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Is family history of depression a risk factor for poststroke depression? A meta - analysis

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Abstract

Objective—To determine whether family history of psychiatric disorder constitutes a risk factor for the development of poststroke depression.

Design—A meta-analysis setting: patients examined for depression following stroke seen in acute care, rehabilitation hospital or outpatient care settings.

Participants—All patients who were reported in the world's literature in English language publications in which information was provided about the existence or not of poststroke depression and the presence or absence of a family history of psychiatric disorder.

Measurements—The frequency of family history of psychiatric disorder was determined for each study as well as the relationship of family history to the presence of poststroke depression.

Results—Based on data obtained from 903 patients with stroke, the fixed model analysis found a risk ratio of 1.51 and the random model a risk ratio of 1.46 for the existence of poststroke depression if there is a positive family history of psychiatric disorder compared with a negative family history.

Conclusions—The existence of a positive family history of psychiatric disorder constitutes a risk factor for development of poststroke depression. The role of family history in poststroke depression, however, appears to be substantially lower than among elderly depressed patients without evidence of vascular disease.

Keywords

Poststroke depression; family history; risk factors

Introduction

For many years, empirical studies have shown that mood disorders are heritable (1). Although we have not yet found a specific genetic abnormality that would explain the existence of a large number of mood disorders, familial history of mood disorders is significantly associated with mood disorder even among twins and offspring raised outside the familial environments (2, 3).

A meta analysis of twin studies, for example, has estimated major depressive disorders (MDD) degree of heritability to be 0.33 (95% confidence interval, 0.26-0.39) (1). The rate of MDD in the relatives of probands with subthreshold depression (24.3%) was significantly lower than the relatives of probands with MDD (31.9%), but was significantly higher than the relatives

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of probands with no history of mood disorder (NMD; 20.2%).(2) The odds ratio for MDD in children of mothers with lifetime history of severe depressive disorder was between 5.2 and 13.9 (3) .

In contrast to this strong association of MDD with familial inheritance, late onset mood disorders have been more strongly associated with vascular disease manifested by left frontal or basal ganglia infarcts(4,5), silent cerebral infarction (6), and deep white matter hyperintensities on MRI scan than family history of mood disorder (7,8) , In fact, the vascular depression hypothesis (7,9) is based in part on the presence of a lower frequency of familial mental disorder than nonvascular depression (10). A comparison of 37 patients with vascular depression and 52 patients without vascular depression found the odds ratio of having a family history of mental illness among vascular compared to non-vascular depressions was 0.36 (95% CI 0.9-1.48) (7). Thus, the question of a lower family history of mood disorders in vascular depressions remains unproven and, furthermore, an analysis of family history of mood disorder among patients with overt stroke and depression (one of the clinical presentations of vascular depression) has never been conducted. We therefore undertook the present study to perform a meta-analysis of the literature comparing patients with and without poststroke depression for the frequency of family history of mental disorder.

Methods

A search was performed using search terms of poststroke depression, stroke and depression, poststroke depression and family history in data bases from MEDLINE, PubMed and the Cochrane Library. More than 130 articles were retrieved regarding poststroke depression. They were reviewed using the following criteria: the study examined only poststroke depression; structured interviews were used (e.g. Structured Clinical Interview for DSMIV diagnosis [SCID]) to elicit diagnostic criteria for major (DSM-III and DSM-IV defined) and minor depression (i.e. DSM-III and DSM-III R for dysthymic disorder without 2 year duration criteria or DSM-IV minor depression, research criteria), and the study examined the relationship between poststroke depression and clinical correlates or risk factors such as family history of psychiatric disorders. Of the 130 articles, 22 were focused on risk factors. Of these 22 studies, only 6 examined the relationship between the poststroke mood disorders and family history of psychiatric disorder. These 6 studies contained data which allowed us to identify 4 types of patients: 1) depressed with positive family history of psychiatric disorder, 2) non-depressed with positive family history, 3) depressed, without family history, 4) non-depressed, without family history.

Statistic analysis

The data was analyzed using Comprehensive Meta-analysis Software. This software has been analyzed and shown to have good accuracy and usability in a recent publication.(11) Random and fixed models were applied. Heterogeneity was evaluated based on I^2 measure defined as $I^2 = 100 (Q-df)/Q$, where Q is Cochran's heterogeneity statistic and df is the degrees of freedom (12). Negative values of I^2 are recorded as zero, so that I^2 lies between 0% and 100%. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity. A comparative search of 509 meta-analyses in the Cochrane Database of Systematic Reviews showed that average heterogeneity was approximately $I^2 = 30\%$, with no heterogeneity found ($I^2 = 0\%$) among 250 of these meta-analyses (12).

Results

The 6 studies used in this analysis are shown in Table 1. The 92 Iowa stroke patients were in-patients or community patients who agreed to participate in a randomized treatment study

within 6 months of acute stroke and provided data on family history of psychiatric disorder. The 291 Baltimore patients were examined during their hospitalization following acute stroke (the vast majority of whom were examined within 1 month following stroke) and are comprised of patients from several different studies who provided data on family history (13,14). These 291 acute stroke patients, however, were combined in a single manuscript examining poststroke anxiety disorder (13). The Morris et al. study (15) was based on a consecutive series of patients given a structured mental status examination and treated in a rehabilitation hospital following an acute stroke. The Hsieh et al. study (16) included 207 outpatients who were examined approximately 14 months following stroke. The 165 patients in the Leentjens et al. study (17) were examined in-hospital at approximately 1 month following stroke with follow-up over 1 year. The Storor and Byrne study (18) included 61 patients hospitalized for acute stroke and examined within 15 days following cerebral infarction. Thus, there were a total of 903 patients examined at inpatient hospitals, rehabilitation hospitals, outpatient clinics and community settings.

The numbers of patients with and without positive family histories in each study are shown in Table 2 with odds ratios of having a depression if you have a positive family history of psychiatric disorder. The results of the meta analysis are shown in Figure 1. Using the fixed model, the risk ratio was 1.51 (95% CI=1.22-1.87, Z=3.81, p<.001). The findings are graphically displayed on the right hand side of the tables. The random model, however, also gave essentially the same finding with a risk ratio of 1.46 (95% CI=1.11-1.92). The heterogeneity I^2 was 34.5%, (Cochran's Q=7.63, df=5, p<0.18). Thus, the heterogeneity was about average for all meta analytical studies and the p value for heterogeneity was not significant.

The pooled data from the present study showed that 60 of 310 patients (19.4%) with poststroke depression had a positive family history. This was compared with data from Krishnan et al. (7) who reported that 37 of 52 elderly patients (71.2%) with nonvascular depression had a positive family history of psychiatric disorder. ($\chi^2=58.3$, df=1, p<0.0001).

Discussion

This study using a meta analysis including 903 patients with stroke, found that patients with a positive family history of psychiatric disorder were about 1.5 times more likely to have a poststroke depression than similar patients without a positive family history. Only one study failed to find a higher rate of depression among patients with a positive family history. Thus, among patients with poststroke depression, family history of psychiatric disorder is significantly associated with the frequency of depression.

Before discussing these findings, it is important to acknowledge the limitations of this study. The main limitation was the relatively small number of studies included in the analysis. Although 903 patients were included, the majority of studies which have examined depression following stroke did not assess the role of family history. Secondly, it is likely that there was great inconsistency in the methods used to assess family history—structured family history interviews were probably not done (the method used to obtain a family history was not specified) and none of the studies identified the nature of the familial mental disorder. A third limitation is that these were cross sectional assessments and some patients had depressions in the acute stroke period while others were many months post stroke. Thus, there may, for example, have been a stronger association with late onset compared with early onset depressions. Finally, we know that some of these patients had a previous personal history of mood disorder, which probably overlapped with a positive family history of psychiatric disorder. Thus, we do not know whether prior personal history or family history played a stronger role in the development of depression.

Given these limitations, how might these findings be construed? The implication of these findings is clearly that a positive family history of psychiatric disorder increases the risk of development of poststroke depression. Although we and others have shown that lesion location, particularly left frontal, left basal ganglia (19) and proximity of the lesion to the frontal pole (20) are associated with depression during the first several months following stroke, there are numerous other factors such as severity of impairment in activities of daily living (21-23), limitations in social support (24), previous personality (15) that have also been associated with increased risk of developing poststroke depression. Furthermore, we have previously reported that among patients with poststroke mania, there was a strong association with family history of mood disorder (25). Thus, it is not surprising that family history represents a risk factor for depression even among patients with stroke related depression.

Perhaps the most relevant question, however, is whether family history plays less of a role in poststroke depression compared to depression among elderly patients without vascular disease. Our results showed that the frequency of positive family history among stroke patients was significantly lower than the frequency reported among elderly depressives without vascular disease. Furthermore, the frequency of positive family history among patients without poststroke depression in our meta analysis was 79 of 594 (13.3%) which is similar or lower than the Lewinsohn et al. (2) report of 20.2% positive family history among probands with no history of mood disorder.

In summary, this study has shown for the first time that, using meta analysis, family history of psychiatric disorder does appear to be a risk factor for depression after stroke. The findings, however, are consistent with the vascular depression hypothesis that family history is less frequently associated with vascular, compared with nonvascular, depression in the elderly. Our meta analysis indicated that patients with a family history of psychiatric disorder were one and a half times more likely to develop a poststroke depression than patients without a family history of psychiatric disorders. It is not surprising that a genetic vulnerability might confer some increased risk of depression after an ischemic brain lesion. Further research will need to directly examine the relationship between depression and family history of specific psychiatric disorders in patients with cerebral ischemia compared with patients without cerebral ischemia.

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Figure 1.
Meta-analysis

Table 1

Studies included in the meta analysis

Study	Number of patients included	Diagnostic criteria and severity rating scales	Where study was conducted
Iowa treatment study patients	92	DSM -IV - HDRS	Outpatient and acute hospital
Baltimore stroke study patients	291	DSM - IV - HDRS	Inpatient and Outpatient
Morris, et al. (26)	88	DSM - III R	Rehabilitation unit
Hsieh, et al. (16)	207	HDRS > 10	Outpatient
Leentjens, et al.(17)	165	DSM - IV, SCID -D	Inpatient
Storor.,Byrne (18)	60	DSM - IV, CIDI	Inpatient

Table 2
Number of patients with and without family history of psychiatric disorder

Study/Patient group	FH/Depressed	FH/Non depressed	NoFH/Depressed	No FH/Non depressed	Odds ratio	95% confidence interval
Iowa stroke treatment	9	8	30	46	1.725	0.599-4.967
Baltimore stroke studies	9	18	95	169	0.889	0.384-2.058
Morris et al. (26)	16	20	18	34	1.511	0.632-3.610
Hsieh et al. (16)	10	4	61	132	5.410	1.632-17.936
Leentjens et al. (17)	14	16	41	94	2.006	0.896-4.490
Storor/Byrne(18)	2	13	5	40	1.231	0.231-7.119