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The body intervenes: How active inference explains depression's clinical presentation

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ABSTRACT

The low mood that characterises depression is accompanied by changes in bodily processes, manifested in symptoms such as insomnia, reduced appetite and fatigue. The active inference framework provides an explanation as to how mood-related symptoms are linked. It suggests that affective experiences arise from predictions about interoceptive states and their corresponding prediction errors, with the relative influence of each modified by precision weighting. Moods reflect long-term predictions about the state of the body, incorporating parameters related to sleep, appetite and energy levels. Depression emerges from the interplay between reduced confidence in long-term prospects and heightened expectation of shorter-term negative affect, which sees a re-weighting of the precision of interoceptive prediction errors. The ensuing bodily changes contribute to the emergence of depressed mood; and underpin disturbances in shorter-term interoceptive predictions and the experience of emotions such as anxiety and irritability. This framework details how interoceptive processes shape the phenomenological and symptomatic experience of depression, helping us to understand the disorder's multifaceted and often idiosyncratic clinical presentation, and with implications for the way we understand and treat depression and its co-morbidities.

> All day, all night the body intervenes; blunts or sharpens, colours or discolours … The creature within can only gaze through the pane—smudged or rosy; it cannot separate off from the body.
>
> Virginia Woolf, On Being Ill (Woolf, 1926, pp. 32–33)

1. Introduction

The experience of a pervasive low mood is often the impetus for a person to seek clinical care. They feel terrible and want action taken to alleviate their suffering. Their low mood is the essential feature of depression, but it is only one among an array of symptoms. Depression involves changes in bodily processes, with many people experiencing symptoms such as insomnia, poor appetite and fatigue. People with depression are likely to also experience changes in the frequency and intensity of emotions, with a shift towards those with negative valence and away from positive emotions.

Our understanding of the mechanistic links between depressed mood and the symptoms that accompany depression remain unclear. Why is it that depressed mood is associated with changes in the basic physiological processes that underlie sleep, appetite and energy levels? How does depressed mood relate to the changed array of emotional experiences? We lack conceptual frameworks that can explain why depression presents the way it does.

1.1. Moods and emotions

There is consensus about many of the features of moods. They tend to be diffuse and unfocused, providing a background atmosphere and context for experiences. They are relatively sustained, lasting hours to days to months. They are not usually reflective of anything in the immediate environment, and it is often difficult for a person to identify what has caused their mood to appear the way it has (Aho, 2019).

Clinically, to describe mood "is simply to equate it with whatever the patient reports as his or her subjective emotional state" (Trzepacz and Baker, 1993, p. 40). This leaves it to the patient to reflect on the character of their internal affective states, drawing on folk conceptions of moods when they describe them to their clinician. They will often provide a summary of their mood over a span of time: for example, over the

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past few months if at an initial assessment, or since last seeing their clinician if at a review.

Emotions have features that contrast with moods. They usually arise in response to objects and events in the immediate environment. They are short-lived; and rather than sit in the background, they dominate attention. Emotions are better articulated than moods, and we can often apply labels to them: as feeling worried, happy, angry, or surprised (Beedie et al., 2005; Clore and Huntsinger, 2007; Kagan, 2007).

1.2. The affective stream

The term "affect" is used in varied ways in different contexts. It is often used as an umbrella term that encompasses all emotional and mood-related experiences, which is how McHugh and Slavney define it: "Affect is a broad term encompassing moods, emotions, motivations, and such feelings as pleasure, confidence, depression, and discouragement" (McHugh and Slavney, 1998, p. 72).

Affect has both an internal, subjectively experienced, *felt* quality, and bodily manifestations that can be observed by others. The latter conception is what clinicians describe as affect in their mental state examinations. Affect – in this narrower clinical sense – is said to be observed by the clinician rather than self-reported like mood. The clinician notes the moment-to-moment changes in a patient's affective expression and makes comment on its characteristics: such as its type, range, intensity, and congruence with what the patient is discussing (Trzepacz and Baker, 1993; Sims, 2002).

The subjective component of affect forms part of the stream of consciousness, a concept proposed by James (1890) to refer to the continuous rolling experience of waking life. The stream of consciousness is often used synonymously with the stream of thought, as if consciousness was made up of only cognitive content. But affective experiences, which are "sensibly continuous, like time's stream", are fundamental to James's conception of it (James, 1884, p. 6). This affective stream is constituted by moods and emotions, and also by what Panksepp (1998) refers to as bodily affects, which includes experiences such as hunger, thirst and pain.

The clearer sense we have of emotions has given them prominence in discussions of affect. But as phenomenologists have argued, moods provide the conditions for emotions. They set the parameters of the affective stream, determining the space of possible affective experiences (Ratcliffe, 2009). Particular moods make particular emotions more likely. A depressed mood, for example, entails greater likelihood of experiencing irritability, anger and fear, and lesser likelihood of joy, anticipation and hope (Chaplin, 2006).

Moods exist at a deeper phenomenological level than emotions: serving as the container for them. They are directed at the world as a whole rather than at particular situations, and constitute our feelings of being (Aho, 2019). Our description of ourselves as being *in* a mood, while we *have* an emotion, hints at their phenomenological differences (Ratcliffe, 2009). Heidegger describes this sense of a mood as being something we inhabit. A mood, he says, is something that is "already there … like an atmosphere in which we immerse ourselves" (Heidegger, 1995, p. 65).

1.3. Disturbed moods

Moods are less easily categorised than emotions. Even when disordered, as in depression, the mood state is said to be difficult to describe (Ratcliffe, 2015). Patients might simply use the term "depressed", a descriptor that Styron says has "a bland tonality" and as being "a true wimp of a word" (Styron, 1990, p. 37). Metaphorical descriptions get closer to describing a depressed mood, which writers have likened to a "bleak shadowland" (Shaw, 1997, p. 25); or a "darkness … closing in" (Radden, 2009, p. 172); or as "like a hole. You are stuck in the hole. You can't get out." (Fusar-Poli et al., 2023, p. 355).

A depressed mood is typically accompanied by insomnia (despite fatigue), a lack of appetite, psychomotor slowing, reduced sex drive and physical complaints; although sleep, appetite disturbances and psychomotor activity can change in the opposite directions too (Fried et al., 2016). Energy levels are low and there are no feelings of pleasure, but instead, feelings of guilt and low self-worth (Fusar-Poli et al., 2023). Other biological changes might also be evident, including changes in inflammatory markers and measures of autonomic activity (Sgoifo et al., 2015; Beurel et al., 2020).

2. Affective experiences and interoception

Affective experiences arise through interoception: they are internally sensed, appearing to arise from internal sources. Interoception, which refers to "the processes by which an organism senses, interprets, integrates, and regulates signals from within itself" (Chen et al., 2021, p. 3), emerges out of interactions between the nervous system and the rest of the body: i.e., those parts of the body that are not the nervous system. The processes can sometimes be perceived – e.g., as pain, hunger, fatigue and fear – although mostly do not rise to conscious awareness (Owens et al., 2018). When there is awareness of interoceptive processes they usually have affective qualities: the processes become known to us as feelings.

2.1. An active inference account of interoception

Recent developments in theoretical neuroscience – and in particular the active inference account of brain function proposed by Friston (2010) – can help us to make sense of how affective experiences and interoceptive processes are connected. Detailed explanations of active inference have been provided elsewhere (Hohwy, 2013; Barrett and Simmons, 2015; Friston et al., 2017; Seth, 2021; Clark, 2023), and I provide here a summary to serve as a framework for understanding interoception and how it applies to mood. The active inference framework provides a conceptual model of brain function. It is a formal theoretical approach grounded in Bayesian inference and variational calculus; and while there are plausible mechanisms for how it is enacted in the brain, empirical support is only starting to emerge (Hodson et al., 2024; Eckert et al., 2025).

The usual concept of the brain is that it first receives sensory information, then processes that information to form models of the world, which then creates the basis for action. The active inference account upends this. It proposes that the brain starts by generating models of the world, acts to selectively sense features of the world according to its models, and then updates the models to more accurately reflect what the sensory data tells it. Instead of the brain performing within a *sense–think–act* framework, it is an inference machine that tests and updates its beliefs by actively sampling the world (Seth, 2021).

The mechanism by which the brain's generative models are brought into alignment with sensory input is by the minimisation of prediction errors (Friston, 2010; Parr et al., 2022). In the interoceptive domain, the brain generates predictions about interoceptive sensory data, and where the actual sensory data differs from modelled expectations, prediction errors are created. The brain seeks to minimise these prediction errors in one of two ways: by updating its models to better account for the data, referred to as perceptual inference; or by pursuing actions that produce sensory data that better accord with the models, referred to as active inference[1] (see Fig. 1).

Active inference is especially apt for understanding interoception.

[1] The term "active inference" is used for the broader framework as well as for the specific component within the framework (active inference is an extension to the older idea of perceptual inference). Other roughly synonymous terms include predictive processing and the Bayesian brain. They are implementations of the free energy principle, an overarching concept that will not be explored in this manuscript.

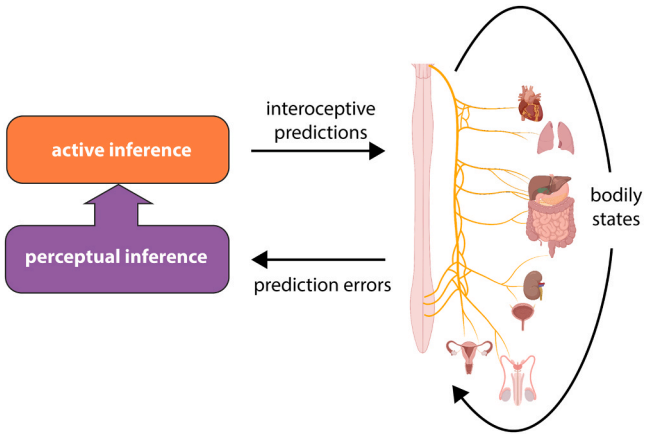

Fig. 1. Active and perceptual inference. Active inference and perceptual inference work in parallel to minimise prediction errors. Interoceptive predictions model the expected bodily signals, and deviations from those predictions ascend as prediction errors. These errors can be minimised by either updating the generative models (perceptual inference) or by adjusting visceromotor output so that the predictions align with the sensory signals (active inference). These processes occur together, to a greater or lesser degree. For example, when environmental temperature exceeds predictions, the brain simultaneously updates its predictions about expected temperatures while initiating vasodilation and perspiration in an attempt to resolve the prediction error.

The classical conception of the active inference model provides an account of motor control, whereby the motor cortex generates predictions of how its actions will affect proprioception, and adjusts its actions to accord with the predicted proprioceptive inputs (Seth and Friston, 2016). For example, it might predict the proprioceptive sensations that would accrue when the arm is drawn back to throw a ball. The process starts with a prediction about the sensory consequences of the action, and action then proceeds to match the proprioceptive input to the proprioceptive predictions via the minimisation of prediction errors. Where proprioceptive predictions model the arm moving backwards, but the arm is in fact at rest in front of the body, a prediction error is created that is resolved by the arm's backward movement.

Interoceptive processes are similar to proprioceptive processes in that they guide action – but via the visceromotor system rather than musculoskeletal. In an active inference account of interoception, the brain generates models of anticipated bodily changes, and where the interoceptive sensory data deviates from predictions, the brain attempts to explain away the prediction errors via visceromotor actions that fulfill the predictions (Stephan et al., 2016). This will often occur unconsciously: e.g., when increased body pH is anticipated the respiratory rate is increased to expel carbon dioxide and maintain body pH at its expected levels. But other prediction errors will rise to conscious awareness as feelings, compelling behaviours to resolve them: e.g., hunger that compels locating and preparing food to satiate it, or fear that promotes preparedness to flee.

2.2. The role of precision-weighting

The third component of the active inference framework relevant to understanding interoception – in addition to perceptual and active inference – is the precision-weighting of prediction errors. Precision is a measure of how reliable the prediction errors are expected to be – it is the inverse of their variance. The precision of the prediction errors impacts the degree to which they update the generative models; an impact that is varied by having a gain function applied to them (i.e., by being weighted). The brain generates models for the precision-weighting of prediction errors, akin to its models for its sensory predictions. These second-order expectations about precision are overlaid on the first-order sensory predictions (Hohwy, 2013).

Prediction errors with high precision will tend to be amplified and those with low precision attenuated. The weightings also depend on the confidence held in the generative models (i.e., the precision of the models). Where confidence in a generative model is high, prediction errors in domains specified by the model will be expected to have very high precision, while prediction errors outside of those domains will be suppressed. These highly precise prediction errors will often be explained away by low-level reflex arcs (i.e., via active inference). When confidence in the prior models is low, however, the gain on the prediction errors is broadly up-weighted: the brain becomes more reliant on prediction errors to update and increase confidence in the models (i.e., via perceptual inference) (Stephan et al., 2016). Precision weighting is therefore influenced by two factors: by the expected precision of the prediction errors themselves, and by the confidence in the generative models. When confidence in the models is low, even low-precision prediction errors are up-weighted. In balancing active and perceptual inferential processes, the brain can be seen to instantiate a dynamic interplay between top-down suppression of prediction errors and bottom-up modification of predictions – an interplay that varies according to context, reflected in the confidence the brain has in its generative models (Hohwy, 2013).

2.3. A neuroanatomical model of interoceptive inference

Plausible neuroanatomical frameworks for active inference models of interoception have been elaborated along similar lines to those for proprioception (Barrett and Simmons, 2015; Seth and Friston, 2016; Stephan et al., 2016). The key cortical regions for generation of interoceptive predictions are the anterior insular and rostral anterior cingulate cortices. Both are agranular, akin to the agranular M1 cortex that generates proprioceptive predictions (Barrett and Simmons, 2015). As agranular regions, they lack the layer IV stellate cells that receive sensory afferents, and are instead specialised for generating predictions about the interoceptive sensory signals that are expected to result from autonomic, neuroendocrine and immunological processes (Shipp et al., 2013; Barrett and Simmons, 2015). The visceromotor regions send predictions to subcortical regions (including the hypothalamus, amygdala, striatum, periaqueductal grey, parabrachial nucleus and solitary tract nucleus); and in addition, send efference copies to other cortical regions. The latter are copies of the generative models that have been sent to lower-level brain regions, and inform higher cortical networks of the interoceptive predictions (Barrett and Simmons, 2015; Stephan et al., 2016).

The insular cortex has a key role in integrating ascending prediction errors from the periphery with higher-level models that provide context for somatic predictions. It consists of a granular posterior region and agranular anterior region, with a transitional region between them (Nieuwenhuys, 2012). The posterior insular receives ascending afferents via complex circuits involving regions in the brain stem, mid-brain and diencephalon (Stephan et al., 2016; Fermin et al., 2022). Within these subcortical circuits many of the ascending prediction errors are explained away via autonomic and neuroendocrine reflex arcs. Prediction errors that cannot be resolved by these mechanisms ascend to granular regions of the posterior insular cortex for further processing – from where conscious awareness of them likely emerges (Solms and Friston, 2018).

The prediction errors that are first processed by the granular posterior insula are domain specific: there is evidence of topographical organisation of the different interoceptive modalities (Nieuwenhuys, 2012). The mid insular cortex, which shows an intermediate dysgranular cytoarchitecture, receives prediction errors from the posterior insular cortex, with the nature of the interoceptive representations becomes more integrated and general in nature. These are fed to the agranular anterior insula, which works in concert with rostral anterior cingulate cortex to generate somatic predictions (Craig, 2009).

2.4. Interoception within higher level cognitive networks

The predictions generated by the visceromotor cortices are informed by higher level cortical networks. The anterior insular and rostral anterior cingulate cortices are richly connected cortical hubs that contribute, respectively, to the salience and default mode networks, the brain's major large-scale integrative networks (van den Heuvel and Sporns, 2011). Bodily predictions (and the expected precision of the prediction errors) are thereby integrated into and informed by the wider environmental context – which is integral to the allostatic role of interoception. The default mode network (DMN) sits at the apex of the brain's cortical networks, composed of anatomical regions that are furthest removed from the regions that support sensorimotor functions (and pointing towards the abstract nature of its representations) (Buckner and DiNicola, 2019). The DMN, fittingly, is most active when a person is at rest and is not attending to external phenomena, including when a person is thinking about the past and future, and when focusing on interoceptive processes such as their breathing and heartbeat (the latter in conjunction with other brain regions) (Buckner et al., 2008). These higher-level interoceptive functions – reflecting on internal processes and their location within a temporal field – are important for contextualising predictions about the body.

Overlaid on these models are the second-order precision-weighting models, which are believed to be primarily generated by the salience network (Barrett et al., 2016; Barrett, 2017a; Seeley, 2019). Precision-weighting is enacted in large part by the monoaminergic systems, which arise from brainstem, midbrain and diencephalic nuclei (Shaffer et al., 2022). Neurotransmitters such as dopamine, serotonin and noradrenaline have modulatory effects on neurotransmission. They modify the activity of the major excitatory and inhibitory neurones (which utilise glutamate and GABA as neurotransmitters, respectively), influencing the relative balance between them (Marder, 2012; Shaffer

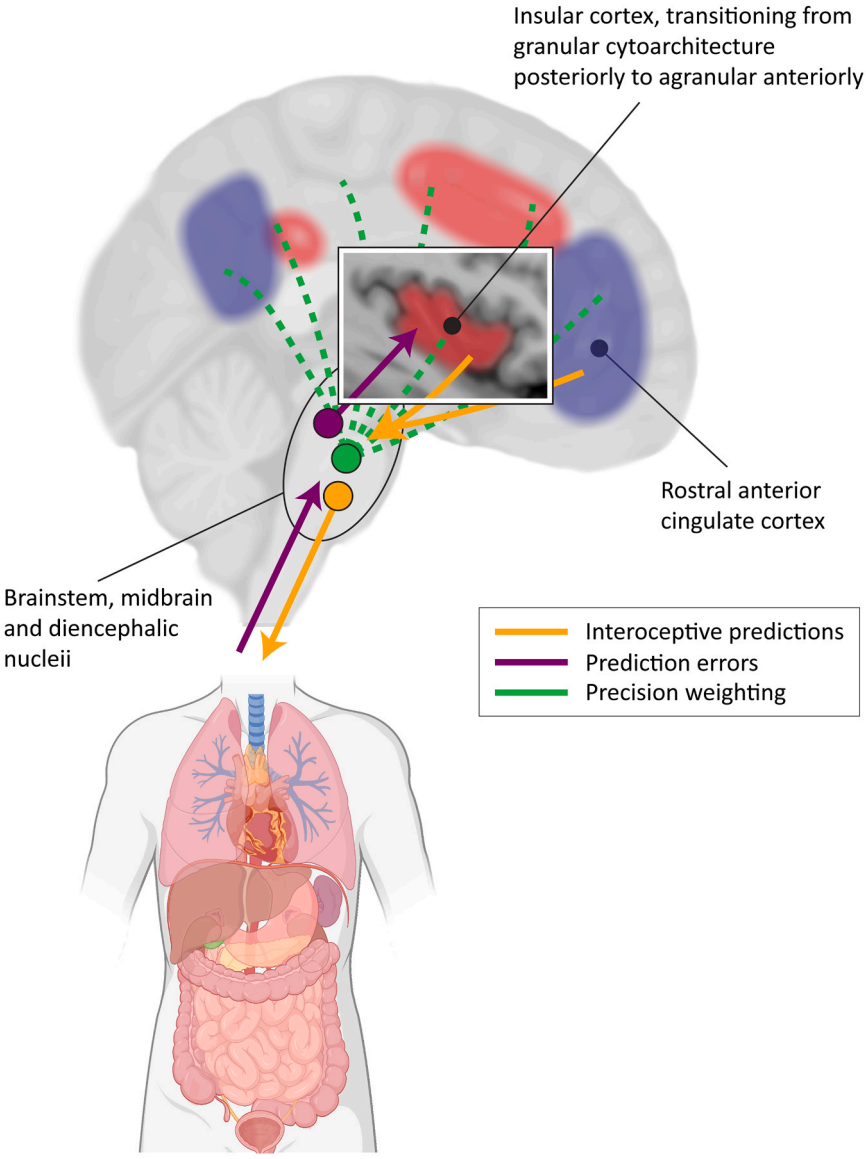

Fig. 2. A brain model of interoceptive active inference. Interoceptive predictions (orange) are generated by agranular anterior insular cortex and rostral anterior cingulate cortex. The resulting prediction errors (purple) ascend via subcortical regions to granular posterior insular cortex. The balance between top-down predictions and bottom-up prediction errors is modulated by precision weighting (green), which is largely enacted by monoaminergic nuclei in brainstem, midbrain and diencephalon. These processes are embedded in higher-order largescale brain networks. The default mode network (blue) supports domain-general integration of interoceptive processes with information about the self in the context of the psychosocial environment. The salience network (red) is thought to provide top-down regulation of precision-weighting, also in the context of broader environmental contingencies. Note that the insular cortex is represented in an inset box (it is located more laterally), and that the location of monoaminergic nuclei are schematic and not intended to be anatomically accurate.

et al., 2022). Activity of the neuromodulators influences the balance between confidence in the generative models and the influence permitted the ascending prediction errors (see Fig. 2 for a brain model of the active inference framework for interoception).

2.5. Affect as precision-weighted interoceptive prediction error

Affective experiences arise as precision-weighted interoceptive prediction errors that have not been explained away by lower-level reflex arcs, and that press themselves on consciousness to change behaviours in the interests of allostasis (Solms and Friston, 2018). As Freud puts it, affect is "a measure of the demand made upon the mind for work in consequence of its connection with the body" (Freud, 1915, p. 122). Simple bodily affects such as hunger and thirst can be understood as generating behaviours to alleviate them: finding food to eat and fluid to drink. Emotions create more complex behavioural programs, but that can nonetheless be understood as creating tendencies to act in particular ways in relevant contexts to preserve bodily and psychological integrity in the face of external demands (Barrett, 2017a).

Interoceptive prediction errors provide the basis for affective experience. As noted, most interoceptive processes occur unconsciously, with active inference seeing the adjustment of visceromotor and neuroendocrine processes to explain away prediction errors via low-level reflex arcs. But when interoceptive processes require behavioural changes to explain away the prediction errors, they are given a weighting that sees them rise to conscious awareness. Emotions such as fear and anger are experienced when the environmental context engenders threat and uncertainty and the need for appropriate action. Confidence in our prior models is low: we increase the weighting of interoceptive prediction errors so that they enter conscious awareness and influence our behavioural stance towards the world (Hohwy, 2013; Barrett, 2017b).

2.6. The temporality of mood

The brain mostly functions to create predictions about the sensory world as it unfolds into the present, extending ahead for only fractions of seconds as we see and hear and move. Affective processes invoke generative models that predict changes further into the future: they can extend for days (Seth and Friston, 2016; Barrett, 2017a). Control of heart rate, respiratory rate, perspiration, and muscle blood flow occur over seconds to minutes as predictions about the body change in response to environmental contingencies (Pasquini et al., 2023). Other predictions have longer timeframes: predictions related to hunger and satiety occur over hours, and those related to sleep (and other circadian functions) occur over the course of a day and beyond (Van Drunen and Eckel-Mahan, 2021).

The forward-looking nature of the brain's projections is exemplified by our mind's contents while we are alone with our thoughts. We spend about half of our waking hours thinking idle thoughts without meaningfully engaging with the external world (Killingsworth and Gilbert, 2010). When people are randomly probed as to the nature of these thoughts, they are about twice as likely to be about the future as about the past; and mostly about a future that extends over the course of the current day and into the day or two ahead (Stawarczyk et al., 2013). These future thoughts are predominately about our goals and plans (Kvavilashvili and Rummel, 2020), and represent the social environment we anticipate encountering.

This introspection is associated with activity of the DMN, the apex cortical network that coordinates subordinate networks, including interoceptive regions (Andrews-Hanna et al., 2014; Buckner and DiNicola, 2019). Interoceptive expectations are modelled in the context of the expected future, reflecting our confidence in what we will encounter and providing a shape to how we will encounter it (Seth and Friston, 2016; Barrett, 2017a). The future is scaffolded by our expectations for it, and our mood reflects the sturdiness of the scaffold. Are we expecting a world that we will navigate with ease, that will provide us with what we seek? Or is it a world that will be uncertain and dangerous, and that will provide us not with pleasure but with suffering? With what certainty do we hold these beliefs?

3. An active inference account of depression

The active inference framework provides a conceptual model for how we can understand the clinical presentation of depression, helping to explain how interoceptive processes shape depression's phenomenological and symptomatic experience. Others have used the active inference framework to explain complementary aspects of depression, including the cognitive distortions (Kube et al., 2020), rumination (Berg et al., 2022) and interpersonal difficulties (Kirchner et al., 2024a) that often accompany the disorder. It should be noted that this account, like the other accounts, provides a model, and its validity should be assessed by its internal consistency, by its ability to parsimoniously explain observations, and ultimately, by whether it can inform hypotheses that can be tested empirically (Gelfert, 2016). While empirical support needs to be bolstered, the framework can nonetheless provide a useful perspective on depression and how it relates to bodily processes. It explains how depressed mood arises alongside changes in the basic physiological processes that underlie sleep, appetite and energy levels; and why the emotional landscape changes when a person is depressed, with the experience of more negative and less positive emotions.

3.1. Mood and long-term interoceptive predictions

The active inference framework suggests that moods represent our long-term model of interoceptive predictions, incorporating the brain's predictions for the body (and the expected precision of the predictions) into the future (Clark et al., 2018). When there is a change in model confidence our precision estimates are re-weighted, and our patterns of interoceptive experience are altered. Transient changes in our mood can be experienced when interoceptive processes are waylaid directly (and not in response to changes in higher-level models reflecting social uncertainty). After a night of poor sleep – caused by say persistent loud noise – our mood will show qualitative lowering; and we experience something similar when we are unwell with a viral illness. These disturb our interoceptive prediction frameworks directly, causing adjustment of the precision-weighting of predictions errors, and making it more likely we experience dysphoric emotions and bodily discomforts (Yirmiya et al., 2000; Tomaso et al., 2021). In normal functioning, the precision-weightings will revert to their long-term averages after a night of restorative sleep or resolution of the viral illness.

More enduring changes in our moods reflect changes in our confidence in interoceptive models that are embedded in an extended temporal matrix. Much of this uncertainty relates to expectations about the social environment and entails interoceptive predictions that extend hours and days into the future. It leads to revised setpoints for the predictions (and the precision-weighting of the prediction errors) for interoceptive processes that have these time-courses, including those related to appetite, sleep and energy levels, and the complex processes underlying immune system function.

3.2. Depression as altered expectations and re-weighted prediction error

The active inference framework suggests that depression arises when there is uncertainty about our future prospects: we lose confidence in the social environment that our bodies will encounter, and anticipate short-term negative affect in the context of that uncertainty. Depression develops when higher-level (or longer-term) generative models encode an increased expectation of the short-term uncertainty encoded by lower-level models (Clark et al., 2018). In other words, there is increased certainty that the setpoints for the shorter-term interoceptive parameters that underpin emotional experiences are uncertain. There are ensuing changes in predictions related to longer term interoceptive

processes that manifest in symptoms such as insomnia, anorexia and fatigue (the mechanisms by which they arise in depression remains unclear, and the fact some symptoms can change in opposite directions adds to the explanatory difficulty). The higher-level models establish hyperpriors for the lower-level models, constraining their range and the likelihood of inhabiting particular states. The change in mood entrains the emotions – the expectation of increased negative affect becomes self-fulfilling.

In depression, the anticipation of bodily states that support negative affect along with an increased confidence in these predictions sees changes in longer-term interoceptive predictions that make the shorter-term predictions more likely (Clark et al., 2018). There is a low expectation of reward – nothing stands out as compelling, and the depressed person loses confidence that any actions they take will produce pleasure or satisfaction (Ramstead et al., 2023). This is especially true of social expectations, and it contributes to the social withdrawal that is characteristic of depression (Badcock et al., 2017; Kirchner et al., 2024b). With this expectation of increased negative affect, together with the inertia that develops with reduced expectation of positive affect, the brain becomes "locked in" (Barrett et al., 2016).

The depressed person's reduced interest in the external world and increased sensitivity to internal processes sees them develop an inward-facing preoccupation. This impaired ability to adaptively switch between internal and external focuses manifests as difficulties with concentration (Davey et al., 2017). There is rumination, which can be viewed as prediction error that is not being explained away: people with depression become trapped in a recursive cycle of sampling possible solutions to their dilemmas without finding resolution (Berg et al., 2022). This leaves the depressed person with a pervasive sense of unease and tension. The emotional landscape has changed: with the experience of fewer positive emotions and more negative emotions, the generative models that predict these outcomes are reinforced.

These changes in long-term interoceptive predictions manifest in changes to a person's sense of themselves. The experiential self – that part of the self that we know at once, without reflection – rests on longer-term interoceptive processes and the feelings they generate (Davey and Harrison, 2022). Such feelings constitute "the feeling of life itself, the sense of being" (Damasio, 1994, p. 150). The fundamental role that moods have in contributing to the experiential self means that when they are waylaid, as they are in depression, the self is set awry too. This is manifested in cognitive distortions about the narrative self – that part of the self that is consciously constructed – which is seen as unlovable, without merit, and deserving of suffering (Davey and Harrison, 2022).

3.3. *The clinical presentation of depression*

The active inference framework helps to explain the many and varied clinical presentations of depression. One patient might present with marked insomnia, restlessness, agitation and anxiety; another with hypersomnia, motor slowing, anhedonia and gastrointestinal discomfort (Fried and Nesse, 2015). The active inference account helps us to make sense of how the presentations of depression can be so diverse, with its proposal that depression arises due to the re-weighting of long-term interoceptive prediction errors in the face of increased uncertainty about the future. The characteristics of a person's generative models are idiosyncratic, reflecting their unique genetic constitutions and developmental experiences (Seth and Friston, 2016; Bouizegarene et al., 2024). So too, their psychosocial circumstances will have distinctive features. The nature of the perturbations to their precision-weighting models will reflect the interactions between a person's interoceptive predictions and social environments.

The common feature of depression is depressed mood (Zimmerman et al., 2006). We cannot be certain that one person's experience of a depressed mood is the same as another's, although the description of an enduring, negative mood state is relatively consistent (Ratcliffe, 2015; Fusar-Poli et al., 2023). A depressed mood, according to the active inference framework, arises as a product of the long-term interoceptive prediction errors that manifest in disturbed sleep, appetite and energy levels. The nature of these changes is variable and can be anticipated to give rise to mood states that show corresponding variance. The changes in precision-weighting associated with longer-term interoceptive processes affects the nature of the shorter-term, context-dependent processes that underlie emotions and bodily affects (Table 1). These too will be variably affected, and the way emotional and somatic experiences are altered will show distinct differences between patients. This accords with how a clinician's assessment of a patient's affect in the consulting room can show marked differences between one patient and the next – even when both give the same description of their mood as being "depressed".

Re-establishing aberrant precision-weighting is the goal of treatments for depression. Antidepressant medications do this directly: selective serotonin reuptake inhibitors, for example, modulate precision-weighting via their effects on the serotonergic system, and ketamine acts on NMDA receptors, modulating excitatory glutamatergic activity. For some, but not all, patients, this shift in neuromodulatory activity results in changes in interoceptive processes – reflected in improved sleep, appetite and energy levels – with corresponding alleviation of depressed mood (Chekroud et al., 2017; Zhou et al., 2022).

Other treatments affect precision weighting indirectly. Psychotherapies, which come in many forms, have in common their aim of improving the confidence a person has in their social supports. Cognitive behavioural therapy, for example, focuses on the dysfunctional thoughts a person has about themselves, their world and their future (Beck, 1979); while interpersonal therapy focuses on strengthening important relationships (Klerman et al., 1984). Both therapies aim to improve the confidence a person has in their generative models, and there is good evidence for their effectiveness (Cuijpers et al., 2021). Psychotherapies and medications can both be seen as attempts to alter the balance between a person's interoceptive predictions and their confidence in their anticipated futures in their efforts to alleviate the symptoms of depression.

4. Future directions and concluding remarks

Active inference accounts of depression provide theoretical explanations for different aspects of the disorder: the focus here is on how alterations to interoceptive processes manifest in the symptoms of depression that present clinically, including how disturbances in sleep, appetite and energy levels are associated with the experience of depressed mood; and how these disturbances change the array of

Table 1
Moods, emotional affects and bodily affects.

	Mood	Emotional affects	Bodily affects
Time course	Hours to days	Minutes to hours	Minutes to hours
Subjective experience	Background feelings, often difficult to label	In the foreground, often a distinct feeling that can be labelled	Qualitatively distinct experiences of hunger, thirst, pain, etc
Interoceptive correlates	Changes in sleep, appetite, motor activity, sex drive, energy levels	Changes in heart rate, respiratory rate, skin perfusion, muscle tension	Different modes for different affects: e.g., changes in plasma osmolality for thirst, nociceptive pathways for pain
Environmental influences	Social environment and internal factors	Social environment, influenced by mood	Internal factors, influenced by mood
In depression	Qualitatively lower	Increased anxiety, anger, irritability; less joy, pleasure, reward	Increased pain, gastrointestinal discomfort, inflammation

emotions that are experienced. A theory is given weight by proposing hypotheses that can be tested empirically, and this account suggests potential studies. The relationships between interoceptive alterations and the experience of depression can be examined in more detail by assessing patients longitudinally using new technologies, with the application of network approaches to analyse them (Borsboom, 2017; Westhoff et al., 2024). Features of mood can be more readily tracked, with ecological momentary assessment allowing for polling of mood and related symptoms during different times of the day (Armey et al., 2015). We can use smart devices to measure parameters such as sleep, heart rate (and its variability), exercise activity and distance walked. We can obtain measures of interpersonal and social activity: such things as geographical mobility via GPS data (how much time is spent out of the home? In novel environments?), typing speed, and the sentiment of text entered into chats and social media apps (Sheikh et al., 2021). We can hypothesise that changes in interoceptive processes respond to changed environmental contingencies, and that these precede, but are also augmented by, the experience of depressed mood. There is evidence, for example, that reduced sleep has a stronger effect on next-day mood than vice versa (Triantafillou et al., 2019), and that circadian phase disruptions have causal influences on depressed mood but not vice versa (Song et al., 2024). More complex, hierarchical models that incorporate a wider array of parameters will provide more complete explanations (Forbes et al., 2023; Westhoff et al., 2024), and could catalyse the development of formal accounts of an active inference model of depression.

An empirically fortified model might address one of the main problems that bedevils depression research, and that is the uncertain parameters of the diagnosis itself. Depression has been operationalised as "major depressive disorder" (MDD) since the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (American Psychiatric Association, 1980). The diagnosis unified multiple disorders described in previous nosologies, and its criteria capture a heterogenous group of patients (Fried and Nesse, 2015). In the DSM's defence, there are not compelling data to support the division of MDD into different depressive disorders based on differential treatment outcomes (Uher et al., 2011; Arnow et al., 2015). The monolithic MDD diagnosis contrasts with the DSM's treatment of anxiety disorders, which are divided into diagnoses including social anxiety disorder, panic disorder, agoraphobia and generalised anxiety disorder. These disorders are highly co-morbid with MDD, and many patients will meet diagnostic criteria for three or four diagnoses, which is often a surprise to them: their experience suggests one all-encompassing problem (Newson et al., 2021). The data that can be collated about the symptomatic experiences of patients, together with objective assessment of physiological parameters, might inform a reconceptualisation of the disorders and the development of a contemporary nosology (Fried, 2022).

5. Conclusion

Our moods, as Heidegger says, are "already there", setting the foundations for our affective experiences. This philosophical insight is supported by an active inference account of moods and how they arise from our predictions about interoceptive processes that endure beyond a day's period of wakefulness. The framework gives our understanding of moods greater conceptual depth, providing a perspective on depression that helps us to understand its multifaceted and often idiosyncratic clinical presentation. It shows us that depression is fundamentally tied to the body: to a body that is moving towards a future that the brain has modelled as being uncertain and has no confidence in (if there is confidence, it is that the world is uncertain and capricious). The framework provides us with a means of thinking about depression that breaks down the mind-body dualism that often characterises it. Depression emerges from biological processes that are deeply embedded in the social environment, and can be best understood as arising out of the interaction.

Declaration of Competing Interest

There are no declarations of interest.

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References

Aho, K., 2019. Affectivity and its disorders. In: Stanghellini, G., Broome, M., Raballo, A., Fernandez, A.V., Fusar-Poli, P., Rosfort, R. (Eds.), The Oxford Handbook of Phenomenological Psychopathology, 1187. Oxford University Press, USA.
American Psychiatric Association, 1980. Diagnostic and Statistical Manual of Mental Disorders. Third Edition): DSM-III. American Psychiatric Association, Washington.
Andrews-Hanna, J.R., Smallwood, J., Spreng, R.N., 2014. The default network and self-generated thought: component processes, dynamic control, and clinical relevance. Ann. N. Y. Acad. Sci. 1316, 29–52. https://doi.org/10.1111/nyas.12360.
Armey, M.F., Schatten, H.T., Haradhvala, N., Miller, I.W., 2015. Ecological momentary assessment (EMA) of depression-related phenomena. Curr. Opin. Psychol. 4, 21–25. https://doi.org/10.1016/j.copsyc.2015.01.002.
Arnow, B.A., Blasey, C., Williams, L.M., Palmer, D.M., Rekshan, W., Schatzberg, A.F., Etkin, A., Kulkarni, J., Luther, J.F., Rush, A.J., 2015. Depression subtypes in predicting antidepressant response: A report from the iSPOT-D trial. Am. J. Psychiatry 172, 743–750. https://doi.org/10.1176/appi.ajp.2015.14020181.
Badcock, P.B., Davey, C.G., Whittle, S., Allen, N.B., Friston, K.J., 2017. The depressed brain: An evolutionary systems theory. Trends Cogn. Sci. 1, 32–44. https://doi.org/10.1016/j.tics.2017.01.005.
Barrett, L.F., 2017b. Functionalism cannot save the classical view of emotion. Soc. Cogn. Affect. Neurosci. 12, 34–36. https://doi.org/10.1093/scan/nsw156.
Barrett, L.F., 2017a. The theory of constructed emotion: an active inference account of interoception and categorization. Soc. Cogn. Affect. Neurosci. 12, 1–23. https://doi.org/10.1093/scan/nsw154.
Barrett, L.F., Simmons, W.K., 2015. Interoceptive predictions in the brain. Nat. Rev. Neurosci. 16, 419–429. https://doi.org/10.1038/nrn3950.
Barrett, L.F., Quigley, K.S., Hamilton, P., 2016. An active inference theory of allostasis and interoception in depression. Philos. Trans. R. Soc. B 371, 20160011. https://doi.org/10.1098/rstb.2016.0011.
Beck, A.T., 1979. Cognitive Therapy of Depression. Guilford Press.
Beedie, C., Terry, P., Lane, A., 2005. Distinctions between emotion and mood. Cogn. Emot. 19, 847–878. https://doi.org/10.1080/02699930541000057.
Berg, M., Feldmann, M., Kirchner, L., Kube, T., 2022. Oversampled and undersolved: depressive rumination from an active inference perspective. Neurosci. Biobehav. Rev. 142, 104873. https://doi.org/10.1016/j.neubiorev.2022.104873.
Beurel, E., Toups, M., Nemeroff, C.B., 2020. The bidirectional relationship of depression and inflammation: Double trouble. Neuron 107, 234–256. https://doi.org/10.1016/j.neuron.2020.06.002.
Borsboom, D., 2017. A network theory of mental disorders. World Psychiatry 16, 5–13. https://doi.org/10.1002/wps.20375.
Bouizegarene, N., Ramstead, M.J.D., Constant, A., Friston, K.J., Kirmayer, L.J., 2024. Narrative as active inference: an integrative account of cognitive and social functions in adaptation. Front. Psychol. 15, 1345480. https://doi.org/10.3389/fpsyg.2024.1345480.
Buckner, R.L., DiNicola, L.M., 2019. The brain's default network: updated anatomy, physiology and evolving insights. Nat. Rev. Neurosci. 20, 593–608. https://doi.org/10.1038/s41583-019-0212-7.
Buckner, R.L., Andrews-Hanna, J.R., Schacter, D.L., 2008. The brain's default network: anatomy, function, and relevance to disease. Ann. N. Y. Acad. Sci. 1124, 1–38. https://doi.org/10.1196/annals.1440.011.
Chaplin, T.M., 2006. Anger, happiness, and sadness: Associations with depressive symptoms in late adolescence. J. Youth Adolesc. 35, 977–986. https://doi.org/10.1007/s10964-006-9033-x.
Chekroud, A.M., Gueorguieva, R., Krumholz, H.M., Trivedi, M.H., Krystal, J.H., McCarthy, G., 2017. Reevaluating the efficacy and predictability of antidepressant treatments: a symptom clustering approach. JAMA Psychiatry 74, 370–378. https://doi.org/10.1001/jamapsychiatry.2017.0025.
Chen, W.G., Schloesser, D., Arensdorf, A.M., Simmons, J.M., Cui, C., Valentino, R., Gnadt, J.W., Nielsen, L., Hillaire-Clarke, C.S., Spruance, V., Horowitz, T.S., Vallejo, Y.F., Langevin, H.M., 2021. The emerging science of interoception: Sensing, integrating, interpreting, and regulating signals within the self. Trends Neurosci. 44, 3–16. https://doi.org/10.1016/j.tins.2020.10.007.
Clark, A., 2023. The Experience Machine: How Our Minds Predict and Shape Reality. Random House, New York.
Clark, J.E., Watson, S., Friston, K.J., 2018. What is mood? A computational perspective. Psychol. Med. 1–8. https://doi.org/10.1017/S0033291718000430.
Clore, G.L., Huntsinger, J.R., 2007. How emotions inform judgment and regulate thought. Trends Cogn. Sci. 11, 393–399. https://doi.org/10.1016/j.tics.2007.08.005.
Craig, A.D., 2009. How do you feel–now? The anterior insula and human awareness. Nat. Rev. Neurosci. 10, 59–70. https://doi.org/10.1038/nrn2555.

Cuijpers, P., Karyotaki, E., Ciharova, M., Miguel, C., Noma, H., Furukawa, T.A., 2021. The effects of psychotherapies for depression on response, remission, reliable change, and deterioration: a meta-analysis. Acta Psychiatr. Scand. 144, 288–299. https://doi.org/10.1111/acps.13335.
Damasio, A.R., 1994. Descartes' Error: Emotion, Reason, and The Human Brain. Putnam, New York.
Davey, C.G., Harrison, B.J., 2022. The self on its axis: a framework for understanding depression. Transl. Psychiatry 12, 23. https://doi.org/10.1038/s41398-022-01790-8.
Davey, C.G., Breakspear, M., Pujol, J., Harrison, B.J., 2017. A brain model of disturbed self-appraisal in depression. Am. J. Psychiatry 174, 895–903. https://doi.org/10.1176/appi.ajp.2017.16080883.
van den Heuvel, M.P., Sporns, O., 2011. Rich-club organization of the human connectome. J. Neurosci. 31, 15775–15786.
Eckert, A.L., Fuehrer, E., Schmitter, C., Straube, B., Fiehler, K., Endres, D., 2025. Modelling sensory attenuation as Bayesian causal inference across two datasets. PLoS ONE 20, e0317924. https://doi.org/10.1371/journal.pone.0317924.
Fermin, A.S.R., Friston, K., Yamawaki, S., 2022. An insula hierarchical network architecture for active interoceptive inference. R. Soc. Open Sci. 9, 220226. https://doi.org/10.1098/rsos.220226.
Forbes, M.K., Fried, E.I., Vaidyanathan, U., 2023. Studying fine-grained elements of psychopathology to advance mental health science. J. Psychopathol. Clin. Sci. 132, 793–796. https://doi.org/10.1037/abn0000872.
Freud, S., 1915. Instincts and their vicissitudes. In: In: The Standard Edition of the Complete Psychological Works Sigmund Freud, 14. Hogarth Press, London, pp. 117–140.
Fried, E.I., 2022. Studying mental health problems as systems, not syndromes. Curr. Dir. Psychol. Sci. 31, 500–508. https://doi.org/10.1177/09637214221114089.
Fried, E.I., Nesse, R.M., 2015. Depression is not a consistent syndrome: an investigation of unique symptom patterns in the STAR*D study. J. Affect. Disord. 172, 96–102. https://doi.org/10.1016/j.jad.2014.10.010.
Fried, E.I., Epskamp, S., Nesse, R.M., Tuerlinckx, F., Borsboom, D., 2016. What are 'good' depression symptoms? Comparing the centrality of DSM and non-DSM symptoms of depression in a network analysis. J. Affect. Disord. 189, 314–320. https://doi.org/10.1016/j.jad.2015.09.005.
Friston, K., 2010. The free-energy principle: a unified brain theory. Nat. Rev. Neurosci. 11, 127–138. https://doi.org/10.1038/nrn2787.
Friston, K., FitzGerald, T., Rigoli, F., Schwartenbeck, P., Pezzulo, G., 2017. Active inference: A process theory. Neural Comput. 29, 1–49. https://doi.org/10.1162/NECO_a_00912.
Fusar-Poli, P., Estradé, A., Stanghellini, G., Esposito, C.M., Rosfort, R., Mancini, M., Norman, P., Cullen, J., Adesina, M., Jimenez, G.B., da Cunha Lewin, C., Drah, E.A., Julien, M., Lamba, M., Mutura, E.M., Prawira, B., Sugianto, A., Teressa, J., White, L. A., Damiani, S., Vasconcelos, C., Bonoldi, I., Politi, P., Vieta, E., Radden, J., Fuchs, T., Ratcliffe, M., Maj, M., 2023. The lived experience of depression: a bottom-up review co-written by experts by experience and academics. World Psychiatry 22, 352–365. https://doi.org/10.1002/wps.21111.
Gelfert, A., 2016. How To Do Science With Models. Springer International Publishing, Cham.
Heidegger, M., 1995. The Fundamental Concepts of Metaphysics: World, Finitude, Solitude. Indiana University Press.
Hodson, R., Mehta, M., Smith, R., 2024. The empirical status of predictive coding and active inference. Neurosci. Biobehav. Rev. 157, 105473. https://doi.org/10.1016/j.neubiorev.2023.105473.
Hohwy, J., 2013. The predictive mind. Oxford University Press.
James, W., 1884. On some omissions of introspective psychology. Mind 9 1–26.
James, W., 1890. The Principles of Psychology. Holt and Company, New York.
Kagan, J., 2007. What Is Emotion?: History, Measures, and Meanings. Yale University Press.
Killingsworth, M.A., Gilbert, D.T., 2010. A wandering mind is an unhappy mind. Science 330, 932. https://doi.org/10.1126/science.1192439.
Kirchner, L., Eckert, A.-L., Berg, M., Endres, D., Straube, B., Rief, W., 2024a. An active inference approach to interpersonal differences in depression. N. Ideas Psychol. 74, 101092. https://doi.org/10.1016/j.newideapsych.2024.101092.
Kirchner, L., Kube, T., Berg, M., Eckert, A.-L., Straube, B., Endres, D., Rief, W., 2024b. Social expectations in depression. Nat. Rev. Psychol. 4, 20–34. https://doi.org/10.1038/s44159-024-00386-x.
Klerman, G.L., Weissman, M.M., Rounsaville, B.J., Chevron, E.S., 1984. Interpersonal Psychotherapy of Depression. Basic Books, New York.
Kube, T., Schwarting, R., Rozenkrantz, L., Glombiewski, J.A., Rief, W., 2020. Distorted cognitive processes in major depression: a predictive processing perspective. Biol. Psychiatry 87, 388–398. https://doi.org/10.1016/j.biopsych.2019.07.017.
Kvavilashvili, L., Rummel, J., 2020. On the nature of everyday prospection: A review and theoretical integration of research on mind-wandering, future thinking, and prospective memory. Rev. Gen. Psychol. 5, 142–162. https://doi.org/10.1177/1089268020918843.
Marder, E., 2012. Neuromodulation of neuronal circuits: Back to the future. Neuron 76, 1–11. https://doi.org/10.1016/j.neuron.2012.09.010.
McHugh, P.R., Slavney, P.R., 1998. The Perspectives of Psychiatry. JHU Press.
Newson, J.J., Pastukh, V., Thiagarajan, T.C., 2021. Poor separation of clinical symptom profiles by DSM-5 disorder criteria. Front. Psychiatry 12, 775762. https://doi.org/10.3389/fpsyt.2021.775762.
Nieuwenhuys, R., 2012. The insular cortex: a review. Prog. Brain Res. 195, 123–163. https://doi.org/10.1016/B978-0-444-53860-4.00007-6.
Owens, A.P., Allen, M., Ondobaka, S., Friston, K.J., 2018. Interoceptive inference: from computational neuroscience to clinic. Neurosci. Biobehav. Rev. 90, 174–183. https://doi.org/10.1016/j.neubiorev.2018.04.017.
Panksepp, J., 1998. Affective Neuroscience: The Foundations of Human and Animal Emotions. Oxford University Press, New York.
Parr, T., Pezzulo, G., Friston, K.J., 2022. Active Inference: The Free Energy Principle in Mind, Brain, and Behavior. The MIT Press, Cambridge, Massachusetts.
Pasquini, L., Noohi, F., Veziris, C.R., Kosik, E.L., Holley, S.R., Lee, A., Brown, J.A., Roy, A.R.K., Chow, T.E., Allen, I., Rosen, H.J., Kramer, J.H., Miller, B.L., Saggar, M., Seeley, W.W., Sturm, V.E., 2023. Dynamic autonomic nervous system states arise during emotions and manifest in basal physiology. Psychophysiology 60, e14218. https://doi.org/10.1111/psyp.14218.
Radden, J., 2009. Moody Minds Distempered. Oxford University Press, New York.
Ramstead, M.J.D., Wiese, W., Miller, M., Friston, K.J., 2023. Deep neurophenomenology: An active inference account of some features of conscious experience and of their disturbance in major depressive disorder. In: Cheng, T., Sato, R., Hohwy, J. (Eds.), Expected Experiences: The Predictive Mind in an Uncertain World. Routledge, New York, pp. 9–46.
Ratcliffe, M., 2009. The phenomenology of mood and the meaning of life. In: Goldie, P. (Ed.), The Oxford Handbook of Philosophy of Emotion. Oxford University Press, pp. 349–371.
Ratcliffe, M., 2015. Experiences of Depression. Oxford University Press, Oxford.
Seeley, W.W., 2019. The salience network: A neural system for perceiving and responding to homeostatic demands. J. Neurosci. 39, 9878–9882. https://doi.org/10.1523/jneurosci.1138-17.2019.
Seth, A., 2021. Being You: A New Science of Consciousness. Faber & Faber, London.
Seth, A.K., Friston, K.J., 2016. Active interoceptive inference and the emotional brain. Philos. Trans. R. Soc. B 371. https://doi.org/10.1098/rstb.2016.0007.
Sgoifo, A., Carnevali, L., Alfonso, M.L., Amore, M., 2015. Autonomic dysfunction and heart rate variability in depression. Stress 18, 343–352. https://doi.org/10.3109/10253890.2015.1045868.
Shaffer, C., Westlin, C., Quigley, K.S., Whitfield-Gabrieli, S., Barrett, L.F., 2022. Allostasis, action, and affect in depression: Insights from the theory of constructed emotion. Annu. Rev. Clin. Psychol. 18, 553–580. https://doi.org/10.1146/annurev-clinpsy-081219-115627.
Shaw, F., 1997. Out of Me: The Story of a Postnatal Breakdown. Viking, London.
Sheikh, M., Qassem, M., Kyriacou, P.A., 2021. Wearable, environmental, and smartphone-based passive sensing for mental health monitoring. Front. Digit. Health 3, 662811. https://doi.org/10.3389/fdgth.2021.662811.
Shipp, S., Adams, R.A., Friston, K.J., 2013. Reflections on agranular architecture: predictive coding in the motor cortex. Trends Neurosci. 36, 706–716. https://doi.org/10.1016/j.tins.2013.09.004.
Sims, A., 2002. Symptoms in the Mind: An Introduction to Descriptive Psychopathology. Saunders, London.
Solms, M., Friston, K., 2018. How and why consciousness arises: Some considerations from physics and physiology. J. Consc. Stud. 25, 202–238. https://doi.org/10.3389/fnhum.2016.00247.
Song, Y.M., Jeong, J., de Los Reyes, A.A., Lim, D., Cho, C.H., Yeom, J.W., Lee, T., Lee, J. B., Lee, H.J., Kim, J.K., 2024. Causal dynamics of sleep, circadian rhythm, and mood symptoms in patients with major depression and bipolar disorder: insights from longitudinal wearable device data. EBioMedicine 103, 105094. https://doi.org/10.1016/j.ebiom.2024.105094.
Stawarczyk, D., Cassol, H., D'Argembeau, A., 2013. Phenomenology of future-oriented mind-wandering episodes. Front. Psychol. 4, 425. https://doi.org/10.3389/fpsyg.2013.00425.
Stephan, K.E., Manjaly, Z.M., Mathys, C.D., Weber, L.A., Paliwal, S., Gard, T., Tittgemeyer, M., Fleming, S.M., Haker, H., Seth, A.K., Petzschner, F.H., 2016. Allostatic self-efficacy: A metacognitive theory of dyshomeostasis-induced fatigue and depression. Front. Hum. Neurosci. 10, 550. https://doi.org/10.3389/fnhum.2016.00550.
Styron, W., 1990. Darkness Visible: A Memoir of Madness. Random House, New York.
Tomaso, C.C., Johnson, A.B., Nelson, T.D., 2021. The effect of sleep deprivation and restriction on mood, emotion, and emotion regulation: three meta-analyses in one. Sleep 44, zsaa289. https://doi.org/10.1093/sleep/zsaa289.
Triantafillou, S., Saeb, S., Lattie, E.G., Mohr, D.C., Kording, K.P., 2019. Relationship between sleep quality and mood: Ecological momentary assessment study. JMIR Ment. Health 6, e12613. https://doi.org/10.2196/12613.
Trzepacz, P.T., Baker, R.W., 1993. The Psychiatric Mental Status Examination. Oxford University Press.
Uher, R., Dernovsek, M.Z., Mors, O., Hauser, J., Souery, D., Zobel, A., Maier, W., Henigsberg, N., Kalember, P., Rietschel, M., Placentino, A., Mendlewicz, J., Aitchison, K.J., McGuffin, P., Farmer, A., 2011. Melancholic, atypical and anxious depression subtypes and outcome of treatment with escitalopram and nortriptyline. J. Affect. Disord. 132, 112–120. https://doi.org/10.1016/j.jad.2011.02.014.
Van Drunen, R., Eckel-Mahan, K., 2021. Circadian rhythms of the hypothalamus: From function to physiology. Clocks Sleep. 3, 189–226. https://doi.org/10.3390/clockssleep3010012.
Westhoff, M., Berg, M., Reif, A., Rief, W., Hofmann, S.G., 2024. Major problems in clinical psychological science and how to address them. Introducing a multimodal dynamical network approach. Cogn. Ther. Res. 48, 791–807. https://doi.org/10.1007/s10608-024-10487-9.
Woolf, V., 1926. On Being Ill. Criterion 4, 32–45.
Yirmiya, R., Pollak, Y., Morag, M., Reichenberg, A., Barak, O., Avitsur, R., Shavit, Y., Ovadia, H., Weidenfeld, J., Morag, A., Newman, M.E., Pollmächer, T., 2000. Illness,

cytokines, and depression. Ann. N. Y. Acad. Sci. 917, 478–487. https://doi.org/10.1111/j.1749-6632.2000.tb05412.x.

Zhou, J., Liu, S., Mayes, T.L., Feng, Y., Fang, M., Xiao, L., Wang, G., 2022. The network analysis of depressive symptoms before and after two weeks of antidepressant treatment. J. Affect. Disord. 299, 126–134. https://doi.org/10.1016/j.jad.2021.11.059.

Zimmerman, M., McGlinchey, J.B., Young, D., Chelminski, I., 2006. Diagnosing major depressive disorder I: A psychometric evaluation of the DSM-IV symptom criteria. J. Nerv. Ment. Dis. 194, 158–163. https://doi.org/10.1097/01.nmd.0000202239.20315.16.