Harnessing Synaptic Plasticity to Treat the Consequences of Emotional Traumatization by Amygdala Depotentiation Techniques: An Electrochemical Model

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Abstract
A new understanding of how sensory input can change the brain is presented here. It is proposed that activation of AMPA receptors on the lateral nucleus of the amygdala, either by purposeful recall or inadvertent stimuli, of a previously traumatically encoded event make them vulnerable to depotentiation. Subsequent stimulation of peripheral touch receptors, on the upper arms, palms and face along with distracting tasks appear to permanently remove these AMPA receptors by causing them to become internalized. This depotentiation process disrupts the

pathway that, through appropriate stimulation, had previously reproduced the consequences of an encoded trauma. The emotional as well as the other components of the traumatic memory are thus irrevocably altered.

Key Words: AMPA Receptor (AMPAR), Amygdala, Calcineurin, Depotentiation, Phosphokinase M zeta, Potentiation, Psychosensory therapy, Sensory input, Synaptic encoding, Thalamo-amygdala pathway

The body is generally thought of as an electrochemical organ and, as in the nature of light, which is both wave and particle, the electrical and chemical components of the body are two sides of the same coin. There is no chemical release without electrical stimulation and there is no electrical activity without chemical release. In the brain, these electrochemical signals (and the magnetic field that develops as a consequence), as well as the numerous neurological pathways underlying them, are posited as the mechanism by which the body perceives, interprets, remembers and communicates.

Chemicals produce and store energy, provide our physical structure, modulate information processing and motivate us to action. Electrical impulses cause the release of stored energy, alter neuronal activity, are converted into magnetic fields, and affect every aspect of bodily function, from the immune system to our memory. That said, we must remember that we are more than an almost infinitely complex system of electrified bio-chemical neuro-pathways. However, for the purposes of this paper we will focus on these two components.

Through evolution a method for handling certain type of threatening situations has been created. Under certain conditions an event is encoded as a traumatic memory. This type of memory is immutably stored. Recall of the event is out of conscious control and leads to a maladaptive response. This recall causes the release of stress hormones and alters the brain, leading to disease. Remarkably, as will be discussed, it is possible by understanding the underlying biology of this process we can remove these unwanted, maladaptive encoded memories and alter the consequences of that trauma.

Sensory input to the brain, whether it comes from outside the body or from within, is transformed into an electrochemical signal. Thus, all sensory input is translated into the language of our body. It is how the head speaks to the feet. It is how we know what to do to survive. It is how we experience the world around us and within us.

Sense	Input Signal	Transduced Signal
vision	→ electromagnetic →	electrochemical
sound	→ compressed air →	electrochemical
smell and taste	→ chemical →	electrochemical
touch	→ mechanical →	electrochemical
visceral	→ mechanical, chemical, electrical →	electrochemical

A typical sensory input, such as touch, produces amazingly complex responses, some of which are driven directly by receptor activation and some by how we interpret that activation. Receptors imbedded in the skin

produce sensations of pressure, position, pain, temperature, texture and movement. Everyone experiences these sensations to a greater or lesser degree when the appropriate receptor is stimulated. In addition, sensory input can also have consequences beyond those produced by receptor stimulation. Some of these responses are hard-wired at birth, such as the calming effect of a mother's gentle touch, or fear that arises from hearing low rumbling thunder, or the physiological arousal at the sight of a threatening circumstance. Other sensory responses are learned. For example, for some there is delight in the smell of chicken soup wafting out of the kitchen. For others, seeing pictures of 9/11 produces great distress. We all have responses to sensory input that can produce pleasure or aversive feelings, an extrasensory response. By extrasensory, we mean those sensations that arise unbidden and are outside the particular properties of sense receptors. Proust's journey as described in *Remembrance of Things Past* [1] begins with such an extrasensory response to a spoonful of tea soaked in a Madeline cake.

"No sooner had the warm liquid and the crumbs with it, touched my palate, a shudder ran through my whole body, and I stopped, intent upon the extraordinary changes that were taking place. An exquisite pleasure had invaded my senses, but individual, detached, with no suggestion of its origin. And at once the vicissitudes of life had become indifferent to me, its disasters innocuous, this brevity, illusory—this new sensation having had on me the effect which love has of filling me with a precious essence; or rather this essence was not in me, it was myself. I had

ceased not to feel mediocre, accidental and mortal. Whence could it have come to me, this all powerful joy?"

It is unlikely that another person tasting this Madeline cake would have experienced such an effect. So how does this sensory input produce an extrasensory response? While the mechanism by which this occurs is shrouded within the complexity of the brain, an extrasensory response must be the result of a perceived 'meaning' either innate or learned, for the organism.

A Third Pillar

A new field of study, a third pillar if you will, called ***psychosensory therapy*** [2,3] is proposed here. This therapy involves the application of sensory input to generate an extrasensory response to produce a beneficial change, either transiently or permanently within the organism. The nature of the input and the mechanism of action differentiate this technique from talk therapy (psychotherapy, the first pillar) and drug therapy (psychopharmacology, the second pillar). Psychosensory therapies have been studied, but in a fragmented way, and here we wish to bring them under one heading. A partial list of techniques that use sensory input to alter symptoms, behavior, mood and thought include:

The psychosensory therapies can be grouped into two major divisions, one in which the mind is activated by an event or feeling at the time of sensory input (above the line) and those where the mind is unengaged (below the line). Those above the line target specific memories and have the potential to de-encode these events and their sensory components. Those below the line produce a down regulation of stress responsiveness, a more generalized desensitization. Can we use the extrasensory response to sensory input to eliminate the consequences of an encoded traumatized event? This paper presents a hypothesis of how this might be accomplished.

The remarkable effect of touch on encoded traumatic events is due to the nature of encoding and the extrasensory

response of touch that is part evolutionary biology and part electrochemistry. It is well accepted that trauma is encoded both in and by the right amygdala, a part of the primitive limbic system that detects and responds to threats and prepares us to flee or fight [4]. In addition, the amygdala causes the moment to be highlighted in our memory for rapid and easy recall.

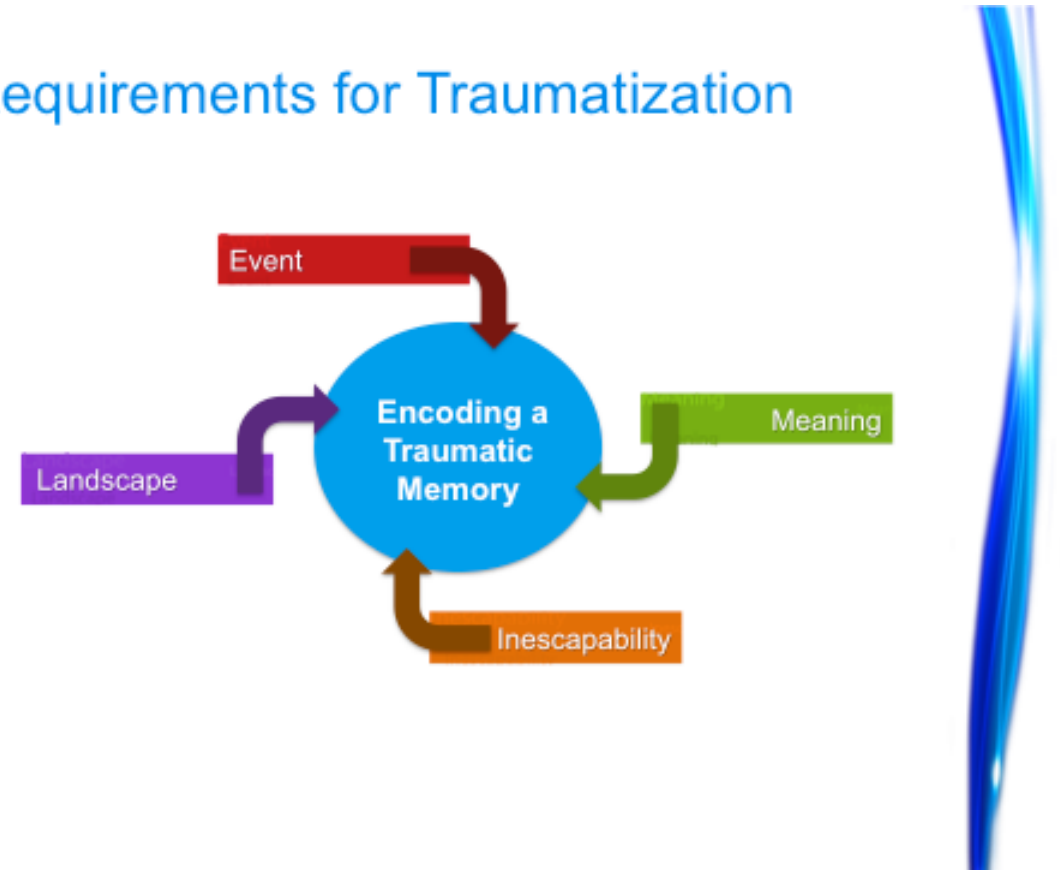
An Encoding Moment

A traumatic encoding moment produces a permanent engram.

We define traumatization at the neural level

… as the process that permanently encodes and synaptically consolidates linkages between the emotional, cognitive, autonomic and somatosensory components present during the traumatizing event. Any one of the components of the encoded memory consciously recalled or triggered inadvertently causes us to experience some or all of the components as if they were happening for the first time.

Traumatization requires four elements [3]. First, an **event** must occur. We can experience this event either first, second or third hand. We can be part of it, we can witness it or we can be told of it. Secondly, the event has to have **meaning**. We must have some attachment to the event so that it can generate an emotional response that is required for traumatic encoding. Attachment arises from something we are or have.



We are attached to living, our bodies, our friends, and our sense of whom we are in the community, feeling safe, and those material things we treasure. We are hard-wired for survival: the thalamo-amygdala pathway (see below) is designed to help us survive by activating the requisite physiology (what biologists call the fight or flight response). It is this attachment to survival that produces meaning. The **landscape of the brain** is the electrochemical state at the time of the event; it is what makes us either resilient or vulnerable to what is unfolding before us. Finally, if the moment is **perceived inescapable**, such as in a car accident where we are tumbling out of control, there is the potential for traumatization. It is this last element that is crucial for our understanding of the therapeutic actions of the extrasensory response to touch.

Traumatic encoding starts with activation of a neuron or neurons in the lateral amygdala where the event begins to map out a pathway that leads to encoding a traumatic memory. On these neurons are many types of receptors, but for our purposes, it is AMPA [5] glutamate receptors that are critical and they become potentiated (increase in number and permanence) at surface of the post-synaptic neuron of the thalamo-amygdala pathway by the emotion-producing stimulus. It is these receptors that are activated when the event is first experienced or recalled after encoding. These receptors are activated by an emotion-producing unconditioned threat stimulus (UTS). These activated receptors then become associated with the conscious threat stimulus (e.g. surroundings), which could be considered the conditioned stimulus.

For example, a bridge phobia is generated when the requirements, including inescapability, for traumatization are met. Here, perceiving we are above ground and cannot get off the bridge at that moment. The UTS (heights) generates fear, but we are unaware of why, so instead we consciously associate the fear with the bridge (the content, which is the conditioned stimulus). This information enters the amygdala directly from the thalamus. Milliseconds later, the complex content (e.g. the color of the bridge) and

the context (e.g. the sky was cloudy), which are the non-emotional aspects of the event, enter the amygdala via the cortex and hippocampus [6] and are bound to the emotion-producing stimulus basolateral complex (BLA) in the amygdala (See Figure 1).

When the requirements are met, a specific enzyme called PKM zeta [7] (PKM zeta, a phosphokinase, is an enzyme that phosphorylates AMPA receptors) is activated. This enzyme maintains the AMPA receptors at the synapse so that they can rapidly conduct information along the pathway that the traumatic moment produced. PKM zeta has a unique biology. It does not contain a regulatory domain that allows for it to be shut off and once activated remains so. This is not the whole story but it helps explain the permanence of a traumatic memory.

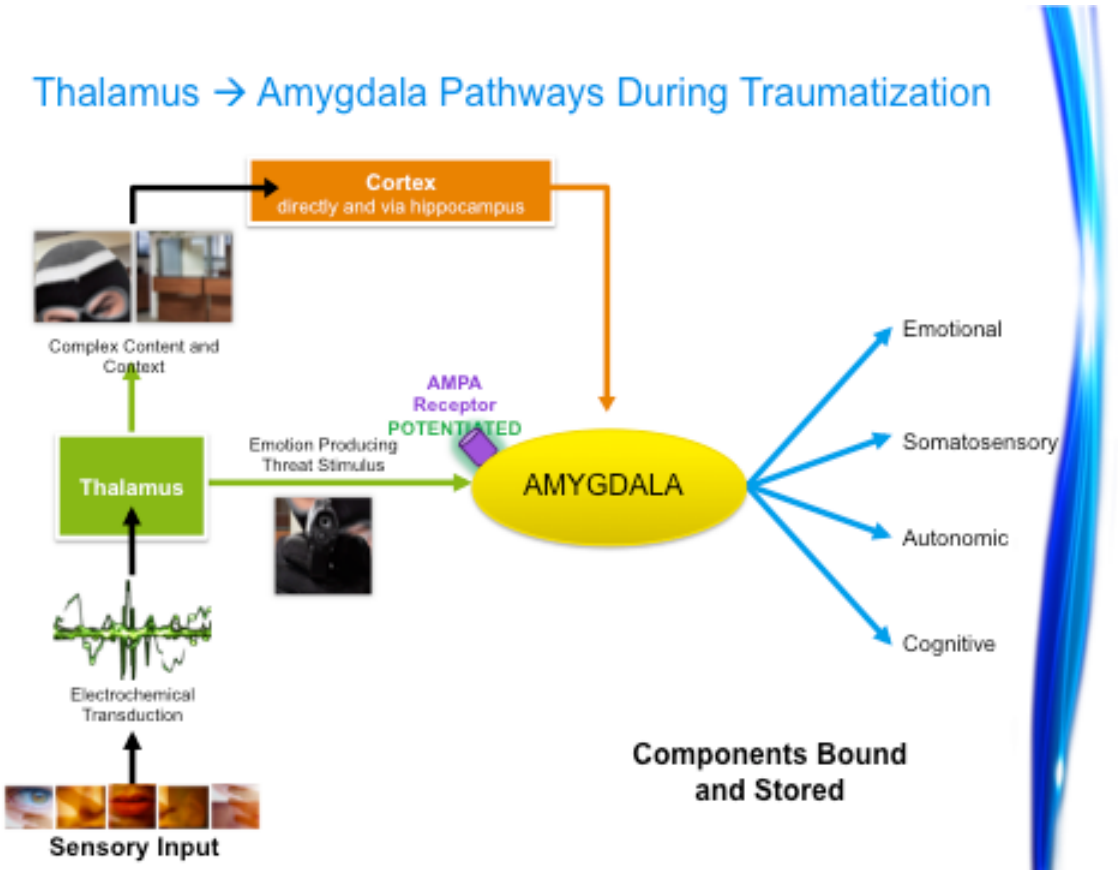


Figure 1

Components of a Traumatized Memory

A traumatic event contains four components [8]. These include the emotional content (e.g. the felt sense), the memory itself (which includes the emotion producing content, the non-emotional content and context), the autonomic reaction of the body (e.g. sweating, blushing) and the somatic aspects (e.g. pain). The amygdala co-encodes these components simultaneously during a traumatization.

FOUR COMPONENTS OF A TRAUMATIC EVENT
Emotional content
Cognitive Components
Autonomic reactions
Somatosensory aspects

Reactivation of the pathway by event recall or by inadvertent stimulus recapitulates the neurobiological pathway that occurred during encoding and reproduces some or all of the experience of the event. We speculate that if one could produce an extrasensory response at the moment of recall that signals safety and escape, a perceived escapability, one of the requirements for encoding of the emotional event, would be lost. The entry into the pathway would be disrupted and the down stream pathways would lose their connectivity. Subsequent attempts at recall or inadvertent exposure to a reminder stimulus would no longer be able to activate the pathway that was produced by the original traumatization. Is this possible and what is the evidence?

Amygdala depotentiation depends on the ability to remove the AMPA receptor from the surface of the post-synaptic neuron in the lateral nucleus of the amygdala. If we can produce a sense of safety, the relationship between the emotion and the immutably encoded traumatic event is disrupted. This prevents subsequent stimuli from activating

the encoded pathway and the direct consequences of the trauma are eliminated.

There are three aspects to amygdala depotentiation. First is activation of the emotional content of the event by imaginal recall. This activates the phosphorylated AMPA receptors that have been encoded at the time of the event. Touch, a gentle and soothing touch, is then applied to the upper arms, palms and around the eyes. It produces an extrasensory response of safety that arises from the evolutionary equivalent of what a mother's touch does at the time of birth. It is innately wired. Concurrently with havening touch the therapist distracts the individual. Since the mind cannot hold two thoughts simultaneously, the use of distraction displaces the recalled event from working memory and prevents it from re-activating the amygdala. Distraction techniques can be visual, auditory or cognitive, such as imagining climbing stairs, humming a tune or counting backward. While the process might seem curious, its effects are almost immediate and profound.

In the brain, it is speculated that soothing touch produces an electrical (a 1-2 Hz) delta wave [5]. Touch (and the delta wave it produces) opens voltage-dependent calcium channels of the post-synaptic lateral amygdala neurons allowing for calcium to enter the cell. This leads to the production of another enzyme called calcineurin [9,10]. This enzyme, a phosphatase, removes phosphorus from activated AMPA receptors but leaves inactive AMPA receptors intact. This dephosphorylation causes the synaptically placed AMPA receptors to lose their hold on the neuronal surface and they become internalized, depotentiating [11] the receptor. The disappearance of the

AMPA receptors from the surface of the post-synaptic neuron is the neurobiological equivalent to de-linking the event from its down stream consequences (See Figure 2). The rapid time course for these events (seconds to minutes) suggests that the process is indeed electrochemical in nature.

It is likely that EFT and EMDR as well as observing another being touched can produce similar effects.

After the emotion-producing receptor is eliminated, subsequent recall of the event only allows for the non-emotional, cortically encoded complex content and context to be brought to conscious awareness (Figure 3). With the amygdala no longer activated, these stimuli cannot produce emotion-laden memories. Once depotentiated, the memory and its co-encoded components are lost and cannot be reconstituted. The key and often the most difficult part of this approach is to find the event that produced the pathway. Once uncovered, activating the emotional component and applying havening successfully de-traumatizes the event and the memory no longer has the power to cause distress.

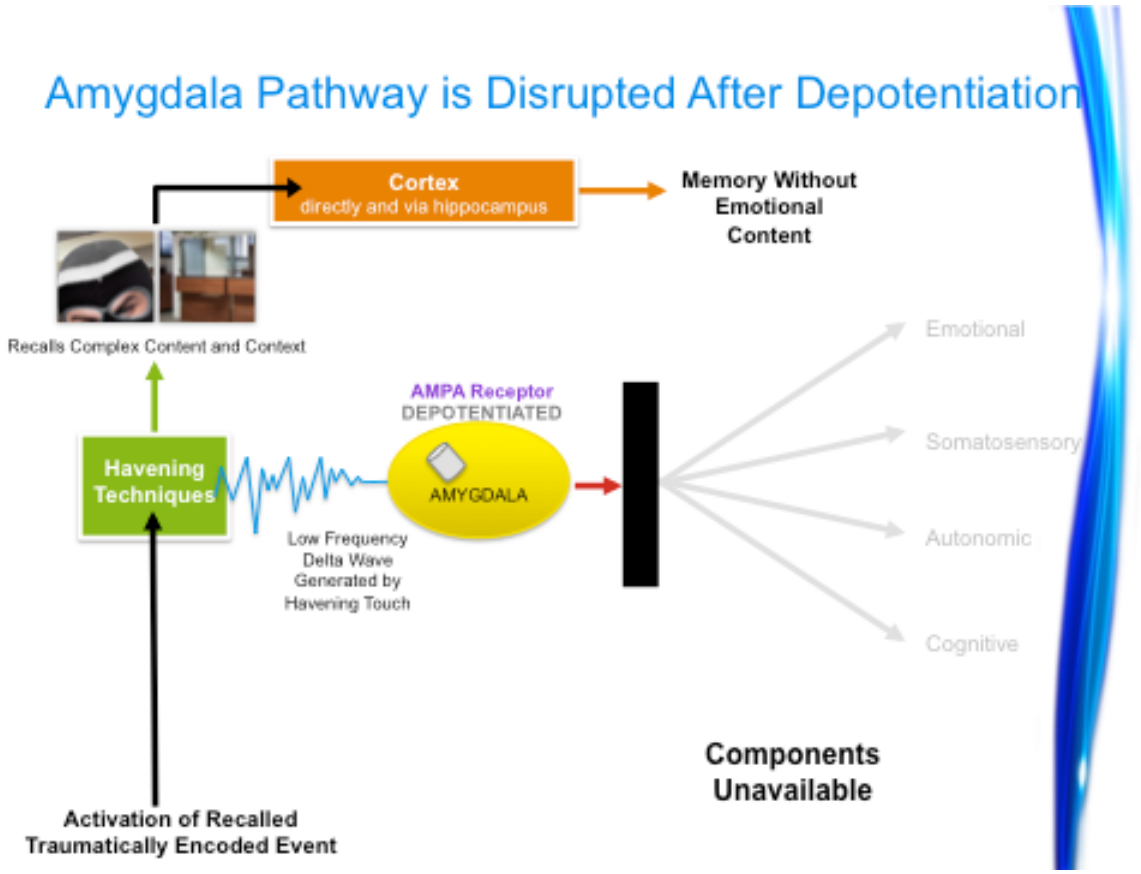


Figure 3

Psychosensory therapies are powerful tools that can eliminate traumatic memories. These memories and the problems they create are staggering in their variation and add hugely to human suffering. Traumatic encoding that involves fear, anger, grief, guilt, pain, remorse, shame, craving and so on are reflected in disorders such as phobias, PTSD, chronic pain syndromes, pathological emotions, somatization, panic and craving.

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