

Review Article

A short historical review of SCNP with special reference to the UKU

Bech P, Ban TA. A short historical review of SCNP with special reference to the UKU

Objective: To give a review of the history of SCNP since the first meeting in 1960 with specific focus on UKU.

Methods: Consulting the appropriate minutes from the meetings.

Results: One of the major goals of the SCNP was the standardization of clinical trials with psychotropic drugs. In 1969, the SCNP established a Committee for Clinical Investigations (UKU) with the representation of clinical investigators and the drug industry; moreover, during the 1970s and '80s, the UKU initiated clinical trials and contributed to the methodology of clinical investigations with psychotropic drugs. With the decrease in governmental funding and increasing influence of the US Food and Drug Administration on the methodology of clinical investigations around the world in the 1990s, the UKU was dissolved. The changes had a detrimental effect on the developments on the methodology of clinical investigations, and the lack of clinical feedback led to an impasse in psychotropic drug development with some pharmaceutical companies abandoning research in the central nervous system area.

Conclusion: It is suggested that a revival of UKU to provide a platform for dialogue among government, industry, and academia could help break the impasse.

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Summations

- One of the major goals of the newly established Scandinavian College of Neuropsychopharmacology (SCNP) in 1960 was to facilitate the development of clinical methodology for the evaluation of psychotropic drugs. To achieve this objective, the SCNP established a Committee for Clinical Investigations (UKU) with representation of clinical investigators and the drug industry.
- In the 1970s and '80s, the UKU made important contributions to psychotropic drug development. The UKU was instrumental in the demonstration of lithium's effectiveness in endogenous depression, and in the development of assessment instruments to be used in clinical investigations, such as the UKU side effects scale and the UKU scales for the diagnosis and severity of mental disorders.
- Abolishment of UKU in the 1990s led to the dominance of the pharmaceutical industry in psychotropic drug development in Scandinavian countries without the necessary clinical feedback and guidance.

Considerations

- The decade from the dissolving of the UKU to the establishment of the SCNP's official journal has been insufficiently covered.

First SCNP meeting in Copenhagen 1960

At the XII meeting of the Nordic Psychiatric Congress in Copenhagen in 1958, the subcommittee on

psychopharmacology had discussed the perspective of a Scandinavian Society of Psychopharmacology. Parallel with this initiative, the executive of the Collegium Internationale Neuro-Psychopharmacologicum (CINP)

contacted the Scandinavian colleagues about establishing a Scandinavian section of the CINP. It was the marked rise in psychotropic drugs in the 1950s (chlorpromazine and imipramine in Europe and the monoamine oxidase inhibitors in United States of America) that resulted in the birth of CINP in 1958.

On 5 February 1960, the SCNP was established (1) with Arvid Carlsson (Sweden) as the Founding President and Jørgen Ravn (Denmark) as the Founding Secretary. Other board members were Erik Jacobsen (Denmark) and David H. Ingvar (Sweden). Present at this meeting were also (among others) Odd Lingjærde (Norway), Gunnar Lundqvist (Sweden), Carl-Gerhard Gottfries (Sweden), Asser Stenbäck (Finland), and Mogens Schou (Denmark) while Paul Kielholz from Switzerland was one of the guests from the Continent.

One of the major goals for establishing the SCNP was the standardisation of clinical trials with psychotropic drugs in Scandinavia.

Second SCNP meeting 1961

The 1961 meeting was the first ordinary congress of the College (2). The board was elected at this meeting by the general assembly with Gunnar Lundqvist (Sweden) as the President and Jørgen Ravn (Denmark) as the Secretary. The other members of the board were Arvid Carlsson (Sweden), Erik Jacobsen (Denmark), and Tollak Sirnes (Norway).

Since then, the SCNP has held annual congresses. Table 1 shows the list of SCNP Presidents. Until 2009, the scientific contributions were all published in the *Nordic Journal of Psychiatry*. Starting in 2010, however, only the abstracts from the SCNP congresses were published every year and no longer in the Nordic journal; however, in *Acta Neuropsychiatrica*, the official journal of the SCNP.

Table 1. SCNP Presidents

1960–1962	Arvid Carlsson (CINP President 1980)
1962–1972	Gunnar Lundqvist
1972–1980	Tollak Sirnes
1980–1985	Carl-Gerhard Gottfries
1985–1989	Lars Gram
1989–1992	Hans Ågren
1992–1995	Annette Gjerris
1995–2000	Ulrik Fredrik Malt
2000–2004	Torgny Svensson (CINP President 2008)
2005–2006	Birte Glensthøj
2007–2013	Ole Andreassen
2013	Gregers Wegener

SCNP, Scandinavian College of Neuropsychopharmacology; CINP, Collegium Internationale Neuro-Psychopharmacologicum.

Udvalg for Kliniske Undersøgelser (UKU); Committee for Clinical Investigations

At the first SCNP congress in 1960, Asser Stenbäck (Finland) stated that we Scandinavians ought to promote drug efficacy assessment with rating scales by focussing on target symptoms. ‘In this way we would achieve a greater consensus as to the results...’.

At the 8th SCNP congress in 1967, Odd Lingjærde (Norway) became a member of the SCNP board and in 1968 he took the first initiative to establish the UKU. The UKU was then founded as a subcommittee of the SCNP. The UKU had one member from each of the Nordic countries (Denmark, Finland, Norway, and Sweden), and one member representing the pharmaceutical industry. Starting in 1969, the UKU became a standing subcommittee of SCNP with Odd Lingjærde as chairman and Erik Sarau-Kristiansen (Denmark), Pekka Tienari (Finland), and Folke Sjöqvist (Sweden) as committee members.

In 1969, on behalf of the UKU, Odd Lingjærde carried out a questionnaire-based study on the use of psychiatric rating scales at Scandinavian institutions for mental disorders (3). In total, 131 departments responded and of these 102 were in favour of using rating scales in the evaluation of mental disorders. The remaining departments were in doubt, but no one disagreed. With regard to the question of how many items a scale for depression or schizophrenia should include, 100 respondents preferred brief scales, whereas the remaining felt that a lengthier scale (more than 20 items) should be considered. In response to the question of which scales they had experience with, the Hamilton Depression Scale was the one most frequently mentioned, followed by the Cronholm–Ottosson Depression Scale, the Beck Depression Inventory, and the Brief Psychiatric Rating Scale (BPRS). These scales were typically used in clinical trials.

The first UKU initiated trial was conducted by Odd Lingjærde in which the HAM-D was used to evaluate the effect of lithium carbonate in combination with tricyclic antidepressants (TCA) in endogenous depression (4). After 4 weeks of treatment, it was found that 79% of the subjects responded favourably to the lithium + TCA combination, whereas only 58% showed a similar response to the placebo + TCA combination ($p < 0.05$).

The most widely known UKU contribution is the UKU side effect scale (5,6). It was developed by Odd Lingjærde (Norway-chairman), Ulf Göran Ahlfors (Finland), Per Bech (Denmark), Sven Jonas Dencker (Sweden), and Kjell Elgen (Norway). The study was initiated by Åke Liljestrand and Kjell Strandberg at the Swedish National Board of Health and Welfare

Department of Drugs with the hope that it would help treating physicians in the detection and reporting of side effects with psychotropic drugs. Michael Trimble (UK), Philip May (US), and George Simpson (US) made valuable suggestions to the working team for the analysis of data and preparation of the report on this scale.

Another major UKU publication was the 'Scales for the assessment of diagnosis and severity of mental disorders' in which UKU members collaborated with Ulrik Malt (Norway) and Tony Lewander (Sweden) (7).

The major UKU publications on rating scales in neuropsychopharmacology have all been published in *Acta Psychiatrica Scandinavia* (APS). Over the decades, two outstanding editors of APS, Erik Strömngren and Jan-Otto Ottosson, showed great interest in clinical psychometrics and were frequent attendees of SCNP congresses.

At the 25th SCNP anniversary in 1984, a symposium was organised on Current Scope of Psychopharmacological Research in Europe (8). At this symposium, the idea of founding the European College of Neuropsychopharmacology (ECNP) was put forward by Carl-Gerhard Gottfries and Per Bech. Three years later, Bech and Gottfries became the Founding President and the Founding Secretary of ECNP, respectively, when the College was established in Brussels in 1987 (9).

In 1991, a European Committee for Standardization of Clinical Trials with Psychotropics (ECST) was established in Strasbourg (France), acting as a sub-committee of ECNP. The objective of the ECST was to promote the exchange of ideas on issues concerning the clinical validity of psychotropic drugs in the treatment of mental disorders via a dialogue between the pharmaceutical industry, academia, and the regulatory authorities in Europe (10). However, before long, the ECNP decided that the ECST should continue as an autonomous body.

In the 1990s, the SCNP dissolved the UKU because by then the influence of the US Food and Drug Administration (FDA) had significantly increased and the industry felt that it would be safer to adhere to the clinical trial model endorsed by the American drug regulatory agency. It should be noted that since the 1970s there were no major changes in scales measuring outcome in clinical trials with psychotropic drugs. The most frequently used scales are still the Hamilton Depression Scale (HAM-D), the BPRS, or the Hamilton Anxiety Scale (HAM-A).

In his 1987 review of the current status of psychiatric research in Denmark for the journal *Psychiatrie & Psychobiologie* (which in 1991 became *European Psychiatry*), Erik Strömngren (11) drew this rather pessimistic conclusion: '...although

Denmark is one of the wealthier countries of the world, its government seems to facilitate decisions on disastrous cuts in budgets; several research institutes of international fame have been closed'. Reviewing in 2000 the changes in the United States, Max Fink (12) noted that the US Government also started to reduce from the mid-1970s the generous sponsorship of psychopharmacology by the US National Institute of Mental Health in the 1960s. As a result of the decrease in available funding, the medical industry, using the FDA guidelines for marketing approval of psychotherapeutic drugs, took over the sponsorship of randomised clinical trials. In the new era, the leading investigators move freely from NIH or academia to industry and vice versa.

In the late 1980s, many psychiatrists of the SCNP who were involved in clinical research became more and more dissatisfied with the growing influence of the industry at the annual meetings, and with their diminished role in clinical investigations. This was not the case in basic research, in which the laboratory studies of researchers like Arvid Carlsson have continued to have an impact on new drug development. The dissatisfaction was to the extent that Erik Sarau Kristiansen (Denmark), a member of the first UKU committee in 1969, sent a letter of resignation from his membership to the SCNP committee in which he gave as a reason of his resignation the downgrading of clinical relevance in psychopharmacology research.

On the other hand, at the annual SCNP congresses in the 1990s, the second-generation antipsychotics and antidepressants were presented very extensively. In 1995, Peter Kramer presented his 'Listening to Prozac', which had just been translated into Swedish with an introduction by Marie Åsberg (13). Presentations from the meetings might then be published as short communications in *Nordic Journal of Psychiatry*, for example, about plasma concentration and clinical effects (14), which can be considered as a traditional Scandinavian approach (Marie Åsberg, Lars Gram, and Svein Dahl).

Fifty years' anniversary of the SCNP

At the 50 years' anniversary of the SCNP in 2009, the opening session had three speakers: first was Arvid Carlsson who briefly told how he in the period up to the mid-1960s explained the function of dopamine and the reuptake inhibition of clomipramine on serotonin. Then Carl-Gerhard Gottfries told us how he had been behind the first clinical trials with citalopram, the drug that took over after zimeldine had to be withdrawn because of its side effect profile. Finally, Per Bech gave a short review of UKU activities, especially with regard to the development of the UKU Side Effect Rating Scale.

Perspective

The first SCNP president Arvid Carlsson received the Nobel Prize in 2000 (for his outstanding studies on the neuropsychiatric function of dopamine). In the 1960s, he discovered that in the antidepressant action of clomipramine serotonin reuptake, inhibition plays an important role. It led to the development of the first selective serotonin reuptake inhibitor (SSRI), zimeldine (15). Other SCNP members, for example, Erik Jacobsen (the effect of disulfiram on the metabolism of alcohol) or Mogens Schou (the mood-stabilising effect of lithium) made also important contributions to the development of neuropsychopharmacology.

Our present SCNP president Gregers Wegener has currently reported that a CINP workgroup recently concluded that virtually no new antidepressant has been developed since the introduction of SSRIs in the late 1970s (16). The consequence of this lack of success in developing new and more effective antidepressants is that several high-profile pharmaceutical companies have decided to shut down research activities in the central nervous system area.

Paradoxically, this report, on the one hand, recognises that research on psychotropic drugs is very profitable for the industry because of the rather high 12-month prevalence of mental disorders (~38% of the EU population), whereas on the other hand, it suggests that the symptom-based scales on which this prevalence estimate has been calculated are the major reason, because of their lack of objectivity, for their failure in the past three decades to discover new classes of more effective and selective psychotropic drugs.

In our opinion, the re-establishment of the UKU in the SCNP and ECST in the ECNP would provide suitable platforms for stimulating the dialogue between industry, governments, and academia to break the impasse in the development of novel psychotropic drugs for the treatment of mental disorders.

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