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Research paper

The interplay between diabetes, depression and affective temperaments: A structural equation model

Martino Belvederi Murri[a,b,*], Sara Mamberto[c], Lucia Briatore[d], Chiara Mazzucchelli[e], Mario Amore[a], Renzo Cordera[c]

[a] Section of Psychiatry, Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Italy
[b] Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[c] Department of Internal Medicine, University of Genova, Genova, Italy
[d] Internal Medicine Unit, Pietra Ligure Hospital, ASL 2 Savonese, Italy
[e] Diabetes Unit, Ospedale Imperia, ASL 1 Imperiese, Italy

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ABSTRACT

Background: Diabetes and depression are reciprocally linked, but few studies modeled their interplay considering the influence of affective temperaments (AT) and demographic factors.
Methods: Participants with type 1 and type 2 diabetes (T1DM and T2DM, n = 279) recruited from Diabetes Units were assessed with the Beck Depression Inventory (BDI), Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire version (TEMPS-A), Morisky Medication Adherence Scale (MMAS), Diabetes Distress Scale (DDS) and Cumulative Illness Rating Scales (CIRS). Glycosylated hemoglobin levels (HBA1C) was used as index of glycemic control. The bi-directional association between glycemic control, depression and candidate mediators was examined with Structural Equation Modeling, testing the impact of moderator variables (AT, diabetes type, age and gender) with multigroup comparison.
Results: The association between HBA1C and depressive symptoms was mediated by diabetes-related distress,, while there was no definite evidence of depression influencing HBA1C through changes of adherence, tiredness, appetite, alcohol intake or smoking. Among individuals with AT, distress was unrelated to HBA1C and had a higher impact on depression; adherence was inversely association with HBA1C. Moreover, physical comorbidities impacted on depression. While diabetes type had a moderation role, age and gender did not affect the model.
Limitations: Cross sectional design, lack of objective measures of diet and physical activity.
Conclusions: Glycemic control seem to influence the severity of depressive symptoms, but the reciprocal association seems non-significant. AT and diabetes type may shape this relationship influencing distress and adherence to medications. Findings may aid interventions aimed at improving patients' care and quality of life.

1. Introduction

Diabetes and depression seem reciprocally linked, but few studies have attempted to model their interplay considering factors related to personality (Gois et al., 2011).

Several studies suggest that individuals with diabetes have an increased risk to develop depression, compared with non-diabetic controls (Buchberger et al., 2016; Nouwen et al., 2010). Diabetes may increase the risk for depression because of illness-related distress, psychological reactions to complications and adaptation to complex medication regimens, and also through neurobiological changes (Bartoli et al., 2016). Whereas, depression may increase the risk to develop type 2 diabetes (Knol et al., 2006), worsen glycemic control (Buchberger et al., 2016) and ultimately increase diabetes-related mortality (van Dooren et al., 2013). This, again, may depend both on lifestyle modifications (e.g. unhealthy behaviors, unbalanced diet and physical inactivity) (Chiu et al., 2010; Zhang et al., 2015) or through dysregulation of neuro-immuno-endocrine systems (Alexopoulos et al., 2011; Belvederi Murri et al., 2014).

Recent studies, however, have cast doubts on the specificity and on the magnitude of the association between depression and diabetes: first, the link between these disorders could be less relevant than previously

* Correspondence to: Section of Psychiatry, Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Largo Rosanna Benzi, 10, Genova 16132, Italy.
E-mail address: martino.belvederi@gmail.com (M. Belvederi Murri).

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estimated (Hasan et al., 2013). Second, a bi-directional *causal* role for these conditions seems not supported by robust findings (Tabak et al., 2014). In particular, the finding of a direct correlation between measures of depression and glycemic control has not been consistently replicated, and might be confounded by several extrinsic factors (Tabak et al., 2014).

The co-occurrence of diabetes and depression seems mainly related to environmental, rather than genetic factors, and individual, rather than familial risk (Mezuk et al., 2015). This calls into question whether individual psychological characteristics such as personality could have an important moderating role on the association between diabetes and depression. Personality, in fact, can impact on lifestyle choices, self-care, treatment adherence and other factors that could in turn influence glycemic control (van Dooren et al., 2016). In addition, personality or temperamental variability determine individual stress reactivity and psychological adjustment to diabetes, which may lead to the onset of depressive symptoms (Gois et al., 2012a, 2012b). Previous studies on this topic indeed found that individuals with T2DM and depressive and anxious temperaments adjusted differently to diabetes, had worse self-management and metabolic control than subjects without a predominant affective temperament (Gois et al., 2011; Hall et al., 2009; Shamsi et al., 2014). However, it would be important to examine how the presence of affective temperaments *shapes* the complex association between diabetes and depression with models that take in account potential bi-directional effects.

Thus, the aims of this study were: (1) to examine the link between depressive symptoms and glycemic control by testing the theoretical model of a bi-directional association; (2) to examine the role of putative mediators of such association (i.e. adherence to medications, cigarette use, alcohol use, appetite changes and tiredness); (3) to examine the role of affective temperaments, age, gender and diabetes type as potential moderators. Our hypotheses were that the pathway from glycemic control to depression would be mediated by diabetes-related distress, while the pathway from depression to glycemic control would be mediated by non-compliance with diabetes medications, changes in appetite/energy and unhealthy behaviors (i.e. smoking cigarettes and drinking alcohol) (Eliasson, 2003; Pietraszek et al., 2010). Second, we hypothesized that affective temperaments, diabetes type, age and gender would affect the relationship between variables in the model (putative moderators).

2. Methods

2.1. Participants

Participants were recruited among consecutive attenders to three outpatient Diabetes Units (University Hospital of S. Martino of Genova, Ospedale Santa Corona, Pietra Ligure, ASL 2 Savonese and Ospedale Imperia, ASL 1 Imperiese) in the index month of November 2015. Patients were proposed participation in the study while in the waiting room before being seen by a diabetologist for their routine diabetes care. A researcher (S.M.) aided the physician in the interviews; potential doubts on clinical information were solved by discussion and obtaining information from the clinical chart. Patients with difficulties filling out questionnaires were assisted to minimize selection bias. Inclusion criteria were broad: older than 18; suffering from either type 1 or type 2 diabetes (T1DM, T2DM), diagnosed by a diabetologist; fluency in the Italian language. Patients with gestational diabetes, diabetes induced by steroids and severe cognitive problems were excluded from the study.

Of 407 patients who were approached, 279 accepted to take part in the study (response rate 68.6%).

Included subjects had no missing data. Patients provided informed consent and the study was approved by the local Ethics Committees.

2.2. Assessments

We collected data on sociodemographic characteristics (age, gender, civil status, education, and occupation), alcohol consumption and smoking habits (number of cigarettes per day), diabetes history (duration, insulin therapy, chronic complications, glycemic control as HbA1c), number of concomitant medication, BMI (body mass index — kg/m^2), sitting at rest blood pressure, previous episodes of depression, treatment with antidepressant drugs and familiar history of depression.

We collected information with different instruments. Depressive symptoms were assessed with the validated Italian version of the 21 item Beck Depression Inventory (BDI), which rates the severity of each symptom on a scale from 0 to 4, with higher scores indicating higher severity (Beck et al., 1996). Item 20, related to tiredness and item 18, related to appetite changes were analyzed separately as possible mediators.

Temperament was evaluated with the Memphis, Pisa, Paris and San Diego- Autoquestionnaire (TEMPS-A), in the short 39 item version, validated against the longer version (Akiskal et al., 2005) and validated in the Italian language (Preti et al., 2013). Temperaments scores (depressive, anxious, cyclothymic, irritable and hyperthymic) were transformed into categorical variables with a cut-off point corresponding to 1 z-score, the minimal value for beginning the excessive temperament. Compliance to diabetes medications was assessed with the Italian version of the four-item version of the Morisky Medication Adherence Scale (MMAS) (Morisky et al., 1986). The scale is based on four yes/no questions, and showed good concordance with objective measures of adherence (Shi et al., 2010). Of note, higher scores indicate lower levels of adherence. Diabetes-related distress was assessed with the Italian version of the 17 item Diabetes Distress Scale DDS (Polonsky et al., 2005). Cronbach alpha values in our sample were high for the BDI (0.92), the TEMPS (0.83) and the DDS (0.91), but lower for the MMAS (0.34). Physical comorbidities were rated by the clinician using the Cumulative Illness Rating Scale CIRS (Miller et al., 1992). Glycemic control was assessed by routine measurement of glycosylated hemoglobin (HBA1C) levels. The assay was based on ion- exchange high-performance liquid chromatography method (Tosoh HLC-723G7HbA1c Variant Mode). Reference values for the normal range are 4.9–6.2%.

2.3. Statistical analysis

To examine the relationship between diabetes, depression and other factors we used a Structural Equation Modeling (SEM) approach. SEM is a powerful analytical technique allowing to test complex, theoretical models using clinical data. Briefly, in a SEM model, it is possible to depict multiple causal pathways between measured or latent factors, and to estimate their relative effect towards one or more outcome variables. Moreover, it is possible to estimate if one or more factors may act as mediators of such putative causal associations/chains. In addition, SEM allows to assess if other variables that are not implicated in a model (moderators) can influence the magnitude or direction of the associations between each factor in the model. The validity of each hypothesized models is tested by examining how well it fits real-world data: specific indices express such degree of fitness and allow cross-model comparison (Chiu et al., 2010). Although SEM analysis of cross-sectional data cannot directly establish causation, it provides important cues to causal relationships (Bullock et al., 1994).

We first tested a SEM model built on pre-specified theoretical assumptions. Subsequently we planned to re-specify the model by trimming nonsignificant associations and re-evaluating its fitness. To test how well the models fitted the observed data we used the χ^2 test, where a *nonsignificant* p value ($p > 0.05$) represents an adequate model fit. As other measures of model fitness we used the Root Means Square Error of Approximation (RMSEA), the Comparative Fit Index (CFI), and the Tucker-Lewis Index (TLI). A RMSEA value less than 0.05 and CFI and TLI values more than 0.95 indicate an acceptable model fit (Hu et al., 1999).