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Wired for Despair

The Neurochemistry of Emotion and the Phenomenology of Depression

Abstract: *Although depression is characterized as a mood disorder it turns out that, like moods in general, it cannot be explained independently of a theory of emotion. In this paper I outline one promising theory of emotion (Multicomponential Appraisal Theory) and show how it deals with the phenomenon of depressive mood. An important aspect of MAT is the role it assigns to peripheral information processing systems in setting up emotional responses. The operations of these systems are automatic and opaque to consciousness, but they represent information about the significance of the environment for the subject, bias cognition and behaviour, and have a characteristic phenomenology. I show how understanding the nature of peripheral appraisal provides a principled way to link neurochemistry and mood via an information processing theory of the circuitry targeted by antidepressant treatment. The discussion is organized around Matthew Ratcliffe's distinction between pre-intentional and intentional feelings and suggests that the MAT might provide a way to link phenomenological and mechanistic accounts of feeling states characteristic of depression.*

1. Introduction

Persistent and pervasive feelings of estrangement, depersonalization, emptiness, grandiosity, or desolation are not in themselves emotional experiences. Rather they condition the space of emotional possibilities. Someone who feels the world to be a desolate or dangerous place, for example, becomes liable to experience episodes of sadness or fear.

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Such pervasive feelings are often described as moods and contrasted with emotional feelings that arise as part of an emotional episode with a specific object and discrete duration. This contrast, however, does not quite capture the way pervasive feeling states influence the experience of emotion. Such states darken or lighten the emotional landscape, affecting the ability of emotional feelings to colour features of that landscape. Only when the nature of these pervasive feelings changes radically, as in depression, anxiety, or other psychiatric disorders, does their fundamental importance become apparent. Even then, however, because moods, unlike emotions, do not have specific objects and are produced by tacit cognitive processes and experienced bodily, their meaning is not readily available to introspection or reflection. Matthew Ratcliffe has introduced the concept of 'existential feelings' to capture some of the elusive properties of these persistent and pervasive phenomenal states (Ratcliffe, 2005; 2008; 2009a,b).

Ratcliffe describes existential feelings as 'pre-intentional' rather than intentional to capture the way they preconfigure the range of emotional experiences for a subject. Ratcliffe also suggests that a simple distinction between bodily experiences and experiences of the world cannot do justice to the phenomenology of existential feelings. This extends a point familiar to theorists of emotion to the case of existential feelings: emotional feelings are bodily feelings, but they also represent the significance of the objects of emotion for us. Similarly, pre-intentional feelings are bodily feelings that also carry information, not about specific objects, but about our mode of emotional orientation to the world. As Ratcliffe (2010) puts it, 'something can be both a bodily feeling and, at the same time, an experience of worldly possibilities'. We might say that existential feelings signal the way the emotional world is preconfigured.

Emotions are not moods, and emotional feelings are not existential feelings, but there is a connection between emotions and moods phenomenologically and conceptually which has proved hard to articulate (Frijda, 1993a). By redirecting attention to the configuring role of persistent and pervasive feeling states, the concept of existential feeling is helpful in linking the phenomenology to the neurobiology and explaining some puzzles about the way treatment for mood disorders works.

In this paper I give an account of the cognitive properties of some neural mechanisms that enable existential feelings to configure the emotional world in this way. The account takes as a case study change in depressive mood consequent on the administration of selective

serotonin re-uptake inhibitors (SSRIs) in antidepressant treatment. Where such treatment works the world is experienced in a different way before and after treatment. I argue that such changes reflect the influence of SSRIs on neural circuits involved in emotional processing.¹ The important point is that the cognitive properties of these circuits explain how existential feelings preconfigure the emotional world.

The account depends on a particular theory of emotional processing: the Multicomponential Appraisal Theory (MAT). Appraisal theory is familiar to theorists of emotion as the theory that emotions are representations of the significance of events for the organism. The intentional content of an emotion represents a core relational theme (CRT) (Frijda, 1986; 2001; 2009; Scherer, Schorr and Johnstone, 2001). The CRT of fear is danger or threat, of sadness, loss, and so on. This core relational theme is sometimes called the *formal object* of an emotion. *Concrete objects* of emotion are the specific objects or events appraised as instantiating the formal object. For example, in an episode of sadness a specific event such as a death is *appraised* as an irreversible loss for the subject of the emotion (Kenny, 1963; Prinz, 2004). Appraisal theory is well placed to explain how emotions derive their intentional content.

Early appraisal theorists assimilated appraisals to judgments: beliefs about the properties of the objects of emotion (Kenny, 1963; Solomon, 1988; 1989). Consequently appraisal theory has been criticized as overly intellectualistic and as ignoring the felt aspect of emotion. Grief, for example, is a visceral state whose essence is a feeling, not a judgment, runs the objection. Equally an emotional feeling may arise or persist in the absence of, or in opposition to, a judgment. Thus accounting for the intentionality of emotional feelings in terms of judgments is an oversimplification.

MAT avoids this objection since it locates many dimensions of appraisal at different, subpersonal, levels of cognitive processing (Grandjean and Scherer, 2008, p. 488; Sander, Grandjean and Scherer, 2005). It retains the idea that appraisals are mental representations of subjective relevance, but suggests that many such representations

[1] It should be noted that there are empirical grounds for scepticism about the role of antidepressants in mood disorder. For sceptics like Kirsch (2009; Kirsch *et al.*, 2008) antidepressant effects are essentially placebo effects. Both sceptical and standard accounts in fact need an account of the mechanisms and cognitive processes involved in mood. Once that account is provided it becomes an open possibility that plasticity in those mechanisms and resultant cognitive changes could be produced by pharmacology or placebo. In what follows, however, I assume the standard account in which depressive mood remits following antidepressant treatment.

depend on processes which use coding formats and timescales which make them unavailable for explicit reflective thought. Most emotional appraisals are in fact conducted by neural circuits which automatically link perception to the automatic regulation of visceral and bodily responses so that they issue almost instantaneously in feelings which reflect the nature of that appraisal.

An example of a subpersonal appraisal process is provided by responses to perceived changes in emotional expression or posture of conspecifics. The mind has mechanisms that constantly compute the relevance of such changes for the subject and initiate appropriate responses. When we recognize a familiar person and see her smile, for example, the significance of that information for us has been represented and that representation used to initiate a response within a few hundred milliseconds (Adolphs, 2010; Sander *et al.*, 2003; 2007; N'Diaye, Sander and Vuilleumier, 2009).

When information processing in this type of circuitry becomes rigidly biased, the repertoire of possible appraisals is limited, effectively limiting the range of possible emotional responses for the subject. Feeling states reflect those biases, lingering and becoming entrenched even in the absence of specific emotional elicitors. In depression, for example, the subject becomes 'wired for despair' as very fundamental appraisal systems become biased to the detection and processing of negative information and consequent disengagement from the world, especially the social world. The consequence is to install automatic bodily and behavioural emotional responses whose sustained presence is experienced as the depressive mood (Colombetti and Thompson, 2008). Or, as Ratcliffe might put it, as existential feelings of despair and desolation.

2. Feelings as Emotion Components

One difference between MAT theories of emotion (and mood) and various feeling theories is that appraisal theories treat feelings as one of many *components* of emotion (Frijda, 1986; 1993b; Frijda *et al.*, 1989). These components are cognition (at different levels of complexity and explicitness ranging from low-level reflexive processes to high-level reflective deliberation), motivational action tendencies, physiological response patterns, motor expression, and feelings (Sander, Grandjean and Scherer, 2005; Brosch *et al.*, 2010). The emotional phenotype for any emotion refers to the way these components are *coordinated* (see below) in the face of their objects, formal and concrete, in an emotional episode.

The essential feature of appraisal theories is that the coordination of emotion components is explained in terms of appraisals. That is, representations of the significance of an object for the subject of the emotion. A prototypical episode of fear organizes components adaptively to respond to the danger. These components include high-level cognition (beliefs about the nature and significance of the object and consequences of action); lower-level cognition (detection of hostile facial expression, vocalization, or posture, and continued monitoring for threat by specialized neural circuits); characteristic autonomic and somatovisceral changes, sensed as feelings; and motor responses, including facial expression. The adaptive coordination of these components in an episode of fear depends on the appraisal of a stimulus as dangerous. The point to note is that these components, while they can occur independently under other conditions, co-occur in a typical pattern in an emotional episode in virtue of the appraisal.

Thus the feeling characteristic of an emotion is a component of the overall emotional state, consequent an appraisal. It is a way of being aware of the bodily state produced by the representation of an emotionally salient property (Colombetti and Thompson, 2008). A bodily feeling in an emotional episode does double duty. It tells the subject about her body *and* about the object or state of the world whose appraisal led to that body state. This dual role for bodily feeling is explained in different ways by different theorists. Prinz (2004), for example, following basic emotion theorists, gives a teleological theory of the emotional intentionality of bodily feelings. Peter Goldie (2000) developed a subtle phenomenological account of what he called 'feeling towards' in episodes of emotion. The MAT explains the intentionality of emotional experience in virtue of the representational content of processes of appraisal that generate it.

Cognitive neuroscience has identified circuits, essential for this coordination of feeling with other components of emotion, which function as 'hubs' of distributed circuits that determine the *subjective relevance* of information. Lower level hubs implement rapid online appraisals while upper level hubs link this information acquired by low-level appraisal systems to higher level, cognitively explicit, forms of appraisal, including belief fixation.

A crucial lower level appraisal hub is the amygdala. Initially the activity of the amygdala was interpreted narrowly as a substrate for 'fear' of standard elicitors. Subsequently this interpretation was replaced by a wider one which treats it as the basis of context-sensitive 'aversion' or 'negative affect'. Further evidence of its role in many conditions involving the rapid and automatic processing of self

relevant information, including positive and rewarding information, led to further theoretical revision. It is now described as a *hub* of an appraisal system (Hsu *et al.*, 2005; Adolphs, 2010; Brosch *et al.*, 2010; Vuilleumier *et al.*, 2003). An example is the processing of information in facial expression. Typically faces are scanned for emotionally significant information (such a smiles, frowns, direction and return of gaze) in parallel with other face processing operations such as the detection of identity. As faces are scanned and information gathered, appropriate autonomic and physiological responses are initiated. The scanning process and the initiation of downstream response are coordinated by activation in the amygdala. Thus, although the amygdala does not itself represent all information necessary to establish the emotional relevance of a stimulus, it coordinates the relevant distributed processing. It is thus the hub of a distributed appraisal processing system whose operations are fast, automatic, and not available to conscious control. We can call these types of appraisals *peripheral* in the jargon of cognitive neuroscience since they are rapid, quasi-perceptual, and not under voluntary control.

A higher level hub of appraisal is the ventromedial prefrontal cortex, a structure which traffics the information acquired by low-level hubs to so-called central or higher level processes. In effect the ventromedial prefrontal cortex recapitulates at a higher level the properties of the amygdala. In so doing it associates emotional information with explicitly represented information used in reflective decision making and planning (Ochsner *et al.*, 2002; Bechara *et al.*, 2000). It thus allows the subject to make more explicit appraisals using so-called 'central' processes. In general peripheral appraisals involve posterior circuitry that evolved to manage the sensorimotor interface with the world, while central appraisals depend on prefrontal structures which evolved to allow stimulus-independent metacognition. What appraisals at these different levels of explicitness have in common is the representation of the significance of an object or situation for the subject.²

As Grandjean and colleagues put it summarizing studies on the communication between the amygdala, hippocampus, and prefrontal systems:

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- [2] The idea that the ventromedial prefrontal cortex computes subjective relevance of centrally represented information predicts that deficits would manifest as an inability to take and incorporate a *personal perspective* on centrally processed information (Goel *et al.*, 1998; Koenigs *et al.*, 2007; Buckner, Andrews-Hanna and Schacter, 2008; Adolphs *et al.*, 2002).

empirical findings of neuronal synchronisation in the human brain in response to emotional stimuli highlight the importance of functional coupling between different distant and local neuronal assemblies and suggest continuous cross talk between different brain regions during the processing of emotional stimuli. (Grandjean and Scherer, 2008, p. 488; see also Sander, Grandjean and Scherer, 2005)

Thus the concept of interacting neural circuitry specialized for peripheral and central appraisal is empirically supported. Not only that, but this circuitry drives the coordination of emotion components.

3. Feelings and Moods: State and Trait Appraisal Bias

People develop *appraisal biases*, tendencies to evaluate objects in characteristic ways and to coordinate emotion components accordingly (Scherer and Brosch, 2009). When we say that someone is depressed or anxious we do not mean that they are unhappy or worried about a specific object. Rather we mean that any object they encounter tends to be appraised in ways that initiate the coordination of components of unhappiness or anxiety. Similarly we explain optimism as a trait not in terms of attitude to a specific object but as an appraisal bias (perhaps installed history of rewarding interactions with the world). The concept refers to characteristic patterns of emotional responses based on biased processing of information.

Anxiety provides an example. Someone with an anxiety disorder has a persistent feeling characteristic of appraising situations as threatening and/or beyond her control. The feeling may wax and wane according to the way attention is captured or directed, but it unfortunately persists in the phenomenological background. Its persistence can be explained by the way in which both peripheral and central appraisal systems are ‘rewired’ from below, primed to detect and respond to threats. Someone with an anxiety disorder, for example, will typically show unusual patterns of face scanning, avoiding the eyes. This avoidance pattern is produced entirely below the threshold of conscious control by peripheral visuomotor systems driven by the amygdala. Typically in such cases hyperactivity of the amygdala itself is driven by lower level brainstem systems. A consequence of very low-level peripheral appraisals driven by the amygdala is mutually-reinforcing physiological changes. As a result an anxious person experiences a characteristic bodily feeling which is a consequence of the fact that her body is primed for avoidance even though there may not currently be a threatening stimulus.

I am not claiming here that dispositions *per se* have a phenomenology, but that the typical pattern of appraisals installed by an emotional disposition, or appraisal bias, has a persistent residual phenomenology. Feelings produced by physiological responses initiated by peripheral appraisals tend to linger and exert an influence on central appraisals whose net effect is to reinforce the feeling. The anxious person will tend to 'dwell in imagination on possible disasters' as Ryle (2009) put it, a tendency which has feedback effects throughout the hierarchy of appraisal systems.

Goldie (2000) gives the excellent example of someone who continues to feel angry long after the initial episode (in his case an upsetting marital argument). This person remains tense and irritable for the rest of the day. They grip the steering wheel tightly driving to work, swear at other drivers, don't show their normal good humour in social encounters. Were they to attend to their feelings they might detect their over-arousal. Often such a residual feeling is at odds with the current situation because it is the lingering result of temporally distant appraisals whose content is not available to consciousness. And precisely because of this residual over-arousal, which tends to short circuit reflective deliberation and crowds out the capacity for positive appraisal, such a person might then start to react angrily to neutral situations, or be inattentive to positive information, reinforcing the problem.

This is an example of an episode of emotion producing a relatively short-lived existential feeling of irritability. Other more dramatic cases may arise where sustained grief at the death of a loved one ultimately installs a pervasive appraisal bias leading to depression and the characteristic existential feeling of emptiness and desolation. In such cases an emotional feeling with a specific object leads to an existential feeling which influences the overall pattern of emotional appraisals.

4. Neurochemistry, Appraisal, and Feeling in Depression

These facts suggest that the existential feelings characteristic of depression could result from biases in appraisal which may operate well below the threshold of explicit cognition. And in fact recent work on the pharmacology of depression has adopted this hypothesis to explain why it is that the phenomenology of depression is so persistent and pervasive in the face of antidepressant treatment.

One clinical approach to depression is the administration of drugs which increase levels of 5hydroxytryptamine (5HT), also known as

serotonin, in the synaptic cleft. The role and efficacy of these drugs is controversial but the consensus is that, typically after some delay, they help resolve or alleviate symptoms.

One governing hypothesis here has been that these drugs elevate mood, perhaps not immediately or directly but eventually, with favourable flow-on effects for the rest of the subject's psychological economy. Perhaps if the subject *feels happier* and more optimistic, her patterns of thought and behaviour will realign appropriately, removing negative appraisal biases.

This presupposes two things: first that antidepressants change mood, and second that mood has a *primary* causal force in coordinating other symptoms of depression. Let us call the conjunction of these two claims the 'mood is chemistry hypothesis' (MIC). If MIC is right we should be able to remove depression by changing the characteristic mood by intervening at the neurochemical level.

It is certainly true that moods can be changed by neurochemical intervention. Feeling states are often instantaneously sensitive to neurochemical changes. However, I do not think the evidence supports the idea that SSRIs are effective in depression as a result of direct alteration of feeling states. Nor does it support the idea that a change in feeling state leads directly to a change in appraisal bias.

In fact in the case of SSRIs the direction of explanation goes the other way. SSRIs do not change appraisal biases by changing mood. Rather they change mood by changing appraisal biases. In particular, antidepressants change peripheral appraisals by changing the information processing properties of peripheral appraisal circuits. The best example comes from recent work on the effects of antidepressants on the interaction between the amygdala, the hub of the peripheral appraisal system, and the systems it regulates.

There is now a body of work which explains the fact that mood does not resolve immediately following antidepressant treatment in terms of the timescale of effects on peripheral appraisal systems of antidepressants. For example, after one week's administration of serotonin, which changes the balance of norepinephrine and serotonin action in the amygdala, patients' amygdala response to masked fearful faces was reduced and the responses of the facial fusiform areas to happy faces was increased. This is an example of the role of the amygdala as a hub of peripheral appraisal. These effects occur well below the threshold of explicit awareness. Patients' explicit judgments about emotional expressions also change accordingly. Patients are more likely to correctly identify positive emotional expressions, for example. Memory for positive words also increased (see Harmer *et al.*,

2009, for a discussion). These effects have now been demonstrated repeatedly (Di Simplicio *et al.*, 2011; McCabe *et al.*, 2011; Pringle *et al.*, 2011; Harmer, 2008).

However, although peripheral appraisals of facial emotional expression change quite quickly, the depressive mood persists for a much longer period, suggesting that ‘antidepressants are able to modify behavioural and neural responses to emotional information *without any change in subjective mood*. Moreover the changes in emotional processing can be seen across different stimuli types and extend outside conscious awareness’ (Harmer *et al.*, 2009, my italics).

Summarizing recent work in the area, Harmer and collaborators pointed out that delay in the remission of mood is not a puzzle if mood is understood as a downstream effect of changes to peripheral appraisal systems with consequent reorganization of emotion components, including feelings. They concluded that ‘antidepressant drug treatments may target these *underlying processes supporting mood rather than targeting mood directly*’ and ‘the therapeutic effect of noradrenaline and serotonin enhancement may depend on how far positive shifts in *automatic emotional processing* [peripheral appraisal in our terminology] can lead to altered conscious emotional appraisal and improved mood’ (*ibid.*).

This view of the evidence about the relationship between peripheral appraisal and mood is consistent with MAT. For MAT, feelings of sadness, grief, or despair are a ‘global broadcast’ of the organismic state that results when cognitive, psychomotor, and affective systems (mal)function in withdrawal mode. At the level of conscious awareness the subject experiences the consequences of biased peripheral appraisals as low mood.

Central appraisals, which depend on communication between central and peripheral appraisal systems, are also affected in depression. For example, the ability to remember and make use of positive autobiographical information is compromised by changes in circuits linking the amygdala, hippocampus, and prefrontal cortex (Ressler and Nemeroff, 2001; Davidson *et al.*, 2000; D’Sa and Duman, 2002; Fuchs *et al.*, 2004; Roozendaal *et al.*, 2009). These circuits implement the communication between the hubs of peripheral and central appraisal and are crucial to the learning and recall of affective contingencies. In fact, the volume of these circuits is often reduced in severe depression (Bremner *et al.*, 2000; Sheline *et al.*, 1996; Videbech and Ravnkilde, 2004). This is consistent with findings that depressive subjects cannot down-regulate their ventromedial prefrontal cortex when appraising potentially negative or depressing stimuli (Sheline *et al.*,

1996; Videbech and Ravnkilde, 2004; Northoff, 2007). Negative autobiographical information is excessively salient to these people. It is not an accident that patients with ventromedial lesions, as well as having characteristic cognitive and behavioural deficits, *are not depressed*. This is explained in terms of a 'lack of the cognitive/affective symptoms associated with self-awareness' (I paraphrase the conclusion of Koenigs and Grafman, 2009, p. 46).

Depressive mood, or existential feelings of despair, reflect an appraisal bias. Since appraisal biases operate in a hierarchical, recurrent fashion and are mutually reinforcing with other components of the emotional systems such as feelings, psychomotor tendencies, and cognition, there is no *a priori* reason to think that intervention at any point in the system is a privileged way to change an appraisal bias. Indeed practitioners of CBT intervene at the level of explicit judgment, changing the pattern of explicit appraisal. Sometimes this approach succeeds in alleviating depressive mood, which suggests that mood is not independent of high-level cognition.

Similarly it *may* be possible to remove the appraisal bias by changing mood directly, as MIC suggests. However, as a matter of fact this does not seem to be how SSRIs work. SSRIs work not by changing mood but by changing the receptive properties of neurons in appraisal circuits, both making them more responsive to positive information and enabling plasticity effects in distributed circuits to which they project. It can take weeks or months to undo entrenched biases in the coordination of emotion components which have been established by patterns of negative peripheral appraisal (Harmer *et al.*, 2009). Downstream bodily feeling and mood aspects persist because they are causally dependent, not only on the prior action of SSRIs on appraisal processes, but on the introduction of a new pattern of appraisal.

This is why Castren (2005) argued that the key to understanding the role of SSRIs in depression is rejecting the MIC hypothesis. Levels of serotonin do not represent positive appraisals. But where appraisal circuits have become biased to process negative information, changing the balance of serotonin/norepinephrine changes the properties of circuits which regulate coordination of emotion components: '[A]ctivity dependant neuronal communication might underlie depression... and antidepressants might work by improving information processing in the affected neural networks' (*ibid.*, p. 2002). Harmer's interpretation of this evidence is novel in psychiatry, which has tended to ignore information processing approaches that emphasize cognitive architecture, in favour of either neurochemical (versions of the

MIC hypothesis) or cognitive behavioural approaches which target what we have called central appraisals.

The crude idea that ‘mood is chemistry’ is perhaps a straw man, but seeing what is wrong with it helps us identify something crucial about the nature of emotions. Emotions have multiple interacting components implemented by interacting neural circuits, and feeling is only one of these components.

Consequently it is not surprising that changing neurochemistry does not always change mood immediately in cases where mood is a consequence of appraisal bias. An organism which is withdrawn, anhedonic, avolitional, has psychomotor poverty and rigid patterns of aversive behaviour, and pessimistic and self-accusing thoughts rapidly receives environmental and bodily feedback that it is failing. Thus all of its appraisal systems represent failure and consolidate the depressive pattern of organization of emotion components.

Ultimately, the beneficial effect of SSRIs in depression treatment is to alter the information processing properties of neural circuits responsible for peripheral appraisals. The effects of pharmacological treatment are very indirect because they depend on neural plasticity in these networks: synaptic connections need to be rebuilt and potentiated. Not only that, but in so far as depression arises in a personal and social context, *activity-dependent* plasticity effects require either changes in the *milieu* or significant cognitive and behavioural work to uninstall dysfunctional appraisals. Restoring the *ability* to detect positive emotional expression will not help unless the patient is consistently exposed to a positive social milieu sufficient to rehabilitate the relevant circuitry.

5. Conclusion

The relationship between feeling states such as mood, physiology, and neural processes is controversial for many phenomenologists. While no one would deny that feeling states are neural representations of body state, the nature of the intentional relationship between feelings and their objects is obscure. While most theorists of emotion and certainly those influenced by phenomenological traditions would accept that feelings in these cases are ‘directed’, the nature of the representational relationship between bodily feeling and the world is not always clear. The aim of this paper has been to clarify that relationship for the case of depressive mood.

In this respect the category of existential feelings, understood in the way Ratcliffe describes, as forms of emotional orientation to the world, or the taking of the world as a set of possibilities for engage-

ment, provides a potential link if understood as a manifestation of appraisal bias. MAT offers an information processing approach with potential to bridge the gap between neurophysiology and phenomenology precisely because it involves forms of tacit representation and processing known to be intimately involved in the regulation of bodily feeling. The fact that resolution of mood relates indirectly to administration of SSRIs turns out, slightly paradoxically, to be another point in favour of MAT. The relationship between neurochemistry and alteration in mood depends on plasticity effects that change the bias in neural circuitry which forms a hub of peripheral appraisal. The nature of peripheral appraisal biases helps account for the fundamental pre-intentional role of existential feeling.

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