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Review

Genetic Basis of Emotional Regulation: Integrative Analysis of Behavioral and Neurobiological Data

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Abstract

Emotional regulation (ER) is the process by which people change their physiology, expressions, and emotional experiences to operate in their daily lives. Deficits in emotion control may be connected to physical and mental health consequences. This review aims to identify genetic variants, understand neurobiological mechanisms, and explore behavioral phenotypes

associated with ER. In our study, we included English studies from online databases such as Web of Science, Cochrane Library, Google Scholar, PubMed, and Scopus using the following keywords “genetic factors”, “genetic markers”, “Emotional regulation”, “emotional dysregulation”, “neurobiology”, and “behavior” till June 2024. The result of the search utilizing our search strategy was 2107 studies. We screened the articles relevant to our topic by screening these articles. We involved 12 studies that met the inclusion criteria of our narrative review. Our study involved 6114 individuals divided into 4511 females and 1603 males. The mean age of the included participants was 18 years. Out of all the genes studied in relation to ER, SLC6A4 was the most frequently found. The findings show that individuals homozygous for the l allele were less likely to misbehave on the task than those with two or one copy of the s allele of the 5-HTTLPR polymorphism. There are essential therapeutic implications from comprehending the genetic basis of ER. It can help with the creation of individualized interventions for people with emotional dysregulation (ED) linked to psychiatric diseases, such as depression and anxiety disorders. For example, the identification of genetic markers may aid in predicting treatment response to particular therapeutic approaches (such as medicine vs cognitive-behavioral therapy) customized to a person's genetic profile. This review is limited by the small sample size and insufficient studies identifying the genetic variants and behavioral phenotypes associated with ER. In conclusion, the current research presents empirical proof that environmental and genetic factors impact individual variances in ER. Moreover, it's significant to note that shared genetic effects play a role in the relationship between neurobiology, behavior, and ER.

Keywords
Genetic factors; genetic markers; emotional regulation; ED; neurobiology; behaviour

1. Introduction

Emotional regulation refers to individuals' strategies and processes to manage and modify their emotional experiences in response to internal or external stimuli. It plays a crucial role in mental health, social functioning, and overall well-being, enabling individuals to navigate challenges, maintain stable moods, and sustain healthy relationships [1]. Effective emotional regulation helps reduce stress, improve coping abilities, and prevent the development of emotional disorders like depression and anxiety. In contrast, emotional dysregulation, characterized by difficulties in controlling emotional responses, can lead to a range of psychological issues and maladaptive behaviors [2].

The neural mechanisms underlying emotional regulation involve key brain regions, including the prefrontal cortex (PFC), amygdala, anterior cingulate cortex (ACC), and insula. The PFC, particularly the dorsolateral and ventromedial areas, is critical for cognitive control and executive functions such as cognitive reappraisal, which involves reinterpreting a situation to alter its emotional impact [3]. The amygdala processes emotions, especially fear and threat, and emotional regulation often involves modulating its activity. Successful regulation typically requires top-down control from the PFC to inhibit excessive emotional reactivity in the amygdala [4].

The ACC and insula also monitor emotional states and regulate emotional responses. These brain regions form networks that balance emotional reactivity and cognitive control [5]. Disruptions in these circuits, particularly in the connectivity between the PFC and amygdala, are often linked to emotional dysregulation and conditions like anxiety, depression, and borderline personality disorder [6].

From a psychological perspective, emotional regulation strategies can be adaptive or maladaptive. Adaptive strategies, such as cognitive reappraisal and problem-solving, promote emotional resilience and healthier psychological outcomes. In contrast, maladaptive strategies, such as rumination (repetitively focusing on negative emotions) and suppression (inhibiting emotional expression), can exacerbate negative emotional states and are associated with poor mental health [7].

Genetic factors play a significant role in determining individual differences in emotional regulation. Studies have identified genetic variations that affect neurotransmitter systems involved in emotion regulation, including serotonin, dopamine, and oxytocin pathways [8]. For example, the 5-HTTLPR gene regulates serotonin reuptake and has been linked to emotional sensitivity and heightened reactivity to negative stimuli. Individuals with the short allele of this gene often show increased amygdala activity and reduced prefrontal control, making it more difficult for them to regulate emotions effectively, especially under stress [9].

Similarly, the COMT gene, which affects dopamine metabolism in the PFC, influences cognitive control processes involved in emotional regulation. Variants of this gene (e.g., the Val158Met polymorphism) can affect dopamine levels in the PFC, leading to differences in cognitive flexibility and the ability to reappraise emotional situations [9].

Understanding the genetic basis of emotional regulation is important because it provides insights into why some individuals are more prone to emotional dysregulation and psychological disorders than others. It also helps explain the variability in how people respond to environmental stressors, trauma, or therapeutic interventions [10]. By integrating genetic research with neuroscience and behavioral studies, clinicians can develop more personalized approaches to treatment. For instance, individuals with certain genetic predispositions may benefit more from cognitive-behavioral therapy (CBT), stress-reduction techniques, or pharmacological treatments tailored to their neurobiological profile [11].

Overall, investigating the genetic underpinnings of emotional regulation can lead to more targeted and effective treatments for emotional disorders, contributing to advances in precision mental health care.

Understanding how variations in genes influence individual distinctions regarding the capacity to regulate emotions successfully is at the center of the research problem concerning the genetic basis of ER. This field of research aims to identify the precise genetic markers, genes, and biological processes that regulate emotions, as well as how these elements interact with external factors to determine how people behave and react emotionally. The goal of studying the genetic basis of ER is to comprehend how differences in human genetics affect how people process and respond to their emotions. This area combines genetics, behavioral science, psychology, and neuroscience to investigate the molecular, neurological, and behavioral processes underlying ER. This review aims to identify genetic variants, understand neurobiological mechanisms, and explore behavioral phenotypes associated with ER.

1.1 Behavioral Phenotypes and Their Regulation

Attention deployment and rumination are central mechanisms in influencing emotional regulation, and understanding how they function can shed light on their powerful impact on emotional experiences. This mechanism involves shifting focus or directing attention to manage emotions. Focusing on specific aspects of a situation significantly impacts how we experience and regulate emotions. One of the most common strategies is distraction, where an individual deliberately shifts focus away from an emotionally charged stimulus. For example, when someone feels anxious, they may divert their attention to a neutral or pleasant activity, such as listening to music or working on a hobby. This can prevent the emotion from escalating by limiting exposure to the trigger. An effective distraction can help downregulate intense negative feelings in the moment, reducing distress. However, over-reliance on distraction can lead to avoidance, which might prevent long-term emotional processing [7].

Attention deployment can also be used in a mindful way, where the individual focuses entirely on the present moment without judgment. Mindfulness encourages attention to the current experience (thoughts, emotions, sensations) without trying to change it. This allows emotions to be experienced more fully but with less reactivity [12]. This can help reduce emotional reactivity and promote a more balanced emotional response, enhancing the ability to manage emotions rather than suppress them. People may also focus on particular aspects of a situation to regulate their emotions. For example, in a stressful event, focusing on the positive aspects (e.g., what can be learned) can help reduce emotional intensity and foster a more adaptive emotional response. This selective attention to positive or neutral stimuli can help reframe negative emotions and enhance emotional resilience [13].

The cognitive change is the broadest group of mental regulating approaches. It is described as a shift in perspective regarding a particular circumstance or the options for addressing it. Like the attention shift, the cognitive change is one of the anticipatory strategies employed when a situation creating conditionally negative emotions cannot be prevented or modified [14]. At that time, changing one's mental attitude becomes a helpful tactic for altering one's emotional state. However, the tasks employed in studies on cognitive change are incredibly diverse. They deal with various facets and interpretations of an emotional interaction [15]. One can differentiate between those that prompted a reevaluation of a particular circumstance and the identification of its advantages and those that resulted in the adoption of an alternative viewpoint, such as the observer's viewpoint or a reevaluation of the emotional experience [16]. A few academics also used a combination of the strategies mentioned earlier. We concentrated on the cognitive change technique known as reappraisal, which involves giving a situation a new meaning or adopting a different person's point of view [17].

1.2 Notable Practices for Skill Development in Emotional Regulation

The Acceptance and Commitment Therapy (ACT) method aims to develop a quality of life that accepts the pain of leading a purposeful life. Personally held values must be defined and clarified as the cornerstone for goal-setting and behavior modification [18]. ACT helps patients to: (1) accept internal occurrences (e.g., successfully handling painful thoughts and challenging emotions without avoidance); and (2) define and clarify these values. Psychological flexibility, or the capacity to live in the present, accept one's experiences with openness, and act according to one's values to

accomplish what is important, can lead to changes in behavior [19]. Providers may observe psychological inflexibility in patients who exhibit low self-awareness or excessive focus on the past (depression) or future (anxiety) during their interactions with them. To overcome resistance and identify the reasons for change, ACT urges clinicians and patients to explore "unworkable actions" and the inconsistency between principles and behavior in a nonjudgmental manner while practicing mindfulness and curiosity. There is evidence to support the use of ACT for people with pain, disabilities, chronic pain, anxiety, and related medical disorders (Figure 1) [20].

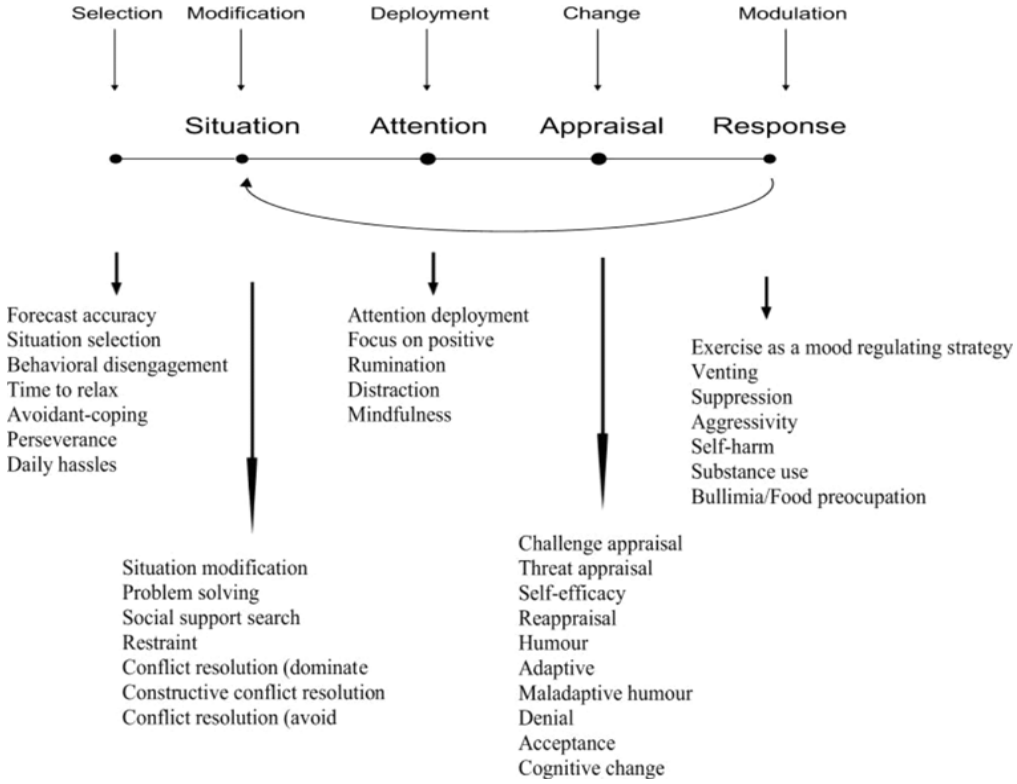

Figure 1 The process model of ER [21].

Although it was first intended to treat borderline personality disorder, dialectical behavior therapy (DBT) is a cognitive-behavioral, biopsychosocial intervention that has also been shown to be beneficial in treating anxiety, alcohol abuse, and eating disorders. The goal of DBT is to help people acquire coping mechanisms for managing emotions, including both excessive and insufficient control. The hypothesis of emotion dysregulation put out by DBT involves emotional susceptibility to external and internal stresses as well as an inability to control severe emotional arousal or verbal and nonverbal expressive emotional responses, even with the best of intentions, or to self-soothe [22].

Furthermore, some people have difficulty returning gradually to their emotional baseline after having strong reactions. DBT includes improved impulse control, interpersonal efficacy, and distress tolerance techniques. The idea of a "WISE mind," which describes reacting to circumstances that elicit emotional solid arousal while maintaining emotional equilibrium, is presented to patients. Assisting patients in developing coping mechanisms that don't require high emotional stimulation will improve their capacity to achieve their lifestyle objectives [23].

1.3 Neural Mechanisms Supporting Emotional Regulation

Although there are other techniques for consciously controlling one's emotions, reappraisal- an intentional modification of one's interpretation of an emotionally charged stimuli or circumstance- is the technique most frequently examined in brain imaging studies. The distinction between implicit and explicit ER-implicit forms, such as reappraisal, in which automatic processes may facilitate emotional change and there may be no conscious objective to regulate, has drawn more attention [24]. Explicit forms of regulation involve active goal-setting and require effortful control processes. Future research has to examine how the developmental trajectories of implicit and explicit modes of ER vary.

It has been demonstrated that reappraisal works well to enhance or suppress responses in systems related to affective responding. The amygdala, a subcortical region crucial for indicating the existence of and adjusting the encoding of affect-relevant stimuli, is foremost among them. The insula, a cortical region that represents information about the bodily conditions connected to affective responses, and the ventral striatum, another subcortical tissue implicated in signaling the desirable value of stimuli, are both affected by reappraisal [25].

A network of regions involving the posterior parietal cortex (PPC), anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (dlPFC), posterior medial prefrontal cortex (mPFC), and ventrolateral prefrontal cortex (vlPFC) are thought to be recruited during reappraisal, which modulates these regions. This group of brain areas is frequently active in tasks demanding cognitive control and is not specific to ER [26]. Working memory and selective attention tasks often cause the dlPFC to become active, which may help remember emotion-regulation techniques. vlPFC is frequently active during inhibition and response selection, which could be helpful when choosing a suitable reappraisal strategy. Lastly, activities requiring selection among conflicting responses often engage mPFC and ACC, which may aid in determining whether regulation is needed [27].

1.4 Genetic Foundations of Emotional Regulation

The process by which people control their emotions in response to external and internal stimuli is called ER. It is a complicated phenomenon influenced by many elements, including psychological, environmental, neurobiological, and hereditary influences. In recent years, there has been a rise in the number of studies devoted to comprehending genetics' role in ER. This has provided insight into the genetic foundations of emotional responses, diseases, and the variation in people's capacities for good ER [28].

Via a variety of processes, genetics significantly influences how well a person can regulate their emotions. These pathways include temperamental qualities, sensitivity to emotional illnesses, genetic predispositions influencing neurobiological processes, and gene-environment interactions. Neurobiological processes, including brain regions, neural circuits, and neurotransmitters, are the basis of ER. Genetic differences can affect these mechanisms, affecting how people experience, think through, and control their emotions [29].

1.4.1 Neurotransmitter Systems

Emotional reactions can be influenced by genetic polymorphisms in the genes encoding neurotransmitter systems, such as norepinephrine (NE), dopamine (DA), and serotonin (5-HT). For

example, disparities in emotional reactivity and susceptibility to mood disorders, including anxiety and depression, have been connected to polymorphisms in the serotonin transporter gene (SLC6A4). Genetic differences in serotonin activity are essential for ER since this neurotransmitter plays a role in emotional processing and mood regulation [30].

1.4.2 Brain Structure and Function

Brain regions that regulate emotions, like the anterior cingulate cortex (ACC), amygdala, and prefrontal cortex (PFC), are developed and operate differently depending on genetic variables. The amygdala is essential for processing emotional stimuli and producing emotional reactions, and the PFC is critical for cognitive control over emotions. Genetic differences can affect these brain regions' activity, connection, and structure, affecting how well someone can control their feelings [31].

1.4.3 Hormonal Systems

Genetic differences in genes that control hormonal systems, such as the hypothalamic-pituitary-adrenal (HPA) axis, can impact ER and stress reactions. Cortisol is a significant hormone involved in the HPA axis, which controls the body's response to stress. Changes in the genes that encode cortisol receptors (NR3C1, for example) or the enzymes involved in cortisol metabolism can impact resilience to stress and ER [32].

1.5 Serotonin Transporter Gene 5-Httlpr Polymorphism

The duration and amount of serotonin synaptic signaling during neurotransmission are controlled by a polymorphic serotonin-transporter-linked polymorphic region (5-HTTLPR) and serotonin transporter gene (5-HTT). The serotonin transporter's mRNA transcription is lower among carriers of the long-rs25531(G) (Lg) allele and the short (S) allele than in carriers of the long-rs25531(A) (La) allele variation [32]. It has been discovered that people without the La allele create roughly 50% less mRNA than people who are homozygous for the La allele. It has been demonstrated that this polymorphism correlates with the degree of emotion reactivity and mood dysregulation. According to a meta-analysis, the 5-HTTLPR polymorphism explains ten percent of the variations in activation of the amygdala, a brain area that regulates emotions. The study used a genotype of serotonin transporter and the amygdala activation [33].

Additionally, various emotional events have been demonstrated to cause increased amygdala activation, which is correlated with the S allele. People who have either the S or Lg allele are more than twice as likely to exhibit violent behavior than people who have at least one La allele, according to a study done on 82 children and adolescents [34]. The short allele of the 5-HTTLPR polymorphism has also been linked to mood instability, a defining feature of borderline personality disorder. According to a different study, including 91 teenagers, attachment may alter the impact of the 5-HTTLPR short allele on violent behaviors. These results imply that the 5-HTTLPR polymorphism regulates emotions and that environmental factors may moderate its influence on mood symptoms and related behaviors. Further investigation is required to corroborate these results and better comprehend this polymorphism's function in ER [35].

1.6 Other Genetic Polymorphisms Implicated in ED

Although serotonin is the main target of pediatric research on genetic variables related to emotion dysregulation, several additional loci may potentially be involved. A mutation from valine to methionine at position 158 (Val158Met) rs4680 in the enzyme that breaks down dopamine is encoded by a functional single-nucleotide polymorphism in COMT gene. Compared to the Met form, the Val version catabolizes dopamine more actively. Previous research has demonstrated a link between the COMT Met allele and more severe ED in kids and teenagers [36]. According to a study involving 277 kids and teenagers, those who carry the Val allele are more prone than their counterparts who do not feel agitated when they do not receive the expected rewards immediately. These findings imply that the link between dopaminergic tone and mood control may not be linear, which may confound the role of COMT (Val158Met) polymorphisms in the regulation of mood [37].

Emotion dysregulation may also be influenced by additional genetic variants linked to D2 dopamine receptor binding affinity, such as the kinase domain, one polymorphism, and the dopamine receptor D2 (DRD2/ankyrin repeat). The DRD2 Taq A1 variant has been linked to increased emotionality and sensitivity to negative feedback while concurrently lowering sensitivity to positive input, according to research on 65 children. Additionally, in event-related potential trials, children with the short allele (S) for the 5-HTTLPR gene may exhibit increased sensitivity to error processing, according to the same study. When comparing the S-allele cohort to the homozygous L-allele cohort, there was a significant increase in both early error-related negativity and later error-related positivity. These electrophysiological signals are believed to represent anterior cingulate activity [38].

Preclinical and clinical investigations, mostly on adults, have identified other genetic variations linked to mood dysregulation. It's also important to consider how these variations affect mood dysregulation in children. Adolescent carriers of the monoamine oxidase-A (MAOA) promoter variants linked to a reduced gene expression may be more violent and impulsive than carriers of the MAOA promoter variant connected with a higher gene expression. When exposed to an anger trigger, people with low-expression MAOA variants may have less activation in the left middle frontal gyrus, left amygdala, and posterior thalamic regions than the control group [39].

2. Materials and Methods

2.1 General Background

Several potential genes and genetic variations linked to ER have been found through genetic research. These genes frequently affect neurodevelopmental pathways and neurotransmitter systems (such as dopamine and serotonin), which affect how emotions are processed and regulated. Variations in these genes can influence individuals' perception, experience, and regulation of emotions in response to internal and external events. Results can be influenced by the interaction of environmental circumstances and genetic predispositions to ER. The way that genetic variants manifest in ER capacities and vulnerability to mental health illnesses, for instance, can be modulated by early life experiences, cultural variables, social support, and stress. Integrative analyses consider the relationships between genes and environments to comprehend how contextual circumstances and genetic predispositions interact to affect ER throughout life.

2.1.1 Inclusion Criteria

Studies were included according to the following PICO: Population: individuals with various behaviors; Intervention: the role of identifying genetic variants, neurobiological mechanisms, and behavioral phenotypes; Comparator: no comparator. And outcome: the emotional regulation and behavioral changes.

- Research methodology includes Randomized clinical trials (RCTs), observational studies, cohort studies, and case-control studies.
- We selected articles from 2010 to 2024 to refresh our knowledge.
- Studies that highlighted the genetic basis of ER.

2.1.2 Exclusion Criteria

- Secondary articles, non-peer review articles such as study proposals, opinions, meta-analyses, and letters to the editor.
- Articles not related to our topic.

2.1.3 Information Sources

We performed our study according to the PRISMA guidelines. We searched multiple online databases including; Web of Science, Cochrane Library, Google Scholar, PubMed, and Scopus. We used the following keywords in the search, “genetic factors”, “genetic markers”, “Emotional regulation”, “emotional dysregulation”, and “behavior” throughout the process. It helped us encompass possibly every academic article related to the research topic for analysis.

2.2 Data Collection

The involved articles were assessed in three phases. The first step started with importing the results of our research strategy from online databases into a sheet of Microsoft Excel utilizing EndNote Software, which removed duplicate studies. During the second phase, the titles and abstracts of the papers put into the Excel sheet were reviewed by two independent authors. The evaluation of the relevant citations from Stage Two came next. We also double-reviewed the research' citations to make sure no ones were overlooked. Finally, three authors performed the data extraction process, and a fourth revised them.

2.3 Qualitative Analysis

We carried out a qualitative analysis of the earlier research findings. Since our study is a narrative review, we were unable to do a quantitative analysis. In order to conclude, it is necessary to identify and compare more than two studies that provide data on the outcomes that will be examined in the quantitative analysis. To get strong evidence and current results and conclusions, we conducted a qualitative analysis of papers relevant to our topic, presented their findings, and compared them.

3. Results

3.1 Summary of the Included Studies

Our search results are demonstrated in the PRISMA flow chart (Figure 2). We involved 12 studies [40-51] that met the inclusion criteria of our narrative review. Our study involved 6114 individuals divided into 4511 females and 1603 males. The mean age of the included participants was 18 years. Table 1 demonstrates the characteristics of the involved studies and patients.

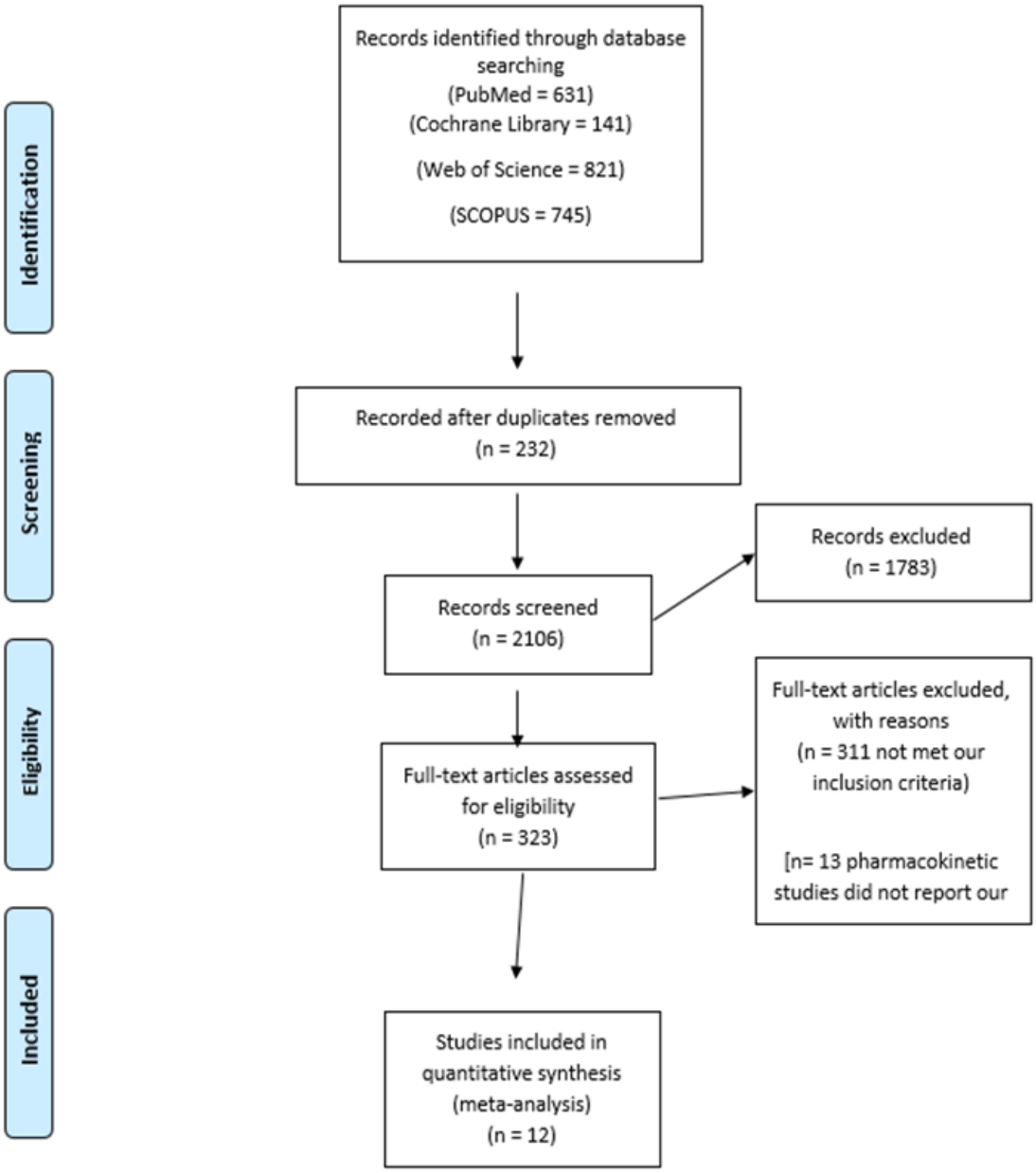

Figure 2 PRISMA flow diagram of literature search.

Table 1 Demonstrates the characteristics of the involved studies and patients.

Study ID	Year	Tool used to assess ER	Genetic association	Polymorphisms studied	Sample population	Genes
Amstadter et al. [40]	2012	BIRD	5-HTTLPR biallelic, rs4680	5-HTTLPR biallelic, rs4680	218 early adolescents	SLC6A4, COMT
Yen et al. [43]	2018	ASQ	G	ESR α-Xbal	100 Taiwanese women with PMMD; 96 controls	Estrogen Receptor α Gene (ESR1)
Bîlc et al. [41]	2018	Tasks	---	rs6265	266 students from Romania	BDNF
Weiss et al. [42]	2014	SEAS	COMT: G (in the Intra-personal Domain)	5-HTTLPR biallelic COMT: rs4680	289 healthy women from Germany	SLC6A4, COMT
Byrd et al. [44]	2020	PAI-BOR	rs53576 (GG)	rs53576, rs2254298	2450 American female children	OXTR
Viddal et al. [51]	2017	ERC	S (association present only at age 6)	5-HTTLPR biallelic	602 Norwegian children	SLC6A4
Halldorsdottir et al. [45]	2017	CERQ	---	rs9296158, rs3800373, rs1360780, rs9470080	1345 genotyped adolescents of Portuguese descent	FKBP5
Propper et al. [50]	2012	ERC	rs1800497 (in males)	DRD4: VNTR EX3, DRD2: rs1800497	206 children were evaluated through ERC by teachers and parents.	DRD2, DRD4
Kataja et al. [46]	2020	Tasks	---	rs4570625	330 Finnish children (8 months of age)	TPH2
Noroña et al. [49]	2018	DCS	---	5-HTTLPR triallelic	99 children aged 3 from the USA	SLC6A4
Murakami et al. [48]	2009	Tasks	S	5-HTTLPR biallelic	24 undergraduate and graduate students from Japan	SLC6A4
Kochanska et al. [47]	2009	Tasks	(association present only in 'insecurely attachment' sample)	5-HTTLPR biallelic	89 American children	SLC6A4

3.2 Results of Quality Assessment

We assessed their quality using Cochrane's tool since we included twelve observational studies [40-51]. Cochrane's tool indicated that the mean score of the observational studies was 9.07 out of 14. The quality evaluation of the observational studies in detail in Table 2.

Table 2 Shows the quality assessment of the included studies.

	Amstadter et al. [40]	Bîlc et al. [41]	Byrd et al. [44]	Halldorsdottir et al. [45]	Kataja et al. [46]	Kochanska et al. [47]	Murakami et al. [48]	Noroña et al. [49]	Propper et al. [50]	Viddal et al. [51]	Weiss et al. [42]	Yen et al. [43]
1. Was this paper's goal or research question made clear?	1	1	1	1	1	1	1	1	1	1	1	1
2. Was the target population for the study well-defined and specified?	1	1	1	1	1	1	1	1	1	1	1	1
3. Was at least 50% of eligible individuals participating?	1	1	1	1	0	1	1	1	1	0	1	0
4. Did all the participants come from the same or comparable populations, and did they all participate over the same period?	0	1	1	1	1	0	1	1	1	1	1	1
5. Was there a power description, an explanation for sample size, or estimates of effect and variance?	0	0	0	0	0	0	0	0	0	0	0	0
6. Were the exposure(s) wanted to be measured before the outcome(s) were determined for the	1	1	1	1	1	1	1	1	1	1	1	1

analysis in this paper?												
7. Was the duration such that one could fairly anticipate seeing it if a relationship between outcome and exposure existed?	1	1	1	1	1	1	1	1	1	1	1	1
8. Was the study's relationship between different exposure levels and outcomes for exposures that can change in quantity or degree (such as exposure categories or exposure measured as a continuous variable) examined?	1	1	1	1	1	1	1	1	1	1	1	1
9. Were the exposure measures, or independent variables, well-defined, legitimate, dependable, and applied similarly to every study participant?	1	1	1	1	1	1	1	1	1	1	1	1
10. Was there a repeated evaluation of the exposure(s) throughout time?	0	0	1	0	0	0	0	1	0	0	0	0
11. Were the dependent	1	1	1	1	1	1	1	1	1	1	1	1

variables, or outcome measurements, properly defined, dependable, valid, and applied similarly to every study participant?												
12. Were the people evaluating the results blinded to the participants' exposure status?	*	*	*	*	*	*	*	*	*	*	*	*
13. Was the follow-up loss 20% or less of the baseline?	1	1	1	1	1	1	1	1	1	1	1	1
14. Has the impact of important potential confounding variables on the link between outcome(s) and exposure(s) been quantified and statistically adjusted?	1	0	1	1	1	1	0	1	1	1	1	1
Total score (out of 14)	10/14	10/14	12/14	11/14	10/14	10/14	10/14	12/14	11/14	10/14	11/14	10/14

Key: 1 = Yes, 0 = No, * = Not reported, N/A = Not applicable.

Out of all the genes studied in relation to ER, SLC6A4 was the most frequently found. In an attempt to reconcile the existing genetic data at the time with the findings from neurology, a few hypothetical models were put up. The primary hypothesis was that, depending on the polymorphism, SLC6A4 functional variations would cause the amygdala nuclei to be more or less reactive to outside events, resulting in a weaker or stronger emotional reaction [52].

Six gene-association studies were discovered regarding SLC6A4 and its relationship to ER, with the majority focusing on adolescents and children. Of these, three confirmed the null hypothesis [42, 47, 49], two indicated a relationship with the short allele, and one indicated a relationship with a polymorphism (rs4680) [40, 48, 51]. Furthermore, no relationship was found between SLC6A4 and ER in genome-wide association studies. Associations with catechol-ortho-methyltransferase (COMT) were discovered in two studies [40, 42]. A correlation with the oxytocin receptor was found in many young girls. Indeed, the possibility that such a gene could have psychological and mental effects is not unreasonable. It's interesting to note that prosocial behavior, angry reactions, and- most crucially, in this context- empathy appear to be correlated with blood and brain levels of oxytocin [44].

The findings show that individuals homozygous for the l allele were less likely than those with two or one copy of the s allele of the 5-HTTLPR polymorphism to misbehave on the task (i.e., decide to give up). In addition, compared to Met homozygotes, those with the Val allele of the COMT Val158Met polymorphism were likelier to give up on the task. The two polymorphisms were combined to form a summative risk allele score, and each risk allele was linked to a 1.75-fold greater odds of giving up the job. According to exploratory analyses, emotional abuse mediated the association between the genetic risk allele and BIRD performance and the 5-HTTLPR [40].

A child's attachment security reduced the impact of their genotypes: 5-HTTLPR polymorphism-possessing a short allele, ss, or sl-was linked to a reduced ability to regulate one's behavior in the preschool age. But by the end of the first year, that risk was only natural for kids with an insecure attachment to their mothers; it didn't exist for kids with a secure attachment [47].

The CATT haplotype (carriers against non-carriers) was estimated using the genotypes rs1360780, rs3800373, rs9296158, and rs9470080. Adolescent CATT haplotype carriers with greater levels of childhood psychological trauma indicated higher levels of both catastrophizing and rumination compared to non-carriers, which is consistent with our predictions and earlier findings.

The results of this study point to potential psychological mechanisms explaining why FKBP5 haplotype carriers who experience childhood psychological trauma are more likely to develop a psychiatric problem later in life, given the correlation between these maladaptive emotion-regulating systems and mental disorders [45].

4. Discussion

Determining how genetic factors affect how people perceive, experience, and control emotions is a multifaceted endeavor combining genetics, neuroscience, and behavioral sciences. This thorough investigation covers the complex relationships between the environment and genes and spans multiple levels of research, from behavioral traits to molecular genetics.

Individual variations in ER have been connected to temperamental variability, physiological processes, and parental behaviors; genetic factors have not received much attention as a possible source of variability in early childhood ER. The current data are consistent with our hypothesis,

which states that working memory and ER are related because of substantial genetic overlap and that differences in ER in toddlerhood are caused by environmental and genetic factors [53]. Genetic impacts may demonstrate the extensive effects of genetic factors on individual variations in ER, a mixture of various psychological systems. Genetic effects may impact temperamental traits, physiological processes, and parental behaviors, which are sources of variability in ER. These effects may overlap with those in the ER. In another way, the relationships among physiological functions, temperaments, parenting, and ER may have a hereditary component [53].

Interestingly, the impacts of genetics and/or environment could be dynamic over time as opposed to static (i.e., the effects could vary with age). For example, visuospatial working memory capacity showed an age × genotype relationship. In particular, the impact of the COMT gene's Val158Met polymorphism on working memory varies with age. Compared to Val carriers, those with the Met/Met genotype experienced higher levels of working memory beyond the age of ten but lower levels before that [54]. Additionally, at 6-7 months, but not at 18-20 months, the Val158Met polymorphism of the COMT gene was linked to positive affect, a temperamental trait associated with ER, which may indicate a potential developmental shift in the genetic effects on ER. It seems plausible that the genetic covariation between working memory and ER may alter with age, given the evidence of differing genetic influences across age groups. Further research is required to investigate the longitudinal routes (such as a genetically informative cross-lagged study) that support the development of working memory and ER [53].

A possible pathway through which deficiencies in working memory and ER may emerge in the illnesses is the hereditary connection between the two functions. People with trouble controlling their emotions may benefit from treatment tactics that increase working memory, and vice versa, because of the overlapping mechanisms underlying individual variability in working memory and ER. Therefore, treatments that focus on only one of them may be able to improve working memory and ER.

Emotion dysregulation in adolescents completely mediated the OXTR-moderated link between general psychopathology and early threat exposure, and the strength of this impact was driven by allele-dependent changes in the correlation between emotion dysregulation and early threat exposure [55]. Increased emotion dysregulation in adolescents predicted general psychopathology for all women, and this was especially true for those who inherited at least one copy of the rs53576 A allele and were exposed to early threats. This aligns with earlier studies that found links between threat exposure, OXTR, and dysregulated emotions [56]. Additionally, a larger body of literature has shown that ER problems are a significant transdiagnostic measure of risk [57].

Early childhood (ages 3 to 6) sees a decline in ED in children, and gene-environment interactions partly explain individual differences in the developmental trajectories of ER. The genotype of the serotonin transporter interacts with both conditionally good and conditionally bad parenting styles to predict ED growth trajectories. Under highly positive or minimally negative parenting, children with the SS genotype seemed to experience a reduction in ED at a faster rate.

The ED trajectories of kids with the SL/LL genotype were not significantly impacted by parenting [49].

Propper et al. demonstrate that risk alleles for dopamine receptor genes (dopamine receptor D2 for males, dopamine receptor D4 for females) are linked to less responsive parenting, based on numerous waves of data from the Durham Child Health and Development Study. Parenting mediates the relationship between the D4 dopamine receptor and all academic results in females.

Evidence suggests that parental involvement impacts girls' withdrawn classroom behavior, which in turn affects instructors' evaluations of students' academic achievement. There is evidence that parenting affects boys' ability to regulate their emotions, and this ability is linked to both the Woodcock-Johnson subscales and instructors' evaluations of their academic behavior [50].

There is growing evidence that stress and peripheral inflammatory signals play a part in the multifactorial etiology and physiopathology of mental illnesses. Notably, inflammatory insults and peripheral inflammation may affect the neuroimmune milieu of the central nervous system, with neuronal circuits responsible for regulating emotions being susceptible. A previous narrative review confirmed the connection between ED and the inflammatory process [58].

The convergence of behavioral data and neurobiological findings demonstrates that genetic factors, brain function, and neurotransmitter systems influence emotional regulation. Genetic variants, such as those in 5-HTTLPR, COMT, and OXTR, affect the structure and functioning of key brain regions like the prefrontal cortex and amygdala, influencing emotional regulation behaviors.

Behavioral assessments show that genetic influences manifest in different emotional regulation strategies, such as cognitive reappraisal or expressive suppression. Moreover, gene-environment interactions and epigenetic changes highlight the importance of genetic predispositions and environmental factors in shaping emotional regulation across the lifespan. Through integrative analysis, it becomes clear that genetic variation influences emotional regulation by modulating neurobiological systems reflected in observable behavioral patterns.

This review is limited by the small sample size and insufficient studies identifying the genetic variants and behavioral phenotypes associated with ER. Future research in emotional regulation should focus on expanding the scope of integrative, longitudinal, and multi-faceted studies that bridge genetic, behavioral, and neurobiological approaches.

5. Conclusions

The significant findings highlight that genetic, neurobiological, and environmental interactions shape emotional regulation. Genetic variants, such as 5-HTTLPR and COMT, influence brain regions critical for emotion regulation (e.g., prefrontal cortex, amygdala), while neurotransmitter systems (serotonin, dopamine) modulate emotional reactivity and regulation strategies. Gene-environment interactions and epigenetic changes further shape emotional regulation across the lifespan, particularly in response to stress and trauma. These insights have significant clinical implications, particularly for developing personalized treatments. By understanding an individual's genetic predispositions, clinicians can tailor interventions like cognitive-behavioral therapy (CBT), mindfulness, or pharmacotherapy to suit their emotional regulation profile. For example, individuals with heightened emotional reactivity due to specific genetic markers may benefit more from targeted stress-reduction strategies or therapies that strengthen cognitive control. Ultimately, integrating genetic profiles into clinical practice could lead to more effective, individualized approaches to managing emotional dysregulation and mental health disorders.

Author Contributions

Mykhailo Zhylin: Conceptualization, writing – original draft, formal analysis, writing – review and editing. Viktoriia Mendelo: Software, writing – review and editing. Svitlana Bondarevych: Methodology, writing – review and editing. Yuliia Kokorina: Conceptualization, writing – original

draft, writing – review and editing. Andrii Tatianchykov: Supervision, validation, writing – review and editing.

Competing Interests

The authors have declared that no competing interests exist.

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