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Review

Are there depression and anxiety genetic markers and mutations? A systematic review

Sally França Lacerda-Pinheiro [a], Roberto Flávio Fontenelle Pinheiro Junior [a], Marcos Antonio Pereira de Lima [a], Claúdio Gleidiston Lima da Silva [a], Maria do Socorro Vieira dos Santos [a], Antonio Gilvan Teixeira Júnior [a], Pedro Neto Lima de Oliveira [a], Karla Denise Barros Ribeiro [a], Modesto Leite Rolim-Neto [a,*], Bianca Alves Vieira Bianco [b]

[a] Federal University of Cariri, Divine Salvior Street, 284, Center, Barbalha, Ceara, Brazil
[b] Faculty of Medicine of ABC, Santo André, São Paulo, Brazil

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ABSTRACT

Background: Genetic factors may encourage or even cause the occurrence of mood disorders such as anxiety and/or depression. However, despite the significant amount of work and sophisticated technology is not fully elucidated which genes or regions of nuclear or mitochondrial DNA, or which types of genetic changes, alone or in combination, can represent reliable genetic markers of anxiety and/or depression.
Objective: To identify whether there are genetic changes that can cause depression or anxiety and if there are genetic markers that can be used to detect these changes.
Methods: A systematic review of 01.01.2004 to 03.28.2014 was held by VHL (Virtual Health Library). The search was performed with the descriptors "anxiety", "depression", "mutation" and "genetic markers". The selected articles were indexed in MEDLINE. The information pertinent to the study was selected, categorized and analyzed. Of the 374 articles found, 29 met the eligibility criteria.
Results: FMR1 gene polymorphisms, dopaminergic (DAT, DRD, COMT), serotonin (5-HTTLPR, HTR1A, HTR2A), interleukins, MCR1, HCN (potassium channel), neurorregulinas, GABAergic (GABA, GAD, DBI) DBI, GABA (Gabra) receptors and GAD genes (GAD1, GAD2) appear to contribute to generate condition of depression or anxiety like. Mutations in mitochondrial DNA in 124pb allele of D2S2944 in ofil 1 and 2 loci of chromosomes 4 and 7, respectively, and the chromosomes 8p, 17p and 15q appear to be associated with the origin of depression or anxiety.
Conclusion: Some studies show only associations with one of the disorders, mainly anxiety. Few have shown association with both simultaneously. Other studies showed specific association of gender, or even specific ethnic groups. It was noticed, controversies over certain markers. Interesting results were observed in combination of changes, especially in cases of SNPs, indicating that perhaps this is the most appropriate way to find reliable markers.

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* Corresponding author. Tel.: +55 88 99042979.
E-mail address: modestorolim@yahoo.com.br (M.L. Rolim-Neto).

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1. Introduction

The emergence of depression and its possible association with anxiety raises a debate about neurochemical reconfiguration, which attempts to highlight the connections between genetic indicators of this phenomenon and the mutations involved in this process. Thus, several studies have indicated genetic susceptibility in understanding the development of depression and anxiety, by considering polygenic *loci* and their environmental factors.

Vendruscolo et al. (2006), based in classic studies, claim that the influence of genetic factors on such psychopathologies has been widely demonstrated (Vendruscolo et al., 2006; Cloninger 1987; van de Wetering et al., 1999), but this effect is still poorly understood at the molecular level. Therefore, the identification and characterization of predisposing genes would certainly be a major advance for preventing and treating psychological disorders such as alcoholism and anxiety.

As a result of gaps in diagnosis and etiology of depression/anxiety, there was a need for studies that show genetic influence in the origin of those disorders. Holmans et al. (2007) emphasize that when performing a study of genomewide linkage scan, families with at least a pair of ill relatives (other than parent–child pairs) were recruited, and DNA markers at all chromosomes were assayed to search for locations where ill subjects have inherited the same sequence variants (within families) more often than expected by chance. Those markers are likely to be close to genes that contribute to disease susceptibility, which can be identified by using other methods. The Genetics of Recurrent Early-Onset Depression (GenRED) sample was recruited to carry out a large-scale genome scan.

It is known that a portion of psychopathologies, such as anxiety and depression, can have in their etiology considerable genetic factors (Goodson et al., 2012) and, because of that, this study is based in the following research questions: are there genetic changes able to cause depression or anxiety diagnosis? And, are there genetic markers that can be used to detect such changes? This survey was conducted through a systematic review aiming to identify which genetic markers are known at present, so that new clinical therapeutic approaches are used, improving the diagnosis, treatment and prognosis of people affected.

2. Methods

It was performed a qualitative systematic review of articles about genetic markers, mutations, and their relations with depression and anxiety published in electronic databases previously selected.

It was conducted a search in the literature through the online databases of the Virtual Health Library (VHL), that hosts the base of MEDLINE, in March 2014, by limiting itself to articles published between January 1, 2004 to March 28, 2014. The reason to limit the search between 2004 and 2014 was because before this period, a number of published works were little expressive and at the same time not addressed directly to the genetic markers and the mutations related to depression and anxiety. In addition, after completion of the sequencing of the human genome in 2003, genetics has gained much importance in the context of the etiology of various diseases considered idiopathic. Initially, the following descriptors were used, in Portuguese, for searching in the VHL:

#1. “genetic markers” (Descriptors in Health Sciences [DeCS, in Portuguese]);
#2. “mutation” (DeCS term);
#3. “anxiety” (DeCS term); and
#4. “depression” (DeCS term).

A similar search strategy was held in the PubMed database, by using the same terms mentioned above.

The analysis of the article followed eligibility criteria previously determined. The survey was carried out in four phases: 1 AND 3, 1 AND 4, 2 AND 3, 2 AND 4. Initially, a search was conducted for those combinations by using the filter “subject descriptor”, but it did not find results either for combination 1 AND 3 or for combination 1 AND 4, it was found only for combinations 2 AND 3 and 2 AND 4. Therefore, the following search strategy was performed: in the first and second times, it searched articles by using the filter “title, summary, subject”; in the third and fourth times, it searched articles by using the filter “subject descriptor “; it adopted the following inclusion criteria: (1) written publications in English, in Spanish or in Portuguese; (2) studies about the topic mutations that cause anxiety or depression; (3) studies about genetic markers for anxiety or depression; (4) original articles with full text accessible through the Portal de Periodicos CAPES (The Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), a virtual library connected to the Brazilian Ministry of education with content restricted to authorized users; and (5) prospective or retrospective observational studies (descriptive or analytical, except for case studies), experimental or almost experimental. The exclusion criteria were as follows: (1) other study designs, e.g. case reports, case series, literature reviews and comments; (2) non-original studies, including editorials, reviews, forewords, short communications and letters to the editor.