

TOWARDS A VULNERABILITY MODEL FOR MAJOR DEPRESSIVE EPISODES

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SUMMARY

Background: While many studies have investigated depression risk factors, few attempts have been made to weight, and compare them. Therefore, we conducted a prospective comparison of a sample of subjects suffering from major depressive disorder and a group of healthy subjects. We compared classic risk factors with internal elements such as personality, family dynamics and health locus of control. We also looked for prognostic factors.

Methods: Forty people with major depressive disorder (the MDD group) were randomly assigned to different treatment groups and followed for two years. In parallel, we followed a group of 21 healthy subjects (healthy group). At the beginning of the study, sociodemographic data were recorded and all subjects were asked to complete the Multidimensional Health Locus of Control (MHLC) scale, the NEO Five-Factor Inventory (NEO-FFI), and the Family Adaptation and Cohesion Scale (FACES III). During the study, subjects were regularly assessed using the Hamilton Depression Scale (HDS) and the Short Form Health Survey (SF-12).

Results: Of the 23 explanatory variables, 13 were statistically different ($p \leq 0.05$): age, gender, number of people living together, income, extravert personality and neuroticism, Internal HLC, Powerful others HLC, Adaptability of the current couple and the family of origin, and Cohesion of the ideal and nuclear family and family of origin. The accumulation of risk factors doubles the chances of suffering from MDD (odds ratio 1.905*). Independent of treatment, among the 13 variables, the first nine explain 34.1% of change in depression measured on the HDS scale ($p < 0.001$).

Conclusion: While the size of our sample limits the robustness of our results, our study suggests that some risk factors are also prognostic. The respective weights of these factors vary as a function of age group. Finally, some, such as health locus of control, family dynamics or extraversion, can be modified as an adjunct to pharmacological treatment.

Key words: risk factors - depression - prognosis

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INTRODUCTION

Although the stress vulnerability model for depression is not new (Holmes & Rahe 1967, Krantz et al. 1985, Masuda & Holmes 1967) we still lack a synthetic model that can predict either the risk or the evolutionary factors of depression. The model is incomplete, notably because in recent years it has become apparent that the identified risk factors vary in some subpopulations. The most recent studies focus on adolescents (Mohammadi et al. 2019), postpartum women (Monteiro et al. 2018), middle-aged patients (Stegenga et al. 2012), women (Accortt et al. 2008), migrants (Giacco et al. 2018), and urban versus rural areas (Crowell et al. 1986).

At present, no model has integrated these variations in risk factors into a dynamic model that modulates overall risk, although Stegenga et al. (2012) is clearly the most advanced in this respect, as the authors seek to weigh various risk factors as a function of age. Similarly, Kendler and Gardner (2016) show how genetic vulnerability to depression and stress factors have a decreasing influence on a succession of depressive episodes.

Here, we are interested in the weightings between more internal factors that have been little explored to date, such as the health locus of control (Wallston et al. 1987), personality traits, and external factors such as family dynamics (Olson 1986). Our earlier work (Zdanowicz et al. 2006) showed that among adolescents,

family cohesion and adaptability together with internality (Internal Health Locus of Control) protected against depression. Conversely, a high level of belief in chance (Chance Health Locus of Control) was associated with a higher risk of major depressive disorder (MDD). We found similar results by comparing adult inpatients suffering from MDD admitted via the consultation department or the emergency room (Zdanowicz et al. 2017).

In this prospective study, we investigate not only whether these dimensions may represent more global risk factors, but also whether they predict long-term trends. Two groups of subjects, one suffering from MDD (the MDD group) and the other in good health (the healthy group, HG), were followed for two years. HG results were published in 2012 (Zdanowicz et al. 2012). The MDD group was treated, and in this study we isolate the dimensions assessed independently of treatment subgroups. The results for treatment subgroups were published earlier in Zdanowicz et al. (2017).

SUBJECTS AND METHODS

Subjects

We carried out a randomized, open-label study from 1 June 2012 on the first 40 inpatients meeting inclusion criteria. Patients were followed up for two years. Inclusion criteria for the MDD group were as follows:

- The patient must meet DSM-IV-R criteria for a major depressive episode;
- It must be the patient's first or second depressive episode;
- No symptoms of depression during the preceding two years;
- No history of other psychiatric disorders on Axis I of the DSM-IV-R;
- No history of gastritis, or gastric or oesophageal ulcers;
- Aged between 18 and 63 years;
- At the beginning of the study the patient must be free of any other medical condition.

Patients taking depressogenic drugs (e.g. beta blockers, morphine derivatives) were excluded, and no formal psychotherapy took place during the study.

Volunteer screening was conducted, and written consent was validated by the local ethics committee (under agreement number B03920072846). In total, 40 patients completed the study.

In parallel, we formed a second group of 'healthy' subjects. Twenty Caucasians were selected at random from the telephone directory and enlisted following written agreement and signed consent. Subjects who had been diagnosed with any psychiatric disorder on Axis I of the DSM IV or who suffered from any physical pathology (unless it was chronic and stable) were excluded.

Methods

No further medication was administered to patients in the MDD group who were in remission (disappearance of all of diagnostic criteria for a major depressive episode) at six months, but follow-up continued until the end of the study. For patients who left, the last score obtained was recorded for the remaining assessments (Last Observation Carried Forward method). The protocol outlined below was applied to all members of both groups: At time 0, the following assessments were carried out:

- The Mini-International Neuropsychiatric Interview: to exclude any past or present psychiatric pathology.
- Sociodemographic data: age; gender; number of people in the household; and socioeconomic status, evaluated by approximate net income per month (€; < 1000, 1000–2000, 2000–3000, 3000–4000, > 4000).
- The Family Adaptation and Cohesion Scale FACES III (Olson 1986): to investigate family dynamics. This model evaluates two dimensions of the functioning of a relational system: cohesion and adaptability. Cohesion is defined as "the emotional ties that every member develops with regard to the others". Adaptability is "the ability of the system to change its power structure, its roles and rules in response to stressful situations".

- Wallston's MHLC scale (Multidimensional Health Locus of Control) (Wallston et al. 1987). This model explores how people relate to their own health. While certain individuals think they can act to avoid or fight disease (an internal health locus of control), others attribute the causes of their health to destiny, or the influence of 'others' (members of the family or health professionals). The MHLC distinguishes three sub-scales: *Internality* (IHLC, Internal Health Locus of Control), *Powerful Others* (PHLC, Powerful Others Health Locus of Control), and *Chance* (CHLC, Chance Health Locus of Control).
- Personality was measured according to the NEO-FFI typology (Costa 1992). This instrument explores five dimensions of personality: neuroticism, extraversion, openness, agreeableness and conscientiousness. Neuroticism refers to emotional stability and adaptability. The more present this dimension, the more the subject feels negative affect such as fear, sadness, anger, guilt, disgust and embarrassment. Extraverts are sociable, although gregariousness is only one facet of extraversion. Extravert people prefer large groups, are active, energetic, verbose and optimistic. Open people are curious about everything that originates in their internal and external universe, and their life is rich in experiences. They typically conceive new ideas, adopt unconventional values, and experience intense positive and negative emotions. Individuals who have low scores on the openness dimension tend to be conservative and conventional in their opinions and behaviours. People who score high on agreeableness are altruistic, likable, helpful, and think they are likely to get help in return. Conversely, people who score low are egocentric, suspicious of others' intentions, and are more likely to compete than cooperate. Conscientiousness refers to the capacity to manage one's desires. This capacity for self-control supports active planning, organizing and carrying out tasks. A positive score is associated with academic and professional success. A negative score is correlated with exaggerated and painful requirements, a compulsive need for order and cleanliness, and work overload.

Patients were assessed with the 17-item Hamilton Depression Scale (HDS) at 0, 0.5, 1, 1.5, 2, 3, 6, 12, 18 and 24 months. Physical health (physical functioning, physical daily life functioning, physical pain and general health), and mental health (vitality, social functioning, daily mental life functioning and mental health) were evaluated with the Short Form Healthy Survey (SF-12) (Ware et al. 1996) and were recorded at 0, 6, 12, 18 and 24 months.

A parametric statistical analysis was carried out using SPSS 25, taking Type 1 and 2 errors into account. No post hoc tests were carried out. A Pearson correlation analysis was run to identify potential covariates. When necessary, linear or logistic regressions

were run. Qualitative variables were compared with the Chi-squared test, and means were compared using Student's *t*-test. Significance levels were set at $p > 0.95$ and $p < 0.05$.

RESULTS

Inter-group comparisons of explanatory variables

A total of 23 explanatory variables were divided into four domains: sociodemographic variables (age, gender, number of people living with the subject, income), personality (extravert, neurotic, open, agreeable, conscientious), MHLC variables (IHLC, CHLC, PHLC, Internality/Externality HLC ratio), FACES III variables

Table 1. Inter-group significant differences

Variable	Average MDD/Healthy	t (or χ^2)
Sociodemographic		
Gender ratio ♀/♂	4.7/1.3	10.09**(χ^2)
Age (years)	40.33/29.17	2.87**
No. living together	2.73/4.05	3.209**
Income	1800/2500	3.094**
Personality		
Neuroticism	44.88/32.90	5.219***
Extraversion	35.63/42.38	4.087***
MHLC		
IHLC	19.8/23.71	3.444**
PHLC	22.78/19.14	2.093*
FACES III		
Family of Origin Cohesion	28.55/35.33	2.889**
Family of Origin Adaptability	21.08/25.62	3.238**
Ideal Family Cohesion	39.85/42	2.249**
Nuclear Family Cohesion	32.19/39.29	2.005*
Current Couple Cohesion	18.38/32.64	3.225**
Adaptability		

* $p = 0.05-0.001$, ** $p = 0.01-0.000$, *** $p < 0.000$

(Cohesion and Adaptability of: the family of origin; the nuclear family; the ideal family; the current couple and the ideal couple). Table 1 lists the 13 variables for which a significant difference was found between the two groups.

Inter-group risk explanatory variables

Table 2 shows odds ratios for these risk factors. It should be noted that apart from family factors (with the exception of Adaptability of the current couple) all classes of variables are associated with statistical risk. Neuroticism is the highest risk factor associated with the MDD group and, conversely, income is the most protective factor.

Table 2. Odds ratio of explanatory variables

	B	S.E.	Sig.	OR
Sociodemographic				
Age	0.068	0.027	0.013	1.071
Gender	-2.125	0.809	0.009	0.119
No. living together	-0.368	0.249	0.139	0.692
Income	-0.932	0.483	0.05	0.394
Personality				
Neuroticism	0.184	0.055	0.001	1.202
Extraversion	-0.290	0.104	0.005	0.748
MHLC				
IHLC	-0.292	0.091	0.001	0.747
PHLC	0.145	0.069	0.036	1.156
FACES III				
Family of Origin Cohesion	0.001	0.064	0.983	1.001
Family of Origin Adaptability	-0.065	0.095	0.494	0.937
Ideal Family Cohesion	0.039	0.120	0.744	1.040
Nuclear Family Cohesion	-0.199	0.109	0.069	0.820
Current Couple Cohesion	-0.131	0.059	0.028	0.878
Adaptability				

Table 3. Change in HDS scores as a function of explanatory variables

	HDS score		Physical Health		Mental Health	
	dt	r	dt	r	dt	r
Sociodemographic						
Age			24	-0.331***		
Gender	24	-0.281	24	0.305*		
No. living together	24	-0.411**	24	0.281*	24	0.334**
Income	24	0.269*	24	0.38**		
Personality						
Neuroticism	12	0.262*	24	-0.253*	18	-0.259*
Extraversion	24	-0.426**	24	0.289*	24	0.305*
MHLC						
IHLC	24	-0.374**	24	0.414**		
PHLC					24	-0.287*
FACES III						
Current Couple Adaptability			24	0.390		

* $p = 0.05-0.001$, ** $p = 0.01-0.000$, *** $p < 0.000$; dt: maximum number of months where a correlation was found

A logistic regression based on risk increasing factors (age, neuroticism, PHLC) gives a multiplicative factor of 1.905 ($p=0.017$).

The evolution of the coefficients of significance as a function of age group show that extraversion is most significant in the 10–20 age range, neuroticism and adaptability in the family of origin are highest in the 41–50 age range, and income is highest in the 51–60 age range.

Change in HDS scores as a function of explanatory variables

As shown in Table 3, of the 13 variables that discriminate between the two groups, nine influence the long-term prognosis of at least one dependent variable (level of depression, physical or mental health).

A linear regression of the HDS score for gender, number of persons living together and income gives a predicted variance of 20.1%** (adjusted R^2). A linear regression for physical health, also including age, explains 27.7%*** (adjusted R^2) of the variance.

A linear regression for personality gives a predicted variance of 16.8%** (adjusted R^2) for the HDS score, 8.9%** for physical health, and 9%** for mental health. Taking into account all dimensions (sociodemographic, personality, MHLC and FACES III), a linear regression explains 34.1% of the evolution of scores on the HDS scale ($p<0.001$), 26.2% of physical health ($p<0.001$), and 16.5% of mental health ($p<0.001$).

In addition to the 10 variables that were not statistically different between the two groups, two (Chance HLC and the Internality/Externality HLC ratio) were found to have a long-term influence on HDS scores in the MDD group at two years (CHLC $r=0.440$ **; I/E $r=0.403$ **).

DISCUSSION

Although the number of participants in our study is clearly a limiting factor, cumulative risk factors can double the risk of MDD. Like Stegenga and Kendler (cfr supra), our study finds that the respective weights of risk factors change as a function of age. This allows us to draw a composite portrait of the person at risk. The subject is a woman in her forties with an average income and a neurotic personality. She relies heavily on others to be in a good health condition. Her couple tends to be rigid. Conversely, the most protected person is a man under forty years of age with a higher than average income. He is extraverted, relying above all on himself to manage his health. He lives in a couple with organizational flexibility.

The prognosis of the depressive episode is a function of family size, gender and income. The ability to express feelings rather than sink into neuroticism, and the couple's ability to adapt to stress are other determining factors.

Finally, the finding that is most important for clinicians relates to the observation that in all these factors, there are dimensions that can be modified and used as levers to reduce risk and improve the prognosis: the couple's dynamics, health locus of control and the ability to express emotions.

CONCLUSION

While the size of our sample limits the robustness of our results, our study suggests that certain risk factors are also prognostic factors. The respective weights of these factors vary as a function of age group. Finally, some, such as MHLC, family dynamics or the ability to express emotions are modifiable as an adjunct to pharmacological treatment.

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Contribution of individual authors:

All authors made a substantial contribution to the design, and/ or acquisition, and/or analysis and interpretation of data.

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