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Genetics and personality affect visual perspective in autobiographical memory

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ABSTRACT

Major depression is associated with a decrease of 1st person (versus 3rd person) visual perspective in autobiographical memory, even after full remission. This study aimed to examine visual perspective in healthy never-depressed subjects presenting with either genetic or psychological vulnerability for depression. Sixty healthy participants performed the Autobiographical Memory Test with an assessment of visual perspective. Genetic vulnerability was defined by the presence of at least one S or L_G allele of the polymorphism of the serotonin-transporter-linked promoter region (5-HTTLPR). Psychological vulnerability was defined by high scores of harm avoidance measured by the Temperament and Character Inventory. Life stress exposure, depressive mood, rumination, and familial history of depression were assessed through standardized procedures. Visual perspective for positive memories was independently predicted by both harm avoidance and a gene by environment interaction between the 5-HTTLPR polymorphism and life stress exposure. Visual perspective and vulnerability for depression may share some biological bases.

1. Introduction

Autobiographical memory (AM) grounds the self by providing coherent narratives organized to elicit a sense of identity across the time (e.g. remembering academic achievements may support the self as knowledgeable) (Conway, 2005). "Autobiographical memories can be retrieved from either the 1st person perspective (or 'field' perspective), in which individuals see the event through their own eyes, or from the 3rd person perspective (or 'observer' perspective), in which individuals see themselves and the event from the perspective of an external observer" (Sutin & Robins, 2008, p.1386). A growing body of research suggests that the visual perspective from which a memory is retrieved may play a role in both emotional regulation and self-related processes (see Sutin & Robins, 2008 for a recent review).

Because major depression is associated with both decreased emotional regulation (Beck, 2008) and increased self-focus (i.e. increased attention to the self) (Mor & Winquist, 2002), it offers a unique opportunity to examine the biological and psy-

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chological correlates of visual perspective. Recent studies found a decrease of 1st person perspective not only in currently depressed adults (Lemogne et al., 2006) and adolescents (Kuyken & Howell, 2006), but also in previously depressed adults experiencing full remission (Bergouignan et al., 2008). Building on these findings, we hypothesized that visual perspective may be partially determined by biological or psychological features associated with vulnerability for depression rather than with depression itself. The present study aimed to examine visual perspective in healthy never-depressed subjects presenting with either a 'genetic' or a 'psychological' vulnerability for depression.

Genetic vulnerability for depression was based on one candidate gene in major depressive disorder, namely the polymorphism of the serotonin-transporter-linked promoter region (5-HTTLPR), which regulates the expression of the serotonin transporter gene in cell lines. The 5-HTTLPR is considered as a triallelic locus with alleles designated as either short (S) or long (L), the latter being subdivided with respect to a single-nucleotide polymorphism (SNP rs25531) into functional variants designated as L_A and L_G (Lesch et al., 1996; Nakamura et al., 2000). The S and L_G alleles are associated with comparable levels of gene expression in cell lines, both of which being lower than the gene expression associated with L_A. Individuals with at least one S or L_G allele exhibit more depressive episodes in relation to life stress than individuals homozygous for the L_A allele, indicating a gene by environment ($G \times E$) interaction (Caspi et al., 2003; Kaufman et al., 2004; Kendler, Kuhn, Vittum, Prescott, & Riley, 2005).

Psychological vulnerability for depression was defined according to the dimensional model of personality proposed by Cloninger, Svrakic, and Przybeck (1993). In this model, harm avoidance (HA) is a trait strongly associated with negative affect, quantifying individual differences in the extent to which a person is anxious, pessimistic, and shy versus risk-taking, optimistic, and outgoing. A high level of HA is associated with an increased risk of depression (Cloninger, Svrakic, & Przybeck, 2006; Farmer et al., 2003).

Note that the present study does not assume a dualistic distinction between genetic and psychological vulnerability. The 'genetic' and 'psychological' labels only refer to the different methods used to assess vulnerability for depression (i.e. molecular biology and psychometric assessment, respectively).

According to previous findings in currently and previously depressed adults (Bergouignan et al., 2008; Lemogne et al., 2006), we expected a decrease of 1st person perspective for positive memories in never-depressed subjects presenting with vulnerability for depression. More specifically, we aimed to test two hypotheses. First, 1st person perspective for positive memories would be lower in individuals with at least one S or L_G allele than in individuals homozygous for the L_A allele. Second, 1st person perspective for positive memories would be negatively correlated with HA.

2. Methods

2.1. Participants

All volunteers were native French-speaking Caucasian medical students and gave written informed consent after complete description of the procedure. The study was carried out in accordance with the latest version of the Declaration of Helsinki and was approved by the Ethics Committee for Biomedical Research of the Pitié-Salpêtrière Hospital. Eighty-five volunteers were screened for past and present DSM-IV diagnoses with the Mini International Neuropsychiatric Interview (Sheehan et al., 1998). Twenty-five volunteers were not included in the study because of personal history of mood disorders or substance use disorders. The remaining sixty volunteers (30 men, 30 women, mean age: 23.45 ± 1.98 years) were included in the study.

2.2. Materials

2.2.1. Genotyping

Genomic Deoxyribonucleic Acid (DNA) was extracted from endobuccal cell swabs with the BuccalAmp DNA Extraction Kit (Epicentre). All subjects were genotyped for the 5-HTTLPR polymorphism, including SNP rs25531 (A/G), according to published protocols (Dannlowski et al., 2008) with minor variation. Primers 5′-GGCGTTGCCGCTCTGAATGC-3′ and 5′-GAG GGACTGAGCTGGACAACCAC-3′ (10 pM each) were used for a 25 μl Polymerase Chain Reaction (PCR) containing 5 μl DNA (20–100 ng), 200 mM dNTPs, 0.5 U Taq Polymerase (Eurobio), 1.5 mM $MgCl_2$ and 1X Buffer (Eurobio), with an initial 15 min denaturation step at 95 °C followed by 35 PCR cycles of 94 °C (60 s), 64 °C (60 s) and 72 °C (120 s) and a final extension step of 10 min at 72 °C. PCR products were digested with HpaII at 37 °C overnight, and separated in 3% agarose gels, stained with SYBRsafe DNA stain (Invitrogen), which resulted in fragments between 62 and 340 bp length allowing differentiation and assignment of all 5-HTTLPR genotypes.

Allele and genotype frequencies were compared with chi-square tests and the test for Hardy–Weinberg equilibrium was performed. Due to the dominant effect of the S and L_G alleles, we considered two groups according to their putative level of gene expression, distinguishing subjects with (SS, SL_A, SL_G, L_GL_G, and L_GL_A) versus without (L_AL_A) the potentially at-risk genotypes, henceforth referred to as S′ and L′ subjects, respectively.

2.2.2. Autobiographical Memory Test (AMT)

Autobiographical memory was assessed with the French version of the AMT (Nandrino, Pezard, Poste, Réveillère, & Beaune, 2002; Williams & Scott, 1988). This test includes 20 cue words: 10 with a positive valence (e.g. happy, safe, successful)