Journal of Psychosomatic Research 71 (2011) 256–263

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

Genetic influences on alexithymia and their relationship with depressive symptoms

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ARTICLE INFO

Article history:
Received 17 June 2010
Received in revised form 2 February 2011
Accepted 15 February 2011

Keywords:
Alexithymia
Depression
Twins
Behavioral genetics

ABSTRACT

Objective: The factors involved in the etiology of alexithymia are still unclear. While a few studies suggested substantial genetic influences on alexithymia, it remains to be determined if these influences are independent of genetic influences on other mental health variables correlated with alexithymia, such as depression. This study is aimed at confirming previous findings of a genetic contribution to alexithymia, examining whether there are genetic or environmental influences common to alexithymia facets, and investigating whether genetic influences on alexithymia are independent of genetic influences on depression.
Methods: The 20-item Toronto Alexithymia Scale and a validated measure of depression were administered to a sample of 729 twins (45% males) aged 23–24 years drawn from the population-based Italian Twin Register. Genetic structural equation modeling was performed with the Mx program.
Results: Genetic factors accounted for 42% of individual differences in alexithymia. Unshared environmental factors explained the remaining proportion of variance. There was a substantial (0.65) genetic correlation between alexithymia and depression. The inclusion of depression as a covariate in the genetic models reduced the heritability estimate for alexithymia to 33%.
Conclusions: Despite some limitations, this study corroborates the notion that genetic factors contribute substantially to individual differences in alexithymia, with unshared environmental factors also playing an important role. Also, it suggests a genetic link between alexithymia and depression.

Introduction

The term 'alexithymia' (from the Greek *a* = lack, *lexis* = words and *thymos* = emotion, mood) was introduced in the early seventies to describe some cognitive and affective characteristics that were often observed among patients with so-called psychosomatic disorders [1,2]. The alexithymia construct, which has gradually taken on a key role within psychosomatic medicine, encompasses limited ability to identify and verbally express emotions, to distinguish emotions from bodily sensations, impoverished fantasy life, and reduced symbolic thinking with a concrete, stimulus-bound, action-oriented thinking style similar to the 'pensée opératoire' [3].

While considerable research has been devoted to the association between alexithymia and physical and mental health problems and its possible causal implications, only relatively few studies have attempted to identify which factors are involved in the etiology of alexithymia. Most of these studies pointed to a role of childhood family factors [4–11]. Although such factors seem to be entirely environmental in nature, in recent years behavioral genetic studies revealed that the exposure to many features of the family environment is at least partly under genetic influence [12,13].

There are several mechanisms that may account for the contribution of genetic factors to individual differences in alexithymic characteristics. The genes potentially involved in variation in alexithymia may influence the transcription of neuronal receptors or neurotransmitters, or may affect neurodevelopment. Genetic factors significantly contribute to variation in brain structures [14,15], and a recent study reported an association between alexithymia and the catechol O-methyltransferase Val108/158Met gene polymorphism [16]. Some family studies found a significant association of mothers' [17–19] and fathers' [19] alexithymia scores with alexithymia scores in the offspring. While these studies suggest an intergenerational transmission of alexithymia, they cannot establish whether the observed familial aggregation originates from genetic or environmental influences shared by family members.

The twin study design is the most suitable to disentangle the role of nature and nurture. Given that monozygotic (MZ) twin pairs share all genes, while dizygotic (DZ) pairs share on average 50% of them, a higher phenotypic resemblance observed among MZ pairs for a trait suggests a substantial role of genetic factors in its expression. To date, only three twin studies of alexithymia have been performed. Two

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doi:10.1016/j.jpsychores.2011.02.016

pioneer studies suggested genetic influences on alexithymia [20] or at least its externally oriented thinking facet [21]. However, these studies suffered from limitations in sample size [20,21] and measurement [20]. Recently, a very large population-based study of 8785 twin pairs strongly supported a genetic contribution to individual differences in all facets of alexithymia [22].

While these studies suggest genetic effects on alexithymia, there are several related issues that deserve further investigation. First, no study used multivariate models to examine whether there are genetic or environmental influences common to alexithymia facets. Second, it remains to be determined if genetic influences on alexithymia are independent of genetic influences on other mental health variables, such as depression, which are correlated with alexithymia [23–25] and are known to be genetically influenced [26,27].

In this study, we measured alexithymia and depression in a general population sample of MZ and DZ twins reared together, with the aim of confirming previous findings of a genetic contribution to individual differences in alexithymia, examining whether there are genetic or environmental influences common to alexithymia facets, and investigating whether genetic influences on alexithymia are independent of genetic influences on depression.

Methods

Participants

The study sample was derived from the population-based Italian Twin Register (ITR) [28], which currently contains information on approximately 23,000 Italian twins belonging to different age groups and geographical areas and is involved in both general population- and clinical-based studies on various complex phenotypes, some conducted within large European networks [29].

A total of 2930 twins enrolled in the ITR and aged 23–24 years were contacted by mail and invited to participate in a study concerning emotional life and well-being, conducted as part of a larger survey aimed at investigating the genetic and environmental influences on several anthropometric measures. In the same mail contact, the twins received the study assessment instruments. A total of 758 twins (25.9%) agreed to participate and returned the questionnaires. This response rate is comparable to that of previous ITR studies [29]. Respondents and non-respondents did not significantly differ in zygosity, education, and geographical area of residence.

Zygosity was assigned by means of a standard questionnaire evaluating the degree of physical similarity of twins during infancy. This is a well-established method in twin studies, which is known to have an accuracy of approximately 95%. The reliability of this method in the ITR population was recently estimated in a sample of 158 same-gender adult twin pairs using nine microsatellite markers; 149 pairs (94.3%) were correctly classified by the questionnaire.

After the exclusion of twins with either missing psychometric data or unknown zygosity owing to missing responses to questions about similarity of appearance with the co-twins, 729 twins entered the analysis. Of these, 327 (44.9%) were males, 653 (89.6%) had completed high school, and 717 (98.4%) were unmarried. Participants belonged to 275 complete pairs and 179 pairs in which only one member participated (unmatched pairs). Out of the 275 complete pairs, 136 were MZ (65 male and 71 female) and 139 were DZ (37 male, 54 female and 48 opposite gender). The 179 twins from unmatched pairs belonged to 71 MZ pairs (32 male and 39 female) and 108 DZ pairs (23 male, 31 female and 54 opposite gender). Twins from complete pairs and twins from unmatched pairs did not significantly differ in education, marital status, alexithymia item-response profiles, and correlations between alexithymia dimensions.

Assessment

Alexithymia was measured with the validated Italian version [30] of the 20-item Toronto Alexithymia Scale (TAS-20), a widely used instrument with established reliability and validity [31,32]. It gives a total score and three subscale scores, measuring the difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and the tendency to focus on concrete details of external events rather than on feelings, fantasies, and other aspects of inner experience ('externally oriented thinking', EOT). Higher scores indicate greater alexithymic characteristics. In the current sample, the internal consistency reliability as measured by coefficient alpha was 0.77, 0.79, 0.73, and 0.54 for the total score and the DIF, DDF, and EOT subscales, respectively.

Depression was measured with the Positively-phrased Depression Scale (PDS), a validated self-report questionnaire consisting of 10 items, each scored on a 5-point scale. The items inquire about the main symptoms of depression (depressed mood, loss of interest and pleasure, feelings of unhappiness, loss of energy, feelings of worthlessness, unrefreshing sleep, difficulty in starting the day, agitation, difficulty concentrating and thought retardation) and are phrased in a positive way to reflect symptom absence (i.e., 'Did you feel happy and in a good mood?', 'Was there something you enjoyed doing or were interested in?', 'Did you think you were happy to live?', 'Did you feel active, full of energy?', 'Did you feel useful?, 'Did you wake up fresh and rested?', 'Did you wake up happy to start the day?', 'Did you feel calm and relaxed?', 'Were you able to concentrate on what you were doing?' and 'Were you able to think clearly?'). The items are scored inversely, so that higher PDS scores indicate greater severity of depressive symptoms. The time period covered is the last month. The PDS was preferred to other self-rated measures of depression as it was considered more suitable for a study presented as dealing with emotional life and well-being. Test–retest reliability at the item level after 2 weeks was found to be 0.60 or higher for all items [33]. Also, in a sample of 104 psychiatric outpatients, those with a depressive disorder scored significantly higher on the PDS than patients with other mental disorders. Also, the PDS displayed high internal consistency reliability (alpha=0.90) and convergent validity against both patient-rated and clinician-rated depression scales, as the PDS score was found to be highly correlated with the Zung Depression Scale (ZDS) (r=0.76), the 9-item Patient Health Questionnaire (PHQ-9) (r=0.76), and the Hamilton Depression Rating Scale (r=0.55). Correlations of similar magnitude between the PDS and both the ZDS (r=0.66) and PHQ-9 (r=0.64) were observed in a sample of 88 university students [34]. In the current sample, the internal consistency reliability as measured by coefficient alpha was 0.86.

Statistical analyses

Sample descriptives

For the TAS-20 total and subscale scores, descriptive statistics including mean and standard deviation, by zygosity and gender, were computed for twins as individuals using the software Stata (version 9.2).

Correlations

For the TAS-20 total score, the correlations between twin and co-twin were estimated in MZ and DZ pairs separately via the maximum-likelihood method as implemented in the software Mx [35], using a univariate saturated model fitted to raw data from MZ and DZ twins. Unlike the approach based on variance–covariance matrices, the Mx's raw data model-fitting method allows one to handle missing data using all available information, and thus also enables the inclusion of single twin responders from unmatched pairs in the analysis, which maximizes the statistical power of the study. While those pairs would