Master's thesis

Stress Responses and their Role in Recurrence and Relapse of Depression: A Review of the Literature

Name and initials: Suprabha

Student number: S4943139

E-mail address: s.suprabha@student.rug.nl

First assessor: prof. dr. P. (Peter) de Jonge

Second assessor: prof. dr. A. (Anna) Lichtwarck-Aschoff

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Abstract

Stress, depression, and its recurrence or relapse have been extensively researched which has led to the emergence of theories to describe the relationship among them. Additionally, the literature provides sufficient evidence for a positive association between stress, depression, and its recurrence or relapse. The association occurs through stressor-induced stress responses, which are crucial for (timely) interventions for depression. Particularly, they are important for pre-emptively acting upon them to reduce the risk of recurrence and relapse. Although there is significant theoretical research related to a stressor - stress response - depression relations, there has been less focus on stress responses associated with depression and its recurrence/relapse. The thesis conducts a theoretical scoping review to synthesize the literature pulling the focus toward the stressor-induced stress responses linked with depression and its recurrence/relapse. Articles included in the review elaborate on the theoretical underpinning of stress mechanisms in terms of stress responses and their association with recurrent depression. The four categories of stress responses — cognitive, behavioral, emotional, and physiological — are examined. Cognitive responses encompass problems like cognitive dysfunction, dysfunctional attributional and inferential styles; emotional responses include concerns related to low mood, emotion-oriented coping styles, and high expressed emotions; behavioral responses include issues related to sleep disturbance and avoidance coping mechanisms; and physiological responses are linked to biological expressions of stress and depression through hormones. The cognitive responses were studied the most in contrast to physiological responses which were studied the least. In conclusion, by undertaking a scoping review of the literature, this study adds to the body of knowledge that can inform the development of targeted interventions and advance the understanding of the complexity of recurrent depression and its relationship to stressors and stress responses.

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Introduction

Stressful experiences have found their way into everyday situations in varying degrees of severity and in different forms, such as demanding work, financial pressure, and family conflict, leading to a wide range of responses. Today, the term stress has become common jargon for such experiences. Although more frequently used as an umbrella term for any form of (psychological) discomfort, from a scientific standpoint, stress offers crucial insights into understanding the origins, development, and recurrence of clinical psychiatric illnesses such as depression (American Psychological Association [APA], n.d.). The literature illustrates and supports a positive relationship between stressors and stress-related disorders (Bartz & Hollander, 2006) including depression. Particularly, chronic stress exposure can lead to the recurrence and relapse of depression (Kalin, 2020; Rohde et al., 1990; Segal et al., 1996). The interaction between stressors and depression occurs through stress responses such as physiological, behavioral, cognitive, and emotional responses (Roos et al., 2022). In addition, the number of years lost to depression is comparatively higher than other psychopathologies (Buckman et al., 2018) due to its relatively prolonged course through recurrence and relapse, calling for effective (real-time) interventions. In tandem, the thesis investigates the theoretical explanation of how stressor-induced stress responses relate to depression, its recurrence, and relapse as a building block toward designing (real-time) interventions.

Stress and Stressful Life Events

Everyday life stressors (normative life events) such as job demands and financial concerns, and major life events (non-normative life events) such as accidents and the loss of a loved one, are known to cause stress (Schwarzer & Schulz, 2003). Some of the stressors examined in the literature are spousal abuse, child abuse, interpersonal conflict, assault,

divorce, marital dispute, family conflict, illness, and relationship stresses (Tennant, 2002). These stressors lead to stress responses that in the short term can be adaptive but can have negative physical and mental health consequences when persistent (Dhabhar, 2018).

Stress Responses

The stress manifestations, also called stress responses, are the physiological or psychological responses to internal or external stressors (APA, n.d.). Some stress responses include palpitations, perspiration, parched mouth, shortness of breath, restlessness, rapid speech, negative emotions such as melancholy and irritation, dysfunctional cognition, and a variety of undesirable behaviors (APA, n.d.).

Understanding the nature of stress and how one responds to it is crucial in comprehending its effect on physical and mental health (Schwarzer & Schulz, 2003). Consequently, human stress responses have gained precedence and are well-researched. The literature broadly categorizes stress responses into emotional, physiological, behavioral, and cognitive (Roos et al., 2022) which bear the following definitions.

Emotional responses are an intricate response pattern that encompasses feelings such as fear, sadness, and anger to deal with a significant experience or an event. Physiological responses include aspects related to the functioning of the individual along with the respective chemical and physical processes, for example, numbing of body parts, fatigue, and accelerated heart beating. Behavioral responses are reactions to external or internal stimuli, for example, accelerated speech, difficulty in communication, difficulty in sleeping, and some coping styles. The behaviors can be observable (external), unobservable (internal), conscious, or unconscious processes. Cognitive responses include all forms of knowing and awareness, such as perceiving, conceiving, remembering, reasoning, judging, imagining, and

problem-solving. Some examples of cognitive responses include biased memory retrieval, negative perceptions, and negative appraisal of the environment.

Frequent exposure to stressful events or elongated exposure to stressors, as noted earlier, can magnify its effect on mental health conditions such as depression to cause its recurrence or relapse. According to the American Psychological Association, depression is the most common mental health disorder in recent times that is treatable (APA, n.d.) consequently, it has been extensively explored. For instance, a simple search ‘depress*’ in the five psychological databases in EBSCO (EBSCOhost Research Platform | EBSCO, n.d.) such as PsychINFO, ERIC, SocINDEX, PsycARTICLES, and MEDLINE results in around one million hits, illustrating the widespread research on depression. Additionally, depression outcomes such as recurrence and relapse (temporal aspect in the course of depression) are related to chronic stress exposure (Rohde et al., 1990; Segal et al., 1996), making it a suitable option for research into how stressors affect depression over time.

Depression

Depression is a prevalent mood disorder characterized by a persistent sad mood (National Institute of Mental Health, 2023; World Health Organization, 2019). The term "depression" has gained popularity due to changing lifestyles leading to more sedentary behaviors, and loneliness, to name a few (Hidaka, 2012). Depression is symptomatically heterogeneous (Slavich & Irwin, 2014), and hence, Diagnostic Statistical Manual (DSM) occasionally falls short of comprehensively evaluating the strengths and resources of the individual in addition to the disruptions brought on by depression (Calarco & Krone, 1991). It is particularly important when attempting to develop appropriate interventions that would be successful for that individual by accounting for individual differences in the symptomatology of depression (Calarco & Krone, 1991). The design of interventions is not only influenced by

disruptions caused by depression but also by other factors such as stressors, stress responses, and their implications on individuals.

Depression is often recurrent and the rates of depression recurrence and relapse increase with time (Belsher & Costello, 1988). For instance, 20- 24% of individuals reported relapsing from unipolar depression two months after the onset, around 30% of individuals relapsed after six months, around 40% showed relapse in 12 months, and finally, around 50% showed relapse post two years (Belsher & Costello, 1988). The statistics not only indicate the prevalence of depression recurrence/relapse but also guide research into the corresponding processes related to it such as recurrence or relapse of depression. Calarco & Krone (1991) nicely juxtaposes depression prevalence to medical disorders as "depression is the common cold of the mental disorders".

In light of its heterogeneous nature, the definition of depression in literature has ranged from a sad mood to clinical depression (Calarco & Krone, 1991). Therefore, to allow some consistency, the following definitions are employed concerning depression and its life course. Depression is defined as *a negative affective state, ranging from unhappiness and discontent to an extreme feeling of sadness, pessimism, and despondency, that interferes with daily life* (APA, n.d.). Remission is the state where symptoms are normalized for about two months or more (Brouwer et al., 2019). Relapse is the re-emergence of the major depressive disorder before attaining remission (Brouwer et al., 2019). Recovery is referred to as prolonged remission or can be described as the period where the symptoms are normalized for four months marking the end of major depressive disorder (Brouwer et al., 2019). Recurrence is a development of a new major depression disorder after a phase of recovery (Brouwer et al., 2019). An episode is an isolated occurrence of the illness, which in this case is an instance of depression (APA, n.d.).

Depression, additionally, tends to co-occur with other illnesses (Kali, 2020), and some examples of comorbidity are studied by Olfson et al., (2012) and Kang et al., (2015) with other psychopathologies and physical illnesses respectively. The comorbidity increases the likelihood of a spurious correlation between stressors and depression. Therefore, the thesis focuses on unipolar depression with no comorbidity meaning only persistent depression with no manic, hypomanic, mixed episodes, or any physical illness to discern the association of stressors and depression exclusively.

The Stressor - Stress Response - Recurrent Depression

Stressors are one of the most common precursors of depression and its recurrence (Epel et al., 2018). Stressors, depression, and its recurrence have temporal precedence implying stressors precede depression onset (Epel et al., 2018). Additionally, stressors and depression are related through the corresponding stress responses (Roos et al., 2022). Currently, numerous studies have attempted to understand and conceptualize the relationship between stressors, stress responses, and depression for designing interventions, but it often occurs post hoc making it challenging to pre-emptively assess and design interventions in real - time. Thus, studies that take into account temporal factors and thorough conceptualization of stressors and stress response mechanisms in relation to depression can advance the development of real-time intervention design that accommodates dynamic interplay between context, time, and person-specific factors.

Numerous theories that do attempt to capture the mechanism of stress and its effects on depression incorporating the temporal aspect are distributed and limited. Similarly, the research related to stress responses, crucial for conceptualizing the relationship between stressors and depression, is also dispersed. As a first step towards designing interventions in real time, knowledge synthesis from this distributed literature to develop a comprehensive

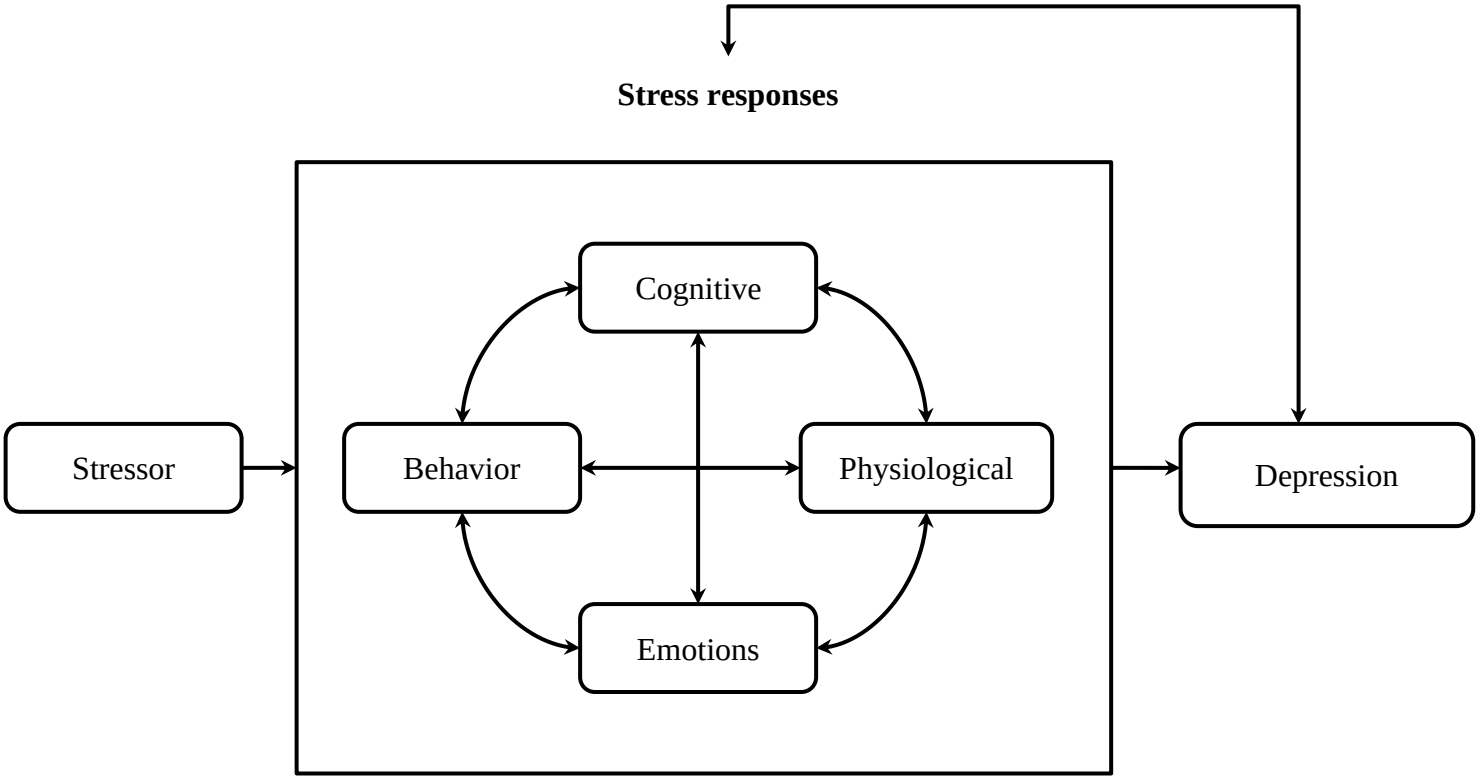
model that can account for stressor, stress response, depression, and its development over time is necessary. This study aims to take a step toward developing a comprehensive conceptualization of stress responses and recurrent depression by adopting a model (see Figure 1) to integrate the literature and review the theory-based articles to inform the evidence supporting the model.

The model (Figure 1) is a representation of a possible stress mechanism related to depression that incorporates responses such as behavioral, cognitive, emotional, and physiological responses to stressors that have been examined in the literature. The model explicitly draws a relation between stressors and depression through these stress responses with an additional component, time, implicitly present in the model accounting for the recurrent nature of depression. For example, behavioral responses such as sleep disturbance (Holsboer-trachsler & Seffritz, 2000) and cognitive responses such as selective attention (Farb et al., 2015) mediate the relationship between stressors or stressful life events that precede onset and recurrence.

A feedback loop from depression to stressor indicates the bidirectionality where the current depression episode can act as a stressor for the upcoming episodes (Kessler & Magee, 1994). Liu (2013) elaborates on such relationship between stressors and depression and how it changes over time. This change feeds back into the stress generation process, changing the implications for impending recurrence or relapse of depression. Repetition of the feedback loop over time leads to multiple occurrences of depression modifying the association between stressors and depression. For instance, poor interpersonal problem-solving skills (stress response) caused by childhood adversity (stressor) can cause more interpersonal stress (stressor) reinforcing the increasing risk for depression (Liu, 2013).

Figure 1

Model: Stress - Stress Response - Depression



Stress and Depression Mechanisms

In depression literature, one vastly used idea introduced by Post (1992) is sensitization (Monroe & Harkness, 2005). The stress sensitization model explains that the onset of depression ensues major life stress events (Stroud et al., 2008), and subsequently, the major life events become less crucial or not necessary to initiate later episodes implying lower stress becomes capable of recurrence/relapse, if at all required (Monroe & Harkness, 2005; Paykel, 2003; Stroud et al., 2008; Tennant, 2002). Altogether, the relationship between stress and its capability to induce episodes is reduced over time, and evidence for the same is provided by Segal et al., (1996) in a neurobiological context.

Although the mechanisms such as the one elaborated above, capture how stress relates to depression and its recurrence, the involvement of different stress responses is limited.

Identification of stress response mechanisms would be a crucial successful initial step toward the long-term objective of creating real-time interventions since it indicates where and how to intervene. Furthermore, such identification can support individualizing the interventions based on the corresponding stress responses. The thesis sheds an explicit focus on stress responses and how it relates to the stressor and subsequently to depression and its recurrence/relapse.

Research Question

The aim of the thesis is to conduct a scoping review of theoretical literature systematically to compile the information that elaborates on stress mechanisms in terms of stress responses and their development over time in relation to depression (see Figure 1) and also to identify the less researched areas in the model.

Methods

A scoping review was conducted to answer the research question aiming to identify the stress responses involved in the stressors - stress responses - depression (recurrence/relapse) relation. The reasoning for choosing scoping review as opposed to systematic review was twofold. One, the goal was to identify and integrate the evidence on stress responses to a model of depression and its recurrence/relapse (see Figure 1). More specifically, the project aims to identify evidence supporting the proposed models rather than synthesize all the evidence in the literature related to stress and depression and its recurrence/relapse (Munn et al., 2018). Two, performing a scoping review will not only help portray the evidence for the model but also indicates the knowledge gaps in terms of limited evidence in the literature (Munn et al., 2018). The proposal for this scoping review was approved on January 31, 2023, by the Graduate School of Behavioral and Social Sciences, University of Groningen.

The PICO (Population, Intervention, Comparison, and Outcome) method was used in the scoping review to generate the search terms, with the population being adults between the ages of 18 and 60; comparisons are drawn between different stress responses brought on by stressors and recurring depression; the outcome being the recurrence of depression. The intervention did not apply to this study. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was employed to seek studies and select them for further analysis. The results of these processes are detailed in Appendix A.

Search Strategy

The search to identify the relevant literature was carried out via an electronic search strategy in the EBSCOhost Research Platform (EBSCOhost Research Platform | EBSCO, n.d.) from five databases such as ERIC, MEDLINE, APA PsycARTICLES, APA PsycINFO,

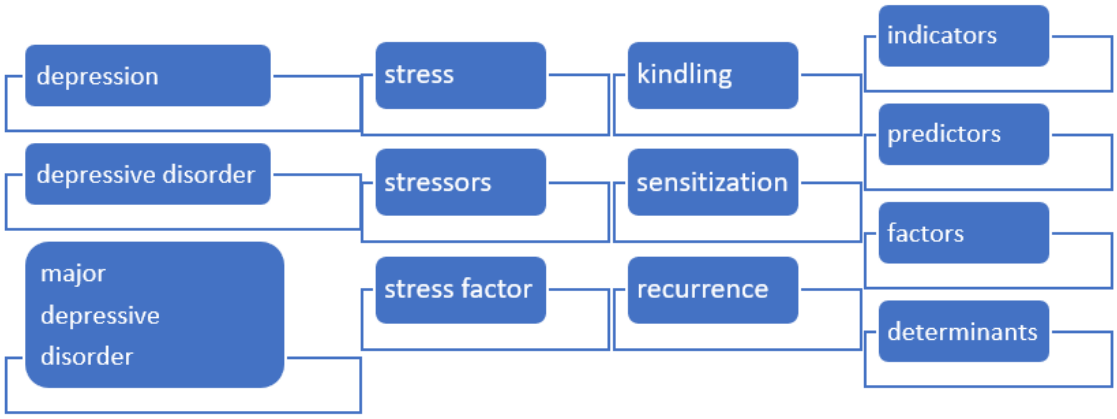
and SocINDEX with the terms listed in Figure 2. Additionally, a backward citation method was employed to identify additional articles that are relevant to answer the research question if it is not already included in the earlier literature search results.

Search Terms

The search terminology derived from the research question and the proposed model (see Figure 1) is presented in Figure 2. Since depression is the focus of the study, ‘Depression* or Depressive episode’ was included. The potential for depression relapse sheds light on chronic stress exposure in depression (Rohde et al., 1990; Segal et al., 1996) and incorporates the temporal aspect of the model and the chronic stress outcomes, terms such as ‘Kindling or Sensitization or Recurrence’ were added. Terms like 'Predictors or Factors or Indicators or Determinants' were adopted to emphasize the stress response categories. These search phrases eased the process of identifying articles that examined stress response factors or predictors of depression and its recurrence/relapse. And finally, to guide the research focus, ‘Stress or Stressor or Stress response’ was incorporated. The complete search query was “depression or depressive disorder or major depressive disorder AND stress or stressors or stress factor AND kindling or sensitization or recurrence AND predictors or indicators or factors or determinants”.

Figure 2

Search Terms Used in the Review



Study Selection Procedure

Selection Procedure

Upon performing the search in the aforementioned databases, the obtained results were exported to RefWorks (ProQuest RefWorks, n.d.) in RIS format. Title screening was carried out based on the inclusion and exclusion criteria that were highly inclusive. The inclusion criteria were: a) Studies focused on depression and stress. b) Studies focused on kindling, sensitization, and recurrence. c) Studies that had longitudinal study design. d) Studies that were peer-reviewed. e) Studies reported in English. The exclusion criteria consisted of a) Studies based on animal research. b) Studies that were retrospective.

The results of the title screen were subjected to the abstract screening with more detailed and stricter inclusion criteria as follows: a) Studies that had a longitudinal design. b) Studies that explored the theoretical underpinning of stress mechanisms in relation to depression. The exclusion criteria employed were as follows: a) Studies focused on other

forms of depression related to postpartum, childhood trauma, and suicidal ideation. b) Studies that addressed depression as a comorbidity condition.

A backward citation search was employed to locate other relevant articles. Articles identified by all means (database search and backward citation search) were subjected to full-text review to mark their eligibility to address the research question. Articles that sought to depict the relationship between stressors, depression, and its recurrence/relapse through stress responses such as cognitive, behavioral, physiological, or emotional were deemed eligible for the scoping review. The corresponding articles were retrieved from online sources, and in some cases, the retrieval process was extended through the library to procure them from exclusive journals and authors. A detailed flow diagram of the screening process is presented in Figure 4 and Appendix A.

Quality Criteria

From the perspective of the scoping review, the quality assessment was restricted to peer-reviewed articles. The decision followed the aim of the thesis which was to scope the relevant literature to the model proposed in Figure 1 and not necessarily to perform a complete knowledge synthesis and summarize the entire relevant literature (Munn et al., 2018).

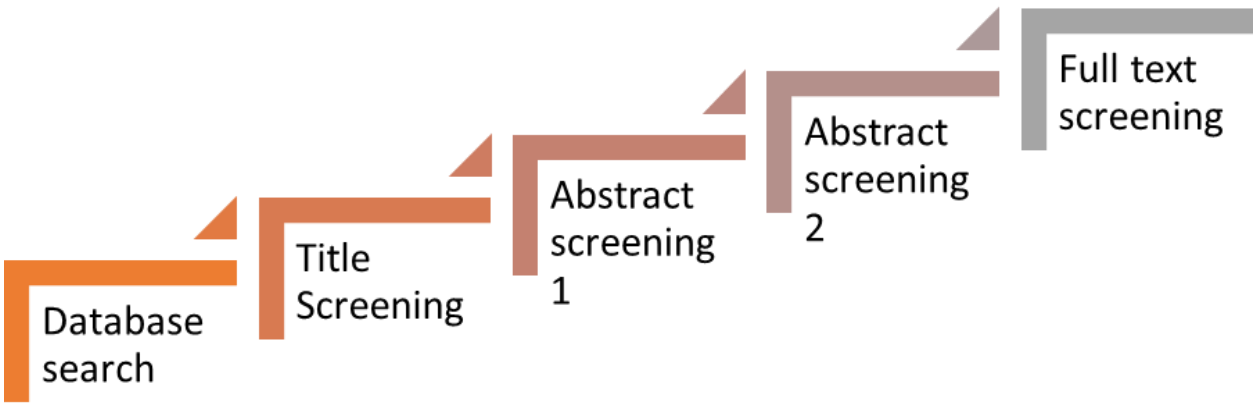
Results

Study Selection Results

The study selection procedure employed is depicted in Figure 3. The search was performed on March 1, 2023, in five databases - ERIC, MEDLINE, APA PsycARTICLES, APA PsycINFO, and SocINDEX with the terms listed in Figure 2. The search results (*n* = 711) were imported and were subjected to deduplication in RefWorks which highlighted one article as a duplicate. Additionally, RefWorks did not report any non-exact replicas that might appear if the formatting was altered. Overall, 99.4% (*n* = 710) of the articles were retained for further screening.

Figure 3

Study Selection and Search Procedure



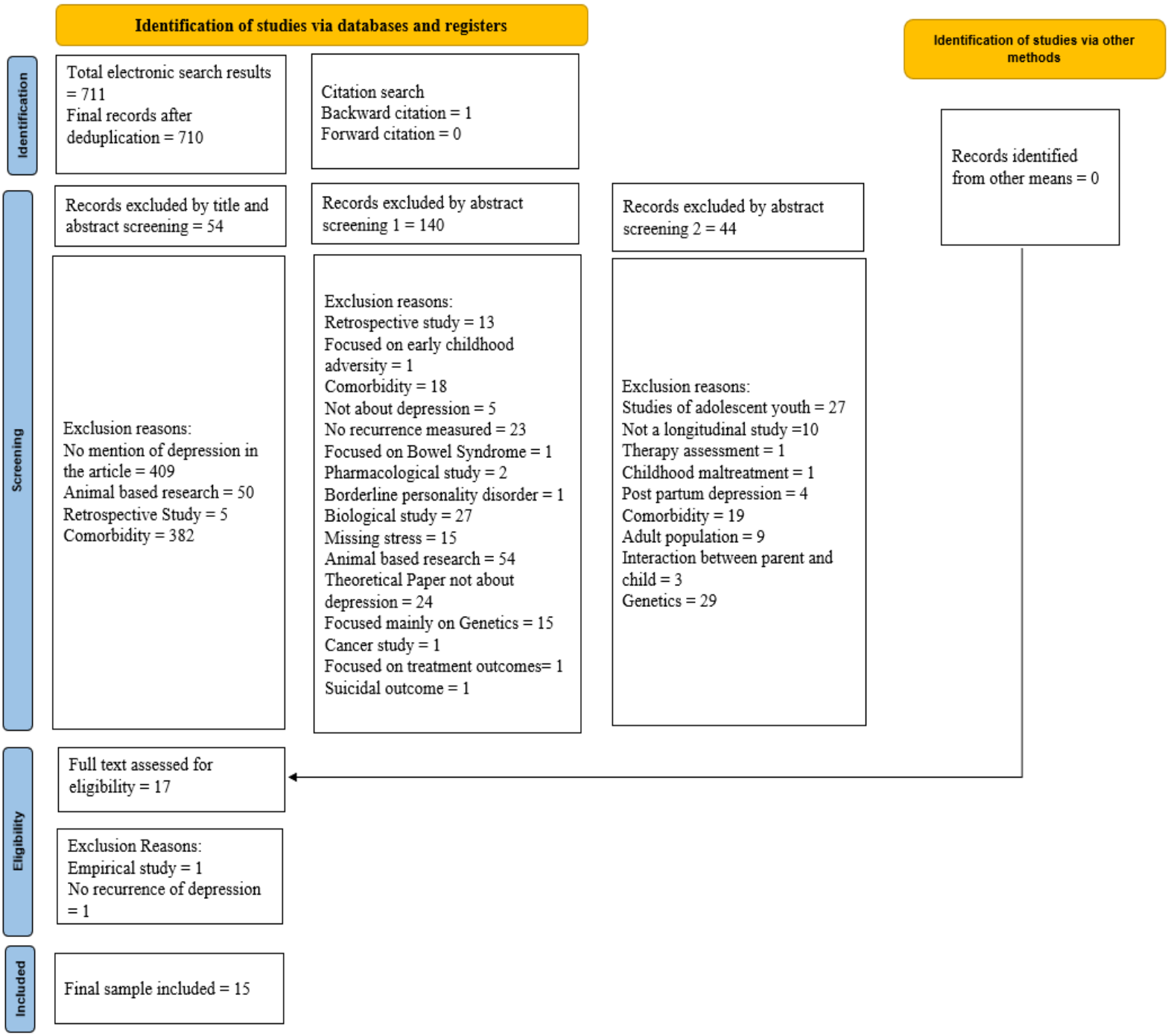
Screening of titles led to the inclusion of 249 articles (35% of the total articles). Next, abstract screening resulted in the inclusion of 109 articles (15% of the total articles). A second round of abstract screening was conducted to restrain the focus solely on studies focusing on adulthood depression and stress, restricting to depression in adults in the age range of 18 to 60 years. The abstract screening procedure yielded *n* = 65 articles (9% of the

total articles). As the scope of the thesis was constrained to the theoretical explanation of stressor-induced stress response and depression, which will be further referred to as theory-based articles, the articles were coded as either empirical or theory-based articles. The coding resulted in *n* = 49 empirical studies (7% of the total articles) and *n* = 16 theory-based studies (2% of the total articles) constituting the two-step scoping review for comprehensive evaluation of the model. The backward citation screening resulted in the inclusion of an additional article for full-text screening.

Theory-based articles were chosen as the focus of the study and the 17 articles (16 articles from database search and one from backward citation searching) were subjected to full-text screening and coded to indicate the eligibility to address the research question. The summary of the coding based on different inclusion and exclusion criteria derived from the research question is presented in Figure 4. Of the 17 full-screened articles, 15 fulfilled the selection criteria (88% of the full-text screened articles). Of the two excluded, one exclusion was due to the type of study which was a purely empirical study (Kessler & Magee, 1994), and another was due to its lack of focus on the recurrence/relapse of depression (Harris, 2001).

Figure 4

Study Coding Process



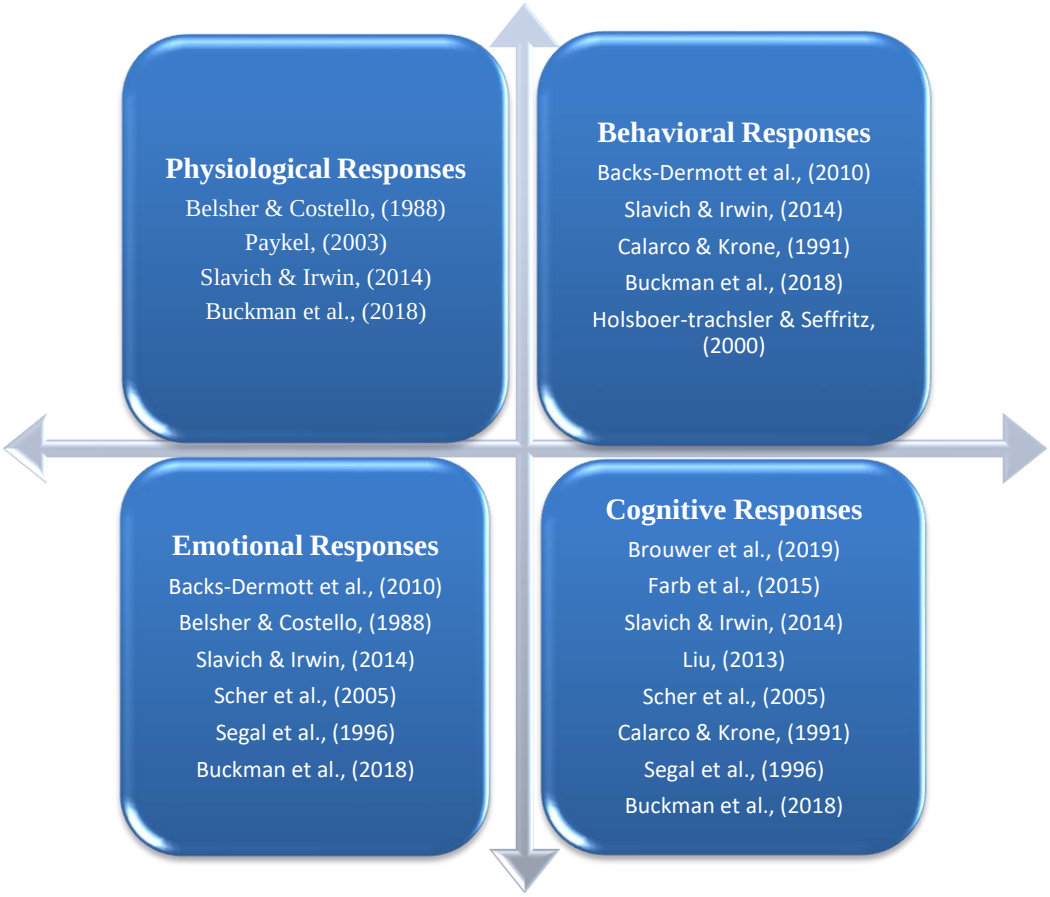
Study Characteristics

The detailed distribution of included articles among the various stress responses with examples is noted in Appendix B, however, article distribution based on the stress responses is represented in Figure 5. Eight articles studied cognitive responses, five articles examined

behavioral responses, six articles investigated emotional responses, four articles studied physiological responses and two articles did not study any responses explicitly. Merely two articles integrated all four types of stress responses.

Figure 5

Mapping of Articles Across Physiological, Behavioral, Emotional, and Cognitive Responses



Primary Findings

The key factors under investigation - stress responses (physiological, behavioral, emotional, and cognitive), and depression recurrence/relapse - were examined in 15 included articles. The following sections will explicitly discuss the respective stress responses due to stressors and their relationship to depression recurrence/relapse.

Cognitive Responses

Stress has been historically associated with cognitive outcomes (Liu, 2013) and has been in focus of research for over two decades, for example, see Segal et al., (1996). Additionally, cognition is an important factor in depression and its relapse and recurrence (Scher et al., 2005). The cognitive effects from exposure to stressors leading to cognitive vulnerability increased the risk of depression and its recurrence/relapse (Scher et al., 2005). Some of the examined cognitive responses to stressors are dysfunctional belief (Brouwer et al., 2019), dysphoric attention and dysphoric elaboration (Farb et al., 2015), negative cognitions including self-blame and themes of inadequacy (Calarco & Krone, 1991; Scher et al., 2005; Segal et al., 1996), negative inferential styles (Liu, 2013), and selective activation of attention, memory search, difficulty in concentrating (Slavich & Irwin, 2014). More generally, negative cognition due to stressors guides self-knowledge and information subsequently, influencing the negative appraisal of the stimulus (Scher et al., 2005). As mentioned earlier, the cognitive effects of stressors predispose an individual to a recurrence or relapse of depression, and the corresponding mechanisms are further elaborated.

Generally, cognitive responses to the stimulus are similar among both depressive and non-depressive prior to the onset of depression, however, they change when exposed to stressors that led to the onset of depression (Scher et al., 2005). The underlying framework responsible for cognitive responses is schemas (Farb et al., 2015). A schema is a form of cognition that directs self-awareness and information that informs stimulus evaluation (Scher et al., 2005). It develops during the early developmental phase of an individual (Calarco & Krone, 1991; Scher et al., 2005; Segal et al., 1996) in response to different kinds of stressors and therefore, the vulnerability to depression also arises early in life. The schemas can remain dormant until they are activated by relevant stimuli (Segal et al., 1996) and once activated, the schema provides access to a complex system of selective attention, memory, and

cognition forming a pattern of information processing that leads to depression. Some examples of negative cognitions include self-blame and themes of inadequacy (Calarco & Krone, 1991; Scher et al., 2005; Segal et al., 1996). Furthermore, the same schemas are also responsible for dysphoric attention and dysphoric elaboration (Farb et al., 2015).

Dysphoria attention and dysphoric elaboration together form the two-factor model of recurrence/relapse proposed by Farb et al., (2015), which describes mechanisms that can lead to depression or its recurrence/relapse. The two factors are malleable and can reinforce each other into a downward spiral. According to the model, sensitization of schema occurs as a result of fixation (sustained representation of negative over positive aspects of the event) and rumination (bringing the fixed viewpoint to the dysphoric schema about one's self, future, and role in the world) (Scher et al., 2005). The fixation is a characteristic of dysphoric attention and rumination is a characteristic of dysphoric elaboration, which jointly describe cognitive dysfunction (Scher et al., 2005). Though the relationship between dysphoric attention and dysphoric elaboration as a cause-and-effect relationship has not been established, it seems to have some neurological basis (Farb et al., 2015).

Additionally, the more depressive episodes an individual has, the easier it is to activate the schema and elaborate the negative associations (Calarco & Krone, 1991; Scher et al., 2005; Segal et al., 1996). If the schema is active, a mild stimulus can rekindle and trigger cognitive dysfunction leading to depression as in the case of stressful life events (Scher et al., 2005), an illustration of Post's work (Post, 1992) on kindling and seizure sensitization (Segal et al., 1996). In the words of the neural system, the threshold for activating the scheme decreases due to sensitization or otherwise called an experience effect, and hence knowledge structures associated with depression are brought to life swiftly. The cues for initial activation reduce upon repeated activation and mutually reinforce leading to a downward spiral, progressing from a mild dysphoria state to a full-blown depressive episode. For example,

information and thoughts associated with a particular stress response are retrieved swiftly when exposed to it (Segal et al., 1996).

Dysfunctional cognition guides the development of dysfunctional attitudes (Scher et al., 2005). A dysfunctional attitude developed as a result of such repeated access to negative schema due to a stressor (Liu, 2013; Scher et al., 2005) giving rise to dysfunctional belief and attributional styles which increases the risk of relapse/recurrence of depression (Brouwer et al., 2019). As cognition is the guide to self-knowledge and information recall, a negative cognition developed by exposure to a stressor leads to negatively toned representations that are capable of biased recall (Scher et al., 2005), selectively activating attention, memory search, difficulty concentrating (Slavich & Irwin, 2014), and development of negative inferential styles (Liu, 2013). The negative inferential styles consequently develop a risk for depression relapse (Scher et al., 2005).

Behavioral Responses

Stress elicits various behavioral responses some of which increase the risk of depression, its recurrence/relapse. The behavioral responses to stressors that are known to increase the risk for recurrence are avoidance coping mechanisms (Backs-Dermott et al., 2010), socio-behavioral withdrawal due to lack of social support and social interaction (Backs-Dermott et al., 2010; Belsher & Costello, 1988; Harris, 2001; Slavich & Irwin, 2014), neurotic behaviors (Brouwer et al., 2019; Buckman et al., 2018), psychomotor retardation (Slavich & Irwin, 2014), and sleeping problems (Holsboer-trachsler & Seffritz, 2000).

Some behavioral stress responses such as avoidance coping mechanisms (Backs-Dermott et al., 2010) are more associated with the recurrence or relapse of depression than stress responses such as sleeping problems resulting from inadequate social support and

social interaction which are associated with both onset (Harris, 2001; Slavich & Irwin, 2014) and recurrence/relapse (Backs-Dermott et al., 2010; Belsher & Costello, 1988).

Physiological Responses

Articles about stress and its physiological aspects have been explored extensively for the past 80 years and are ongoing (Slavich & Irwin, 2014; Szabo et al., 2017). Over the years, numerous physiological responses have been linked with depression and its recurrence/response. For example, inflammatory processes (Slavich & Irwin, 2014), persistently blunted response to Thyrotropin-Releasing Hormone (TRH), short Rapid Eye Movement (REM) latency (Belsher & Costello, 1988), and high cortisol level (Paykel, 2003), to name a few.

The biological processes related to depression are preceded by stress responses such as high cortisol levels (Paykel, 2003). Therefore, psychological aspects such as the perception of threat can initiate similar responses that include biological and behavioral changes and pose a risk for depression (Slavich & Irwin, 2014). For example, psychological stress can elicit inflammatory processes, which is usually a primary response to physical injury or infection (Slavich & Irwin, 2014).

Emotional Responses

Depression (and its recurrence/relapse), by its definition, is characterized by a persistent sad mood (World Health Organization, 2019) and is a serious mood disorder (National Institute of Mental Health, 2023), highlighting the involvement of emotions. Most frequently, the emotional responses to stressors precede depression and its recurrence or relapse (Backs-Dermott et al., 2010). As a result, stressors and depression recurrence are associated with emotional responses. For example, emotion - oriented coping mechanisms

due to stressors have proven to be related to relapse of depression (Backs-Dermott et al., 2010), and extreme emotions such as severe humiliation precede the onset of depression (Backs-Dermott et al., 2010).

Inflammation, a physiological response, can precipitate depressive symptoms such as sad mood, anhedonia, and fatigue (Slavich & Irwin, 2014), and subsequently, the negative mood precedes both onset and depression recurrence (Scher et al., 2005; Segal et al., 1996). The negative mood further advocates more negative moods (Scher et al., 2005; Segal et al., 1996) leading to a sensitization effect similar to the one described by Post (1992). Repeated exposure to stressors eliciting emotional responses would result in minor stressors becoming capable of causing severe emotional responses, increasing the risk for depression (Segal et al., 1996). The emotionally driven responses were predicated by neuroticism further adding to the risk of relapse and recurrence (Brouwer et al., 2019).

Moderating Factors

Although most responses to stressors that are associated with depression and its recurrence/relapse can be exclusively categorized among physiological, cognitive, emotional, and behavioral responses, some factors stand apart from these categories either due to their complexity, their nature of possibly belonging to multiple categories or due to its indirect association with both stressor and depression. One example of such a factor is personality (Backs-Dermott et al., 2010). Personality influences one's response to stress and depression respectively and it also influences stressor - stress response - recurrence of depression processes. Additionally, personality influences all responses to depression directly and indirectly. The indirect effect may provide the impression that personality has no bearing on the course of depression (Backs-Dermott et al., 2010), however, Tennant (2002) found that personality also has a direct effect on recurrence/relapse.

Closely related to personality, neuroticism is another construct that was difficult to categorize based on definitions employed in this study; however, it influences how one experiences and responds to a stressor (Schneider, 2004). It is also proven to influence emotional, cognitive, behavioral, and physiological responses (Schneider, 2004). An example by Buckman et al., (2018) suggested that neuroticism dictates the emotional response to stressors.

Similarly, attachment styles are not typical responses but influence the responses to stressors. For instance, attachment styles due to early life stressors such as childhood trauma moderated the effects of stressors on stress responses (Kessler & Magee, 1994). Dismissive and preoccupied attachment styles characterized by anxious attachment, excessive reassurance-seeking, and dependency guide the stress response to a stressor (Liu, 2013). The attachment styles influence physiological responses to stressors for instance, dismissive attachment styles direct the dysregulation of HPA (stress response) through higher cortisol levels (Kidd et al., 2011). Additionally, the effect of attachment styles on cognitive responses to stressors is illustrated by examples where individuals with anxious attachment styles display higher negative affect (stress response) (Sheinbaum et al., 2015) and individuals with an avoidant attachment style decrease their positive affect states (stress response) when exposed to stressors (Sheinbaum et al., 2015). As a result, feeling unloved, rejected, and unwanted due to attachment styles predisposes one to depression (Scher et al., 2005).

Lastly, age and gender are also not stress responses; however, literature has pointed out their influences on stress response and the recurrence of depression (Stroud et al., 2008). Age and gender significantly moderated the effects between stress, depression, and its recurrence/relapse. For example, as age increases, the difference between the proportion of people experiencing a severe life event before onset and the proportion of people experiencing a severe life event prior to a recurrence increases. The gender effects showed

that the percentage of female participants increased, and the difference in the proportion of people experiencing a severe life event prior to onset to that recurrence decreased (Stroud et al., 2008). Thus, personality, attachment styles, neuroticism, age, and gender moderate the risk of depression recurrence/relapse.

Precursors to Stress - Recurrent Depression Relation

Factors such as childhood adversity and genetics act as precursors for depression. Childhood adversity is extensively studied with outcomes for depression (see, for instance, Wainwright & Surtees, 2002) and with stress responses (Wu et al., 2023). In the context of the thesis, it does not appear as a stress response but is related to depression in a way it increases the vulnerability to the recurrence of depression (Kessler & Magee, 1994) through stress responses such as cognitive dysfunction (Scher et al., 2005). Childhood adversity could be related to parental death, parental divorce, deprivation of adequate care, and physical and sexual abuse, and studies show that it increases rates of depression and difficulty in transitioning to early adulthood (Paykel, 2003). In addition, depression history moderates the relationship between childhood adversity and the recurrence/relapse of depression (Kessler & Magee, 1994). Chronic stress, on the other hand, mediates the relationship between childhood adversity and the recurrence of depression (Kessler & Magee, 1994). Thus, childhood adversity is a precursor influencing the relation between stressors, stress response, and recurrent depression.

Genetics is another precursor that influences responses to stress directly and indirectly, thereby guiding the stress responses resulting in the risk of depression recurrence/relapse (Harris, 2001; Paykel, 2003). An example of indirect influence is observed in serotonin transporter gene polymorphism which influences the stress response processes in the presence of stressors (Liu, 2013). Furthermore, Liu, (2013) notes that dependent stressors

that involve the individual are more heritable through genes than independent stressors that do not directly involve the individual. Provided that dependent stressor has a major role in stress responses, the risk of depression recurrence/relapse also increases in offspring (Liu, 2013). An example of the direct influence of genetics is observed when sleep problems in depressive individuals are compared to those of non-depressive individuals. Additionally, the sleep patterns among the depressive are similar to those of depressed ancestors indicating the transmission of genetic risk of depression and its recurrence (Holsboer-trachsler & Seffritz, 2000).

External Factors

Other effects such as contagion effects that are external to the individual also influence stress response and depression onset and recurrence. The tendency of the depressed individual to influence the onset or relapse of depression in their social network is referred to as depression contagion (Liu, 2013). Interpersonal dependent factors and behavioral responses are related to contagion mechanisms thereby providing insight into interpersonal and intergenerational transmission. For example, in an excessive assurance-seeking relationship, a stress response to a stressor can have two outcomes. One, interpersonal rejection (individuals create an aversion to the depressed individual and leave); Two, becoming depressed themselves when exposed to stress (an individual who bears on the needs of the depressed people and enduring the aversion) (Liu, 2013).

Discussion

The purpose of the thesis was to do a theoretical scoping review of the literature to collate knowledge from the literature that utilizes theoretical grounding to explain the stress mechanism in terms of stressor-induced stress responses, and its evolution through time, in recurrent depression.

Strengths of the Study

The study has numerous strengths. 1) It systematically explores literature and identifies the evidence supporting the model proposed with a focus on the stress responses (see Figure 1) to help unfold the mechanisms of the stressor - stress response - recurrent depression relation that feeds back into the stress-generating process. 2) It attempts to synthesize knowledge related to stress - stress response - depression and its recurrence/relapse 3) It adds to the literature on the development of a comprehensive model of stressor - stress response - psychopathology by identifying varied stress responses in relation to depression and its recurrence/relapse. 4) This review helps take the first step toward real-time interventions for stress and depression. 5) The study also highlights the stress responses that are researched more frequently such as cognitive dysfunction (Buckman et al., 2018; Calarco & Krone, 1991; Farb et al., 2015; Liu, 2013; Segal et al., 1996b; Slavich & Irwin, 2014).

Despite the study's advantages, some shortcomings and deviations are outlined below. These are divided into three categories: deviations in research selection procedures, discrepancies and restrictions in the co-morbidity of depression and other related issues, and disparities and limitations in stressors and stress responses.

Deviations from the Study Selection Procedure

The first of the deviations concerns the inclusion of empirical study (i.e., Backs-Dermott et al., 2010), an exception to the aim of the thesis to synthesize theoretical knowledge related to a stressor - stress responses - recurrent depression. The inclusion was based on the fact that it was rooted in theory and its evaluation following the rationale that theories are constructed from empirical evidence. Specifically scouring for theoretical articles might have sidestepped the theoretical articles grounded in empirical evidence. Further, the two-step scoping review also accommodates the inclusion of screened empirical articles in the second step to expand the scope of the study and add to the current findings.

On the other hand, an additional article (Buckman et al., 2018) identified through a backward citation search was not retrieved through the database search with the employed search terms (Figure 2). The reason for the miss could be related to key terms used in the article being different from the search terms. For example, the terms ‘stress or stressor or stress factor’ would explicitly look for articles that highlight stress or have it as one of their keywords. The article by Buckman et al., (2018) did not have the stress terms included in the title or the keywords, leading to its miss. Furthermore, several studies were excluded due to not having stress terms in the title or keywords or even in the abstract though they studied stress. The fact that Buckman et al., (2018) article was not identified by the search terms or the screening process shows that there might have been an oversight of articles that do not explicitly mention studying stress.

Another deviation in the study selection process is the employment of two-step abstract screening. The results from the first abstract screening were too broad to fit into the scope of the thesis. Hence, a second abstract screening with supplementary inclusion and exclusion criteria was conducted (see Figure 4). The second abstract screening resulted in *n* =

65 articles which were further segregated into empirical or theory-based studies (two-step scoping review). The thesis begins with a theoretical perspective drawn from theory-based studies (n = 16), after which it must combine empirical papers (n = 49) for a complete comprehensive review.

Comorbidity of Depression and Unipolar Depression

According to Kalin (2020), depression can co-occur with other illnesses such as anxiety-related disorders. Even though the focus was on unipolar depression, because of its significant comorbidity the presence of other illnesses might have been overlooked. Some examples of this are explored in Olfson et al., (2012) where depression comorbidity with other psychopathologies such as panic, generalized anxiety, substance use, and dysthymic disorders. In addition, Kang et al., (2015) explores depression comorbidity with physical sickness such as cancer, stroke, and acute coronary syndrome. Moreover, most of the studies did not discern between primary, secondary, and double depression (Belsher & Costello, 1988). Thus, the stress responses found for depression might not be exclusively related to unipolar depression.

Calarco & Krone (1991) further pointed out that the definitions for depression used by authors span from sad mood to a clinical level of depression determined by the range of psychological and physiological symptoms resulting in ambiguity and inconsistency in pinpointing effects associated with clinically diagnosable depression (Belsher & Costello, 1988; Buckman et al., 2018; Monroe & Harkness, 2022). The ambiguity is also present in other terminology associated with depression such as relapse, recurrence, remission, and episode, further complicating the implications of stress responses to depression and its recurrence/relapse. To complicate the matter even more, even though the constructs and stress responses utilized for the characterization of onset, maintenance, relapse, and

recurrence are the same, the underlying processes could be different (Segal et al., 1996). A comprehensive definition of onset, recurrence, and relapse is the starting point for the exclusive characterization of stress responses associated with them respectively (Monroe & Harkness, 2022).

Furthermore, the focus of the study was restricted to depression, more specifically, unipolar depression hence, the findings also bear the same restriction and cannot be easily extended to other psychopathology, even for other types of depression. To broaden the scope, additional types of depression, such as postpartum depression, and other psychopathologies, such as anxiety disorder and bipolar disorder, must be considered.

Another limitation arises due to the employed exclusion criterion that permitted only adulthood depression. The decision was made hypothesizing that depression in childhood or adolescence or older adults can be different from those in adulthood (Lindner Center of Hope, 2019). Additionally, it helped confine the scope to fit the thesis but at the same time constrained the findings. Life experience of depression would require one to consider the aforementioned populations as they form an integral part of the life course.

Stressors and Stress Responses

The study broadly explores the relationship between stressor - induced stress response - depression, but the stressors itself is not explicitly studied even though they could have a varied influence on depression. Stressors can be normative or non-normative, and mostly, the distinction is not made explicitly in the included studies. Similarly, not distinguishing between independent (negative life events that are out of the individual's control) or dependent stressors (negative life events that are at least partially influenced by the individual's behavior) (Liu, 2013) can lead to misattribution of stress responses and depression outcomes to corresponding stressors. Following this, it was challenging to

distinguish between different stress responses based on the kind of stressors because most studies neglected to address the type of stressors.

Similarly, the severity of the stressor is just as crucial. For example, Tennant, (2002) studied the severity and duration of stress and concluded to have a positive association with onset and recurrence/relapse. Since details about the stressors were rarely mentioned, it is difficult to discern its effects on stress response and consequently on depression recurrence or relapse.

Stress responses studied in the included articles spread across the four categories. Two of the 15 papers discussed all four stress reactions, which could be due to the following two reasons. 1) Articles generally focus on one or two categories of the stress response (in total 10 articles). 2) The articles which studied all four response articles are review articles (Buckman et al., 2018; Slavich & Irwin, 2014) and could be the reason for inclusiveness. Considering the two viewpoints, it can be speculated that articles generally concentrate more on one or two types of stress responses. Additionally, two articles were included in the review that did not investigate any specific stress response however, they did examine stress responses on a meta-level in addition to the recurrence of depression, and mechanisms associated with them. One of them was a meta-analytical review (Stroud et al., 2008) and the other was a review article on stress mechanisms related to depression and its recurrence/relapse (Monroe & Harkness, 2022).

The review additionally demonstrated that some stress responses were researched more than others. For instance, eight studies investigated the cognitive stress response while only four, five, and six studies, respectively, examined the physiological, behavioral, and emotional stress responses. On the contrary, stress responses such as physiological responses have been researched for a very long time (Szabo et al., 2017), and yet relatively fewer

theory-based articles were included in this review implying that it may be less researched with recurrent depression as opposed to onset of depression. This suggests that future studies would benefit from looking more closely at individual stress responses as well as all stress responses collectively in relation to depression recurrence.

The four response categories were inclusive of most of the types of responses. However, some were hard to categorize such as personality, neuroticism, and attachment styles as they are not stress responses but individual characteristics that influence stress responses. Personality can be viewed as an interaction between physiological, behavioral, cognitive, emotional processes (Hart et al., 2005) and genetics. Genetics, on the other hand, is a precursor to depression similar to childhood adversity. Therefore, these constructs that are not stress responses yet have a bearing on stress responses. Furthermore, due to its complex congregation of multiple factors, it is difficult to discern its effect precisely.

Stress responses do not occur in isolation and some studies highlighted the possible interaction among them. One study elaborated a multi-factor model taking into account stress generation processes based on interaction among cognitive vulnerability, and the behavioral and social context of depressed people to draw out the mechanism associated with relapse (Liu, 2013). For instance, a negative inferential style can be restrictive in engaging in physical activity which is protective in depression incidence/relapse by eliciting anti-depression effects (Kandola et al., 2019). Such increasing withdrawal from activities can reinforce the stress-generation process contributing to increasing negative appraisal of stressors (Liu, 2013).

Another instance of interaction among the stress responses is illustrated by Segal et al., (1996) where the author elaborates on mechanisms associated with interaction between emotion and information processing. For example, the depressed mood (emotional response)

can recall selective memories (cognitive response) that are associated with being depressed or information learnt in a prior depressed mood. Strengthening the associated information to the negative mood due to its repeated access also reduced the positive information access due to its infrequent access (Segal et al., 1996).

A few articles also mentioned the instances where stress response caused other stress responses. For example, consider the case where sleep disturbance, which is a physiological factor, causes behavioral problems in depressive individuals (Holsboer-trachsler & Seffritz, 2000). Another example includes mood (emotional responses) linked to cognitive reactivity-predicted relapse (Scher et al., 2005). Cognitive reactivity could also be due to the feeling of being unloved, rejected, and unwanted as a result of dismissive attachment styles (Scher et al., 2005). In some cases, responses are associated with other external factors, for example, sleep disturbances (behavioral response) are related to the choice of anti-depression medication (external factor) (Holsboer-trachsler & Seffritz, 2000).

Additionally, some stress responses could belong to multiple categories such as coping styles which can be both behavioral and cognitive responses to stressors (Rekhi, n.d.). In the thesis, however, coping styles are considered to be a behavioral response to stressors leading to depression based on the definition employed but it could also refer to cognitive coping styles. From the aforementioned examples, interaction among the stress responses and multi-category responses develops a complex relation rendering difficulty in discerning the corresponding causes and response effects. Exclusively studying these responses can assist in localizing the stress response and risk for depression recurrence/relapse.

The prevalence related to recurrence in depressed persons has been said to be exaggerated (Buckman et al., 2018; Monroe & Harkness, 2022), leading to misclassifying those who are at risk for recurrence and relapse when compared to those who are not (single

episode depression). Such misidentification might result in uncovering of responses and mechanisms associated with the recurrence of depression as they may be distinct from those of a single episode of depression (Belsher & Costello, 1988), thereby creating barriers in developing a clear conceptualization of stressor - induced stress response and depression recurrence and relapse.

Lastly, the mechanism of stressor - stress response - recurrent depression is also influenced by the context in which it occurs (Cutrona et al., 2006; Martell et al., 2001); nevertheless, for this thesis, the focus is limited to the model involving the interaction among stressors - induced stress responses, and recurrent depression as these are considered the fundamental components irrespective of context. For example, highly neurotic individuals (context) have increased vulnerability to the stressor (Schneider, 2004), consequently influencing the stressor - stress response - recurrent depression. More precisely, neurotic individuals are more reactive to stress in the form of emotional and cognitive responses. For simplicity, the study focused on the model and its components and hopes that future research will incorporate the context of the model.

Conclusion

The purpose of the thesis was to conduct a scoping review of theoretical literature to understand the stress mechanism in relation to depression and its evolution over time, through stress responses. The literature suggests that stress and life events contribute to the likelihood of relapse in depression and are also associated with the onset and recurrence of depression (Belsher & Costello, 1988).

Stressful life events have been found to precede both the onset (Harris, 2001; Paykel, 2003) and recurrence/relapse of depression (Belsher & Costello, 1988). The relationship between stress and depression is explained through various stress responses, including physiological, emotional, behavioral, and cognitive responses. Examples of these stress responses include cognitive dysfunction (Calarco & Krone, 1991), extreme emotions (Belsher & Costello, 1988), sleep disturbances (Holsboer-trachsler & Seffritz, 2000), and inflammation (Slavich & Irwin, 2014), among others, as described in this study.

Examining the different stress responses that contribute to depression recurrence or relapse, opens the possibility of designing an intervention that targets specific stress response patterns. This knowledge can be utilized in designing real-time interventions and developing tailored interventions based on individual stress response profiles. Furthermore, it is also important to realize that stress responses can vary between the onset of depression and its recurrence or relapse when considering interventions and treatment approaches (Segal et al., 1996). Overall, by conducting a scoping review of the literature, this study contributes to building information that can guide the development of targeted interventions and improve our understanding of the complexities of recurrent depression and its relationship with stressors and stress responses.

Future Research

The current study contributes to the literature and knowledge base of stress - stress response - depression (and its recurrence/relapse) however, the study's scope can be expanded to incorporate screened empirical studies (second steps of two-step scoping review) along with the already outlined theory-based articles (the current study). A more comprehensive model (stressor - stress response - psychopathology) of what was investigated in the current study can be tested by incorporating more illnesses starting with various kinds of depression and, more widely, other psychological disorders such as anxiety-related disorders. Further, it can be extended to include depression and recurrence/relapse in other populations such as adolescents and older adults to describe the life course experiences of depression.

Since the interaction of the stress responses may make it challenging to pinpoint a specific effect, an isolated assessment of stress responses can aid in determining the origin and effect of stress responses. Lastly, given that only a few studies focused on all kinds of stress responses, a further inquiry examining all four components can advance the understanding of the various kinds of stress responses.

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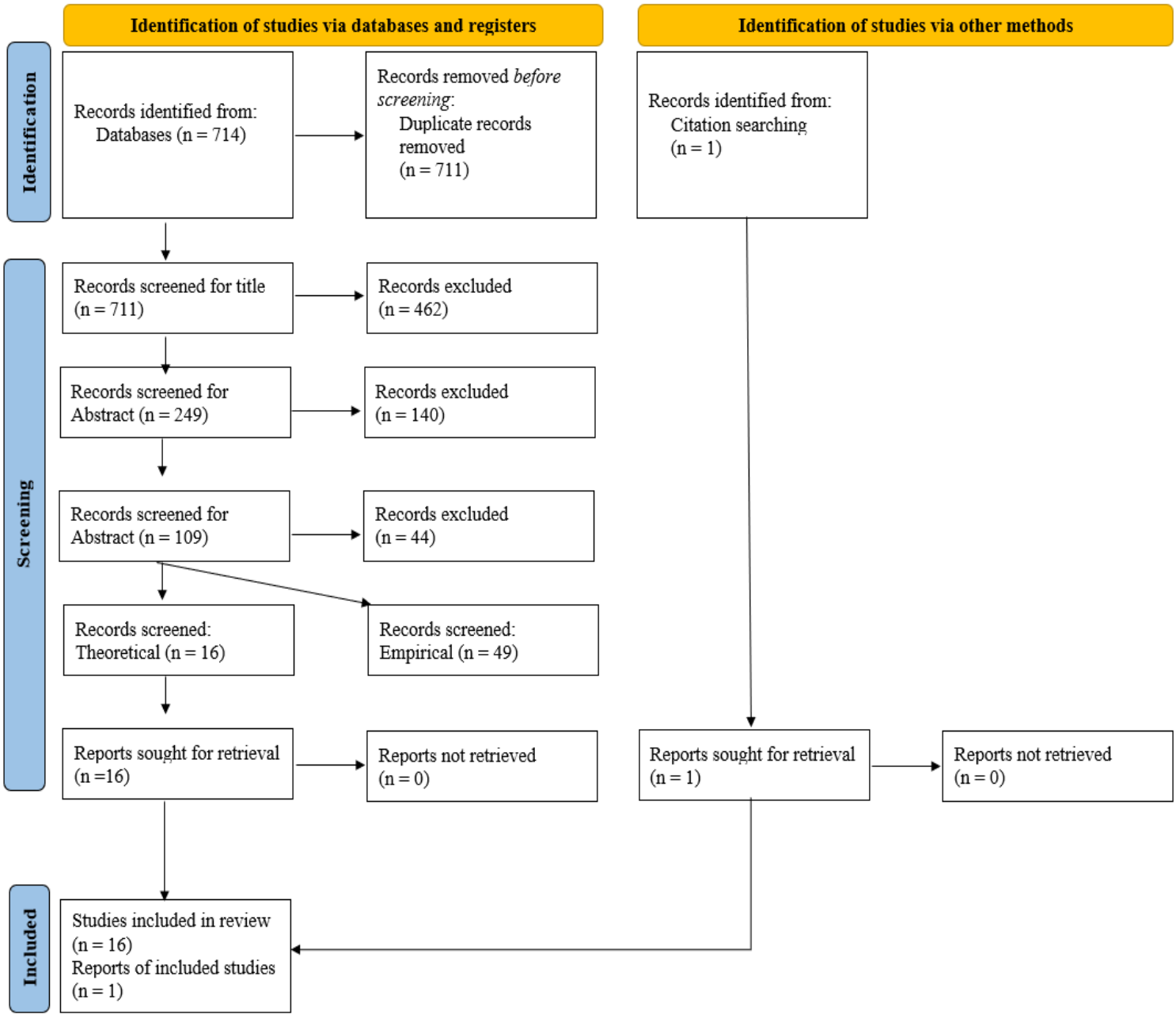
Appendix A

Figure 6

PRISMA 2020 Scoping Review Flow Diagram



Appendix B

Table 1

Stress Responses Examined in the Included Articles

Article	Stress Responses				Moderators	Precursors
	Cognitive	**Behavioral**	**Emotional**	**Physiological**		
Backs-Dermott et al., (2010)		1. Avoidance coping style	1. Emotional oriented coping style			
Monroe & Harkness, (2022)						
Belsher & Costello, (1988)			1. High expressed emotion	1. Persistently blunted response to TRH 2. Short REM latency		
Paykel, (2003)				1. High cortisol levels		1. Genetics
Tennant, (2002)						1. Genetics

Article	Stress Responses				Moderators	Precursors
	Cognitive	**Behavioral**	**Emotional**	**Physiological**		
Brouwer et al., (2019)	1. Dysfunctional beliefs 2. Attributional styles				1. Neuroticism	
Farb et al., (2015)	1. Dysphoric attention 2. Dysphoric elaboration					
Slavich & Irwin, (2014)	1. Difficulty concentration	1. Psychomotor retardation 2. Socio-behavioral withdrawal 3. Sleep disturbances	1. Sad mood 2. Anhedonia 3. Fatigue	1. Inflammation		
Liu, (2013)	1. Dysfunctional attitudes 2. Negative inferential styles 3. Problem solving skills				1. Attachment styles	
Holsboer-trachsler & Seffritz, (2000)		1. Sleep disturbances 2. Sleep deprivation				

Article	Stress Responses				Moderators	Precursors
	Cognitive	**Behavioral**	**Emotional**	**Physiological**		
Stroud et al., (2008)						
Scher et al., (2005)	1. Negatively toned representations 2. Selectively activated attention 3. Selective memory search and recall 4. Irrational belief 5. Dysfunctional attitudes 6. Interpretive bias		1. Negative mood		1. Attachment styles	
Calarco & Krone, (1991)	1. Dysfunctional cognition	1. Motor retardation				
Segal et al., (1996)	1. Information processing bias		1. Emotion processing bias			
Buckman et al., (2018)	1. Cognitive bias 2. Information processing bias 3. Cognitive reactivity 4. Rumination 5. Worry	1. Avoidant coping style	1. Worry	1. Neuro endocrine dysfunction	1. Neuroticism	1. Genetics