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R. Heun · H. Müller

Interinformant reliability of family history information on psychiatric disorders in relatives

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Abstract Knowledge on the reliability of family history information is essential for every family study. However, systematic analyses of interinformant reliability of family history information on individual relatives have not yet been published. Consequently, family history information on 1306 first-degree relatives and spouses of patients and of control subjects was collected from at least two other family members using questionnaires. Interinformant reliability was acceptable for dementia [Kappa = 0.58, 95% confidence interval (CI) = 0.48–0.68], but less so for alcoholism (Kappa = 0.41, CI = 0.23–0.59), depression (Kappa = 0.26, CI = 0.14–0.38) and anxiety disorders (Kappa = 0.19, CI = 0.05–0.43). Demographic variables of subjects and informants and their familial relationship did not influence diagnostic agreement on the diagnosis of dementia. Diagnostic agreement on depression was significantly reduced when information from siblings of index subjects was compared with information from spouses of index subjects. The interinformant agreement for the diagnosis of depression was higher in younger than in older subjects (relative risk for disagreement 1.08/additional year, CI = 1.02–1.15). Siblings of index subjects seem to provide different, but not necessarily less relevant, family history information in comparison with other relatives. Researchers should be aware of the problem that depression in the elderly can be easily missed by family history. It seems more important for the diagnosis of depression than for a diagnosis of dementia to get information from multiple informants.

Key words Interinformant reliability · Family history information · Dementia · Depression

R. Heun (✉) · H. Müller
Department of Psychiatry, University of Bonn,
Sigmund-Freud-Strasse 25, D-53105 Bonn, Germany

Introduction

In family studies frequencies of psychiatric disorders in first-degree relatives of patients and of controls are compared (Gershon et al. 1986). Diagnoses of relatives are derived either from direct interviews or from surrogate information provided by informants, i.e. other family members. The first approach is called the family study method, the second represents the family history method (Andreasen et al. 1986; Weissman et al. 1986). Even if direct interviews are intended, not every subject can be interviewed, i.e. some relatives may already be deceased or may be unavailable for other reasons at the time of the study. Thus, surrogate information, i.e. family history information, is essential in every family study.

Several factors may influence the validity of family history information, e.g. psychiatric disorders of the informants (Breslau et al. 1988; Chapman et al. 1994; Kendler et al. 1991), the number of informants (Gershon and Guroff 1984) and the relationship of informants to their relatives (Mendlewicz et al. 1975; Pickle et al. 1983; Thompson et al. 1982). Andreasen et al. (1986) recommended the use of a second informant in addition to the index subject in family studies to increase the sensitivity of the family history. However, she did not mention the possibility of divergent information. Such divergent information on two demented subjects provided by different informants has recently been described by Walstra et al. (1995).

The use of more than one informant raises the question on the interinformant reliability of family history information. It might also be asked which parameters influence and possibly reduce the reliability of this information, i.e. the agreement of both informants information on psychiatric symptoms. These questions are addressed in the present study. Another reason to examine interinformant reliability of family history is the fact that reliability of a diagnostic instrument provides the upper limit for possible validity. A systematic analysis of interinformant reliability has not been previously published.

Methods

Subjects and diagnostic procedures

The study data are part of a comprehensive family study conducted at the department of Psychiatry, University of Mainz: 203 patients with dementia of Alzheimer Type (DAT) or depression (DSM-III-R criteria; age at onset > 40 years) and 80 control subjects from the general population (i.e. 283 index subjects) and their available first-degree relatives and spouses were interviewed using the Composite International Diagnostic Interview (CIDI; WHO 1990). Subjects above 55 years were additionally interviewed with the Structured Interview for the Diagnosis of Dementia of the Alzheimer Type, Multiinfarct Dementia and Dementias of other Aetiology (SIDAM; Zaudig et al. 1991). The CIDI allows DSM-III-R diagnoses for various psychiatric disorders, and the SIDAM allows a detailed differential diagnosis of dementing disorders. Further details of methods and data analysis of the whole family study have been described recently (Heun et al. 1995, 1996).

Family history information on all first-degree relatives and spouses of patients and of control subjects (i.e. the subjects) were individually collected from other relatives (i.e. the informants) using the Family History Questionnaire (Andreasen et al. 1977, adapted to include DSM-III-R criteria), the Dementia Risk Questionnaire (Breitner and Folstein 1984) and the Dementia Questionnaire (Silverman et al. 1986). Family history information on index subjects of families i.e. patients or control subjects was not included in the present study. The Family History Questionnaire is used for diagnosing schizophrenia, affective disorders, anxiety disorders, substance abuse and other psychiatric disorders (providing information comparable with the CIDI). The Dementia Questionnaire and the Dementia Risk Questionnaire provide different information on dementia in relatives; thus, they were used in combination for diagnosing dementia. Consequently, comparison of both instruments is neither useful, nor feasible. The information from these instruments are related to SIDAM data. Diagnostic decisions on the psychiatric disorder of all living or deceased family members based on family history information (lifetime diagnosis according to DSM-III-R criteria) were individually made by the consent of two psychiatrists (i.e. interview information was not used for family history diagnosis); this information represents the dependent variable in logistical regression analysis.

All diagnostic decisions were made without knowledge of the diagnosis of the index subject of the family and of the familial relationships of subjects and informants.

The present analysis focuses on interinformant reliability of surrogate information on relatives of index subjects, i.e. DSM-III-R diagnoses resulting from family history information given by other relatives. Therefore, data analysis is restricted to subjects on whom at least two informants had provided family history information. If more than two informants could provide family history information on one subject, two informants were randomly selected. Thus, every pair of informants can be seen as an independent unit of observation. Table 1 gives a description of subjects on whom family history was given; Table 2 describes the informant samples (i.e. first and second informants). There were no significant differences between first and second informants as can be expected from the randomisation procedure.

The information of relatives given on psychiatric problems of others was rarely detailed enough to make precise diagnoses using the five-digit DSM-III-R diagnostic code. Identical diagnostic codes for a family member resulting from different informants were also rare. Consequently, diagnoses had to be combined for further analysis; i.e. the diagnosis of dementia included dementia of Alzheimer type, multi-infarct dementia, amnestic disorder and dementia NOS. The diagnosis of depression included major depressive disorder, bipolar disorder, dysthymia, adjustment disorder with depressed mood and depressive disorder NOS.

Table 1 Description of the subjects on whom at least two other relatives could provide surrogate (i.e. family history) information on psychiatric disorders

Variable	
N	1306
Living	51.5%
Interviewed	29.6%
Age (years, mean ± SD)	60.3 ± 18.9
Gender	47.2% (F)
	52.8% (M)
Relationship to index subject	
Parents	26.9%
Child	25.1%
Sibling	37.0%
Wife/husband	10.9%
Best estimate diagnoses (DSM-III-R)	
Dementia	7.8%
Depressive disorder	3.1%
Anxiety disorder	4.0%
Alcohol abuse and dependence	1.5%
Substance abuse and dependence	0.2%
Other psychiatric disorders	2.0%
Any psychiatric disorder	15.4%

Table 2 Description of informants and their relationship to the subjects on whom they provided information

Variable (unit)	First informant	Second informant
Age (years, mean ± SD)	57.9 ± 16.3	57.9 ± 15.9
Gender (%)	62.6 (F) 37.4 (M)	62.3
Relationship of informants to relatives		
Parent (%; i.e. informant is father or mother)	8.8	8.3
Uncle/aunt (%)	6.1	4.7
Sibling (%)	26.5	28.0
Child (%)	19.1	18.5
Nephew/niece (%)	16.2	14.8
Wife/husband (%)	2.8	2.8
Others (%)	20.6	23.0

Statistical analysis

Diagnostic agreement of informants was measured using Kappa values including 95% confidence intervals (CI). Kappa values indicate chance-corrected proportional agreement (Altman 1994).

To evaluate the role of factors which might influence diagnostic accuracy and thus affect reliability, stepwise logistical regression analyses (forward and backward) were performed on agreement vs disagreement between informants for the presence of a subject diagnosis (i.e. dementia or depression, respectively) as dependent variable (i.e. agreement: both informants indicated dementia or depression, respectively; disagreement: the first informant indicated dementia or depression, respectively, and the other indicated no diagnosis).

Independent variables were subject age, subject gender, living vs deceased subject, the relationship of informant to index subject of the family study (children, sibling, parent and spouses of index subjects, or the index subject; spouses were selected as reference

group), identical vs different familial relationship of informants to subject (i.e. both informants had identical familial relationship to the subject on whom they provided information, e.g. both were either children, siblings or, alternatively, the two informants had different relations, e.g. one informant was a child, the second a sibling, etc.; for familial relationship, see Table 2), age difference and gender difference of informants, presence of any psychiatric disorder in one of the two informant vs presence or absence of psychiatric diagnoses in both informants.

Both kinds of familial relationships were included in the statistical analysis: firstly the relationship of the informant to the index because the awareness for psychiatric symptoms might be influenced by the closeness of a relationship with a diseased index subject; secondly, the relationship of relative and informant because the closeness of this relationship might independently influence the knowledge on psychiatric disorders of the relative by the informant. However, due to the limited numbers of affected relatives, it was not possible to examine all combinations of different relationships of two informants to the subject on whom they provided information, thus limiting possible conclusions concerning the latter relationship.

A priori, the presence of interview-based diagnoses of dementia and depression were not included in the models because this would have led to a reduction of the analysis to those subjects currently alive. However, the interview-based diagnosis was introduced in a second model as independent variable to examine the consistency of the negative finding, i.e. that no informant or subject variable influenced the agreement of two informants on dementia in a relevant other (see below). This resulted in a significant influence of this variable on diagnostic agreement on dementia and thus supported the adequacy of calculations leading to the negative results (see below).

The forward and backward logistical regression analyses were performed stepwise using a change in log likelihood < 0.0001 as the criterion for the end of inclusion or exclusion of a variable in the model. Results for individual variables were reported as significant if the significance level of $p < 0.05$ was received in forward and backward logistical regression analysis. Interactions could not be evaluated due to limitations of sample size. For the same reason logistical regression analyses were not performed for anxiety disorders, alcoholism and other psychiatric disorders.

The study design was approved by the ethics committee of the Medical Board of Rheinland-Pfalz (Germany). Subjects gave informed consent that their data, including family history could be used in the study. All subjects were asked to inform their relatives of the study and additionally agreed to inform us of possible unwillingness of family members to allow their data to be included in this study. Family history information on two subjects was excluded because these subjects did not want any information on them used.

Results

Agreement of informants on dementia in family members

The degree of diagnostic agreement of two randomly selected informants on 1306 subjects as indicated by Kappa coefficient is described in Table 3. The interinformant reliability is acceptable for dementia (> 0.5), but less so for alcoholism, depression and anxiety disorders. Sensitivity and specificity of the informants in comparison with the other informant were given for descriptive purposes. Sensitivity, specificity and predictive values are ineffective indicators of test performance because no informants can provide the gold standard for comparisons.

Forward and backward stepwise logistical regression analysis revealed no significant predictor of agreement of informants for a diagnosis of dementia, except the presence of dementia as indicated by personal interview; i.e. subject age, subject gender, living vs deceased, familial relationship of subject to the index subject, difference in relationship of informant to relative, age difference between informants, gender difference of informants, presence of psychiatric disorder in one of both informants did not influence diagnostic agreement concerning a diagnosis of dementia (see Table 4). Forward and backward stepwise regression with the first model (i.e. without interview-based diagnosis as an additional independent variable) stopped after one step without inclusion of any variable, after ten iterations and exclusion of all variables, respectively. The calculations of the control model (i.e. inclusion of an interview-based dementia diagnosis) stopped after step 1, i.e. the inclusion of a dementia diagnosis as indicated by a personal interview. The variables age of subject, gender of subject, relationship of subject to index proband, living vs dead, age difference of informants, gender difference of informants, difference in familial relationship of relative to both informants, presence of psychiatric disorder in one informant vs in no (both) informants were not included in the model. Backward stepwise regression stopped after nine iterations after the exclusion

Table 3 Agreement of diagnostic information of the informant pairs provided by one of their respective relatives. Sensitivity and specificity of diagnosis for each informant refers to the psychiatric disorder identified by the other informant

Diagnostic subgroup	Sensitivity informant 1 (%)	Specificity informant 1 (%)	Sensitivity informant 2 (%)	Specificity informant 2 (%)	Kappa coefficient (95% CI)
Dementia	64.8 (46/71)	97.2 (1200/1235)	56.8 (46/81)	98.0 (1200/1225)	0.58 (0.48–0.68)
Depressive disorder	27.8 (15/54)	97.2 (1217/1252)	30.0 (15/50)	96.9 (1217/1256)	0.26 (0.14–0.38)
Anxiety disorders	15.4 (2/13)	99.6 (1288/1293)	28.6 (2/7)	99.2 (1288/1299)	0.19 (0.05–0.43)
Alcohol abuse and dependence	40.7 (11/27)	98.9 (1265/1279)	44.0 (11/25)	98.8 (1265/1281)	0.41 (0.23–0.59)
Other psychiatric disorders	34.2 (13/38)	98.2 (1245/1268)	36.1 (13/36)	98.0 (1245/1270)	0.33 (0.19–0.47)
Any psychiatric disorders	56.1 (97/173)	93.1 (1055/1133)	55.4 (97/175)	93.3 (1055/1131)	0.49 (0.42–0.56)

Table 4 Results of forward and backward stepwise logistical regression analysis. In the model predicting agreement of two informants on a diagnosis of dementia in another family member, other variables, except the presence of dementia indicated by personal interview, were not included or excluded, respectively. Agreement of two informants on depression in a family member was significantly better for younger relatives; siblings of an index subject of a family were worse informants than others. For non-significant variables see Methods

[a] This is the result of a post-hoc analysis in the sample of living subjects after having primarily found no subject or informant variable significantly affecting diagnostic agreement between two informants

Variable	Regression coefficient B	Standard error of B	χ^2 (Wald statistic)	*df*	*p*	Relative risk (exp B)
Agreement on dementia						
Presence of dementia in the subjects as indicated by interview[a]	1.54	0.489	9.94	1	0.0016	4.67
Agreement on depression						
Age of subject	–0.0815	0.0315	6.69	1	0.0097	0.92
Relationship of subject to index proband	–	–	7.75	4	0.10	–
Index subject vs spouse	1.25	0.822	2.29	1	0.12	3.47
Parent vs spouse	–0.130	0.756	0.030	1	0.86	0.88
Sibling vs spouse	–2.07	0.938	4.86	1	0.027	0.13
Child vs spouse	–0.455	0.566	0.64	1	0.41	0.63

of these variables, the variable presence of dementia diagnoses by interview being the one which remained relevant in the control model.

Agreement on depression in family members

Diagnostic agreement was significantly reduced when information from siblings of index subjects was compared with information from spouses of index subjects (siblings vs spouses: OR = 0.13, CI = 0.02–0.80), but not when information from spouses of index subjects was compared with those of parents or children of index subjects or of index subjects (see Table 4). The agreement for the diagnosis of depression of two informants was higher in younger subjects than in older subjects (relative risk for disagreement 1.08/additional year of age; CI = 1.02–1.15). No other of the above-mentioned factors was a significant predictor for diagnostic agreement of informants on depression in a relevant other. Forward regression had stopped after 4 iterations and the inclusion of age of subject and relationship of informant to the index subject. Backward stepwise regression analysis stopped after iteration 11 and the exclusion of irrelevant variables.

Discussion

Diagnostic agreement on dementia in relatives

The degree of diagnostic agreement on dementia based on information from two relatives was acceptable. As expected, the observed reliability as indicated by its Kappa value was higher than the validity (Heun et al. 1997). Most importantly, there was no relevant factor which influenced the diagnostic decisions of informants on the presence of dementia in the subject, except the presence of dementia supported by an interview examination. Thus, our results indicate that no group of relatives can be seen and consequently selected as best informants, i.e. all relatives seem to be equally good or bad informants concerning dementia. This is in agreement with our finding that validity of dementia by family history does not depend on any informant parameter (Heun et al. 1997). In agreement with these results, Jacomb et al. (1994) found that gender of informants, and relationship of informant to subject, did not influence validity of the family history for dementia. La Rue et al. (1993) observed that younger relatives reported more initial symptoms of dementia than spouses. However, this special issue had not be examined in the present study.

Diagnostic agreement on depression in relatives

The reliability of a diagnosis of depression based on family history information was low. This might indicate that not every family member is aware of symptoms of depression in other relatives. This is in agreement with our recent observation that the detection of depression in and by relatives increases with the number of informants (Heun et al. 1997). Thus, it is advisable that several informants, especially first-degree relatives, have to be asked on symptoms of depression on unavailable relatives in family studies.

The agreement on depression in subjects was low when information from sibling and spouses of index subjects was compared. In contrast, validity of this information was not significantly reduced in siblings in comparison with other relatives (Heun et al. 1997). This might indicate that siblings of index subjects provide different, but not necessarily less relevant, family history information in

comparison with other relatives (i.e. spouses, children and parents of index subjects). Various authors provided evidence in support of the view that siblings provide more accurate family history information on the patient's early life, whereas more accurate information on later life is obtained from spouses and children (Mendlewicz et al. 1975; Orvaschel et al. 1982; Thompson et al. 1982; Pickle et al. 1983). Therefore, we propose that family history information from siblings of index subjects is supplemented by information from other first-degree relatives (and vice versa).

The diagnostic agreement of informants on depression was lower in older than in younger relatives. However, validity of family history did not depend on the patients age according to our previous analysis (Heun et al. 1997). The most likely reason for this discrepancy might be that the sample was enlarged and information on elderly unavailable and deceased relatives was included in the present analysis. Our results additionally indicate that the reduced accuracy of family history information on older subjects is not related to the informants' age. Therefore, it seems most likely that depressive episodes in older and deceased subjects might have been forgotten by some informants, or that many episodes might not even be known to some of the present informants, or both. Due to the unavailability of more precise information, we cannot decide which possibility is more appropriate. There is no solution to the problem that surrogate information on depression in dead or otherwise unavailable relatives might be inaccurate. Consequently, researchers should at least be aware of the problem that the risk to miss a depression by family history is much higher for older, in comparison with younger, subjects.

In the present reliability analysis informant diagnoses did not influence agreement of informants on depression diagnosis in the subjects. In contrast, the validity of family history information was increased when the informant had a lifetime diagnosis of depression, but was reduced if the informant had any other psychiatric diagnosis (Heun et al. 1997). The failure to find an influence of informant psychiatric disorder on agreement of informants might be a limitation of statistical power in the present analysis since only 15 subjects were assumed to have a lifetime diagnosis of depression by both informants.

Diagnostic agreement on other psychiatric disorders in relatives

The reliability of anxiety disorders seems lower than that of other disorders, including alcohol-related disorders. This observation might be consistent with the findings of Thompson et al. (1982) who reported a low sensitivity of different groups of relatives to detect anxiety disorders in other relatives, but a moderate sensitivity of different groups of informants to detect and report alcohol-related disorders in others. It might be speculated that periodically acute disorders are less likely to be detected by relatives than chronic disorders. Alcoholism might additionally raise the awareness of other family members due to its social, psychopathological and medical consequences. However, due to the relatively small sample size of diseased subjects in these groups and of other subjects with further psychiatric disorders in the present study, confidence intervals of kappa values were high and partially overlapping, thus limiting further conclusions concerning these less frequent disorders.

General conclusions and limitations

A general limitation of all family studies seems to be the impossibility to receive very precise psychopathological and temporal information on all family members allowing completion of the DSM-III-R five-character diagnostic code. The fact that diagnoses based on information from different relatives are completely identical, and perfectly match with interview-derived diagnoses (see Heun et al. 1997), is the exception rather than the rule. Consequently, diagnoses in relatives have to be grouped for comparisons of relatives groups in family studies. If such surrogate diagnoses are not detailed enough or cannot be usefully combined in a family study, comparisons of frequencies of disorders have to be based on personal interviews. However, this approach is prone to a selection bias excluding deceased, uncooperative and unavailable relatives.

The observed reliability of family history information for dementia as indicated by Kappa values on dementia was higher than its validity observed in the same sample. The observation that the information on a possible diagnosis of dementia received from different informants is not influenced by other factors does not indicate that the diagnoses are valid. This simply indicates that these factors do not significantly influence the reliability. Thus, information provided from different family members on dementia in other relatives has acceptable reliability, even though the detection of dementia by relatives is not highly sensitive. However, the information provided by different informants is comparable, and there are no relatives which might be seen as more helpful than others for providing family history information on dementia.

In contrast, the information on depression in family members is different for different informants. Thus, it is useful to ask several informants for family history for depression on each individual subject. Information from siblings of index subjects seems to differ from that of other relatives and might be seen as useful complements. The agreement of informants on depression in older subjects is lower than in younger relatives. This might be the result of the low sensitivity of informant information on elderly and deceased subjects. Consequently, it is most important to get information from several informants on a possible history of depression in elderly and deceased relatives.

It might be argued that the present study cannot decide whether the observed low reliability of family history information is the result of the different abilities of various informants to provide diagnostic information on relevant

other, or alternatively, of technical shortcomings such as inadequate interviews or bad family history questionnaires. We suppose that the former is more likely: the main excuse given by many informants for inadequate information on some, but not all other relatives was the lack of previous or current regular personal contact; there was rarely any problem to understand or answer the questions.

Data analysis was based on 1306 subjects. Even in this large sample, the influence of all relevant factors which might affect the reliability of the family history information on different diagnoses cannot be assessed. This results from the fact that valuable data for statistical analysis can only be received if enough subjects and informants with specific features or combinations of these features were included in the sample. This gets increasingly less powerful if the influence of rare features, such as a history of depression in the informant, should be examined. Consequently, the influence of such factors on diagnostic agreement of informants can only be assessed in much larger samples.

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