Recent advances in molecular genetics have stimulated basic and clinical research, and opened up access to hypothesis-driven and unbiased genetic approaches. With knowledge of the genes involved in complex basic functions like the stress response, and of multifactorial diseases like stress-related disorders, we can improve our understanding of the mechanisms and moderators involved in the biology of normal and altered stress response, which in turn will help to identify new drug targets and interventions for stress-related disorders.

Stress response and stress-related disorders

Though there is no generally accepted definition, stress is usually defined as a state of disturbed homeostasis evoking a multiplicity of somatic and mental adaptive reactions, which are summarized as stress response aim-
The perception of a stressful situation activates a large number of neuronal circuits in the prefrontal cortex and limbic system, including the hypothalamus, where the sympathetic nervous system is activated; this in turn leads to a widespread release of noradrenalin from the postganglionic fibers and to the release of adrenalin (and noradrenalin) from the adrenal medulla. Additionally, the parvocellular neurons of the hypothalamus are stimulated to secrete the neuropeptides corticotropin-releasing hormone (CRH) and vasopressin (AVP) into the portal vessel system to activate the synthesis and release of corticotropin (ACTH) from the anterior pituitary. ACTH, in turn, stimulates the adrenal cortex to synthesize and release glucocorticoids, in particular cortisol (in humans). These hormones have a multiplicity of functions, which are necessary for the adaptation to acute stress, but can be pathogenic when the organism is persistently exposed. Therefore, a fine-tuned regulation of the sympathetic system and of the HPA axis is essential to avoid the development of a pathological dysregulation that can progress to stress-related disorders, which can be defined as illnesses whose causation, onset, or development is substantially influenced by stress and its neurobiological correlates. Among others, cardiovascular dis-

### Selected abbreviations and acronyms

- **ACTH**: adrenocorticotropic hormone, corticotropin
- **AVP**: (arginin)-vasopressin
- **CRH**: corticotropin-releasing hormone
- **DEX**: dexamethasone
- **GR**: glucocorticoid receptor
- **HPA**: hypothalamic-pituitary-adrenocortical
- **MR**: mineralocorticoid receptor
- **RAAS**: renin-angiotensin-aldosterone system
- **TSST**: Trier Social Stress Test
orders such as hypertension and coronary artery disease, as well as psychiatric diseases such as bipolar disorder and unipolar depression, are examples of stress-related disorders that will be discussed in this review.

The main central structure for the regulation of the autonomic nervous system is the hypothalamus, which receives input from cortical and subcortical structures, as well as from peripheral receptors and organs. The primary regulatory elements of the HPA axis are the corticosteroid receptors, glucocorticoid receptors (GR), and mineral corticoid receptors7 (for details see ref 8).

As indicated in the left panel of Figure 1, activation of the HPA axis leads to the secretion of cortisol (in humans), which induces a negative feedback inhibition to CRH and AVP (at the level of the hypothalamus) and to ACTH (at the level of the anterior pituitary). Impaired corticosteroid signaling results in an attenuation of the negative feedback inhibition, which could result in the failure to sufficiently suppress CRH and AVP release from the hypothalamus and ACTH from the anterior pituitary, which in turn leads to chronically elevated levels of cortisol (Figure 1, right panel). The attenuated negative feedback inhibition can be most sensitively diagnosed with a neuroendocrine challenge test of the HPA axis, the combined dexamethasone (dex)/CRH test.

Impaired HPA axis regulation during an acute episode is the most consistent laboratory finding in depression and bipolar disorder (see refs 13 to 15 for reviews), which corresponds to the concept of stress-related disorders. Accordingly, the majority of depressed patients exhibit an exaggerated ACTH and cortisol response to the combined dex/CRH test (Figure 2).

These alterations were shown to normalize after successful antidepressant treatment,11,16-18 suggesting that altered HPA axis regulation and its normalization is involved in the pathogenesis of and recovery from depression, respectively.

**Genetics of stress response**

Evidence for heritability is a prerequisite for the involvement of genetic factors. The most efficient way for evaluating heritability is twin studies comparing phenotypic similarity between monozygotic and dizygotic twins. Twin data are available for the Trier Social Stress Test (TSST),19 which is a standardized procedure for the assessment of the psychosocial stress response. Briefly, this test comprises a public speaking task involving a mock job interview and a mental arithmetic task. Subjects are asked to prepare a presentation for promoting their candidacy for a position that is tailored to their education. After the preparation time, subjects give their presentation in front of a panel of judges who are evaluating the talk. After 5 minutes, subjects are requested to perform an unexpected mental arithmetic task for a further 5 minutes. HPA axis activity (plasma ACTH and cortisol and/or salivary cortisol) is evaluated before and after the tasks as well as during recovery. Federenko and coworkers20 reported a heritability estimate (h²) of 0.32 for the plasma cortisol response to the TSST in 33 monozygotic and 25 dizygotic twin pairs, suggesting moderate heritability, but this increased up to 0.98 in two repetitions of the test. Heritability estimates for ACTH and salivary cortisol were distinctly smaller in the first test session, but increased markedly in the repeated test sessions. A previous study by Kirschbaum and coworkers21 with 13 monozygotic and 11 dizygotic twin pairs also reported only marginal heritability for the salivary cortisol response to a single administration of the
TSST. High heritability was observed for salivary cortisol after stimulation with 100 µg human CRH (without dex suppression) and no heritability was found for the salivary cortisol response to strenuous physical exercise (ergometer activity).21

No heritability data are available for the combined dex/CRH test. However, in the Munich Vulnerability Study,22,23 the combined dex/CRH test was conducted in healthy first-degree relatives of patients with a major depressive disorder, who are assumed to carry a genetic vulnerability for affective disorders. These so-called high-risk probands (HRPs) are characterized by a moderately elevated hormonal response to the combined dex/CRH test, which was significantly higher compared with controls without a personal or familial history of psychiatric disorders, but less pronounced compared with the response in acutely depressed patients. Modell and coworkers24 replicated these findings in still unaffected HRPs who were re-examined in a follow-up investigation about 4 years later (Figure 3), suggesting that this trait-like impaired regulation of the HPA system could reflect the genetic vulnerability for affective disorders in these subjects.

Despite the statistical evidence for a considerable heritability of the stress response, the number of significant genetic findings is small, and the conclusiveness rather limited. The findings are summarized in Table I. Due to the importance of the HPA system for the stress response, which is primarily regulated by GR, the GR gene has been proposed as the primary candidate for the

![Figure 3. Cortisol response to the combined dex/CRH test is moderately elevated in high risk probands for affective disorders (AUC, \(P < .05\)), which was stable over time at the group level (AUC, \(P = .758\)) as well as at the individual level (Pearson correlation, \(r = .51, P < .05\)) in a follow-up investigation 4 years later. Dex, dexamethasone; CRH, corticotropin-releasing hormone; AUC, area under the curve](image)

| Genes                        | Chromosomal position | Results                                                                                                                                                                                                 |
|------------------------------|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| **Psychosocial stress response** |                       |                                                                                                                                                                                                                   |
| Glucocorticoid receptor (GR, NR3C1) | 5q31.3               | Combined Bcll and N363S polymorphisms associated with salivary cortisol response to psychosocial stress (Trier Social Stress Test, TSST) in male mono- and dizygotic twins25; replicated in male unrelated subjects but not in female subjects (Kumsta and Wüst, 2006; personal communication) |
| GABA(A) α6 receptor subunit (GABRA6) | 5q34                 | T1521C polymorphism associated with ACTH, cortisol, and blood pressure response to psychosocial stress (TSST) in healthy subject26                                                                 |
| Opioid receptor μ1 (OPRM1)   | 6q24-q25             | A118G polymorphism associated with cortisol response to psychosocial stress (modified TSST) in healthy subject27                                                                                           |
| **Endocrine HPA challenge tests** |                       |                                                                                                                                                                                                                   |
| Glucocorticoid receptor (GR, NR3C1) | 5q31.3               | Bcll and N363S polymorphisms associated with ACTH and cortisol suppression after oral low-dose dexamethasone (dexamethasone suppression test) in elderly subjects28,29                                                                                      |
| Angiotensin-converting enzyme (ACE) | 17q23.3             | Insertion/deletion polymorphism associated with hormonal response to the combined dexamethasone suppression/CRH stimulation test in acute major depression20,21                                                                                                   |
| Brain-derived neurotrophic factor (BDNF) | 11p13             | Val66Met polymorphism associated with ACTH and cortisol response to the combined dexamethasone suppression/CRH stimulation test in acute depression21                                                                                       |

**Table I.** Genetic associations with stress response in human paradigms. GABA, γ-aminobutyric acid; ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; HPA, hypothalamic-pituitary-adrenal
Genetic association studies. Significant associations between GR and psychosocial stress response were reported, but only when a haplotype approach is applied or when male subjects are separately analyzed (Kumsta and Wust, 2006; personal communication). Further genetic associations, not yet replicated, are reported for the γ-aminobutyric acid (GABA) A6 receptor subunit gene and for a nonsynonymous exon single-nucleotide polymorphism (SNP) of the micro-opioid receptor 1 (MOR) gene. Additional evidence for an involvement of the GR gene in the genetics of the stress response has been provided by two other studies (Table I) employing a low-dose dex suppression test in elderly subjects. In this test, plasma cortisol levels after oral administration of dex are interpreted as an indicator for GR sensitivity, which is the major regulator of the stress hormone activity at the pituitary level. Two other studies in patients suffering from major depression reported associations between the angiotensin-converting enzyme (ACE) gene and the hormonal response to the combined dex suppression/CRH stimulation test, which is the most sensitive challenge test for evaluating stress hormone regulation. ACE is involved in the so-called renin-angiotensin cascade of water regulation, which in turn affects blood volume and blood pressure. A recent study observed an association between the combined dex/CRH test and brain-derived neurotrophic factor (BDNF) in depressed patients, which has been interpreted as evidence for an involvement of a reduced neuroplasticity in the development of disturbed HPA axis regulation. Taken together, there are only a limited number of studies examining the association between candidate genes and the stress response. Besides genes involved in the sympathetic (ACE) or HPA axis-mediated (GR) stress response, further genes constituting different biological systems implicated in emotional regulation and neuroplasticity (BDNF) have been examined. However, the results show only moderate effect sizes, although heritability estimates suggest a strong involvement of genetic factors. Further evidence for genes involved in the regulation of the stress response could be provided by clinical studies investigating genetic vulnerability factors for stress-related disorders. These genetic risk factors are assumed to be responsible for an inappropriate response to repeated and/or continuous stress and thus for mediating the vulnerability for stress-related disorders.

Genetics of stress-related disorders

A large number of diseases can be understood as stress-related disorders, and most of them are characterized by an at least moderate heritability. In this review, we focus on the most prevalent stress-related disorders, hypertension and coronary artery disease, as examples of cardiovascular disorders, and on bipolar disorder and unipolar depression as examples of psychiatric disorders. Cardiovascular disorders are the leading cause of mortality in the Western world, and are projected to become the leading cause of disease burden worldwide in 2020. Essential hypertension is the most common cardiovascular disorder, with a lifetime prevalence of above 50% in most western communities, affecting approximately 1 billion individuals worldwide; heritability estimates around 30% have been reported. Myocardial infarction is a serious outcome of coronary artery disease. Twin studies suggest that the risk for myocardial infarction is fairly heritable, with a heredity estimate of 60% in females and 26% in males. A large number of case-control association studies in essential hypertension are available (Table IIa) focussing on a number of candidate gene systems. The majority of findings have been obtained with candidates from the sympathetic system, including adrenergic genes, genes of the renin-angiotensin-aldosterone system (RAAS), and genes involved in vascular regulation. Despite the large number of studies, only a few associations can be regarded as convincing, including the associations with the angiotensinogen (AGT), aldosterone synthase (CYP11B2), and with the renin (REN) gene, all involved in the RAAS. Several studies report gene x gene interaction effects, eg, between the endothelin 1 (EDN1) and serotonin receptor 2a (5HTR2A) genes, and between the ACE, aldosterone synthase (CYP11B2), and α adducin (ADD1) genes. Several candidate genes from other biological systems (eg, DRD2, GNB3, ACSM3) have been proposed, but no unambiguous conclusion can yet be drawn from the findings from these studies. As for hypertension, a large number of genetic association studies have also been conducted for coronary artery disease. However, the results are more difficult to interpret than in hypertension, since different clinical conditions, including myocardial infarction and arteriosclerosis/stenosis, are integrated as coronary artery disease. Most candidate genes showing replicable associations...
have been derived from the concept of inflammation as a major risk factor for coronary heart disease. Convincing evidence for genetic associations has been reported for genes involved in innate immunity or genes moderating the inflammatory reaction, such as leukotrienes and lymphotoxins (Table IIb).

The number of positive results outweighs the negative findings, and most effect sizes were in at least moderate range. Nevertheless, not all candidate genes derived from potent endophenotypes show convincing associations. One example of this divergence is lipoprotein A, which has been identified as a potent vulnerability factor for coronary artery disease, even though there is only a little evidence for a genetic association of the lipoprotein A (LPA) gene. Further gene candidates have been derived from studies in mendelian disorders involving premature coronary artery diseases such as familial hypercholesterolemia, familial defective apolipoprotein B (APOB), sitosterolemia, and Tangier disease. An overview of these findings is provided by Watkins and Farrall. However, the translation of these findings to multifactorial cardiovascular disorders is limited.

Besides cardiovascular diseases, bipolar disorder and unipolar depression are further examples of burdensome stress-related disorders with a distinct heritability and a high prevalence in the general population, especially unipolar depression, which is projected to become the second leading cause for disease burden in 2020.

Lifetime prevalence of bipolar disorder is around 1% according to population-based epidemiological studies in Europe as well as in the US, while lifetime prevalence of unipolar depression is distinctly higher, with a similar rate of 17% in Europe and in the USA. Twin studies suggest a high heritability for bipolar disorder, with heritability estimates, ranging between 80% and 90%, and a moderate heritability for unipolar depression with h² between 33% and 42%.

Most candidate genes for association studies with bipolar disorder and unipolar depression have been derived from neurotransmitter systems involved in antidepressant research.

### Table IIa. Replicated findings of genetic associations with hypertension

| Genes                                      | Chromosomal position | Results                                      |
|--------------------------------------------|----------------------|----------------------------------------------|
| **Adrenergic system**                      |                      |                                              |
| β2-adrenoceptor (ADRB2)                    | 5q31-q32             | Significant associations reported in Caucasian and Asian populations, but also several negative findings |
| β3-adrenoceptor (ADRB3)                    | 8p12-p11.2           | Significant associations reported in Caucasian population and in male type 2 diabetics |
| **Renin-angiotensin-aldosterone system**   |                      |                                              |
| Angiotensin-converting enzyme (ACE)        | 17q23.3              | Significant small to moderate effects, but also several negative reports |
| Angiotensinogen (AGT)                      | 1q42-q43             | Largest number of positive studies, but also some negative findings |
| Aldosterone synthase (CYP11B2)             | 8q21-q22             | More positive than negative reports          |
| Angiotensin (AT1) receptor (AGTR1)         | 3q21-q25             | Mixed results, positive findings as well as negative reports |
| α Adductin (ADD1)                          | 4p16.3               | Mixed results, positive findings as well as negative reports |
| Atrial natriuretic peptide (NPPA, NPPB)    | 1p36.2               | Less positive findings than negative reports |
| Renin (REN)                                | 1q32                 | Predominance of positive findings            |
| 11β-hydroxysteroid dehydrogenase 2 (HSD11B2) | 16q22 | Weak positive effects are reported |
| **Vascular system**                        |                      |                                              |
| Endothelin 1 (EDN1)                        | 6p24.1               | Significant association with blood pressure in obese subjects, some evidence for association with hypertension, in interaction with 5-HTR2A |
| Nitric oxide synthase (NOS3)               | 7q36                 | Less positive findings than negative reports |
| **Other genes**                            |                      |                                              |
| D2 receptor (DRD2)                         | 11q23                | Associated with hypertension and with elevated blood pressure in personality disorder |
| G protein J3 subunit (GNB3)                | 12p13                | Less positive findings than negative reports |
| SAH (ACSM3)                                | 16p13.11             | Mixed results, positive findings as well as negative reports |

5-HT, serotonin; SAH, SA hypertension-associated homolog.
sant drug action. Only some of the findings could be consistently replicated, including associations between the monoaminoxidase A (MAOA) and catechol-o-methyltransferase (COMT) gene and bipolar disorder and tryptophan hydroxylase 2 (TPH2) gene and unipolar depression (Table III). Further conclusive evidence exists for an involvement of the D-aminoacidoxidase activator DAOA (G72)/G30 locus in the susceptibility for bipolar disorder, but also for schizophrenia. A large number of studies have examined the genetic associations between

| Genes | Chromosomal position | Results |
|-------|----------------------|---------|
| Innate immunity | | |
| CD14 molecule (CD14) | 5q31.1 | Significant associations with myocardial infarction, but also negative reports 
| Toll-like receptor 4 (TLR4) | 9q32-q33 | Significant associations reported for acute coronary events and myocardial infarction but not with coronary stenosis |
| Leukotrienes | | |
| Arachidonate 5-lipoxygenase-activating protein (ALOX5AP) | 13q12 | Evidence for an association with myocardial infarction and arteriosclerosis |
| Leukotriene A4 hydrolase (LTA4H) | 12q22 | Significant association with ethnicity-specific risk for myocardial infarction in different ethnic samples |
| Other genes | | |
| Lymphotoxin α (LTA) | 6p21.3 | Significant association with myocardial infarction in Japanese populations as well as arteriosclerosis in Caucasians, but also negative reports |
| Galectin 2 (LGALS2) | 22q13.1 | Associated with myocardial infarction; protein interacts with LTA |

Table IIb. Replicated findings of genetic associations with coronary artery disease.

| Genes | Chromosomal position | Results |
|-------|----------------------|---------|
| Bipolar disorder | | |
| Monoaminoxidase A (MAOA) | 5q31.3 | Significant associations with a modest effect size confirmed by meta-analyses suggesting greatest effects in female patients |
| Catechol-o-methyltransferase (COMT) | 22q11.21 | Meta-analysis revealed a modest effect size and has been suggested as a common susceptibility gene for bipolar disorder and schizophrenia |
| 5-HT transporter (SLC6A4) | 17q11.1-q12 | A number of positive studies confirmed in meta-analyses, but also negative studies for 5-HTTLPR, one negative meta-analysis |
| D-aminoacidoxidase activator DAOA (G72)/G30 | 13q33-q34 | Several positive reports with polymorphisms in the proximity of these nested genes, but also with schizophrenia, suggesting a common susceptibility locus |
| Brain-derived neurotrophic factor (BDNF) | 11p13 | Family-based association studies showed significant effects but most replication studies were negative; one study suggested association with a subgroup of patients displaying rapid cycling |
| P2X ligand-gated ion channel 7 (P2RX7) | 12q24 | Significant associations reported |
| Unipolar depression | | |
| Tryptophan hydroxylase 2 (TPH2) | 12q21.1 | Significant associations with major depression and suicide |
| 5-HT transporter (SLC6A4) | 17q11.1-q12 | More depressive symptoms in carriers of the short 5-HTTLPR allele, but also negative reports |
| Glucocorticoid receptor (NR3C1) | 5q31.3 | Bcll and ER2223EK polymorphisms associated with susceptibility to recurrent unipolar depression |
| P2X ligand-gated ion channel 7 (P2RX7) | 12q24 | Significant associations with unipolar depression reported |

Table III. Replicated findings of genetic associations with bipolar disorder and unipolar depression. 5-HT, serotonin
polymorphisms in the serotonin (5-HT) transporter (SLC6A4) gene and bipolar disorder and unipolar depression. Most attention focused on a functional insertion/deletion polymorphism in the promoter region to SLC6A4, known as 5HTTLPR. Despite several positive results, the number of negative replications is increasing, and the relevance of this polymorphism for the susceptibility to bipolar disorder or unipolar depression is meanwhile being challenged.

Besides SLC6A4, P2X ligand-gated ion channel 7 is the only gene showing replicated effects for susceptibility to both bipolar disorder and unipolar depression. This gene codes for a cation-selective ion channel expressed in central glial cells as well as in neurons, and is assumed to regulate immune function and neurotransmitter release. In summary, genetic association studies in stress-related disorders have provided evidence for an involvement of several other genes not identified by basic genetic studies on stress response. Since an inappropriate response to repeated and/or continuous stress mediates the susceptibility to stress-related disorders, these genes are also assumed to moderate the stress response. We have reviewed genetic association studies in hypertension, coronary artery disease, bipolar disorder, and unipolar depression. Due to the large and rapidly increasing number of publications, it is impossible to provide a complete overview. However, we have tried to summarize the most consistent and most frequently discussed findings. It is important to note that different classes of candidate genes have been investigated in the four diagnostic groups reported in this review, despite their common relationship to stress and inappropriate stress response. While candidate genes in hypertension and coronary artery disease are primarily related to the RAAS and to inflammation/immune response, respectively, the majority of candidate genes in bipolar disorder and unipolar depression are derived from monoaminergic neurotransmitter systems. This makes it clear that our actual knowledge of the complex interplay between genetic factors, altered stress response, and stress-related disorders is still limited, and that further research and new approaches are required to improve our understanding of these complex functions.

**Conclusion and outlook**

The summarized findings do not provide an exhaustive and satisfying answer about the genetics of stress response and stress-related disorders. Many single findings are still unconnected, and the restriction of the gene selection to established candidates has retarded our understanding of the complex interplay between genetic factors, stress response, and stress-related disorders. Sophisticated models, especially those aiming to integrate the findings from basic and clinical research as well as from the different types of stress-related disorders, are required to close the gap in our knowledge. The new chip-based whole-genome technologies, Affymetrix GeneChip and Illumina Genotyping BeadChip, are powerful tools for this endeavor. With this technology, the advantages of an unbiased approach as provided by linkage analysis, and the statistical power of association studies are combined to identify new candidate genes. However, results from unbiased approaches are always preliminary, and require validation in confirmatory studies. This means that independent replication studies are needed, but also clinical studies taking gene x gene and gene x environment interactions into account. For causal inferences, preclinical experiments are required, including (conditional) genetic modification and the development of specific compounds as research tools for the protein targets. Finally, text- and information-mining tools, which are already available but have to be further developed, will be very helpful to integrate all findings into sophisticated models delineating the pathways from genes to stress response and stress-related disorders. There is still a long way to go—but the prerequisites for success are more present than ever.

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Genetica de la respuesta al estrés y de los trastornos relacionados con el estrés

Los descubrimientos principales en la genética de y de los trastornos relacionados con el estrés son: i) las variaciones de los genes implicados en el sistema simpático o en el eje hipotálamo-hipófisis-corteza suprarrenal están asociadas con respuestas alteradas al estrés; ii) los genes relacionados con el sistema renina-angiotensina-aldoesterona o la respuesta inflamatoria/inmunitaria están asociados a los trastornos cardiovasculares; iii) los genes implicados en los sistemas neurotransmisores monoaminérgicos están asociados al trastorno bipolar y a la depresión unipolar. La inmensa mayoría de estos estudios de asociación siguen un enfoque convencional, impulsado por hipótesis, lo que restringe la selección de genes candidatos conocidos. Este método tan conservador ha retrasado el conocimiento de la interrelación compleja entre los factores genéticos, la respuesta al estrés y los trastornos relacionados con éste. Las tecnologías de chip para el estudio de todo el genoma abrirán las puertas a métodos nuevos, objetivos y eficaces, lo que estadísticamente permitirá identificar nuevos genes candidatos que serán validados minuciosamente en estudios confirmatorios clínicos y preclínicos. Todo ello, sumado al uso de nuevos instrumentos para la explotación de texto e información, nos ayudará a integrar todos los datos dentro de modelos complejos que delimiten las vías desde los genes hasta la respuesta al estrés y los trastornos relacionados con el estrés.

Génétique de la réponse au stress et des troubles liés au stress

Voici les principaux résultats sur la génétique de la réponse au stress et des troubles liés au stress: 1) les variations des gènes impliqués dans le système sympathique ou l’axe hypothalamo-hypophyso-sur-rénalien sont associées à des anomalies de la réponse au stress ; 2) les gènes liés au système rénine-angiotensine-aldostérone ou à une la réponse inflammatoire/inmunitaire sont associés avec des maladies cardiovasculaires ; 3) les gènes impliqués dans les systèmes de neurotransmission monoaminérgiques sont associés aux troubles bipolaires et à la dépression unipolaire. La grande majorité de ces études d’association a suivi une approche conventionnelle hypothético-déductive, limitant donc la sélection des gènes aux candidats établis. Cette approche très conservatrice a retardé notre compréhension des interactions complexes entre les facteurs génétiques, la réponse au stress et les troubles liés au stress. Les technologies de puce à ADN sur le génome entier ouvriront la voie à de nouvelles approches non biaisées et statistiquement efficaces qui permettront d’identifier de nouveaux gènes candidats. Ces derniers devront être minutieusement validés dans des études cliniques et précliniques de confirmation. Ces technologies, associées à de nouveaux outils d’analyse des textes et des informations, nous permettront d’intégrer plus facilement tous les résultats dans des modèles sophistiqués précisant les voies qui vont des gènes à la réponse au stress et aux troubles liés au stress.

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