The Association between Endocrine Functioning and the Manifestation of Psychotic, Mood and Anxiety Symptoms: A Scoping Review

Jelle van der Galiën

Master Thesis - Clinical Neuropsychology

S3836312
July 2024
Department of Psychology
University of Groningen
Examiner/Daily supervisor:
Dr. Daouia Larabi

Abstract

INTRODUCTION: This review explored and summarized current research on how endocrine functioning influence the manifestation of psychotic, mood, and anxiety (PMA) symptoms, considering their roles in physiological processes and impacting brain functions. It delves into the bidirectional relationship between endocrine functioning and PMA symptoms, emphasizing the need for further understanding in both clinical and research contexts.

METHODS: This scoping review systematically synthesized the current literature on the association between endocrine functioning, hormone imbalances and the manifestation of PMA symptoms. Literature search for the last ten years on PsycINFO and MEDLINE and subsequent screening led to 51 included studies. Data were extracted and analyzed to identify trends, gaps, and potential mechanisms linking endocrine functioning to PMA symptomology. The review adhered to PRISMA-ScR guidelines for comprehensive reporting.

RESULTS: Key hormone types found to be associated with PMA symptoms include sex hormones, stress hormones, thyroid hormones, appetite hormones, and oxytocin. Key findings underscore sex-specific effects of sex hormones related to the sexually dimorphic PMA symptom presentation. A dysregulated HPA axis, including high cortisol levels, shows significant associations with psychotic symptoms and increased susceptibility for mood and anxiety symptom development, particularly following early-life stress. Thyroid hormone imbalances can mimic and exacerbate neuropsychiatric symptoms, and appetite and metabolic hormones showed associations with psychotic and anxiety symptoms via metabolic dysregulation and neuroinflammatory pathways. Lastly, oxytocin modulates stress and social cognition, with low levels impacting PMA symptoms.

CONCLUSION: This study revealed the complex interplay between endocrine functioning and PMA symptoms. Findings were often heterogeneous and associations limited. Hormone-symptom relationships are not solely causal but interact with genetic, biological, and

environmental factors, influencing brain function and predisposing individuals to PMA symptoms. Future transdiagnostic and multidisciplinary research strategies could enhance diagnostic and treatment approaches related to these manifestations.

Keywords: endocrine system, endocrine functioning, anxiety symptoms, mood symptoms, hormones, psychotic symptoms, psychiatric symptoms, sex hormones, thyroid hormones, stress hormones, appetite hormones, oxytocin

Contents

The Association Between Endocrine Functioning and the Manifestation of Psychotic, Mood and Anxiety Symptoms

The endocrine system, also known as the hormone system, is an important regulator of homeostasis for numerous physiological processes. It plays crucial roles in (neuro)physiological functions such as growth and development, reproduction, regulating metabolism, immune function and controlling mood and emotions (Salvador et al., 2019). Conjoinedly, it is well-established that hormones and endocrine functions influence phenomena that are related to psychiatric symptoms, including mood, behavior, and cognition. The development of psychiatric symptoms - and by extension, psychiatric disorders – involves a multifaceted pathogenesis, including the interaction of psychological, psychosocial, and biological factors (Glannon, 2022). A deeper understanding of the endocrine system's role in the manifestation of psychiatric symptoms could aid in the improvement of diagnostic and therapeutic strategies.

The Endocrine System

Endocrinology refers to the scientific domain of studying and explaining cell communication within the context of the physiological system of an organism through chemical messengers called *hormones* (Norman & Litwack, 1997, p. 1). The endocrine system encompasses the network of glands and organs that facilitate the communication between cells and various anatomical regions by excreting hormones. Specific hormone receptors receive these messengers, triggering a cascade of biochemical reactions that can impact mood, behavior and cognition through various mechanisms (Norman & Litwack, 1997, p. 7).

According to the Environmental Protection Agency (2024), over 50 different types of hormones – and even more neurotransmitters – have currently been identified in humans. Given this complexity, the current study delves into hormones that have garnered significant

attention in the scientific literature for their associations with the manifestation of psychotic, mood and anxiety symptoms.

Hormone Classifications

Hormones can be classified in various ways, based on their chemical structure, mechanism of action, or function. While a certain hormone can be involved with various functions, his study handles simplified classifications based on function. The types of hormones associated with the manifestation of psychiatric symptoms in the current study include: (1) *sex hormones* (i.e. testosterone and estrogen), (2) *stress hormones* (i.e. cortisol), (3) *appetite and metabolic hormones* (i.e. ghrelin and insulin), (4) *thyroid hormones*[1] (i.e. thyroxine and thyroid-stimulating-hormone) and (5) *socio-behavioral hormones* (i.e. oxytocin[2]). A full overview and description of included hormones and related terms can be found in the Glossary in Appendix A.

Psychotic Symptoms, Mood Symptoms and Anxiety Symptoms

In a clinical context, psychiatric symptoms encompass behavioral or psychological features that aid in diagnosing various psychiatric conditions. Clinicians assess the presence, severity, duration, and frequency of symptoms to determine their pathological significance. Clinical interviews, observations, and diagnostic criteria such as those outlined in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-V) are used for this process (American Psychiatric Association, 2013).

Prominent examples of psychiatric symptoms include psychotic, mood and anxiety (PMA) symptoms, which occur frequently in the general population (Stochl et al., 2015). Firstly, (1) *Psychotic symptoms* (PS) refer to false beliefs, delusions, hallucinations, and

[1] As an exception, thyroid hormones are not classified by function but rather by their site of synthesis: the thyroid gland. In the scientific literature, they are commonly grouped together under the 'thyroid hormone' category (Puchalapalli & Mahmood, 2020).

[2] Oxytocin is a neuropeptide hormone that functions both as a neurotransmitter and a hormone (Norman & Litwack, 1997, p. 128). For this reason, it is still of interest for this study.

disorganized behavior or thinking. They can occur in disorders such as schizophrenia, schizotypal disorder or bipolar disorder. These symptoms are often accompanied by cognitive impairments in social cognition and attention, which is prevalent in disorders associated with psychotic symptoms (Nuevo et al., 2012).

Second, (2) *Mood symptoms* (MS) manifest as discordance between life circumstances and emotional states. These are typical manifestations in disorders like major depressive disorder (MDD) and bipolar disorder. These symptoms include sadness, decreased energy, hopelessness, and in some cases, mania or irritability. They are often accompanied by cognitive impairments in attention, memory, and executive functions (Harvey, 2011).

Lastly, (3) *anxiety symptoms* (AS) arise from perceived threats or dangers, characterized by feelings of nervousness, restlessness, and physical symptoms like increased heart rate and rapid breathing. Generalized Anxiety Disorder (GAD) and panic disorder are common disorders associated with these symptoms (Glannon, 2012).

The three distinct PMA symptom domains share etiological factors in their development and manifestation, such as genetic, neurobiological and environmental influences (Stochl et al., 2015). Moreover, PMA symptoms - and psychiatric disorders in general - show a high rate of comorbidity within individuals, and patients often present with multiple symptoms spanning across these categories (Stochl et al., 2014). Considering this, understanding the interplay between endocrine functioning and PMA symptoms and exploring these domains in an integrated fashion may contribute to the development of unified theoretical models and holistic treatment approaches.

Aim

Increasingly, a bidirectional relationship between endocrine disorders and psychiatric manifestations is being established in relevant studies and literature (Salvador, et al., 2019; Mishra et al., 2022). On the one hand, endocrine dysfunctioning may contribute to various

psychiatric manifestations. On the other hand, an altered psychological state, such as experiencing chronic anxiety, may contribute to the development of endocrine dysfunctioning (Salvador, et al., 2019; Mishra et al., 2022).

Overall, the association between hormone imbalances and symptoms observed in depression and anxiety are often discussed in existing literature. For psychotic symptoms associated with schizophrenia and bipolar disorder, the role of the endocrine system and hormone imbalances are less explored (Ranabir & Reetu, 2011). Furthermore, even when there are strong associations between a disorder and endocrine functioning, psychiatric disorders exhibit considerable heterogeneity in symptom presentation between individuals and across contexts (Glannon, 2022). Due to this heterogeneity and the complex interplay of various factors contributing to the manifestation of psychiatric symptoms, it is often still unclear what specific symptoms are related to which hormonal imbalance.

In this context, understanding hormone profiles of patients holds potential clinical value for diagnosing, treating, and preventing psychiatric symptoms and disorders (Altemus, 2010). For instance, it is a stated goal of the DSM-V to incorporate biological pathophysiology or biomarkers into psychiatric diagnostic criteria. To date, no such markers have reliably been identified that predict psychiatric disorders sufficiently to warrant inclusion to diagnostic criteria (Altemus, 2010; Glannon, 2022).

The current study aims to summarize and explore the current understanding and research regarding the relationship between hormonal imbalances and PMA symptoms, considering underlying brain mechanisms, cognitive mechanisms and pathophysiological processes. This exploration of subjects will be guided by the following research question: *How is endocrine functioning associated with the manifestation of psychotic, anxiety and mood symptoms, also considering possible underlying brain mechanisms and pathophysiological processes?*

Methods

To achieve this, the current study employed a scoping review. Literature scoping reviews are increasingly being implemented as an approach to review health-related research (Pham et al., 2014). A scoping review is a method of knowledge synthesis, following a systemic approach to collect and summarize evidence and understanding of a topic. In this manner, concepts, theories, sources, and knowledge gaps can be identified. Scoping reviews do not rigorously weigh the quality of studies like systematic reviews do (Tricco et al., 2018). They do not extract quantitative data or effect sizes, and generally include a results' discussion that is predominantly qualitative in nature, as opposed to quantitative. Therefore, scoping reviews are suited for broader research questions and less stringent exclusion criteria. The guidelines and explanation posed by Tricco et al. (2018) in the *PRISMA Extension for Scoping Reviews* (PRISMA-ScR) will be adhered to in the present study. The PRISMA-ScR checklist can be found in Appendix B.

Procedure

For the search strategy development, a librarian from the University of Groningen was consulted. The search was conducted via the databases *PsycINFO and MEDLINE.* In April 2024, databases were searched from January 2014 to April 2024 with the following terms: ("anxiety symptom*" OR "cognitive symptom*" OR "psychotic symptom**" OR "mood symptom*") AND ("endocrine system*" OR "endocrine disorder*" OR "hormone*"). Terms were searched in keywords, titles, and abstracts. In total, 1324 peer-reviewed articles were obtained from the databases using the keywords listed above. The program Zotero (Corporation for Digital Scholarship, n.d.) was used to gather and organize the studies, and the online tool Rayyan (Ouzzani et al., 2016) was used for the screening process.

Eligibility Criteria and Study Selection

After duplicate removal, the titles and abstracts of 608 published studies were screened by the sole author of this project. The articles had to meet the criteria outlined below in order to be considered for inclusion.

Inclusion Criteria

(1) Studies that explored the association between hormones, endocrine functioning and the development, continuation or exacerbation of psychotic, anxiety or mood symptoms were included; (2) experimental studies, longitudinal designs, cross-sectional designs, qualitative research and reviews (including meta-analyses, narrative reviews and systematic reviews) were considered eligible; and (3) articles written in English were considered.

Exclusion Criteria

Furthermore, papers were excluded if they met any of the following criteria: (1) Studies focusing only on mood, anxiety, or psychotic symptoms in the context of a specific (neurodegenerative) disease unrelated to endocrine functioning; (2) articles focusing only on messengers of the endocrine system that exclusively function as neurotransmitters (i.e. serotonin or dopamine); (3) studies on endocrine alterations in the context of pregnancy during the pre-, post-, or peri-partum phase; (4) papers discussing psychotic symptoms, anxiety symptoms, or mood symptoms as an effect of exogenous hormonal treatment were not included; (5) articles that not primarily focusing on human studies but on animal studies; and lastly, (6) no books, opinion pieces, case reports, letters or conference abstracts were considered.

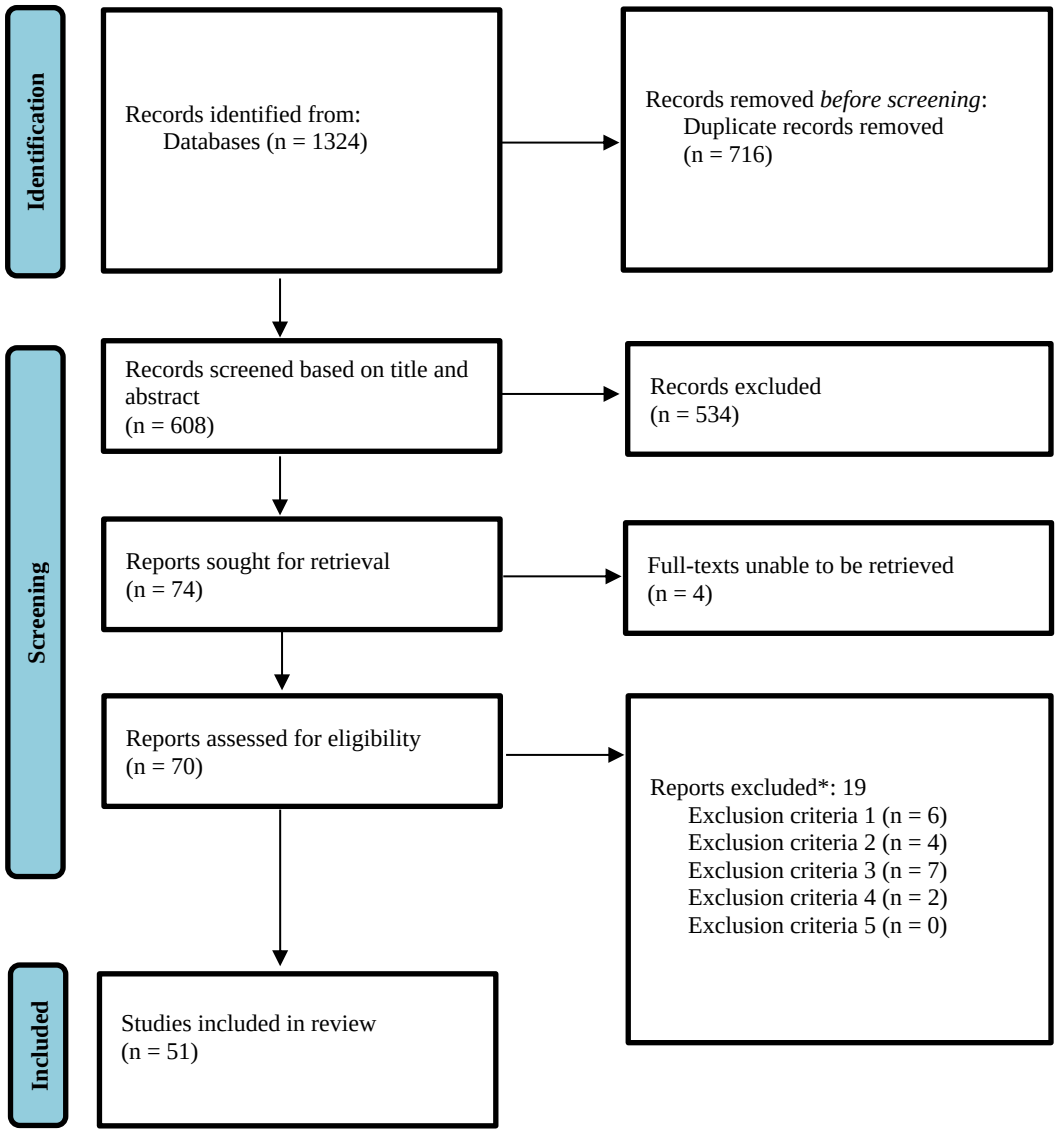
Full-Text Assessment

After the initial screening process, 74 reports were sought for full-text assessment, of which 70 were successfully retrieved. These articles were read entirely by the author to further assess for eligibility based on the aforementioned criteria. 19 additional articles were

excluded during this stage for reasons mentioned in the flow chart (Fig. 1). Full-text assessment identified 51 articles of potential relevance for this review.

Figure 1

PRISMA flow diagram



Note. *Please refer to the exclusion criteria on page 12 for further details.

Data Assessment, Extraction, Analysis and Reporting

Subsequently, the selected studies were summarized and analyzed. The following data were extracted and recorded in a data extraction table (see Appendix C): author(s), title, year of publication, study design, relevant participant characteristics (sex, diagnosis, age),

endocrine/hormonal measure, psychiatric symptom domains, main outcomes, notable limitations and - when provided - proposed mechanisms.

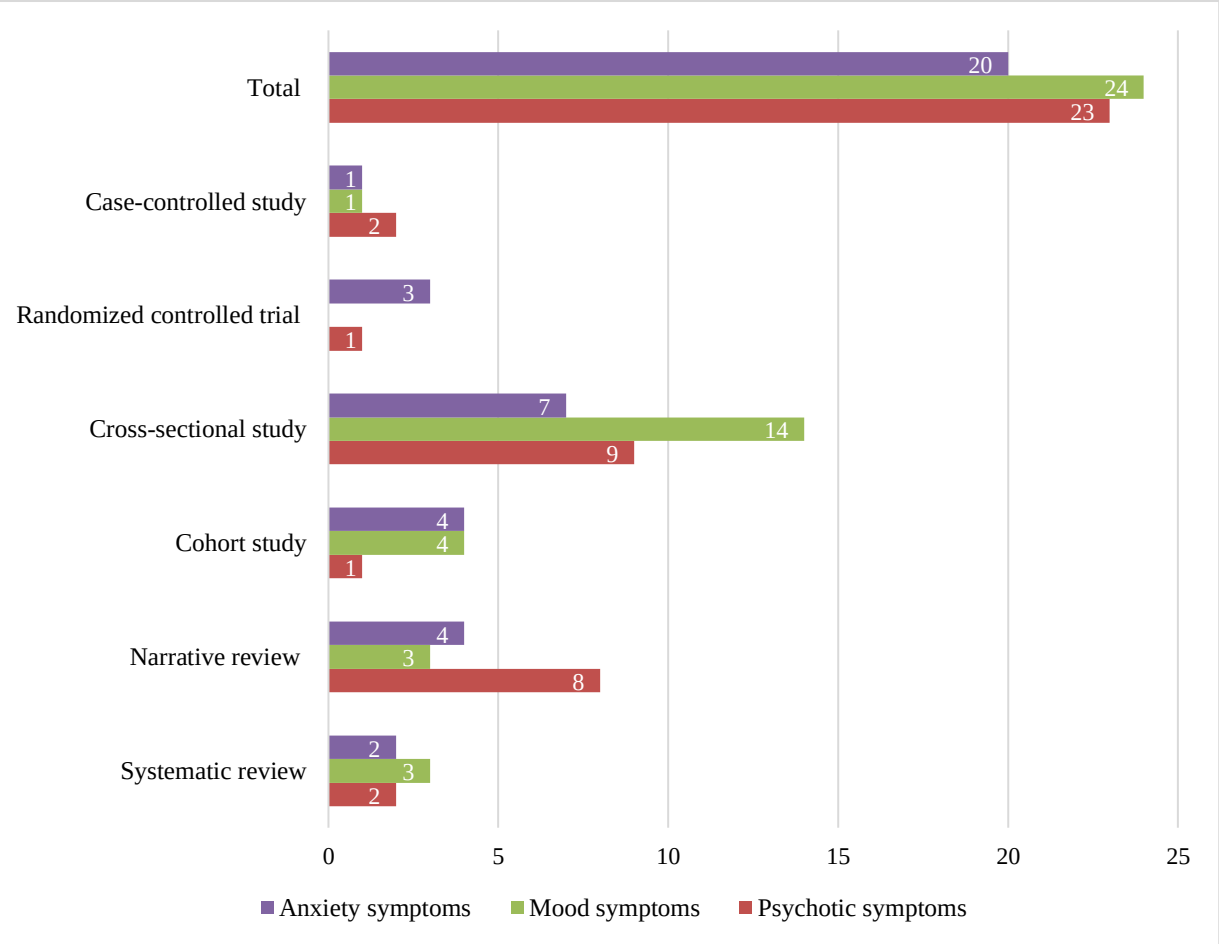
Results

Descriptive Summary of Included Studies

A total of 51 studies were included in the review. Of these, 23 examined psychotic symptoms, 24 discussed mood symptoms and 20 addressed anxiety symptoms. Articles were recounted per domain. A full overview of the included study designs is shown below in Figure 2 and in Appendix C. For the comprehensive data extraction table, see Appendix C, Table C2.

Figure 2

Distribution of included study designs across symptom domains

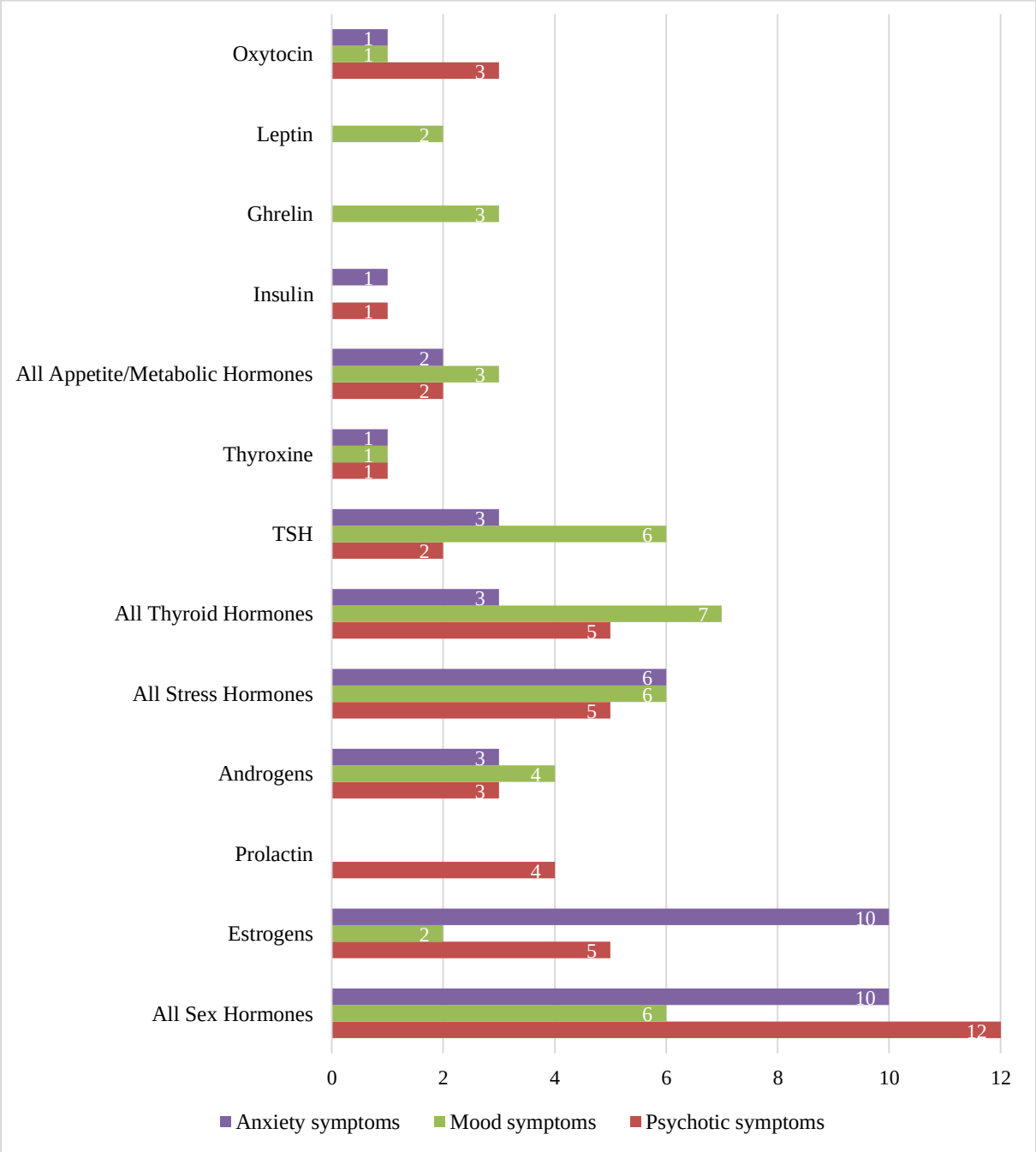


Note. 51 reports were included. Studies discussing multiple symptom types are *recounted* for each symptomatic domain. Numeric values indicate number of studies included.

Analysis and data synthesis of included reports resulted in the following hormone types relevant to the manifestation of PMA symptoms: *sex hormones*, *thyroid hormones*, *stress hormones*, *socio-behavioral hormones (oxytocin)* and *appetite/metabolic hormones*. A distribution of explored hormone types by symptom domain is shown in Figure 3.

Figure 3

Number of studies exploring hormone types across symptom domains



Note. TSH = thyroid stimulating hormone. Numeric values denote number of studies included.

The sources of evidence for each hormone type and their association with PMA symptoms will be discussed, along with any relevant psychopathology, cognitive mechanisms or neurophysiological processes.

Sex Hormones and PMA Symptom Manifestations

The majority of the included studies (n = 26) discussed the relationship between sex hormones and the manifestation of PMA symptoms. An overview of the main findings pertaining to sex hormones is shown in Table 2.1 below.

Table 2.1

Main Findings Regarding the Link Between Sex Hormones and Psychotic, Mood, and Anxiety Symptoms

Psychotic Symptoms		Mood Symptoms		Anxiety Symptoms	
Main findings	References	Main findings	References	Main findings	References
In women, *estrogens* delay onset of PS, improves cognitive functions and reduces symptom severity. Results inconclusive in men.	McGregor et al., 2017; Hodgetts & Hausmann, 2020; Brand et al., 2021; Barendse, 2023	*Estrogen* fluctuations impact brain regions involved in social and cognitive processing, increasing risk for MS manifestation.	Toffoletto et al., 2014; Chronister et al., 2021	Higher *estradiol* linked to increased threat vigilance and attentional bias in women: risk for AS manifestation.	Graham and Shin., 2018; Nouri et al., 2022
Testosterone correlated with less severe positive symptoms in women, but inversely correlated with negative symptoms in men.	Gonzalez et al., 2017; Barendse et al., 2023;	In women, higher *androgen* levels in PCOS linked to increased anger, anxiety, depression, and cognitive impairment.	Balikci et al., 2014; Sukhapore et al., 2022; Lee et al., 2017	Elevated *DHEA-S*: mixed results, correlated with increased anxiety in boys but decreased in girls; high *DHEA/ testosterone* linked to anxiety via increased amygdala connectivity.	Barendse et al., 2018; Mulligan et al., 2020
Hyperprolactinemia common in psychotic disorders in women, linked to cognitive dysfunction and positive symptoms.	Labad, 2019; Jen et al., 2020; Medina-Loera et al., 2020	Lower *DHEA* levels correlated with higher depressive symptoms and poorer cognitive functions; lower *DHEA-S* linked to manic symptoms in men.	Walther et al., 2019; Lee et al., 2017		

Note. PS = psychotic symptoms; MS = mood symptoms; AS = anxiety symptoms; SZ = schizophrenia; PCOS = polycystic ovary syndrome.

The various sex hormones show varied and sex-specific effects in their relation to PMA symptom manifestation. Multiple studies (n = 8) noted limited findings and a lack of research regarding sex hormones' relationship with PMA symptoms in men (Medina-Loera et al., 2020; Brand et al., 2021).

Sex Hormones & Psychotic Symptoms

Twelve articles discussed sex hormones in the context of psychotic symptoms. Especially for women, there is evidence that fluctuations in sex hormones are associated with psychotic symptoms.

Female Sex Hormones & Psychotic Symptoms

According to various reviews (n = 5: 1 systematic review; 4 narrative reviews), estrogens (including estradiol) play a protective role by delaying the onset of psychosis in women by reducing symptom severity and improving cognitive functions. Conversely, low levels may lead to vulnerability and more severe symptoms (McGregor et al., 2017; Hodgetts and Hausmann, 2020; Brand et al., 2021). Estrogens may work their effects through proposed mechanisms such as enhanced synaptic and bilateral neuroplasticity, modulating dopamine signaling, and stress response attenuation (Hodgetts and Hausmann, 2020; Brand et al., 2021).

Prolactin and Psychotic Symptoms

Prolactin is also implicated and related to psychotic symptoms according to included studies, (n = 4: 2 narrative reviews; 1 case-controlled study; 1 cross-sectional study) with effects differing by sex. For example, hyperprolactinemia can lead to low estrogen and is associated with increased vulnerability for psychotic symptoms in women in various studies, including two reviews (Brand et al., 2021; Culbert et al., 2022). In a cross-sectional study, high prolactin levels were correlated with cognitive dysfunction and negative symptoms in men (Medina-Loera et al., 2020). Contrarily, low prolactin levels in schizophrenia patients

showed increased risk for both sexes in developing a rebound in psychotic symptoms in a case-controlled study (Jen et al., 2020).

Testosterone and DHEA and Psychotic Symptoms

The association of psychotic symptoms with androgenic steroids and precursors such as DHEA and DHEA-S is similarly marked by sex-specific effects, albeit less explored in the included studies (n = 3: 1 narrative review; 1 randomized controlled trial (RCT); 1 cross-sectional study). For example, females with higher testosterone were shown to exhibit less severe positive symptoms (Gonzalez et al., 2017). Conversely, elevated levels in adolescent males were correlated with less negative symptoms in a narrative review. A proposed mechanism suggests that higher testosterone levels during adolescence may impact striatal functioning and improve reward-responses, leading to fewer negative symptoms (Barendse et al., 2023).

Sex Hormones and Mood Symptoms

Four studies (1 systematic review; 2 cross-sectional studies; 1 cohort study) indicate noteworthy sex-specific hormone-mood relationships in the context of sex hormones, related mostly to estrogen and androgen fluctuations (Balikci et al., 2014; Toffoletto et al., 2014; Chronister et al., 2021; Lyu et al., 2023).

Female Sex Hormones and Mood Symptoms

Female sex hormones, including progesterone and estrogens, play a role in the manifestation of mood symptoms by exerting effects on brain regions involved in emotional and cognitive processing (amygdala, anterior cingulate cortex (ACC) and the inferior frontal gyrus), as described in a systematic review on women with depression (Toffoletto et al., 2014). Reflecting this pattern, elevated estradiol levels in boys appeared to be associated with increased depressive symptoms in a cohort study (Chronister et al., 2021).

Male sex hormones and Mood Symptoms

Four cross-sectional studies on women with PCOS showed higher specific androgen levels to be related to significantly increased anger, anxiety, depression, and cognitive impairment (Balikci et al., 2014; Sukhapore et al., 2022; see also Lee et al., 2017). For instance, the precursor DHEA has been implicated in mood regulation in studies on women; low levels correlated with more severe mood (manic and depressive) symptoms (Lee et al., 2017; Walther et al., 2019). Additionally, one case-controlled study found a negative correlation between DHEA-S levels and manic symptom severity in both sexes (Lee et al., 2017).

Sex Hormones and Anxiety Symptoms

Ten studies discussed sex hormones in the context of anxiety. Females are twice as likely to develop anxiety disorders and experience greater symptom severity compared to males. Hormonal fluctuation differences may contribute to this disparity (Graham & Shin, 2018).

Female Sex Hormones and Anxiety Symptoms

Fear extinction and attentional bias are crucial processes in the development and maintenance of anxiety. Estradiol levels were positively correlated in 2 RCTs with attentional bias for threat in female participants, contributing to the development of anxiety (Graham & Shin., 2018; Barendse et al., 2020; Nouri et al., 2022).

Testosterone, DHEA, DHEA-S and Anxiety Symptoms

Proneness for anxiety often develops early in life. The three studies (1 longitudinal cohort study, 2 cross-sectional studies) exploring this topic showed mixed results. For example, elevated DHEA-S levels revealed increased amygdala connectivity and anxiety in boys, but decreased amygdala connectivity and anxiety in girls (Barendse et al., 2020). Higher DHEA and testosterone levels were linked to increased amygdala connectivity with the visual

cortex and ACC, correlating with anxiety symptoms in both boys and girls (Barendse et al., 2018; Mulligan et al., 2020).

Stress Hormones and PMA Symptom Manifestations

Twelve of the included studies discussed stress hormones in relation to PMA symptoms. An overview of the main findings related to stress hormones is shown in Table 2.2. Stress hormones show associations with PMA symptoms through various mechanisms, mainly related to a dysregulated hypothalamic-pituitary-adrenal (HPA) axis[3], which is linked to the pathophysiology of various psychiatric manifestations (Mikulska et al., 2021). Overall, elevated stress hormone levels are common across PMA symptom domains.

Table 2.2

Main Findings Regarding the Link Between Stress Hormones and Psychotic, Mood, and Anxiety Symptoms

Psychotic Symptoms		Mood Symptoms		Anxiety Symptoms	
Main findings	References	Main findings	References	Main findings	References
Increased *cortisol* levels common in individuals with (risk for) PS; impairs cognition: atrophy and inflammation in hippocampus and PFC.	Wingenfeld & Wold, 2015; Labad, 2019; Merritt et al., 2020; Schatzberg, 2015	Dysregulated *HPA axis* prevalent in MDD, affecting stress responses and cognitive functions.	Wingenfeld & Wolf, 2015; Chronister et al., 2021	Early life stress triggers *HPA axis*, leading to increased *stress hormone* secretion, altering amygdala connectivity and increasing AS susceptibility.	Pagliaccio et al., 2015; Raymond et al., 2018; Yuen et al., 2017; Mesdrakis et al., 2020
Elevated *cortisol* levels more strongly associated with anxiety than PS, suggesting stress as epiphenomenon in PS.	Karinakas & Garyfallos, 2015; Labad, 2019; Schatzberg, 2015	Early adversity causes sustained *cortisol* elevation, reduced hippocampal volume, altered amygdala connectivity, affects cognitive function and emotion regulation: MS proneness.	Pagliaccio et al., 2015; Yuen et al., 2017; Raymond et al., 2018	Chronically elevated *cortisol* detrimental for anxiety symptoms, reduces hippocampal activity.	Wingenfeld & Wolf, 2015; Pagliaccio et al., 2015; Raymond et al., 2018

Note. PS = psychotic symptoms; MS = mood symptoms; AS = anxiety symptoms; PFC = prefrontal cortex; HPA = hypothalamic-pituitary-adrenal.

[3] The HPA axis (see glossary) regulates immune response, stress response and cortisol excretion.

Stress Hormones & Psychotic Symptoms

Stress hormones may contribute to the manifestation of psychotic symptoms by means of disrupted HPA axis functioning, as elevated stress hormone levels are frequently observed in psychosis (Wingenfeld & Wold, 2015; Labad, 2019; Merritt et al., 2020). A proposed mechanism is that chronic glucocorticoid excess may affect the PFC and hippocampus, alter dopamine signaling, reduce connectivity, reduce plasticity and cause inflammation, hampering cognitive functions such as learning, social cognition and memory; implicating risk for PS development (Labad, 2019; see also Schatzberg, 2015).

Results in the reports (n = 5: 1 systematic review; 4 narrative reviews) are somewhat inconsistent, however. Elevated cortisol levels appear to be most strongly associated with anxiety measures, rather than psychotic symptoms (Karinakas & Garyfallos, 2015; Labad, 2019; see also Schatzberg, 2015). This implies that elevated levels may also be an epiphenomenon related to the experienced stress and anxiety in individuals with PS (Labad, 2019).

HPA Axis Dysregulation Contributes to Mood & Anxiety Symptoms

A dysregulated HPA axis, including cortisol hypersecretion and reduced feedback sensitivity to cortisol, is highly prevalent in MDD patients (Schatzberg, 2015; Wingenfeld & Wolf, 2015; Chronister et al., 2021). According to the accredited review by Wingenfeld & Wolf (2015), this dysregulation could implicate stress hormones receptors, which may negatively affect stress responses. In line with this, three studies (2 narrative reviews; 1 cohort study) noted that stress hormones are also associated with the manifestation of mood and anxiety symptoms through early adversity. For instance, childhood stress can induce brain changes and sustained cortisol elevation, leading to reduced hippocampal volume and altered connectivity with the amygdala. These alterations affect cognitive functions and emotion

regulation, increasing susceptibility to mood and anxiety manifestations (Pagliaccio et al., 2015; Yuen et al., 2017; Raymond et al., 2018)

Thyroid Hormones and PMA Symptom Manifestations

Thyroid hormones and thyroid disorders are associated with PMA symptoms according to various articles (n = 9) included in the current review. An overview of the main findings can be found in Table 2.3 below.

Table 2.3

Main Findings Regarding the Link Between Thyroid Hormones and Psychotic, Mood, and Anxiety Symptoms

Psychotic Symptoms		Mood Symptoms		Anxiety Symptoms	
Main findings	References	Main findings	References	Main findings	References
Higher *T4* levels associated with better cognitive performance in early psychosis.	Barbero et al., 2015	*HT* increases susceptibility to treatment-resistant MDD and slows treatment response in BD.	Puchalapalli & Mahmood, 2020	Similarly to MS, elevated *TSH* levels contribute to more severe anxiety symptoms in mood disorders.	Yang et al., 2014
HT prevalent in depressed individuals with psychotic symptoms.	Dai et al., 2023; Merritt, 2020	*HT* can mimic neuropsychiatric symptoms including MS	Puchalapalli & Mahmood, 2020	*HT* can mimic neuropsychiatric symptoms including AS	Puchalapalli & Mahmood, 2020
High *TSH* levels linked to increased risk of developing psychotic symptoms via chronic inflammation.	Dai et al., 2023; Wang et al., 2024	Subclinical *HT* and elevated *TSH* linked to more depression and suicide attempts.	Lang et al., 2020; Liu et al., 2021; Zu et al., 2024		
HT can mimic neuropsychiatric disorders such as myxedema psychosis.	Merritt et al., 2020; Puchalapalli & Mahmood, 2020				

Note. PS = psychotic symptoms; MS = mood symptoms; AS = anxiety symptoms; T4 = thyroxine; TSH = thyroid stimulating hormone; HT = hypothyroidism.

Thyroid hormone imbalances can cause symptomatic manifestations resembling neuropsychiatric symptoms, these generally recede with recovery of thyroid function (Merritt

et al., 2020; Puchalapalli & Mahmood, 2020). Conversely, specific thyroid hormone imbalances have been associated with a risk of developing neuropsychiatric disorders (Dai et al., 2023; Wang et al., 2024).

Thyroid Hormones and Psychotic Symptoms

As described in a systematic review by Puchalapalli & Mahmood (2020) and the narrative review by Merritt et al. (2020), hypothyroidism (HT) can mimic psychosis, presenting with PS. HT is also more prevalent in depressed individuals with PS, compared to without (Merritt et al, 2020; Dai et al., 2023). Furthermore, long-term elevated thyroid stimulating hormone (TSH) was associated with inflammation and higher psychotic manifestations in two cross-sectional studies. This may result in structural changes and altered neuronal processes, contributing to the manifestation of cognitive dysfunction and psychotic symptoms (Dai et al., 2023; Wang et al., 2024).

Thyroid Hormones and Mood and Anxiety symptoms

Similarly, elevated TSH levels are associated with more severe mood and anxiety symptoms, and higher suicide occurrence in mood disorders (Huang et al., 2023; Luo et al., 2023; Yang et al., 2023). Beyond mimicking neuropsychiatric disorders, HT is implicated as a risk factor for increased mood and anxiety symptoms across three studies (1 systematic review; 2 cross-sectional studies) and may increase susceptibility to treatment-resistant mood symptoms (Lang et al., 2020; Puchalapalli & Mahmood, 2020).

Appetite and Metabolic hormones and PMA Symptom Manifestations

Although few studies (n = 6: 2 systematic reviews; 1 narrative review; 2 cross-sectional studies; 1 cohort study) included in the current review discussed appetite or metabolic hormones, evidence indicates that these hormones play roles in the manifestation of psychotic, mood and anxiety symptoms. Results varied across specific hormones, different studies, populations and conditions. For an overview of findings, refer to Table 2.4.

Table 2.4

Main Findings Regarding the Link Between Appetite and Metabolic Hormones and Psychotic, Mood, and Anxiety Symptoms

Psychotic Symptoms		Mood Symptoms		Anxiety Symptoms	
Main findings	References	Main findings	References	Main findings	References
Diabetes/insulin insensitivity associated with psychosis, potentially due to effects of blood-sugar on brain and neuro-inflammation.	Merritt et al., 2020	Higher *ghrelin* levels observed in BD I and II compared to MDD and controls; higher levels linked to more severe depressive symptoms in older adults.	Chen et al., 2022; van Andel, 2022;	More severe AS in *diabetes*, this can affect systems such as HPA axis, increasing risk for other psychiatric manifestations.	Kershaw et al., 2023
		Higher *leptin* and *ghrelin* levels associated with depressive symptoms, possibly due to neuroinflammatory pathways.	Scott et al., 2023		

Note. PS = psychotic symptoms; MS = mood symptoms; AS = anxiety symptoms; BD = bipolar disorder; MDD = major depressive disorder.

Insulin, Diabetes and Psychotic Symptoms

Only one narrative review discussed psychotic symptoms in the context of metabolic hormones. Diabetes mellitus (involving insulin insensitivity) includes disrupted blood-sugar levels and can be associated with psychosis. This potentially links insulin dysregulation and psychotic symptoms through mechanisms such as elevated blood sugar levels in the brain and inflammation associated with diabetes (Merritt et al., 2020).

Insulin, Diabetes and Anxiety Symptoms

Likewise, higher anxiety levels were observed in diabetes patients compared to the general population, according to a large-scale systematic review (Kershaw et al., 2023). Through a bidirectional mechanism, anxiety levels may also affect other physiological systems, such as the HPA axis, increasing risk for other psychiatric manifestations (Kershaw et al., 2023).

Ghrelin, Leptin and Mood Symptoms

In a cross-sectional study on bipolar I and II patients, higher levels of ghrelin were observed compared to those with MDD and healthy controls. Interestingly, the same study found higher ghrelin level to be associated with improved executive functions in BD patients, indicating potential neuroprotective effects (Chen et al., 2022). Conversely, a cohort study found that higher ghrelin levels are linked to more depressive symptoms in older adults. This relationship was influenced by age and waist-hip ratio (van Andel, 2022).

In the same study, leptin levels were also associated with depressive symptoms in older adults, with age and waist-hip ratio once again modifying this relationship (van Andel, 2022). Correspondingly, the systematic review by Scott et al. (2023) found that higher leptin and ghrelin levels are associated with depressive symptoms in youth, possibly due to neuroinflammatory pathways.

Oxytocin and PMA Symptom Manifestations

The search yielded a limited number (n = 4) of cross-sectional studies on the association of PMA symptoms with oxytocin (OXT). An overview of findings regarding OXT and PMA symptoms is provided in Table 2.5.

Table 2.5

Main Findings Regarding the Link Between Oxytocin and Psychotic, Mood, and Anxiety Symptoms

Psychotic Symptoms		Mood Symptoms		Anxiety Symptoms	
Main findings	References	Main findings	References	Main findings	References
Lower *OXT* levels linked to more stress and impaired social cognition, potentially contributing to PS development.	Merritt et al., 2020	Higher *OXT* levels are associated with well-being, less MS and reduced stress.	Chen et al., 2022; van Andel, 2022;	*OXT* is negatively correlated with stress hormones, anxiety, and fear symptoms. Higher levels are associated with reduced stress and less AS..	Masdrakis et al., 2023; Morgan et al., 2023

Note. PS = psychotic symptoms; MS = mood symptoms; AS = anxiety symptoms; OXT = oxytocin

Oxytocin is known to be a regulator of behavior, mood and cognition (Masdrakis et al., 2023). OXT is negatively correlated with stress hormones, anxiety, and fear symptoms, and higher levels are associated with well-being and with reduced stress and anxiety (Masdrakis et al., 2023; Morgan et al., 2023). Conversely, lower OXT levels are linked to more stress and impaired social cognition, potentially contributing to psychotic symptoms (Mutu et al., 2018; Rubin et al., 2018; Veras, 2018).

Discussion

This scoping review is one of the few reviews that aimed to summarize and highlight the current state of the scientific literature on the associations between endocrine functioning, hormonal imbalances and the manifestation of psychotic, mood and anxiety symptoms in a comprehensive manner. Findings highlight the evidence for complex and interrelated associations between sex hormones, stress hormones, thyroid hormones, appetite hormones, and the socio-behavioral hormone oxytocin with regard to PMA symptoms.

Sex-specific effects of Sex Hormones on PMA symptoms

Sex hormone fluctuations show sex-specific effects related to the manifestation of PMA symptoms. This may be attributed mostly due to different, fluctuating and interacting sex hormone levels. While this review found limited findings in men, the differences in sex hormone levels between men and women may be an explanation for the sexually dimorphic presentation of PMA symptoms across various disorders.

Influence of Sex Hormones on Psychotic Symptoms

Estrogen's Protective Effect against Psychotic Symptoms

The course and presentation of psychotic disorders varies significantly between sexes. This may partially be due to estrogens' neuroprotective effects against neurodegeneration associated with psychotic symptoms (Mu et al., 2024). Studies indicate that estrogen has protective effects in women against the manifestation of psychotic symptoms, with limited findings in men (McGregor et al., 2017; Hodgetts & Hausmann, 2020; Brand et al., 2021), consistent with recent reviews (Mu et al., 2024).

Prolactin, Androgens, and Psychotic Symptoms

Furthermore, elevated prolactin can lower estrogen and is linked to psychotic symptoms and cognitive dysfunction in both sexes, potentially through this mechanism (Labad, 2019; Jen et al., 2020; Medina-Loera et al., 2020). Findings on androgens were limited, but some studies hinted higher testosterone to be protective against positive symptoms in females and decrease negative symptoms in men, reflecting the sexually dimorphic presentation of psychotic disorders (Gonzalez et al., 2017; Barendse et al., 2023; Buoli et al., 2016).

Impact of Sex Hormones on Mood and Anxiety symptoms

This review revealed robust evidence for the impact of female sex hormones on mood manifestations by exerting effects on brain regions involved with emotional and cognitive

processes (Toffoletto et al., 2014). Furthermore, limited evidence hints that lower specific androgen levels in women are linked to increased anxiety, depression and cognitive impairment (Balikci et al., 2014; Lee et al., 2017 Sukhapore et al., 2022). In this regard, the current review found limited findings in men. However, the comprehensive systematic review by Salvador et al. (2019) concluded that androgen deficiency in men is also associated with depressive mood and cognitive impairment.

Women exhibit twice the risk for anxiety and mood disorders compared to men. Considerable evidence implicates sex hormone fluctuations in women as a major factor behind these sex differences (Kundakovic & Rocks, 2022). These findings were reflected in the current project.

Conclusion on Sex Hormones and PMA Symptoms

Estrogen's protective effects against psychotic symptoms are well-documented in women, potentially explaining the gap in psychosis presentation between sexes. Sex hormone fluctuations throughout developmental stages, coupled with environment and genetical predisposition contribute to the manifestation of PS. Likewise, sex hormone fluctuations increase the *risk* for anxiety and mood symptoms. However, they are not solely *causative*; their impact involves complex interactions among hormone status, genetics, and environmental influences affecting brain structure and function (Kundakovic & Rocks, 2022).

Stress Hormones and their Role in PMA symptoms

Stress hormones are linked to PMA symptoms through mechanisms involving the HPA axis, as elevated cortisol and a dysregulated HPA axis are common in disorders involving PMA symptoms.

Impact of Chronic Stress on Psychotic Symptoms

High stress hormone levels are common in individuals with PS or those at risk (Karinakas & Garyfallos, 2015; Schatzberg, 2015). Studies propose that cortisol excess

impairs cognitive functions and alters dopamine functioning, which may increase risk for PS. However, elevated cortisol levels may also reflect the stress experienced due to psychosis itself, as they are more strongly associated with anxiety (Karinakas & Garyfallos, 2015; Labad, 2019). This suggests that the stress experienced due to psychosis may modulate the relationship of HPA axis functioning and PS, consistent with the comprehensive systematic review by Bradley & Dinan (2010). However, it is likely that stress hormone dysregulation contributes to risk for psychosis - and poorer physical and mental health overall (Bradley & Dinan, 2010).

Effects of Chronically Elevated Cortisol on Anxiety and Mood Symptoms

The current review indicates that elevated cortisol and a dysregulated HPA axis are also commonly associated with anxiety and mood symptoms. For instance, there is strong evidence that chronically elevated stress hormone levels adversely affect stress responses and cognitive functions (Schatzberg, 2015; Wingenfeld & Wolf, 2015; Chronister et al., 2021). Furthermore, chronically high cortisol can be neurotoxic, especially during early development. This may alter brain regions involved in cognitive functions and emotion regulation, thereby increasing susceptibility to the development of mood and anxiety symptoms (Pagliaccio et al., 2015; Yuen et al., 2017; Raymond et al., 2018).

Conclusion on Stress Hormones and PMA Symptoms

Childhood stress, early adversity and chronic stress can increase susceptibility to mood and anxiety symptoms by dysregulating the HPA axis, influencing brain structure and cognition through chronically elevated cortisol. Additionally, - and consistent with large reviews - anxiety and stress are known to increase risk for psychotic symptoms (van Winkel et al., 2008), emphasizing that (early) stress management is crucial in the mitigation of PMA symptom manifestation.

Thyroid Hormones and their Role in PMA symptoms

Thyroid hormones are implicated in the manifestation of PMA symptoms through thyroid dysfunction, which can mimic neuropsychiatric symptoms. Long-term thyroid hormone imbalances also increase the risk of developing PMA symptoms related to neuropsychiatric disorders that don't resolve with thyroid restoration.

Hypothyroidism and PMA Manifestations

Strong evidence from the current project and other reviews confirm that hypothyroidism (HT) can induce symptoms such as psychosis, anxiety and mood manifestations (Puchalapalli & Mahmood, 2020; Lekurwale et al., 2023). These symptoms recede as thyroid functions recover and are therefore distinguishable from neuropsychiatric symptoms related to psychiatric disorders. Conversely, HT was identified as a risk factor for more severe mood and anxiety symptoms that do not recede with restored thyroid functioning (Puchalapalli & Mahmood, 2020).

Impact of TSH Imbalances on PMA Symptoms

Additionally, large cross-sectional Chinese studies reported that elevated thyroid stimulating hormone may contribute to cognitive dysfunctioning and psychotic symptoms through mechanisms such as neuroinflammation leading to structural changes and altered neuronal processes (Dai et al., 2023; Wang et al., 2024). Elevated TSH was also related to more severe AS and MS in included cross-sectional studies (Huang et al., 2023; Luo et al., 2023; Yang et al., 2023). These findings are somewhat in line with a large systematic review by Bathla et al. (2016), who concluded that abnormal TSH levels are common in mood and anxiety disorders, but data were contradictory whether direction of the association involved high or low TSH levels.

Conclusion on Thyroid Hormones and PMA symptoms

Given the heightened risk for developing PMA symptoms associated with thyroid imbalances, one may conclude the need for regular monitoring of thyroid function, particularly in individuals with depression, as it may predispose them to treatment-resistant forms of the condition.

Appetite and Metabolic Hormones and PMA Symptoms

A limited number of studies included discussed appetite and metabolic hormones. These studies did find evidence for associations of insulin, leptin and ghrelin with PMA symptom manifestation, however.

Impact of Insulin Dysregulation on Psychotic and Anxiety Symptoms

Metabolic hormone dysregulation, specifically insulin sensitivity associated with diabetes, is linked to psychotic symptoms. This may be due to disrupted blood-sugar levels and inflammation impacting the brain, contributing to psychosis (Merritt et al., 2020). These findings are coherent with a large-scale meta-analysis from Perry et al. (2016), who concluded that impaired glucose tolerance and insulin resistance are associated with first-episode psychosis; indicating a potential predictive marker. However, no causality was established in their review, similar to the findings of the current scoping review.

In the context of anxiety symptoms, robust evidence from a systematic review revealed heightened anxiety levels among diabetes patients compared to the general population (Kershaw et al., 2023). However, this does not provide evidence that endocrine mechanisms associate with diabetes contribute to the manifestation of AS. The increased anxiety may be a psychological epiphenomenon due to increased stress levels experienced with diabetes, similar to elevated cortisol levels in psychosis. Conversely, it is established in reviews in the literature that stress has significant impact on metabolic function, and long-

term anxiety and stress can contribute to metabolic disorders, such as diabetes (Sharma et al., 2022)

Impact of Leptin and Ghrelin on Mood and Anxiety Symptoms

The current review provides evidence that dysregulation of the appetite hormones leptin and ghrelin are associated with anxiety and mood symptoms. Leptin may influence mood and anxiety by contributing to neuroinflammation and reduced neuroplasticity, whereas elevated ghrelin levels have been linked to increased neuroinflammatory responses, which can similarly affect brain function and structure, impacting emotional regulation and cognitive processes, resulting in increased depressive symptoms (Chen et al., 2021; van Andel et al., 2022). The systematic review by Scott et al. (2023) further reinforces these findings, demonstrating that elevated leptin and ghrelin levels are linked to depressive symptoms in youth, potentially through neuroinflammatory pathways.

Conclusion on Appetite and Metabolic Hormones

The bidirectional nature of the relationship of appetite and metabolic hormones with stress, other physiological systems and PMA symptoms highlights the need for a comprehensive approach to understanding and treating psychiatric conditions that considers both metabolic and psychological factors.

Socio-behavioral Hormones: Oxytocin and PMA symptoms

The current review included limited results for the neuropeptide oxytocin (OXT), likely due to search strategy limitations. Being a well-documented regulator of mood and behavior, OXT levels are inversely correlated with stress hormones, anxiety and fear symptoms, while higher levels mark improved well-being, mood and reduced anxiety (Masdrakis et al., 2023; Morgan et al., 2023).

Conversely, low levels may contribute to the development of psychotic symptoms. This may be explained by increased stress and impaired social cognition, which are hallmarks

of psychosis (Mutu et al., 2018; Rubin et al., 2018; Veras, 2018). Low oxytocin level may also interfere with dopamine signaling. Altered dopamine signaling is implicated and often associated with PS (Kesby et al., 2018). Potentially for this reason, exogenously administered oxytocin is being used to treat individuals at risk for psychosis, which has shown therapeutic effects on social cognition, positive symptoms and emotion regulation (Keng Goh et al., 2021).

Conclusion on Oxytocin and PMA symptoms

Overall, OXT has anti-inflammatory and neuroplastic effects, which are crucial for maintaining brain functions and mitigating PMA symptoms. Evidence from a large systematic supports the role of OXT in PMA disorders and symptomatic manifestations. This may be unsurprising due to the hormone's role in social functioning, considering many PMA symptoms are characterized by, or related to, social functioning (Cochran, 2013).

Implications

This review aids in synthesizing the current standing of research related to endocrine functioning and PMA symptom manifestations. In this manner, it explored possibilities for future directions in research as well as potentially informing clinical decisions. Understanding hormonal influences on the manifestation of mood, anxiety and psychosis at the symptom level could inform diagnostic and treatment recommendations.

For instance, the findings emphasize the potential of personalized and holistic treatment approaches, whereby endocrine disorders and hormonal profiles are taken into consideration in mental health practice. Furthermore, this review highlights the value of mitigating the effects of long-term PMA symptoms and associated stress on endocrine functioning and subsequent mental health problems. This review could guide interdisciplinary research, wherein expertise from endocrinology, neurology, psychiatry and psychology is

adopted to further the understanding of the interactions between endocrine functioning and mental health.

Gaps, Limitations and Future Directions

Despite a multitude of findings and possible implications, results from this scoping review were often heterogeneous and lacked clear relationships to specific symptoms of the PMA domains. This may contribute to the broad conclusions and general associations found in existing reviews and studies on the topic. Moreover, provided mechanisms are often speculative, requiring more research. All this may be due to various limitations and gaps in the literature.

Research Gaps and Limitations

Firstly (1), the heterogeneity of symptom and disorder presentation make it difficult for researchers to draw clear conclusions on an association. Second (2), the development of PMA symptoms includes genetic, epigenetic, biological, psychological and environmental factors. These interactions affect hormone status, endocrine functioning, mood, behavior, and cognition in a multidirectional manner (Kershaw et al., 2023). In this regard, true unifying and multidisciplinary models and reviews - integrating (epi)genetic, biological, environmental, behavioral and cognitive research - are lacking. Third (3), associations were usually researched in included studies within the context of disorders, instead of specific symptoms. This makes drawing specific connections with symptoms difficult (Sukhapore et al., 2022), which was reflected in the current project. Lastly (4), the three symptom types often overlap and interact. For example, psychotic symptoms increase risk of anxiety, and vice versa. The conclusions of studies regarding specific hormone-symptom relationships are often limited due to this interaction.

These limitations potentially indicate shortcomings regarding symptom and disorder classifications in research and diagnostical practice. A transnosological approach, such as the

Research Domain Criteria (RDoC) framework (National Institute of Mental Health, 2024), may be better suited to understand symptom-hormone relationships. This method focuses on studying underlying mechanisms such as cognitive processes, social processes and units of analysis (in this context: i.e. hormonal imbalances and symptom phenomena) independent of traditional diagnostic categories. In this manner, the RDoC framework could aid in identifying more precise and personalized symptom-hormone relationships, potentially leading to more effective and tailored treatment strategies benefiting a wide range of patients, irrespective of specific diagnoses.

Limitations of the Current Review

The current review also has several limitations of its own. As mentioned, the majority of the included studies discussed hormonal functioning in the context of a disorder. Therefore, symptom-hormone associations were often derived from psychotic, mood and anxiety disorders, which usually include a diverse and heterogeneous range of (comorbid) symptoms. This made it difficult to identify patterns across studies with depth and detail regarding hormone-symptom associations.

The second limitation refers to the heterogeneity of included studies. Including a diverse range of methodologies has advantages for exploratory purposes. However, it also led to difficulties drawing definitive conclusions about findings and patterns.

Lastly, the search, screening and analysis was done by a single author, potentially increasing risk of bias in study selection and a possible overrepresentation of certain viewpoints found in the literature.

Future Directions

Given the breadth of the topic, future research could delve deeply into each subject covered in this review. Using a transdiagnostic approach, future studies should focus on specific hormones in more detail. This could take the form of a systematic review,

synthesizing the results of longitudinal studies with homogenous designs to help determine causal relationships between endocrine functioning and specific PMA symptom manifestations (i.e. only focusing on the relationship with positive symptoms in psychosis). In this regard, it is also crucial for future research to integrate multidisciplinary approaches to help create comprehensive models that better explain the interactions between endocrine function, PMA symptoms and mental health in general.

Conclusion

The findings from this scoping review indicate intricate associations between specific hormone functions and PMA symptoms. The available literature on the topic is extensive and not all could be included.

Key Findings

(1) Key findings include the sex-specific effects of sex hormones: estrogens are potentially protective against psychosis in women while imbalances of these hormones increase the risk for anxiety and mood symptoms. This emphasizes the need for more research, particularly in men where data are lacking.

(2) A dysregulated HPA axis and stress hormones are linked to psychotic symptoms, although further clarification is needed. HPA axis dysregulation shows clearer associations with mood and anxiety symptoms, predicting increased risk. Early adversity and chronic stress can alter brain function, increasing susceptibility to mood and anxiety symptoms, underscoring the importance of managing stress and stress hormones, especially during critical developmental periods.

(3) Moreover, thyroid hormone imbalances show an association with psychotic, mood and anxiety symptoms and cognitive dysfunction, as in the case with TSH. Hypothyroidism can mimic PMA symptoms by itself and is also indicated as a risk factor for more severe

mood symptoms and anxiety, especially in an already existing psychiatric disorder such as MDD.

(4) Appetite and metabolic hormones, including ghrelin, leptin and insulin were also reviewed, highlighting their associations with diabetes and their relationship with psychotic and anxiety symptoms via metabolic dysregulation and neuroinflammation.

(5) Lastly, oxytocin mitigates stress and anxiety, whilst low levels impair social cognition and may contribute to psychotic and mood symptoms.

It is crucial to note that the relationships of hormonal fluctuations with PMA symptoms are not solely causal. Fluctuations often co-occur with symptomatic manifestations, reflecting broader physiological and psychological processes. However, endocrine dysfunctioning can heighten the risk of developing certain symptoms through short and long-term effects on physiological processes and brain regions.

Overall, genetic, biological, and environmental factors interact in a complex manner to influence endocrine functioning, mood, behavior, and cognition; shaping the development of psychotic, mood, and anxiety symptoms. In this context, using transdiagnostic and multidisciplinary research strategies may help to elucidate the interplay of these factors, potentially informing and improving diagnostic and treatment strategies in mental health care.

References

Altemus, M. (2010). Hormone-specific psychiatric disorders: do they exist? *Archives Of Women's Mental Health*, *13*(1), 25–26. https://doi.org/10.1007/s00737-009-0123-0

Balikci, A., Erdem, M., Keskin, U., Zincir, S. B., Gulsun, M., Ozcelik, F., Akgul, E. O., Akarsu, S., Oztosun, M., & Ergun, A. (2014). Depression, Anxiety, and Anger in Patients with Polycystic Ovary Syndrome. *Nöro Psikiyatri Arşivi*, *51*(4). https://doi.org/10.5152/npa.2014.6898

Barbero, J. D., Gutiérrez-Zotes, A., Montalvo, I., Creus, M., Cabezas, Á., Solé, M., Algora, M. J., Garcia-Parés, G., Vilella, E., & Labad, J. (2015). Free thyroxine levels are associated with cognitive abilities in subjects with early psychosis. *Schizophrenia Research*, *166*(1–3), 37–42. https://doi.org/10.1016/j.schres.2015.04.030

Barendse, M. E., Simmons, J. G., Byrne, M. L., Patton, G., Mundy, L., Olsson, C. A., Seal, M. L., Allen, N. B., & Whittle, S. (2018). Associations between adrenarcheal hormones, amygdala functional connectivity and anxiety symptoms in children. *Psychoneuroendocrinology*, *97*, 156–163. https://doi.org/10.1016/j.psyneuen.2018.07.020

Barendse, M. E., Simmons, J. G., Patton, G., Mundy, L., Byrne, M. L., Seal, M. L., Allen, N. B., & Whittle, S. (2020). Adrenarcheal Timing Longitudinally Predicts Anxiety Symptoms via Amygdala Connectivity During Emotion Processing. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *59*(6), 739-748.e2. https://doi.org/10.1016/j.jaac.2019.04.018

Barendse, M., Lara, G., Guyer, A., Swartz, J., Taylor, S., Shirtcliff, E., Lamb, S., Miller, C., Ng, J., Yu, G., & Tully, L. (2023). Sex and pubertal influences on the neurodevelopmental underpinnings of schizophrenia: A case for longitudinal research

on adolescents. *Schizophrenia Research*, *252*, 231–241. https://doi.org/10.1016/j.schres.2022.12.011

Bathla, M., Singh, M., & Relan, P. (2016). Prevalence of anxiety and depressive symptoms among patients with hypothyroidism. *Indian Journal Of Endocrinology And Metabolism*, *20*(4), 468. https://doi.org/10.4103/2230-8210.183476

Bradley, A. J., & Dinan, T. G. (2010). Review: A systematic review of hypothalamic-pituitary-adrenal axis function in schizophrenia: implications for mortality. *Journal Of Psychopharmacology*, *24*(4_suppl), 91–118. https://doi.org/10.1177/1359786810385491

Brand, B. A., De Boer, J. N., & Sommer, I. E. (2021). Estrogens in schizophrenia: progress, current challenges and opportunities. *Current Opinion in Psychiatry*, *34*(3), 228–237. https://doi.org/10.1097/yco.0000000000000699

Buoli, M., Caldiroli, A., Serati, M., Grassi, S., & Altamura, A. C. (2016). Sex Steroids and Major Psychoses: Which Role for DHEA-S and Progesterone? *Neuropsychobiology*, *73*(3), 178–183. https://doi.org/10.1159/000444922

Chen, M., Hsu, J., Huang, K., Tsai, S., Su, T., Li, C., Lin, W., Tu, P., & Bai, Y. (2020). Role of appetite hormone dysregulation in the cognitive function among patients with bipolar disorder and major depressive disorder. ˜ *The œ World Journal Of Biological Psychiatry*, *22*(6), 428–434. https://doi.org/10.1080/15622975.2020.1819566

Chronister, B. N., Gonzalez, E., Lopez-Paredes, D., Suarez-Torres, J., Gahagan, S., Martinez, D., Barros, J., Jacobs, D. R., Checkoway, H., & Suarez-Lopez, J. R. (2021). Testosterone, estradiol, DHEA and cortisol in relation to anxiety and depression scores in adolescents. *Journal Of Affective Disorders*, *294*, 838–846. https://doi.org/10.1016/j.jad.2021.07.026

Cochran, D. M., Fallon, D., Hill, M., & Frazier, J. A. (2013). The Role of Oxytocin in Psychiatric Disorders. *Harvard Review Of Psychiatry*, *21*(5), 219–247. https://doi.org/10.1097/hrp.0b013e3182a75b7d

Culbert, K. M., Thakkar, K. N., & Klump, K. L. (2022). Risk for midlife psychosis in women: critical gaps and opportunities in exploring perimenopause and ovarian hormones as mechanisms of risk. *Psychological Medicine*, *52*(9), 1612–1620. https://doi.org/10.1017/s0033291722001143

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. (2013). In *American Psychiatric Publishing, Inc. eBooks*. https://doi.org/10.1176/appi.books.9780890425596.893619

Glannon, W. (2022). Biomarkers in psychiatric disorders. *Cambridge Quarterly Of Healthcare Ethics/CQ. Cambridge Quarterly Of Healthcare Ethics*, *31*(4), 444–452. https://doi.org/10.1017/s0963180122000056

Gleeson, P. C., Worsley, R., Gavrilidis, E., Nathoo, S., Ng, E., Lee, S., & Kulkarni, J. (2015). Menstrual cycle characteristics in women with persistent schizophrenia. *Australian And New Zealand Journal Of Psychiatry*, *50*(5), 481–487. https://doi.org/10.1177/0004867415590459

Goh, K. K., Chen, C., & Lane, H. (2021). Oxytocin in Schizophrenia: Pathophysiology and Implications for Future Treatment. *International Journal Of Molecular Sciences*, *22*(4), 2146. https://doi.org/10.3390/ijms22042146

González-Rodríguez, A., Bernardo, M., Penadés, R., Arias, B., Cortés, V. R., Seeman, M. V., & Catalán, R. (2017). Do FSH/LH ratio and gonadal hormone levels predict clinical improvement in postmenopausal schizophrenia women? *Archives Of Women's Mental Health*, *20*(5), 613–620. https://doi.org/10.1007/s00737-017-0757-2

Graham, B. M., & Shin, G. (2018). Estradiol moderates the relationship between state-trait anxiety and attentional bias to threat in women. *Psychoneuroendocrinology*, *93*, 82–89. https://doi.org/10.1016/j.psyneuen.2018.04.018

Guan, L. Y., Hou, W. L., Zhu, Z. H., Cao, J. Q., Tang, Z., Yin, X. Y., Xu, D. W., Yu, X., Jia, Q. F., Tang, W. J., Zhang, J., & Hui, L. (2021). Associations among gonadal hormone, triglycerides and cognitive decline in female patients with major depressive disorders. *Journal Of Psychiatric Research*, *143*, 580–586. https://doi.org/10.1016/j.jpsychires.2020.11.022

Harvey, P. D. (2011). Mood symptoms, cognition, and everyday functioning: in major depression, bipolar disorder, and schizophrenia. *PubMed*. https://pubmed.ncbi.nlm.nih.gov/22132366

Hodgetts, S., & Hausmann, M. (2020). Antipsychotic effects of sex hormones and atypical hemispheric asymmetries. *Cortex*, *127*, 313–332. https://doi.org/10.1016/j.cortex.2020.02.016

Huang, X., Sun, Y., Wu, A., & Zhang, X. (2023). Prevalence and clinical profile of abnormal glucose in first-episode and drug-naïve patients with major depressive disorder with comorbid abnormal thyroid function: a large-scale cross-sectional study. *BMC Psychiatry*, *23*(1). https://doi.org/10.1186/s12888-023-04842-5

Jen, Y., Hwang, T., Chan, H., Hsieh, M. H., Liu, C., Liu, C., Hwu, H., Kuo, C., Lin, Y., Chien, Y., & Chen, W. J. (2020). Abnormally low prolactin levels in schizophrenia patients after switching to aripiprazole in a randomized trial: a biomarker for rebound in psychotic symptoms? *BMC Psychiatry*, *20*(1). https://doi.org/10.1186/s12888-020-02957-7

Karanikas, E., & Garyfallos, G. (2015). Role of cortisol in patients at risk for psychosis mental state and psychopathological correlates: A systematic review. *Psychiatry And Clinical Neurosciences*, *69*(5), 268–282. https://doi.org/10.1111/pcn.12259

Kershaw, K. A., Storer, B., Braund, T., Chakouch, C., Coleshill, M., Haffar, S., Harvey, S., Newby, J., Sicouri, G., & Murphy, M. (2023). The prevalence of anxiety in adult endocrinology outpatients: A systematic review and meta–analysis. *Psychoneuroendocrinology*, *158*, 106357. https://doi.org/10.1016/j.psyneuen.2023.106357

Kundakovic, M., & Rocks, D. (2022). Sex hormone fluctuation and increased female risk for depression and anxiety disorders: From clinical evidence to molecular mechanisms. *Frontiers in Neuroendocrinology*, *66*, 101010. https://doi.org/10.1016/j.yfrne.2022.101010

Labad, J. (2019). The role of cortisol and prolactin in the pathogenesis and clinical expression of psychotic disorders. *Psychoneuroendocrinology*, *102*, 24–36. https://doi.org/10.1016/j.psyneuen.2018.11.028

Lang, X., Hou, X., Shangguan, F., & Zhang, X. Y. (2020). Prevalence and clinical correlates of subclinical hypothyroidism in first-episode drug-naive patients with major depressive disorder in a large sample of Chinese. *Journal Of Affective Disorders*, *263*, 507–515. https://doi.org/10.1016/j.jad.2019.11.004

Lee, S., Wang, L., Chang, C., Wu, C., Chen, H., Lin, S., Chu, C., Lu, T., & Lu, R. (2017). Serum DHEA-S concentration correlates with clinical symptoms and neurocognitive function in patients with bipolar II disorder: A case-controlled study. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, *74*, 31–35. https://doi.org/10.1016/j.pnpbp.2016.11.006

Lekurwale, V., Acharya, S., Shukla, S., & Kumar, S. (2023). Neuropsychiatric Manifestations of Thyroid Diseases. *Curēus*. https://doi.org/10.7759/cureus.33987

Liu, F., Huang, L., Zhu, R., Peng, C., & Deng, X. (2021). The thyroid dysfunction of suicide attempts in major depression. *Annales Médico-psychologiques*, *179*(4), 329–333. https://doi.org/10.1016/j.amp.2020.12.022

Luo, G., Li, Y., Yao, C., Li, M., Li, J., & Zhang, X. (2023). Prevalence of overweight and obesity in patients with major depressive disorder with anxiety: Mediating role of thyroid hormones and metabolic parameters. *Journal Of Affective Disorders*, *335*, 298–304. https://doi.org/10.1016/j.jad.2023.05.008

Lyu, N., Zhao, Q., Fu, B., Li, J., Wang, H., Yang, F., Liu, S., Huang, J., Zhang, X., Zhang, L., & Li, R. (2023). Hormonal and inflammatory signatures of different mood episodes in bipolar disorder: a large-scale clinical study. *BMC Psychiatry*, *23*(1). https://doi.org/10.1186/s12888-023-04846-1

Masdrakis, V. G., Legaki, E., Papageorgiou, C., & Markianos, M. (2020). Pituitary-adrenal axis hormones in early-onset versus late-onset panic disorder. *International Journal Of Psychiatry in Clinical Practice*, *26*(1), 72–78. https://doi.org/10.1080/13651501.2020.1828929

Masdrakis, V. G., Papageorgiou, C., & Markianos, M. (2022). Correlations of plasma oxytocin with clinical and hormonal parameters in panic disorder. *Nordic Journal Of Psychiatry*, *77*(3), 221–226. https://doi.org/10.1080/08039488.2022.2083675

McGregor, C., Riordan, A., & Thornton, J. (2017). Estrogens and the cognitive symptoms of schizophrenia: Possible neuroprotective mechanisms. *Frontiers in Neuroendocrinology*, *47*, 19–33. https://doi.org/10.1016/j.yfrne.2017.06.003

Medina-Loera, S., Flores-Medina, Y., Escamilla-Orozco, R. I., Saracco-Álvarez, R. A., Rosel-Vales, M., Flores-Ramos, M., & Mondragón-Maya, A. (2020). Association between

prolactin serum levels and cognitive function in chronic schizophrenia patients. *Salud Mental*, *43*(1), 21–25. https://doi.org/10.17711/sm.0185-3325.2020.004

Merritt, J., Tanguturi, Y., Fuchs, C., & Cundiff, A. W. (2020). Medical Etiologies of Secondary Psychosis in Children and Adolescents. *Child And Adolescent Psychiatric Clinics Of North America*, *29*(1), 29–42. https://doi.org/10.1016/j.chc.2019.08.005

Mikulska, J., Juszczyk, G., Gawrońska-Grzywacz, M., & Herbet, M. (2021). HPA Axis in the Pathomechanism of Depression and Schizophrenia: New Therapeutic Strategies Based on Its Participation. *Brain Sciences*, *11*(10), 1298. https://doi.org/10.3390/brainsci11101298

Mishra, K., Sawant, N., & Garg, S. (2022). Management of psychiatric disorders in patients with endocrine disorders. *Indian Journal Of Psychiatry/Indian Journal Of Psychiatry*, *64*(8), 402. https://doi.org/10.4103/indianjpsychiatry.indianjpsychiatry_30_22

Morgan, J. K., Conner, K. K., Fridley, R. M., Olino, T. M., Grewen, K. M., Silk, J. S., Iyengar, S., Cyranowski, J. M., & Forbes, E. E. (2023). Adolescents' Hormonal Responses to Social Stress and Associations with Adolescent Social Anxiety and Maternal Comfort: A Preliminary Study. *Child Psychiatry And Human Development*. https://doi.org/10.1007/s10578-023-01521-0

Mu, E., Gurvich, C., & Kulkarni, J. (2024). Estrogen and psychosis — a review and future directions. *Archives Of Women's Mental Health*. https://doi.org/10.1007/s00737-023-01409-x

Mulligan, E. M., Hajcak, G., Crisler, S., & Meyer, A. (2020). Increased dehydroepiandrosterone (DHEA) is associated with anxiety in adolescent girls. *Psychoneuroendocrinology*, *119*, 104751. https://doi.org/10.1016/j.psyneuen.2020.104751

National Institute of Mental Health (NIMH). (2024). *About RDOC*. National Institute Of Mental Health (NIMH). Geraadpleegd op 1 juli 2024, van https://www.nimh.nih.gov/research/research-funded-by-nimh/rdoc/about-rdoc

Norman, A. W., & Litwack, G. (1997). *Hormones*.

Nouri, S., Biedermann, S. V., Joue, G., Auer, M. K., Sommer, T., & Fuss, J. (2022). Effects of circulating estradiol on physiological, behavioural, and subjective correlates of anxiety: A double-blind, randomized, placebo-controlled trial. *Psychoneuroendocrinology*, *138*, 105682. https://doi.org/10.1016/j.psyneuen.2022.105682

Nuevo, R., Chatterji, S., Verdes, E., Naidoo, N., Arango, C., & Ayuso-Mateos, J. L. (2010). The Continuum of Psychotic Symptoms in the General Population: A Cross-national Study. *Schizophrenia Bulletin*, *38*(3), 475–485. https://doi.org/10.1093/schbul/sbq099

Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan—a web and mobile app for systematic reviews. *Systematic Reviews*, *5*(1). https://doi.org/10.1186/s13643-016-0384-4

Pagliaccio, D., Luby, J. L., Bogdan, R., Agrawal, A., Gaffrey, M. S., Belden, A. C., Botteron, K. N., Harms, M. P., & Barch, D. M. (2015). Amygdala functional connectivity, HPA axis genetic variation, and life stress in children and relations to anxiety and emotion regulation. *Journal Of Abnormal Psychology*, *124*(4), 817–833. https://doi.org/10.1037/abn0000094

Pek, T. M., Yazici, E., Guzel, D., Kose, E., Yazıcı, A. B., & Erol, A. (2019). The relationship between oxytocin, vasopressin and atrial natriuretic peptide levels and cognitive functions in patients with schizophrenia. *Psychiatry And Clinical Psychopharmacology*, *29*(4), 798–810. https://doi.org/10.1080/24750573.2019.1653149

Perry, B. I., McIntosh, G., Weich, S., Singh, S., & Rees, K. (2016). The association between first-episode psychosis and abnormal glycaemic control: systematic review and meta-analysis. ˜ *The œLancet. Psychiatry*, *3*(11), 1049–1058. https://doi.org/10.1016/s2215-0366(16)30262-0

Pham, M. T., Rajić, A., Greig, J. D., Sargeant, J. M., Papadopoulos, A., & McEwen, S. A. (2014). A scoping review of scoping reviews: advancing the approach and enhancing the consistency. *Research Synthesis Methods*, *5*(4), 371–385. https://doi.org/10.1002/jrsm.1123

Puchalapalli, A., & Mahmood, A. (2020). Neuropsychiatric comorbidities in hypothyroidism: A systematic review. *Neurology, Psychiatry & Brain Research/Neurology, Psychiatry And Brain Research*, *37*, 79–86. https://doi.org/10.1016/j.npbr.2020.06.005

Raymond, C., Marin, M., Majeur, D., & Lupien, S. (2018). Early child adversity and psychopathology in adulthood: HPA axis and cognitive dysregulations as potential mechanisms. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, *85*, 152–160. https://doi.org/10.1016/j.pnpbp.2017.07.015

Rubin, L. H., Wehring, H. J., Demyanovich, H., Carter, C. S., Pournajafi-Nazarloo, H., Feldman, S. M., Earl, A. K., August, S., Gold, J. M., & Kelly, D. L. (2018). Peripheral oxytocin and vasopressin are associated with clinical symptom severity and cognitive functioning in midlife women with chronic schizophrenia. *Schizophrenia Research*, *195*, 409–411. https://doi.org/10.1016/j.schres.2017.09.041

Salvador, J., Gutierrez, G., Llavero, M., Gargallo, J., Escalada, J., & López, J. (2019). Endocrine Disorders and Psychiatric Manifestations. In *Endocrinology* (pp. 1–35). https://doi.org/10.1007/978-3-319-66362-3_12-1

Schatzberg, A. F. (2014). Anna-Monika Award Lecture, DGPPN Kongress, 2013: The role of the hypothalamic–pituitary–adrenal (HPA) axis in the pathogenesis of psychotic major

depression. ˜ *The œWorld Journal Of Biological Psychiatry*, *16*(1), 2–11. https://doi.org/10.3109/15622975.2014.916414

Scott, S. R., Millwood, S. N., & Manczak, E. M. (2023). Adipocytokine correlates of childhood and adolescent mental health: A systematic review. *Developmental Psychobiology*, *65*(3). https://doi.org/10.1002/dev.22379

Sharma, K., Akre, S., Chakole, S., & Wanjari, M. B. (2022). Stress-Induced Diabetes: A review. *Curēus*. https://doi.org/10.7759/cureus.29142

Stochl, J., Khandaker, G. M., Lewis, G., Perez, J., Goodyer, I. M., Zammit, S., Sullivan, S., Croudace, T. J., & Jones, P. B. (2014). Mood, anxiety and psychotic phenomena measure a common psychopathological factor. *Psychological Medicine*, *45*(7), 1483–1493. https://doi.org/10.1017/s003329171400261x

Sukhapure, M., Eggleston, K., Fenton, A., Frampton, C., Porter, R. J., & Douglas, K. M. (2022). Changes in Mood, Anxiety, and Cognition with Polycystic Ovary Syndrome Treatment: A Longitudinal, Naturalistic Study. *Neuropsychiatric Disease And Treatment, Volume 18*, 2703–2712. https://doi.org/10.2147/ndt.s385014

Toffoletto, S., Lanzenberger, R., Gingnell, M., Sundström-Poromaa, I., & Comasco, E. (2014). Emotional and cognitive functional imaging of estrogen and progesterone effects in the female human brain: A systematic review. *Psychoneuroendocrinology*, *50*, 28–52. https://doi.org/10.1016/j.psyneuen.2014.07.025

Tricco, A. C., Lillie, E., Zarin, W., O'Brien, K. K., Colquhoun, H., Levac, D., Moher, D., Peters, M. D., Horsley, T., Weeks, L., Hempel, S., Akl, E. A., Chang, C., McGowan, J., Stewart, L., Hartling, L., Aldcroft, A., Wilson, M. G., Garritty, C., . . . Straus, S. E. (2018). PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals Of Internal Medicine*, *169*(7), 467–473. https://doi.org/10.7326/m18-0850

Van Andel, M., Van Schoor, N. M., Korten, N. C., Heijboer, A. C., & Drent, M. L. (2022). Ghrelin, leptin and high-molecular-weight adiponectin in relation to depressive symptoms in older adults: Results from the Longitudinal Aging Study Amsterdam. *Journal Of Affective Disorders*, *296*, 103–110. https://doi.org/10.1016/j.jad.2021.09.069

Van Winkel, R., Stefanis, N. C., & Myin-Germeys, I. (2008). Psychosocial Stress and Psychosis. A Review of the Neurobiological Mechanisms and the Evidence for Gene-Stress Interaction. *Schizophrenia Bulletin*, *34*(6), 1095–1105. https://doi.org/10.1093/schbul/sbn101

Walther, A., Tsao, C., Pande, R., Kirschbaum, C., Field, E., & Berkman, L. (2019). Do dehydroepiandrosterone, progesterone, and testosterone influence women's depression and anxiety levels? Evidence from hair-based hormonal measures of 2105 rural Indian women. *Psychoneuroendocrinology*, *109*, 104382. https://doi.org/10.1016/j.psyneuen.2019.104382

Wang, Q., Ren, H., Liu, T., & Zhang, X. (2024). Serial multiple mediating roles of anxiety and thyroid-stimulating hormone in the relationship between depression and psychotic symptoms in young adults with anxious depression. *Journal Of Affective Disorders*, *351*, 8–14. https://doi.org/10.1016/j.jad.2024.01.208

Wingenfeld, K., & Wolf, O. T. (2015). Effects of cortisol on cognition in major depressive disorder, posttraumatic stress disorder and borderline personality disorder - 2014 Curt Richter Award Winner. *Psychoneuroendocrinology*, *51*, 282–295. https://doi.org/10.1016/j.psyneuen.2014.10.009

Yang, W., Qu, M., Jiang, R., Lang, X., & Zhang, X. (2022). Association between thyroid function and comorbid anxiety in first-episode and drug naïve patients with major

depressive disorder. *European Archives Of Psychiatry And Clinical Neuroscience*, *273*(1), 191–198. https://doi.org/10.1007/s00406-022-01457-x

Yuen, E. Y., Wei, J., & Yan, Z. (2017). Molecular and Epigenetic Mechanisms for the Complex Effects of Stress on Synaptic Physiology and Cognitive Functions. *International Journal Of Neuropsychopharmacology*, *20*(11), 948–955. https://doi.org/10.1093/ijnp/pyx052

Zotero | Your personal research assistant. (n.d.). https://www.zotero.org/

Appendix A

Glossary of hormones and related terms

Term	Definition	Reference
Sex hormones	Hormones that affect sexual development and reproduction.	Barendse et al., 2023
Estrogens	Steroid hormones that promote female characteristics, regulating menstrual cycle, reproduction, mood and cognition.	Barendse et al., 2023
Estradiol	Primary form of estrogen, regulates reproduction, bone, skin and cardiovascular health.	Hodgetts and Hausmann, 2020
Progesterone	Steroid hormone preparing regulating menstrual cycle and prepares for pregnancy.	Toffoletto et al., 2014
Testosterone	Primary male sex hormone, essential for reproductive tissues, muscle, bone density. Influences mood and cognition.	Balikci et al., 2014
Dehydroepi-androsterone (DHEA)	Adrenal hormone, precursor to sex/androgen hormones, affects energy, immune function, mood.	Balikci et al., 2014
Dehydroepi-androsterone sulfate (DHEA-S)	Stable hormone reservoir that is convertible to DHEA as needed.	Balikci et al., 2014
Prolactin	Pituitary hormone stimulating breast-milk production, has roles in metabolism and immune system.	Medina-Loera et al., 2020
Stress hormones	Hormones involved with immunal and stress responses.	Pagliaccio et al., 2015
Cortisol	Adrenal cortex steroid hormone responding to stress, glucose levels, and involved in immune suppression.	Pagliaccio et al., 2015
HPA axis	Not a hormone, the HPA axis comprises the interaction the hypothalamus, the pituitary gland, and the adrenal glands; regulates immune response, stress response and cortisol excretion.	Pagliaccio et al., 2015
Thyroid hormones	These hormones play important roles in regulating metabolism, growth, and development throughout the body, including the brain.	Puchalapalli & Mahmood, 2020
Thyroxine (T4)	Thyroid hormone regulating metabolism, growth and development.	Puchalapalli & Mahmood, 2020
Thyroid Stimulating Hormone (TSH)	Pituitary hormone stimulating thyroid hormone production.	Puchalapalli & Mahmood, 2020
Hyperthyroidism and hypothyroidism	Hypothyroidism (underactive thyroid) and hyperthyroidism (overactive thyroid), can disrupt normal functioning of the thyroid gland, leading to imbalances in thyroid hormone levels.	Aslan et al, 2009

Term	Definition	Reference
Appetite and Metabolic hormones	These hormones work together to maintain energy balance, control hunger and appetite. Some thyroid hormones also function in regulating metabolism.	Merritt et al., 2020
Leptin	Appetite hormone from fat cells, controls hunger, satiety and food intake.	Scott et al., 2023
Ghrelin	Stomach and pancreatic hormone that stimulates appetite, food intake and fat storage.	Scott et al., 2023
Insulin	Pancreatic hormone that manages blood-glucose (sugar) levels.	Merritt et al., 2020
Socio-behavioral hormones	These hormones influence social behaviors, interactions and emotions. Some sex hormones also function as socio-behavioral hormones.	Mutu et al., 2018
Oxytocin	Hypothalamic-pituitary neuropeptide hormone that supports social bonding, reproduction, childbirth. Also known as the 'love' hormone. Can be classified based on many other properties: e.g.; neuropeptide; neurotransmitter etc.	Mutu et al., 2018

Note. The total amount of hormones is vast, included here are only the ones discussed in the review.

Appendix B

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	6 - 8
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	8 - 9
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	N.A.
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	9 - 10
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	9
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	9
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10 - 11
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	10 - 11
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	11
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N.A.
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	12 - 13

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	13
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	14
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	14 - 15
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	55 - 66
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	16 - 26
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	26 - 33
Limitations	20	Discuss the limitations of the scoping review process.	34 - 35
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	35 - 37
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	N.A.

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

Appendix C

Table C1

Overview of included study designs per symptom domain

Study design	N	Number of included studies per domain		
		Psychotic symptoms	Mood symptoms	Anxiety symptoms
Systematic review	6	2	3	2
Narrative review	11	8	3	4
Cohort study	5	1	4	4
Cross-sectional	21	9	14	7
Randomized controlled trial	3	1		3
Case-controlled	4	2	1	1
Total	51	23	24	20

Note. Blank cells indicate that no studies of that design were included for that category. Studies discussing multiple symptom types are recounted in each relevant domain column. N = total studies.

Table C2

Data extraction overview

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
1. Role of cortisol in patients at risk for psychosis mental state and psychopathological correlates: {A} systematic review (Karanikas & Garyfallos, 2015)	Systematic review (N = 16) Patients at risk for psychosis (ARP)	Cortisol	Psychotic	Trend towards higher cortisol levels in ARP. Minimal prodromal psychosis relation to cortisol; association most strong with anxiety measures	Heterogeneity of factors contributing to symptoms. Lack of specificity of association cortisol with symptoms.
2. The role of cortisol and prolactin in the pathogenesis and clinical expression of psychotic disorders (Labad, 2019)	Narrative review At risk mental states with psychotic symptoms (ARMS)	Glucorticoids and HPA, prolactin	Psychotic	Differences in cortisol secretion ARMS that transition to psychosis vs those that don't. Basal cortisol findings inconsistent in longitudinal studies. Hyperprolactinemia observed in ARMS/FEP: altered dopamine signaling. Inflammation, stress induced HPA alterations.	Increased prolactin may be stress related epiphenomenon rather than direct cause. Need more research to elucidate mechanisms between stress hormones, cogntition and psychosis.
3. The role of the hypothalamic–pituitary–adrenal (HPA) axis in the pathogenesis of psychotic major depression (Schatzberg, 2015)	Narrative review MDD patients	Cortisol / glucocorticoid receptor gene	Psychotic Mood, depressive	Cortisol may affect dopamine activity, potentially contributing to the development of delusions in psychotic depression.	Narrative review
4. Effects of cortisol on cognition in major depressive disorder, posttraumatic stress disorder and borderline personality disorder—2014 {Curt} {Richter} {Award} {Winner} (Wingenfeld & Wolf, 2015)	Narrative review	Cortisol and HPA	Depressive, Cognition in MDD, PTSS	Dysregulated HPA (hypersecretion and reduced feedback sensitivity prominent in MDD), inconsistent associations cortisol and CI, some negative correlation with memory function. Cortisol's effects on memory vary across mental disorders. MDD patients show hippocampal dysfunction and GR resistance, resulting in a lack of cortisol effects on memory.	Non-systematic review (but based on systematic reviews)
5. Testosterone, estradiol, {DHEA} and cortisol in relation to anxiety and depression scores in adolescents (Chronister et al., 2021)	Longitudinal cohort study. N = 522 adolescents	Estradiol testosteron Cortisol	Depressive and anxiety	Elevated cortisol, estradiol, and testosterone levels were associated with increased odds of elevated depression and anxiety symptoms. Effect modifaction by testosterone and cortisol on hormone-mood associations; gender differences	

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
6. Impacts of stress and sex hormones on dopamine neurotransmission in the adolescent brain (Sinclair et al., 2014)	Narrative review Focused on literature on adolescents	Testosterone, estrogen and glucocorticoids	Stress Psychotic	Adolescence is marked by increased responsiveness to sex and stress hormones, which influence maturing dopaminergic circuitry. Testosterone, estrogen, and glucocorticoids interact and exert distinct, brain region-specific effects on dopamine neurotransmission during adolescence and throughout postnatal life. These hormones modulate dopamine neurotransmission in the brain	Non-systematic review (but based on systematic reviews)
7. Amygdala functional connectivity, {HPA} axis genetic variation, and life stress in children and relations to anxiety and emotion regulation (Pagliaccio et al., 2015)	Longitudinal cohort study n=120	HPA axis	Anxiety Depressive mood	HPA profile predicted altered connectivity to several brain regions. Childhood stress predicted altered connectivity with ACC. Alterations in amygdala connectivity were influenced by both genetic factors related to the HPA axis and early life stress. Weakened connectivity observed in frontal and subcortical regions; implicated in anxiety and depression.	Single summary variable used for genetic varation measure
8. Molecular and epigenetic mechanisms for the complex effects of stress on synaptic physiology and cognitive functions (Yuen et al., 2017)	Narrative review	HPA axis Stress hormones	Depression Anxiety PTSD	Corticosteroids U-shaped effect on brain homeostasis: acute or moderate levels is adaptive to stress, chronic harms brain function and CFs. Chronic stress causes structural changes in PFC, dendritic atgrophy. Various molecular players: genes, inflammation, epigentics mediate effects of stress on CFs. Genomic activation of CS: activate MC + CS receptors, leading to changes in gene expression. Nongenomic: influences synaptic activities within amygdala, PFC and HC	Non-systematic review, but based on meta-analyses and SRs.

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
9. Early child adversity and psychopathology in adulthood: {HPA} axis and cognitive dysregulations as potential mechanisms (Raymond et al., 2018)	Narrative review	HPA Stress hormones	Cognitive functions Stress	EA increases vulnerability to mental illness. Hippocampal volume reductions are seen in adults with EA history. Prefrontal cortex volume alterations are observed in EA-exposed individuals. Amygdala volume changes are inconsistent but may be influenced by EA. Functional neuroimaging shows dysregulated brain activation in EA-exposed individuals. Hippocampus, prefrontal cortex, and amygdala support cognitive functions crucial for stress regulation. EA affects cognitive functions, including memory, executive functions, and emotion regulation. EA-exposed individuals display deficits in visual and working memory, inhibition, attention, and emotion regulation.	Multifactorial pathogenesis of mental illness makes causal associations difficult. Reliance on limited number of cognitive functions measures as a proxy for the mentioned brain functions.
10. Pituitary-adrenal axis hormones in early-onset versus late-onset panic disorder, (Masdrakis et al., 2020)	Observational cross-sectional N = 54 Early and late onset PD	ACTH, DHEAS, cortisol, HPA	Panic and anxiety symptoms	Early-onset PD patients had longer illness duration. Early-onset PD patients had significantly higher levels of ACTH and DHEAS, and marginally higher levels of cortisol. Early onset PD may have distinct biological features compared to late-onset regarding HPA axis functioning.	
11. Adolescents' hormonal responses to social stress and associations with adolescent social anxiety and maternal comfort: {A} preliminary study (Morgan et al., 2023)	Preliminary case-controlled study N = 47 adolescents, and n = 47 mothers of A	Stress hormones Oxytocin	Social anxiety symptoms	Cortisol levels increase in response to stress but decrease after receiving support, while oxytocin levels decrease in response to stress but increase after receiving support. Higher social anxiety -> higher cortisol response at baseline but greater declines after maternal support. Social anxiety did not affect OXT response.	No control group. Varying saliva measuring intervals
12. Sex steroids and major psychoses: {Which} role for {DHEA}-{S} and progesterone? (Buoli et al., 2016)	Cross-sectional observational study. N = 89 male SZ or mood disorder patients	Sex hormones (DHEA-S)	Psychotic and depressive	Patients with abnormal DHEA-S levels were more likely to have a family history of major depressive disorder. Higher DHEA-s in patients with history of psychotic symptoms. DHEAS levels associated with higher probability of psychotic symptoms in lifetime.	Need validation in larger studies

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
13. Menstrual cycle characteristics in women with persistent schizophrenia (Gleeson et al., 2016)	Cross-sectional from clinical trial. N = 139. Women with a psychotic disorder	Estradiol, sex hormones	Psychotic and mood symptoms	Regular menses are associated with higher estradiol levels and higher rates of cyclical mood symptoms but not with severity of psychotic symptoms.	
14. Estrogens and the cognitive symptoms of schizophrenia: {Possible} neuroprotective mechanisms (McGregor et al., 2017)	Systematic review N = 99	Estrogen	Psychotic and cognitive	Low E associated with increased symptom severity in SZ. SZ women often hypoestrogenic. E shows effects on domains like episodic memory, WM and EFs	Need to elucidate mechanisms underlying effects of estrogen on cognition
15. Do {FSH}/{LH} ratio and gonadal hormone levels predict clinical improvement in postmenopausal schizophrenia women? (Gonzalez et al., 2017)	12-week clinical trial cross-sectional N=136	Sex hormones Testosterone	Psychotic symptoms and cognitive symptoms	higher FSH/LH ratios were still associated with improvement in positive psychotic symptoms but also with worsening global psychotic symptoms, particularly cognitive symptoms. Not significant after Bonferroni adj. Testosterone showed trend associated with improved (reduction of) positive symptoms. Potential correlation with negative symptoms.	Small sample, multiple testing
16. Antipsychotic effects of sex hormones and atypical hemispheric asymmetries (Hodgetts and Hausmann, 2020)	Narrative review	Estradiol	Psychotic symptoms	There are speculative mechanisms by which estradiol may exert antipsychotic effects, including its influence on GABAergic PV neurons and its ability to enhance bilateral brain activity in a neurocompensatory manner.	Limited research on men
17. Association between prolactin serum levels and cognitive function in chronic schizophrenia patients (Medina-Loera et al., 2020)	Cross-sectional study observational N= 31 SZ patients	Prolactin	Psychotic symptoms and CFs.	No correlations found between prolactin levels and symptom severity, but male patients showed significant negative correlations between prolactin levels and cognitive function. Male SZ patients more vulnerable to cognitive effects of hyperprolactinemia	Need more research to understand differential response in men and women
18. Abnormally low prolactin levels in schizophrenia patients after switching to aripiprazole in a randomized trial: {A} biomarker for rebound in psychotic symptoms? (Jen et al., 2020)	Non-randomized clinical trial on SZ patients Case-controlled N = 62	Prolactin	Psychotic symptoms	Patients with abnormally low prolactin levels (PRL) were more likely to experience a rebound in psychotic symptoms. Low PRL may identify patients at risk for psychotic rebound.	

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
19. Estrogens in schizophrenia: {Progress}, current challenges and opportunities (Brand et al., 2021)	Narrative review Focus on SZ patients	Estrogen Prolactin	Psychotic	Low estrogenic phases associated with increased psychosis vulnerability. E has neuroprotective effects: reduces neuroinflammation, promotes synaptic plasticity and influences dopamine signaling. Deficiency common in SZ, especially women. Hyperprolactinemia can lead to low E.	Limited findings on men
20. Risk for midlife psychosis in women: {Critical} gaps and opportunities in exploring perimenopause and ovarian hormones as mechanisms of risk (Culbert et al., 2022)	Narrative review Women ARP	Ovarian/Sex hormones	Psychotic	Clinical evidence indicates that fluctuations in ovarian hormones across reproductive phases are associated with changes in psychotic symptoms in women with schizophrenia. Menopausal transition overlaps with spike in psychosis vulnerability.	Only women researched
21. Sex and pubertal influences on the neurodevelopmental underpinnings of schizophrenia: {A} case for longitudinal research on adolescents (Barendse et al., 2023)	Narrative review	Sex hormones	Psychotic	Dysfunction in the frontal-limbic network is associated with affective and psychotic symptoms, while disruptions in the frontal-striatal network are linked to negative symptoms in SZ. Sex difference seen in SZ, men more negative, women more positive. Higher testosterone levels during adolescence are associated with stronger striatal response to reward and fewer negative symptoms in males with SZ. Dysfunction in the frontal-striatal network, influenced by testosterone during puberty, may contribute to the prevalence of negative symptoms in males with SZ. Evidence suggests that the frontal-limbic network, involved in affective and positive symptoms, is influenced by pubertal development and estradiol.	Methodological inconsistencies limit specific conclusions in this area.
22. Depression, anxiety, and anger in patients with polycystic ovary syndrome (Balikci et al., 2014)	Cross-sectional study N = 44 Females with PCOS	LH, DHEAS, Testosteron	Mood symptoms, anxiety	Women with PCOS had higher levels of BMI, insulin, LH, DHEAS, and total testosterone compared to controls. Significant differences were observed in trait anger, anger control, outward and inward anger, anxiety, and depression scores between the two groups. Elevated DHEAS levels were correlated with anxiety scores but not depression scores. Hormonal changes in PCOS may directly influence anxiety levels, while depressive symptoms could be secondary to psychosocial factors.	

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
23. Emotional and cognitive functional imaging of estrogen and progesterone effects in the female human brain: {A} systematic review (Toffoletto et al., 2014)	Systematic review (N = 33)	Estrogen Progesterone	Mood and cognitive	Hormonal fluctuations, such as those occurring during the menstrual cycle (follicular and luteal phases), COC use, and CSHT, impact brain regions involved in emotional and cognitive processing, including the amygdala, anterior cingulate cortex, and inferior frontal gyrus.	Functional recruitment of brain regions varied across groups and domains in the study, suggesting complex interactions with hormonal milieu and brain function.
24. Serum {DHEA}-{S} concentration correlates with clinical symptoms and neurocognitive function in patients with bipolar {II} disorder: {A} case- controlled study (Lee et al., 2017)	Clinical sample case-controlled study N = 32 BP-II patients and N = 30 HC's	DHEA-S	Mood symptoms and cognitive functions	Lower CF scores in BP-II. Serum DHEA-S levels were inversely correlated with verbal memory and composite scores of cognitive function in BP-II patients. There was a negative correlation between serum DHEA-S levels and manic symptom severity.	Small sample, lack of control for stressful events. Need for research on mechanism.
25. Do dehydroepiandrosterone, progesterone, and testosterone influence women's depression and anxiety level s? {Evidence} from hair-based hormonal measures of 2105 rural {Indian} women (Walther et al., 2019)	Cross-sectional study N = 2105 women	Hair-sampled sex hormone DHEA	Depression and anxiety symptoms	The study aligns with previous research showing both positive and negative associations between DHEA and depressive symptoms, as well as varied associations between testosterone and depressive symptoms in women. Results regarding anxiety symptoms and hormone levels are mixed, with negative associations observed for DHEA and positive associations for testosterone, though sensitive to treatment of non-detectable values. No association was found between progesterone levels and either depressive or anxiety symptoms, consistent with some existing literature.	
26. Associations among gonadal hormone, triglycerides and cognitive decline in female patients with major depressive disorders (Guan et al., 2021)	Cross-sectional study N = 183 with MDD	Sex hormones Estradiol Testosteron	Cognition in depression	Depression associated with CI. Decreased gonadal hormone levels may contribute to higher trygcliceride levels in female MDD patients. HTG: females exhibited poorer CFs. No sign diff in male patients.	Small N. Confounding factors like antidepressants and diet

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
27. Changes in mood, anxiety, and cognition with polycystic ovary syndrome treatment: {A} longitudinal, naturalistic study (Sukhapore et al., 2022)	Pre-post intervention study with HC's Cohort study N = 33 PCOS N = 40 HCs	Sex / ovary hormones	Mood and anxiety symptoms	PCOS associated with mood and anxiety. Evidence of CI in PCOS women. Treated PCOS showed reduced symptoms. CF improvement attributed to practice effects.	Heterogeneous medication treatment
28. Hormonal and inflammatory signatures of different mood episodes in bipolar disorder: {A} large-scale clinical study (Lyu et al., 2023)	Cross-sectional clinical study N = 8332 BD patients	Sex hormones: Testosterone, estradiol, progesterone, CRP	Mood symptoms	Patients in manic episodes showed higher levels of testosterone, estradiol, progesterone, and CRP, and lower levels of ACTH compared to depressive episodes. Gonadal hormones, stress, and inflammatory markers showed different associations with mood episodes based on age and sex. For instance, testosterone levels were associated with mood episodes in adult men, while estradiol and progesterone levels differed in middle-aged and elderly men.	No HC's. No consideration for effect of medication
29. Estradiol moderates the relationship between state-trait anxiety and attentional bias to threat in women (Graham and Shin, 2018)	Mixed design within- and between-subjects RCT N = 104	Estradiol	Anxiety symptoms	Fear extinction and attentional bias to threatening stimuli are key psychological processes in anxiety. Estradiol levels were positively correlated with attentional bias to threat among female participants. Estradiol moderated the relationship between state-trait anxiety, symptoms of anxiety and stress, and attentional bias in women. Specifically, higher estradiol levels were associated with vigilance to threat in individuals with higher anxiety, while lower estradiol levels were associated with avoidance of threat. Effects not seen in men.	Limited findings in men

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
30. Associations between adrenarcheal hormones, amygdala functional connectivity and anxiety symptoms in children (Barendse et al., 2018)	Cross-sectional N = 83 children	Adrenarcheal hormones / sex hormones	Anxiety symptoms	Boys with higher DHEA and testosterone levels showed increased amygdala connectivity with visual cortex and anterior cingulate cortex (ACC), which was indirectly associated with greater social anxiety and obsessive-compulsive symptoms. In girls, higher DHEAS levels were associated with reduced amygdala connectivity with fusiform face area (FFA) and insula, indirectly linked to lower total anxiety, social anxiety, and specific phobia symptoms. Sex-specific associations between hormone levels, amygdala connectivity, and anxiety symptoms suggest unique roles for each hormone and neural mechanism in anxiety during adrenarche. Highlights sex differences. Amygdala connectivity important neural mechanism underlying link between adrenarcheal hormones and anxiety symptoms	
31. Adrenarcheal timing longitudinally predicts anxiety symptoms via amygdala connectivity during emotion processing (Barendse et al., 2020)	Longitudinal cohort design N = 64 children	Sex hormones DHEA-S	Anxiety symptoms	Higher levels of DHEA sulfate (DHEAS) at age 9 were associated with increased amygdala connectivity over time in boys but decreased connectivity in girls. Higher DHEA levels related to altered amygdala connectivity and increased anxiety symptoms.	
32. Increased dehydroepiandrosterone ({DHEA}) is associated with anxiety in adolescent girls (Mulligan et al., 2020)	Cross-sectional trial N = 286 girls	DHEA	Anxiety symptoms	DHEA concentrations were positively associated with scores on panic, generalized anxiety, and social anxiety subscales.Participants with higher DHEA levels were more likely to have an anxiety disorder, particularly generalized anxiety disorder (GAD).	Focus on girls, may not generalize to boys
33. Effects of circulating estradiol on physiological, behavioural, and subjective correlates of anxiety: {A} double-blind, randomized, placebo-controlled trial (Nouri et al., 2022)	Double blind randomized controlled trial RCT	Estradiol	Anxiety symptoms	The study highlights sex differences in anxiety-related behavior, with women generally showing higher levels of anxiety compared to men. However, estradiol does not significantly alter this pattern.	Need for further elucidation on complex relationship sex hormones and anxiety

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
34. The prevalence of anxiety in adult endocrinology outpatients: {A} systematic review and meta–analysis (Kershaw et al., 2023)	Systematic review / MA N = 59 on N = 25176 endocrinology outpatients	General endocrine disorders Appetite hormones	Anxiety	GAD most frequent diagnosis among the outpatients. PD higher. PD higher in non-diabetes vs diabetes. Outpatients in developing countries higher anxiety. Females diabetes patients higher anxiety. Anxiety occurs morge frequently in outpatients than general population.	Prevalence estimates were higher when assessed with self-report scales compared to diagnostic interviews
35. Role of appetite hormone dysregulation in the cognitive function among patients with bipolar disorder and major depressive disorder (Chen et al., 2021)	Cross-sectional N = 58 BP-I, 36 BP-II 40 MDD, 40 HCs	Appetite hormones	Mood symptoms and CFs	Patients with bipolar I or II disorder had higher ghrelin levels compared to patients with major depressive disorder and controls. A positive association between ghrelin levels and executive function was observed in patients with bipolar disorder, highlighting potential neuroprotective and neurocompensatory effects of ghrelin on CF in BP-II	Further research is needed to elucidate the underlying mechanisms and validate the findings, especially in the context of major depressive disorder; Using only one measure of cognitive function
36. Ghrelin, leptin and high-molecular-weight adiponectin in relation to depressive symptoms in older adults: {Results} from the {Longitudinal} {Aging} {Study} {Amsterdam} (van Andel et al., 2022)	Longitudinal cohort study N = 898	Appetite hormones	Mood / depressive symptoms	Ghrelin and leptin levels were associated with depressive symptoms in older adults, with age and waist-hip-ratio modifying the association.	Possible selection bias
37. Adipocytokine correlates of childhood and adolescent mental health: {A} systematic review (Scott et al., 2023)	Systematic review N = 28 on children	Appetite hormones	Mood and anxiety symptoms	Higher levels of leptin and ghrelin were associated with depressive symptoms in youth due to inflammatory pathways, while associations with other adipocytokines varied across different disorders and symptoms.	
38. Medical Etiologies of Secondary Psychosis in Children and Adolescents (Merritt et al., 2020)	Narrative review	Thyroid hormones Appetite hormones HPA axis	Psychotic symptoms	Inadequate synthesis of thyroid hormone can lead to myxedema psychosis, resolves with treatment. Diabetes mellitus can occur with psychosis, most common in hypoglycemia. Elevated cortisol levels seen in people at risk for psychosis.	

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
39. Free thyroxine levels are associated with cognitive abilities in subjects with early psychosis (Barbero et al., 2015)	Cross sectional clinical study N = 70 patients with psychotic disorder	Thyroid hormones	Psychotic symptoms	Higher FT4 levels, but not TSH or thyroid antibodies, were associated with better cognitive performance in attention/vigilance and overall cognition among individuals with early psychosis.	
40. Serial multiple mediating roles of anxiety and thyroid-stimulating hormone in the relationship between depression and psychotic symptoms in young adults with anxious depression (Wang et al., 2024)	Cross-sectional N = 369 YA's with anxious depression	Thyroid hormones, TSH	Psychotic symptoms, Mood symptoms, Anxiety symptoms	Anxiety and depression increases risk for psychotic symptoms. Anxiety mediates relation depression and PS. TSH mediator too. Higher TSH levels were found to be positively correlated with the presence of PS. This association suggests a potential link between thyroid dysfunction and the development of psychotic symptoms in young adults with AD.	
41. Prevalence and clinical correlates of subclinical hypothyroidism in first-episode drug-naive patients with major depressive disorder in a large sample of {Chinese} (Lang et al., 2020)	Cross-sectional N = 1706 MDD patients	Thyroid hormones	Mood symptoms	Positive symptoms may be related to severe SCH in MDD patients. A higher prevalence of positive symptoms was found in patients with concurrent MDD and severe SCH compared to those without. TSH levels were positively correlated with depressive symptoms in first-episode MDD patients, consistent with some previous studies. Association between SCH and suicide attempts.	Need for establishing causal mechanisms. No HC group
42. Association between subclinical hypothyroidism and psychotic features in {Chinese} young adults with first-episode and untreated major depressive disorder (Dai et al., 2023)	Cross-sectional 481 young MDD patients	Thyroid hormones	Psychotic and Mood symptoms	elevated TSH levels may increase the risk of psychotic symptoms through inflammatory pathways and neuronal processes involving the central nervous system.	
43. Neuropsychiatric comorbidities in hypothyroidism: {A} systematic review (Puchalapalli & Mahmood, 2020)	Systematic review (N = 66) on hypothyroidism in depression and bipolar disorder patients	Thyroid hormones	Mood symptoms	Hypothyroidism can mimic neuropsychiatric disorders. Thyroid hormone interacts with serotonin and norepinephrine systems, impacting mood. Hypothyroidism increases susceptibility to treatment-resistant depression and slows treatment response in bipolar depression. Hypothyroidism shares neuropsychiatric deficits with depression but also presents with distinct symptoms. Depression may be marked by abnormal thyroid states. Treating HT can restore metabolic activities in brain areas involved in regulating affect and cognition.	

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
44. The thyroid dysfunction of suicide attempts in major depression (Liu et al., 2021)	Cross-sectional N = 1589 MDD	Thyroid hormones	Mood symptoms Anxiety symptoms Psychotic symptoms Suicide attempts	Thyroid dysfunction, specifically higher levels of ATPO, was independently associated with suicide attempts in MDD patients, even after controlling for confounding factors. Suicide attempters showed higher levels of thyroid antibodies (ATPO and ATG), thyroid-stimulating hormone (TSH), and prevalence of psychotic symptoms and anxiety disorders compared to non-attempters.	Lack of causal interference, cross-sectional
45. Association between thyroid function and comorbid anxiety in first-episode and drug naïve patients with major depressive disorde (Yang et al., 2023)	Cross-sectional N = 1718 MDD outpatients	Thyroid hormones	Anxiety symptoms Mood symptoms	Patients with MDD and comorbid anxiety had significantly higher serum levels of thyroid-stimulating hormone (TSH), thyroglobulin antibody (TGAb), and thyroid peroxidase antibody (TPOAb) compared to those without anxiety. TSH and Tgab levels potential biomarkers for identifying MDD with comorbid anxiety.	Limited generalizibility. Cross- sectional
46. Prevalence and clinical profile of abnormal glucose in first-episode and drug-naïve patients with major depressive disorder with comorbid abnormal thyroid function: {A} large-scale cross- sectional study (Huang et al., 2023)	Cross-sectional N = 1718 MDD patients	Thyroid hormones	Mood symptoms	The prevalence of abnormal glucose in MDD patients with comorbid thyroid dysfunction is high, with higher rates of suicide attempts, severe anxiety, and psychotic symptoms. Higher Hamilton Rating Scale for Depression (HAMD) scores and thyroid-stimulating hormone (TSH) levels are independently associated with abnormal glucose in MDD patients with thyroid dysfunction.	Need to establish causal relationships
47. Prevalence of overweight and obesity in patients with major depressive disorder with anxiety: {Mediating} role of thyroid hormones and metabolic parameters (Luo et al., 2023)	Cross-sectional N = 1718 MDD patients	Thyroid hormones	Mood symptoms	Gender differences in MDD and suicide. Females mor MDD, anxiety and somatic symptoms. Males more suicidal and addictive behaviours. There is a correlation between thyroid function, particularly TSH levels, and suicide risk among individuals with MDD. Higher TSH levels were associated with suicide attempts in both males and females.	Need to establish causal relationships

Study	Design and participant characteristics	Endocrine measures	Symptom Domains	Key findings and proposed mechanism	Limitations
48. The relationship of oxytocin, vasopressin, and atrial natriuretic peptide levels with cognitive functions in patients with schizophrenia (Mutu et al., 2018)	Cross-sectional comparative study N = 63 SZ patients	Oxytocin Vasopressin	Psychotic symptoms	Blood levels of oxytocin, vasopressin, and atrial natriuretic peptide did not significantly differ between patients with schizophrenia and healthy controls. Oxytocin levels were associated with recognition of certain facial expressions and response times in both patients and healthy controls.	
49. Rare missense coding variants in oxytocin receptor ({OXTR}) in schizophrenia cases are associated with early trauma exposure, cognition and emotional processing (Veras, 2018)	Case-controlled study N = 48 SZ patients	Oxytocin	Psychotic symptoms	Early environmental factors, such as parental bonding and trauma, can interact with oxytocin expression and OXTR gene methylation, potentially influencing schizophrenia risk and symptomatology. Schizophrenia cases with rare missense coding OXTR SNVs exhibit cognitive deficits, particularly in processing speed and perceptual organization, which may precede the onset of psychotic symptoms. Interaction of genetic vulnerability and environmental stressors.	
50. Peripheral oxytocin and vasopressin are associated with clinical symptom severity and cognitive functioning in midlife women with chronic schizophrenia (Rubin et al., 2018)	Cross sectional N = 26 women with SZ	Oxytocin	Psychotic symptoms Cognitive functions	Lower OT levels were associated with more severe overall symptomatology, particularly in thought disorder and hostility. Higher AVP levels were associated with worse anhedonia-asociality. Higher OT levels were associated with worse overall cognitive performance, delayed memory, and language. Cortisol and estradiol were better predictors of cognitive function in HC than in SZ.	Understanding the role of neuroendocrine factors in schizophrenia requires larger-scale, longitudinal studies to elucidate their impact on cognitive and symptom outcomes.
51. Correlations of plasma oxytocin with clinical and hormonal parameters in panic disorder (Masdrakis et al., 2023)	Cross sectional N = 24 Panic disorder patients	Oxytocin	Anxiety symptoms	OXT implicated in reducing fear and anxiety. OXT plasma levels are more relevant to general anxiety than specific panic psychopathology in acutely-ill PD patients. Potential biological explanation includes the role of OXT in respiratory functions and its effects on the 'fear circuit'. Previous studies have shown both positive and negative associations between OXT levels and psychopathology in various clinical conditions.	

Note. Measures marked in red demarcate stress hormones; measures in blue demarcate sex hormones, green demarcates appetite/metabolic hormones; orange demarcates thyroid hormones; purple demarcates neuropeptides. Blank cells indicate no notable limitations of relevance to this scoping review were provided.