April 2008

newsletter 19

A network for people

Competence Network Schizophrenia

www.schizophrenianet.eu

Univ.-Prof. Dr. med. W. Gaebel
(Speaker of the German Research Network on Schizophrenia)

Dear Colleagues,

Looking back on the activities of the GRNS in the year 2007 I think that there is no doubt that the most important event was the First European Conference on Schizophrenia Research, organized by the head office of the GRNS. Some of the highlights of this conference will be reported in this issue of our newsletter.

This 1st ECSR has been a remarkable success. Speakers as well as participants encouraged us to pursue our initial plans to establish this conference on a biannual basis. Thus, it is our pleasure to invite you already now to attend the 2nd European Conference on Schizophrenia Research (ECSR), which will take place in **Düsseldorf, Germany, September 23 – 25, 2009.** As in 2007 the ECSR will be cosponsored by the Association of European Psychiatrists (AEP), the World Psychiatric Association (WPA) and its section on schizophrenia, and the German Society for Psychiatry, Psychotherapy, and Nervous Diseases (DGPPN).

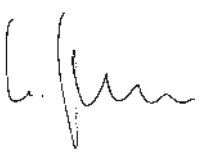
According to our objectives as well as the participants' needs documented in the comments on the evaluation sheets of last year's conference and in order to stand out from other congresses in the field of schizophrenia our concept is to focus on the transfer of research findings into every day practice. None the less the ECSR 2009 will still be a forum for European network research.

The Scientific Committee invites authors to submit outlines for core symposia and abstracts to be considered for inclusion into the programme. **Deadline for submission of symposia is December 21, 2008. Abstracts for oral presentations and posters can be submitted until March 15, 2009.**

We are looking forward to receiving your contribution and to welcoming you at the ECSR in 2009.

Yours sincerely

Wolfgang Gaebel

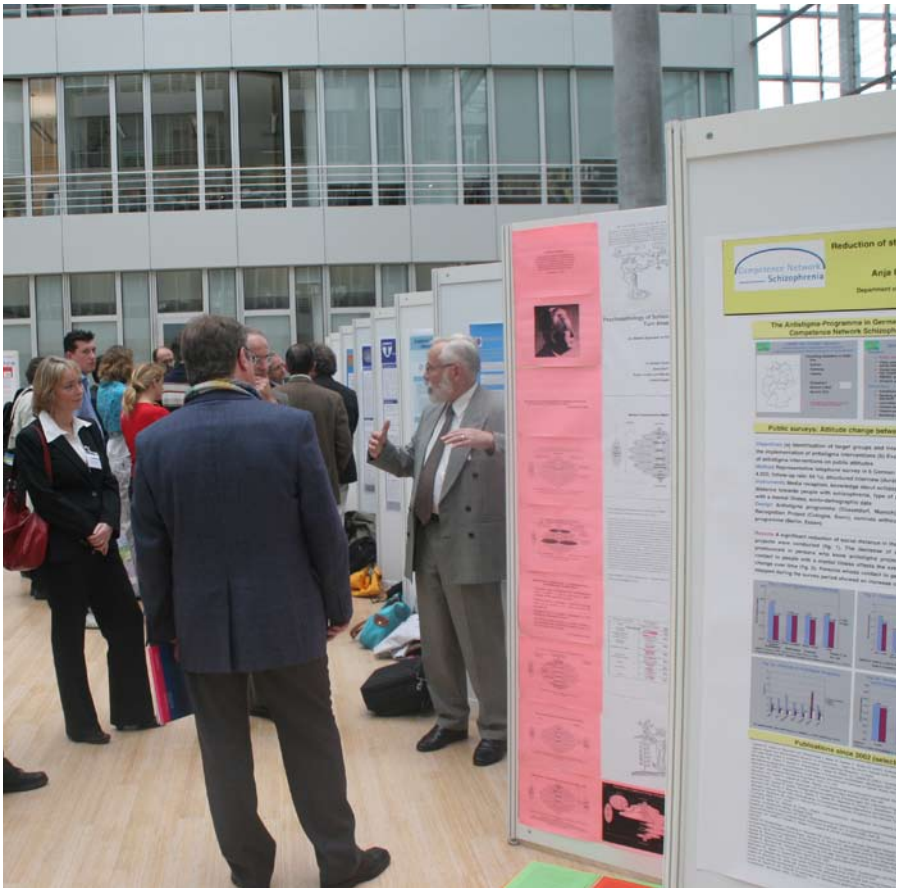


1st European Conference on Schizophrenia Research

In autumn 2007 international psychiatrists, psychotherapists and interested colleagues of other disciplines met in Düsseldorf to update their knowledge especially with regard to early recognition and early treatment of psychosis, as well as concerning the therapeutic challenges of first episode schizophrenia, and other topics like genetics, brain imaging, or neuro-psychology just to name some.

The ECSR was organized by the German Research Network on Schizophrenia but was not only meant for presenting the results of own research projects.

It was likewise a kick-off meeting for further biannual European Conferences on Network-Research in Schizophrenia being a forum to present results of national and transnational research projects, and also to discuss innovative concepts for research transfer into the health care system. The presidential symposium dealt with „Future perspectives in diagnosing schizophrenia" and discussed different aspects in the process of reviewing current classification systems.



Poster Session ECSR 2007

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Future Perspectives in Diagnosing Schizophrenia

The Presidential Symposium, which opened the conference and was organized in honour of the 60th birthday of Wolfgang Gaebel, the speaker of the GRNS, reflected the discussion on the disease concepts of schizophrenia with regard to the revision of the currently used diagnostic classification systems. Against the background of new findings on the neurobiological aspects of this disease as well as on a changing view on its phenomenology the speakers looked critically on the diagnostic criteria actually defining schizophrenia.

H.-J. Möller, Munich started with a historical view on the development of psychopathology in the last century, the rediscovery of this approach in the field of evolutionary psychology with the concept of massive modularity and its implementation in psychopathology and the classification of mental disorders.

Critical aspects of current classification systems

H.-J. Möller pointed out that psychiatrists face many problems when classifying and diagnosing schizophrenia. Diagnostic systems do not attempt to find homogeneous groups. Quite the opposite, the diagnostic entity of schizophrenia currently comprises a heterogeneous collection of interrelated and relatively distinct phenotypes. These variants relate to relatively distinct brain-behavioural modules each with either overlapping or separate aetiology, pathophysiology, course characteristics and treatment response. At present, over one hundred combinations of symptoms can lead to a diagnosis of schizophrenia according to DSM-IV. Furthermore, the requirements that need to be fulfilled for a diagnosis of schizophrenia are not the same in the different diagnostic systems; for example, ICD-10 requires characteristic symptoms to have been present for at least one month, DSM-IV for at least 6 continuous months, raising questions about the validity of each system. Studies have shown that the frequency of diagnostic groups in large patient samples not only depends on the diagnostic system applied but also on the particular version of that system. The schizophrenia/bipolar dichotomy has validity problems since a large proportion of individuals fall into the overlap area between schizophrenia and bipolar disorder and are currently diagnosed as schizoaffective, or Psychotic/Mood Not Otherwise Specified.

"At the moment, people with schizophrenia are grouped into categories, whereas it may be more clinically relevant to group symptoms (e.g. positive symptoms, negative symptoms, depression, mania, cognitive decline and functional impairment) into dimensions. Some evidence suggests that a dimensional approach may be superior to a categorical approach in terms of clinical usefulness and prognostic ability, but the question of diagnostic usefulness still has to be clarified.", Möller concluded. Factors such as duration, time course and aetiopathogenesis (e.g., emotional, cognitive, social) are important for the treatment and outcome of schizophrenia but are not covered by current diagnostic systems.

Therefore Möller proposed a new conceptual model of classification of psychotic illnesses that is based on simultaneous ordering of individuals according to two levels of their biological and phenomenological complexity. This model is supposed to be conceptually similar to the periodic table of the elements whereby objects grouped together on the basis of one organizing principle were at the same time subjected to ordering along a second axis. He expected that a true two-axis classification of psychotic illnesses would provide a basis for new sampling strategies for biological and clinical research that would be different from the sampling strategies derived from the existing classification models.

The role of cognition in the diagnosis of schizophrenia

When talking about weaknesses of the current classification system the aspect of cognitive impairment is especially critical, said Richard Keefe from Durham. Neurocognitive impairment is, on average, severe to moderately severe compared to healthy controls, and almost all patients with schizophrenia demonstrate cognitive decrements compared to their expected level if they had not developed the illness. Compared to patients with affective disorders, cognitive impairment in schizophrenia appears earlier, is more severe, and is more independent of clinical symptoms. Cognitive impairment in schizophrenia is more predictive of dysfunction in our increasingly complex society than positive and negative symptoms a fact that is reflected in the low percentage of people working fulltime and being capable of living fully independently. Cognitive impairment is considered to be a core component of schizophrenia, and is increasingly investigated as a potential treatment target. Accordingly the US FDA has indicated that the recognition of cognitive impairment in the diagnostic nomenclature would be an important step towards warranting a pharmacologic indication to a drug that improves cognition.

The current description of schizophrenia within DSM-IV includes several references to cognitive impairment. Yet is not a part of the criteria or typology.

The cognitive experts in the Measurement And Treatment Research to Improve Cognition in Schizophrenia (MATRICS) project concluded that "schizophrenia and schizoaffective disorder share a similar pattern of cognitive impairments, which is distinct from patterns in major depression, bipolar disorder, and Alzheimer's dementia." (Buchanan et al, *Schiz Bull*, 2005)

Even if cognitive information does not increase the point of rarity (its ability to improve the distinction between two entities and thus create an increased nonoverlap between them) between psychotic disorders and thus does not meet a crucial determinant in order to achieve a diagnostic refinement, it may "provide useful information not contained in the definition of the disorder that helps in decisions about management and treatment." (Kendell and Jablensky, 2003)

The following criterion is now proposed for consideration in the diagnostic criteria for DSM-V and ICD-11 schizophrenia: "A level of cognitive functioning suggesting a consistent severe impairment and/or a significant decline from premorbid levels considering the patient's educational, familial, and socioeconomic background".

Keefe commented on this: "If these diagnostic systems focus less on specific criteria in favor of a completely dimensional approach, the above recommendation could be easily revised to include cognitive impairment as one of the key dimensions."

In his summary he described several challenges that must be met before this suggestion will be accepted. Research is needed to determine

- if such a criterion will increase the point of rarity between schizophrenia and other diagnostic entities;
- if clinicians are able to evaluate cognition reliably with brief formal assessment instruments or interview-based methods;
- if the inclusion of such a criterion will improve the value of the diagnosis of schizophrenia for prognosis, treatment outcomes, and the identification of its biological and genetic determinants.

The future contribution of genetics to the diagnosis of schizophrenia

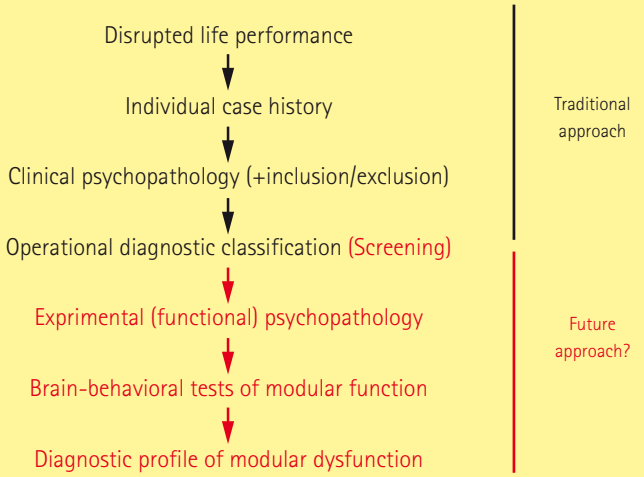
Genetics is currently providing the major cue to the etiological multifactorial diagnosis of disorders like schizophrenia. Diagnosis of schizophrenia is exclusively based on psychopathological patterns and temporal criteria without reference to any explicit etiological determinant. Despite the limitations of this symptom based diagnosis it became possible through the tools of molecular genetic to identify a growing number of susceptibility genes and causal determinants. Yet, apparently the expected diagnostic specificity of schizophrenia associated genetic markers is becoming more and more questionable given the current state of evidence. A reason for this transnosological nature of genetic determinants might be that they are impacting on a set of neurobiological characteristics some of which are shared between diagnoses. Symptoms and symptom patterns are apparently too complex and under the additional influences of various environmental forces to show a specific relationship to DNA-sequence variations. W. Maier, Bonn: "This constellation raises the question if symptom based mental disorders can be rooted in distinct etiologies, and which might be the consequences for future diagnostic systems."

Besides susceptibility genes common risk alleles for schizophrenia became available through candidate and genome wide association study. Thus a translational characterization of their impact on brain structure and function provides an important tool to discover new disease-associated mechanisms. Findings of Meyer-Lindenberg and co-workers implicate that genes and circuits related to dopaminergic neurotransmission (COMT, DARPP32), glutamatergic neurotransmission (GRM3) and neural plasticity (BDNF), among others, are contributing to the genetic risk in the pathophysiology of schizophrenia.

Functional psychopathology: A future framework for diagnosing schizophrenia?

While schizophrenia is diagnosed in a descriptive manner based on psychopathologically defined clinical symptoms, the functional origin of symptoms – if known at all – is rarely involved into the diagnostic process, W. Gaebel criticised the current disease concept. For the future advancements of diagnostic systems considering the functional basis of psychopathology beyond nosological categories may be of increasing importance, W. Gaebel argued. The aim of such an approach should be the development of a functional psychopathology, characterizing symptoms not only on a descriptive level but dissecting them in their component parts, i.e. into the basic psychological dysfunctions underlying these symptoms. Such an approach may help to elucidate the nonspecificity of biological variables related to psychiatric disorders and may increase the chance of finding meaningful relations between biological and behavioural variables. A modular connectionist diagnostic system of mental disorders may be apt to integrate modern neurobiological and genetic findings in psychiatry on the background of a bio-psychosocial approach.

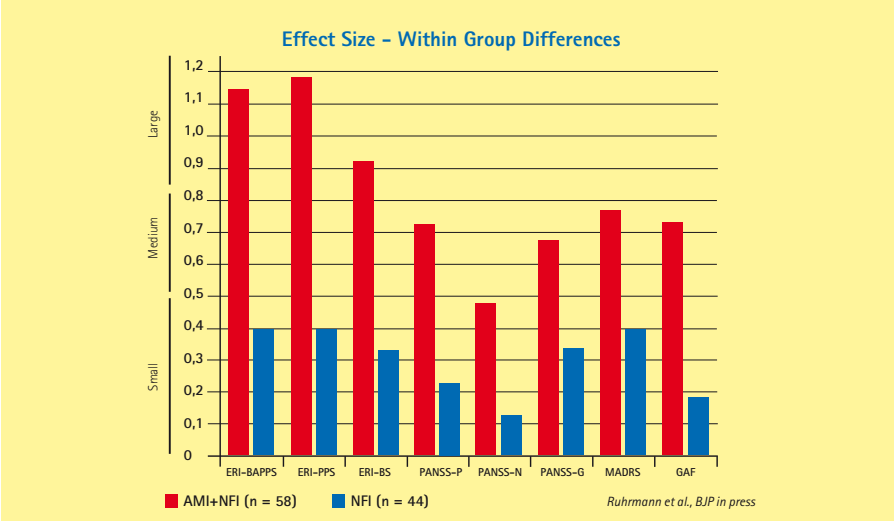
Towards a Modular Classification of Neurodermental Dysfunctions



Conclusion

Valid diagnostic classification is crucial for clinical research and practice. Data, rather than opinion or tradition, must inform classification. Research data from many fields are inconsistent with a dichotomous classification. Powerful new research tools provide biological validators for classification. Current classifications are inhibiting progress in research and clinical practice. Simple steps can, and should, be taken immediately as "first aid" measures. Development of biologically valid classification will be an iterative process. Key desirable properties can already be identified for new classification systems.

Early recognition and early intervention



Early intervention for psychosis has become an international initiative for the improved treatment of young people in the earliest phases of psychotic illness. The rationale for this includes the perceived link between duration of untreated psychosis and clinical outcome, as well as the importance of tailoring specific interventions to young people with no prior experience of mental health services. The approach is based on specific interventions in three areas: drug treatments, psychological treatments and service level interventions. Shôn Lewis, Manchester, UK: "The experimental use of drug treatments or cognitive therapy to prevent transition to full psychosis in people seeking help for at risk mental states, or prodromal symptoms has recently been evaluated and it appears that both drug treatments and psychological treatments are likely to be effective."

Prevention has become a major task in the treatment of psychosis. Within the German Research Network on Schizophrenia a unique two-phase approach was evaluated. S. Ruhrmann, Cologne presented the data of128 patients being putatively in an early initial prodromal state (EIPS) of psychosis, defined by cognitive-perceptive basic symptoms or a combination of functional decrease and biological risk indicators. They were randomized to either cognitive behaviour therapy (CBT) or supportive counselling (SC) for 12 months, with another follow-up after 24 months. 124 patients being putatively in the late initial prodromal state (LIPS), defined by attenuated or transient full-blown positive symptoms, were randomized to either a needs-focused intervention (NFI) or a combination of NFI with amisulpride (AMI+NFI) for up to 24 months. In the EIPS study, significant lower conversion rates were observed with CBT after 12 and 24 months. Both treatment conditions produce a comparable significant symptomatic and functional improvement. In the LIPS study, combined treatment with amisulpride yielded a superior acute 12-weeks treatment effect on positive, negative, affective and functional measures. First analysis of six-months effects showed a significant lower conversion rate with AMI+NFI. S. Ruhrmann: "Both treatment approaches – NFI and AMI+NFI – appear to at least delay the onset of psychosis, opening up the opportunity to adapt indicated prevention to the current needs of the patients."

Early course of schizophrenia: Functional and neurobiological disturbances

This symposium was organized by one of the cosponsors of the 1st ECSR, the WPA Section on Schizophrenia. Merete Nordentoft (Denmark) presented an insightful talk on the association of premorbid functioning, duration of untreated psychosis (DUP) and outcome among patients with first-episode schizophrenia spectrum disorders. Against the background of the Danish OPUS-trial, a longitudinal study of first episode psychotic patients, she concluded that the association of DUP and illness outcome was highly consistent even over a time period of five years, supporting the case for programmes that aim to reduce DUP. Furthermore she postulated another illness dimension beginning long before actual psychosis breakout characterized by low premorbid adjustment, negative symptoms and social/vocational problems. From a neurobiological viewpoint, Birthe Glenthoj (Denmark) pointed out the predictive relation of dopamine D2 receptors binding potentials in neuroleptic-naive first-episode schizophrenia patients to treatment outcome. In addition she has found evidence that schizophrenic symptomatology is influenced by frontal and thalamic D2/3-receptor activity, and that antipsychotic drugs not only exerts their therapeutic actions via D2 blockade in the striatum but also via frontal and thalamic D2/3-receptors. A further illustrative talk delivered by Wiebke Cahn (Netherlands) brought up the topic of neurotoxicity of psychosis being the detrimental effect of psychosis on brain metabolism und morphology. Conclusively, Peter Falkai (Germany) elucidated the mechanisms underlying hippocampal pathology in schizophrenia, considering bilateral hippocampal volume reduction as the most frequent brain structural change in schizophrenia patients. According to Falkai, this anomaly can be traced back to genetical factors (NRG-1) as well as to environmental influences. Additionally, he indicated failures both in synaptogenesis and neurogenesis as key factors in the development of schizophrenia and suggested that specific non-pharmacological interventions, e.g. physical exercise, may exert a beneficial influence on functional and structural deficits.

ECSR News Ticker

Aretaeus Schizophrenia Award

Aretaeus of Cappadocia (AD 81–138).

On the occasion of the ECSR 2007 the German Research Network on Schizophrenia awarded for the first time a prize for young scientists who stand out due to excellent empirical studies in the field of schizophrenia research. This prize is named after the Greek physician Aretaeus of Cappadocia (Asia Minor), who practiced in Rome and Alexandria at the beginning of the second century. Aretaeus not only gave the earliest clear account of diabetes, but also left many fine descriptions of diseases including a systematic classification of mental disorders. This contained a first description of schizophrenic behaviour, recorded within a comprehensive medical compendium, which for the first time differentiated between acute and chronic disorders. This prize is worth 5000 Euro and is donated by the PsychoseNetz, the supporting association of the GRNS.

In 2007 Dr. med. Johannes Hamann from the Department of Psychiatry and Psychotherapy, Technical University Munich and Dr. rer. soc. Andreas Wittorf from the Department of Psychiatry and Psychotherapy, University of Tübingen received the Aretaeus Schizophrenia Award.

The physician Johannes Hamann was awarded for a study on shared decision making and its short- and longterm effects published in Acta Psychiatrica Scandinavia and *Journal of Clinical Psychiatry.* The psychologist Andreas Wittorf was awarded for a study on the predictive validity of neuropsychological, clinical and sociodemographic variables on community outcome. The study has recently been accepted for publication in European Archives of Psychiatry and Clinical Neurosciences.

Workshop: Network Research in Schizophrenia – A European Perspective?

"Future European Conferences on Schizophrenia Research shall explicitly be a forum to present data generated in different national networks as well as by networking on a European level." Wolfgang Gaebel, the speaker of the GRNS, has stated in his welcome address. According to this objective representatives of European Networks dealing with different aspects of schizophrenia came together in a workshop in order to

1. Learn from other European Networks – their focus in research, their experiences in transferring research results into practice as well as their unmet needs
2. Initiate joined European efforts for fighting schizophrenia and evaluating underlying causes of this disorder.
3. Discuss future European research activities and a forward-looking strategy for taking research results into the clinics and identifying bottlenecks
4. Define/identify common research interests as a basis for possible transnational research collaboration, including the option of a joined funding application to the EU (7th EU framework program?)
5. Discuss options for a harmonization of research methods in order to pool data from different studies more efficiently (example: MATRIX-initiative in the US)

The participants from Brain-Net Europe, GROUP (Genetic Risk and Outcome of Psychosis Network), MHN (Mental Health Research Network), FERN (The First Episode Research Network), EPOS (European Prediction of Psychosis Study), SWEPP (Swiss Early Psychosis Project), SeGrid (Joint ebased database for sensitive data), and GRNS (German Research Network on Schizophrenia), as well as the President of the Association of European Psychiatrists AEP, Cyril Höschl (Prague, CZE), and Alfredo Cesario (Brussels, BEL), European Commission – Medical and Public Health Research, and Dieter Dollase (Brussels, BEL), EU Liason Office of German Research Organisations (KoWi) discussed future concepts of working together on a European level with the perspective of establishing transnational networks of excellence or at least strategic partnerships. With regard to upcoming EU-calls on schizophrenia which are supposed to be published in early summer 2008 the EU-representatives emphasized the limitations for collaborating centres within such calls: project partners involved should not exceed 6 to 8 centres. Cesario announced these calls for May/June 2008 having a deadline three months after publication. D. Dollase from KoWi strengthened the essential aspects for applying within the FP7-programme.

- Good experience with EU projects
- Real commitment for R&D with colleagues on a European/international level
- Project needs European involvement
- Brings forward young researchers
- Get aware of enterprises/relevant organisations and access to knowledge
- Building of longterm relations of mutual interest

All participants agreed that their objectives meet these criteria, strengthening their motivation to collaborate in European research projects on schizophrenia. They explicitly declared their interest in a joint application within FP7. Part of the group will meet again on the occasion of the AEP in Nice to continue the fruitful discussion.

Bildunterschrift kommt noch

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Scientific Events 2008

5. - 9. April 2008	**AEP Congress 2008, Nice** www.kenes.com/aep
21. - 25 June 2008	**1st International Schizophrenia Society Scientific Meeting, Venice** www.schizophreniasirs.org
13. - 17. July 2008	**XXVI Congress of the CINP, Munich** www.cinp2008.org
18. - 19. Sept. 2008	**GRAS – 3rd International Symposium on Schizophrenia, Göttingen** www.gras.em.mpg.de
20. - 25. Sept. 2008	**WPA 2008 – The 14th World Congress of Psychiatry, Prague** www.wpa-prague2008.cz
09. - 11. Oct. 2008	**DGBP – 7. Drei-Länder-Symposium für Biologische Psychiatrie, Göttingen** www.dgbp-kongress.de
20. - 22. Oct. 2008	**IEPA – 6th International Conference on Early Psychosis, Melbourne (Aus)** www.iepa2008.com
26. - 29. Nov. 2008	**DGPPN Kongress 2008, Berlin** wwww.dgppn-kongress.de

Announcement of the 2nd European Conference on Schizophrenia Research

The ECSR 2009 will again take place in Düsseldorf from **September 23–25**. Psychiatrists, psychotherapists and other professionals specializing in the field of schizophrenia are invited to submit abstracts for posters and oral presentations, as well as for symposia. The deadline for online submissions of abstracts

- for symposia is **December 21, 2008**
- for oral presentations and posters **March 15, 2009**

For more information please visit the conference- website **www.schizophrenianet.eu** or contact the German Research Network on Schizophrenia (Kompetenznetz Schizophrenie) by email **info@kompetenznetz-schizophrenei.de** or phone +49-(0)211-922-2770.

Imprint

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