Prediction Errors Drive UCS Revaluation and not Classical Conditioning: Evidence and Neurophysiological Consequences

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Abstract

Nowadays, the experimental study of emotional learning is commonly based on classical conditioning paradigms and models, which have been thoroughly investigated in the last century. On the contrary, limited attention has been paid to the revaluation of an unconditioned stimulus (UCS), which, as experimentally observed by various researchers in the last four decades, occurs out of classical conditioning. For this reason, no analytical or quantitative theory has been developed for this phenomenon and its dynamics. Unluckily, models based on classical conditioning are unable to explain or predict important psychophysiological phenomena, such as the failure of the extinction of emotional responses in certain circumstances. In this manuscript an analytical representation of UCS revaluation learning is developed; this allows us to identify the conditions determining the “inextinguishability” (or resistant-to-extinction) property of emotional responses and reactions (such as those observed in evaluative conditioning, in the nonreinforcement presentation of a conditioned inhibitor, in post-traumatic stress disorders and in panic attacks). Furthermore, an analysis of the causal relation existing between classical conditioning and UCS revaluation is provided. Starting from this result, a theory of implicit emotional learning and a novel interpretation of classical conditioning are derived. Moreover, we discuss how the proposed theory can lead to the development of new methodologies for the detection and the treatment of undesired or pathological emotional responses, and can inspire animal models for resistant-to-extinction responses and reactions.

Keywords: Amygdala, classical conditioning, conditioned inhibitor, emotional learning, evaluative conditioning, misattribution, prediction error, PTSD, resistant-to-extinction, UCS revaluation, unconscious emotion.

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Introduction

Emotions are critical for the environmental adaptation of individuals and for their survival. In fact, emotions prepare any organism to act in some specific ways without the need of experiencing a physical effect that originates from a specific source of stimulation; for instance, the perception of a snake evokes an innate reaction [1, 2, 3] before experiencing (or re-experiencing) a physical elicitation (e.g., a snake attack). This is due to the fact that the representation of some stimuli and the associated emotional reactions are innate [1, 2, 3], being shaped by evolution.

The emotional system plays also an important role in many psychiatric and psychological diseases, in decision making [4] and in the clinical field (e.g., in drug treatment; [5, 6, 7, 8, 9]). Moreover, experimental evidence suggests that subliminal emotional stimulation (through emotional pictures) can improve sport or endurance performance [10, 11], and that emotions influence pain perception [12, 13, 14]. This leads to the conclusion that any influence at emotional level may substantially affect human behavior and perception.

Nowadays, the experimental study of emotions and of their related phenomena is usually based on classical conditioning paradigms [15]. Classical conditioning occurs when a conditioned stimulus (CS) is paired with an unconditioned stimulus (UCS). Generally speaking, a CS is a neutral/innocuous stimulus (e.g., a sound or a neutral visual cue), whereas the associated UCS is a source of stimulation (e.g., an electric shock or food). By repeated CS-UCS pairings, a CS can come to elicit a conditioned response (CR), which is often similar to the unconditioned response (UCR), i.e., to the response directly elicited by the paired UCS [16, 17, 15]; however, the repetitive presentation of the CS without that of the paired UCS leads to CR extinction, since the CS itself will not be longer able to signal (or predict) the UCS.

Classical conditioning theory provides an explanation of the emotional learning mechanism involved in repeated CS-UCS pairings. However, this is not the only emotional learning mechanism, as originally understood by [13]. In fact, Rescorla noticed the difference between the learning mechanisms involving two independent emotional memories, one concerning CS-UCS pairing, the other one the UCS outcome evaluation (and re-evaluation). This viewpoint has been shared by other researchers (e.g., see [19, 20, 21, 22]). However, as far as we know, until now no mathematical (or quantitative) model has been developed for the second type of emotional learning, i.e., for UCS revaluation (in other words, for the learning and the re-valuation of an UCS outcome). For this reason, no quantitative description can be given for many psychophysiological effects and phenomena driven by the emotional system. In fact, this requires the knowledge of a model able to properly describe the dynamics of the interactions between the emotional system and a primary stimulus (i.e., an UCS).

In this manuscript we tackle the problems of developing a novel theory and a new model for implicit emotional learning; we also lay foundations for the development of new methods for the modulation of emotional reactive responses. Our solutions to the above mentioned problems are based on the analysis and the interpretation of various experimental results acquired in different disciplines. In fact, we propose a unifying framework that provides a comprehensive and coherent description of the emotional learning system.

The article begins by illustrating a multidimensional representation of the emotional response to a given stimulus. The proposed representation, which is supported by experimental evidence showing the involvement of distinct and specific neuronal populations in emotional responses [23, 24] (and is also supported by other experimental results based on pharmacological conditioning [25, 26, 27]), accounts for the different types of emotional response and, in particular, for active responses (which are actively sustained by external physical mechanisms, like pharmacological or mechanical stimulation), reactive responses (which are not sustained by any physical mechanism, but “self-instantiated” by the emotional system) and passive residual responses (due to the excitatory residuals from previous emotional elicitations; [28, 29]). Moreover, in our representation plays an important role the source attribution and misattribution phenomena [30, 31, 32, 33, 34] and the modeling of contrast effects [35]. We then develop a novel model describing the emotional response of an organism elicited by a source of stimulation (i.e., an UCS). The derivation of our model relies on the assumption that, similarly as various mathematical models describing classical conditioning (e.g., Rescorla-Wagner model [36, 37] or temporal difference (TD) models [38, 39, 40, 41]), or probabilistic (Bayesian) “perception” and “action” learning models (i.e., the predictive coding (PC) [42] and the active inference models [43, 44]), coding of emotional and behavioral responses involves the computation of a specific error signal. In our work this error signal is defined as the difference between the response expected from the considered source of stimulation and the response actually perceived by the elicited organism. This definition is equivalent to that adopted in TD and PC models, and relies on experimental observations acquired in functional imaging studies [45, 38, 46], or directly measured in dopaminergic circuits (e.g., in the ventral tegmental area, VTA) or in other fear-related circuits [47, 48, 49, 50, 23, 51, 24, 52, 53]. The relationship between the mechanisms of classical conditioning learning and that of UCS revaluation learning is taken into consideration next. In particular, we analyse the different mechanisms involved in the encoding of a CS and of an UCS, and show how the two resulting neural representations lead to specific different properties. Furthermore, we show that a) what is observed during classical conditioning is actually an interrelated effect of both associative and UCS revaluation learning mechanisms, b) only the latter is driven by the emotional system through the computation of emotional error signals (this important result is supported by experimental evidence obtained from optogenetic manipulations [54, 55]). After showing how the Rescorla-Wagner equation for classical conditioning can
be analytically derived from the proposed model for implicit emotional learning under specific conditions, we propose a more complete model for Pavlovian conditioning; in doing so, the stochastic Hebbian plasticity rule \[56, 57, 58, 59, 60, 61\] is exploited. The proposed model is able to predict specific phenomena which cannot be explained by the currently available classical conditioning models (such as the dependence of asymptotic responding on CS intensity and US intensity; \[35, 52\]). Furthermore, we discuss how the conditioned inhibition \[63\] and some related phenomena (such as the failure of the extinction of conditioned inhibition through nonreinforced presentations of the inhibitor; \[64, 65\]), which cannot be described in terms of classical conditioning \[65, 56\], can be quantitatively predicted by the proposed theory. Then, we analyse the case in which the emotional system is elicited by a continuous time-varying source of stimulation (e.g., a time-varying acoustic stimulation, such as music; \[66\]), and we show how our model can be extended to provide some mathematical and neurophysiological indications. Our model is then exploited to quantitatively describe some (system-level) mechanisms leading to a resistance-to-extinction of an emotional response (i.e., inextinguishability over successive trials or over time) under certain conditions, and to illustrate some mechanisms through which an emotional reactive response associated with a primary stimulus can be artificially strengthened/mitigated. This provides new insights on various psychiatric pathologies, like panic attacks \[67\], post traumatic stress disorder (PTSD; e.g., see \[68, 69, 70\]), and psychological phenomena like evaluative conditioning (EC) \[71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81\] (which are known to be resistant to extinction \[72, 73\]).

Finally, we summarise our main findings and discuss the potential implications of our results on future research on emotion processing.

Methods

1. Response representation

This Section is organized as follows. In Section 1.1 the emotional and non-emotional components of the central nervous system (CNS) response to a given stimulus are analysed and vector representations for such a response are developed. Then, in Section 1.2 the active and reactive components of an emotional response are introduced. Finally, the specific features of the reactive response are discussed in Section 1.3.

1.1. Components and vector representation of a brain response

Generally speaking, in a mammalian CNS the response (i.e., the effect) elicited by a given stimulus consists of distinct components, each involving a multitude of neuronal and receptor families; this response (or effect) can be determined by hormonal, mechanical, acoustic, pharmacological and/or other effects originating from the peripheral systems or from the CNS itself. In the following each component of a CNS response is associated with a specific neuronal (e.g., dopaminergic, serotonergic, opioidergic, etc.) population within a given brain region (e.g., the population of dopaminergic neurons in the ventral tegmental area, VTA). For this reason, if \( N \) distinct components can be identified in the CNS, the considered response can be represented as a row vector \( \mathbf{y} = [y_1, y_2, \ldots, y_N] \) belonging to a \( N \)-dimensional space, called CNS space in the following; moreover, this vector can be expressed as the linear combination of \( N \) versors (i.e., unit norm vectors) \( \{y_i; i = 1, 2, \ldots, N\}\); this set of versors, being associated with different neuronal populations, form a complete basis \( \mathcal{B} \) for the considered space. Then, we have that

\[
\mathbf{y} = \sum_{i=1}^{N} y_i \mathbf{v}_i, \quad (1)
\]

where \( y_i \) is a real quantity representing the product between the mean number of elicited neurons and their mean firing rates for the \( i \)-th neuronal population (with \( i = 1, 2, \ldots, N \)); consequently, \( y_i \) takes on a positive (negative) value if the response produces an increase of (a decrease or inhibition of) the activity for the \( i \)-th population, and is equal to zero whenever the response does not involve any adjustment for the baseline activity of the population. It is also important to point out that, generally speaking, the versors forming the basis \( \mathcal{B} \) are not orthogonal, since a specific component can be (linearly or non-linearly, and directly or indirectly) related with other components. This fact is exemplified by the dopaminergic nigrostriatal population (associated with motor functions) and the dopaminergic neurons within the mesolimbic system (associated with motivation and reward functions); in fact, these populations are not simply differentiated from an anatomic viewpoint and significant functional interactions between them have been observed (e.g., see \[82\] and references therein).

Furthermore, given a specific region, a neuronal population can influence another population (e.g., the noradrenergic neuronal population can interact with the dopamine neurons \[83\]). From a neurochemical perspective, the motivation for the interdependencies between different components is represented by the fact that a given neurotransmitter may simultaneously interact with all the various isoforms of its receptor on neurons that also are under the influence of multiple other afferent pathways and their transmitters \[84\].

The components forming the response elicited by a given stimulus can be classified on the basis of different criteria. A fundamental criterion consists in distinguishing emotional components from non-emotional ones. In practice, the emotional component of a given response is due to all the emotional and motivational neuronal systems and influences the mesocortical limbic structures contributing to approach and avoidance behaviors \[85\]. On the contrary, the non-emotional components originate from all the neuronal systems not belonging to the emotional/motivational systems (e.g., to the nigrostriatal dopaminergic system or the sensorimotor system). Note that, generally speaking, emotional and non-emotional components can be interdependent; for instance, they can be
causally related (e.g., physical and emotional pains are correlated) or indirectly related (e.g., emotional components can influence the immune response [86, 5, 87, 88, 89]). This differentiation between emotional and non-emotional components can be included in the vector model sketched above by identifying an emotional sub-space within the CNS space, as exemplified by Fig. 1.

Furthermore, the emotional (non-emotional) response components are collected in the vector \( y_{em} \) (\( y_{ne} \)) and overall CNS can be represented as the concatenation of the two aforementioned vectors, i.e. as
\[
y = [y_{em}, y_{ne}]. \tag{2}
\]

Finally, it is worth noting that our response representation is suited to properly model various experimental results evidencing that the mammalian CNS is able to discriminate different emotional rewarding components (e.g., different dopaminergic populations related to appetitive or rewarding stimulations). In particular, some results illustrated in [23, 24] have lead to the conclusion that neurons can discriminate between cocaine and liquid rewards (or between cocaine and heroin), possibly even better than between natural rewards, and that in rats some neurons can be activated by lever pressing regardless of drug injection, whereas other neurons by pressing a lever of a specific drug or natural rewards only. This shows that every external stimulus, such as food, a natural liquid reward or a rewarding drug, is able to elicit in the rat CNS some specific emotional components related to specific neuronal populations.

1.2. Active and reactive emotional responses

In this manuscript the following definitions are adopted in relation to a source of emotional stimulation.

**Definition 1. Source of emotional stimulation**

An emotional source of stimulation is defined as any source or primary stimulus able to elicit a response involving an emotional or motivational component.

Note that the term “primary stimulus” is employed here to exclude any secondary stimulus (i.e., CS [15, 37]) conditioned to a source stimulus through classical conditioning; nevertheless, even a CS previously paired with a primary stimulus (i.e., an UCS) is able to elicit an emotional response. In the following we assume that a given UCS is always able to elicit an emotional component (e.g., an electric shock device or food), so that both the terms UCS and emotional source of stimulation could be used indiscriminately.

**Definition 2. Active stimulation and active response**

An active emotional response is defined as any emotional component elicited by a primary stimulus through direct physical (e.g. mechanical, chemical, pharmacological, etc.) mechanisms. Furthermore, the stimulus elicitation is defined as active stimulation.

It is worth mentioning that the adjective “active” refers to the fact that the considered response is sustained through an active and physical action of the considered external source of stimulation.

Real world examples of a stimulus eliciting an active response are provided by a drug able to stimulate an emotional or motivational component (through pharmacological mechanisms), a pain stimulus (originating, for instance, from an electric shock delivery), or food.

Generally speaking, the active response can be represented as a non-linear and time-varying function of the physical stimulation generating it and of the internal physiological states (note that the time-variance of this function accounts, for instance for habituation effect or for receptor upregulation and downregulation [84]). Moreover, the active response may be influenced by various physical features of the source stimulus, such as its frequency, rate of change and magnitude of the elicitation.

**Definition 3. Reactive stimulation and reactive response**

A reactive emotional response (or non-active response) is defined as any emotional component “self-induced” by the perception of a stimulus; such a response is not actively sustained by any external physical (e.g. mechanical, chemical, pharmacological, etc.) mechanism. Furthermore, the stimulus elicitation is defined as reactive stimulation.

It is worth noting that the adjective “reactive” refers to the fact that the considered response is reactively elicited as the stimulus is perceived and it is not sustained through any direct physical mechanism.

A real world example of a stimulus eliciting a reactive response is provided by a CS previously paired with a primary stimulus; in this case the elicited reactive response is called conditioned reflex [15]. The non-active response can be elicited also through the mere perception of a primary source of stimulation, such as a threatening stimulus (e.g. a spider or a snake) or food. Such a source of stimulation could be innate (e.g., represented by a biological/phylogenetic fear-related threat, such as a spider, a snake or an angry face [11, 23]) or learned (e.g., an ontogenetic source like a gun [1]).

It is important to point out that, from an evolutionary perspective, emotional reactive responses are fundamental for
the survival of individuals since they can elicit behavioral responses without the need for individuals to physically re-experiencing a given source elicitation (e.g., a snake bite), or they act to turn individual attention to positive valenced sources, such as food. For this reason, reactive responses are learned through the emotional system in order to induce a proper reaction whenever individuals face sources of stimulation or other cues signalling a primary stimulus. As it will be discussed in more detail in Section 2.1, reactive responses are elicited through the amygdala, since, in the absence of an intact amygdala, no reactive response or conditioned reflex can occur [91]. It is also worth mentioning that a primary stimulus is able to elicit both an active emotional response and a reactive emotional response; on the contrary a secondary stimulus (i.e., a CS) can elicit a reactive response only.

Given the definitions and the considerations illustrated above, the emotional vector \( y_{em} \) can be expressed as

\[
y_{em} = y_{aem} + y_{rem} \tag{3}
\]

where \( y_{aem} \) (\( y_{rem} \)) represents the active (reactive) portion of \( y_{em} \).

In the literature various results are available about the latency and decay of emotional responses. First of all, the latency of an emotional response is usually deemed negligible; however, its decay is a time-consuming process for all nontrivial or pronounced emotional states [31, 92, 28]. In analysing the decay of a response, it should be always kept into account that any emotional response can be decomposed in two main functional factors, namely the dominantly neurally controlled factor and the dominantly humorally controlled factor. The former factor has a faster decay after the end of the stimulation, whereas the latter one is relatively slower [28] and can elicit neural responses. For this reason, the different factors of both reactive and active responses extinguish after their elicitation at different speeds. For this reason, it can be always assumed that at least a portion of both active and reactive responses extinguishes quite slowly (e.g., this portion is related to hormones and neuromodulators decay). Moreover, at a given instant a generic active or reactive response can be in its passive state (e.g., instantiated, or during an active elicitation) or in its passive state (i.e., during the decay interval following the end of an active elicitation).

The most important ideas illustrated in this Section can be summarized in Fig. 2, which shows the different types of the emotional response that can be elicited by a generic source of stimulation and the mathematical notation adopted to denote them.

1.3. On the nature of reactive emotional responses

As already stated in the previous Section, a generic CS can elicit a reactive emotional response only, unless it also represents a primary source of stimulation. For this reason, the observation of the responses elicited by different CSs can unveil the specific properties of reactive responses. Various results are already available about this issue in the literature. In particular, it is well known that the unconscious/implicit placebo/nocebo effect can be interpreted as a conditioning process in which a primary stimulus (e.g., a drug) become paired with a CS (e.g., the substance administration or other cues) [5, 94, 95, 96, 97, 98, 99, 100, 101, 102, 8, 103]. After some effective pairings, a successive presentation of the CS (e.g., the administration of an inert substance), in the absence of any active physical/pharmacological stimulation, is able to elicit a purely reactive response which mimics the previous active response due to the primary stimulus. This claim is confirmed by various brain imaging data, evidencing that placebos can mimic the effect of active drugs and activate the same brain areas; this occurs for placebo-dopamine in Parkinson’s disease, for placebo-analgesics or antidepressants, and for placebo-caffeine in healthy subjects (see [27] and references therein). Moreover, in [25] it is shown that pharmacological conditioning, like conditioning with opioids, produces placebo analgesia mediated via opioid receptors administering saline infusions, and that, if conditioning is performed with nonopioid drugs, other nonopioid mechanisms are involved, so that conditioning activates the same specific neuronal populations as the primary stimulus. Similar results and conclusions have been obtained in mice experiments [26]. This line of reasoning is also supported by a further experiment [104] showing that an increase in dopamine release in the ventral striatum, measured through microdialysis, are observed not only when rats self administer cocaine (representing the UCS in the considered experiment), but also when they are solely presented with a tone (representing the CS) that has been previously paired with cocaine administration. Furthermore, experimental verification of the influence of nonconscious conditioned stimuli on placebo/nocebo effects [98, 99] show that a reactive stimulus is able to interfere with a given active stimulation (e.g., an active drug or a painful stimulation), by increasing or decreasing the effect of the active response. This suggests that common active and reactive response components can be additive or competing and, hence, both contribute to the determination of the overall elicited response. The last observation is also supported by further experimental results [12, 13, 14] which show that emotional reactive stimulations (e.g., the perception of emotional pictures or other reactive stimuli) modulate pain perception. For these reasons, if the active and the reactive elicited responses involve some common components, these, in turn, add up in an algebraic sense (see Eqs. (3) and (1)). A further support of this conclusion come from the experimental evidences described in [31, 92, 28, 29] which show that, under some conditions, an emotional excitation can be transferred to a successive independent source of stimulation, energizing it, because of the residual excitation due to the incomplete decay of the previous emotional elicitation. This phenomenon is called excitation transfer [28, 29].

Additional results illustrated in [105] reveal the differentiation between emotional and non-emotional components, and reactive and active responses in nociceptive stimulation (in this case the pain network involves both affective or emotional components, and sensory components). In particular, func-
tional imaging experiments have evidenced that both physically receiving a pain stimulus (i.e., an active stimulation) or observing a signal indicating that a loved person - present in the same room - is receiving a similar pain stimulus (i.e., a reactive emotional pain-related stimulus mediated through empathy) activates the bilateral anterior insula (AI), the rostral anterior cingulate cortex (ACC), the brainstem and and the cerebellum. These results have also shown that, on the contrary, activity in the posterior insula/secondary somatosensory cortex, the sensorimotor cortex (SI/MI), and the caudal ACC was specific to physically receiving pain (i.e., that non-emotional components were exclusively due to the active response) \[105\].

All the results mentioned above evidence that a CS (or a generic reactive stimulus) can elicit specific neural populations and that these populations reflect or mimic the same systems elicited by the primary stimulus paired with the conditioned CS; in other words, as far as the emotional components are concerned, a reactive response mimics the original active response. Moreover, active and reactive responses which involve the same emotional components add up in algebraic sense. This observation leads us to the following two important remarks:

Remark 4.

A reactive response can mimic, at least, the emotional subspace of a previously associated elicited active response.

Nonetheless, we argue that a reactive response can certainly determine also some non-emotional components provided that these are causally related to the emotional ones (e.g., the emotional system can influence the immune response \[86\] [85] [87] [88] [89], or the dopaminergic mesolimbic system can interact with the nigrostriatal dopaminergic system \[106\] [107] [82]). Furthermore, we argue that even the humoral immune response sub-space (in particular the components of the CNS such as the hypothalamic-pituitary-adrenal axis, HPA, or the sympathetic nervous system, SNS; [87]), other than the emotional sub-space, can be mimicked from an active response elicitation; this last assertion is supported by experimental results related to conditioned immune response and pharmacological conditioning with immunosuppressive drugs [5] [87] [108]. Note also that Remark \[4\] is fundamental on the description of the emotional dynamics (see Section 3).

Remark 5.

If a reactive and an active responses involve the same components, the reactive response can strengthen/weaken (energize/inhibit) the emotional components of the primary active response since they are qualitatively indistinguishable. Hence, Eq. (3) can be applied.

As it will become clearer in Section 3, this remark will play a fundamental role in the description of emotional dynamics.

One can argue that, in some cases, a reactive response learned from its active counterpart does not mimic the original emotional response. For instance, this occurs in aversive conditioning, when an electric shock is used as unconditioned stimulus; in particular, it has been observed that heart rate decreases during the presentation of a CS and, on the contrary, it increases when an active electric shock is given \[109\]. For this reason, at first glance reactive and active responses seem to be qualitatively different as they lead to distinct behaviors. Actually, a different interpretation of these results can be formulated. In fact, it should not be forgotten that the active response to a pain stimulus consists of two components (one emotional, the other one non-emotional) and the non-emotional component could result in a behavior substantially different than that produced by the elicitation of the emotional component alone. Moreover, generally speaking, in the complex mammalian CNS, different level of a specific neurotransmitter within a given brain region (determined by the elicitation of a specific emotional component) could lead to different (even opposite) behavioral observations \[84\] (this last assertion will be discussed in more detail in Section 6.2).

2. Error-driven learning

In this Section the basic mechanisms involved in emotional learning are reviewed; in particular we focus on the
role played by the amygdala (and other important systems) in emotional learning and on the mechanisms for the generation of the error signals on which such a learning is based.

2.1. On the role of the amygdala in emotional learning

In complex vertebrates the amygdala represents the core center in the formation and storage of emotional events and in the elicitation of emotional responses. In particular, it is well known that the amygdala plays a fundamental role in encoding emotional memories, in fear responses and in skin conductance response (SCR) classical conditioning. In fact, various results are available in the literature about the involvement of the amygdala in the acquisition and encoding of relevant emotional memories [110][111][112][113][114], and about the fact that these mechanisms are based on its synaptic plasticity [115][112][116]. In addition, in a growing body of literature [117][118][119][120][121][122] it is shown that amygdala is necessary for fear responses, and no reactive fear responses are instantiated in the absence of an intact amygdala [118]. Finally, the analysis of patients with a damaged brain has evidenced the importance of amygdala in SCR classical conditioning. This emerges, for instance, from the results illustrated in [91], where the case of a patient with selective bilateral destruction of his amygdala is analysed; in fact, this patient shows an unconditioned SCR to a UCS, but no SCR conditioning to the paired CS, although he is well aware of the CS-UCS relation.

All the results illustrated above lead to the conclusion that the amygdala is necessary for the elicitation of an emotional reactive response; note, however, that, if the amygdala is damaged, an active elicited response (e.g., an unconditioned painful stimulus) can be still elicited. Further results available in the literature evidence that the amygdala mediates the emotional reaction, and that directly and indirectly elicits emotional and motivational areas of human brain [123][52][124]. In particular, on the basis of information coming from the subcortical (i.e. thalamus) and cortical pathways (from which perception and the representation of the features of any source originates) the amygdala arouses both the cortex and the emotional and motivational brain regions directly and indirectly through different systems [125][126], that is the nucleus accumbens (NAcc), the prefrontal cortex, the midbrain, the hypothalamus, the autonomic nervous system, the endocrine system and others). In the following analysis we briefly refer to this group of systems as system chain. In fact, the amygdala sends projections to a variety of systems, and it consists of several interacting subnuclei that may provide specific individual contribution to the overall emotional computation [127][126][125] (in particular, different subnuclei of the amygdala can process and elicit specific emotional components [128][129][130][54][127]). Research activities in this field have also evidenced that the representation of any UCS is stored within the basolateral amygdala (BLA) [54][55]. Note also that the amygdala mediates both appetitive (i.e. rewarding) and aversive stimuli [111][131][120][121][122][132]; in the former case the BLA neurons project onto the NAcc, whereas in the latter one onto the centromedial amygdala (CeM) [112].

2.2. On the generation of error signals in emotional learning

Neurons in several brain structures appear to code specific signals, that are called error signals and, generally speaking, represent the difference between a really experienced response and its expected counterpart [51][24]. In the literature a number of results are available about the role played by specific neuronal populations in coding error signals and the nature of such signals. In particular the error signals are coded in relation to rewards, punishments, external stimuli, and behavioral reactions [48][51][53]. In some cases, dopamine neurons, norepinephrine neurons, and nucleus basalis neurons broadcast prediction errors as teaching signals to large postsynaptic structures; in other cases, error signals are coded by selected neurons in the cerebellum, superior colliculus, frontal eye fields, parietal cortex, striatum, and visual system, where they influence specific subgroups of neurons. In general, prediction errors can be used in postsynaptic structures for the immediate selection of behavior or for synaptic changes underlying emotional and behavioral learning [46][51].

Evidences of coding of error signals during learning have been found in various neuroimaging studies [45][38][46].

More specifically, as evidenced by a growing body of literature [133][48][134][23][24][53], in emotional learning, populations of dopaminergic neurons encode the error signal evaluating the difference between what is expected (i.e., the expected reward) and what is really occurring; furthermore, this error signal is exploited to correct and modulate the individual’s emotional and behavioral response. The error signal computed in these dopaminergic regions can be positive or negative and can drive appetitive or aversive emotional reactions [48].

On the basis of all the above illustrated results, it can be stated that error signals driving emotional responses are evaluated in different brain regions, depending on the nature of the involved emotional components; however, in emotional learning (and in the computation of the associated error signal), a fundamental role is played by the orbitofrontal cortex (OFC) [135], which represents a key structure in coding and maintaining the representations of a stimulus response (i.e., the representation of the expected outcome associated with a stimulus) [136][135]. In fact, various experimental results have evidenced that the OFC generates information about expected outcomes (e.g., see [137] and references therein), which are deemed critical in the computation of prediction errors; these results are consistent with the relation between the reward-related activity in OFC and VTA dopamine neurons [137].

Experimental results have also evidenced that, when OFC and midbrain data are juxtaposed, anticipatory activity observed in the OFC is inversely related to dopaminergic error signaling downstream [138]. This shows that the error signals in other brain areas might depend partly on OFC input for properly calculating the errors [139][138]. This idea has been partially confirmed for error signals in midbrain
2.3. On error-based emotional learning

On the basis of the experimental results summarised in the previous Section, it can be assumed that, during emotional learning, an error signal is computed in different brain regions (e.g., the VTA), depending on the nature of the elicited emotional response. In this process the OFC plays an important role since it interacts with these brain regions and codes the expected response to a given stimulus (i.e., the expected UCR). Moreover, the error signal which is broadcasted to other brain regions including the OFC, may undergo processing and fusion with other information (even at a higher cognitive level) and is certainly sent to the amygdala, since this part of the brain is necessary for the elicitation of an emotional reactive response, for conditioning and for the storing process of emotional stimuli.

It is also important to point out that the extended network for computing and coding the emotional error-signals (which we call error computing distributed network) can be represented as a distributed system consisting of different sub-systems and, in particular, the OFC, the prefrontal cortex (PFC), the VTA, the midbrain, the striatum and others; all these interact in an iterative fashion. However, the study of these multiple neural interactions is behind the scope of our analysis. For this reason, in the following we assume that, whenever a stimulus elicits an emotional response, an error signal is computed and transmitted to the amygdala for updating the corresponding reactive emotional response; note that this error-driven mechanism enables adaptivity in emotional learning. As it will be shown in the following sections, this mechanism can be quantitatively described and analysed by representing the emotional learning system as a dynamic system, characterised by memory elements (due to the amygdala and to the OFC), fed by a time-varying error signal, and generating the emotional responses (i.e., the vector $y_{em}$ in Eq. (3)).

It is useful to mention that the ideas of relating brain learning to an error-prediction signal and of modelling this process as a dynamic adaptive control system have been already developed in various theories. The most relevant example of this approach is provided by Rescorla and Wagner in their theory about classical conditioning. In fact, in this case the human brain is assumed to learn from a prediction error, defined as the discrepancy between a reference value and what is actually perceived by the considered subject [36 37]. In particular, learning occurs through a mechanism that updates the expectations about the outcome in proportion to a prediction error, so that, across trials, the expected outcome converges to the actual outcome [37]. A variant of the Rescorla-Wagner theory is represented by the so called temporal difference (TD) learning [38 39 40 41], which accounts for the time evolution of the response within each trial. The goal of TD learning is providing a prediction, for each instant $t$ in the trial during which a CS is presented, of the total future reward to be gained in that trial from time $t$ to the end of the trial itself [38].

A more recent theory (known as predictive coding theory [42]) formalizes the notion of the Bayesian brain, in which neural representations in the higher levels of cortical hierarchies generate predictions of representations in lower levels. These top-down predictions are compared with representations at the lower level to compute a prediction error. The resulting error-signal is passed back up the hierarchy to update higher representations; this recursive exchange of signals lead to the minimization (ideally the suppression) of the prediction error at each and every level to provide a hierarchical explanation for sensory inputs that enter at the lowest (sensory) level. In the Bayesian jargon neuronal activity encodes beliefs or probability distributions over states in the world that causes sensations [42]. In predictive coding theory the notion of precision (or confidence, which is the inverse of the variance) of the error signals is also formalised, and the mechanism through which the brain has to estimate and encode the precision associated with the prediction errors is explained. The prediction errors are then weighted with their precision before being assimilated at a high hierarchical level. Generally speaking, predictive coding assumes that organisms minimize an upper bound on the entropy of sensory signals (the free energy), which, under certain simplifying (Gaussian) assumptions is equivalent to the prediction error. The minimization of the error-signal (at the different hierarchical levels of a neural network) is generally computed through a generalized gradient descent [44]. Hence, predictive coding theory leads to model the brain activity by means of a neural network with multiple neuronal layers (from the top high hierarchical level, to the bottom sensory level) which is governed by the backpropagation algorithm [148]; this algorithm leads to the minimization of the error signal, adjusting, iteratively, the weights of the prediction errors at different network layers (such weights correspond to the precisions). In machine learning and engineering fields artificial neural networks have been extensively applied to a large number of learning problems [148] (for classification, regression or parameters estimation). Hence through a neural network architecture, in principle, any nonlinear function or distribution can be learned. Predictive coding theory and the above mentioned concepts have been successfully applied to perception [42] and motion (action) learning (the so called active inference the-
As already mentioned in Section 2.3, a mathematical representation based on multidimensional vectors should be adopted to properly describe the error signal involved in emotional learning and defined as the difference between the actually perceived response and its expected counterpart; this is due to the fact that multiple (and specific) emotional components could be elicited by a primary stimulus. However, in the following we focus on the dynamics of a single component to ease the reading. This choice, however, does not entail any loss of generality, since our model can be applied to any component.

Indistinguishability between the emotional component of an active response and the corresponding reactive learned response - As illustrated in Section 1.3, a learned reactive response mimics the emotional components of the active response elicited by a primary stimulus. For this reason, we assume that the reactive and the active responses add up, so generating the emotional component $y_{em}$ (see Eq. (2) and Remark 5).

The essential neural network and the related neural functions - The considered error signal is computed by a distributed and dynamically interconnected neural network whose master element is supposed to be the OFC (see Sections 2.2 and 2.3). This error-signal is transmitted by the network to the amygdala, which, in turn, updates the emotional reactive response associated with the representation of the primary stimulus. The processing of the error signal inside the amygdala is represented by the (unknown) amygdala function, denoted $F_A(\cdot)$ in the following.

As already discussed in Section 2.1, whenever a primary stimulus is perceived, the amygdala elicits the reactive response previously coded for that stimulus. In particular, the amygdala is able to arouse the cortex, and the emotional and motivational brain regions directly and indirectly; this process involves the system chain described in Section 2.3 and operating between the amygdala output and the emotional brain systems. In the proposed model, the biological functionality of this system chain is described by the (unknown) system chain function $F_{Ch}(\cdot)$. Note that this function does not lend itself to a simple description, since it is influenced by iterative mechanisms involving neuronal and hormonal systems, and various brain regions. In practice, $F_{Ch}(\cdot)$ represents the processing which turns all the amygdala output signals into emotional and motivational responses. These ideas are summarised in Fig. 3, which shows the functional representation proposed for the implicit emotional learning system.

Functional approximations - Generally speaking, the functions $F_A(\cdot)$ and $F_{Ch}(\cdot)$ may change over time, and are expected to be influenced by the internal physiological states at the time the stimulus is encountered. External circumstances and various features of the eliciting stimulus. Moreover, it is expected that the amygdala function depends also on the elicited sensory modality (e.g., auditory, visual, olfactory). Finally, the behavior of these functions change from component to component. However, in the following it is always assumed, for simplicity, that these functions are static; consequently, the influence of all the...
Figure 3: Discrete-time representation of the mechanisms on which the implicit emotional learning system is based. The functional connections between the involved actors and the processing task accomplished by each block are shown. In particular, a stimulus could exert an active stimulation, a reactive stimulation or both; in case of a reactive stimulation, the stimulus is perceived and, successively, the amygdala elicits the associated reactive response. The amygdala output is being processed by the system chain network, which involve all the systems between the amygdala output and the emotional/motivational brain regions (e.g., the nucleus accumbens, the sympathetic system, the hypothalamus and others). The orbitofrontal cortex updates the expected response associated to a given stimulus and drives the error computation network for the computation of the emotional error signals. The error signals are sent to the amygdala which updates the reactive responses associated to the given stimulus. The processes involved in the discrete-time emotional system are discuss in detail in the following sections.
above mentioned factors and possible habituation effects are not taken into consideration. Moreover, their dependence on the considered emotional component is not highlighted by the adopted mathematical notation since, as already mentioned above, we focus on a single emotional component.

3. A novel discrete-time dynamic model for the implicit acquisition (and inflation) and devaluation (and extinction) of an emotional source

In this Section the discrete-time dynamic models for implicit emotional learning during the source acquisition (and inflation) and devaluation (and extinction) are developed. In particular, the source acquisition represents the process through which an emotional source of stimulation (i.e., UCS) is detected and coded within the brain; the inflation (devaluation), instead, represents the process through which an UCS outcome (i.e., an UCR) increases (decreases) with respect to the previously coded UCR. At the beginning of our study some additional hypotheses needed in the development of our model (and complementing the hypotheses illustrated in Section 2.4) are listed and properly motivated, and some details about the adopted mathematical notation are provided.

3.1. Additional hypothesis and mathematical notation

Unless explicitly stated, the following hypotheses hold in the development of our model.

H.1 - Discrete trials - Multiple trials in the interaction between a source and a subject are considered; the trial duration \( \Delta T \) is assumed to be relatively small and, in particular, negligible with respect to the inter-trial interval (ITI) \( T \). For this reason, each trial can be ideally associated with a specific point on the time axis and the corresponding emotional response can be deemed constant, so that a discrete time scale can be adopted in the representation of the considered phenomena.

H.2 - Residual response from previous trials - The time constant \( \tau \) associated with the decay of the response elicited during each trial is deemed negligible with respect to the inter-trial interval \( T \); consequently, when a new trial takes place, the emotional response due to the previous trials has already vanished.

H.3 - Novelty of the source of stimulation - The stimulus eliciting the emotional response is assumed to be neutral before the start of the trials (e.g., it is not a phylogenetic innate source of stimulation).

H.4 - Stimulus perception - The perceived stimulus is the same in each trial, so as the associated contextual information and boundary conditions. This assumption states that, if a stimulus elicits a subject during the first trial in a specific context (e.g., place, timing, and specific boundary conditions), it has to be considered that the stimulus perception in the following trials involves exactly the same contextual and boundary conditions. In the absence of such an assumption the reactive response elicited by the stimulus perception might be modulated by the different contextual information and boundary conditions. For instance, the perception of a threatening stimulus (e.g., a snake) at a short distance and without barriers should elicit a reactive response stronger than that due to the same stimulus perceived at a larger distance or in the presence of a separation barrier (i.e., with different boundary conditions and context).

H.5 - Response evolution - During the process of source acquisition, the emotional response increases monotonically over successive trials; this assumption is motivated by the definition of acquisition and consolidation of a source stimulus (hence, the extinction or devaluation processes are not taken into consideration in this case). On the contrary, during the process of source devaluation or extinction, a monotonical decrease of the emotional response is observed.

H.6 - Stability of the emotional system - The emotional response does not diverge (i.e., does not tend to infinity) as the number of trials increases.

In our analysis the following mathematical notation is adopted. The emotional response and the active emotional component characterizing the \( n \)-th trial are denoted \( y_n \) and \( x_n \), respectively (note that these quantities correspond to the terms \( y_{em} \) and \( y_{aem} \), respectively, in Eq. (3)). where \( n \) is the trial index (with \( n = 1, 2, \ldots \)). In principle, the dependence of \( y_n \) and \( x_n \) (and that of the amygdala function \( F_A(\cdot) \) and of the corresponding system chain function \( F_{CH}(\cdot) \); see the last part of Section 2.4) on the emotional space component they refer to should be indicated; in the following, however, such a dependence is omitted to ease the reading. Note also that H.3 entails that

\[
y_0 = 0,
\]

since the first trial corresponds to \( n = 1 \), whereas H.5 leads to the inequality

\[
y_n \geq y_{n-1}
\]

for the acquisition (and inflation) process and to

\[
y_n \leq y_{n-1}
\]

for the devaluation process (with \( n \geq 2 \) in both (5) and (6)). Finally, H.6 can be formulated as

\[
\lim_{n \to \infty} |y_n| < \infty
\]

3.2. Quantitative analysis of source acquisition and inflation

In the following analysis the considered active source of stimulation (see Definitions 1 and 2) could be represented, for instance, by an electric shock device or by a drug administration. We argue that the last mentioned case represents the acquisition of an implicit or unconscious placebo response.

In the first trial (i.e., for \( n = 1 \)) the source stimulates the subject for the first time, so eliciting the emotional response

\[
y_1 = x_1.
\]
The error (or difference) signal (defined as the difference between the expected response and the really perceived response; see [4] and [5])

\[ e_1 \triangleq y_1 - y_0 = x_1 \]  

(9)
is evaluated in parallel. Then, this signal is transmitted from the error evaluation network to the amygdala, which computes and stores (within the amygdala itself) the amygdala reactive response

\[ i_{A,1} = F_A(e_1) \]  

(10)\this quantity is associated with the representation of the eliciting stimulus (i.e., the acquired source of stimulation, UCS). Such a stimulus representation is also stored within the amygdala and, in particular in the BLA [55, 54] (other related contextual information are stored in the hippocampus [55]).

As already mentioned previously (see subsection 2.1), after the acquisition process described above, whenever the subject perceives the source of stimulation, his/her amygdala elicits the previously coded (and stored) reactive response \( i_{A,1} \) (the stimulus perception process has to be interpreted in the sense given in H.4). At the level of emotional and motivational brain areas the direct and indirect effects of \( i_{A,1} \) result in the reactive response

\[ i_{R,1} = F_{Ch}(i_{A,1}) \]  

(11)\which depends on the full system chain (i.e., on all the systems elicited by the amygdala and their interactions). Note that \( i_{R,1} \) is elicited independently of the fact that the source stimulates actively (i.e., physically) the subject, because of its reactive nature.

In the second trial, if the subject, after perceiving the stimulus and having triggered the emotional reactive response associated with it, is also physically stimulated, the emotional response is updated on the basis of the active response \( x_2 \) elicited by the source and the elicited reactive response \( i_{R,1} \) (determined by the amygdala in the previous trial, during which the emotional response has been learned). Then, we have

\[ y_2 = x_2 + i_{R,1} \]  

(12)\here \( x_2 \), which represents the response originating from the physical interaction between the subject and the source stimulus in the second trial, cannot be smaller than \( x_1 \), since the source acquisition/inflation is being considered (see H.5). After the response \( y_2 \) has been elicited, the new error signal (see [9])

\[ e_2 \triangleq y_2 - y_1 \]  

(13)\encoding the difference between what was expected (\( y_1 \)) and what is experienced (\( y_2 \)) is sent to the amygdala; this, in turn, updates the stored emotional reactive response accordingly (note that the stimulus remains unchanged over all the trials, so that in the absence of cognitive or suggestion processes the expected value \( y_1 \) is exclusively due to the value implicitly stored at the end of the previous source-subject interaction; see H.4). Moreover, the updated reactive response, which is computed and stored within the amygdala, is given by the sum of the previous reactive component with the increase due to the last error signal \( e_2 \). For this reason, it is given by

\[ i_{A,2} = i_{A,1} + F_A(e_2). \]  

(14)\The amygdala reaction \( i_{A,2} \), in turn, reflects the emotional response in the emotional/motivational brain areas, which is given by

\[ i_{R,2} = F_{Ch}(i_{A,2}) \]  

(15)\Similarly, in the third trial, the response

\[ y_3 = x_3 + i_{R,2} \]  

(16)\is elicited. The last equation can be easily rewritten (see Eqs. [10], [13], [14] and [15])

\[ y_3 = x_3 + F_{Ch}(i_{A,2}) = x_3 + F_{Ch}(i_{A,1} + F_A(e_2)) = x_3 + F_{Ch}(F_A(e_1) + F_A(e_2)) = x_3 + F_{Ch}(F_A(y_1 - y_0) + F_A(y_2 - y_1)). \]  

(17)\Following the line of reasoning illustrated above leads easily to the general expression

\[ y_n = x_n + F_{Ch}\left(\sum_{k=1}^{n-1} F_A(e_k)\right) \]  

(18)\holding for \( n \geq 2 \). It is important to point out that the sum appearing in the right hand side of (18) represents the storing process within the amygdala (i.e., the emotional learning process involving all the past experience); however, no quantitative result can be inferred from (18) in the absence of some information about the structure of the functions \( F_A(\cdot) \) and \( F_{Ch}(\cdot) \). As far as the last point is concerned, in the following it is assumed that \( F_A(0) = 0 \) and \( F_{Ch}(0) = 0 \), and that both \( F_A(\arg) \) and \( F_{Ch}(\arg) \) can be properly approximated as linear functions for small values of \( |\arg| \). Consequently, the first order Taylor approximations

\[ F_A(\arg) \simeq \gamma \cdot \arg \]  

(19)\can be adopted, where \( \gamma \) and \( \Gamma \) denote the first derivatives of \( F_A(\arg) \) and \( F_{Ch}(\arg) \), respectively, evaluated at \( \arg = 0 \) (\( \gamma \) and \( \Gamma \) denote the reactivity of the amygdala and the system chain, respectively, and take on real values and, similarly as the parameter \( \alpha \) defined below, depend on the selected emotional component). Then, if the parameter

\[ \alpha \triangleq \gamma \cdot \Gamma \]  

(21)\is defined, Eq. (18) can be approximated as
\[ y_n = x_n + \alpha \cdot \sum_{k=1}^{n-1} e_k = x_n + \alpha \cdot \sum_{k=1}^{n-1} (y_k - y_{k-1}), \]  
(22)

which represents a first order approximation model. The last equation can be reformulated, after some manipulations, as (see also (4))

\[ y_n = x_n + \alpha \cdot (y_{n-1} - y_0) = x_n + \alpha \cdot y_{n-1} \]  
(23)

which shows the recursive nature of the emotional dynamic learning system, described by a first order non-homogeneous model [160]; note that emotional stability (see H.6) requires the modulus of the parameter \( \alpha \) to be strictly less than unity [160] (i.e., \( |\alpha| < 1 \)).

From the last result and our previous assumptions it easily inferred that a complete dynamic model describing emotional learning in an approximate fashion is expressed by (23).

\[ y_{n+1} > y_n \]  
(24)

for any \( n \in \mathbb{N} \) (with \( y_0 = 0 \)) and

\[ y_n = y_{n-1} \]  
(25)

when the error signal \( e_n \) is equal to zero.

Let us now analyse the implications of Eqs. (23)-(25). we assume that, without any loss of generality, the active elicited response is constant at every trial (e.g., the amplitude of the stimulus is constant, so as the elicited active response), so that

\[ x_n = X \]  
(26)

for \( n \geq 1 \), where \( X \) denotes a constant. Then, (23) turns into

\[ y_n = X + \alpha \cdot y_{n-1} \]  
(27)

which can be interpreted in terms of eq. (3), since \( X \) represents the active response, whereas \( \alpha \cdot y_{n-1} \) the associated reactive response \( (i_R) \). It is easy to show that, in this case, the emotional response in the \( n \)-trial is given by

\[ y_n = X \cdot \left( \frac{\alpha^n}{\alpha - 1} - \frac{1}{\alpha - 1} \right) \]  
(28)

so that it approaches the asymptotic value

\[ y^* = X \cdot \frac{1}{1 - \alpha} \]  
(29)

as \( n \) increases (in practice, after a few source-subject interactions, \( y_n \) closely approaches \( y^* \)). Then, substituting (29) in the right-hand side of (27) yields

\[ y^* = X + \frac{\alpha}{1 - \alpha} X \]  
(30)

which, once again, shows that the emotional response consists of an active component \( (X) \) and a reactive component

\[ i^*_R = \frac{\alpha}{1 - \alpha} X \]  
(31)

On the basis of the last results, it is not difficult to show that, if \( \alpha > 0.5 \), the emotional reactive response \( (i_R) \) becomes greater than its active counterpart as the number of trial increases. This phenomenon can occur, for instance, in a limited number of repeated trials if the reactivity of the amygdala, at least for a specific emotional component, is relatively strong (i.e., \( \gamma \) takes on a large value). In this case the acquired emotional reaction could become very intense after some trials, even in the presence of a modest active response due to a source physical stimulation. It is worth mentioning that the amygdala reactivity could be increased, for instance, by stress hormones (through direct and indirect mechanisms) [161].

Finally, it is worth mentioning that, if the source of stimulation is a phylogenetic source (i.e., a prepared biological and evolutionary fear relevant stimulus coded in the mammalian amygdala since birth [162, 1, 2, 90]), an emotional reaction \( Y_0 \) can be natively coded and stored within the amygdala [90]. For this reason, as soon as this source is perceived, an emotional reactive response \( Y_0 \) could be elicited even in the absence of previous source-subject interactions. In this case the dynamic model for the increase (inflation) of the emotional response

\[ y_n = X + Y_0 + \alpha \cdot (y_{n-1} - Y_0) \]  
(32)

can be easily derived from (23).

3.2.1. Theorem: On the necessity of both the reactive response and the expected (predicted) outcome for the stability of the emotional system

It is important to point out that the reactive response determined by the amygdala \( (i_R) \) and the expected outcome (i.e. to \( y_{expected} \); this, on the basis of our assumptions, can be considered equal to the last occurred outcome, i.e. to \( y_{n-1} \)) are both required in order to ensure that the elicited response does not diverge if the number of successive trials increases (in other words, the response does not becomes arbitrarily large as the number of UCS stimulation trials increases; see H.6).

Proof. Proof by contradiction (reductio ad absurdum) \( \square \)

Hypothesis 1: the reactive response associated with a stimulus representation (i.e., with an UCS representation) coincides with the expected (predicted) outcome, and the expected or predicted outcome converges to the experienced outcome.

Hypotheses H.1 - H.6 and the Remarks [4] holds.

Hypothesis 1 asserts that a unique reactive signal predicting the UCS outcome exists, and that this signal coincides with the reactive response elicited when the UCS is perceived; furthermore, the predicting signal converges (by learning) to the actual experienced elicitation. The last assumption has been formulated to include a more general scenario than that considered in our initial assumptions, in which the expected outcome coincides with the last experienced outcome. From a mathematical viewpoint, the expected outcome can be computed using any supervised learning method (or, alternatively, TD methods [40]) in which the predicted outcome is evaluated
on the basis of the past \( m \) predictions (i.e., of the predicted outcomes in the last \( m \) trials) and of the actual outcome, minimizing the error between the prediction and the experienced outcome. Otherwise it can be assumed that the predicted outcome coincides with the last experienced outcome.

1. Let the UCS be an active source of stimulation (e.g., a painful stimulation or a drug administration).

2. The UCS is perceived by a given subject on successive trials, then it exerts an active elicitation (i.e., it elicits the active response \( X \)). During the first trial the response is exclusively due to the active UCS elicitation, that is \( y_1 = X \). After the first trial (for instance, during the UCS perception in the second trial), the predicted (reactive) response, called \( y_{predicted,1} \), is computed.

3. In the second trial, after the UCS perception, the predicted outcome \( (y_{predicted,1}) \) adds up to the successive UCS active elicitation, so that the outcome can be expressed as \( y_2 = y_{predicted,1} + X \). Furthermore, since \( y_{predicted,1} \) does not coincide with the actual experienced outcome, the new prediction \( y_{predicted,2} \) is computed after the second trial: it can be easily proved that \( y_{predicted,2} > y_{predicted,1} \) (since the experienced outcome has been strengthened and the error signal has to be minimized).

4. In the third trial the experienced outcome can be written as \( y_3 = y_{predicted,2} + X \); since \( y_3 > y_2 \geq y_{predicted,2} \) a new value for the predicted response is computed, called \( y_{predicted,3} \) such that \( y_{predicted,3} > y_{predicted,2} \).

5. In the \( n \)-th trial the outcome can be expressed as \( y_n = y_{predicted,n-1} + X \); it is easy to prove that \( y_n > y_{n-1} \geq y_{predicted,n-1} \). Moreover, if the number of trials tends to infinity, the outcome grows indefinitely (i.e., \( \lim_{n \to \infty} y_n = \infty \)).

6. The last statement is absurd, as it contradicts hypothesis H.6.

3.2.2. Quantitative analysis of source devaluation and extinction

Let us assume now that in the \( n_0 \)-th trial (corresponding to the beginning of the extinction process), the considered source does cease to stimulate actively the subject (e.g., an inert drug is administered, after that the asymptotic response expressed by Eq. \( 25 \) has been reached through the administration of an effective active drug in the previous trials). In this case, Eqs. \( 23 \)–\( 25 \) turn into

\[
y_n = \alpha \cdot y_{n-1}
\]

for \( n > n_0 \),

\[
y_0 = Y_0
\]

and

\[
y_n = y_{n-1}
\]

when the error signal \( \epsilon_n \) is equal to zero, respectively. These formulas show that, even if the active stimulation drops to zero, the corresponding reactive response, which depends on the previous source-subject interactions, does not vanish abruptly, but exhibits a decay rate depending on the value of the parameter \( \alpha \). In particular, if \( n_0 = 0 \) and \( Y_0 \) denotes \( y_0 \) (note that \( 1 \) does not hold in this case), from \( 33 \) it is easily inferred that

\[
y_n = Y_0 \cdot \alpha^n
\]

This result shows that, if \( |\alpha| < 1 \), \( y_n \) asymptotically tends to zero in the absence of an active elicitation.

3.3. Emotional response dynamics in discrete time scale

The mathematical results derived in Sections 3.2 and 3.2.2 taken together, can be employed for evaluating the emotional response to an arbitrary pattern of physical source elicitation, that is in the general case of source revaluation \([18, 22, 20]\). Hence, the emotional adaptation, on the basis of the variability of the phisical stimulation of a given stimulus (UCS) during successive trials, can be quantitatively described.

Moreover, we argue that, in investigating the emotional response in the presence of an arbitrary active stimulation, it is important to understand under which conditions the equality \( 25 \) holds, i.e. the error signal is equal to zero (excluding, of course, the trivial cases in which the source is extinguished, i.e., \( y_n = 0 \), or the response reaches its asymptotic value \( 29 \)). In fact, this should allow to acquire a deeper understanding and a quantitative description of diverse psychophysiological phenomena, like particular forms of placebo/nocebo effects, evaluative conditioning phenomena, and some psychiatric and psychological disorders, like panic attacks, post traumatic stress disorders (PTSD) and others. Further details about this issue are provided in the next Sections 4.2 and 8.

3.4. On the impact of excitation decay

The proposed dynamic model can be modified to account for the excitation decay \([31, 22, 23, 28]\), because of which a certain time (denoted \( \tau \)) is needed to dissipate an elicited response. In practice, this phenomenon becomes relevant through successive trials when the inter-trial interval \( T \) is relatively small with respect to the time constant \( \tau \) characterizing the dominantly humorally controlled factor of the emotional response (and, consequently, H.2 does not hold). In fact in \( 28 \) it is shown that, under some conditions, an emotional excitation can be transferred even to a successive independent source of stimulation, because of the residual excitation due to the incomplete decay of the previous source stimulation. This phenomenon is called excitation transfer \([28, 29]\). In these conditions, the response aroused in each trial is due to both the actual (both physiological/active and reactive) elicitation and to the residual excitation from the previous trial; moreover, the dissipation rate of the emotional response (i.e., the value taken on by the parameter \( \tau \)) is influenced by the intensity of the aroused response, intervening distractions, fatigue \([31\) and other factors \([92]\).

If an exponential decay is assumed for the dominantly humorally controlled response, the recursive equation
depression effect

stead, the "undershoot" experienced after a negative contrast increases; see H.6 in Section 3.1.

emotional response does not diverge as the number of trials increases; see Eq. (37) in Section 3.1.

α + \xi \cdot \exp(-T/\tau) < 1

(38)
can be easily inferred. Moreover, on the basis of Eq. (37) it can be easily proved that the final emotional value associated with the source of stimulation increases as T gets smaller. In some cases, however, the ITI could change over the sequence of trials. For instance, a “fast” emotional acquisition, resulting from a group of some very close trials, could be followed by another group of trials characterized by a larger ITI. In this case, if the second group starts only after the end of the excitation decay of first group, then the response will naturally decrease according to Eq. (40) until the asymptote expressed by (41) is reached. Finally, we note that, from a quantitative perspective, the effects of an excitation decay in close trials could be illusorily perceived as a larger value for the parameter \alpha as long as the trials are temporally close to each other.

3.5. On the inclusion of contrast effects in the discrete-time model

In the literature it is well documented [35] [163] that surprising reward omissions, that is, the absence or reduction of an expected reward, are accompanied by aversive emotional reactions, at least in mammals [163]. On the contrary, surprising increases in the expected reward result in an appetitive emotional reaction. In particular, positive and negative contrast effects, arising from unexpected shifts in the obtained reward (whose value is greater or smaller than that previously experienced), depend on the comparison of the sensory property of the present stimulus with information stored in memory [164] and lead to an emotional response overshoot or undershoot, which is independent from the absolute value of the real reward. For instance, in [164] it is shown that rats, in the presence of a shift from 32% to 4% of the administered sucrose solution, displayed a successive negative contrast (i.e., a depression effect [35]) by initiating significantly fewer bouts of licking than control rats maintained on 4% sucrose. Furthermore, no significant increase in the dopamine efflux in the NAcc was observed during the consumption of 4% sucrose by rats that experienced the shift from 32%; on the contrary, the consumption of 4% sucrose by control rats was accompanied by a significant increase in the DA efflux in the NAcc.

Generally speaking, the emotional “overshoot” experienced during positive contrast is termed elation effect; instead, the “undershoot” experienced after a negative contrast is termed depression effect [35].

Contrast effects can be interpreted in terms of emotional responses, as indirectly suggested by the effects of drugs on contrast [35]. In fact, experimental data reveal that drugs having anxiolytic effects on humans (e.g., amobarbital, ethanol, and benzodiazepines) tend to reduce negative contrasts. Interestingly, the barbiturate drug reduces negative contrast, but does not have any effect on positive contrast [35]. The hypothesis according to which emotional responses are involved in contrasts is also supported by the experiments reviewed in [35] and showing that an increased release of adrenocorticosteroid hormones is detected in the presence of negative contrasts; this proves that a negative contrast is able to activate a component of the sympathetic response to stress. In addition, the responses evoked by negative contrasts are often characterized by a long duration and sometimes do not dissipate by the end of the experiment [35].

Experimental evidence also shows that contrast exhibits an inverse dependence on the inter trial interval T and a direct dependence with the magnitude difference between the preshift and the postshift values (in other words, it is proportional to the error signal, defined as the difference between the expected outcome and the perceived outcome). For this reason, prior experience (e.g., prior trials) with the source of stimulation determining the expected value (or outcome) plays a fundamental role in determining contrast effects.

Given the empirical results illustrated above, we argue that contrast effects can be included in the proposed model for implicit emotional learning by adding a new function, called contrast function and denoted \( C(e_A; T) \); this function exhibits a nonlinear dependence on T and on the actual error-signal, defined as

\[ e_{A,n} \triangleq (x_n + \alpha \cdot y_{n-1}) - y_{n-1} \]

for the n-th trial; note that this definition is motivated by the fact that the error signal refers to the present trial (instead of the previous one), since contrast effects occur in parallel with the actual outcome. Consequently, the emotional response during the n-th trial can be evaluated as (see Eq. (23))

\[ y_n = x_n + \alpha \cdot y_{n-1} + C(e_A; T) \cdot e_{A,n} \]

if \( e_{A,n} \neq 0 \) and

\[ y_n = y_{n-1} \]

if \( e_n = 0 \) and \( e_{A,n} = 0 \)

The following properties can be reasonably assumed for \( C(e_A; T) \): a) \( C(e_A; T) \cong 0 \) if \( 0 \leq e_A \leq T_A \), where \( T_A \) is a proper threshold; b) \( C(e_A; T) \cong K \) (where \( K \) is a positive constant) if \( e_A > T_A \) for a fixed \( T \); c) \( C(e_A; T) \) is inversely proportional to the ITI (i.e., \( C(e_A; T) \propto 1/T \)). Property (a) derives from the fact that no contrast effect is expected for a relatively small error signal; (b) is based on a first order approximation and (c) comes from empirical observations [35].

The quantities \( T_A \) and \( K \) have to be experimentally estimated. Moreover, it is reasonable to assume that they could depend on the specific emotional component elicited during
the stimulation (e.g., the dopaminergic neuronal population in the NAcc).

It is not difficult to show that a simple continuous function approximately satisfying the above mentioned conditions is

\[ C(e_A; T) = \frac{K}{1 + e^{-(e_A - \tau_A) / \alpha}} \cdot \frac{1}{T} \]  

(42)

This can be approximated by the linearized model

\[ C(e_A) \approx K \cdot e_A \]  

(43)

If Eq. (43) is adopted to model the contrast effect, an unexpected UCS elicitation (i.e., an active UCS stimulation which is not signalled by a CS nor by the UCS perception, such as, for instance, a permanently-connected electric shock device elicitation) determines the response

\[ y_{UCS} = X + K \cdot X, \]  

(44)

and is attributed to the UCS. Furthermore, depending on the value expected for the UCS before the unexpected elicitation, the error signal is computed and the reactive response associated with the UCS is updated accordingly; in particular, if the expected response before the unexpected elicitation is equal to \( X + \alpha X \), the error signal becomes \( e = X \cdot (K - \alpha) \). Moreover, if another unexpected UCS elicitation occurs, the resulting error signal is equal to zero since the expected outcome (which coincides with the last outcome) is now equal to the actually experienced outcome, which is given by \( X + K \cdot X \) (i.e., the active elicitation and the contrast contribution due to the unexpected elicitation). This mathematical result is important because shows that a series of trials of unexpected UCS elicitations lead to an error signal different from zero only during the first unexpected elicitation, in fact, in the successive unexpected trials this leads to a static situation in which the error signal remains equal to zero and a constant reactive contribution (i.e., \( K \cdot X \)) due to the contrast effect is elicited.

Moreover, if the Eq. (43) is adopted to model the contrast effect and if it is assumed that \( 0 < K < 1 \), it is easy to demonstrate that Eq. (40) becomes

\[ y_n = (1 + K) \cdot x_n + (\alpha + K \alpha - K) \cdot y_{n-1}. \]  

(45)

Furthermore, if it is assumed that \( x_n = X \) for every trial (see Eq. (29)), the asymptotic solution for the Eq. (45) coincides with the one obtained in the absence of the contrast effect (see Eq. (29)). This last result is motivated by the fact that during successive trials the contrast effect decreases, since the expected outcome (which is signalled by the UCS perception before the UCS active elicitation) approaches the experienced outcome (i.e., both the error signal and the actual error signal tend to zero over successive trials). Note also that the contrast effect could be negative, for instance, if the experienced outcome is smaller than its expected counterpart a response inhibition occurs. For this reason, if the active elicitation \( x_n \) drops to zero, the response decreases faster than in the case in which no contrast is considered, since the term \((\alpha + K \alpha - K)\) in the second side of Eq. (45) is smaller than \( \alpha \) (see Eq. (23)).

Finally, we argue that, if the contrast effect and the effect of the excitation decay are included in our discrete-time model (see also the classical conditioning model in Section 6.4), such a model should also be able to justify the spontaneous recovery effect [36], which could occur after a classical conditioning extinction. This phenomenon, which consists in the possibility of experiencing a conditioned response some time after a complete conditioned extinction, cannot be described in terms of the Rescorla-Wagner model [36]. Moreover, we argue that the passive residual response due to a contrast effect (e.g., an inhibitory response due to the lack of an expected UCS elicitation) is able to counteract the effect of a residual conditioned Pavlovian response, which, in turn, it can not be detected. For this reason, after the dissipation of a contrast passive response, the conditioned reflex can be observed again. Our viewpoint is partially supported by the fact that spontaneous recovery is stronger when conditioning extinction occurs through massed trials (i.e., in the presence of a small ITI, which are known to enhance contrast effects) and weaker when extinction occurs through widely spaced trials (i.e., in the presence of a larger ITI which determines a smaller contrast effect) [165].

4. Misattribution of a source of stimulation and evaluative conditioning

When a source of emotional stimulation elicits a subject, the process of encoding emotional memory starts; this involves various interactions between the amygdala and the hippocampus [113]. This encoding results in the processing and storage of different pieces of information, such as contextual information, the elements determining internal states and the elicited response. Generally speaking, the hippocampus (and, in particular, the dentate gyrus, DG) encodes contextual information, whereas the BLA encodes emotional valence and unconditioned stimulus representation [54, 55]. The encoding of emotional memory requires that the source of stimulation is correctly detected and attributed. When an emotional response due to a source of stimulation is attributed to a wrong source, an event of source misattribution occurs (e.g., see [31, 32, 33], and references therein). Note that misattributions may result either from conscious, accessible and measurable controlled processes, or from spontaneous, inaccessible, automatic processes [30, 34]. In the last case this phenomenon is called implicit misattribution (e.g., see [30, 79, 14]). A quantitative description of the source misattribution phenomena can be developed on the basis of our dynamic model; moreover, the new results about this topic sheds new light on the problem of evaluative conditioning (EC). Both these issues are illustrated in the remaining part of this Section.

4.1. Source misattribution: a quantitative analysis

Let us focus again, like in the previous Section, on multiple trials of the interaction between a given aource and a subject and assume a discrete-time scale in our analysis. In a generic trial one of the following mutually exclusive events

\[ y_{UCS} = X + K \cdot X, \]  

(44)
might happen: 1) the elicited response is correctly attributed to the source of stimulation, so that the emotional reactive response is computed and coded according to Eq. (27); 2) no source of stimulation is identified and, consequently, no reactive response is encoded and associated with the source; 3) the elicited response is misattributed to another (others) source(s) of stimulation. In the following we focus on the last event and assume, without any loss of generality, that the misattributed source of stimulation is initially neutral (i.e., it does not elicit an active or a reactive emotional response). Actually, this event encompasses the following three mutually exclusive cases:

a) The misattribution occurs in the presence of an active response; for instance, this occurs when an hidden active source of stimulation (e.g., the hidden administration of a given drug able to elicit an emotional component) is misattributed to another insignificant source of stimulation.

b) The misattribution occurs in the presence of a residual (i.e., passive) response decay only (in other words, no active or reactive responses are elicited); in this case the misattribution trial follows the elicitation trial and occurs during the excitation decay.

c) The misattribution occurs when a purely reactive source of stimulation is eliciting the subject, so that the associated response is purely reactive.

If the misattributed source of stimulation is not neutral but elicits a response, the response elicited during the misattribution process will result from the superposition of the actual source response with the previous non-attributed emotional state [28]. For this reason, in this case the previous non-attributed emotional state “energizes” the actual source.

In the following the above mentioned three cases are analysed in the framework of the dynamical model developed in the previous Section; moreover, it is assumed that misattribution always occurs in the first trial and that the previous reactive response is equal to zero (i.e., \( y_0 = 0 \)).

**Case a): Misattribution occurring in the presence of an active response.**

In this case, the response in the first trial is only due to the active component (i.e., to \( X \); see Eq. (27)) elicited by a non-attributed source of stimulation (e.g., an hidden administered drug). Consequently, the error signal in the first trial, denoted \( e_1 \), is equal to \( X \) and the corresponding reactive component (expressed by \( \alpha \cdot X \)) is coded for the new misattributed source of stimulation. If the original (i.e., true) source of stimulation ceases to actively elicit the subject in the following trials (i.e., the physical active component becomes zero), a negative error signal is computed. In this case, after repetitive exposures of the misattributed source without active elicitation, the emotional response asymptotically tends to zero (according to a mathematical law similar to that expressed by Eq. (36)).

**Case b): Misattribution occurring in the presence of a decaying residual response only.**

This case is known in literature as transfer paradigm (described in the Hullian drive theory [92]) or excitation transfer [166, 28, 29], and refers to the influence of a prior episode of arousal on subsequent emotional responses. In this case, since environmental elements about the actual source of a residual arousal are missing, such an arousal is misattributed to a subsequent stimulus; this may result in an intensification of the subject’s emotional response to the new stimulus (see [166] and references therein). In this case, in the first trial the registered response is due to a passive (residual) response only, which is denoted \( \xi \) in the following. Consequently, the error \( e_1 \) in the first trial is equal to \( \xi \) and the reactive response stored for the misattributed source is equal to \( \alpha \cdot \xi \). Moreover, if the subject is elicited by the misattributed source in a successive trial, the corresponding reactive response is given again by \( \alpha \cdot \xi \), which is smaller than what was expected for that source (i.e., \( \xi \)), so that a negative error signal is computed. Therefore, if further trials occur, the emotional response asymptotically tends to zero, similarly as in the previous case.

**Case c): Misattribution occurring in the presence of a purely reactive source of stimulation eliciting the subject.**

In this case, the response in the first trial (when the misattribution is occurring), called \( i_U \), is due to a purely reactive response elicited by another unrevealed source (e.g., a subliminal emotional stimulation [162, 119, 167]). Hence, the response attributed to the new source (because of the misattribution) is equal to \( i_U \), which, in this case, is exactly what the amygdala is eliciting, so that the error \( e_1 \) in the first trial is equal to zero (i.e., the elicited response coincides with the expected response). Hence, during the second trial, the exposure to the new source determines the reactive response elicited by the amygdala during the first trial (\( i_U \)); furthermore, since the contribution due to the error signal is equal to zero, the overall response remains equal to \( i_U \). For the same reason, the response remains constant during the successive trials. These results, that hold if habituation or mere exposure phenomena [168] are neglected, show that an inextinguishable (i.e., not vanishing through repetitive trials of source perception) reactive response can be obtained through a complete misattribution of a purely reactive emotional response. Note that, generally speaking, a source of stimulation is expected to elicit an active component too, and when this active component is no longer present, a negative error signal drives the response extinction through repetitive exposures, as illustrated in the Section 3.2.2. On the contrary, our mathematical results show that, if the stored response associated with a stimulus is purely reactive (i.e., no active component is expected), the error signal is equal to zero in each trial, because the reactive response corresponds to the expected response; for this reason, no updating of the emotional reactive response occurs. A concrete example of such effect is the EC through implicit misattribution [79, 33] (see Section 4.2).

Let us define now a non-active stimulus as a stimulus eliciting a reactive (or null) response only; given this definition, our
main finding can be summarised in the following corollary.

**Corollary 1**

If a purely reactive emotional response is attributed to a non-active stimulus, this stimulus becomes a resistant-to-extinction source of reactive emotional stimulation.

Corollary 1 allows us to justify the inextinguishability of EC due to implicit misattribution (see [79, 33] and references therein), and could suggest a mechanism for other forms of resistant-to-extinction responses. In practice, through the repeated application of Corollary 1, in each misattribution stage the reactive response is given by the sum of the previous reactive responses evoked by the considered stimulus (because of the resistant-to-extinction nature of the reactive stimulus itself) with the actual misattributed reaction (in other words, the reactive response is cumulative). This could explain why an emotional additive increase can be obtained naturally in every day life through the so called incubation effect [68, 19] (note that even a summation of different reactive sources could be misattributed to one single target stimulus). More specifically, some neurotic individuals can reexperience a trauma in their minds, or people can misattribute some background emotional states (such as mood and others irrelevant and disconnected emotional events) forward a target stimulus, which, in turn, becomes able to elicit a stronger arousal at every misattribution or rumination stage [19].

Furthermore, Corollary 1 provides theoretical basis for the development of purely reactive emotional stimuli: in principle, an additive and a resistant-to-extinction emotional reaction can be obtained in a controlled environment, through repetitive interactions between a subject, a non-detectable reactive emotional source (the misattributed source) and a target stimulus (to be attributed). In practice, a confounding source (or a compound of confounding sources) of reactive stimulation could elicit a subject in the presence of a target stimulus, which has to become the attributed source of stimulation. Moreover, through repetitive elicitations, the target stimulus is expected to produce an inextinguishable and increasing reactive response. One method to obtain a compound of confounding reactive sources is to develop a subliminal masked exposure of an emotional and sufficiently strong aroused stimulus [1, 169, 170, 2, 90], while a target stimulus has to be clearly perceived by the subject. To this aim the confounding reactive stimulus has to elicit the same emotional components as the target, in order to obtain the superposition (i.e., the algebraic sum) of multiple contributions, i.e. the process we call implicit accumulation effect. We believe that further research activities are needed to understand how to construct and optimize a suitable target stimulus (which must be easily attributable by a subject in relation to the emotional induced response) and which sensory elements (e.g., tactile, visual or auditory elements) should be included, in order to optimize the effect. Furthermore, it is important to consider that a misattribution mechanism requires that the response evoked by the UCS could feasibly have arisen from the target CS, so some minimal degree of feature matching is a necessary condition; without it, source confusion (and misattribution) is unlikely to occur [33].

Finally, it is important to point out that a practical exploitation of our results could be represented by the development of novel methods to mitigate an undesired emotional reaction. In fact, in principle, an undesired reactive response could be weakened through the misattributed elicitation of an opposite valenced reactive response (for instance the pain perception can be weakened through the stimulation with rewarding reactive stimulus, or it can enhanced through the stimulation with anxiety related or emotionally threatening reactive stimulus [12, 13, 14]), or through a reactive inhibition. This might represent a valid supporting tool for treating certain psychopathologies for which the mere exposure treatment, even if coupled with drug administration, could fail to extinguish an undesired emotional reactive response (see Section 8.1).

### 4.2. Evaluative conditioning through implicit misattribution

As already mentioned above, the EC phenomenon represents the formation (or change of the valence) of a stimulus, called CS, originating from a prior pairing of the CS itself with another stimulus, called UCS [171, 75, 73, 172, 79, 33]; unlike Pavlovian conditioning, a CS response acquired through EC seems to be resistant to extinction [72].

In recent years various research activities have been devoted to investigate the role played in EC by the awareness of contingencies between a CS and its paired UCS [71, 171, 75, 79, 173]. In particular, experimental evidence illustrated in [79] leads to the conclusion that the EC occurrence can be justified by different mechanisms, like classical conditioning (and, consequently, the awareness of CS-UCS contingencies) and implicit misattribution (in this case, awareness is not required). In the same reference it is also shown that sequential CS-UCS presentations are subject to UCS revaluation, retroactive inference from subsequent learning and contingency awareness (these phenomena are typically related to classical conditioning); on the contrary, a simultaneous CS-UCS presentation, which, generally speaking, prevents awareness and facilitates the source misattribution, can produce EC effects which are robust against all the factors mentioned above. Moreover, in [33] it is shown that, according to the implicit misattribution model, responses to UCSs can be misattributed without awareness to the CS, and that the implicit misattribution depends on source confusability, in other words the subject has to confuse which multiple coocurring stimuli in her environment is evoking the evaluative response. Furthermore, manipulations of the variables related to the potential for the misattribution of an evaluation, (i.e., the source confusability) show that greater EC occurs with an higher degree of confusability [33]. Hence, as already discussed in the previous Section, the inextinguishability of the CS valence in EC phenomena due to implicit misattribution can be explained in terms of Corollary 1; in other words, it is motivated by the fact that the UCS (e.g., a reactive stimulus such as an emotional picture) behaves like a purely reactive source of stimulation, and the reactive outcome is attributed
(at least partially) to the CS, so that the response stored and expected for that stimulus is purely reactive (see also the Case c in the Section 4.1 for the quantitative analysis). This result is also supported by Baeyens and colleagues [171], who found that EC was not sensitive to the degree of statistical contingency between the CS and US, but EC should increased with the absolute number of pairings because each provides an opportunity for misattribution, and such misattributions could act cumulatively [33]. It is worth mentioning that EC could also be determined by other mechanisms, or by the combinations of different mechanisms [33], such as, classical conditioning, the formation of particular beliefs about the CS and conceptual recategorization of the CS [33].

5. Differences and relations between the implicit emotional model and the predictive coding model

The predictive coding (or active inference) version of interoception [150] [151] [152], described in Section 2.2, cannot be applied to implicit emotional learning because the theorem derived in Section 3.2.1. In fact, since the prediction signal (which coincides with the reactive response in predictive coding) and the active (bottom-up sensory) elicitation sum up, the prediction response would increase indefinitely over successive trials. One might argue that the precision associated with the error signal originating from the reactive (self-made) emotional response should be reduced by attentional mechanisms, like in active inference in primary motor cortex (M1), where the gain (or precision) associated with the sensations originating from the self-made action are reduced [150] [174] (see also the corollary discharge; e.g. [175]). Nevertheless, this cannot occur within the emotional system, since the reactive and the active emotional responses are indistinguishable and, for this reason, add up in algebraic sense, as shown by the experimental evidence described in Section 1.3.

Despite this, we argue that the predictive coding principle could be applied under the assumption that different hierarchical neural networks operate in succession, and others in parallel, during implicit emotional learning. More specifically, if an active stimulus elicits a given subject, a first neural network, describing perception, determines which is the most probable stimulus responsible for the elicitation (i.e., the source attribution process) through the maximization of the Bayesian posterior probability distribution (or the free energy minimization, which leads to the “surprise” or entropy minimization [43] [44]), then the network for the computation of the expected outcome (managed by the OFC) interacts with the network which computes the updating of the reactive responses (within the amygdala). However, our model provides a system level representation of implicit emotional learning and, for this reason, the details about the iterative computations (and messages passing) between neurons or between different neuronal hierarchical levels of the involved signals (such as error signals, expected outcomes or reactive responses, and the neural computations leading to source attribution) are behind the scope of our analysis. For instance, our system-level model assumes that a distributed network computes error signals without entering into the details of such a computation; hence, for example, our model cannot be accounted for phenomena or physiopathologies originating from a defect in the error computation processes (such as a pathological dopamine system unable to properly compute the precisions associated with the error signals). Nevertheless, our model can specifically predict phenomena and pathologies originating from system-level problems (in other words, it provides a macro-level perspective). Furthermore, our model does not describe the computations leading to source attribution, instead it describes the effects originating from the cases in which, during a stimulation, a stimulus is correctly attributed, misattributed or even not attributed. Finally, it is worth mentioning that an important similarity between the proposed implicit emotional learning model and the active inference model is represented by the fact that the brain can experience a reactive stimulation (i.e., a prior bayesian belief, in the active inference terminology) shaped by prior experiences and learning, even if the stimulus does not actively elicitate the subject. However, it is important to stress out that in our model the reactive response is differentiated from the expected outcome, which represents a value (more precisely a function over internal physiological states) of the elicitation that the brain (OFC) expects to experience from a given UCS. In other words, expecting a given response does not coincide with the “self-induction” of that response (see the Theorem in Section 5.2.1). Furthermore, a variation of the active (sensory or bottom-up) stimulation leads to an update or modulation of the expected outcome and of the reactive emotional response associated to the given stimulus.

6. On the emotional learning in classical conditioning and UCS evaluation

In this Section the intrinsic differences and the relations between the mechanism of learning in classical conditioning and that previously described for UCS revaluation learning are illustrated. Then, it is shown that the Rescorla-Wagner equation for classical conditioning represents an approximation of a specific case of emotional learning, since it can be derived from our model, exploiting the stochastic Hebbian plasticity rule [56] [57] [58] [60] [61] and taking into account specific approximations.

6.1. Introduction

In classical conditioning a CS, which is usually a neutral/innocuous stimulus like a sound or a neutral visual cue, is paired with a source of stimulation (e.g., an electric shock or food), which is called UCS. Through repeated CS-UCS pairings the CS can elicit a CR, called unconditioned response (UCR), which is often similar to the response aroused by the paired UCS [16] [17] [15]. When the UCS represents an aversive stimulus, the CS-UCS pairing phenomenon is called Pavlovian fear conditioning [16] [17]. In fear conditioning with humans, an indirect estimate of the autonomic CR can
be obtained measuring the changes in skin conductance level (SCL), i.e. the so called skin conductance response (SCR). Note, however, that in the analysis illustrated in the previous sections, the UCR (i.e., the response elicited by a source of stimulation) is not simply represented by indirect measurements, such as SCR or the degree of salivation [15]. In fact, it represents the response associated with the brain neural populations elicited by the UCS and, consequently, includes both non-emotional and emotional components. More specifically, the UCR consists of a reactive response component \( y_{rem} \), a component due to the active (physical) stimulation of emotional brain areas \( y_{rem} \); see Eq. (3) and a contribution due to non-emotional stimulation \( y_{ne} \). For this reason, the SCR acquired during a specific UCS stimulation, like an electric shock delivery, represents only an indirect and correlated measure of the full response \( y \) expressed by Eqs. (12).

### 6.2. Different emotional learning mechanisms: for a primary stimulus (UCS) and for a stimuli association (CS-UCS)

Even if both a CS and the paired UCS could be able to eliciting the same emotional reaction under some circumstances, we argue they are qualitatively different entities and, most important, they might be learned through independent mechanisms. In fact, on the one hand, through classical conditioning, which represents the learning of stimulus contingencies, a CS acquires the capacity to elicit a response because it is able to signal a likely occurrence of the UCS elicitation. On the other hand, during implicit emotional learning (or UCS evaluation), an element acquires the capacity to elicit a response because of a direct attribution of the outcome forward that element (i.e., the UCS). Furthermore, the UCS outcome revaluation (i.e., inflation and deflation) is also driven by implicit emotional learning.

Our claims are supported by various results available in the literature [19, 20, 21, 18, 22]. In particular, [18], on the basis of the results of various experiments in which inflation (UCS increase) is performed after conditioning, came to the conclusion that organisms form memories of a given UCS independently of associative connections with a CS. Furthermore, in [22], it is shown that the automatic response associated with a UCS (SCR) changes through the revaluation of the UCS itself in the absence of a variation in the probability of the CS-UCS contingency. In [20], it is shown that a UCS inflation, even during trials of conditioning extinction, results in a larger CR. In [19], starting from contemporary models of Pavlovian conditioning in humans, it is inferred that the processes of CS-UCS association and UCS revaluation may be largely independent. In particular, UCS revaluation can be obtained in different ways (including verbal suggestions and cognitive processes) and this modifies the strength of a CR in the absence of any change in stimulus contingencies. Moreover, in the experiment reported in [21], thirty subjects were randomly assigned to the inflation (UCS increase) or the deflation (UCS decrease) group, after a common classical conditioning acquisition procedure (i.e., after experiencing the same UCR strength). During the test session the indicators of the CR intensity were SCRs and subjective aversion to the conditioned stimulus (CS). The main results obtained in that case can be summarized as follows: a) the CR strength measured by SCR was increased by the UCS inflation and decreased by the UCS deflation; b) the subjective aversiveness to the CS was not sensitive to both manipulations of the UCS intensity.

All the above mentioned results lead us to the following conclusions: a) UCS revaluation occurs out of classical conditioning and, implicitly, is able to modify the CR; b) the strength of an autonomic CR might be influenced by the subjective revaluation of a UCS, even when the CS-UCS contingency remains the same; c) the probability of a CS-UCS contingency (i.e., the CS prediction of the occurrence of a UCS) through Pavlovian conditioning is independent of the UCS revaluation. For these reasons, the UCS evaluation (and revaluation) cannot be described by classical conditioning, so that a specific model (i.e., a model for implicit emotional learning or UCS revaluation, like that illustrated in Section 3) is necessary. These concepts are summarized in Fig. 4, where the CS representation is related to the UCS representation through a connection whose strength is proportional to the probability (or the belief) of stimulus contingency, i.e. to the probability \( \text{Pr}\{\text{UCS/CS}\} \) of the UCS stimulation conditioned on the CS perception (briefly, the CS-UCS contingency probability updated through the classical conditioning learning). It is worth noting that the probability \( \text{Pr}\{\text{UCS/CS}\} \) can be increased through repetitive CS-UCS pairings or reduced through a CS exposure without UCS elicitation. These probability/belief updatings reflects the CR during testing, according to the classical conditioning learning (e.g., through the results given by the Rescorla-Wagner equation (27)). Note also that, in Fig. 4 the connection between the UCS and the corresponding reactive response (\( \text{IR} \), see Eqs. (10-11)) is highlighted.

The schematic representation illustrated in Fig. 4 is in agreement with various recent results available in [54] and [55]. In particular, the experimental results shown in [55] have evidenced that the hippocampal engram memory (which codes the contextual CS) is neutral and could freely associate with either positive or negative emotions (through the UCS representation) coded within the BLA. The connection between the contextual CS coded in the DG in the hippocampus and the UCS coded within the BLA could also be switched by optogenetic technology manipulation. In practice, a CS-UCS connection (denoted CS-UCS #1) can be switched to another CS-UCS connection (denoted CS-UCS #2) of opposite valence with respect to the first one (e.g., from a fear emotional response to a reward emotional response). Indeed, the optogenetic reactivation of the DG engram-bearing cells during the presentation of a UCS having valence opposite to the original one strengthens the connectivity of these DG cells with a new subset of BLA neurons, while weakening the connections established during the original learning [55]. From these results it can be inferred that the CS memory engram is neutral and that a CS can elicit an emotional reaction through the
connection to an UCS in the BLA. Additional results about the effects of optogenetic manipulation are illustrated in [54], where it is shown that the projection of a CS representation onto a UCS ensemble in the BLA is required for the expression of a learned behavior, and that a CS (e.g., auditory or olfactory) activates an UCS representation in the BLA to generate a learned behavior.

On the basis of our previous analysis we can state that a CS elicitation, in turn, arouses a UCS reactive response \(i_R\) through a probabilistic (or belief) connection; furthermore, the value of the associated probability (or belief) \(\Pr\{UCS/CS\}\) is determined by classical conditioning (or even by optogenetic manipulations [55]). For instance, at the end of a conditioning acquisition, the probability \(\Pr\{UCS/CS\}\) is close to unity, since a CS predicts almost certainly the UCS "imminent" elicitation. In this case a trial test produces a CR expressed by \(\Pr\{UCS/CS\} \cdot i_R \approx i_R\) and, consequently, given by \(i_R\), which represents the reactive response, determined by the amygdala reaction computed and stored within the amygdala itself for the considered UCS (see Eqs. (10-11)). When the value of \(\Pr\{UCS/CS\}\) is between zero and unity, the CR can be computed, for instance, through the Rescorla-Wagner equation [57] and has to equal the product \(\Pr\{UCS/CS\} \cdot i_R\). Therefore, at the end of a conditioning acquisition process, there is no real difference, in terms of emotional reactive response, if the subject perceives a CS alone or the paired UCS alone (note that the term “response”, and not “behavior”, is adopted here, since different intensities of the components of the same emotional response may lead to distinct observable behaviors; this issue is discussed in more detail below). This is exemplified by the case of the dog observed at the end of a conditioned acquisition in the conditioning experiments performed by [15]: in fact, as far as the degree of salivation (i.e., the behavioral outcome due to the reactive response \(i_R\)) was concerned, perceiving the food (UCS) or perceiving the bell (CS) which signalled the incoming food, did not really make any difference (at least during the first trial, before the eventual extinction process). Note that this does not mean that the CS becomes a substitute of the UCS, as initially supposed by Pavlov in the so called “Stimulus-Substitution Theory” [109], but that the CS triggers the reactive response \(i_R\) through the elicitation of the representation of the paired UCS within the BLA (such an UCS elicitation through the CS perception could be “partial” or “total” depending of the CS-UCS connection strength; see Fig. 4 and [55]). In fact, as already stated in Section [1] a CR and the corresponding UCR are not identical, and only in specific conditions they could be similar (in addition, a UCR, unlike a CR, may involve an active component, \(X\)). In practice, the CR mimics the emotional components elicited by the corresponding UCR (see Section [1,3] and Remarks [5] and [2]) but, generally speaking, with a lower intensity, since the emotional system has to be stable (i.e., \(|\alpha| < 1\) is required; see H.6 in Section [3] and because the active component \(X\) is no longer present in a purely reactive stimulation. These considerations could be useful to explain the fact that, in specific circumstances, the CR might represent an opposite behavioral response with respect to the original UCR; for instance, one unconditioned response to morphine is represented by the reduced sensitivity to painful stimuli; however, the conditioned response to stimuli associated with morphine is represented by an increased sensitivity to painful stimuli [159]. Phenomena like this could be explained considering that, generally speaking, the degree of elicitation of a neuronal population (or the quantity of a specific type of released neurotransmitter), due to a CR is smaller than the original one generated by the corresponding UCR (e.g., an active morphine administration) because of the above mentioned reasons. In particular, in neuropharmacology it is well known that an excitatory effect is commonly observed with low concentrations of certain depressant drugs (e.g., alcohol, morphine, general anesthetics) because of either the depression of inhibitory systems or a transient increase in the release of excitatory transmitter (note that an excitatory state occurs only with low concentrations of the depressant). Consequently, within the complex CNS structure, different doses of a specific receptor agonist or of a specific neurotransmitter (i.e., different intensities of a specific component of a response) could lead to very different (even opposite) observable behavioral responses (see [84] for an exhaustive review about this topic).

Generally speaking, the typical scenario of a laboratory, where the UCS is represented by an electric shock device, which is permanently connected to the subject who does not know when the electric shock will be effectively delivered (unless signalled by the paired CS), leads to the impossibility of observing the emotional reactive response \(i_R\) when the source of stimulation (i.e., the UCS electric shock device in the above mentioned scenario) is perceived by the subject. On the contrary, we argue that, if the electric device is repeatedly connected to the subject and disconnected from him/her in each trial of electric stimulation, the subject perception of the connected UCS device will elicit \(i_R\) exactly as the CS perception does (after a conditioned acquisition for the CS). One may argue that, in this case, the CS is represented by the

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**Figure 4:** Schematic representation of the connections between a CS, the paired UCS and the reactive response \(i_R\) associated with the representation of the UCS itself. The reactive response \(i_R\) is determined by the UCS revaluation learning, instead the connection strength between CS and UCS \(\alpha_{CS-UCS}\) is determined by classical conditioning learning. Note that this schematic representation is in agreement with the experimental results shown in [54][55].
electric shock device and that the electric shock delivery represents the UCS. Note, however, that in the considered scenario the device represents a primary source of direct stimulation (i.e., the UCS), whereas the shock delivery represents the physical elicitation of that source, which supports the active elicited response (i.e., the term $X$, see Eq. (27), or the term $Y_{stim}$, see Eq. (5)). Note also that the same considerations can be expressed when the primary stimulus is represented by food [15], but do not hold for a neutral CS (e.g., a neutral sound) signalling the UCS, since, in the last case, the CS cannot sustain a direct physical stimulation.

6.3. Conceptual difference between encoding a stimulus as a primary stimulus (UCS) or as a conditioned stimulus (CS)

Another important issue related to the differences in the learning mechanisms analyzed in the previous Section concerns the regions of the brain in which a CS and a UCS are memorised. If a contextual CS is considered, the CS engram and the the associated UCS are stored in the DG and in the BLA, respectively [55]; however, it is still unclear if the same rule applies to any non-contextual CS. Note also that phylogenetic fear-relevant stimuli, which are sources of stimulation according to the definition provided in Section 1.2, are natively stored in the mammalian brain [2, 90].

In the following we summarise the most important experimental results which concern the subliminal elicitation of UCSs and the failure in subliminal elicitation of "previously-neutral" conditioned CSs. Then, some important conclusions about CS/UCS memorisation in specific regions of the brain are inferred from them.

Subliminal elicitation of UCSs - In various experiments accomplished by Öhman et al., the awareness of visual stimuli was blocked by means of backward masking [162, 176]. In this case a target picture, representing a CS, is presented in a short interval (lasting less than 50 ms) and is followed by the presentation of a masking picture having similar luminosity and colour features, and shown in the same area of the visual field [177]. The presentation of this masking stimulus interrupts the cortical processing of the target stimulus [178, 179]; hence, the target is invisible to the conscious and awareness of the subject [180]. Moreover, in these experiments snake- or spider-fearful subjects have been exposed to phylogenetic fear-relevant masked stimuli (snakes or spiders) and neutral masked stimuli (flowers and mushrooms). The acquired experimental results have evidenced that only the phylogenetic stimuli were able to elicit an automatic SCR response in phobic patients [90]. These findings agree with the hypothesis about amygdala functionality proposed by LeDoux [181, 126]. In fact, LeDoux has hypothesized the existence of a thalamic pathway to the amygdala; such a pathway would allow to automatically detect evolutionary prepared visual stimuli (like emotional faces, spiders, snakes, injuries). Note that this model is also supported by other results acquired by different researchers that have employed masking in normal participants [182, 170] or have observed brain activity in patients affected by cortical blindness [183, 184]. According to this model about amygdala functionality, the superior colliculus stimulates the pulvinar nucleus of the thalamus, which then arouses the amygdala [126, 183, 186]. This mechanism is also supported by various brain imaging studies, which show that masked facial stimuli activate the amygdala exactly as masked pictures of threatening animals (such as snakes and spiders) do [185]. This suggests that the salient features representing an aversive source of stimulation could be stored in the amygdala.

Failure in subliminal elicitation of “previously-neutral” conditioned CSs - Other experimental results available in the literature help us to understand what happens when a neutral stimulus (i.e., a CS) conditioned on an active source of stimulation (i.e., an UCS, like an electric shock) elicits a subject, and in particular, if the CS representation is stored in the same region as a phylogenetic aversive stimulus. Note that, from a supraliminal perspective, both a purely reactive UCS (e.g., a snake picture) and a previously conditioned CS (e.g., a neutral picture conditioned to an electric shock) are able to elicit a similar autonomic response, at least in subjects suffering from a phobia towards the phylogenic stimulus represented on the exposed pictures [20]. A more interesting case is that of subliminal perception, where only the sub-cortical thalamic-amygdala pathway is elicited because of the backward masking procedure described above. Various results, acquired by Öhman and Soares in experiments of differential conditioning, are available about this case [2].

In these experiments, a neutral stimulus, denoted CS+ (e.g., flowers or mushrooms) was paired with an electric shock UCS (i.e., an active source of stimulation) during the acquisition phase, and a different neutral stimulus, denoted CS-, was presented in the absence of the UCS. The results acquired during the extinction phase have evidenced that the conditioned CS+ was able to elicit a differential response (in particular, an SCR response different from the baseline level of the CS-response) only in the presence of supraliminal perception; on the contrary, no differential SCR response has been observed in the case of masked perception. This means that, unlike the case of a reactive UCS (such as spiders, snakes or angry faces), which is able to elicit an emotional reaction both through supralimnarily or subliminally perception [90], a previously neutral conditioned CS elicits an emotional response through supraliminal perception only. Therefore, the sub-cortical thalamic-amygdala pathway (i.e., the so called high road [126]) is unable to elicit a representation of the given CS; this representation, instead, can be elicited only through the thalamus-cortex-amygdala pathway. These considerations lead us to the conclusion that a CS representation might not be directly stored within the amygdala (or, in any case, not in the same region as an UCS representation) even if it predicts an aversive-related stimulus.

Finally, it is worth mentioning that the same conditioning paradigms have been used when employing biologically fear-related (phylogenetic) stimuli [2], angry faces [162, 187], and even ontogenetic pictures (i.e., pictures of cultural threats
such as guns directed toward a subject) for CS+ and CS−. In all the seen experiments, even if the employed CSs were conditioned stimuli, they were not neutral, since they represented reactive aversive emotional sources (i.e., reactive UCSs). This qualitative difference with respect to a neutral CS (i.e., to a CS not representing a reactive emotional source) reflects the different behavioral results provided by the considered experiments and, in particular explains, the fact that, even during the masked extinction procedure, the CSs+ have been able to elicit an emotional response through the sub-cortical thalamic-amygdala pathway.

The experimental results illustrated above have lead us to the following conclusions. It is likely that any representation of an emotional source of stimulation, such as an innate biological fear-related threat (in other words, a phylogenetic source) or a cultural threat (i.e., an ontogenetic source), is able to elicit an emotional response through the sub-cortical thalamic-amygdala pathway; hence, this source is expected to be stored in a rapid access site of the amygdala. On the contrary, in the case of classical conditioning, a previously-neutral conditioned CS is unable to elicit a reactive emotional response through the thalamic-amygdala pathway; consequently, it should be stored in other regions of the brain or in a region of the amygdala different from that employed for primary stimuli. Therefore, which is the qualitative difference between a reactive UCS (e.g., an emotional picture) and a previous neutral CS conditioned through classical conditioning? Both UCS and CS are able to elicit similar responses supraliminarily, but such stimuli are stored in different brain regions. We argue that the main qualitative difference between these two cases is represented by how initially the stimulus has acquired the capacity to elicit an aversive emotional response, that is by how the stimulus has been encoded (as a primary stimulus or as a conditioned stimulus). In fact, a phylogenetic source might be innate and natively stored within the amygdala; moreover, an ontogenetic emotional source, such as a gun [1], might be acquired through learning mechanisms different from those of classical conditioning. It is reasonable to suppose that a generic UCS, like an electric shock device or a weapon, is acquired through an active and direct stimulation (or even cognitively, exploiting aversive experiences of other individuals through social fear learning [188] [189]; consequently, the corresponding outcome will be directly attributed to that active source. In brief, a UCS represents a stimulus able to directly elicit a response (i.e., it is encoded as a primary stimulus); on the contrary, a CS does not have such a capability and its role is limited to statistical signalling of an incoming UCS. We also argue that the experiments described above should also lead to similar conclusions if a new active source of stimulation (i.e., an UCS which does not represent a phylogenetic threatening stimulus nor an ontogenetic stimulus), experimentally generated, is adopted. In particular, the correctness of the last claim could be assessed by modifying the experimental procedure described in [1]; in particular, this would require the following two steps: a) introducing an additional phase in the experimental procedure described in [1], in order to generate (starting from a neutral stimulus) a newly ontogenetic source of stimulation for a group (through UCS evaluation), and a new conditioned stimulus for another group (through classical conditioning learning); b) analyzing the behaviors of the two different groups at the end of the learning procedure. We expect to find out that both groups will be able to show an emotional reaction (e.g., an SCR) through a supraliminal stimulus perception, whereas only the group who has encoded the stimulus as a primary stimulus (i.e., as UCS) will be able to show an emotional reaction through subliminal perception (i.e., through the thalamo-amygdala pathway). If such a result will be obtained, it will also definitively prove that the mechanism through which the aversive object has been encoded (i.e., through classical conditioning acquisition or by direct or implicit response attribution) makes the difference and determines the brain region in which the stimulus representation will be stored.

In the absence of further experimental results, we believe, on the basis of the existing literature, that the only reasonable claim that can be made about the nature of a coded stimulus, is given by the following remark.

Remark 6.

If a subliminally perceived cue elicits an emotional reaction, then this means the cue representation is stored within the amygdala and it represents a source of emotional stimulation (i.e., an UCS).

Note that this remark is useful when analysing experimental results in which a subliminally perceived stimulus elicits a measurable emotional reaction.

6.4. Derivation of the Rescorla-Wagner Equation for Classical Conditioning and a corrected formulation

In this section it is shown how the Rescorla-Wagner equation for CS-UCS Pavlovian conditioning can be derived starting from our model about the implicit learning of an UCS outcome.

Our derivation relies on the assumption that the CS-UCS synaptic connections are governed by the mechanisms of stochastic Hebbian plasticity [56] [57] [58] [59] [60] [61]. This hypothesis is supported by both some experimental results shown in [55] and [54], and other models relying on the fact that a CS-UCS pairing entails the Hebbian potentiation of the CS inputs onto the UCS representations in the BLA [190] [191] [125]. In practice, Hebbian learning is based on the idea that synapses between neurons being simultaneously active become stronger. Consequently, “neurons that fire together could wire together” through an increase in synaptic efficacy mediated by long term potentiation (LTP, see [192]); on the contrary, a decrease in synaptic efficacy is mediated by long term depression (LTD) [193]. In particular, in [55] it is shown that the optogenetic reactivation of the DG engram-bearing cells coding a contextual CS, during the presentation of a new UCS having valence opposite to the original UCS (which was previously paired with the CS itself), strengthens the connectivity of these cells with a new subset of the BLA neurons, while weakening the connections established during
the original learning process. In other words, the simultaneous activation of a CS neural representation and of a new UCS strengthens a CS-UCS connection (through LTP) and, at the same time, weakens the connection (through LTD) between the CS and the previously associated UCS, which is not simultaneously active.

As illustrated in [194], the main task of the sensory system is to detect (and model) correlations through neuron firing, in order to exploit ‘suspicious coincidences’ in complex incoming information. These correlations may form the ‘objects’ or ‘features’ of the representations of any stimulus. After being detected by primary sensory areas, such correlations can be used for binding elementary features into more elaborate percepts. These binding phenomena are based on the concept of neuronal assemblies, which are usually defined as a group of neurons that transiently undergo synchronous firing [194, 59]. This transient synchrony could form the basis of a common input to later stages of integration, and so promote responses that are specific to a given ensemble of features [197]. These mechanisms rely on the fact that cortical neurons are very efficient at detecting correlations [198], as evidenced by computational models [199]. On the basis of these results it can be assumed that the representation of a CS and that of its associated UCS are formed by a neuronal assembly, which, in turn, is composed by cells assemblies representing specific features, and that connections between the CS and the UCS neuronal assemblies are established through Hebbian plasticity. The implications of this assumption are analysed in the following part of this Section, where a new sequence of trials, involving CS-UCS-subject interactions, is taken into consideration.

In these trials we assume that: a) the source of stimulation (UCS) has been acquired (i.e., properly coded as a source stimulus), and the emotional learning for the UCS source has encoded the reactive response \( i_R \) (which can be assumed to be equal to \( \alpha \cdot X \), with \( X \) representing the active induced response); b) a new cue (denoted CS) becomes paired with the source UCS in the first trial and, hence, an UCR associated with this UCS is elicited; c) in the first trial (i.e., for \( n = 1 \)) the strength \( \alpha_{\text{CS-UCS}}^{(1)} \) (ranging from 0 to 1, as evidenced below) of the CS-UCS connection (which, in turn, is related to \( i_R \); see Fig. 4) is equal to zero (in other words, no connection has been established before the start of the pairing process); d) the CS remains the same during all the considered trials; e) the UCS elicitation is signalled by the CS presentation only and not by the UCS presentation (e.g., the electric shock device is permanently attached to the subject and the shock delivery is signalled exclusively by the CS presentation). In the following analysis the response elicited by the CS, previously named CR, is denoted \( y_{\text{CS}} \). Then, in the first trial, an unexpected active UCS elicitation \( (X) \) generates the emotional response (see Eq. (30))

\[
y_{\text{UCS}}^{(1)} = X,
\]

which is what was expected for the source UCS. However, since the UCS occurs unexpectedly in time, a reactive contribution due to the contrast effect (see Section 3.5) should be produced (provided that no previous conditioned cue or direct UCS perception signals the active stimulation). Nevertheless, in Section 3.5 it has been shown that successive unexpected UCS elicitation does not entail the computation of an error signal, but certainly involve the elicitation of a reactive response due to the contrast effect, (quantified by the product \( K \cdot X \)). However, without any loss of generality, this reactive contribution can be neglected; furthermore, it can be noted that, during conditioning trials, this contrast contribution will vanish (since no “unexpected stimulation” occurs as the CS becomes progressively able to predict the UCS occurrence) and in place of this contribution the reactive response associated with the UCS \( (i_R) \) will be elicited as the CS is perceived (see Fig. 4). Even if no error signal has to be estimated for the given UCS source during the first trial, the contemporary presence of the CS during the UCS elicitation is sufficient to generate some synaptic connections between the representation of the CS and that of the UCS through the stochastic Hebbian rule; consequently, the strength of this link is potentiated through LTP. In the following it is also assumed that individual plastic synapses exhibit a binary behavior, since they can be in a depressed state or in a potentiated state. For this reason, the strength of a set of plastic synapses is quantified by the fraction of synapse population in the potentiated state [56, 57, 58, 60, 61]: this fraction is called synaptic strength and in the \( n \)-th trial is denoted as \( \alpha_{\text{CS-UCS}}^{(n)} \) for the set of synapses from the neurons representing the CS stimulus onto the encoding neurons for the UCS.

The mechanism through which plastic synapses learn cue-outcome contingencies through stochastic reward-dependent Hebbian modifications is illustrated in [61]. In practice, whenever the neurons encoding a given CS are simultaneously elicited at the activation of the UCS neurons, the plastic synapses from CS onto UCS in the depressed state make a transition to the potentiated state with probability \( \alpha_+ \) (this quantity is called potentiation rate); otherwise, if the CS is elicited without the contingent UCS elicitation, they make a transition in the reverse direction with probability \( \alpha_- \) (this quantity is called depression rate). It is worth mentioning that the parameters \( \alpha_+ \) and \( \alpha_- \) are often called learning rates [60] and that they depend on the firing rate of the postsynaptic neurons of the CS and on the state of the UCS (which is either active or non-active, that is eliciting or not eliciting UCS). The firing rate is low for the neurons which do not represent the perceived CS and, on the contrary, is high for the neurons encoding the CS. Hence, if the CS features are modified during the trials, the learning rates change too. In the following, however, we assume that the CS perception does not change during the trials (see H.4 in Section 3.5), so that the depression and potentiation rates remain constant (and different from zero). It is worth pointing out that the parameters \( \alpha_+ \) and \( \alpha_- \) are scalar quantities (each of them would be replaced by a vector having identical components if multiple emotional components were considered in the evaluation of the reactive response) and they are not related to the parameter \( \alpha \) defined
in Section 3.2 (i.e., $\alpha$ becomes also a vector, but with different components, if multiple emotional components are taken into consideration).

On the basis of the plastic probabilistic Hebbian rule illustrated above, in the $n$-th trial the synaptic strength is updated as

$$\omega^{(n)}_{CS-UCS} = \omega^{(n-1)}_{CS-UCS} + \hat{\alpha}_+ \cdot \left(1 - \omega^{(n-1)}_{CS-UCS}\right)$$  \hspace{1cm} (47)

during a conditioned acquisition (through LTP), and as

$$\omega^{(n)}_{CS-UCS} = \omega^{(n-1)}_{CS-UCS} - \hat{\alpha}_- \cdot \omega^{(n-1)}_{CS-UCS}$$  \hspace{1cm} (48)

during the extinction phase (through LTD). Note that the second term in the right-hand side of (47) describes the change related to the transition of synapses in the depressed state, since a fraction $\left(1 - \omega^{(n-1)}_{CS-UCS}\right)$ of synapses are potentiated with probability $\hat{\alpha}_+$. In the following, we assume, without any loss of generality, that the potentiation and depression rate are equal (i.e., $\hat{\alpha}_+ = \hat{\alpha}_- = \hat{\alpha}$). Then, during acquisition the synaptic potentiation of the CS-UCS connection can be evaluated as follows:

$$\omega^{(n)}_{CS-UCS} = \omega^{(n-1)}_{CS-UCS} + \hat{\alpha} \cdot \left(1 - \omega^{(n-1)}_{CS-UCS}\right)$$  \hspace{1cm} (49)

where the term $\hat{\alpha}$ denotes the learning rate, it represents a scalar value (or a vector with all equals components if more than one emotional components are involved in the reactive response $i_R$).

The synaptic strength $\omega^{(n)}_{CS-UCS}$ evaluated on the basis of Eq. (47) can be exploited to assess the response $y^{(n)}_{CS}$ to the presentation of the CS alone in the $n$-trial; in fact, the intensity of the CR is determined by the product of $\omega^{(n)}_{CS-UCS}$ with the reactive response $i_R$ associated with the paired UCS, i.e. by

$$y^{(n)}_{CS} = \omega^{(n)}_{CS-UCS} \cdot i_R.$$  \hspace{1cm} (50)

Then, substituting (47) in (50) yields the expression

$$y^{(n)}_{CS} = i_R \cdot \omega^{(n-1)}_{CS-UCS} + \hat{\alpha}_+ \cdot \left(i_R - i_R \cdot \omega^{(n-1)}_{CS-UCS}\right),$$  \hspace{1cm} (51)

which can be easily put in the form

$$y^{(n)}_{CS} = y^{(n-1)}_{CS} + \hat{\alpha}_+ \cdot \left(i_R - y^{(n-1)}_{CS}\right).$$  \hspace{1cm} (52)

It is easy to prove that the last formula coincides with the well known Rescorla-Wagner equation for Pavlovian conditioning [36, Sec 1, p. 365, eq. (1-2)],

$$V_{n+1}^x = V_n^x + \alpha x \beta_1 \left(\lambda_1 - V_{n}^x\right)$$  \hspace{1cm} (53)

for the case in which a single CS is considered; in fact, Eq. (53) is obtained from (52) if $\hat{\alpha}_+$ and $i_R$ are replaced with $\alpha \cdot \beta_1$, respectively, and $y^{(n-1)}_{CS}$ is assumed to represent the associative strength $V_{n}^x$. Note that the $V_{n}^x$ coincides with the term $V_{n}^x$ if a single CS (denoted $x$) exists; otherwise it represents the sum of the associative strengths of all CSs (including $x$).

Equation (52) deserves the following comments:

- If the overall CS is composed by $N$ distinct CSs (i.e., a CSs compound is considered), the synaptic strength between the compound and its paired UCS can be still computed on the basis of (49). However, in this case, a fraction of the overall strength should be associated with each component of the compound CS (such a fraction depends on the nature of the considered CS and its neural representation). Then, the contribution to the synaptic strength originating from the $k$-th component (with $k = 1, 2, ..., K$) can be evaluated as (see (47))

$$\omega^{(n)}_{CS_k-UCS} = \omega^{(n-1)}_{CS_k-UCS} + \hat{\alpha}_+ \cdot \left(1 - \omega^{(n-1)}_{CS_k-UCS}\right),$$  \hspace{1cm} (54)

where $\omega^{(n)}_{CS_k-UCS}$ and $\omega^{(n-1)}_{CS_k-UCS}$ represent the synaptic strength originating from the $k$-th CS and the overall synaptic strength originating from the compound, respectively. The last formula is motivated by the fact that each component shares the same full synaptic connection in reaching the neural representation of the stored UCS. It is also worth mentioning that multiplying both sides of (54) by $i_R$ produces

$$y^{(n)}_{CS_k} = y^{(n-1)}_{CS_k} + \hat{\alpha}_+ \cdot \left(i_R - y^{(n-1)}_{CS_k}\right),$$  \hspace{1cm} (55)

which represents the Rescorla-Wagner equation for the case of a CS compound [36 Sec 1, p. 365, eq. (1-2)]. From Eq. (55) it can also inferred that, if a CS or a compound have been conditioned to a UCS, so that their synaptic strength is equal to unity, when a new CS is added to the compound and paired with the given UCS no connection updating can occur, this phenomenon is known as blocking effect [36].

- From a mathematical perspective Eqs. (47) and (54) can be interpreted as simple rules for updating a conditional probability. In fact, the synaptic strength $\omega^{(n)}_{CS-UCS}$ can be interpreted as the probability (or the belief) of that the event of UCS elicitation occurs conditioned on the fact that the given subject perceives the considered CS.

- During the extinction process, the CS is repeatedly sent the UCS (with the term $\hat{\alpha}_-$). In turn, the reactive response $y^{(n)}_{CS}$ is added to the compound and paired with the given UCS by $i_R$ produces

- A straightforward consequence of Eq. (55) is represented by the fact that the maximum response obtained at the end of the conditioning process asymptotically approaches $i_R$, which represents exactly the emotional reactive response associated with the given source of stimulation (i.e., with the UCS). In turn, the reactive response $i_R$ can be increased (inflation) or decreased (devaluation) by UCS re-evaluation (e.g., through a variation of the active stimulation $X$), independently of the Pavlovian conditioning process.

- From the last point it can be inferred that, at the end of the acquisition of a CS-UCS Pavlovian conditioning,
there is no difference, in terms of emotional response, if the CS only or the UCS only is perceived in the absence of an active elicitation. This claim holds only in a supraliminal stimulus elicitation (see Section 6.3).

- Actually, since the CS-UCS connection strength increases during conditioning acquisition, the reactive response $i_R$ associated with the UCS should also become stronger. As a matter of fact, the emotional response $y_{UCS}^{(n)}$ in the $n$-th acquisition trial is due to the elicitation of the CS response (i.e., to $y_{CS}^{(n)} = i_R \cdot \omega_{CS-UCS}^{(n)}$ due to the partial activation of the UCS representation from the CS) and to the active UCS stimulation (i.e., to the term $X$ due, for instance, to an electric shock stimulation; see Eq. (46)), since the overall response is attributed to the UCS (which represents, unlike the CS, a direct source of stimulation). This last claim is supported by the experimental results obtained through optogenetic manipulations [55], which show that a memory engram coding a CS is “emotionally neutral” and could freely associate with different emotional responses through the corresponding UCS representations coded within the BLA. Therefore, it is easy to prove that the associated reactive component $i_R$ grows from the initial value $\alpha \cdot X$ to the value $\alpha \cdot (X + i_R^{(n-1)} \cdot \omega_{CS-UCS}^{(n)})$ because of the error signal (computed as the difference between the expected response $y_{UCS}$ and the experienced outcome). For these reasons, the process of implicit UCS inflation originates from an indirect contribution of the CS; in fact, the CS, signalling the UCS, is able to elicit the reactive response ($i_R$; see Fig. 4) associated with the UCS itself. Therefore, $i_R$ does not remain constant over consecutive acquisition trials, as assumed by the original Rescorla-Wagner model, but evolves according to the recursive equation

$$i_R^{(n)} = \alpha \cdot \left( X + i_R^{(n-1)} \cdot \omega_{CS-UCS}^{(n)} \right)$$

The last formula shows that the CR intensity influences the intensity of the unconditioned response. This result is in agreement with some experimental results [62] (see also [36] and articles therein), evidencing the dependence of asymptotic responding on CS intensity and US intensity; this represents one of the results unpredicted by the Rescorla-Wagner model [36]. It is also important to point out, however, that the changes of $i_R$ over successive trials could be really small, since the term $\alpha \cdot i_R$ in Eq. (56), which is smaller than $\alpha^2 \cdot X$ (since $0 < \omega_{CS-UCS} < 1$), is negligible with respect to the term $\alpha \cdot X$ (since $|\alpha| < 1$). Moreover, it is easy to prove that the asymptotic value of $i_R$ is $\alpha X / (1 - \alpha)$, which is greater than the initial value $\alpha X$. This leads to the conclusion that, since the value of the parameter $\alpha$ is influenced by the selected CS (if the impact of other factors, such as internal psychological states and the selected UCS, is deemed constant), different CSs may result in distinct asymptotic values of $i_R$ (and consequently of $y_{UCS}$; see Eq. (59)).

In summary, we propose to adopt a new classical conditioning model (valid for a discrete time scale), which encompasses the Rescorla-Wagner model and coincides with it only under specific conditions and restrictions. If a single CS is assumed to simplify the notation, this extended model is described by Eq. (47) when the given CS is paired with an UCS, Eq. (48) when the CS is presented alone, by Eq. (56), which has to be updated only in the CS-UCS pairing trials (since $i_R$ does not vary if the CS is presented alone), and, finally, by the formula

$$y_{UCS}^{(n)} = \omega_{CS-UCS}^{(n)} \cdot i_R^{(n-1)},$$

which expresses the $y_{UCS}$ updating.

Note that Eqs. (56) and (57) hold for $n \geq 2$ and that the initial conditions

$$\omega^{(1)} = 0 \quad (58)$$
$$i_R^{(1)} = \alpha \cdot X \quad (59)$$
$$y_{CS}^{(1)} = 0 \quad (60)$$

and

$$y_{UCS}^{(1)} = X \quad (61)$$

should be adopted when employing them. Our extended model provides a more general and accurate description of the emotional response during conditioning than the original Rescorla-Wagner model for at least three different reasons. First of all, it includes the contributions of both the active response ($X$) due to the elicitation of the physical UCS and the reactive response associated with the UCS representation within the BLA ($i_R$). Moreover, the recursive equations describing it are causal unlike those representing the Rescorla-Wagner model. Note that causality ensures that the currently computed response depends only on the past and present values of the stimulus and the response itself, but not on their future values; unluckily, this does not occur for the Rescorla-Wagner model since the evaluation of the current response requires the knowledge of the final asymptotic response (i.e., the term $\lambda$ in Eq. (53)), which is actually unknown to the brain. Finally, in our model the CS-UCS synaptic strength (associative learning) and the consequent UCS inflation are jointly considered: the model shows that classical conditioning learning influences the reactive response associated with the paired UCS; this is due to the misattribution of the CR contribution forward the UCS response. Hence, generally speaking, classical conditioning (i.e., the CS-UCS contingency or associative learning) and implicit emotional learning (i.e., UCS revaluation) are different learning mechanisms, but are closely related; in particular, classical conditioning, is able to indirectly determine the inflation of the UCS. It is also interesting to note that the asymptotic value

$$i_R^{(\infty)} = \alpha \cdot y^* = \frac{\alpha \cdot X}{1 - \alpha} \quad (62)$$

of $i_R$ provided by Eq. (56) is identical to the asymptotic reactive response resulting from implicit learning (see Eq. (30)).
This means that perceiving the source of stimulation (i.e., the UCS) or perceiving a signalling conditioned stimulus before the administration of the active stimulation (X) leads to the same asymptotic reactive response to the given UCS. However, the CS is only a means to strengthen the reactive response associated with its paired UCS, and classical conditioning represents a secondary (indirect) mechanism of emotional learning. In fact, the CS remains neutral [55] and the corresponding CR (i.e., \( Y_{CS} \)) is related to the synaptic connections between the CS representation and the UCS representation in the BLA, which, in turn, is connected to the reactive response which has been strengthened through UCS evaluation (because of a misattribution of the CR). It is also worth mentioning that direct implicit emotional learning (i.e., perceiving the UCS at every trial in place of the CS) allows to achieve the asymptotic response expressed by Eq. (52) in fewer trials than classical conditioning, since in last case the initial value of the synaptic strength \( \omega_{CS-UCS} \) able to elicit the UCS is smaller than unity and increases with trials.

It is also important to note that the proposed model is able to properly predict the fact that, if the CS is presented with a UCS of lower intensity (i.e., with an active component \( X' < X \)) during a generic trial, the reactive response \( i_R \) will be reduced by the influence of the error signal and, at the same time, the synaptic strength \( \omega_{CS-UCS} \) will be independently increased (or will remain constant if the asymptotic value has been already reached), since the synaptic connections between the CS and the UCS are still reinforced by the stimuli contingency (i.e., through associative learning, rather than through an error signal computation), even in the presence of a negative error signal. This result is in agreement with the experimental evidences shown in Section 6.2 note, however, that classical conditioning may determine, indirectly (through the elicitation of the reactive response and its misattribution forward the UCS), an error signal. It is also important to mention that classical conditioning experiments involving the contingency of two neutral stimuli (e.g., the pairing of a neutral tone and a neutral light; see [200] and articles therein) are in agreement with our results, since these show that the associative learning can occur with the pairing of two neutral (not emotional nor motivational) stimuli and, hence, with no computation of any error signal. From these results and considerations it can be inferred that the associative learning is not driven by the emotional system, on the contrary the implicit UCS revaluation learning is driven by the emotional system through the computation of the emotional error signals.

Finally, it is worth mentioning that the asymptotic reactive response associated with a given UCS cannot be increased by means of the conditioning acquisition of a new CS (called CS#2). In fact, if the CS#2 becomes paired with the UCS, in the initial trials the total outcome \( Y_{UCS} \) is smaller than the asymptotic value reached during the previous conditioning due to the first CS (CS#1); this is due to the fact that, at the beginning, the connection strength \( \omega_{CS#2-UCS} \) is smaller than unity. Therefore, in the initial trials a negative error signal will lower the reactive response \( i_R \) and, in the successive trials, a positive error signal will increase it again until the asymptotic value in Eq. (52) is reached.

### 6.4.1. Stochastic Hebbian rule in more complex pattern

When complicated CS patterns are conditioned to an UCS, Hebbian learning leads to self-organizing networks of synaptic connections. Such networks are able to represent complicated statistical regularities characterizing the considered environment [201, 61]; for instance, temporal CS-UCS relations can be also learned assuming the time variable (and temporal relations between stimuli) as a contextual CS [202]. We argue that, even during the implicit emotional learning of the UCS, the temporal trend of the stimulation represents an important contextual information, which might be coded and stored. In addition, we feel that more complicated Hebbian networks simultaneously taking into account several variables could be able to predict more sophisticated phenomena related to classical conditioning paradigms (e.g., second order conditioning [36]).

### 6.4.2. Conditioning to a reactive source stimulus

We argue that the following three possible events can occur when a CS is conditioned to a purely reactive UCS (i.e., an UCS for which no active component elicitation is expected, e.g., an emotional picture): 1) a simple associative connection CS-UCS is generated; 2) the CS is misattributed to be the source of the elicited response, so becoming a new (and independent) reactive source like the original UCS, so that a new reactive response, equal (but independent) to the original \( i_R \), is generated and associated to the CS; furthermore, this misattribution process could occur even during the presentation of the CS alone after conditioning, since the reactive elicitation equals to \( \omega_{CS-UCS} \cdot i_R \) (see Eq. (40)) could be misattributed forward the CS, in this case the reactive response being associated with CS corresponds to the quantity \( \omega_{CS-UCS} \cdot i_R \); 3) a combination of the previous two events happens. Moreover, if one of the two last mentioned events occurs, the conditioned CS will become an inextinguishable element of emotional reaction. In summary, we argue that a CS conditioned to a reactive UCS can become an inextinguishable reactive source of stimulation through different mechanisms; furthermore, a given stimulus could act as both a CS and a primary stimulus (UCS) at the same time, owning even opposite valenced potentials; for instance, the considered stimulus could be conditioned to an aversive UCS and, at the same time, could operate as an appetitive source of reactive stimulation.

### 6.5. On the conditioned inhibitor

In this Section the quantitative description of the so called conditioned inhibitor is developed on the basis of our theory. Operationally speaking, a conditioned inhibitor is a CS that passes a negative summation and retardation tests for conditioned inhibition (see [56] and articles therein). A CS is said to pass a negative summation test for conditioned inhibition if, when it is presented together with a conditioned excitor (i.e., a...
CS which has been paired with an UCS), it reduces the level of conditioned responding to that excitor that would otherwise occur. Moreover, a CS is said to pass a retardation test for conditioned inhibition if it requires a larger number of pairings with the UCS to become an effective conditioned excitor than those required if the CS were novel (i.e., if the CS had not undergone inhibitory training).

The most widely used method to create a conditioned inhibitor consists of not reinforcing the intended inhibitory CS in the presence of another cue that itself has been previously reinforced. Let us analyze the conditioned inhibition on the basis of the model we proposed for emotional learning.

One of the main assumptions made in the development of our model is that the functions involved in the computation of emotional reactions are time invariant (see Section 2.3). Under this assumption, if in a sequence of trials an UCS elicits a subject that always maintains the same internal physiological states (for instance, this case is exemplified by a dog that undergoes some conditioning trials, pairing a ring and some food, in which the intensity of its hunger remains the same), the only source of variation of the response (and of the expected outcome) is represented by the learning process. For this reasons, if the expected outcome for an UCS after the first elicitation trial is equal to \( X \), the reactive response associated with the UCS \( (i_R) \) is equal to \( \alpha X \) (see Eqs. (11, 19 and 20)), whereas the asymptotic value is equal to \( \alpha X / (1 - \alpha) \) (see Eq. (31)). Hence, in both cases, the reactive response \( i_R \) is expressed by

\[
i_R = \alpha \cdot y_{\text{expected}}. \tag{63}
\]

that is by the product of the parameter \( \alpha \) depending on the amygdala and the system chain functions (see Eqs. (19, 21)) with the expected outcome.

Generalizing the last consideration leads to the conclusion that, if the expected outcome for a specific UCS is also influenced by internal physiological states (and not only by the learning process), the reactive response associated with the considered UCS varies according to Eq. (63). From a neurophysiological perspective, we argue that the last result is motivated by the fact that the expected outcome and the biological functions determining the reactive response are controlled by the same internal physiological states (the degree of hunger in the example mentioned above). In practice, if food is presented to a satiated dog, the expected outcome (i.e., the rewarding response which is expected to occur) is very weak and, consequently, the associated reactive response will be weak too (e.g., a low degree of salivation will be observed).

However, this phenomenon does not lead to the extinction (or devaluation) of the UCS, since no error signal is computed; this is due to the fact that the expected outcome coincides with the experienced outcome (actually, in this case the dog could even avoid to eat and hence to experience the actual UCS elicitation). It is also reasonable to assume that, if a tone (CS) is presented together with some food (UCS) to a satiated dog, the CS-UCS association will be reinforced even if no emotional response occurs, and, in any cases, no CS extinction occurs. In other words, the perception of the UCS in a trial in which the internal physiological states of the subject lead to a low expected response (or even to a response equal to zero for the considered UCS) does not lead to the extinction of the UCS itself (nor to a correction of the reactive response through the computation of an error signal); furthermore, the paired presentation of a previously paired CS (excitor) with the considered UCS, during the aforementioned conditions, does not lead to extinction of the CS.

On the basis of the considerations illustrated above the following quantitative analysis of a conditioned inhibitor can be derived. We argue that an inhibitory CS (denoted CSI in the following) represents a stimulus whose neural representation is directly connected to an inhibitory reactive response, denoted \( i_{RI} \) (in other words, a causal attribution of the inhibitory effect forward the CSI occurs, so that the CSI is encoded as a source of stimulation by the emotional system). For instance, if an excitor CS previously conditioned with an electric shock delivery (characterized by the intensity \( X \)) is paired with a new CSI and, simultaneously, with an intensity of electric stimulation equal to zero, the CSI becomes a conditioned inhibitor and, more specifically, becomes connected to an inhibitory (e.g., negative) reactive response \( i_{RI} = \alpha (\neg X) \). If these considerations are generalized like in the previous case of an excitor source of stimulation (see Eq. (63)), the reactive response associated with the CSI is a function of the expected active stimulation which has to be inhibited, so that

\[
i_{RI} = \alpha (\neg y_{\text{expected}}). \tag{64}
\]

On the basis of the last result it should be expected that, if a new CS excitor (denoted CS2 in the following), predicting an UCS stimulation intensity weaker than the one predicted by the conditioned excitor which has been employed for the inhibitory conditioning (to obtain the CSI), called \( X' \) (with \( X' < X \)), where \( X \) represents the UCS intensity predicted by the conditioned excitor employed for the inhibitory conditioning, denoted CS1 in the following), or, equivalently, conditioned with the active stimulation \( X \) at a lower reinforcement rate (which results in the inequality \( \omega_{\text{CS2-UCS}} < \omega_{\text{CS1-UCS}} \)) and such that \( \omega_{\text{CS2-UCS}} \cdot X = X' \), is presented in compound with the CSI, the reactive inhibition becomes equal to \( \alpha (\neg X') \). More specifically, we argue that the CSI is able to proportionally inhibit only the CSs excitors signalling an expected excitatory outcome equal or smaller than \( X \); furthermore, the inhibition for expected outcomes greater than \( X \) remains equal to \( -\alpha X \), since the emotional system does not know how the inhibitor behaves for larger excitatory intensities.

Conversely, if during inhibitory conditioning the CSI has been obtained through a partial reduction of the active UCS elicitation, say from \( X \) to \( X - \Delta X \), the inhibitory reactive response is able to proportionally inhibit only an expected outcome comprised between \( X - \Delta X \) and \( X \), but not smaller than \( X - \Delta X \); this is due to the fact that the emotional system has learned that an outcome smaller than \( X - \Delta X \) represents a residual response which cannot be inhibited. For these reasons, for the last mentioned case, the reactive inhibition re-
response can be expressed as
\[ i_{Ri} = -\alpha \left[ y_{\text{expected}} - (X - \Delta X) \right] \] (65)
when \( X - \Delta X \leq y_{\text{expected}} \leq X \), and as
\[ i_{Ri} = -\alpha \cdot \Delta X \] (66)
when \( y_{\text{expected}} \geq X \), and, finally, as
\[ i_{Ri} = 0 \] (67)
when \( y_{\text{expected}} < X - \Delta X \).

From the above results, it is easily inferred that the CSI inhibitory effect depends not only on the expected excitatory outcome (i.e., \( y_{\text{expected}} \)), but also on the inhibition intensity and on the residual (not inhibited) response generated during the learning process (i.e., \(-\Delta X \) and \( X - \Delta X \), respectively). These concepts are summarised in Fig. 5.

It is worth noting that, if a previously conditioned CSI (which it has to remember is coded as a source of stimulation) is presented alone (i.e., without a paired UCS or CS), an extinction cannot occur since the expected outcome is equal to zero; consequently, the associated reactive response \( i_{RI} \) is equal to zero too (see Eqs. (64) and (67)) and no error signal is computed. Moreover, if the conditioning inhibition has occurred by pairing a CS excitor, the CSI and an UCS stimulation intensity lower than the one employed during CS excitatory conditioning, the presentation of the CSI alone can even strengthen its inhibitory effect. This is due to the fact that the synaptic connection between the CSI and the CS, which in turn is connected to the UCS representation (which is excitatory) is extinguished (or weakened) by repeated presentations of the CSI alone [65]. This effect, indeed, can also be obtained by extinguishing the CS employed in the inhibitory conditioning [65]: this experimental evidence supports the existence of the associative connections CSI-CS-UCS. For these reasons, the CSI could exert even an excitatory response when paired with a new CS2 (i.e., a different CS than that employed during the inhibitory conditioning) predicting (i.e., signalling) an excitatory outcome smaller than \( X - \Delta X \) (i.e., smaller than the residual excitatory response generated during the inhibitory conditioning) [64][65]. In fact, in this case, the reactive inhibitory response \( i_{RI} \) associated with CSI is equal to zero (see Eq. (67)), and the associative synaptic connections, generated during inhibitory conditioning, (CSI-CS-UCS) from CSI to CS (which in turn is connected to the excitatory UCS, which is associated with the reactive response \( i_{RI} \)) determine the reactive response equal to \( \alpha_{\text{CSI-CS}} \cdot \alpha_{\text{CS-UCS}} \cdot i_{RI} \) (if not extinguished through repeated presentations of the CSI alone, or through the original CS extinction). All the results illustrated above, namely the impossibility of extinguishing a CS inhibitor through its repeated presentation (or even its inhibitory strengthen), and the fact that the inhibitory effect of the conditioned inhibitor (CSI) depends on the expected outcome, on the UCS intensity decrease and on the residual (i.e., not inhibited) response generating during the inhibitory conditioning process (see Eqs. (64)[67]), are supported by experimental results illustrated in a growing body of literature (e.g., see [203][64][36][204][205]) and reviewed in [65]. It is worth to mention that the above obtained results cannot be predicted by the simple Rescorla-Wagner model [36], nor by the classical conditioning theory.

Finally, as in the case of some phylogenetic “excitatory” stimuli (i.e., prepared biological and evolutionary fear relevant stimuli, such as angry faces, spiders, snakes and others) which are coded in the mammalian amygdala since birth [164][1][2][90], we argue that also phylogenetic inhibitors could exist since birth; in particular, the food may represent a phylogenetic inhibitor of hunger (which in turn depends on physiological internal states). The last interpretation is in line with the observation that when the degree of hunger is relatively high, the reactive response intensity \( i_{RI} \) associated with food representations is particularly strong (see Eq. (64)). It is also important to note that the inhibitory effect originated by consuming food, could lead to a rewarding experience also because the contrast effect. This last consideration is supported by the Berlyne’s “arousal jag” theory [206], which postulates that a drop from unusually high level of arousal (which is experienced as unpleasant; represented by an high level of hunger in the example mentioned above) to a low level is associated with a feeling of pleasure [207]. This effect is described in more detail (also from a quantitative perspective) in Section 7.2.

7. Emotional Response Dynamics in Continuous Time Scale

In the previous Sections a discrete-time model has been developed for the evaluation of an emotional response in the presence of discrete time trials. In real word conditions, however, an emotional source might elicit continuously a subject in a certain time interval, so that the inter-trial interval \( T \) and the single discrete trial duration \( \Delta T \) tend to zero (in other words, a continuous elicitation can be seen as a series of an infinite number of discrete active elicitations, each of which has an infinitesimal time duration \( \Delta T \) and the temporal spacing between them tends to zero). In these conditions, the emotional response during the source-subject interaction cannot be deemed constant and the dynamics of the response variation have to be carefully assessed. Moreover, the reactive response is continuously updated driven by the continuous time counterpart of the error signal. In the following, the problem of developing a mathematical model for describing the continuous time evolution of an emotional response is investigated, in order to extend our previous findings to the continuous time scale. In principle, the theory of time scale calculus [157] should be applied to the considered problem in order to devise a solution independent of the involved time scale. In our analysis, however, a simpler approach, based on standard engineering methods, is developed.
Figure 5: Representation of the reactive inhibitory response $i_{Ri}$, associated with a conditioned inhibitor CSi (which is encoded by the emotional system as a source of stimulation rather than as a conditioned stimulus), over the expected excitatory outcome. In case a) the reactive inhibition associated with CSi is effective on all the expected excitatory responses greater than zero, since, during inhibitory conditioning, the emotional system learned that the CSi is able to completely inhibit the excitatory response. In case b) the reactive inhibition associated with CSi is not effective for expected excitatory responses smaller than the value given by $X - \Delta X$; this is due to the fact that the emotional system has learned, during conditioning inhibition, that excitatory intensities smaller than $X - \Delta X$ represent a residual response which cannot be inhibited. In both cases, a) and b), if the expected excitatory outcome is greater than $X$, which represents the greatest expected excitatory intensity generated during inhibitory conditioning, the $i_{Ri}$ coincides with the inhibitory intensity associated with $X$; this is due to the fact that the emotional system has not been trained for values higher than $X$. 
To begin, we consider the proposed discrete-time model (see Eqs. (24-25)) and, without any loss of generality, we focus on the model not accounting for the response decay over time nor for the contrast effect (the contrast effect will be discussed in Section 7.2). Moreover, from a quantitative perspective the effects of the exponential decay can be accounted for increasing the value of the parameter \( \alpha \). The so-called bilinear transform method [208] is applied to this model in order to derive a continuous time counterpart of it. It is not difficult to prove that this results in the differential equation

\[
y'(t) = x(t) \cdot \frac{2}{T(1+\alpha)} + x'(t) \cdot \frac{1}{1+\alpha} - y(t) \cdot \frac{2(1-\alpha)}{T(1+\alpha)} \tag{68}
\]

which describes the desired continuous dynamic model. In Eq. (68), the functions \( y(t), y'(t), x(t) \) and \( x'(t) \) represent the elicited response, its first derivative, the active stimulation and its first derivative over time, respectively; the parameter \( T \), which represents the ITI in the discrete time scale, in the continuous time scale model represents the sensory time discrimination threshold [209] (i.e., the smallest temporal interval for which the CNS neurons can discriminate between two distinct consecutive stimulations). Hence, the value of \( T \) depends on the involved perceptive modality (e.g., somatosensory stimulation, visual stimulation or acoustic stimulation).

If the condition \( y_n = y_{n-1} \) (see Eq. (25)) is taken into account, solving this equation by standard methods produces

\[
y(t) = \exp \left( \frac{2(\alpha-1)}{T(1+\alpha)} t \right) \left( -\frac{4\alpha}{T(1+\alpha)^2} \int_0^t \exp \left( -\frac{2(\alpha-1)}{T(1+\alpha)} \tau \right) x(\tau) d\tau \right) + \frac{x(t)}{\alpha+1} \exp \left( -\frac{2(\alpha-1)}{T(1+\alpha)} t \right) - \exp \left( \frac{2(\alpha-1)}{T(1+\alpha)} t \right) x(0) \tag{69}
\]

with

\[
y(t) = y(t^*) \text{ if } y'(t^*) = 0 \text{ and } x(t) = x(t^*) \forall t \geq t^* \tag{70}
\]

and

\[
y(t) = y(t^*) \text{ if } y'(t^*) = 0 \text{ and } x(t) = 0 \forall t \geq t^*. \tag{71}
\]

Note that Eq. (70) represents the continuous time counterpart of \( y_n = y_{n-1} \) (see Eq. (25)). In fact, the condition \( y_n - y_{n-1} = 0 \) turns into the differential condition \( y'(t^*) = 0 \) in the continuous time domain. Therefore, Eq. (70) means that the emotional reactive response is not updated if the first derivative of the response itself is equal to zero at a generic time instant \( t^* \); consequently, the response at an instant \( t \geq t^* \) equals the response at the instant \( t^* \), provided that the active response \( x(t) \) remains constant in the time interval \( (t, t^*) \). In practice, however, it should be expected that \( x(t) \) is a time varying excitation, so that the response will experience continuous changes. A simple interpretation can be also provided for Eq. (71). In fact, this refers to the case in which both the first derivative of the response and the active response are equal to zero at the instant \( t = t^* \). In this case, the response will take on the constant value \( y(t^*) \) for \( t \geq t^* \) in the absence of an active elicitation (i.e. if \( x(t) = 0, \forall t > t^* \)); this means the resulting response will be purely reactive. In practice, it should be expected that, if \( y'(t^*) < \epsilon \) and \( x(t^*) < \kappa \), where \( \epsilon \) and \( \kappa \) are small quantities, the response \( y(t) \) will remain approximately constant over a certain time interval. Moreover, if the active response \( x(t) \) becomes greater than zero at the instant \( t = t^* \) when the condition expressed by Eq. (71) holds, it is not difficult to prove that the response can be expressed as

\[
y(t) = y_1 + y_2(t) \tag{72}
\]

for \( t \geq t^* \), where

\[
y_1(t) = y(t^*) \tag{73}
\]

and

\[
y_2(t) = e \left( \frac{2(\alpha-1)(t-t^*)}{T(1+\alpha)} \right) \left( -\frac{4\alpha}{T(1+\alpha)^2} \int_t^{t^*} \exp \left( \frac{2(\alpha-1)}{T(1+\alpha)} \tau \right) x(\tau) d\tau + \frac{x(t)}{\alpha+1} - \exp \left( \frac{2(\alpha-1)}{T(1+\alpha)} \tau \right) x(0) \right) \tag{74}
\]

The last result shows that the response \( y(t) \) can be considered as the sum of two separate contributions, one representing the inextinguishable reactive response \( y_1(t) \), the other one \( y_2(t) \) accounting for the possible variations of the physical (active) elicited response \( x(t) \). It is also important to point out that, if the condition \( y'(t^*) = 0 \) and \( x(t^*) = 0 \) occurs again at a successive instant \( t = t^* \), a new purely reactive response is elicited and the model (72) can be adopted to represent it. Therefore, our mathematical model leads to the conclusion that an inextinguishable reactive response to a given source of stimulation (e.g., an electric shock source or an acoustic noise source) can be obtained through a suitable choice of the dynamics of an induced active response and that, in principle, this emotional reaction could be indefinitely strengthened by repeating similar dynamics.

Note also that, in order to obtain a reactive resistant-to-extinction response, the dynamics of the active emotional response \( x(t) \) have to meet specific conditions, which, in turn, depend on the dynamics of the physical features (e.g., electric voltage, frequency and amplitude of a noise sound, etc.) of the adopted source. In other words, it should be expected that a specific mapping function between the features of a given...
physical source and the corresponding active emotional response induced by it exists. If this function is known, the physical features of the source can be controlled in a way to generate specific dynamics in the active response; this, in turn, results in the generation of an inextinguishable form of emotional reactive response. Therefore, these theoretical findings suggest that, in principle, the inertial nature of the emotional dynamic system can be exploited to originate a resistant-to-extinction emotional reaction.

It is worth mentioning that the asymptotic response which is obtained from the Eq. 69 assuming $T = 1$ and a constant active elicitation (i.e., $x(t) = X$) is $y = X/(1 + \alpha)$. This last result shows that if a continuous active and constant elicitation occurs over time, the overall response reaches the same asymptotic value which is reached in the discrete-time model during successive trials (see Eq. 29).

Finally, it is worth mentioning that an “hybrid” time scale should be adopted, in some cases, in real world; for instance we could have different discrete trials, each of which is sufficiently extended over time so that the continuous time model should be used to analyse it (note that this type of time scale is indicated by $\mathbb{P}$ in [157]). In this case both the discrete model and the continuous time model have to be employed to describe the dynamics of emotional learning.

7.2. On the inclusion of contrast effects in the proposed continuous time emotional model

In the case of a continuous time source of stimulation (e.g., a continuous acoustic stimulation, such as music) contrast effects can be exploited to evoke specific emotional responses. It is well known that music is able to evoke emotions, for instance, violating expectations or shifting in time the rewards in a balanced mechanism based on frustration (i.e., tension, as a state of dissonance, instability and uncertainty [207]) and satisfaction (resolution towards consonant and stable sounds experienced as pleasurable) [66]. Violation or retardation in resolution produces a tension increase which may result in a successive stronger satisfaction during resolution [207]. In this scenario, the contrast effect can explain, for instance, why a slowly increasing tension could result in a successive higher pleasure and rewarding effect after a sudden and unexpected resolution. A qualitative description of the contrast effect on a continuous time scale is expressed in Berlyne’s "arousal jag" theory [206], which postulates that a drop from unusually high level of arousal (which is experienced as unpleasant) to a low level is associated with a feeling of pleasure [207]. Apparently, the low level arousal alone is not able to elicit a pleasure response; this means that only the contrast between arousal levels produces an emotional pleasure (i.e., a contrast effect). These considerations motivate our interest in including the contrast effect in our continuous-time dynamic model for the emotional system. Unluckily, the discrete-time counterpart described in the Section 5.5 is nonlinear; consequently, the procedure adopted in the derivation of Eq. 68 cannot be applied to this case. Hence, the contrast effect on a continuous time scale can be analysed by numerical simulation. A less refined approach is based on linearizing the function $C(e_A; T)$ (see Eq. 42) and applying the bilinear transform method to derive a new differential equation. In particular, if the Eq. 43 is adopted for the modeling of the contrast effect (and assuming that $0 < K < 1$), the bilinear transform method applied to Eq. 45 leads to the following differential equation

$$y'(t) = x(t) \cdot \frac{2(1+K)}{T(1+\alpha+Ka-K)} + x'(t) \cdot \frac{1+K}{T(1+\alpha+Ka-K)} +$$

$$-y(t) \cdot \frac{2(1-\alpha-Ka+K)}{T(1+\alpha+Ka-K)}$$

(75)

The solution of the last equation is not reported here for the sake of brevity. Finally, it is important to mention that the contrast effect on a continuous time scale represents a further tool that can be exploited to obtain a desired dynamics for an emotional reactive response (e.g., for the elicitation of positive/negative emotional responses, or to obtain a resistant-to-extinction response exploiting the dynamics in a continuous time scale).

8. Resistant-to-extinction emotional reaction through response saturation

Generally speaking, any mathematical function $f(x)$ representing a specific biological response cannot take on arbitrarily large values, because of the limited dynamics of the response itself. In practice, as the value taken on by the argument $x$ grows, the corresponding value $f(x)$ of the function does not steadily increase in proportion to it and, when $x$ crosses a certain threshold, a certain saturation level is reached; in other words, $f(x)$ exhibits a nonlinear behavior for sufficiently large values of $x$. In particular, these considerations hold for the system chain function $F_{CA}(x)$ defined in our dynamic model (see Eq. 18) and involved in the computation of the emotional reaction, and for the amygdala function $F_A(x)$ (see Eq. 10). In the following, we focus on the second function and analyse the implications of its nonlinear behavior; similar considerations, however, can be expressed for the system chain function. In developing our model of UCS revaluation (see Section 3), we have assumed that $F_A(x)$ can be approximated as a linear function (see Eq. 19) if in the $n$-th trial (or at a specific time instant) the error signal takes on a value smaller than a saturation threshold $T_3$, which defines the linearization range for $F_A(x)$ (see Fig. 6).

If, however, the error signal exceeds the saturation threshold $T_3$ (i.e., if the error signal becomes excessively large), a phenomenon of emotional saturation should be expected. This phenomenon could occur during an extremely traumatic event, represented by a unique event over a continuous time scale (see Section 7), or by an event involving successive acquisition trials and stimulations on a discrete time scale (see Section 3). It is worth noting, for instance, that if during a continuous-time active elicitation the reactivity of the amygdala is relatively high (which could be increased by the stress hormones and other factors related to stress [161]), the parameter $\alpha$ increases accordingly (see Eqs. 19, 21), so that the reached asymptotic response, which can be expressed as
When emotional saturation occurs, the source of stimulation (or any associated cue) generating it could produce inextinguishable effects, even in the absence of an active component which corresponds to the term $X$ in eq. (13). In fact, in the linear case, a purely reactive elicitation in the absence of an active component (i.e., with $X = 0$) leads to a negative error signal, since an active component is expected. In turn this error signal weakens the amygdala response (i.e., more precisely it produces a reduction by the amount $-\gamma \cdot X$; see Eqs. (12), (19)), and hence leads to the extinction through successive trials (see Eq. (36)). Conversely, if the amygdala function has previously reached its saturation level, in the first trial of reactive elicitation in the absence of the active component (e.g., a purely reactive visual or auditory cue triggers the reactive emotional response associated with the considered traumatic event) the computed negative error signal is unable to reduce the amygdala response. Hence, in the successive trials the error signal becomes equal to zero and no response updating occurs. More specifically, this is true if the error signal computed in the first trial, whose amplitude is equal to that of the expected active component (i.e., $e_1 = -X$), is smaller than the saturation level reached by the amygdala function (see Fig. 6). These considerations lead us to the conclusion that any stimulus perception, even in the absence of an active elicitation, can trigger a reactive emotional response. This holds both for the perception of the source of stimulation and for any related cue: in fact, a cue (CS) conditioned to the source (UCS) can trigger the reactive response associated with the UCS (i.e., $i_R$), and since such a response is evident and constant at every trial (i.e., the error signal is equal to zero) the contingency between CS and the UCR ($i_R$) is reinforced at every trial. Furthermore, the considerations made in the Section 6,4.2 about a cue conditioned to a purely reactive source of stimulation apply to this case too. We argue that this phenomenon could happen in panic disorders and PTSD [68, 69, 70]. As a matter of fact, in some forms of PTSD and panic disorders the mere repetitive exposure to cues related to a traumatic event does not lead to an extinction of emotional responses or results in a very slow extinction [210, 70, 211]. It is worth noting that during the reactive stimulation (e.g., a panic attack) other previously neutral cues could be associated (i.e., conditioned or misattributed) to the occurring reactive response, and successively these cues might trigger the reactive response; hence, in turn, this phenomenon can lead to a generalization of triggered panic attacks (i.e., panic disorders). Note that the standard classical conditioning model is unable to explain these psychopathologies. Nevertheless, one might argue that in PTSD patients the traumatic stimulus is generally perceived in a context (and also in the presence of boundary conditions) that differ from the one which originally caused the emotional response saturation. Hence, the different perceived context should lead to an (at least partial) inhibition of the elicited reactive response. Nonetheless, it should be kept into account that: a) the inhibitory strength originating from the discrimination of the contextual information could be smaller than the degree of saturation reached by the amygdala response during the considered traumatic event (see Fig. 6); b) contextual information are primarily coded and stored in the hippocampus (conversely, the representation of an aversive stimulus is coded within the BLA), so that, if during the traumatic event the hippocampus does not properly code contextual information, then no effective contextual discrimination can be obtained during further exposures of the stimulus. As far as this last point is concerned, it is worth mentioning that hippocampus functioning and its ability to encode information (especially contextual information) are impaired by uncontrollable stress (see [161] for a review on this topic). In particular, it is well known that the hippocampus of a mammalian brain is a target of stress hormones since it has one of the highest concentrations of receptors for corticosteroids. Consequently, certain hippocampal functions, such as learning and memory, are susceptible to disruption by stress partly mediated by corticosteroid receptors (mainly by the glucocorticoid receptors, GRs). Interestingly, the model developed in [161] shows that alterations in hippocampal functioning require both stress hormones and the active output from the amygdala, which in turn projects both directly and indirectly to the hippocampus. For this reason, the amygdala output is a crucial component on the stress-induced modulation of hippocampal plasticity; in fact, when there is an experimentally induced reduction in the amygdalar input to the hippocampus (as a result of an inactivation or damage of the amygdala), plasticity in the hippocampus remains intact under stress conditions [161]. These results support our hypothesis according to which the saturation of the amygdala response during an extreme traumatic event, together with the release of the stress hormones, could lead to an impairment of the hippocampus functioning and contextual information encoding. In parallel, the saturation of an emotional response component could cancel the effect of the error signal, which, on the contrary, in physiological conditions should produce an extinguishment of the emotional response in few trials.

It is also worth mentioning that chronic stress (e.g., PTSD) may induces hippocampus atrophy [212] and impair neurogenesis, specifically in the DG [161]. This, in turn, may lead to a greater generalization of anxiety disorders, in the impairment of emotional reactions inhibition and of contextual cue processing [211].

8.1. On the reactive response to a stimulus under drug administration

The proposed dynamic model can be also exploited to analyse the emotional response over multiple trials when a reactive (and resistant-to-extinction) response is contrasted by an active drug treatment (e.g., an anxiolytic drug is employed to lower an anxiety reaction or panic attack elicited by a given
Figure 6: Schematic representation of the biological behavior of the amygdala function $F_A(x)$ in its linear zone a) and in its saturation zone b). In case a) the error signal (equal to $-x$) is able to reduce the elicited emotional response. On the contrary, in case b) a negative error signal is unable to produce a similar effect, so that the emotional response remains at its saturation level. In particular, the case b) occurs if the negative error signal (due, for instance, to the fact that the active response $x$ is no more elicited during the stimulation) is smaller than the degree of saturation reached by the amygdala in the previous stimulation(s).
stimulus). Our interest in this analysis is motivated by the possibility of quantitatively assessing the long-term mitigation of an undesired pathological emotional reaction provided that it is administered as an active drug during the elicitation of a reactive response; in particular, we are interested in analysing the effects of the drug withdrawal.

One might argue that, in the considered scenario, the mere exposition to the source stimulus during the administration of a suitable drug could be effective in reducing or extinguishing an undesired pathological reactive response, such as those occurring in panic attacks, PTSD, or phobias. Indeed, as shown in Section 3 if a negative error signal (due to a response reduction) is computed during a trial exposure, the reactive response is modified accordingly, and this results in a less intense emotional reaction. Nonetheless, it can be shown that, after the trial in which the drug administration is suspendend, the reactive response asymptotically increases to its original value, that is to the value of the response occurring before the trial in which drug was administrated. In fact, this result is due to the computed error signal and holds in the absence of any cognitive modulation of the reactive response (i.e., in the absence of emotional reappraisal [213, 214]).

In our study of a reactive response contrasted by an active drug treatment it is assumed that a given stimulus produces an inextinguishable reactive response \( i_R = Y_0 \). Such a response could originate from different events, like response saturation during a traumatic event (see Section 3) or repetitive energizing trials of a reactive response through an accumulation effect (see Section 4.1), or it can be natively stored within the amygdala (e.g., arachnophobia). For this reason, the initial condition

\[
y_0 = Y_0
\]

is given. In the sequence of trials the effect of the administered drug is always represented by an active elicitation, denoted \( A = -\triangle Y_0 \), opposite to the reactive response (i.e., the active drug effect consists of an inhibition of the reactive response). Then, from Eq. (3) it is easily inferred that

\[
y_1 = i_R + A = Y_0 - \triangle Y_0;
\]

so that the error signal computed in the first trial is

\[
e_1 = y_1 - y_0 = -\triangle Y_0.
\]

Note that the active drug (represented by the term \(-\triangle Y_0\) in the last equation) should inhibit the reactive response \( y \), which is expected to become weaker (i.e., should be obtained \( y_1 \geq 0 \)). Furthermore, if the drug withdrawal starts in the second trial, the resulting response \( y_2 \) can be expressed as (see Eq. 23)

\[
y_2 = Y_0 + \alpha \cdot e_1
\]

\[
= Y_0 - \alpha \cdot \triangle Y_0,
\]

so that the resulting error signal is

\[
e_2 = y_2 - y_1 = (1 - \alpha) \cdot \triangle Y_0.
\]

Consequently, the response in the third trial is

\[
y_3 = i_R + \alpha \cdot e_1 + \alpha \cdot e_2
\]

\[
= Y_0 - \alpha^2 \cdot \triangle Y_0.
\]

Following this line of reasoning, the response elicited in \( n \)-th trial (with \( n \geq 2 \)) can be expressed as

\[
y_n = Y_0 - \alpha^{n-1} \cdot \triangle Y_0
\]

The last equation can be also derived from the mathematical model developed for the case of a phylogenetic source of stimulation, that is from Eq. (22) (a phylogenetic stimulus is conceptually different from an undesired reactive response acquired through emotional learning, but the emotional responses appearing in these two cases are functionally identical). Moreover, from Eq. (82) it is easily inferred that, after drug withdrawal, the emotional response asymptotically tends to its initial value \( (Y_0) \) as the number of trials increases (since the inequality \(|\alpha| < 1\) holds). This result confirms that an active response (e.g., the effect of an active drug) can certainly mitigate a reactive one; however, it also shows that, if the active response vanishes (i.e., if the drug is withdrawn in this case), the error signal becomes positive, since the actual outcome is greater than the expected counterpart, and the reactive response progressively returns to its initial value. Note also that an active drug can exert its inhibition effect also through a reduction of the amygdala reactivity (i.e., a reduction of the parameter \( \gamma \) derived from the amygdala function \( F_\gamma (x) \); see Eqs. (10) and, consequently, of the \( \alpha \) parameter. However, it is easy to show that the mathematical result derived above also applies to this case if it is assumed that the amygdala reactivity (i.e., the behavior of \( F_\gamma (x) \)) returns to its original conditions after the drug withdrawal (actually, a time-invariant behavior of the amygdala function has been previously assumed to simplify the development of our model).

Unlike the case of an active drug treatment, if an undesired reactive response (target response) is counteracted through an opposite reactive elicitation (e.g., through a reactive inhibition), then the effect of the counteraction will be permanent, since no active component is expected. Hence, ideally, a reactive counteraction will be learned and permanently sustained by the emotional learning system; on the contrary, an active counteraction needs the presence of an active response at every trial. For instance, psychotherapy and behavioral treatments could be effective inhibitors of a reactive response since they are able to modulate (e.g., reduce) a reactive response within the amygdala through cognitive manipulations. This is due to the fact that the human dorsolateral prefrontal cortex (DLPC) is able to direct higher level cognitive information, such as “self-regulation thoughts”, to the OFC, which, in turn, can integrate these information and modulate the original emotional reaction stored within the amygdala (so that a reappraisal effect is obtained) [213, 214, 146, 145]. In summary, a conscious down-regulation of emotions [213] allows to generate an error signal able to mitigate a reactive response without requiring an external active source, like a drug.
From a mathematical viewpoint, our last considerations can be motivated as follows. The reappraisal (e.g., reduction) of the reactive response of the amygdala by a quantity \(-\Delta Y_0'/\alpha\) through OFC modulation results in the response
\[
y_1 = Y_0 - \Delta Y_0',
\]
so that the error signal computed in the first trial is
\[
\epsilon_1 \triangleq y_1 - y_0 = -\Delta Y_0'.
\]
Hence, if it is assumed that no further session of cognitive reappraisal occurs, the response in the second trial can be expressed as
\[
y_2 = Y_0 - \Delta Y_0' + \alpha \cdot \epsilon_1
= Y_0 - \Delta Y_0' - \alpha \cdot \Delta Y_0',
\]
Note the last equation still contains the term \(-\Delta Y_0'\), since it originates directly from a reactive emotional downregulation (and it is not due to the computation of an error signal after that an active elicitation has been occurred, like in the previous case; see Eq. (77)). Such a reduction can be obtained, for instance, by lowering the amygdala reactivity during the response (e.g., by reducing the release of stress hormones, since these are known to affect the amygdala output; [161]); moreover, multiple sessions of reactive modulation could lead to the extinction of the considered reactive response. Note also that, in the absence of additional sessions of emotional modulation, the asymptotic response can be expressed as
\[
y_{\infty} = Y_0 - \frac{\Delta Y_0'}{1 - \alpha}
\]
and this shows that the effect of the reactive inhibition persists over successive trials.

8.2. Drug treatments, reactive methods and emotional responses

Since pathologies involving emotional disorders, such as panic disorders or PTSD, usually lead to a generalization of their triggered responses (i.e., an increased number of new stimuli becomes able to trigger a pathological reactive response) and to the atrophy or impaired neurogenesis of the hippocampus (in particular, of the DG) [161], specific pharmacological treatments could be effective in blocking and reversing these biological conditions. Nevertheless, as shown in the previous Section, a treatment based on an active drug alone could be unable to counteract the pathological reactive response on a long term (i.e., after the drug withdrawal). This means that active drugs, even if are able to mitigate the symptoms due to strong inextinguishable responses, cannot durably extinguish them. For this reason, the adoption of reactive methods (e.g., psychotherapy treatments [215, 210]) able to extinguish (or mitigate) a pathological reactive response is required. These methods include all the techniques able to counteract a pathological emotional response through an opposite reactive response or a reactive inhibition (consequently, the use of any active component is avoided). We argue that different technologies, like optogenetic manipulation of memory engrams and memory photostimulation, could be adopted to achieve this target. In fact, on the one hand, the optogenetic manipulation of the memory engrams within the DG or the BLA [54, 216] allows to switch the valence of a CS in the DG from a positive (negative) UCS to an opposite one [55]. Some results have evidenced that the chronic reactivation of hippocampal cells associated with a positive memory is able to suppress depression-like behavior in mice [216]. On the other hand, the memory photostimulation of UCS-responsive cells on the BLA has been shown to produce valence-specific behaviors [54]. On the basis of the aforementioned results we argue that, if during trials in which a subject is exposed to the cues related to a traumatic event, positive valenced UCS-responsive cells were photostimulated, then the outcome triggered by such cues (i.e., the target response) could be weakened. In fact, the photostimulation-induced response should be misattributed to the target cue and, consequently, the final cue-related outcome should be due to the superposition of the original target response with the optically elicited response; this should result in a net decrease of the target response. Unluckily, optogenetic neuronal manipulations and memory photostimulation cannot be used on humans today because of their invasiveness. We argue, however, that similar reactive counteractions could be obtained through a subliminal exposure, exploiting the implicit accumulation effect (see Section 4.1). Finally, it is useful to mention that techniques exploiting the misattribution of reactive responses (both conditioned responses and purely reactive responses) could be also employed to strengthen a desired response (e.g., an unconscious placebo response).

Discussion

In this manuscript a novel theory of emotional learning has been illustrated. The theory shows the differentiation (and the relations) between classical conditioning and the UCS revaluation, and provides various new insights on well known psychophysiological phenomena and psychiatric diseases (e.g., panic disorders and PTSD), and a number of new ideas for further research. One of its most interesting implications is represented by the identification of well defined mathematical and neurophysiological conditions ensuring the inextinguishability of specific emotional reactions. In particular, it allows us to establish the following four different mechanisms through which a stimulus can produce a resistant-to-extinction emotional reaction: 1) misattribution of a reactive response (see Corollary 1); 2) classical conditioning of a stimulus to a purely reactive source of stimulation; 3) saturation of emotional response (e.g., of the amygdala reactive response); 4) the exploitation of the inertial dynamics of emotional learning system on a continuous time scale. Further relevant contributions are represented by the proof that the Rescorla-Wagner model for classical conditioning can be obtained as a special case of the proposed model; the derivation of a new model for
conditioning, which accounts for the implicit UCS revaluation and that is able to quantitatively describe important experimental results (such as the impossibility to extinguish a conditioned inhibitor through its repeated presentations), which are unpredictable by existing classical conditioning models. Indeed, classical conditioning has been deeply studied in the last century, while UCS revaluation did not obtain the due attention, and, for this reason, actually, appropriate analytical and experimental models for resistant-to-extinction responses do not exist.

Our result paves the way for various new research activities. First of all, various potential applications of our theory can be envisaged in the hot research area concerning the manipulation of human behaviours and emotional reactions. Note that our theory unveils the real differences between an UCS and a CS from the perspective of the emotional system and, in particular, shows that removing a CS does not ensure the extinction of an undesired emotional reaction, since, as long as a UCS reaction remain stored (or relatively strength), it is able to form other CS-UCS connections, or to duplicate its associated reaction through a misattribution effect or even to strengthen itself through incubation mechanisms. Furthermore, if an UCS reaction is extinguished or weakened, all the associated CSs are weakened. Thus, establishing a well defined differentiation between a cue (i.e., a CS) and a source of stimulation (i.e., UCS) is fundamental in order to eradicate an emotional undesired reaction. This fundamental differentiation could be effectively assessed exploiting Remark (6), i.e. testing the subliminal emotional reactive response through subliminal exposure. Indeed, as shown in our analysis, no difference between CS and UCS might be sensed in the course of a supraliminar perception. In addition, from a conscious perspective, a source or a cue-stimulus could be hardly differentiated, because of misattribution effects or response duplications (e.g., an initial CS could be misattributed and become an UCS); note also these and other related attribution phenomena often occur automatically and unconsciously [30, 34], and are not explained by classical conditioning theory.

Another interesting research topic is represented by the potential applications of Corollary 1, i.e. by the possibility of devising UCSs able to elicitate reactive responses. Such responses could be strengthened through an accumulation effect and potentially exploited to modify the emotional reaction to a given stimulus (e.g., to weaken an opposite valenced emotional reaction or to enhance the unconscious placebo effect of a drug [98, 99]). The idea of generating an accumulated reactive response could be really useful from a therapeutic viewpoint since, in practice, the active modulation of a given reactive response (accomplished, for instance, through the action of a pharmacological drug) vanishes over time if the associated active component decays too (in the considered example this occurs if the administered drug is withdrawn). Furthermore, other “reactive methods” could be exploited in order to modulate (i.e., to increase or decrease) a target response; these methods include but are not limited to: the misattribution of a CR forward the target response, the cognitive reappraisal of an emotional response [213] (e.g., psychotherapy), optogenetic manipulations [54, 216, 55].

Once again, it is worth stressing that these results rely on the differentiation between the types of emotional response (such as active, reactive and passive residual responses) that can come into play during a stimulation (and, more precisely, during UCS revaluation) and the concepts of source attribution and misattribution, and that these relevant factors are not taken into consideration in classical conditioning models.

A further relevant research topic concerns the applications of our model of emotional learning on a continuous time scale. Generally speaking, this model could be exploited to analyse the emotional reaction generated by any physical stimulation which varies continuously over time (e.g., a time-varying acoustic source of stimulation, such as music [66]). We feel, however, that our model is preliminary and that it should be improved by including some features of hippocampus filtering (for instance, the temporal pattern recognition, that is the detection of regular patterns within the time-varying elicited response, should be included).

Finally, it is important to mention that our theoretical framework can be exploited for the development of psychophysiological experimental models for both animals and humans; these, in turn, can potentially provide new insights into emotion-related phenomena and pathologies.
Appendix

In this Appendix we describe an experiment useful to prove that the encoding of an aversive object as a conditioned stimulus (CS) to a primary source of punishment (i.e., CS-UCS encoding through aversive classical conditioning acquisition) or as a primary source of stimulation (UCS) involves different regions of the mammalian brain.

The procedure adopted in this experiment is obtained by including a new part in the procedure followed in [1] and is sketched below. The proposed experiment is based on the use of a specific device, never observed by the involved subjects and having a neutral shape; this device, however, is able to produce an aversive stimulus, like an electric shock or strong noise. Moreover, it involves two distinct groups of subjects, one denoted group+, the other one group-. In practice, the experiment consists of three different phases, each involving multiple trials. In the first phase the selected device has to directly elicit an aversive response for some trials in the members of group+, so that their emotional learning systems attribute the elicited responses to that source of stimulation, learn the associated reactive responses, and finally code and store them within their amygdalas. In the group-, the same device has to be conditioned to an identical aversive response elicited in the group+; however, all the subjects of group- must be aware of the fact that the aversive stimulus originates from another source of stimulation (denoted UCSa) and must learn the stimulus contingencies (in other words, classical conditioning learning occurs for group-, instead of the direct response attribution characterizing group+). In particular, the picture of the new device pointed toward the subject can be easily conditioned instead of the device itself (since, otherwise, it would be quite difficult to perform a conditioning procedure by which the physical object is paired with the UCSa elicitation). In the second phase, a differential conditioning paradigm is adopted. For this reason, each subject of group+ has to be conditioned with the pairing of the picture of this device, pointed toward the subject and denoted CS+, with a new UCS (e.g. and electric shock); the last UCS, called UCSb, must be different from UCSa, that is employed for the conditioning of group-. Moreover, another threatening element (e.g., a gun), called CS-, is presented to the subjects of group+ in the absence of an UCS. The same procedure is followed for the subjects of group-; these have previously acquired the given device as a conditioned cue and not as a direct source of stimulation. Finally, in the third phase, a masked (unmasked) extinction phase for half subjects of group+ (group-) will be able to reveal which CSs+ are able to elicit a differential autonomic response (i.e. a SCR) even under a subliminally (masked) perception. If group+ only will exhibit a differential autonomic response in the masked extinction (with respect to the SCR elicited by the masked CS- perception), it will be inferred that only the representation of the CS+ within group+ can be activated through the sub-cortical thalamus-amygdala pathway; therefore, we will come to the conclusion that the representation of CS+ has been stored within the amygdala in the same site as other UCSs (e.g., phylogenetic or ontogenetic threatening stimuli [162 1 2 3 90]). Conversely, if the subjects of group- are considered, the CS+ (which is the same picture as that employed for group+), represents an aversive object which has not been stored within the BLA, or, in any case, not in a brain region activated by the sub-cortical thalamo-amygdala pathway (like the phylogenetic or ontogenetic stimuli).

We believe that, if the envisaged results will be obtained, they will also definitively prove that the mechanism through which the selected aversive object has been encoded (i.e., through classical conditioning acquisition, or by direct or implicit response attribution) makes the difference.
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