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Unconscious Psychological Treatments for Physiological Survival Circuits

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Abstract

The idea of targeting unconscious or implicit processes in psychological treatments is not new, but until recently it has not been easy to manipulate these processes without also engaging consciousness. Here we review how this is possible, using various modern cognitive neuroscience methods including a technique known as Decoded Neural-Reinforcement. We discuss the general advantages of this approach, such as how it can facilitate double-blind placebo-controlled studies, and minimize premature patient dropouts in the treatment of fear. We also speculate how this may generalize to other similar physiological survival processes.

Keywords

Unconscious interventions; Neural-Reinforcement; Fear; Survival/defensive circuit

Introduction

Conscious emotions are generated by complex networks in the nervous system [1,2]. Some of the key structures in this network, like the amygdala, influence behavior and physiological responses important for survival [2]. According to one influential framework known as the higher-order view, much of these brain processes are unconscious, *unless* they are monitored or meta-represented by some higher-order processes [1,3,4]. Although still debated, this higher-order perspective has gradually gained some empirical traction. Our

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goal here is to discuss its various clinical implications. We will use fear as an example, to focus on how the principles of psychotherapy may be applied to the unconscious physiological components underlying fear processing. We end by speculating how these perspectives may generalize to other survival-related physiological circuits.

Targeting the unconscious: why would it work?

Humans evolved in a complex environment where the timely production of defensive responses could often be a matter of life and death. As a result, fixed and rapid survival reactions such as fighting, fleeing or freezing are response strategies that greatly favored survival [5,6]. While seemingly simplistic, these behaviors involve complex neuronal networks for the detection of threats and for the production of appropriate defensive reactions. Some of these behaviors have been suggested to occur automatically [5,6] without requiring the conscious awareness of the relevant threat.

Various methods have been employed to dissociate between conscious and unconscious processes in the brain [4,7]. Specifically, in the case of fear [9], unconscious stimulus presentations have been shown to increase physiological reactivity [8–15] and to affect behavioral outcomes [16–19] (but see [14,20]). Functional magnetic resonance imaging (fMRI) studies have shown that the amygdala, a central structure in the survival/defensive circuit [2], is one of the key regions activated during unconscious fear perception (for a review, see [21]). Importantly, these findings indicate that, without consciousness, some critical regions associated with fear may not be implicated. These include higher-order regions such as the prefrontal cortex (ventromedial [vmPFC], dorsolateral [dlPFC], dorsomedial [dmPFC], and orbitofrontal), the anterior cingulate cortex, and the insula (although, see [22–24]). These regions were associated with conscious fear perception as they are notably involved in the successful treatment of specific phobia [25–27], panic disorder [28–30], generalized anxiety disorder [31], obsessive-compulsive disorder [32,33], post-traumatic stress disorder (PTSD) [34,35], and social anxiety [35,36]. This dissociation between conscious and unconscious processing is in line with the previous literature indicating the importance of prefrontal regions for consciousness [4,7,37].

The dissociation between conscious and unconscious processes raises the question of how these two brain networks may interact. Is the conscious feeling of fear a late stage ‘read-out’ of the activity of the survival/defensive circuit, or is it part of an independent, parallel process? Although theoretical models are still debated (e.g., [1,38]), in general it seems plausible that the conscious experience of fear isn’t completely independent from or totally unrelated to the unconscious physiological process (see figure 1). In particular, under the higher-order view of consciousness [4], we expect the experience of fear to be different from its physiological basis, but the former should meaningfully reflect the latter in most cases. As such, a clinical intervention designed to target the unconscious survival/defensive circuits alone (see table 1) may ultimately alleviate symptoms at the conscious level.

Advantages of targeting the unconscious

An ‘unconscious’ clinical or therapeutic procedure can refer to: (1) an intervention targeting an unconscious process, or (2) an intervention carried without the patient (and sometime the therapist) being aware of the purpose or content of the treatment. The first idea has been prominent within psychoanalytic traditions: Sigmund Freud is probably best known for popularizing the idea of targeting the unconscious mind. This approach is still at the core of modern psychodynamic treatments [46,47] and unconscious or implicit processes are also involved in most modern psychotherapeutic approaches [48]. Other methods, such as hypnosis [49], eye movement desensitization reprogramming [50], transcranial magnetic stimulation [51], and transcranial direct current stimulation [52] have also been used to change implicit processes in the brain. Our focus here, however, is on the advantages of novel treatments that meet *both* criteria of unconsciousness.

One major advantage for this kind of fully unconscious interventions (i.e., satisfying both criteria (1) and (2) above) is that they can be demonstrated in double-blind placebo-controlled experiments, i.e., where neither the therapists nor the patients are aware of the nature of the intervention [53,54]. Traditionally, this is difficult to achieve, because the nature of many psychotherapeutic treatments cannot be completely hidden from the therapists carrying the intervention. Although many arguments have been made as to why double-blind controls may not be totally necessary under all circumstances [55], the advantages of doing so - when it is possible - are obvious. It allows for rigorous experimentation, which can further integrate psychological treatments with modern medicine. Considering the origins of unconscious treatments, where criticisms that it was unscientific [56] have led to serious repercussions, this point should not be under-appreciated. More generally, the placebo effect is known to be complex and large under many circumstances [57] and not controlling for it casts legitimate doubts to a treatment effectiveness.

To achieve this kind of intervention outside of awareness, we have recently made use of a new method called Decoded Neural-Reinforcement (also called Decoded Neurofeedback, DecNef) [58], in which participants’ brain patterns representing specific content (e.g. visual objects) are paired with reward [58]. Importantly, it has been shown that subjects were generally unaware of the contents of these induced brain activity, as well as the general purposes of the procedure, when they were not explicitly instructed about them [58,59].

We have capitalized on the unconscious nature of this intervention method to overcome one challenge traditionally faced by exposure therapy for common fears. In conventional exposure therapy, patients have to consciously face their fear which is subjectively aversive and high rates of premature attrition have been reported [60]. Also, conscious exposure can lead patients to rely on conscious "safety signals", which have been shown to interfere with the effectiveness of the procedure [61]. By using decoded Neural-Reinforcement, we bypassed these issues, by directly rewarding the spontaneous occurences of the relevant brain representations, to make their valence less negative via associative learning [62,63] (Figure 2).

This approach may open up possibilities of how much we can do ‘under the (conscious) hood’. With advancements in brain decoding [64], it is conceivable that unconscious representations beside those for simple objects could eventually be targeted too. Alternatively, one interesting approach not based on decoded neuroimaging information is to carry unconscious interventions during sleep. Experiments conducted both in animals [65] and in humans [65,66] indicate that memories can indeed be changed by presenting stimuli during slow-wave sleep. Such a procedure has notably been used to achieve olfactory aversive conditioning, to reduce cigarette smoking behavior [67].

Beyond fear?

These proof-of-concept examples (Figure 2) show that an unconscious physiological target may be malleable and subject to the basic psychological principles of Pavlovian (associative) conditioning [2]. If these associative learning mechanisms apply to the unconscious physiological survival circuitry for fear [1], would this apply to other ‘fear-like’ unconscious physiological mechanisms too? To what extent are other survival-related physiological mechanisms ‘fear-like’, where the proposed approach may apply?

Here, we speculate that this issue may have been traditionally unappreciated. Take the immune system for example. Conceptually it shares many features of fear: it detects external ‘threats’ and reacts in a way that is largely effective, but occasionally it overreacts, leading to the paralysis of the entire system, or blockage of other complementary mechanisms, such as in the case of inflammation. Given the supposed ‘physiological’ nature of these mechanisms, we might have been initially reluctant to think of them in Pavlovian terms. But it has been shown that even plants are capable of basic Pavlovian learning [68]. Ultimately, many circuits in the nervous system as well as in other parts of our bodies might have been ‘designed’ under the same principles; all organisms and their evolutionarily older subparts are subjected to similar survival pressure.

Take the immune system for example. It has been reported that it can be conditioned through learning [69]. Placebo effects may happen through such mechanisms as conditioning of the immune system with stimuli or taste of medicine that isn’t otherwise effective [70,71]. As mentioned above, the prevalence of placebo effects is often under-appreciated. To what extent can we apply Pavlovian associative learning models to formulate treatments of immune dysfunction?

Of course, there are also clear differences between fear and basic survival mechanisms such as the immune system. For instance, some basic survival circuits can operate without the need for a self-other distinction at the level of the organism because they do not have to regulate complex interactions with the environment. This is in line with the danger model [72], according to which the immune system do not distinguish between self and nonself, but rather mainly focuses on the differences between safety and danger. So in a sense, we should not expect the immune system to be psychologically as complex as some other brain processes.

However, recent research has also increasingly highlighted the two-way communications between brain processes with other physiological mechanisms in the body, e.g. the brain-gut connections [71]. It is known that these physiological processes, similar to the hormonal mechanisms related to fear, are bidirectionally connected to processes within the central nervous system. So even if the physiological circuits in question themselves aren't exactly psychological in nature, the above argument may still hold that we may be able to apply psychological principles in manipulating them, via brain processes.

To really test the degree to which these physiological mechanisms can be understood in Pavlovian terms, we can evaluate some counter-intuitive predictions. For example, it is known that fear can spread socially via vicarious learning [73]. If autoimmune responses are to be conceptualized as akin to fear, does it mean they may spread through the social network too? While this may seem surprising, the current empirical data is not entirely incompatible with such possibility (Box 1). Future work may be able to explore this contentious hypothesis further.

To conclude, we draw attention to the implications of some of the most powerful and best-understood principles about psychology - namely, Pavlovian conditioning, and explored how they may be applicable to various diseases. By isolating them from consciousness, we hope to show that they are not 'unscientific', as if they were just 'all in our heads'. Instead, they can be demonstrated with experimentally rigorous methods, just like other phenomena in physiological medicine. Importantly, these principles may also have the potential of generalizing beyond processes traditionally thought to be 'psychological'.

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Highlights

- Unconscious physiological survival circuits are involved in various mental illnesses.
- Unconsciously targeting the survival/defensive circuit might benefit anxiety disorders.
- Theoretically, other survival-related physiological circuits could also be targeted.

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Box 1

Do autoimmune diseases spread through the social network?

Incidence rates of autoimmune diseases such as Type 1 diabetes and multiple sclerosis have been increasing with substantial cross-country differences [74]. But the epidemiological findings are equivocal: the geographical and other epidemiological patterns of autoimmune diseases [75–77] are also consistent with a mechanism of unconscious spreading through social networks, as much as they could lend support to the popular hygiene hypothesis [78] or its updated versions that focus more on microbiome diversity [79]. The exact mechanisms remain unclear. One way to make sense of these results may be to conceptualize autoimmune reactions as something akin to fear, whereby the purpose of the process is to pre-emptively respond to an external treat; occasionally such over-reactions lead to problems by blocking the action of other effective mechanisms. In humans as well as other animals, there is direct experimental evidence that some fear-related processes can be transmitted socially through vicarious learning [80,81].

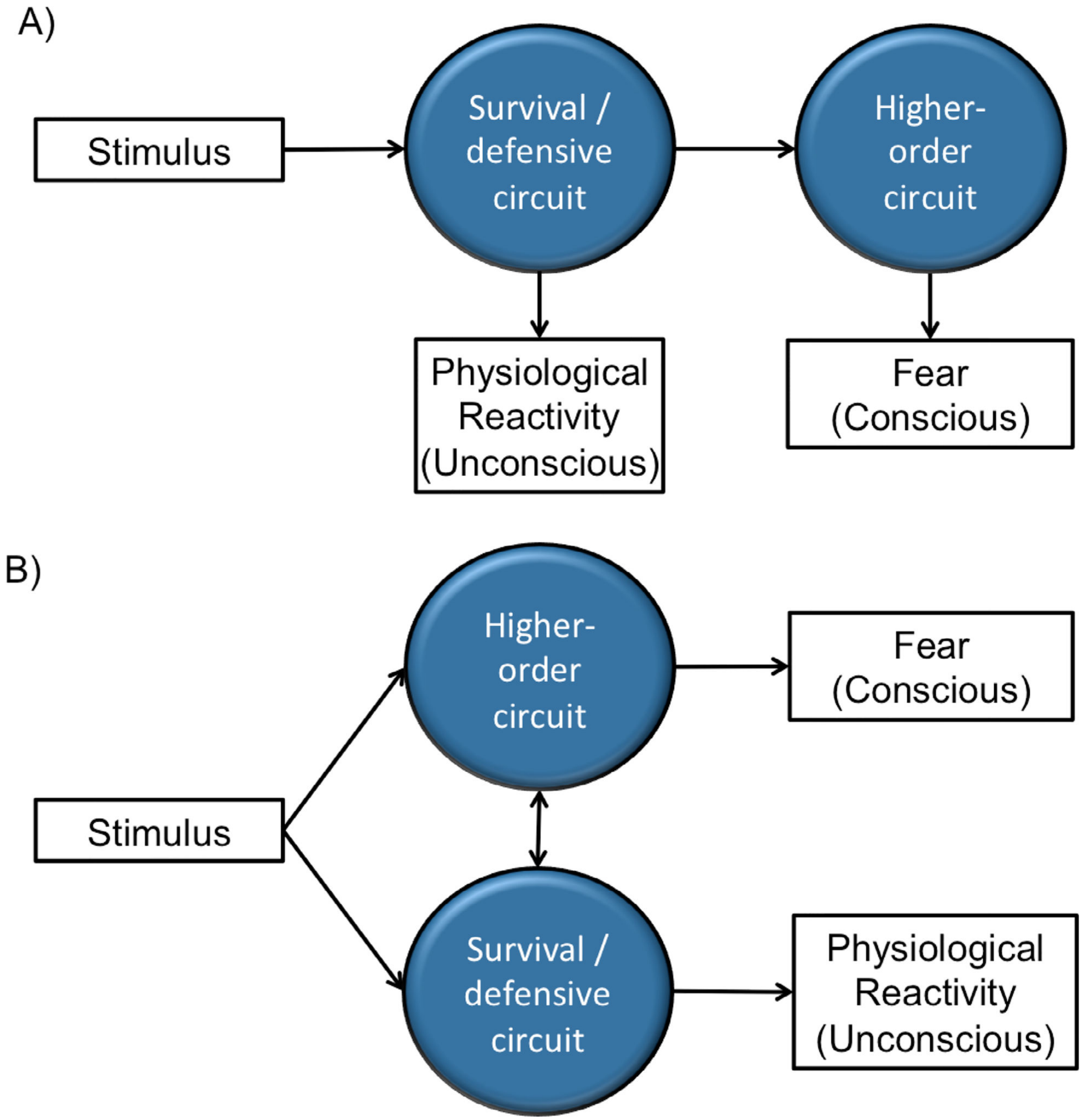

Figure 1. Interactions between the survival/defensive circuit and the higher-order circuit

(A) According to some views (e.g. the higher-order view of consciousness [4]), the physiological mechanism relevant for dealing with immediate threat is considered to be the unconscious bases which ultimately lead to the higher-order process determining the conscious experience of fear. (B) An alternative is to conceptualize the two processes as operating in parallel. But even under such views, few would consider that the two processes do not interact at all.

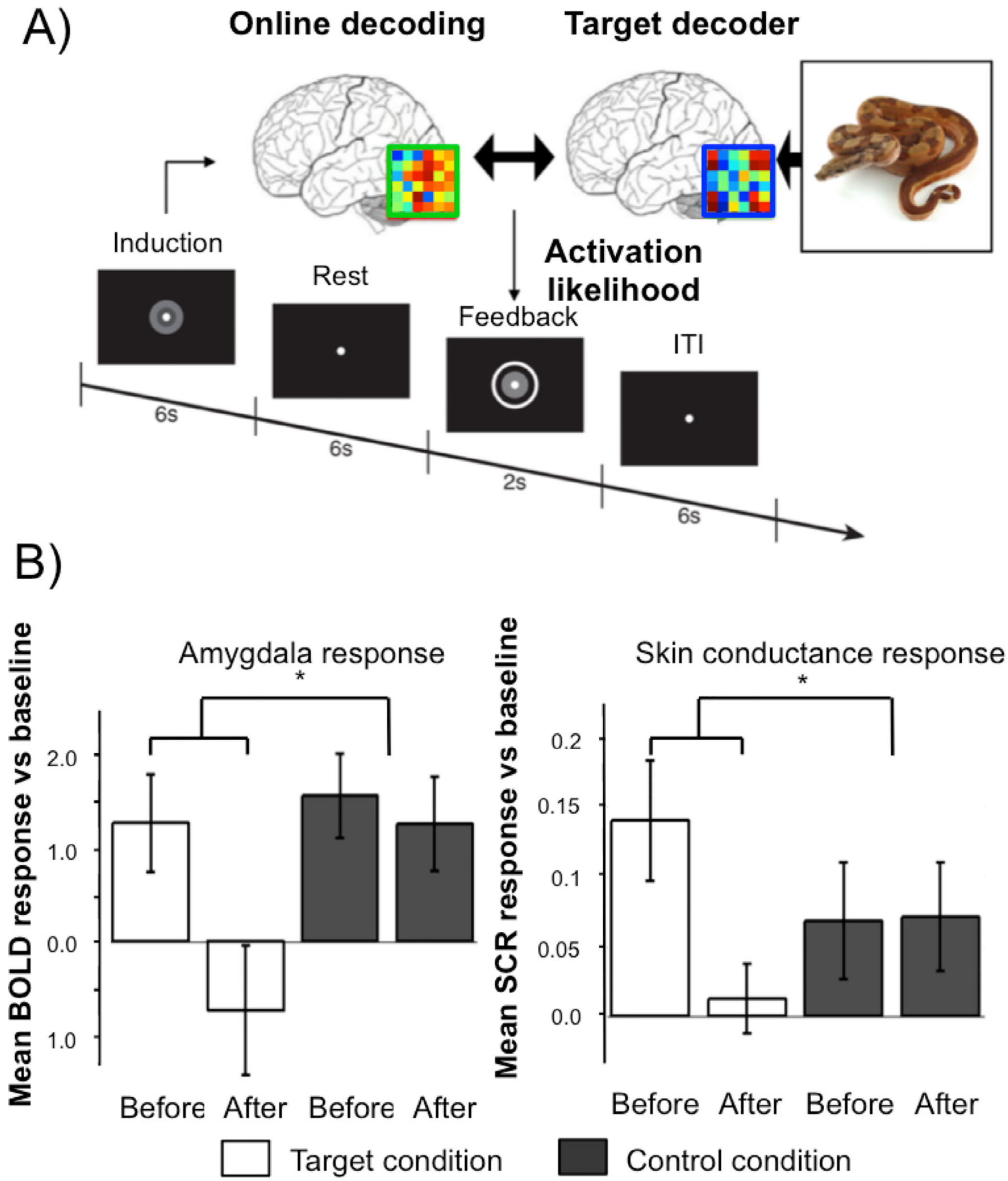

Figure 2. An unconscious Neural-Reinforcement intervention targeting naturally occurring animal fears

(A) Procedure in one trial of Decoded Neural-Reinforcement. Online decoding was used to reinforce occurrences of the multivoxel representation of a feared animal (e.g., a snake). The feedback was proportional to the likelihood of the feared animal being represented. (B) Using this method, we demonstrated in a double-blind placebo-controlled experiment that Neural-Reinforcement can lead to reliable reductions in physiological fear responses measured by amygdala hemodynamic activity (left panel) and skin conductance response (right panel) [63].

Table 1

Some recent studies on the unconscious activation of the survival/defensive circuit in mental illnesses

Population	Methods	Stimuli	Outcome	References
Specific phobia, PTSD, and panic disorder	backward masking	Fearful faces	↗ activity in the left amygdala and ↘ activity in the vmPFC in patients.	[39]
Spider phobia	Backward masking	Spiders	↗amygdala, hippocampus, para-hippocampus, superior temporal gyrus, and dlPFC in patients.	[22]
Trait anxiety	CFS	Threatening faces	Faster break through with higher trait anxiety	[40]
Autism	Backward masking	Fearful faces	↘ pupillary response in patients	[41]
Negative affectivity	CFS	Fearful faces	↗ response in right amygdala and superior temporal sulcus with higher negative affectivity	[42]
Maltreated children	Masked dot probe paradigm	Emotional faces	↗ response in the right amygdala for emotional faces in maltreated children.	[43]
Callous-unemotional traits in conduct disorders	Backward masking	Fearful faces	↗ response in the right amygdala with low callous-unemotional traits.	[44]
Unemotional traits in young violent offenders	CFS	Emotional faces	Faster break through with lower unemotional traits.	[45]

CFS: Continuous flash suppression.