent (Nuffield Department of Clinical Neurosciences, Oxford University Hospitals Trust, UK)*

"There are now several studies in progress looking for these or other autoantibodies in patients with different forms of psychiatric disease, principally psychosis. A few published studies indicate that perhaps 5-10% of patients with psychiatric diagnoses will have antibodies to one of the known targets, but further work is required to identify whether these patients respond to immunotherapies, and to identify other potential target antigens in this important group of diseases."

Angela Vincent will deliver her plenary lecture, 'Autoimmune processes in encephalopathy: a promise for treatment of psychiatric disorders' on Monday 7 October at 13:30-14:15 in the Auditorium.

Reference

1 Vincent A et al. Autoantibodies associated with diseases of the CNS: new developments and future challenges. Lancet Neurology (2011) 10:759-72

CLINICAL RESEARCH

Emotion, cognition and pain – placebo responses and pain processing in mental disorders Room H Sunday 6 October **09:00-10:40**

Uncomfortably numb

Pain processing in borderline personality disorder

Investigations into the way that individuals with borderline personality disorder (BPD) handle pain has shed light on the role of affective and cognitive state in pain processing. Rosemarie Kluetsch (Central Institute of Mental Health, Mannheim, Germany) spoke to *ECNP Daily News* ahead of the congress to discuss her group's work at the Department of Psychosomatic Medicine and Psychotherapy and her work in the default mode network (also known as the task-negative network), a brain system that deals with self-referential and pain processing and one that appears to be altered in BPD.

Why were you interested in looking at pain processing in BPD?

About 80-90% of patients with BPD engage in so-called non-suicidal self-injury, for different reasons. A lot of the patients that do engage in self-injurious behaviour do not report pain during self-injury and have also shown altered pain processing under experimental conditions. Our lab has done a few studies using different modes of pain stimulation, but mostly thermal pain stimulation, where we applied painful thermal stimuli with different temperatures. When comparing a control group and a group of patients with BPD, we would consistently find that the BPD patients have a higher pain threshold. They would be less sensitive, although they would be able to detect the stimuli. It does not seem to be the sensory component of pain processing (which we disentangled using the laser paradigm[1]), but rather the affective-cognitive component that seemed to be altered.

Then my supervisor, Christian Schmahl [Central Institute of Mental Health, Mannheim, Germany], who had originally planned to give this talk, did a study in 2006 where they looked at neural correlates of this so-called hypoalgesia in BPD.[2] They found that there were certain differences compared to the control group: pain produced neural deactivation in the perigenual anterior cingulate gyrus and the amygdala – regions that would ordinarily increase their activation towards painful stimuli. On the other hand, there was upregulation (more activation) in the dorsolateral prefrontal cortex, a region engaged in cognitive control.

From that we were wondering, how we could achieve a better understanding of the neural processes underlying such differences in pain processing? At that time, the approach to analyse brain networks was still unfolding. Ruth Lanius [University of Western Ontario, London, Ontario, Canada], our collaborator in Canada, had already been using the network approach in the analysis of self-referential processing in patients with PTSD [post traumatic stress disorder]. In particular, they had found some interesting results looking at the default mode network.[3] So we thought, why don't we bring the two together? There were also findings of altered default mode function in BPD, and all of the data on altered pain processing. So we put the different strands of research together and examined network connectivity in a dataset that we had previously acquired. We used two different methods (psychophysiological interaction analysis and independent component analysis, respectively) to get a good picture.

> *"Maybe individuals with BPD don't even feel that the painful stimulus is connected to them, or that maybe their body does not feel as connected to them."*
>
> *Rosemarie Kluetsch (Central Institute of Mental Health, Mannheim, Germany)*

What is the message for clinicians here?

One thing that may be helpful is to keep in mind that BPD patients may evaluate painful stimuli differently. This may be due to dissociative symptoms and less integration of what is actually happening (or at least this is what we are speculating), so that maybe individuals with BPD don't even feel that the painful stimulus is connected to them, or that maybe their body does not feel as connected to them.

Is there a specific pattern of pain processing in BPD patients who self-injure, or could this be a more general fingerprint for how those who self-injure deal with pain, regardless of comorbidity?

It is a little difficult to tell, because these individuals with BPD who engage in self-injurious behaviour on a regular basis are very ill. They often meet criteria for several comorbid Axis-I disorders. For example, many fulfil criteria for PTSD and depression, anxiety and somatoform disorders, and sometimes even dissociative disorders above and beyond their diagnosis of BPD. It is hard to disentangle these things. Trying to find individuals that don't have all of these comorbidities leaves you with a sample that is not really representative of the patients in our in-patient unit! So I don't know whether or not this pattern of altered pain processing is specific to BPD. A former colleague of mine, Anja Kraus, has done a subgroup analysis in patients with BPD and comorbid PTSD compared to BPD patients without PTSD.[4] She found that there were actually differences in that the amygdala downregulation that I mentioned earlier was found to a greater degree in patients that had both of the disorders.

Another cross-sectional study was by Petra Ludäscher.[5] She looked at people who had BPD and still self-injured, BPD patients that had stopped, and healthy controls. She found that the people who were still self-injuring had the highest pain threshold. The healthy ones had the lowest, and

the ones who had stopped were somewhere in between. Of course, since it is cross-sectional, we cannot say that it is because those subjects do not self-injure any more, but it certainly gives us a hint in that direction. So, all in all, I don't know whether you could say altered pain processing is specific to BPD, or whether it is actually a correlate of a certain kind of illness severity and combination of symptoms that is also reported in depression and other disorders.

What is your lab working on now?

We are trying to better understand what the motivating components are – what is it about self-injurious behaviour that maintains it or that has people come back to it all the time? So we conducted a study on the effects of pain on stress regulation.

> *"We found that, in line with what clinicians had observed all along, aversive tension as well as heart rate would come down much faster after a stress induction if BPD patients received the incision."*
>
> *Rosemarie Kluetsch (Central Institute of Mental Health, Mannheim, Germany)*

We used an incision model,[6] where we applied an incision to the forearm, so that there was some tissue damage, versus a sham treatment where people would just be touched with the blunt end of the scalpel without injury. We examined a group of BPD patients who had recently self-injured and a group of healthy controls, and each person would receive both treatments. We found that, in line with what clinicians had observed all along, aversive tension as well as heart rate would come down much faster after a stress induction if BPD patients received the incision.

In a next step, we took that paradigm into the MRI environment, and investigated whether the incision would cause changes in brain connectivity in BPD patients. Then, another important thing is looking at the endocannabinoid system in BPD patients who self-injure to see if there are any changes there (and there are probably changes there) and what they look like.

Rosemarie Kluetsch will present 'Alterations in default mode network connectivity during pain processing in borderline personality disorder', which features as part of a broader discussion on altered pain processing in various psychiatric disorders, 'Emotion, cognition and pain – placebo responses and pain processing in mental disorders', taking place today at 09:00–10:40 in Room H.

References

1. Schmahl C et al. Differential nociceptive deficits in patients with borderline personality disorder and self-injurious behavior: laser-evoked potentials, spatial discrimination of noxious stimuli, and pain ratings. Pain. (2004); 110(1-2):470-9.
2. Schmahl C et al. Neural correlates of antinociception in borderline personality disorder. Arch Gen Psychiatry. (2006); 63(6):659-67.
3. Bluhm RL et al. Alterations in default network connectivity in posttraumatic stress disorder related to early-life trauma. J Psychiatry Neurosci. (2009); 34(3): 187–194.
4. Kraus A et al. Amygdala deactivation as a neural correlate of pain processing in patients with borderline personality disorder and co-occurrent posttraumatic stress disorder. Biol Psychiatry. (2008); 65(9):819-22.
5. Ludäscher P et al. A cross-sectional investigation of discontinuation of self-injury and normalizing pain perception in patients with borderline personality disorder. Acta Psychiatr Scand. (2009); 120(1):62-70.
6. Reitz S et al. Stress regulation and incision in borderline personality disorder-a pilot study modeling cutting behavior. J Pers Disord. 26(4):605-15.

CLINICAL RESEARCH

Understanding ADHD in adults Room H Sunday 6 October **14:30-16:10**

Improving knowledge in adult ADHD

While it was once thought to be largely a disorder of childhood, the recognition of adult ADHD is prompting much-needed research into defining its pathophysiology and improving treatment strategies. In an interview with *ECNP Daily News*, Ana Isabel Cubillo Fernandez and Katya Rubia (Institute of Psychiatry, King's College London, UK) described the increasing complexity and associated comorbidities of ADHD as sufferers move into adulthood, and how continuing research can help identify innovative therapies.

As Dr Cubillo Fernandez described, the evidence is consistent for the persistence of ADHD into adulthood in more than 65% of affected children and this tends to be accompanied by a distinct shift in symptomatology. "ADHD symptoms change in their presentation with age with hyperactivity symptoms typically decreasing, but persisting inattention and impulsiveness," she said. "The new version of the DSM-5 has modified the number of symptoms required, their description, as well as the age of onset in order to facilitate the correct identification of adult ADHD cases."

The group's imaging research has shed light on what may be the distinct neural correlates that correspond to the differences in disorder presentation in adults and children. Professor Rubia added: "Our work has shown that children with ADHD have structural and functional abnormalities in several regions of the brain, most prominently the basal ganglia, but also in prefrontal, temporo-parietal regions and the cerebellum. Our meta-analysis of structural MRI studies shows that the basal ganglia abnormalities grow out with age so that adults no longer have deficits in this region. Other studies, however, show that frontal lobe deficits are still present in adult ADHD.

> *"Once we have identified the mechanisms that underlie the remittance of ADHD symptoms into adolescence and adulthood, we can use these to develop better ADHD treatments."*
>
> *Ana Isabel Cubillo Fernandez (Institute of Psychiatry, King's College London, UK)*

"Our fMRI studies and fMRI meta-analyses in ADHD children and adults show that the fronto-striato-cerebellar dysfunctions during disorder-relevant cognitive tasks are strikingly similar in children and adults with ADHD, suggesting persistence of brain function deficits into adulthood. The exceptions are the basal ganglia deficits that were more pronounced in children with ADHD during attention tasks, in line with structural findings that basal ganglia abnormalities may normalise with age."

These more pronounced basal ganglia deficits in childhood ADHD seem to suggest that adult ADHD is a milder form of the disorder at the brain level, as Dr Rubia suggested. With a reminder that ADHD is not simply a deficit in any one brain region, but a disorder of fronto-striato-cerebellar networks, she noted

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CLINICAL RESEARCH

Understanding ADHD in adults Room H Sunday 6 October **14.30-16:10**

Improving knowledge in adult ADHD

Continued from page 5

that several studies have identified persisting frontal lobe deficits in adult ADHD, which implies that the basal ganglia elements of this network may grow out while frontal deficits persist.

"One could speculate that this could explain why some children grow out of the disorder, perhaps those where the problem was more prominently focussed on the basal ganglia, while those where the problem was more prominent with the frontal parts of these networks may persist," Professor Rubia said. "The basal ganglia are innervated by dopamine which is typically lower in ADHD children, hence the treatment with dopamine agonists (stimulants), which enhance dopamine, most prominently in the basal ganglia. The fact that stimulants improve dopamine in the basal ganglia and the fact that the basal ganglia are more affected in children with ADHD could lead to the speculation that dopamine

agonists may possibly be more efficient in children than in adults or could explain why dopamine agonists have limited long-term efficacy once the child grows older. Alternatively, we also have evidence from our PET meta-analysis that the brain adapts to long-term stimulant medication which could also explain limited long-term efficacy."

The factors that influence whether or not the symptoms of any particular child will persist into adulthood are yet to be elucidated, but further work will surely help to define these risks, as Dr Cubillo Fernandez explained: "There is only one longitudinal study and a small number of cross-sectional studies, and these studies show that the brain structure and function of remitters is more similar to that of healthy controls than that of the ADHD persisters. The only longitudinal study conducted so far showed that those patients with more ADHD symptoms (in particular inattention symptoms), had more abnormal cortical thickness. However, findings in adult ADHD have been inconsistent.

"Therefore, more longitudinal studies are crucial to help us identify the factors that mediate the persistence and the remittance of the behavioural symptoms, of the cognitive deficits and of the structural and functional abnormalities into adulthood. They can also identify the role of comorbid disorders in the persistence of symptoms or the severity of their presentation, the role of substance use or abuse, or how medication may mediate in this normalisation process. Once we have identified the mechanisms that underlie the remittance of ADHD symptoms into adolescence and adulthood, we can use these to develop better ADHD treatments."

> *"Our work has shown that children with ADHD have structural and functional abnormalities in several regions of the brain, most prominently the basal ganglia, but also in prefrontal, temporo-parietal regions and the cerebellum."*
>
> *Katya Rubia (Institute of Psychiatry, King's College London, UK)*

Speaking of the research that the group is currently doing in this area, Dr Cubillo Fernandez said: "Our current focus is on developing non-pharmacological treatment for ADHD, such as fMRI-neurofeedback, using the results of our imaging research of under-functioning of the inferior frontal cortex and the basal ganglia. Thus, we will train ADHD adolescents to up-regulate their own activation of these brain regions via the brain-computer interface."

Dr Cubillo Fernandez will present 'Persistence of brain deficits in adult ADHD' as part of the session 'Understanding ADHD in adults', held this afternoon at 14:30-16:10 in Room H.

CLINICAL TREATMENT

An update on the psychopharmacology of bipolar disorder Auditorium Sunday 6 October **14:30-16:10**

New developments in bipolar pharmacotherapy

New compounds tested adjunctively are an important tool to advance the therapeutic strategy of bipolar disorder, delegates will hear this afternoon in a session exploring the psychopharmacology of the illness.

A core aim within the advancement of pharmacological treatment of bipolar disorder is the ability to specifically tailor therapy for each patient. Moreover, while a sustained, long-term response is an attractive goal, this effort may require a multitude of drugs to achieve.

Specifically, when compared to periods of mania, the depressive component of bipolar disorder naturally warrants the most intense focus due to the fact that it is associated with a significantly high suicide rate, as well as other aspects that shorten the lifespan of sufferers (such as weight gain and cardiovascular complications).

"Until August 2013, there was only one monotherapy approved by the Food and Drug Administration [FDA] for the treatment of bipolar depression," Joseph Calabrese (Bipolar Disorders Research Center, Cleveland, Ohio, USA) told *ECNP Daily News*. "That compound is encumbered by a side effect profile which is accompanied by intolerable sedation and somnolence, and significant numbers of patients stop the medication because of poor tolerability. In addition, that compound binds with high affinity at histamine type 1 receptors which stimulates appetite and causes weight gain, which eventually leads to significant metabolic burden."

With this in mind, a great deal of potential lies with two recently trialled compounds that can effectively improve the symptoms of bipolar depression without intolerable sedation and metabolic burden. The first, lurasidone, is an antipsychotic agent whose efficacy is mediated by a combination of D2 and 5-HT2A antagonism, and the efficacy in depression is believed to be mediated by 5-HT7 antagonism. "The absence of intolerable sedation and somnolence and the absence of metabolic burden is extremely important, and somewhat unexpected, with lurasidone because

> *"The absence of intolerable sedation and somnolence and the absence of metabolic burden is extremely important, and somewhat unexpected, with lurasidone because the compound is an atypical antipsychotic."*
>
> *Joseph Calabrese (Bipolar Disorders Research Center, Cleveland, Ohio, USA)*

ECNP Membership

Have you considered **ECNP** membership? myECNP

ECNP membership is available in five broad categories for researchers actively involved in the field of neuropsychopharmacology and related disciplines. ECNP Members can enjoy the benefits of networking with ECNP members across Europe, as well as significantly reduced registration fees for the ECNP Congress, and the opportunity to propose brainstorming ideas. Also included is a free subscription to the journal *European Neuropsychopharmacology* and our newsletter ECNP Matters. The members' pages of the ECNP website gives you the opportunity to peruse employment vacancies in your field, as well as being eligible to apply for the ECNP Seminar, Workshop and Schools of Neuropsychopharmacology, especially intended for Junior Scientists.

Members share exclusive access to the Members' and Faculty Lounge at the ECNP Congress, which offers a relaxed atmosphere in which members and congress faculty can take a moment for themselves between sessions or engage in a conversation with one another during the congress. The lounge is equipped with wireless internet, power outlets, a computer with printer, and refreshments throughout the day.

The ECNP General Assembly is the annual general meeting of members, ECNP's highest deliberative body and the embodiment of one of the College's most fundamental member privileges: the right to vote and help shape ECNP's future. Members have the right to vote at the General Assembly, as well as the opportunity to serve on an ECNP Committee.

The Members' Reception, which takes place right before the Keynote Session, provides the opportunity for ECNP members to mingle with some of the most distinguished scientists present at this year's congress, to share ideas and opinions with speakers and members of our Executive Committee, including the ECNP President Joseph Zohar and President-Elect Guy Goodwin.

The Members' Breakfasts are set up to allow ECNP members to exchange thoughts with members of the Executive Committee on the present and future issues or challenges facing the College in an informal, relaxed environment.

Members' and Faculty Lounge

Location: Level -1 (Palau de Congressos)

Opening hours:

Saturday	09.00-18.00
Sunday	08.30-18.00
Monday & Tuesday	08.30-16.00
Wednesday	08.30-11.00

General Assembly of ECNP Members

Monday 7 October
12.15-13.15 Room F

Members' Reception
Saturday 5 October
17.15–18.00 Foyer 0

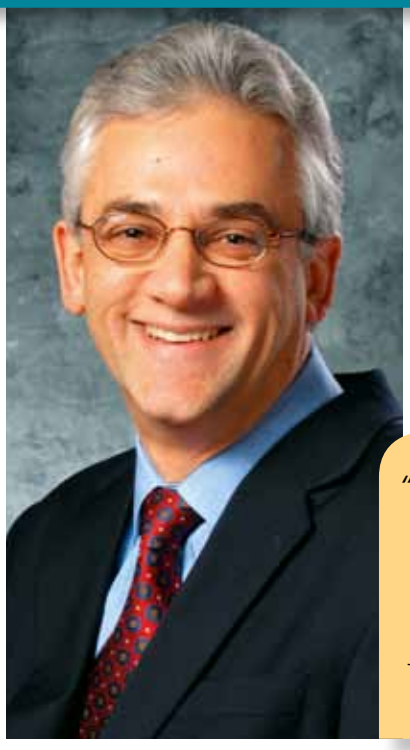
Members' Breakfasts
Sunday 6 and Monday 7 October
07.45–08.45 Foyer 1

Membership application forms can be found in the 'About ECNP' section of the ECNP website: **www.ecnp.eu**

the compound is an atypical antipsychotic," said Dr Calabrese. "Everyone thought sedation and metabolic burden would be a problem."

Development of lurasidone included both monotherapeutic and novel, adjunctive design, the latter utilising lithium/valproate or placebo alongside the compound. Positive results from the studies led to the approval of lurasidone by the FDA in August of this year. Data from the studies will be published in the coming months in two papers in the American Journal of Psychiatry.

The second compound, armodafinil, was tested adjunctively in several studies that incorporated lithium, valproate, lamotrigine, aripiprazole, olanzapine, ziprasidone, or risperidone. "Armodafinil is unique because it acts by dopamine reuptake inhibition, which is a mechanism that has never been implicated in bipolar depression," explained Dr Calabrese.



"Like lurasidone, it is unique in that it does not cause sedation and it is does not cause metabolic burden, but the armodafinil study has been more complicated. Three studies have been done: one separated from placebo, and the two others did not."

While data from the armodafinil studies is in the submission stage at the *Journal of Clinical Psychiatry*, delegates attending the ECNP session will receive an early glimpse of the some of the main data highlights for the compound, as well as an overview of the results for lurasidone.

'New developments in the pharmacotherapy of bipolar disorders', as part of the session 'An update on the psychopharmacology of bipolar disorder', 14:30-16:10, Sunday 6 October, Auditorium.

"Armodafinil is unique because it acts by dopamine reuptake inhibition, which is a mechanism that has never been implicated in bipolar depression"

Joseph Calabrese (Bipolar Disorders Research Center, Cleveland, Ohio, USA)

ECNP INITIATIVES

ECNP Networks

Targeted Network Meetings

The ECNP Networks are an initiative with a primary aim rooted in the desire to foster a multicentre European collaboration that will allow the standardised collection of essential clinical, psychological, biological and therapeutic variables that can then be analysed in clinical studies and pharmacological trials.

Furthermore, at their core the ECNP Networks are a forum for highly qualified investigators to gather and develop projects, as well as assess lessons learned – and future perspectives – in an open format. They are also a platform to foster the development and integration of European neuropsychopharmacology.

The networks are organised by the ECNP Networks Taskforce, an extensive collaborative group whose harnessed expertise is a vital tool in facilitating the development of new proposals by each network, promoting interaction between the individual networks, and monitoring progress and funding statuses.

There are currently nine ECNP Networks, ranging from more established, mature networks to those starting their journey. With this in mind, to order to assist the interaction between members of the different networks, and to cast a wider net that will encourage clinical and basal multidisciplinary minds to gather to share their views, a series of Targeted Network Meetings were held for two days immediately prior to this year's congress, consisting of tailored meetings that concentrated on four of the nine networks, namely: the Neuroimaging Network; the Obsessive Compulsive and Related Disorders Network (OCRN); the Child and Adolescent Neuropsychopharmacology Network; and the Bipolar Disorders Network (ENBREC).

With development of ideas taking centre stage, the actual format of the meetings depends on both the age of the network, and the currently pressing issues it faces. For instance, while one network may focus on recently-obtained results, and discuss them at length, another may tackle how to better circumnavigate the challenges it has previously faced. Conversely, others may look squarely to the future, generating a plan of action, and what they hope to collaboratively achieve in the coming years.

"The ECNP Networks were launched in 2007, and they really aim at addressing shortcomings in the European neuropsychopharmacological research structure and the lack of a common database," ECNP Networks Scientific Coordinator Nic van der Wee (Leiden Institute for Brain and Cognition/Psychiatric Neuroimaging, the Netherlands) told *ECNP Daily News*. "On the other hand, they also explore the idea that there is need, especially nowadays, for a cooperation of European networks in order to foster development in European scientific research."

> *"Ideally we would like to have a mixture of people in the [Targeted Network Meeting] audience. Of course there are always senior researchers present, but we strongly encourage early-career attendees as well."*
>
> *Nic van der Wee (Leiden Institute for Brain and Cognition/Psychiatric Neuroimaging, the Netherlands)*

The database aspect is something the Networks team is particular keen to develop. With great promise for the future of research, a common database for the Networks would allow the sociodemographic characteristics of patients, clinical characteristics, epidemiology of different disorders and all the biological material corresponding to these patients (neuroimaging, genetic materials etc.) to be shared in a potentially powerful way.

"For some networks this kind of database infrastructure is already in place, because they have been able to secure grants, or had continuations from existing collaborations," said Professor van der Wee. "But we're still trying to open an easily accessible database in order to share data among all of the networks."

He added: "It is quite a complicated procedure. You have to develop a database overarching for all of the different networks. If you look at the networks we have, some are advanced or mature networks – those who have obtained and carried out FP7 grants – and you also have starting networks like the Experimental Medicine Network or the Addiction Network. It is these starting networks, especially, that might really profit from an easy accessible overarching database."

In terms of the selection process that governs which four networks will hold symposia prior to the ECNP Congress, the Taskforce and the Scientific Programme Committee take into account a number of factors, including the age of the network, what past or future topics it would like to discuss, the impact this may have and the crosstalk between clinical and basic research. For instance, one of this year's focussed networks, the Obsessive Compulsive and Related Disorders Network, will discuss new translational models, new neuroimaging approaches and classification issues, but it will also discuss its experience with recent grant applications to improve its strategy in this area.

Commenting on what messages are expected to resonate following each Targeted Network Meeting, Professor van der Wee added: "Looking at the excellent quality of the programmes, we believe that the Targeted Networks Meetings will be very productive. The focus will really depend on the developmental stage the network is in. They could well look into what are unmet needs in their specific field in order to formulate a future research agenda, or it could be also a chance for a more mature network to exhibit results from previous work, and discuss their final data. It can really be useful for them to look into whether they have served their original aim. Other experts in the field, and the audience, can think about these results and see how they can help to move things forward."

With an audience of 30, including speakers and moderators, the meetings maintain a personalised atmosphere that lends itself to open and honest discussion. With this in mind, Professor van der Wee is keen to stress that the sessions will really benefit from a wide-reaching audience demographic that is expected to better represent both the overall viewpoints, and more diverse opinions, that may exist in the wider scientific community. "Ideally we would like to have a mixture of people in the audience," he commented, adding "of course there are always senior researchers present, but we strongly encourage early-career attendees as well."

More information about the Targeted Network Meetings held prior to this year's Barcelona Congress can be found on the ECNP website at http://www.ecnp.eu/meetings/tnms.


SOCIAL MEDIA
AT THE ECNP CONGRESS
For informational updates and news flashes during the congress, find us on Facebook and follow us on Twitter.
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neuroscience applied

CLINICAL TREATMENT

Beyond dopamine blockade – new perspective in the treatment of schizophrenia Auditorium Monday 7 October **14:30-16:10**

New paths in schizophrenia treatment

Negative symptoms of schizophrenia will be placed under the spotlight tomorrow in a session that will explore the new treatment perspectives hoped to alleviate the severe impediment these symptoms have on an individual's functional reintegration and quality of life.

In an interview with *ECNP Daily News*, Michael Berk (Deakin University, Geelong, Australia) began by stressing that the negative symptoms of schizophrenia are common and pervasive, and are poorly targeted by existing therapies, thus there is a pressing need for better therapeutic agents: "What triggered us to start looking in this whole area was a study by Kim Do done just over 10 years ago,[1] which showed reduced glutathione in the cerebrospinal fluid and also by [brain MR] spectroscopy in people with schizophrenia," he said.

"Because glutathione is the brain's major free radical scavenger, this suggested two things. Firstly, that there is an abnormality in oxidative metabolism in people with schizophrenia. Secondly, it raised the question of whether one might be able to correct this by using agents that might be glutathione precursors.

"As an interesting aside, when we did a comprehensive scratch around the literature, this reduction in glutathione was actually first published in 1934, so it is not a new finding; in fact it is one of the oldest biomarkers we have in all of psychiatry. So from the outset, we were interested in a compound called N-acetyl cysteine [NAC], which is an amino acid. This is converted in the body to cysteine, which is the rate-limiting step for the synthesis of glutathione. We did a study which looked at whether one can treat the symptoms of schizophrenia by targeting these redox pathways with NAC. This was our primary hypothesis, but we now also know that NAC does a whole host of other things to pathways that we understand are also abnormal in schizophrenia. So it has effects on oxidative stress in addition to inflammation, mitochondrial dysfunction, and apoptosis. Importantly, in terms of schizophrenia, it also has effects on glutamate, which is a neurotransmitter we know is abnormal in schizophrenia."

> *"I don't hold to the view (and I don't think many people do) that [psychiatric disorder] classifications, as much as they are a best solution in an imperfect world, truly do represent the answer to the question of what the pathophysiologies of these disorders really are."*
>
> *Michael Berk (Deakin University, Geelong, Australia)*

During the session, Professor Berk will present research findings supporting the beneficial effect of NAC in reducing negative symptoms of schizophrenia, improving functioning and quality of life, and reducing extra-pyramidal side effects. Following the success of this study, he investigated other psychiatric disorders that were known to convey abnormalities in NAC, with studies of bipolar disorder achieving significant reductions in symptoms during depressive episodes.[3] Professor Berk noted that other research groups had identified significant effects of NAC in the diverse fields of autism and addiction, with strong results being achieved in the reduction of cannabis use.

Speaking of the three novel analyses that he is presenting at the congress, Professor Berk said: "First, we have just finished a study in depression. While the study is not unequivocal, it does show some efficacy of NAC in unipolar major depression. We have also done a post-hoc analysis of a schizophrenia study asking the question, does stage of illness predict who is more likely to get better with NAC? And what we found was that, across the symptoms, but clearly shown in negative symptoms, was that the people with chronic schizophrenia seemed to derive more benefit from NAC than those who were earlier in their course of illness. This was actually contrary to what we expected to find. The last thing that I'll be talking about is, again, a post-hoc analysis of a schizophrenia study following up a clue that others had unearthed on effects of NAC on substance use. We looked at smoking and there was a hint,

although I have to say not unequivocal, of reduction in smoking in people who were given NAC. This whole NAC journey has taken us to places where we never expected it to take us."

While there has been much research evidencing the commonalities between different psychiatric disorders, the very idea of such commonalities is not easily understood. "It depends on how you conceptualise these mental illnesses," said Professor Berk. "If you take our current classifications as biblical documents, making the assumption that they truly do define distinct illnesses with well understood pathophysiology – such that asthma is different from pneumonia, which is different from a heart attack because we know their pathophysiologies – then it makes no sense.

"But it makes sense if you look at it from either one of two perspectives: that these biomarkers are common across illnesses and they might be conceptualised as pathways to neuroprogression or pathways of allostatic load (depending on the theoretical model); it also makes sense if one has doubt as to whether the current boundaries truly represent a cleavage at the joint of these neurobiological disorders. I don't hold to the view (and I don't think many people do) that the classifications, as much as they are a best solution in an imperfect world, truly do represent the answer to the question of what the pathophysiologies of these disorders really are."

> *"This whole NAC journey has taken us to places where we never expected it to take us."*
>
> *Michael Berk (Deakin University, Geelong, Australia)*

Professor Berk will present 'Novel mechanisms to improve negative symptoms – initial success and new directions' as part of the session 'Beyond dopamine blockade – new perspective in the treatment of schizophrenia', taking place tomorrow at 14:30-16:10 in the Auditorium.

References

1. Do KQ, Trabesinger AH, Kirsten-Krüger M, et al. Schizophrenia: glutathione deficit in cerebrospinal fluid and prefrontal cortex in vivo. Eur J Neurosci. (2000); 12(10):3721-8.
2. Looney JM and Childs HM. The lactic acid and glutathione content of the blood of schizophrenic patients. J Clin Invest. (1934); 13(6):963–968.
3. Berk M, Copolov DL, Dean O, et al. N-Acetyl Cysteine for Depressive Symptoms in Bipolar Disorder—A Double-Blind Randomized Placebo-Controlled Trial. Biol Psychiatry. (2008); 64(6):468-75.

INTERFACE RESEARCH

Immunogenetics and psychiatric disorders Room F Monday 7 October **14:30-16:10**

Immune targets offer novel add-on therapy for bipolar and schizophrenia

Evidence for a genetic association between genes coding for immune-related molecules and the incidence of the respective psychiatric disorders will be discussed tomorrow in a session dedicated to immunogenetics and psychiatric disorders. Reviewing the immunogenetic background of schizophrenia and bipolar disorder will be Ryad Tamouza (INSERM, Paris, France), and he spoke to *ECNP Daily News* ahead of the congress to explain why it is so important for researchers to explore the immune response in these disorders.

While immunogenetics – the genetic control of immune responses – is very a familiar term in chronic inflammatory disorders such as diabetes mellitus, it presents a relatively unfamiliar face in the field of psychiatry. "Immunogenetics consists of the study of the control of both arms of the immune response: the innate and adaptive immune response," said Dr Tamouza. "Why now in the psychiatric setting? Because there is now evidence, in schizophrenia, bipolar and other disorders, that there is an immunity component.

"For example, you have low chronic inflammatory processes both in schizophrenia and in bipolar disorder. Our hypothesis, which is not only ours but is accepted worldwide, is that during pregnancy or in the early prenatal period, in individuals susceptible to developing bipolar disorder or schizophrenia, there is a gene environment interaction between the immunogenetic background and infectious disorders such as flu. It is an old concept, because of the concept of seasonality, the fact that there is, for example, a high incidence of patients affected by schizophrenia born during the winter, during infectious windows to common pathogens. Our role is to study how the individual will manage the immune response through the genetic background."

Citing the increased incidence over the control population of medical comorbidities in bipolar disorder and schizophrenia (alongside the more familiar canvas of psychiatric comorbidities), such as cardiovascular diseases, diabetes mellitus, obesity and thyroid dysfunction, Dr Tamouza suggested that a common pathway may play a role in all of these conditions. "This could be the reason that we pinpoint this pathway particularly," he said, emphasising that a proof-of-concept is required in order to clearly demonstrate that the psychopathology of these psychiatric disorders can be affected by their being embroiled in an immune inflammatory process.

> *"You cannot envisage using these drugs on all patients. You have to stratify the patients based on their immunogenetic profile."*
>
> *Ryad Tamouza (INSERM, Paris, France)*

"What we need as a target is to identify biomarkers, and these biomarkers will help to make an early diagnosis and open the way to new innovative therapies," said Dr Tamouza. "In bipolar patients, it is established that there is a background of psychiatric genetic disorder. But if you have immune dysregulation in the same patient – some inflammatory process, for example – you can manage it by add-on anti-inflammatory drugs.

"There are a lot of clinical trials in the US and worldwide using anti-inflammatory drugs such as corticoids, or anti-tumour necrosis factors (anti-TNF), where TNF is a pro-inflammatory cytokine found in bipolar disorder and schizophrenia. We are publishing some papers on this kind of management, which are currently in press."

Understanding the immune component of schizophrenia and bipolar disorder can only come about by gathering patients' genetic data, which can then be correlated with any historical environmental factors, both clinical and social, that could give rise to inflammation. "What I mean by 'environmental' is not only infection, but stress," continued Dr Tamouza. "We know that in early childhood, some trauma leads to stress within the brain. All of these kinds of phenotypes will be analysed in interaction with the genetic background. Right now we are working on the characterisation of the patients and the follow-up of the patients. With the clinical history of infections and so on, when we complete with a significant cohort, we will analyse the gene interactions. You cannot envisage using these drugs on all patients. You have to stratify the patients based on their immunogenetic profile. After that, you will be able to categorise which patients can have this add-on therapy."

Dr Tamouza will present 'Immunogenetic background in schizophrenia and bipolar disorder' as part of the session entitled 'Immunogenetics and psychiatric disorders', taking place tomorrow at 14:30-16:10 in Room F.

Networking opportunities

Members' Reception

Saturday | 17.15-18.00 | Foyer 1
Palau de Congressos

Catch up with other ECNP members, accompanied by drinks and snacks. Hostesses will lead you to specially reserved seats in the Auditorium, just before the start of the Keynote Session.

Members' and Faculty Lounge

Open daily | Level -1 | Palau de Congressos

Enjoy the calm and comforts of the lounge, exclusive to ECNP members and congress faculty.

ECNP Plaza

Open daily | Level -1 | Palau de Congressos

Take a break, meet a colleague, find out what's going on at ECNP.

Welcome reception

Saturday | 19.30-21.00 | Auditorium
Palau de Congressos

Mix and mingle with participants from around the world, while enjoying dinner and a drink.

Science-on-the-Rocks

Sunday | starts 21.00 | Hard Rock Café
Barcelona city centre

Meet and greet other junior scientists at this exclusive networking event.

Hard Rock CAFE BARCELONA

ECNP neuroscience applied

at the ECNP Congress

Members' Breakfasts

Sunday & Monday | 07.45-08.45 | Foyer 1
Palau de Congressos

Share your ideas for the future of the College with other members of ECNP and the Executive Committee.

Poster sessions

Sunday-Tuesday | 11.45-13.30 | Level -1
Palau de Congressos

The ultimate networking moment at the congress, and your chance to interact with poster presenters as well as fellow participants.

Scientific cafés

Sunday-Tuesday | 16.10-16.40 | outside the session rooms | Palau de Congressos

Share ideas and meet new colleagues at these topic-focused, informal gatherings.

Junior Scientists' 'best practices' breakfast

Tuesday | 07.45-08.45 | Foyer 1,
Palau de Congressos | (by invitation only)

Exchange thoughts and experiences with junior scientists and invited guests.

ECNP Junior Scientists Initiative

ECNP Dinner

Tuesday | 20.00-23.00 | Museo Marítimo
(by invitation only)

Make your congress experience complete by connecting with other congress faculty, committee members and invited guests.

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BRAINSTORMING @ ECNP

Consolidation and reconsolidation interventions in the 'golden' hours after trauma Room M1 Monday 7 October **07:45–08:45**

Going for 'gold' in PTSD intervention

A brainstorming session that will explore the intervention strategies following traumatic events will take place tomorrow morning, with a particular focus on examining the crucial time window after trauma that may prove vital in improving the long term outcomes of patients at risk of developing stress-based disorders.

Hosted by experts Harm Krugers (Swammerdam Institute for Life Sciences, University of Amsterdam, the Netherlands) and Eric Vermetten (Central Military Hospital, University Medical Centre Utrecht, the Netherlands), the brainstorming session will serve as a forum for both cutting-edge updates and frank discussion on consolidation, reconsolidation and the benefits that memory intervention can have on post-traumatic stress disorder (PTSD) and other negative outcomes.

Ahead of the session, Dr Krugers offered some background as to what he hopes to explore: "Consolidation and reconsolidation can be seen as at least an opportunity to target fear and fear-related memories," he said. "That's an important concept that has developed over the past years. It has been tested in animal studies, and to some extent in human studies. Some of these studies are promising, some of them are less promising, so I think the point that might come up is what might be some important aspects that determine whether the therapies are feasible and can be successful, and what are the boundary conditions?

"More data is required, and also more test conditions. I think another point that is very important is that it has been tested to a large extent in healthy animals and healthy humans, and what will be important is does it work in people that suffer from fear-related memories and PTSD? Actually these people might respond completely different to treatment when compared to healthy individuals. To a large extent that has not been studied, at least not in detail."

As is reflected in the title of the brainstorming session, the 'golden' window of time that follows immediately after any traumatic event is something that has garnered much focus. Paradoxically, while intervention during this time may prove to be crucial, PTSD symptoms are slow with their onset, thus it is difficult to confidently say who will be most in need of treatment. "Typically you cannot diagnose PTSD in the first four weeks following exposure," said Dr Vermetten.

He added: "Or it could be the late type of PTSD which only manifests itself after six months or later. In my population I work with military personnel, and there is also contextual variables of stigma or denial, so symptoms may only surface years later... and it doesn't mean that the biology will respond accordingly. We think that the biology will need to be treated in the moment of the consolidation and reconsolidation."

In typical emergency care practise, Dr Vermetten stressed that approximately 10-15% of people would be expected to develop a form of clinical disorder following a traumatic experience. Thus it is extremely difficult to gauge what the target population is. That being said, there are of course populations that are expected to be higher risk, such as the armed forces. "Soldiers are exposed to a high risk environment, so while you do not know who will develop PTSD, you know that they are a group that is very likely to develop PTSD based on the traumatic events they have been exposed to," said Dr Vermetten.

With this in mind, the military population would represent an ideal choice for extended study, but once again, paradoxically, a volatile, dangerous military environment would most likely preclude the chance for clinicians to be physically present during or shortly after the respective trauma.

Despite this limitation, Dr Vermetten stressed that extrapolation of intervention models in other settings, such as car accidents, are still sound. "It's translational and well validated, but in a clinical case condition it is not yet tested well enough," he said.

It is clear that while promising, there is still much to consider in the 'golden' window after trauma, but the brainstorming session

> *"Consolidation and reconsolidation can be seen as at least an opportunity to target fear and fear-related memories. That's an important concept that has developed over the past years."*
>
> *Harm Krugers (Swammerdam Institute for Life Sciences, University of Amsterdam, the Netherlands)*

"For this brainstorming session it is good to educate people but also to give some challenges as to what criteria the design needs to have in order to execute a study."

Eric Vermetten (Central Military Hospital, University Medical Centre Utrecht, the Netherlands)

is hoped to promote a collaborative approach that will help crack the complex shell surrounding the topic. Describing his thoughts on how the session will play out, Dr Vermetten continued: "Part of it will be looking at an overview of the compounds, and what are the potential receptors that are involved with the biological systems that we are trying to target.

"Issues like dosing, i.e. how much, what exactly is the golden window (minutes, hours?), and how we need to define the population. Is it predominantly males, females, children? What are the clinical or demographic variables that we need to take into account when we design the study? For this brainstorming session it is good to educate people but also to give some challenges as to what criteria the design needs to have in order to execute a study."

Dr Krugers and Dr Vermetten will host the session 'Consolidation and reconsolidation interventions in the 'golden' hours after trauma: conditions, definitions and opportunities' on Monday morning at 07:45-08:45 in Room M1.

The session forms part of the daily brainstorming programme, filled with three concurrent sessions at 07:45-08:45 on Sunday, Monday and Tuesday mornings in rooms M1, M3 and Y3. Refer to the ECNP Programme for full listings.

TONIGHT!

Junior scientists are invited to attend the 'Science on the Rocks' event held in downtown Barcelona this evening. With emphasis on a relaxed, friendly atmosphere, the event will encourage interaction with peers and offer discussion in a casual setting. There will also be an informal lecture by David Nutt on 'Translational research in Neuropsychopharmacology'.

DON'T FORGET to collect your voucher beforehand at the ECNP Plaza

Time: 21:00
Location: Hard Rock Café, Placa de Catalunya, 21

JUNIOR SCIENTISTS SYMPOSIUM

New preclinical and clinical insights of psychosis, ADHD and addiction Sunday 6 October 14:30-16:10 **Room F**

Reward, dopamine, and the schizophrenia puzzle

Impaired dopamine functioning is a well-known feature of the schizophrenia profile, thought to account for the impairment in the anticipation and receipt of reward that is one of the disorder's emergent characteristics. Investigating how pervasive this characteristic is throughout affected families could provide the basis for further studies, both in the underlying genetics of such deficits as well as in further defining those most at-risk during adolescence. Max de Leeuw (Brain Center Rudolf Magnus, Utrecht, the Netherlands) spoke to *ECNP Daily News* to discuss his recent studies in reward processing using functional MRI (fMRI), which he will be presenting as part of the Junior Scientists symposium this afternoon at the ECNP Congress.

Explaining the difficulty with which negative symptoms can be ascribed to particular cognitive dysfunctions, and hence the difficulty in targeting them with clinical therapies, Dr de Leeuw began: "Reward processing is a cognitive process highly dependent on dopamine. We all know that schizophrenia is a disorder in dopamine levels, and we know that because of the aberrant dopamine levels reward processing is affected in schizophrenia. There are some behavioural studies that have shown that the motivation for reward is decreased in schizophrenia; how you can translate this into clinics is very, very difficult, because the paradigm of the cognitive task is very difficult to apply in that way. It is clear that schizophrenia patients have negative symptoms and do not have very much motivation for anything at all. But the question is whether that is also the underlying mechanism of impaired reward processing – that is very hard to distinguish."

Impaired reward processing has been demonstrated through fMRI studies in comparisons of schizophrenia patients and healthy controls, findings that correspond to impairments in behavioural studies. However, the reward circuitry, although highly dependent on dopamine, is certainly affected in a number of psychiatric disorders. So what could its predictive value be in schizophrenia in particular? De Leeuw said: "Indeed, there are also other psychiatric diseases in which dopamine is affected too. These disorders may influence your reward mechanism, but the question is whether [reward dysfunction] is a result of the symptoms, rather than it being specific for the disease.

"For cognitive processing in general we know, for example, that individuals that are at risk for schizophrenia also show impaired performance during several cognitive tasks. Combined with the fact that cognitive processing is dependent on adequate dopamine functioning, this gives an indication that there is a sort of constitution in their genes that may result in affected dopamine levels or dopamine functioning. That is basically the hypothesis underlying the task we were using, because it is the dopamine story that underlies those deficits we are seeing."

> *"It is clear that schizophrenia patients have negative symptoms and do not have very much motivation for anything at all. But the question is whether that is also the underlying mechanism of impaired reward processing."*
>
> *Max de Leeuw (Brain Center Rudolf Magnus, Utrecht, the Netherlands)*

During the session, Dr de Leeuw will present the results of recent investigations into the way in which unaffected siblings of schizophrenic individuals process reward anticipation and reward outcome. Explaining the design of the study, he emphasised that significant results would lay the foundations of important future work in the at-risk population. "We included 28 siblings of schizophrenia patients and 29 controls," he said. "Both were performing a reward task while we were scanning. We matched for accuracy so that all participants won the same amount. We are using unaffected, non-medicated siblings because if they show impairments comparable to their ill relatives, it provides evidence for a genetic vulnerability and this may be a stepping stone for further research in higher risk subjects, such as young adolescent offspring of schizophrenia patients. If there is such a factor of impaired reward processing in the unaffected siblings, it is very important to go on with the research.

"There are other studies in cognitive processing in unaffected siblings that do show the deficits in fMRI. One that has often been found is in the frontal-striatal network, so that was the network we were especially interested in. We scanned both groups and compared them. What we saw was that, during reward anticipation, siblings have a blunted activation in the ventral striatum. During the outcome of reward those siblings show hyperactivation of the striatum and of the frontal cortex."

Dr de Leeuw explained these results in terms of what is already known about the way in which learning about reward cues is impaired in schizophrenic individuals. "This is about cue processing. For example, a rewarding cue does not provoke activation in the reward network during anticipation. So if they have not learned that they are going to be rewarded, they are extremely rewarded in the outcome and that is why the hyperactivation occurs. Cue processing – learning that you are going to be rewarded – we know is highly dependent on dopamine functioning. So this will give us insight that there is a dopamine function problem in those siblings, and that is in turn consistent with what we find in schizophrenia patients.

"So it is related to the disorder and it is related to schizophrenia, so we know that cue processing and the underlying frontal-striatal dysfunction is to some extent heritable. Further research, which I am going to do as well, is to look at which genes are responsible for those dopamine deficits in that frontal-striatal network."

Max de Leeuw will deliver his presentation 'Reward processing in unaffected siblings of schizophrenia patients: a functional magnetic resonance imaging study' as part of this afternoon's Junior Scientists Symposium, 'New preclinical and clinical insights into the causes of psychosis, ADHD and addiction', taking place at 14.30 in Room F.

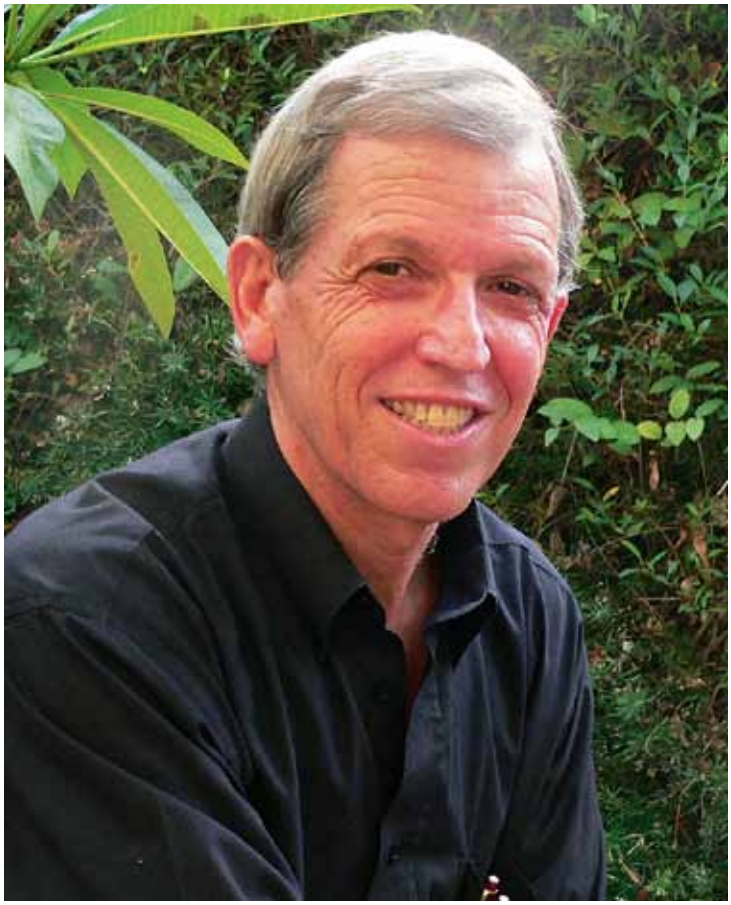
INTERVIEWS

ECNP President

Interview **Joseph Zohar**

ECNP President Joseph Zohar, Professor of Psychiatry at Tel Aviv University, Israel, has led the ECNP Executive Committee since 2010, steering the college through all of the events, initiatives and meetings (including 2012's landmark 25th anniversary congress in Vienna) organised within the extensive and ever-expanding ECNP calendar.

ECNP Daily News took the opportunity to speak to Professor Zohar to see what his particular highlights have been from the last three years, as well as his future visions for ECNP.



What have been the highlights of your presidential term?

Right when we met for the first time as the new Executive Committee I felt that it was essential to clarify and articulate our mission. In December 2010 the Executive Committee agreed (for the first time) on a mission statement for the college that has now accompanied us during the three years of my term. By making clear what our mission is, it helps us to focus on our activities.

Along the lines of promoting better treatment and enhance brain health we opened two new schools. In 2012, a School of Child and Adolescent Neuropsychopharmacology, which took place in Venice, and then this year we opened yet another new School – the School of Old Age Neuropsychopharmacology, which again runs in Venice.

We have also held six interactive seminars. Each ECNP Seminar lasts two days and is carried out in a place in which it is considered necessary. This has included Russia, Latvia, Greece, Romania, Estonia, and Moldova.

One of the highlights of our term was of course the 25th anniversary. This event gave us an opportunity to update the 25 year-old by-laws so that they will fit better within the current structure and activities of the college. We used this opportunity also to present (again for the first time) a code of conduct which was incorporated in the new by-laws, and both were adapted in October 2012 in the General Assembly.

It seems that there has been increasing focus on providing a more inclusive junior member experience in recent times, as well as more interactive elements in general?

We managed to launch formal collaboration with the European Organisation of Psychiatric Residency, and consequently a new committee, called the Junior Members Advisory Panel (J-MAP), was established in 2013. During this Congress we have specific activity, 'Science on the Rocks', initiated by Florian Riese which will take place on Sunday 6 October at 9pm.

In addition, in 2012 we developed the 'ECNP Certificate' programme which offers a unique opportunity for junior colleagues to receive personal mentorship from internationally-renowned figures in a speciality or technique that they would like to explore.

We also expanded on the communication with members, using social media such as Facebook, Twitter, Presidential Blog etc., and we now post educational videos on YouTube. Those 10 minutes educational videos are based on talks given by members and other participants from different meetings including our annual meeting.

> *"[It] has been a very unique and very fulfilling experience. The harmony between the Executive Committee and the Office was really superb, and I think everybody felt like they were serving a worthwhile mission."*
>
> *Joseph Zohar (Tel Aviv University, Israel)*

Now that you are stepping down as President, are there still initiatives and ideas that you would like to see implemented by the committee in the coming years?

When I had my first meeting with the Executive Committee, I put up a slide quoting Charles Darwin, who suggested that it is not the strongest species that survives, but the one that is most able to adapt. I think that we need to be always on the watch to make sure we are facing the dramatic changes that are taking place in the arena of brain research. We need not only to develop new tools but also to work with diligence on better implementation of existing tools, such as eLearning, and sophisticated web-based personal guidelines etc. Recruiting is also a worthwhile consideration.

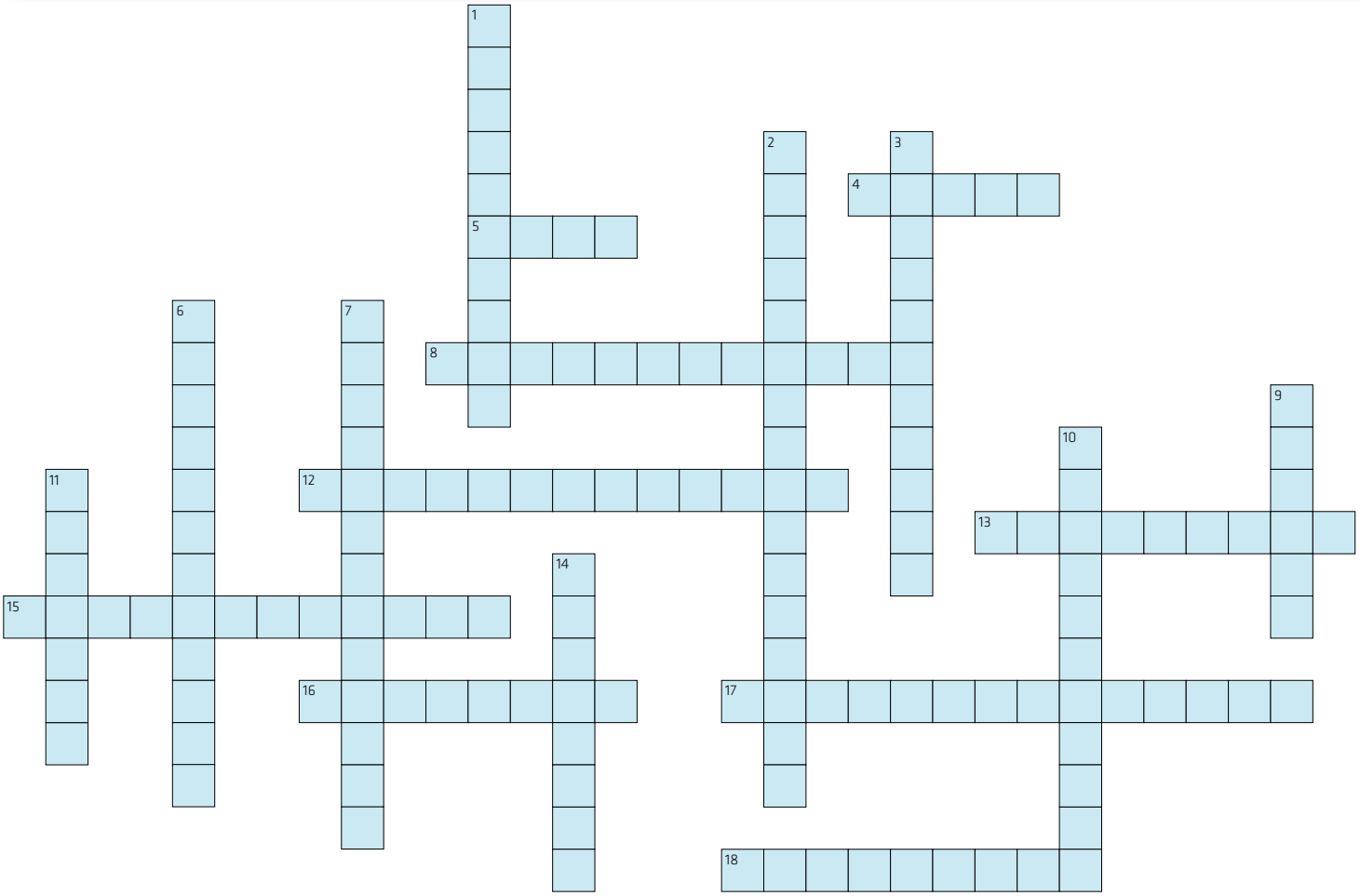
Another focus should be the opening of a channel to the public. We have been trying, and we should do so more in the future, to build a bi-directional bridge between the advances in neuroscience on one side, and clinical treatment on the other. Furthermore we should base it on an open dialogue with the public and policy makers in order to make sure that we really address the right needs.

Along those lines, in 2012 we started the Media Award, a specific award that highlights writing, plays, movies, books, exhibitions etc. that really help to bring balanced, updated knowledge of the brain and brain disorders to the fore.

Finally, from your experience what can every upcoming President expect from their time in the role?

My three-year experience of serving the scientific community, and to some extent the public with regards to building this 'bridge', has been really a very unique and very fulfilling experience. The harmony between the Executive Committee and the Office was really superb, and I think everybody felt like they were serving a worthwhile mission. I believe that this spirit, this atmosphere and this ambience will continue on.

ECNP PUZZLES



Across

4 Who is credited with discovering the neuromodulatory properties of acetylcholine?

5 The term 'cortex' is derived from the Latin word meaning…

8 Famous psychiatrist of the turn of the last century whose middle name was 'Schlomo.'

12 What was the serendipitously discovered antipsychotic chlorpromazine initially intended for?

13 Hippocrates said that the brain was the seat of intelligence. Who thought that the heart played this role, and that the brain was a cooling mechanism for the blood?

15 Which histological fixative is also extensively studied for its widespread occurrence in interstellar space?

16 What is the name of the folk style whose features include cante, toque, baile and palmas?

17 What is the name of the ECNP initiative that assists clinical researchers in accessing pharmacological tools important for the pursuit of their studies?

18 What did Spanish surrealist Dali call "the most serious part of my personality"?

Down

1 Who coined the term 'hypnosis' in 1843?

2 What is the name of the project constructing a synthetic brain down to the molecular level through computational means?

3 What does the 'RD' stand for in RD Laing?

6 Which novel by Pat Barker chronicles poet Siegfried Sassoon's treatment for shell shock by neurologist and psychiatrist WHR Rivers during World War I?

7 Who played the protagonist feigning mental illness in 'One Flew Over the Cuckoo's Nest'?

9 Where will 2014's ECNP Congress be held?

10 What was the name of the American railroad worker who survived an iron rod through his head in 1848, a case which has inspired so much neurological debate since?

11 Which substance of abuse was found to convey most harm, both to users and to others, in a 2010 analysis published in *The Lancet*?

14 Common name of the Persian polymath and author of *The Cannon of Medicine*.

Answers for today's crossword can be found on page 18 in Monday's issue of *ECNP Daily News*.

ECNP CALENDAR OF EVENTS

2014	
6-9 March	ECNP Workshop on Neuropsychopharmacology for Young Scientists in Europe, Nice, France
4-6 April	**ECNP Seminar,** *Veles, Macedonia*
6-11 April	ECNP School of Child and Adolescent Neuropsychopharmacology, Venice, Italy
8-10 May	**ECNP Seminar,** *Croatia*
18-21 October	**27th ECNP** *Congress, Berlin, Germany*
14-16 November	**ECNP Seminar,** *Serbia*
2015	
29 Aug–1 Sept	**28th** *ECNP Congress, Amsterdam, The Netherlands*
2016	
17-20 September	**29th ECNP** *Congress, Vienna, Austria*
2017	
2-5 September	**30th ECNP** *Congress, Paris, France*
2018	
6-9 October	**31st ECNP** *Congress, Barcelona, Spain*
2019	
7-10 September	**32nd ECNP** *Congress, Copenhagen, Denmark*

For regular updates on ECNP initiatives please visit:
www.ecnp.eu and www.ecnp-congress.eu

Stay informed, stay connected

In addition to this newsletter, ECNP offers a variety of other news and media channels designed to keep you at the forefront of our latest activities, initiatives and developments:

Websites (www.ecnp.eu | www.ecnp-congress.eu)
The ECNP websites provide a myriad of information on matters related to our organisation. Follow links to sign up for e-bulletins and news updates.

Message from the President
A monthly personal e-message from the President.

E-news
Monthly overview of latest news within ECNP.

Talk of the Month
Short video talks by distinguished scientists, aimed at making ECNP science more accessible to the general public.

Facebook (www.facebook.com/myECNP)
Find ECNP on Facebook to subscribe to the news feed and join meeting 'events' throughout the year.

Twitter (twitter.com/ECNPtweets)
Follow ECNP on Twitter to receive the latest news and updates, hot off the presses!

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ECNP neuroscience applied