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Genetics and Cognitive-Behavioural Theory Explaining Anxiety

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ABSTRACT

Although occasional anxiety is considered a normal and adaptive emotion, when excessive or persistent, it can lead to significant functional impairment and the development of severe anxiety-related psychopathology. While acknowledging the multifaceted aetiological nature of the anxiety disorders spectrum, this article discusses one biological and one psychological-based approach, delving into the significant roles of genetic predisposition and cognitive-behavioural theoretical framework in understanding anxiety disorders. Genetic factors contribute substantially to their onset, with heritability explaining up to 40% of the variance. Various genetic markers and mutations have been identified, illuminating the intricate interplay between genes and neurobiological pathways. Additionally, cognitive-behavioural theory elucidates how maladaptive cognitive processes perpetuate anxiety. Distorted cognitive schemas and dysfunctional core beliefs characterise the cognitive landscape of anxiety disorders, influencing emotional responses and behaviour patterns. While both genetic predisposition and cognitive-behavioural processes offer valuable insights into anxiety disorders, methodological limitations in existing research, particularly regarding inconsistencies due to self-reported data and measurement tools issues, require reconsideration. Understanding in-depth the interaction between genetic predisposition and cognitive-behavioural processes is crucial for developing comprehensive treatment approaches; still, this remains an area of ongoing research. Future studies should focus on gene-environment interactions and neurobiological mechanisms underlying anxiety disorders, implementing advanced genomic and neuroimaging techniques; additionally, twin studies of molecular genetics could be beneficial in identifying specific genetic markers associated with anxiety-related cognitive biases and maladaptive schemas.

Keywords: Anxiety disorders, aetiology, genetic predisposition, cognitive-behavioural theory

EXAMINING THE COMPLEX AETIOLOGY OF ANXIETY DISORDERS: GENETIC INFLUENCES AND COGNITIVE-BEHAVIOURAL DYNAMICS

Occasional anxiety is by nature a normal and sometimes useful emotion in a daily routine, since, defined as ''non-pathological'', it acts protectively for an individual facing a threatening situation, or it motivates one by making them more productive and able to cope with everyday challenges (Penninx et al., 2021). However, its manifestation's intensity, duration, and frequency often have a detrimental impact on an individual's ability to function effectively in personal, social, and professional settings, resulting in being evaluated as "pathological" (Chand & Marwaha, 2022). Excessive and persistent anxious behaviour has the potential to escalate further and lead to the development of severe anxiety-related psychopathology (American Psychiatric Association, 2013).

Anxiety disorders rank as the most prevalent mental health conditions (Comer, 2012; Hollander & Simeon, 2011), as they appear to affect 18% of the global (Daitch, 2011; Kessler et al., 2005, 2010) and 15% of the European population (Wittchen et al., 2011). An estimated 301 million adults worldwide suffer from anxiety disorders (Institute for Health Metrics and Evaluation, 2019), with a greater prevalence for females (63%) compared to males (37%; World Health Organization, 2017), while in the general population, one in three appear to be experiencing severe anxiety-induced symptoms at some point in their lives (Bandelow & Michaelis, 2015; Kessler et al., 2005). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) lists different types and categories of anxiety disorders, such as Generalized Anxiety Disorder, Panic Disorder, Social Anxiety Disorder, and several Phobia-related Disorders (American Psychiatric Association [APA], 2013). These disorders are marked by cognitive dysfunction and/or emotional distress caused by maladaptive cognitive systems related to the interaction of fear and anxiety (APA, 2013; Nolte et al., 2011). However, there are complexities and differences among them regarding risk factors, age ranges of onset, course, and symptomatology, which makes the detailed investigation of the aetiological factors of anxiety disorders particularly interesting.

AETIOLOGICAL APPROACHES

Given that the majority of scientific opinion agrees that no single causal theory can fully explain mental disorders as their manifestation is due to the interaction of various variables (Barlow et al., 2018; Dobson & Dozois, 2019), it would be ideal to take into account all aetiological approaches. Nevertheless, acknowledging, though, that aetiology is a confluence of various biopsychosocial parameters, this paper is limited to the analysis of two aetiological approaches: i) the biological theory on the axis of (epi-)genetics and ii) the psychological approach based on the Cognitive-Behavioural model.

Biological Perspective on Anxiety Disorders: Genetic Factors

From a biological perspective, family, especially twin studies, clearly indicate the significant involvement of heredity and genetic predisposition, placing them among the most prevalent predictive and possible causal factors (Hettema et al., 2001; Lieb et al., 2000). Findings suggest that the likelihood of developing an anxiety disorder increases when at least one of the parents is already affected (Johnson et al., 2008; Wittchen, 1998) and accretes depending on the severity of the symptoms or any potential comorbidity (Schreier et al., 2008). A wide range of twin studies comparing monozygotic (MZT) and dizygotic twins (DZT), in terms of the general manifestation of anxiety disorders, have shown higher rates in MZTs (Andrews et al., 1990; Kendler et al., 1992a, 1992b; Skre et al., 1993). In particular, Andrews et al. (1990) found a concordance rate of 64% among MZTs and 44% among DZTs for any

anxiety disorder. Studies examining genetic influences on biological traits suggest that in major anxiety disorders such as panic disorder (PD), Specific Phobia (SP), Social Anxiety Disorder (SAD) and Generalized Anxiety Disorder (GAD), similar, possibly inherited, recessive genomes are identified (Kendler et al., 2003) and that mutations on chromosomes 1, 2, 15, and 16 may account for vulnerability to anxiety (Webb et al., 2012).

In PD, the most widely studied anxiety disorder, there is a greater involvement of heredity when compared to the rest of the spectrum (Finn & Smoller, 2001). Genetic factors have a moderate effect on individuals with PD, according to findings from family and population-based twin studies (Lopez-Sola et al., 2014; Maron et al., 2010; Spatola et al., 2011), explaining about 30% of the variance in predisposition. Moreover, Merikangas et al. (2003) argued that individuals with affected first-degree relatives are four times more likely to develop SAD and SP than those without a relevant family history. Additional findings show that the hereditary factor holds an important role in the manifestation of blood-related phobias (e.g. injections, bleeding wounds etc.) and co-attribute the manifestation of situational phobias and zoophobias to similar genes (Czajkowski et al., 2011; Le Beau et al., 2010; Neale et al., 1994). In the case of Neale et al. (1994), however, issues of internal and external validity were underlying, as out of 541 MZT and 388 DZT female twin pairs, only 124 participants appeared to suffer from SP (based on self-reports over the telephone), while only 11 of them perceived it as a ''disorder''. A subsequent study (Gratacòs et al., 2001) found an interesting association involving a specific mutation, the duplication of a certain part of the chromosomal region 15q24–26, and irrational fears and phobias. A limitation of this study, however, was the phenotypic classification of the participants in the absence of a detailed description of their clinical picture (Morris-Rosendahl, 2002).

Family and twin studies also point to a hereditary component for SAD and GAD; observing their onset in several members of the same family reinforces the notion of genetic influences, especially when considering that the presence of the RBFOX1 gene often constitutes a risk factor for developing GAD (Davies et al., 2015; Scaini et al., 2014; Villafuerte & Burmeister, 2003). Interestingly, the genetic predisposition appears to be positively associated with a general vulnerability to the development of acute anxiety and related disorders, alongside significant involvement of the prefrontal cortex, amygdala, and hippocampus (Bas-Hoogendam et al., 2016). Additionally, genetic studies have shown that neuronal abnormalities, such as (hyper-)excitation or inhibition of neurotransmission, are associated with the inheritance of defective genes involved in the neurotransmission structures of glutamate, serotonin, dopamine, and norepinephrine (Maron et al., 2010). Researchers speculate that these neuronal abnormalities serve as the genetic foundation for the modulation of specific personality traits linked to anxiety disorders, including high neuroticism (Hettema et al., 2006) and behavioural inhibition (Smoller et al., 2003). In the causal dimension of general biological vulnerability to anxiety, the Triple Vulnerability Model (Barlow, 2000, 2004) proposes the (potentially inherited) personality traits of neuroticism and introversion, which appear to be positively associated with anxiety disorders (Brown & Naragon-Gainey, 2013). Finally, scholars have argued that the development of anxiety disorders may be induced through epigenetic mechanisms, potentially triggering the development of anxiety even within the fetus (Hompes et al., 2013; Non et al., 2014). Pregnant women with a current diagnosis of anxiety disorder who did not receive treatment have demonstrated methylation of deoxyribonucleic acid (DNA) at the promoter of the glucocorticoid receptor gene, NR3C1, in cord blood and the genome, increasing the risk for the

unborn fetus to develop an anxiety disorder (Non et al., 2014; Patriquin & Mathew, 2017).

As far as the limitations are concerned, biological approaches, while offering scientifically based explanations of genetically related individuals' behaviours, have been criticised for abstract and deterministic reasoning, oversimplifying the complexity of human nature, and failing to account for intervening variables such as cognitive processes and nurture/environment (McLeod, 2017). In addition, gene-related studies may sometimes provide inaccurate findings of questionable reliability due to inconsistencies in replications and small effect sizes (Kendler, 1992a; Shimada et al., 2015). Several aetiologies could be to blame, such as the absence of homogeneity in genetic levels, variation in phenotypic evaluations, and differences in individual characteristics and environment (McLean et al., 2009). Moreover, although the higher coincidence rates in anxiety disorders among MZTs suggest an aetiological genetic background, the time of onset, as well as the type of disorder, often varies, perhaps suggesting the important interference of personal experiences (Gross & Hen, 2004). It is observed that even with the highest rates of genetic factor involvement (40%), the remaining percentage is explained by non-genetic factors. Therefore, given that prediction or correlation does not imply causation, the findings can be interpreted as strong evidence of heritability involvement in combination with other parameters and might help to explore more precise mechanisms of heritability-environment interaction. This is further supported by the Diathesis-Stress model (Broerman, 2017), suggesting that even if there is a genetic predisposition to certain behaviours, the likelihood of manifestation is related to other triggering or causal factors.

Psychological Perspective: The Cognitive-Behavioural Model

One of them is the psychological parameter, which for the present article's objectives was chosen to be developed based on Beck's Cognitive-Behavioural theory, the most scientifically documented to date (Feltham & Horton, 2000). The cognitive-behavioural theory posits that the primary human characteristic, i.e. cognition, along with all senses, receives information, processes it, and evaluates it in interaction with the environment (Beck, 2011). A continuous cyclical process therefore unfolds, consisting of cognitions and beliefs interdependent with emotions, behaviours, and bodily reactions. The model proposes that either the genetic predisposition (for specific personality traits) or learning through prior childhood experiences and interaction with the environment construct cognitive schemas, and it attributes the existence of dysfunctional core beliefs and repetitive patterns of behaviour to distorted fixed schemas (Beck, 2011; Harila,1998).

Particularly for anxiety, the cognitive theory concentrates on content and anxious reasoning, linking the emergence of anxiety disorders to either cognitive distortions (Beck, 2011) or processing issues that result in misinterpretations (Kuru et al., 2018). In terms of cognitive errors, two of the most prevalent in anxiety disorders are catastrophising and personalisation (Kuru et al., 2018), i.e., the tendency to overemphasise negative events or experiences, and attribute full blame or guilt to the self for the negative outcome of a situation, respectively (Beck, 2016). In addition, a perception of a high external locus of control, i.e., a belief of helplessness, with an accompanying feeling of inability to control a situation (and/or behaviour) by the individual (Rotter, 1966; Schepers, 2005), shows a positive correlation with the development of anxiety disorders (White et al., 2006).

Similarly, in terms of problematic processing of stimuli, the way an anxious person thinks negatively about themselves

(vulnerable), others (threatening), and the future (unpredictable/threatening --> need for constant vigilance) constitutes the Anxiety Triad (Blackburn & Davids, 1995). This cognitive vulnerability, considered one of the key risk factors, is characterised by misinterpretation of events due to overestimation of the severity of the threat and underestimation of one's ability to respond (Riskind & Williams, 2006). The individual, therefore, becomes particularly prone to misinterpreting situations as stressful when dysfunctional cognitive schemas interfere with cognition, possibly resulting in the development of "fear of fear" (anticipatory anxiety), a cognitive framework that aptly explains Agoraphobia (Goldstein & Chambless, 1978; Riskind & Williams, 2006). The above position is supported by research, as hypersensitivity, false overestimation of potential threats, and related cognitive distortions are common perpetuation behaviours in disorders such as SP (Wenzel et al., 2005), PD, and Agoraphobia (Busscher et al., 2013; Craske & Barlow, 2014; Sandin et al., 2015).

According to Clark and Beck (1988), when a situation is falsely assessed as dangerous by one suffering from pathological anxiety, a physiological change in the Autonomic Nervous System is triggered (fight-or-flight response), and the individual adopts an abnormal behaviour as a coping strategy. The individual often fails to perceive the true dimension of this dysfunctional behaviour, characterised by endless fear, anxiety, and a constant search for potential dangers, since they construct it as a defence mechanism. This framework seems to apply to those affected by SAD (Austin & Kiropoulos, 2008) and GAD (Clark et al., 1997), and particularly to individuals with PD, who tend to perceive and interpret their bodily responses as potentially fatal because of catastrophising (Austin & Richards, 2001; 2006). This behaviour's stress during the progression of a panic attack episode triggers additional stress-induced physiological responses, which in turn appear even more threatening, creating, thus, a vicious cycle (Ohst & Tuschen-Caffier, 2018).

The primary behavioural model of anxiety development and maintenance is Mowrer's Two-Stage Theory of Fear and Avoidance, proposed in 1947, which suggests that fear of a particular stimulus is the result of learning, as it is generated through Classical Conditioning Learning (Rehman et al., 2022) and maintained through Operant Conditioning Learning (Staddon & Cerutti, 2003). Embedded phobic responses are believed to be maintained by the repetitiveness of specific behaviours modelled by the individual to avoid the distress caused by the fearful stimulus (Krypotos et al., 2015; Mowrer, 1947). The ensuing temporary relief creates a process of Operant Conditioning Learning, which reinforces the perpetuation of avoidance behaviour toward the anxiety-provoking stimulus at hand.

Along with the abovementioned theories of "fear learning," the dimension of learning through modelling and imitation (Bandura & Rosenthal, 1966) is added, completing the theoretical framework of hermeneutic analysis of disorders related to phobic reactions, such as SP, PD, and Agoraphobia (Field & Purkis, 2012; Milosevic & McCabe, 2017). The famous "Little Albert" experiment with the acquired (induced) phobia in rats (Watson & Rayner, 1920) and other studies of children with pre-existing phobias further support this theory (Askew et al., 2016; Reynolds et al., 2017). However, several laboratory studies have called these interpretations into question, as they failed to manipulate the phobic response (Gamble et al., 2010; Milosevic & McCabe, 2017). Moreover, animal, and human experiments attributing the phenomenon to amygdala lesions (Hassoulas et al., 2013; McCue et al., 2014) demonstrate that the model struggles to explain how avoidant behaviour is often adopted without prior overt stimulation (absence of learning conditions). Finally, although the model adequately explains the acquisition and maintenance of phobias, it

cannot be extended and generalised to explain pervasive anxiety and its associated disorders, such as GAD (Behar et al., 2009). These shortcomings gave rise to the development of later cognitive models falling under the umbrella of the Third Wave of Cognitive behaviourism, such as Wells and McNicol's (2014) Meta-cognitive theory, which proposes a discrepancy and ambivalence between positive and negative attitudes towards anxiety and worry (Knowles et al., 2016). Two types of worry are distinguished: excessive, pathological worry about everyday life and ‘’meta-worry’’, i.e., the creation of negative emotions and self-dissatisfaction regarding one's tendency to worry (Craske, 2016; Wells, 2014). Complementing the above, the ''Intolerance of Uncertainty'' theory (Dugas et al., 2012; Freeston et al., 1994), comes to argue that the individual suffers when even imagining that something negative could potentially occur and, thus, becomes particularly vulnerable to the development of anxiety disorders (Koerner et al., 2017). Both theories seem to explain the development of GAD (Dugas et al., 2004; Koerner et al., 2017) and SAD (Boelen & Reijntjes, 2009); particularly, concerning SAD (Boelen & Reijntjes, 2009), the ''intolerance of uncertainty'' trait seems to be associated with excessive social ambitions and expectations of the individual, which develop during childhood within a potentially invalidating, controlling family environment (Osmanağaoğlu et al., 2018; Rodebaugh et al., 2017; Sanchez et al., 2017) and is possibly inherited (Sanchez et al., 2016).

Considering the limitations, despite the aforementioned cognitive-behavioural models appearing to satisfactorily explain the spectrum of anxiety disorders, related studies exhibit methodological limitations. As most data are self-reported, the participant must recall past unpleasant emotions and stressful situations. Given that short-term memory's emotion recall process differs qualitatively from long-term memory (Robinson & Clore, 2002), such methodologies that require participants to self-refer to present distress or, conversely, to recall emotionally negative-valence memories, may lead to inconsistencies and divergent findings. In addition, evidence shows that participants -particularly those affected by GAD- respond differently between methods of physiological measures and self-report (Borkovec & Hu, 1990; Decker et al., 2008). As a result, there is a need for more objective measurement tools in this population, such as the inclusion of historical data, extended or naturalistic observation methods increasing ecological validity, and recordings of physiological measurements.

CONCLUSION

In summary, anxiety disorders constitute a category of mental illnesses that can result in severe functional impairment for those affected, and therefore, thorough investigation and evaluation of risk and aetiological factors through a biopsychosocial prism is considered important. Despite their limitations, both, the biological explanation based on genetic predisposition and the psychological one based on Cognitive-Behavioural Theory, seem to adequately explain how anxiety disorders develop. Future research should focus on gene-environment interactions and neurobiological pathways in anxiety disorders, to investigate how genetic variations and cognitive processes affect brain structure and function areas involved in anxiety regulation, as well as twin studies and molecular genetics to identify genetic markers associated with anxiety-related cognitive biases maladaptive schemas.

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REFERENCES

1. American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). https://doi.org/10.1176/appi.books.9780890425596
2. Andrews, G., Stewart, G., Allen, R., & Henderson, A. S. (1990). The genetics of six neurotic disorders: a twin study. *Journal of affective disorders*, *19*(1), 23–29. https://doi.org/10.1016/0165-0327(90)90005-s
3. Askew, C., Reynolds, G., Fielding-Smith, S., & Field, A. P. (2016). Inhibition of vicariously learned fear in children using positive modelling and prior exposure. *Journal of Abnormal Psychology*, *125*(2), 279. http://dx.doi.org/10.1037/abn0000131
4. Austin, D. W., & Kiropoulos, L. (2008). An internet-based investigation of the catastrophic misinterpretation model of panic disorder. *Journal of Anxiety Disorders, 22*(2), 233–242. https://doi.org/10.1016/j.janxdis.2007.01.013.
5. Austin, D. W., & Richards, J. C. (2001). The catastrophic misinterpretation model of panic disorder. *Behaviour research and therapy, 39*(11), 1277–1291. https://doi.org/10.1016/s0005-7967(00)00095-4
6. Austin, D. W., & Richards, J. C. (2006). A test of core assumptions of the catastrophic misinterpretation model of panic disorder. *Cognitive Therapy and Research, 30*(1), 53–68. https://doi.org/10.1007/s10608-006-9010-4.
7. Bandelow, B., & Michaelis, S. (2015). Epidemiology of Anxiety Disorders in the 21st Century. *Dialogues in Clinical Neuroscience, 17*, 327-335. https://doi.org/10.31887/DCNS.2015.17.3/bbandelow
8. Bandura, A., & Rosenthal, T. L. (1966). Vicarious classical conditioning as a function of arousal level. *Journal of personality and social psychology*, *3*(1), 54–62. https://doi.org/10.1037/h0022639
9. Barlow D. H. (2000). Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *The American psychologist*, *55*(11), 1247–1263. https://doi.org/10.1037//0003-066x.55.11.1247
10. Barlow, D. H. (2004). *Anxiety and its disorders: The nature and treatment of anxiety and panic*. Guilford press.
11. Bas-Hoogendam, J. M., Blackford, J. U., Brühl, A. B., Blair, K. S., van der Wee, N. J. A., & Westenberg, P. M. (2016). Neurobiological candidate endophenotypes of social anxiety disorder. *Neuroscience and biobehavioral reviews*, *71*, 362–378. https://doi.org/10.1016/j.neubiorev.2016.08.040
12. Beck, J. S. (2011). *Cognitive behavior therapy: Basics and beyond* (2nd ed.). Guilford Press.
13. Behar, E., DiMarco, I. D., Hekler, E. B., Mohlman, J., & Staples, A. M. (2009). Current theoretical models of generalized anxiety disorder (GAD): conceptual review and treatment implications. *Journal of anxiety disorders*, *23*(8), 1011–1023. https://doi.org/10.1016/j.janxdis.2009.07.006
14. Blackburn I. M. & Davidson K. M. (1995). *Cognitive therapy for depression and anxiety: a practitioner's guide*. Blackwell Science.
15. Boelen, P. A., & Reijntjes, A. (2009). Intolerance of uncertainty and social anxiety. *Journal of anxiety disorders, 23*(1), 130–135. https://doi.org/10.1016/j.janxdis.2008.04.007
16. Borkovec, T. D., & Hu, S. (1990). The effect of worry on cardiovascular response to phobic imagery. *Behaviour Research and Therapy, 28*(1), 69–73. https://doi.org/10.1016/0005-7967(90)90056-O
17. Broerman, R. (2017). Diathesis-Stress Model. In V. Zeigler-Hill & T. K. Shackelford (Eds.), *Encyclopedia of Personality and Individual Differences* (pp. 1-3). Springer International Publishing.
18. Brown, T. A., & Naragon-Gainey, K. (2013). Evaluation of the unique and specific contributions of dimensions of the triple vulnerability model to the prediction of DSM-IV anxiety and mood disorder constructs. *Behavior therapy*, *44*(2), 277–292. https://doi.org/10.1016/j.beth.2012.11.002
19. Busscher, B., Spinhoven, P., van Gerwen, L. J., & de Geus, E. J. (2013). Anxiety

sensitivity moderates the relationship of changes in physiological arousal with flight anxiety during in vivo exposure therapy. *Behaviour research and therapy*, *51*(2), 98–105. https://doi.org/10.1016/j.brat.2012.10.009

20. Chand, S. P., & Marwaha, R. (2022). Anxiety. In *StatPearls*. Treasure Island, FL: StatPearls Publishing. Updated May 8, 2022. https://www.ncbi.nlm.nih.gov/books/NBK470361/
21. Clark, D. M., & Beck, A. T. (1988). Cognitive approaches. In C. G. Last (Ed.) & M. Hersen, *Handbook of anxiety disorders* (pp. 362–385). Pergamon Press.
22. Clark, D. M., Salkovskis, P. M., Breitholtz, E., Westling, B. E., Öst, L. G., Koehler, K. A., et al. (1997). Misinterpretation of body sensations in panic disorder. *Journal of Consulting and Clinical Psychology, 65*(2), 203–213. https://doi.org/10.1037/0022-006X.65.2.203
23. Comer R. J. (2013). *Abnormal psychology* (8th ed.). Worth.
24. Craske, M. G., & Barlow, D. H. (2014). Panic disorder and agoraphobia. In D. H. Barlow (Ed.), *Clinical handbook of psychological disorders: A step-by-step treatment manual* (pp. 1–61). The Guilford Press.
25. Czajkowski, N., Kendler, K. S., Tambs, K., Røysamb, E., & Reichborn-Kjennerud, T. (2011). The structure of genetic and environmental risk factors for phobias in women. *Psychological medicine*, *41*(9), 1987–1995. https://doi.org/10.1017/S0033291710002436
26. Daitch, C. (2011). *Anxiety disorders: The go-to guide for clients and therapists*. W. W. Norton & Co.
27. Davies, M. N., Verdi, S., Burri, A., Trzaskowski, M., Lee, M., Hettema, J. M., Jansen, R., Boomsma, D. I., & Spector, T. D. (2015). Generalised Anxiety Disorder--A Twin Study of Genetic Architecture, Genome-Wide Association and Differential Gene Expression. *PloS one*, *10*(8), e0134865. https://doi.org/10.1371/journal.pone.0134865
28. Decker, M. L., Turk, C. L., Hess, B., & Murray, C. E. (2008). Emotion regulation among individuals classified with and without generalized anxiety disorder. *Journal of anxiety disorders*, *22*(3), 485–494. https://doi.org/10.1016/j.janxdis.2007.04.002
29. Dobson, K. S., & Dozois, D. J. A. (Eds.). (2019). *Handbook of cognitive-behavioral therapies* (4th ed.). The Guilford Press.
30. Dugas, M. J., Buhr, K., & Ladouceur, R. (2004). The Role of Intolerance of Uncertainty in Etiology and Maintenance. *In R. G. Heimberg, C. L. Turk, & D. S. Mennin (Eds.), Generalized anxiety disorder: Advances in research and practice*, 143–163. The Guilford Press.
31. Feltham C. & Horton I. (2000). *Handbook of counselling and psychotherapy*. SAGE.
32. Field, A. P., & Purkis, H. M. (2012). Associative learning and phobias. In M. Haselgrove & L. Hogarth (Eds.), *Clinical applications of learning theory*, 49–73. Psychology Press. https://doi.org/10.4324/9780203803509
33. Finn, C. T., & Smoller, J. W. (2001). The genetics of panic disorder. *Current Psychiatry reports*, *3*(2), 131–137. https://doi.org/10.1007/s11920-001-0010-5
34. Freeston, M. H., Rhéaume, J., Letarte, H., Dugas, M. J., & Ladouceur, R. (1994). Why do people worry? *Personality and Individual Differences, 17*(6), 791–802. https://doi.org/10.1016/0191-8869(94)90048-5
35. Gamble, A. L., & Rapee, R. M. (2010). The time-course of attention to emotional faces in social phobia. *Journal of behavior therapy and experimental psychiatry*, *41*(1), 39–44. https://doi.org/10.1016/j.jbtep.2009.08.008
36. Goldstein, A. J., & Chambless, D. L. (1978). A reanalysis of agoraphobia. *Behavior Therapy, 9*(1), 47–59. https://doi.org/10.1016/S0005-7894(78)80053-7
37. Gottschalk, M. G., & Domschke, K. (2016). Novel developments in genetic and epigenetic mechanisms of anxiety. *Current opinion in psychiatry*, *29*(1), 32–38. https://doi.org/10.1097/YCO.0000000000000219
38. Gottschalk, M. G., & Domschke, K. (2017). Genetics of generalized anxiety disorder and related traits. *Dialogues in clinical neuroscience*, *19*(2), 159–168.

https://doi.org/10.31887/DCNS.2017.19.2/kdomschke

39. Gratacòs, M., Nadal, M., Martín-Santos, R., Pujana, M. A., Gago, J., Peral, B., Armengol, L., Ponsa, I., Miró, R., Bulbena, A., & Estivill, X. (2001). A polymorphic genomic duplication on human chromosome 15 is a susceptibility factor for panic and phobic disorders. *Cell*, *106*(3), 367–379. https://doi.org/10.1016/s0092-8674(01)00447-0
40. Gross, C., & Hen, R. (2004). The developmental origins of anxiety. *Nature reviews. Neuroscience*, *5*(7), 545–552. https://doi.org/10.1038/nrn1429
41. Hassoulas A., McHugh L., Reed P. (2013). Avoidance and behavioural flexibility in obsessive compulsive disorder. *J. Anxiety Dis*. *28*, 148–153. https://doi.org/10.1016/j.janxdis.2013.05.002
42. Hettema, J. M., Neale, M. C., Myers, J. M., Prescot, A., & Kendler, K. S. (2006). A population-based twin study of the relationship between neuroticism and internalizing disorders. *Am. J.Psychiatry, 163,* 857– 864. https://doi.org/doi:10.1176/ajp.2006.163.5.857
43. Hettema, J.M., Neale, M. C., Kendler, K. S. (2001). A review and meta-analysis of the genetic epidemiology of anxiety disorders. *Am. J. Psychiatry, 158* (10), 1568 – 1578. https://doi.org/10.1176/appi.ajp.158.10.1568
44. Hoehn-Saric, R., & McLeod, D. R. (1985). Locus of control in chronic anxiety disorders. *Acta psychiatrica Scandinavica*, *72*(6), 529–535. https://doi.org/10.1111/j.1600-0447.1985.tb02650.x
45. Hollander, E., & Simeon, D. (2011). Anxiety disorders. *In R. E. Hales, S. C. Yudofsky, & G. O. Gabbard (Eds.), Essentials of psychiatry*, 185–228. American Psychiatric Publishing.
46. Hompes, T., Izzi, B., Gellens, E., Morreels, M., Fieuws, S., Pexsters, A., Schops, G., Dom, M., Van Bree, R., Freson, K., Verhaeghe, J., Spitz, B., Demyttenaere, K., Glover, V., Van den Bergh, B., Allegaert, K., & Claes, S. (2013). Investigating the influence of maternal cortisol and emotional state during pregnancy on the DNA methylation status of the glucocorticoid receptor gene (NR3C1) promoter region in cord blood. *Journal of psychiatric research*, *47*(7), 880–891. https://doi.org/10.1016/j.jpsychires.2013.03.009
47. Institute for Health Metrics and Evaluation. (2019). Global Burden of Disease Study 2019 (GBD 2019) results [Website]. *Global Health Data Exchange*. https://vizhub.healthdata.org/gbd-results?params=gbd-api-2019-permalink/716f37e05d94046d6a06c1194a8eb0c9
48. Johnson JG, Cohen P, Kasen S, & Brook, J. S. (2008). Parental concordance and offspring risk for anxiety, conduct, depressive, and substance use disorders. *Psychopathology, 41,* 124 – 128. https://doi.org/10.1159/000112028
49. Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1992a). Generalized anxiety disorder in women: a population-based twin study. *Archives of General Psychiatry*, *49*(4), 267-272. https://doi.org/10.1001/archpsyc.1992.01820040019002
50. Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1992b). The genetic epidemiology of phobias in women. The interrelationship of agoraphobia, social phobia, situational phobia, and simple phobia. *Archives of general psychiatry*, *49*(4), 273–281. https://doi.org/10.1001/archpsyc.1992.01820040025003
51. Kendler, K. S., Prescott, C. A., Myers, J., & Neale, M. C. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Arch. Gen. Psychiatry, 60*, 929 – 937. https://doi.org/10.1001/archpsyc.60.9.929
52. Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch. Gen. Psychiatry, 62,* 617–27. https://doi.org/10.1001/archpsyc.62.6.61750
53. Kessler, R. C., Gruber, M., Hettema, J. M., Hwang, I., Sampson, N., & Yonkers, K. A. (2010). Major depression and generalized anxiety disorder in the National Comorbidity Survey follow-up survey. *In D. Goldberg, K. S. Kendler, P. J. Sirovatka, & D. A. Regier (Eds.), Diagnostic issues in*

depression and generalized anxiety disorder: Refining the research agenda for DSM-V, 139–170. American Psychiatric Association. https://doi.org/10.1017/S003329170700201 2

54. Knowles, M. M., Foden, P., El-Deredy, W., & Wells, A. (2016). A Systematic Review of Efficacy of the Attention Training Technique in Clinical and Nonclinical Samples. *Journal of clinical psychology*, *72*(10), 999–1025. https://doi.org/10.1002/jclp.22312
55. Koerner, N., Mejia, T., & Kusec, A. (2017). What's in a name? Intolerance of uncertainty, other uncertainty-relevant constructs, and their differential relations to worry and generalized anxiety disorder. *Cognitive behaviour therapy*, *46*(2), 141–161. https://doi.org/10.1080/16506073.2016.121 1172
56. Krypotos, A. M., Effting, M., Kindt, M., & Beckers, T. (2015). Avoidance learning: a review of theoretical models and recent developments. *Frontiers in behavioral neuroscience*, *9*, 189. https://doi.org/10.3389/fnbeh.2015.00189
57. Kuru, E., Safak, Y., Özdemir, İ., Tulacı, R. G., Özdel, K., Özkula, N. G., & Örsel, S. (2018). Cognitive distortions in patients with social anxiety disorder: Comparison of a clinical group and healthy controls. *The European Journal of Psychiatry, 32*(2), 97–104. https://doi.org/10.1016/j.ejpsy.2017.08. 004
58. LeBeau, R. T., Glenn, D., Liao, B., Wittchen, H. U., Beesdo-Baum, K., Ollendick, T., & Craske, M. G. (2010). Specific phobia: a review of DSM-IV specific phobia and preliminary recommendations for DSM-V. *Depression and anxiety*, *27*(2), 148–167. https://doi.org/10.1002/da.20655
59. Lieb, R., Wittchen, H. U., Höfler, M., Fuetsch, M., Stein, M. B., & Merikangas, K. R. (2000). Parental psychopathology, parent-ing styles, and the risk for social phobia in offspring: a pro-spective-longitudinal community study. *Arch Gen Psychiatry, 57*, 859 – 856. https://doi.org/10.1001/archpsyc.57.9.859
60. López-Solà, C., Fontenelle, L. F., Alonso, P., Cuadras, D., Foley, D. L., Pantelis, C., Pujol, J., Yücel, M., Cardoner, N., Soriano-Mas, C., Menchón, J. M., & Harrison, B. J. (2014). Prevalence and heritability of obsessive-compulsive spectrum and anxiety disorder symptoms: A survey of the Australian Twin Registry. *American journal of medical genetics. Part B, Neuropsychiatric genetics: the official publication of the International Society of Psychiatric Genetics*, *165B*(4), 314–325. https://doi.org/10.1002/ajmg.b.32233
61. Maron E, Hettema JM, Shlik J. (2010). Advances in molecular genetics of panic disorder. *Molecular Psychiatry, 15*, 681 – 701. https://doi.org/10.1038/mp.2009.145
62. McCue M. G., LeDoux J. E., Cain C. K. (2014). Medial amygdala lesions selectively block aversive pavlovian–instrumental transfer in rats. *Front. Behav. Neurosci., 8,* 329. https://doi.org/10.3389/fnbeh.2014.00329
63. McLean, C. P., & Anderson, E. R. (2009). Brave men and timid women? A review of the gender differences in fear and anxiety. *Clinical Psychology Review, 29,* 496–505. https://doi.org/10.1016/j.cpr.2009.05.003
64. McLeod, J. (2017). *Pluralistic Therapy: Distinctive Features* (1st ed.). Routledge. https://doi.org/10.4324/9781315398266
65. McLeod, S. A. (2017, February 5). Biological psychology. *Simply Psychology*. https://www.simplypsychology.org/biologic al-psychology.html
66. Merikangas, K. R., Lieb, R., Wittchen, H. U., & Avenevoli, S. (2003). Family and high-risk studies of social anxiety disorder. *Acta psychiatrica Scandinavica. Supplementum*, (417), 28–37. https://doi.org/10.1034/j.1600-0447.108.s417.5.x
67. Milosevic, I. & McCabe, R. (Eds.). (2015). *Phobias: The Psychology of Irrational Fear*. Retrieved from http://publisher.abc-clio.com/9781610695763
68. Morris-Rosendahl D. J. (2002). Are there anxious genes? *Dialogues in clinical neuroscience*, *4*(3), 251–260. https://doi.org/10.31887/DCNS.2002.4.3/d mrosendahl
69. Mowrer, O. H. (1947). On the dual nature of learning—a re-interpretation of "conditioning" and "problem-solving." *Harvard Educational Review, 17,* 102–148.

70. Neale, M. C., Walters, E. E., Eaves, L. J., Kessler, R. C., Heath, A. C., & Kendler, K. S. (1994). Genetics of blood-injury fears and phobias: a population-based twin study. *American journal of medical genetics*, *54*(4), 326–334. https://doi.org/10.1002/ajmg.1320540411
71. Nolte, T., Guiney, J., Fonagy, P., Mayesand, L. C., & Luyten, P. (2011). Interpersonal stress regulation and the development of anxiety disorders: an attachment-based developmental framework. *Frontiers in Behavioral Neuroscience, 55* (5), 1–21. https://doi.org/10.3389/fnbeh.2011.00055
72. Non, A. L., Binder, A. M., Kubzansky, L. D., & Michels, K. B. (2014). Genome-wide DNA methylation in neonates exposed to maternal depression, anxiety, or SSRI medication during pregnancy. *Epigenetics*, *9*(7), 964–972. https://doi.org/10.4161/epi.28853
73. Ohst, B., & Tuschen-Caffier, B. (2018). Catastrophic misinterpretation of bodily sensations and external events in panic disorder, other anxiety disorders, and healthy subjects: A systematic review and meta-analysis. *PLoS ONE, 13*(3), e0194493. https://doi.org/10.1371/journal.pone.0194493.
74. Osmanağaoğlu, N., Creswell, C., & Dodd, H. F. (2018). Intolerance of Uncertainty, anxiety, and worry in children and adolescents: A meta-analysis. *Journal of affective disorders*, *225*, 80–90. https://doi.org/10.1016/j.jad.2017.07.035
75. Patriquin, M. A., & Mathew, S. J. (2017). The Neurobiological Mechanisms of Generalized Anxiety Disorder and Chronic Stress. *Chronic stress (Thousand Oaks, Calif.)*, *1*, 2470547017703993. https://doi.org/10.1177/2470547017703993
76. Penninx, B. W., Pine, D. S., Holmes, E. A., & Reif, A. (2021). Anxiety disorders. *Lancet (London, England)*, *397*(10277), 914–927. https://doi.org/10.1016/S0140-6736(21)00359-7
77. Rehman I, Mahabadi N, Sanvictores T, et al. Classical Conditioning. [Updated 2022 Aug 22]. *In: StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. *Available from:* https://www.ncbi.nlm.nih.gov/books/NBK470326/
78. Reynolds, G., Field, A. P., & Askew, C. (2017). Learning to fear a second-order stimulus following vicarious learning. *Cognition & emotion*, *31*(3), 572–579. https://doi.org/10.1080/02699931.2015.1116978
79. Riskind, J. H., & Williams, N. L. (2006). A Unique Vulnerability Common to All Anxiety Disorders: The Looming Maladaptive Style. In L. B. Alloy & J. H. Riskind (Eds.), *Cognitive vulnerability to emotional disorders* (pp. 175–206). Lawrence Erlbaum Associates Publishers.
80. Robinson, M. D., & Clore, G. L. (2002). Episodic and semantic knowledge in emotional self-report: Evidence for two judgment processes. *Journal of Personality and Social Psychology, 83*(1), 198–215. https://doi.org/10.1037/0022-3514.83.1.198
81. Rodebaugh, T. L., Levinson, C. A., Langer, J. K., Weeks, J. W., Heimberg, R. G., Brown, P. J., Menatti, A. R., Schneier, F. R., Blanco, C., & Liebowitz, M. R. (2017). The structure of vulnerabilities for social anxiety disorder. *Psychiatry research*, *250*, 297–301. https://doi.org/10.1016/j.psychres.2017.01.073
82. Rosen, J. B., & Schulkin, J. (1998). From normal fear to pathological anxiety. *Psychological Review. 105* (2), 325 – 350. https://doi.org/10.1037/0033-295X.105.2.325
83. Rotter, J. B. (1966). Generalized expectancies for internal versus external control of reinforcement. *Psychological monographs: General and applied*, *80*(1), 1.
84. Ruscio, A. M., Hallion, L. S., Lim, C. C. W., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Andrade, L. H., Borges, G., Bromet, E. J., Bunting, B., Caldas de Almeida, J. M., Demyttenaere, K., Florescu, S., de Girolamo, G., Gureje, O., Haro, J. M., He, Y., Hinkov, H., Hu, C., de Jonge, P., … Scott, K. M. (2017). Cross-sectional Comparison of the Epidemiology of DSM-5 Generalized Anxiety Disorder Across the Globe. *JAMA psychiatry*, *74*(5), 465–475. https://doi.org/10.1001/jamapsychiatry.2017.0056
85. Sanchez, A. L., Cornacchio, D., Chou, T., Leyfer, O., Coxe, S., Pincus, D., & Comer, J. S. (2017). Development of a scale to

evaluate young children's responses to uncertainty and low environmental structure. *Journal of anxiety disorders*, *45*, 17–23. https://doi.org/10.1016/j.janxdis.2016.11.006

86. Sanchez, A. L., Kendall, P. C., & Comer, J. S. (2016). Evaluating the intergenerational link between maternal and child intolerance of uncertainty: A preliminary cross-sectional examination. *Cognitive Therapy and Research, 40*(4), 532–539. https://doi.org/10.1007/s10608-016-9757-1
87. Sandin, B., Sánchez-Arribas, C., Chorot, P., & Valiente, R. M. (2015). Anxiety sensitivity, catastrophic misinterpretations and panic self-efficacy in the prediction of panic disorder severity: towards a tripartite cognitive model of panic disorder. *Behaviour research and therapy*, *67*, 30–40. https://doi.org/10.1016/j.brat.2015.01.005
88. Scaini, S., Belotti, R., & Ogliari, A. (2014). Genetic and environmental contributions to social anxiety across different ages: a meta-analytic approach to twin data. *Journal of anxiety disorders*, *28*(7), 650–656. https://doi.org/10.1016/j.janxdis.2014.07.002
89. Schepers, J. (2005). The construction of a normative scale of locus of control. *SA Journal of Industrial Psychology, 31*(3). https://doi.org/10.4102/sajip.v31i3.201
90. Schreier, A., Wittchen, H. U., Höfler, M., Lieb, R. (2008). Anxiety disorders in mothers and their children: prospective longitudinal community study. *The British Journal of Psychiatry, 129*, 308-309. https://doi.org/10.1192/bjp.bp.106.033589
91. Shimada-Sugimoto, M., Otowa, T., & Hettema, J. M. (2015). Genetics of anxiety disorders: Genetic epidemiological and molecular studies in humans. *Psychiatry and Clinical Neurosciences, 69,* 388 – 401. https://doi.org/10.1111/pcn.12291
92. Skre, I., Onstad, S., Torgersen, S., Lygren, S., & Kringlen, E. (1993). A twin study of DSM-III—R anxiety disorders. *Acta Psychiatrica Scandinavica, 88*(2), 85–92. https://doi.org/10.1111/j.1600-0447.1993.tb03419.x
93. Smoller, J. W., Rosenbaum, J. F., Biederman, J., Kennedy, J., Dai, D., Racette, S. R., Laird, N. M., Kagan, J., Snidman, N., Hir-shfeld-Becker, D., Tsuang, M. T., Sklar, P. B., Slaugenhaupt, S.A. et al (2003). Association of a genetic marker at the corticotro-pin-releasing hormone locus with behavioral inhibition. *Biol Psychiatry, 54* (12), 1376–1381. https://doi.org/10.1016/S0006-3223(03)00598-5
94. Spatola, C. A., Scaini, S., Pesenti-Gritti, P., Medland, S. E., Moruzzi, S., Ogliari, A., Tambs, K., & Battaglia, M. (2011). Gene-environment interactions in panic disorder and CO_2 sensitivity: Effects of events occurring early in life. *American journal of medical genetics. Part B, Neuropsychiatric genetics: the official publication of the International Society of Psychiatric Genetics*, *156B* (1), 79–88. https://doi.org/10.1002/ajmg.b.31144
95. Staddon, J. E, & Cerutti, D.T. (2003). Operant conditioning. *Annu Rev Psychol, 54,* 115-44. https://doi.org/10.1146/annurev.psych.54.101601.145124
96. Villafuerte, S., & Burmeister, M. (2003) Untangling genetic networks of panic, phobia, fear and anxiety. *Genome Biol. 4* (8), 224. https://doi.org/10.1186/gb-2003-4-8-224
97. Watson, J. B., & Rayner, R. (1920). Conditioned emotional reactions. *Journal of Experimental Psychology, 3*(1), 1–14. https://doi.org/10.1037/h0069608
98. Webb, B. T., Guo, A.Y., Maher, B.S. et al. (2012). Meta-analyses of genome-wide linkage scans of anxiety-related phenotypes. *European Journal of Human Genetics, 20,* 1078 – 1084. https://doi.org/10.1038/ejhg.2012.47
99. Wells, A., & McNicol, K. (2014). Metacognitive therapy. In P. Emmelkamp & T. Ehring (Eds.), *The Wiley Handbook of Anxiety Disorders*. https://doi.org/10.1002/9781118775349.ch37
100. Wenzel, A., Haugen, E. N., Jackson, L. C., & Brendle, J. R. (2005). Anxiety symptoms and disorders at eight weeks postpartum. *Journal of anxiety disorders*, *19*(3), 295–311. https://doi.org/10.1016/j.janxdis.2004.04.001
101. White, J. B., Langer, E. J., Yariv, L., & Welch, J. C. IV. (2006). Frequent Social Comparisons and Destructive Emotions and

Behaviors: The Dark Side of Social Comparisons. *Journal of Adult Development, 13*(1), 36–44. https://doi.org/10.1007/s10804-006-9005-0

102. Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., Olesen, J., Allgulander, C., Alonso, J., Faravelli, C., Fratiglioni, L., Jennum, P., Lieb, R., Maercker, A., van Os, J., Preisig, M., Salvador-Carulla, L., Simon, R., & Steinhausen, H. C. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European neuropsychopharmacology: the journal of the European College of Neuropsychopharmacology, 21*(9), 655–679. https://doi.org/10.1016/j.euroneuro.2011.07.018

103. Wittchen, H-U., Nelson, C. B., & Lachner, G. (1998). Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. *Psychol Med, 28,* 109 – 126. https://doi.org/10.1017/s0033291797005928

104. World Health Organization. (2017). Depression and other common mental disorders: global health estimates. *World Health Organization.* https://apps.who.int/iris/handle/10665/254610.

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