

## THE CROATIAN VERSION OF DIAGNOSTIC INTERVIEW FOR GENETIC STUDIES

Dubravka Glučina<sup>1</sup>, Dolores Britvić<sup>1</sup>, Davor Lasić<sup>1</sup>, Milenka Dedić<sup>1</sup>, Marko Jakelić<sup>1</sup>,  
Igna Brajević-Gizdić<sup>2</sup>, Žana Kralj<sup>1</sup> & Maja Bucan<sup>3</sup>

<sup>1</sup>Clinic for Psychiatry, Clinical Hospital Split, University School of Medicine, Split, Croatia

<sup>2</sup>Public Health Institute of Split-Dalmatian County, Split, Croatia

<sup>3</sup>University of Pennsylvania, Department for psychiatry, USA

### SUMMARY

*Diagnostic Interview for Genetic Studies (DIGS) is a modern structured interview schedule that has been in use since 1994. Main purpose of the DIGS is to record information regarding to a subject's functioning and psychopathology and it was specifically designed for psychiatric genetic studies. The DIGS is also suitable for making diagnosis, evaluation of comorbidity and other researches. It contents items and sections and has a semi-structured design that gives interviewers the freedom needed to extract the best in formation possible. The validity of a Croatian version of the DIGS was investigated. The original English version was initially translated into Croatian. The Croatian version was then back-translated and compared with the original. In this paper we will describe each item that DIGS contents as well as the use of this diagnostic instrument.*

**Key words:** *diagnostic interview for genetic studies - semi-structured design - psychiatric genetic studies – psychopathology - comorbidity*

\* \* \* \* \*

### INTRODUCTION

Recently genetic studies in psychiatry have increased considerably. Standard diagnostic interviews used in psychiatry were not designed for genetic studies, and that was the main problem for the researchers. In 1994 the National Institute of Mental Health (NIMH) developed a specific instrument for genetic studies: the Diagnostic Interview for genetic Studies-DIGS (Nurnberger et al. 1994). Second version of the DIGS was developed in January 1995, and currently DIGS version 3.0 is in use. That version was developed between November, 1997 and January, 1999 (DIGS 1999). The purpose of DIGS is to record information about subject's functioning and psychopathology. It is specially developed to collect information regarding affective disorders and schizophrenia. Semi-structured design of the DIGS allows us to observe many symptoms associated with other conditions such as personality disorders alcoholism and drug abuse.

The interview is suitable for use in studies of probands and their relatives as well as for the patient selected from the both inpatient and outpatient units. The most suitable personel for administering this instrument are individuals with experience in interviewing and making judgments about manifest psychopathology (DIGS 1999).

The DIGS's semi-structured design gives interviewers possibility to extract the best information possible, without loosing a standardized pattern of interviewing.

DIGS is also a relevant diagnostic criteria. Reliability of the DIGS so far was tested in French version in 1999 in Swiss population, through a study of

136 cases (Preisig et al. 1999). Other translations of the DIGS have reported a good reliability of the DIGS in Hindi population with 20 patients (Deshpande et al. 1998), and more recently in Korean population, in a sample of 53 patients (Eun-Jeong et al. 2004). It was also validated in Columbian (Palacio et al. 2004) and Spanish population (Roca et al. 2006). That is why we decided to translate the DIGS into Croatian and test the validity of a Croatian version of the DIGS. The original English version was initially translated into Croatian. The Croatian version was than back-translated and compared with the original. Next, a group of psychiatric inpatients and outpatients will be interviewed using the Croatian version.

The aim of this report is to introduce Croatian psychiatrists with this semi-structured interview that can be used in many psychiatric genetic studies. It has been translated into Croatian and the validation of the same is still in process.

### INTERVIEW ASPECTS OF THE DIGS

#### Development

Items previously tested in other research interviewers were incorporated into the DIGS. These instruments include the SADS, Structured Clinical Interview for DSM-III-R, Diagnostic Interview Schedule, and Comprehensive Assessment of Symptoms and History. Concurrent development of a research interview for the Collaborative Study on the Genetics of Alcoholism, permitted the inclusion of comparable items in affective disorders and substance abuse sections (Nurnberger et al. 1994).

The DIGS evolved from multiple drafts that were field tested by researchers at the participating centers. Each group conducted field trials with psychiatric inpatients, outpatients, and controls (more than 70 patients in seven sites). Frequent collaborator meetings were held to discuss modifications to the drafts (Nurnberger et al. 1994).

A comprehensive DIGS training manual accompanies the interview. In this manual there are few sections such as background information, administrative procedures, and coding conventions. There are also many examples which can help interviewer to code subject's answers or resolve potentially confusing situations during the interview.

### **Format of the interview**

Coding of the responses should be made properly. The interviewer must note all the examples that can be useful for coding. There are questions and criterion-based definitions that are standard in nowadays psychiatry. If the interviewer sees that a symptom is present, it should be scored, made a marginal note about it, even in those cases when the subject denies existence of that particular symptom.

Sections of the DIGS typically begin with one or two closed-end questions that invite yes or no response. A denial of symptoms in these screening permits one to skip the remainder of the section. If the subject responds positively to the initial screening questions, comprehensive symptom-based information is obtained (Nurnberger et al. 1994).

If no symptoms are reported the interviewer can note that information and move to another section. Organic factors like age of onset, recency, severity frequency and duration of symptoms/syndroms are included. This interview can be conducted in 30 minutes if a subject has no psychiatric illness or it can last for four hours for a patient with different and complex symptoms. The median time required is 150 minutes for affected subjects. After conducting the interview, interviewer needs 30 to 40 minutes to write a narrative and review the answers.

More than 1300 DIGS interviewers have been performed successfully in affected families by the collaborating centers as of October 1993 (Nurnberger et al. 1994).

### **SECTIONS OF THE DIGS**

A modified Mini-Mental State examination is included to permit early termination of the interview with subjects of diminished cognitive capacity. In the demographics section, in addition to standard information, subjects are asked about adoption status and country of birth. Ethnic background is detailed to permit comparisons allele frequencies or disorder rates among subpopulations in genetic studies. The medical history screens for developmental factors and medical

disorders that are known to be associated with psychiatric syndromes including neurological disorders, head injuries, hormonal disturbances, vitamin deficiencies, and birth and developmental abnormalities. Cigarette smoking history is quantified. Female subjects are asked about the association of psychiatric disturbances with pregnancy, childbirth, and menopause and the association of mood disturbance with the premenstrual and menstrual periods (Nurnberger et al. 1994).

### **Somatization**

In this section subjects are asked about problems with body pains in ten physical systems. It also involves subject's medical history. The interviewer should ask about neurological, gastrointestinal, sexual, and other complaints in case that the patient's symptoms are medically unexplained. It is very important to distinguish the panic disorder instead of somatization.

### **Overview**

In this section it is important to record the subject's age at the first psychiatric treatment, any psychotropic agents used, the formal psychiatric assessment, and the number of hospitalizations using subject's medical history as well. The interviewer has a time line and a table for course of illness which provide summarization and chronologic detalization of all the key symptoms. This diagnostic section of the DIGS is particularly useful in making differential diagnoses of mood, schizophrenic, and SA syndromes.

### **Mood Disorder**

The major depression section assesses symptoms for both the current and most severe episode (it is recommended that the two episodes be assessed in series rather than in parallel). If delusions and/or hallucinations have occurred during the episode, descriptive information is obtained to classify symptoms as mood congruent or incongruent. The presence of psychotic symptoms prior to and beyond the resolution of affective symptoms is also assessed (to distinguish DSM-III-R SA disorder). To permit diagnosis using Modified Research Diagnostic Criteria, multiple impairment items are included, and the interviewer must further rate whether the subject was impaired or incapacitated in the major life role. Possible specific precipitants of affective syndromes are considered and an attempt is made to establish the existence of at least one „clean“ episode without such a specific precipitant. A symptom checklist is used for reviewing a second episode to establish recurrent major depression. The age of onset and the number of episodes are also recorded (Nurnberger et al. 1994).

The mania/hypomania section has a purpose to determine if the subject has ever had manic or hypomanic episode and to document a current and most

severe episode. It is very important to assess the functional „incapacitation“ of the patient. That is defined as presence of any psychotic symptom, organic factor, treatment seeking behavior, inability to hold a conversation or to carry out the principal role for at least two consecutive days. The total number of episodes, age of onset, and recency are recorded. Dysthymia is assessed in a separate section. There are many questions that emphasize the phrase „clearly different from your normal self“ with aim to separate clinical mania from usual mood changes.

The cyclothymic personality disorder is adapted from the modified SADS or Gershon and coworkers (Gershon et al. 1982, Mazure et al. 1979.) as a combination of two subsections that assess modified Research Diagnostic Criteria depressive personality and hyperthymic personality. This is similar to cyclothymia as described by Akiskal et al. 1979.

### Substance Use Disorders

The DIGS offers a comprehensive assessment of the consumption of both alcohol and other drugs, abuse and dependence. These sections are similar to those in the Semi-Structured Assessment for Genetic Studies of Alcoholism. Two optional tables at the beginning of the alcohol section permit the interested researcher to record the number of drinks consumed each day of the week prior to the interview and the time it took to consume the alcoholic beverage. A screen is built into the alcohol section to enable a skip-out if the subject reports any of the following: never had a drink of alcohol, never drunk regularly (defined as at least once a week six months or more), never became drunk (operationalized as slurred speech, unsteady gait), or never drank more than three alcoholic beverages in a 24-hour period. The final screening questions are those of the CAGE questionnaire (Mayfield et al. 1974, Bush et al. 1987).

The marijuana section has been separated from the general drug section because the use of marijuana is very common. In the general drug abuse section there is a list of commonly abused drugs in the following categories: cocaine, stimulants, sedatives, hypnotics, tranquilizers, opiates, PCP (phencyclidine hydrochloride), hallucinogens, solvents, combination drugs, and a miscellaneous category. The interviewer should ask patients who are drug users about intravenous drug use.

Alcohol and other drug withdrawal syndromes are assessed by asking about individual symptoms associated with each substance, the co-occurrence of withdrawal symptoms, and whether the subject used the substance to ameliorate the discomfort of withdrawal symptoms. Medical and psychological consequences of substance abuse are evaluated. The clustering of symptoms is assessed for alcohol and drug abuse or dependence by rating the persistence of specific cognitive, behavioral, and physiologic symptoms for at least 1 month. Treatment, age of onset, and the recency and the date of last use of each substance are recorded (Nurnberg et al 1994).

### Psychosis

This section provides diagnostic criteria for psychosis and other psychotic symptoms as well as items in distinguish specific psychotic syndromes. The screening questions assist in determining if the subjects have ever had an episode or period that included psychotic symptoms.

After positive response to probe questions, the subject is initially asked about 25 different types of delusions and hallucinations. Judgments are also made regarding formal thought disorder, bizarre behavior, avolition or apathy, flat and/or inappropriate affect, depersonalization, and derealization (Nurnberger et al. 1994).

Individual symptoms are recorded on a lifetime basis as well as anchored to the current or most recent episode. An array is used to specify whether symptoms occurred during depression, mania, substance use, a medical illness, or the absence of these conditions. The onset of the first symptoms or episode is explored and the number of episodes is recorded (chronic psychosis, including prodromal and residual, is considered to be one extended period of illness). Prodromal and residual symptoms are evaluated separately (Propping et al. 1983, Davison et al. 1969).

The DIGS includes the modified structured interview for Schizotypy to assess schizotypal, schizoid and paranoid personality disorders in relatives if the psychosis was not reported in previous sections. These sections are not used if the psychosis was reported in previous sections.

### Comorbidity

This section was designed to determine relationship between substance abuse and other psychiatric disorders. It is important to establish the temporal relationship between substance abuse, psychosis and major affective disorder. The interviewer should evaluate if one disorder typically or always occurs first, if the disorders always co-occur, if one disorder persist in the absence of the other as well as the duration of the persistence.

### Suicidal Behavior

A separate section for the assessment of suicidal behavior characterizes the most serious suicide attempt in terms of intent, lethality, and the symptomatic context in which is occurred, e.g. during an episode of mood disorder, psychosis, or substance abuse (Nurnberger et al. 1994).

### Anxiety Disorders

This section provides diagnostic criteria for anxiety disorders using DSM-III-R and DSM-IV.

The major anxiety disorders were included because they are common familial conditions with an overlap in

symptom profile and perhaps and genetic vulnerability factors with affective illness (Coryell et al. 1988, Leckman et al.1983, Fyer et al 1990). This section provides diagnostic criteria for Obsessive Compulsive Disorder, Phobia Disorder, Panic Attacks, Panic Disorder with or Without Agoraphobia, as well as questions that help us distinguish Panic Disorder from Generalized Anxiety Disorder, Social Phobia and Specific (Simple) Phobias.

### Eating Disorders

This section provides criteria for anorexia nervosa and/or bulimia nervosa using DS -III-R and DSM-IV. Because some but not all family studies have indicated a familial relationship between affective and eating disorders, sections on anorexia and bulimia were included in the DIGS. The anorexia section includes a table to determine whether the subject meets the DSM-III-R body weight criterion for anorexia (15% below the expected body weight). The table entries are made according to gender, height, and body frame size. Those who continue are assessed for a distortion of body image and presence of an intense fear of gaining weight despite being underweight. Possible organic contributors are ruled out. Symptoms, age of onset, and recency of first and last regularly occurring binges are recorded in the bulimia section (Nurnberger et al 1994).

### Pathological Gambling

In this section diagnostic criteria for pathological gambling is provided using DSM-III-R and DSM-IV. It refers to subject`s preoccupation with gambling, inability to resist impulses to gamble and degree in which gambling disrupts social life and everyday functioning of the patient.

### Sociopathy

This section provides a diagnostic criteria for antisocial personality (ASP) using DSM-III-R and DSM-IV.

Antisocial personality disorder was included as a disorder from a different genetic spectrum that should ally be excluded from studies of affective illness and schizophrenia (Cloninger et al. 1975).

## METHODS

Following consultations with linguists and clinicians the English version of the DIGS 3.0 was translated into Croatian. The Croatian translation was then back-translated by individuals who had not been involved in the initial translation. Next the diagnostic reliability will be tested on a group of approximately 200 patients. Finally interrater reliability will be examined among three of the authors. In this study every patient will be examined two times by three independent interviewers during the same interview and two independent

interviewers will estimate patient`s answers. Five psychiatrists and one psychiatry intern were trained for this study.

### Selecting test administrators

The best way to select personel who will administer the DIGS is to choose professionals who have clinical experience and suitable knowledge. Those are psychiatrists, psychologists, psychiatric social workers and psychiatric nurses.

### Training

The DIGS and the relevant diagnostic criteria should be studied in detail before use so that the interviewer understands the proper procedures for using the instrument and criteria for judging the items, and knows the information needed for critical diagnostic distinctions. If this is not done, the initial interviewers with subjects will be extremely awkward and unnecessarily long because he already has sufficient information, or whether the subject is providing information that is irrelevant with respect to making the required judgments.

Experience has shown that nothing more valuable for training than conducting several interviews. Initially this can be done by having interviews try out the instrument on one another and the person being interviewed assuming the role of a subject. Next, they should try it out on actual subjects, preferably representative of those who will be examined in the research study. If possible, these should be joint interviews with researchers making independent ratings, and there should be discussion of the interviewing technique and of all causes of disagreement in scoring (DIGS 1999).

## CONCLUSION

In this review we wanted to show how the introduction of the Diagnostic Interview for Genetic Studies into clinical practice will improve detail diagnostic of both psychiatric illnesses and comorbidity. This diagnostic instrument is necessary for psychiatric genetic studies that will allow our country to compete and keep up with the global trends in nowadays psychiatry.

## REFERENCES

1. Akiskal HS, Kheni MK & Scott-Strauss A: Cyclothymic temperamental disorders. *Psychiatr Clin North Am.* 1979;2:527-554.
2. Bush B, Shaw S, Clearly P, Delbanco TL & Aronson MD. Screening for alcohol abuse using the CAGE questionnaire. *Am J Med.* 1987;82:231-235.
3. Cloninger CR, Reich T & Guze SB. The multifactorial model of disease transmission, III: familial relationship

- between sociopathy and hysteria (Briquet's syndrome). *Br J Psychiatry*. 1975;127:23-32.
4. Coryell W, Endicott J, Andreasen NC, Keffer MB, Clayton PJ, Hirschfeld RMA, Scheftner WA & Winokur G. Depression and panic attacks: the significance of overlap as reflected in follow-up and family study data. *Am J Psychiatry*. 1988;145:293-300.
  5. Cummings JL: Organic psychoses: delusional disorders and secondary mania. *Psychiatr Clin North Am*. 1986;9:292-311.
  6. Deshpande SN, Mathur MN, Das SK, Bhatia T, Sharma S & Nimgaonkar VL: A Hindi version of the Diagnostic Interview for Genetic Studies. *Schizophr Bull* 1998;24:489-93.
  7. Eun-Jeong J, Yeon-Ho J, Jin-Pyo H, Samuel H, So-Jin M, Jin-Hee H et al. Korean version of the Diagnostic Interview for Genetic Studies: validity and reliability. *Compr Psychiatry* 2004;45:225-9.
  8. Fleiss JL: *Statistical methods for rates and proportions*. 2nd ed. New York: John Wiley; 1981.
  9. Fyer AJ, Mannuzza S, Gallops MS, Martin LY, Aaronson C, Gorman J et al. Familial transmission of simple phobias and fears. *Arch Gen Psychiatry*. 1990; 47:252-256.
  10. Gershon ES, Hamovit J, Guroff JJ, Dibble E, Leckman JF, Sceery W et al. A family study of schizoaffective, bipolar I, bipolar II, unipolar, and normal control probands. *Arch Gen Psychiatry*. 1982; 39:1157-1167.
  11. Leckman Jf, Weissman MM, Merikangas Kr, Pauls DL & Prusoff BA: Panic disorder and major depression: increased risk of depression, alcoholism, panic and phobic disorders in families of depressed probands with panic disorder. *Arch Gen Psychiatry*. 1983;40:1055-1060.
  12. Mayfield D, McLeod G & Hall P: Alcoholism screening instrument. *Am J Psychiatry*. 1974;131:1121-1123.
  13. Mazure C & Gershon ES: Blindness and reliability in lifetime psychiatric diagnosis. *Arch Gen Psychiatry*. 1979;36:521-525.
  14. Nurnberger JI, Blehar MC, Kaufmann CA, York-Cooler CY, Simpson SG, Harkavy-Friedman JH et al.: Diagnostic Interview for Genetic Studies (DIGS). Rationale, unique features, and training. *Arc Gen Psychiatry* 1994;51:849-59.
  15. National Institute of Mental Health. Molecular Genetics Initiative: Diagnostic Interview for Genetic Studies, Reference Manual. Bethesda, Md: National Institute of Mental Health; December 7, 1999.
  16. Palacio CA, García J, Arbeldáez MP, Sánchez R, Aguirre B, Garces IC et al. Validation of the Diagnostic Interview for Genetic Studies (DIGS) in Colombia. *Biomédica* 2004;24:56-62.
  17. Preisig M, Fenton BT, Matthey ML, Barney A & Ferrero F: Diagnostic Interview for Genetic Studies (DIGS): inter-rater and test-retest reliability of the French version. *Eu Arch Psychiatry Clin Neurosci* 1999;249:174-9.
  18. Propping P: Genetic Disorders presenting as schizophrenia: Karl Bonhoeffer's early view of the psychoses in the light of medical genetics. *Hum Genet*. 1983;65:1-10.

Correspondence:

Dolores Britvić  
Clinical Hospital Split  
Šoltanska 1, 21 000 Split, Croatia  
E-mail: dbritvic@globalnet.hr