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Neurobiology and Treatment of Relationships

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The Neurobiology and Treatment of Relationships

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This manuscript is updated frequently as new research and clinical applications appear in the literature. Please read this paper and send me your comments and suggestions. If your suggestions are significant and can be referenced, I will acknowledge your contribution. Please feel free to contact me directly by email or phone call. I will answer your call or get back to you promptly if I am not available. Feel free to text me and suggest a time to talk by phone if you prefer. I welcome your comments and corrections. Any errors in the paper are mine and are unintentional. I appreciate your assistance in developing this theoretical and clinical model of close human relationships.

Introduction

I grew up on a farm in Iowa that my brothers and I still own and operate. I was the oldest of four boys. Our mother was a caring and kind soul who put up with a constant parade of pets, critters we had rescued, and requests for food. She often remarked, "Life wouldn't be so bad if people didn't have to eat!"

My mother and father had a loving relationship. I never heard a cross word between them. My bedroom was upstairs above theirs. I would fall asleep at night and wake up in the morning listening to them talking below me. I had no idea how rare such a close marital relationship can be.

My paternal grandparents lived on the neighboring farm and were married 70 years before my grandfather died. They were like the chickens in our farmyard. They constantly "pecked" at one another but never drew blood. They were what I now call a "conflict habituated couple." Unlike my parents, they were always "after each other" but were inseparable. When my grandfather died, Gramma lamented, "I miss the old fool."

When I left the farm and went off to college, I was required to take courses in psychology and sociology. That ultimately led to a doctorate emphasizing psychology and marriage and family therapy. Since then, life circumstances stimulated an interest in science in general and neuroscience in particular.

After receiving my Ph.D. from the University of Iowa, my first wife and I moved to Texas Tech University where Sue was hired to set up and run the Internal Medicine Department's laboratory. She was an analytical biochemist. I was hired as a psychologist in the University Counseling Center and a faculty member in the Department of Human Development. I founded and directed a doctoral program in marriage and family therapy including a family therapy clinic from 1974 until 1987.

In the spring of 1975, my wife had a "grand mal seizure." The doctors in the medical school had no idea what had caused it. She was very athletic and intellectually brilliant. The incident was written off as a fluke. However, over the next ten years Sue frequently became confused on her way to and from work. She would call me and ask directions. She would also always stop and look around for the door in each room in our home. In all other respects she was extremely intelligent and talented. Her colleagues loved her, and her lab was always filled with happy techs and med students. In 1983, we visited her mother and father in Dubuque, Iowa and I noticed my mother-in-law had difficulty remembering things we had said to her. Her behavior was unusual enough that we took her to the University of Iowa's Department of Neurology for evaluation. To our surprise she was diagnosed with Early Onset Alzheimer's Disease Familial Type. This condition affects only 1 to 2 % of Alzheimer's patients and develops early in life. I suspected immediately that Sue had the same condition, so immersed myself in neuroscience. Sadly, Sue's mother died in her early 50's.

In 1987 I accepted a visiting professorship at Iowa State University and stayed on to found and direct a marriage and family therapy doctoral program. By the time we moved, Sue's condition had progressed to the point that my children and I were caring for her. Sue died in 1994 at age 47.

I share this history with you so you can understand why I have written this paper. I am personally highly invested in understanding how to develop and maintain a good relationship. I am also intrigued by how our nervous and endocrine systems shape our emotions, thoughts, and behavior.

I invite anyone who reads this paper to contact me with any thoughts or suggestions you have to improve the quality of the theoretical model I am attempting to develop. I do not claim to have a definitive model of how relationships develop and how our bodies drive us to seek an intimate partner or produce children. Many colleagues have helped me over the last 35 years, and I request your assistance as well. Please contact me at the email address or phone number listed on the title page.

The paper you are about to read is based on my study of affective neuroscience, human biology, and 50 years of experience working with couples and families. I have attempted to reference or in some way document everything I have written. However, some of my comments are considered "clinical lore"; that is, knowledge shared by mental health professionals that is believed to be true. My colleagues and I are attempting to conduct research to demonstrate that such lore has a scientific basis. I have tried to separate "hard science" from "clinical lore." Please feel free to disagree with my observations and share any scientific findings you believe to be more accurate than what I have stated.

I want to thank Dr. Jack Shelley Tremblay, Chair, Department of Psychology for his assistance. He is an experimental neuropsychologist with expertise in psychophysiology, electroencephalography, and cognitive assessment who oversees the graduate program in Brain and Behavioral Science and a Combined/Integrated Clinical and Counseling Psychology Program. Dr. Shelley-Tremblay and I are Co-principal Investigators of The Neurobiology of Relationships Study at the University of South Alabama.

I would also like to acknowledge Dr. Ralph Davis, formerly a research scientist at the University of Wisconsin-Madison and now an emeritus professor of biology at Northwestern College in Orange City, Iowa. Dr. Davis is a leading expert in nematode neurobiology. He has graciously assisted me.

Finally, I thank my wife Dana Roberts for being a loving partner and patient listener. She has helped me clarify thinking and improve my presentation style.

The comments in this document are my own as are any errors. I hope you enjoy my paper.

The Neurobiology and Treatment of Relationships

Falling in love and attempting to stay in love is a time-honored human tradition. Why we are driven to be in love, and how we behave during the process have been the subject of endless poems, songs and stories. The advent of modern brain imaging technology and continuing research regarding the functioning of the human body have laid the groundwork for this paper about how we fall in love, stay in love, parent children, and lose a close partner though divorce or death. This paper is intended to provide a beginning framework for thinking about how neuroscience relates to couple and family therapy. The framework described here focuses on neurobiological processes that influence intimate behavior. It also may be useful to therapists assisting couples desiring to improve their relationships.

This framework draws from my own research focused on couples in committed relationships and the work of other social science and neurobiological researchers, particularly Jaak Panksepp. Jaak Panksepp (1998, 2011, 2012; Panksepp & Watt, 2011; Davis, Kenneth L & Montag, Christian, 2019) has identified seven Prototype Affective Systems**,** primal emotional circuits common to mammalian brains (See Table 1). My own ongoing couple research has attempted to link these circuits to lifelong stages of love such as lust, attraction, and attachment described by various authors (Fisher, 1996; Fisher, 2016; Fisher, Aron, & Brown, 2005) and later life stages including parenting (Carter, & McGoldrick, 1999) and partner loss (Joanning & Keoughan, 2006). I have also drawn from the work of Lisa Feldman Barrett who has studied the neurology of emotions. In sum, this framework attempts to describe the neurobiology of love relationships throughout the life span. This paper will also apply this neurobiological framework to the treatment of relationships that have become less than satisfactory, and the improvement of relationships that are functioning reasonably well but have some room for improvement.

Where to Stand to Look

Understanding how the human brain operates may require a change in epistemology. Discussions of the brain often describe levels of physiology that generally follow the evolution of brain development from simple organisms to humans. That is a helpful way to conceptualize how the brain came to take on the capabilities it now has. However, when considering how the brain, behavior, and cognition are interrelated, it is helpful to think of "levels of analysis" rather than just structural components/levels of operation. A level of analysis is a philosophical lens that moves from a simple concrete description to a more complex description of physical realities. When describing the brain, a concrete description would be to name and describe the structures and their respective functions as relatively isolated parts of the brain; e.g., brain stem/implementation of autonomic function, amygdala/fear, vigilance, emotion regulation; hypothalamus/control of autonomic, endocrine, emotional and motivational functions, cortex/higher cognitive, sensory and motor integration. I will explore many of these structures and their functions in this paper with everyday examples as wells as summaries of research findings.

When describing how the brain operates, neuroscientists are moving to a more complex description of how brain components interact to function as a highly interconnected, cybernetic or "self-organizing system." Dr. Douglas Watt, noted neuroscientist who has helped me with this paper, and other affective neuroscientist (folks who study emotion), like to talk about "multiple nested feedback loops" that coordinate the activity of brain components. When describing our subjective experience of brain function, our "consciousness" or "mind," we move to an even more complex description. However, there continues to be a physical reality of neuronal circuits, hubs, white matter/axonal pathways that make up these more complex/intricate phenomena. The term "hierarchy" is often used when describing less to more complex physical-functional brain organizations such as the various "levels" of connectomics (comprehensive maps of connections within an organism's nervous system) : micro-connectomics (precise connectomes at the level of individual synapses), meso-connectomics (at the level of neural circuitries within particular brain structures/regions) and macro-connectomics (at the level of the brain component interactions across brain regions and structures. Using a levels of analysis approach avoids the pitfalls of simple "levels" of structures that imply a hierarchy within the brain. No area of the brain is "superior" or "inferior"; that is, more or less important. Many parts of the brain contribute to the phenomenological experiences of feeling, thinking, and behaving. At times one or a few brain areas might have control (akin to veto power) over other areas' neural function/output, depending on what specific process/brain function or circuit we are talking about. However, that ability does not make those areas superior, simply in temporary control.

An example of levels of analysis would be an automobile. The motor, transmission, body, and wheels are the basic components, a first level analysis. The parts put together structurally to constitute an automobile, a second level analysis. The parts, functionally carrying out the functions they were designed to produce when interacting with a human; e.g., being driven, constitute an operational automobile, a third level analysis. All levels of analysis are the same car but considered from different perspectives. Different perspectives do not imply that one perspective is "better" or "higher" than another, simply different.

Another example illustrates how the brain "areas" function. The brain does not have "part" like you may have learned in high school or college biology. The notion of parts is left over from early dissections of the brain hundreds of years ago. The brain can be separated into parts, but these parts, or more accurately, areas, do not function independently. The function of our brain can be compared to a symphony orchestra. All areas of the orchestra are always doing something, but one area of the orchestra, such as the strings, brass, or percussion section may be taking the lead at one time. However, some of the time all areas are playing dramatically in sync with one another. The brain functions in a similar matter. Different areas of the brain "take charge" depending on what you are doing at a given time. All other areas of the brain support the lead area, but the lead area is constantly shifting. If there is a "conductor", it may be the brain waves, the electrical activity in the brain measured by an EEG. Brain waves are generated by the activity of neurons and glial cells (supportive cells that constitute most of the brain). Brain waves also excite activity in neurons and glial cells. This is a self-propagating process. You can see a similar process at a football game when an individual begins a "wave" that is copied by people around that person. The wave spreads throughout the stadium and perpetuates itself. However, the brain waves of our brain never stop, but can increase or decrease in response to our environment. In sum, the brain is a complex system of areas that coordinate with one another to produce emotions, feelings, thoughts, and behaviors that change as our interaction with our environment changes.

Why Do We Fall in Love?

What motivates humans to spend so much time and energy pursuing relationships with other people? Panksepp (2012) and other affective neuroscientists have identified **Prototype Affective Systems (PAS)** or **Primary Emotions** that underlie and motivate all human behavior. These systems are outlined in Table 1.

Table 1: Prototype Affective Systems (PAS)* and Affective Feelings (AF)**

***PAS refer to basic components of emotions, each of which leads to whole families of systems at secondary and tertiary levels that are involved in processing or "creating" emotions as illustrated in Figure 1 below.**

****AF or "Affective Feelings", and cognitive elaborations (thoughts) are more complex extensions of Prototype Affective Systems. "Emotions" exist at multiple levels of analysis simultaneously—primary, secondary, tertiary processing (See Figure 1 below). Feelings and Cognitions are different levels of analysis of Prototype Affective Systems; but all are components of emotions.**

(Based on TED TALK: The Science of Emotions: Jaak Panksepp at TEDxRainier, July 13, 2014)

Prototype Affective Systems	Affective Feelings
• SEEKING/EXPECTANCY	Enthusiastic, Energized, Anticipatory
• RAGE/ANGER	Pissed Off, Irritated
• FEAR/ANXIETY	Anxious, Frightened to Terrified
• LUST/SEXUALITY	Horny
• CARE/NUTURANCE	Tender & Loving, Empathetic
• PANIC/GRIEF	Lonely & Sad to Separation Anxiety (Distress)
• PLAY/JOY	Joyous, Rough and Tumble Play, Humorous

The names of Prototype Affective Systems are all capital letters to distinguish these neurological systems from the everyday language used by humans to describe how they are feeling. These **PAS** have very specific biological characteristics (that will be detailed later) and promote specific behaviors. Our everyday use of these terms is much more variable and less definitive.

To avoid confusion when reading quotes in this paper drawn from various sources, please note that "Prototype Affective Systems" are also called "Primary Emotions," "Executive Operating Systems," "Primary Process Emotions," or "Prototype States." These phrases have the same meaning and are used interchangeably by Panksepp and other affective neuroscientists cited in this paper. I will use the terms Primary Emotions and Prototype Affective Systems interchangeably. The important issue to remember is that these systems are the most basic component of emotions but emotions can be seen to exist at multiple levels of analysis simultaneously. The level being referred to depends on the focus of discussion—primary, secondary, or tertiary processing that we will explore in detail.

These **PAS** produce the basic emotional drives that arise from structures/areas buried deep in the brain, are ancient from an evolutionary perspective, and are highly interconnected systems involving the brain stem, the limbic system, and the neocortex. A**ffective Feelings** arise from more complex processing of Primary Emotions that will be explained later. Affective neuropsychologists and many evolutionary psychologists argue that our emotional experiences in everyday life stem from these **PAS** and are modified by learning and our ability to reflect upon our experiences. For many years, neuroscientists believed that our "thinking brain," the neocortex, generated emotions; but that view is being challenged by recent research. Non-human animals and humans can experience emotions even when the cortex has been damaged or removed (Panksepp, 2011). For purposes of this paper and framework, we will assume that emotions emerge from these primary, more rudimentary systems. These **PAS** involve processing by the limbic system in interaction with the neocortex in complex ways to produce our experienced "feelings" that are an interpretation of these **PAS** influenced by the context of our past and current experience (Damasio, 2000, 2010; Panksepp, 1998, 2011). This notion is explored below.

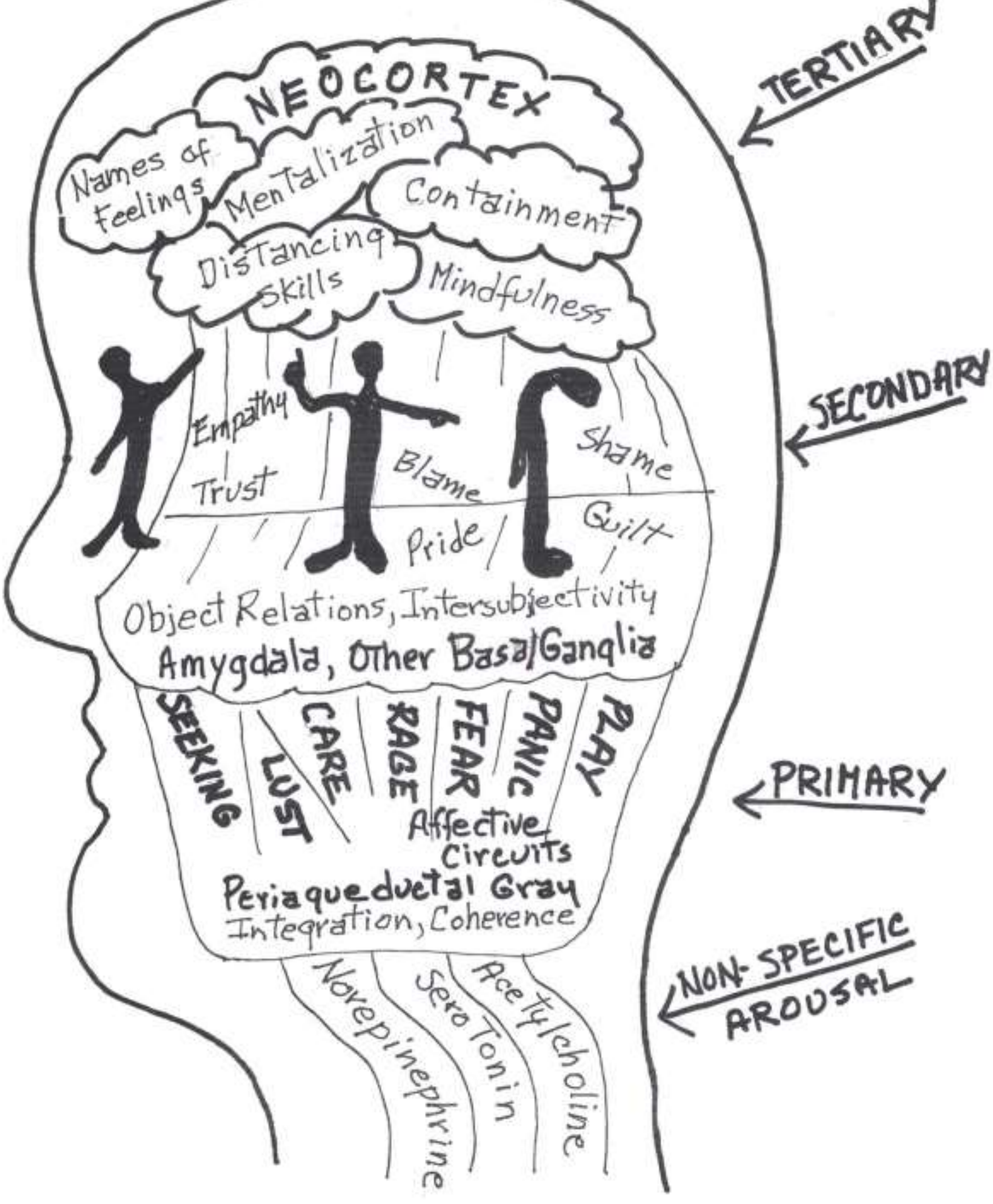
Each primary emotion controls and gives rise to distinct but specific types of behavior associated with many overlapping physiological changes that result in intense feelings, memories, and thoughts about what is happening in our lives. Figure 1 (Adapted from Panksepp, 2012) illustrates these primary emotions and the secondary feelings and tertiary processes that emerge in various regions of the brain.

The following description of Figure 1 is drawn from Panksepp & Biven (2012**) The Archaeology of Mind** which summarizes many studies conducted by Panksepp and other affective neuroscientists. Many of the comments to follow in this manuscript are based on this important neuroscience text unless otherwise specified.

Figure 1

Levels of Processing of Emotions Within the Human Brain

Adapted from Panksepp (2012) Original Drawing by Sandra Paulsen


NEOCORTEX
Names of Feelings
Mentalization
Containment
Distancing Skills
Mindfulness
Empathy
Trust
Blame
Shame
Pride
Guilt
Object Relations, Intersubjectivity
Amygdala, Other Basal Ganglia
SEEKING
LUST
CARE
RAGE
FEAR
PANIC
PLAY
Affective Circuits
Periaqueductal Gray
Integration, Coherence
Norepinephrine
Serotonin
Acetylcholine
TERTIARY
SECONDARY
PRIMARY
NON-SPECIFIC AROUSAL

The Primary Emotions, Prototype Affective Systems or PAS illustrated are ancient systems located at the top of the spinal column that cause us "to move out" (the root of the word Emotion) and behave adaptively. They provide instinctive and subconscious unconditional behavioral reactions based on evolution that help us survive, and provide a basis for our brain to generate "feelings"; also influence our "thoughts". These systems feed information to the "higher" more recently evolved brain (Neocortex) and stimulate hormonal and neural processes. They ultimately produce Endophenotypes, our primary emotional-affective personality profile generated by our individual genome.

These systems are purely physiological and subconscious because they have not yet been processed by the limbic system and cortex; that is, totally outside our awareness. Non-specific arousal emerges as nerve impulses and neural transmitters/hormones (e.g., acetylcholine, serotonin, norepinephrine, dopamine, oxytocin) from throughout our body arrive in our brain as we respond to environmental stimuli. The input information they convey is initially processed by various nuclei in the brainstem, especially the periaqueductal gray, and then passed on to other areas of the brain. These prototype affective systems give rise to "feelings," a secondary processing of Primary Emotions, that occurs within the limbic system, a subcortical region of the brain. Such feelings include pride, blame, shame, confidence, trust, disgust, dominance, empathy and guilt. They are the result of the limbic system interacting with the information the brain receives about the environment in which we live. Tertiary processes are what we typically call "mind" and occur in the neocortex; that is, how we think about Primary Emotions that have been converted into feelings within the environmental context in which the person is living. These secondary feelings and tertiary processes are influenced by the cultural and immediate interpersonal context as we live our lives, and are in part learned.

Most commonly, PAS are not under willful control, nor are they generated by our neocortex (so called "higher mind") but rather are programmed by our subcortical brain ("lower mind"), areas that constitute the processing of the Primary Emotions in conjunction with our early learning (Narvaez, D., Panksepp, J., Schore, A., & Gleason, T., 2012).

In sum, our daily experience of life is largely compelled by unconscious instinct, basic drives, and reflexive responses (lower brain) moderated by life experience and intermittent conscious thinking/reflection (higher brain). As our higher brain thinks and reflects on our day-to-day experiences, our lower brain influences our thoughts although we are not consciously aware of those influences. Primary Emotional systems are raw affects that often help us make important, and when necessary, rapid decisions.

In similar fashion, the somatic marker hypothesis, formulated by Antonio Damasio (1991), proposes that emotional processes guide (or bias) behavior, particularly decision-making. "Somatic markers" are "feelings" arising from and associated with physiological states in our body, that are in turn associated with Primary Emotions, such as the association of rapid heartbeat with anxiety or of nausea with disgust. According to the hypothesis, somatic markers strongly influence subsequent decision-making. Within the brain, somatic markers are thought to be primarily processed in the ventromedial prefrontal cortex (VMPFC) and the amygdala, areas of the brain that will be explored later in this paper. Panksepp argues that these "feelings" are secondary and tertiary processing of PAS involving the limbic system and neocortex.

Our conscious processes create a narrative to explain what is happening in lower brain systems/structures. At times that narrative interprets our Primary Emotions in irrational ways because we are not consciously aware of our **PAS** but need to invent a story, a confabulation, that helps us make sense of the world in which we are living, and how Primary Emotions in the moment relate to or are justified by our current situation or circumstances. Partners in close relationships at times disagree because their individual interpretations of shared life experiences differ. Their individual **PAS** and variably accurate and inaccurate memories interact with their past learning and life experiences to produce personal narratives that are different, leading to disagreements. Couples seen by couple/marital therapists and those involved in my current research and clinical practice demonstrate this phenomenon regularly.

Our Primary Emotions have evolved to help us survive life-threatening stressors and react very quickly if we are exposed to danger (a car runs a stop sign so we have to stop quickly, our partner becomes very angry with us). Consequently, Primary Emotions may "take-over" in during the short term during a threatening situation so we can survive long enough to think about what to do in the future to survive. This is an important theme we will visit again later in this paper.

Lisa Feldman Barret's View of Emotions

Lisa Feldman Barret is a neuroscientist who studies human emotions (2006, 2017, 2020). Although some of her ideas overlap with those of Jaak Panksepp, there are major differences. The following is a summary of her work with some comparisons to Panksepp's concepts. Barret's Conceptual Act Theory argues that emotional systems such as Panksepp describes do not exist. She postulates that consciousness emerges when a stimulus or situation elicits bodily sensations of pleasure or pain and a level of arousal. These bodily sensations are meaningless because we usually hardly noticed. They only become meaningful when we place them in context. Consequently, Barret does not see emotions to be physical reactions as Panksepp does, but rather cognitive interpretations of physical changes in our bodies. Interested readers are encouraged to view her numerous talks available on the internet (See References).

Emotions/Feelings/Thoughts as Constructions

An emotion/feeling/thought is an event in which our whole brain is making meaning of internal sensations in our body in relation to what is going on around us. The same ache in your gut can be anxiety, hunger, longing or distrust depending on what is happening to you, in your current environment, at a particular point in time. In sum, emotions/feelings and thoughts can be variable depending on the "story" of our lives over time.

Our Internal Model of the World

Our brain produces a model of the world. Our brain is connected to our bodies within a social context of other brains and what is happening around us. Consequently, our brain gets information from our senses caused by stimuli in our environment. This information is incomplete, an approximation based on phenomena such as air pressure, light, chemicals, aches, shivers, tightness; that is, the effects of some cause in the world. However, our brain only has access to the effects of the cause in our bodies, not the cause itself, so our brain has to guess what the cause is. This leads to ambiguous conclusions.

Making Sense of Physical Changes

Our brain's job is to make sense out of physical changes in our body. Barrett view is that we invent a story to explain these changes, and that emotions are part of that story, a cognition. Panksepp argues that emotions are the physical component of these changes. Unlike Barrett, he further argues that feelings are your interpretations of these changes. Panksepp maintains that Emotions and Feelings in combination with your memories of prior experiences allow you to generate a story or narrative to explain what the changes in your body from moment to moment mean. Both theories eventually generate a story we use to guide or lives; however, Panksepp argues that emotions are physically based, while Barrett sees them as cognitions regarding changes in our body. Panksepp starts with physical reactions to our environment, emotions; interpretations of emotions given what is happening in our environment at the moment, feelings; and third order processing that includes memories stored in the neocortext, a narrative or story that explains what is happening. See Biven (2022) for a detailed comparison of these arguments.

Are Emotions Different Physically?

It can be hard to tell. Physical changes accompanying various emotions are variable and overlap. Individuals, physicians, and psychotherapists struggle to figure out what is happening physically for a person at any given time. Consequently, determining the best narrative to explain what is happening physically can be ambiguous.

What's Going On?

Our body is constantly attempting to keep itself in homeostasis so it can survive. Physical changes accompanying this process are largely outside of our conscious awareness so we are not constantly distracted by what our bodies are doing to maintain an internal balance. Consequently, we are poor at determining our emotional and feeling state precisely. We tend to have a general impression of our internal physical state so can become confused regarding our feelings and how to explain them. Resolving this confusion is a component of psychotherapies and medical diagnoses.

General Mood vs. Specific Emotions

Our general awareness of what is going on in our bodies is what we experience as “mood” or “affect.” Our brain constantly attempts to link mood to what causes the sensation we are experiencing. Often, this linking process stimulates an emotion that can lead to an interpretation or feeling. We may experience this process as if an emotion/feeling is taking us over and driving our behavior. Our subjective experience may not accurately reveal what is going on inside our body.

Emotional Variability

Emotions are not confined to a specific part of the brain. For example, the amygdala is not "the center of fear." Emotions are generated by complex patterns of activity throughout many areas of the brain as it interacts with our body and external stimulation. Consequently, we experience emotions differently from one time to another depending on the circumstances, the context in which we are imbedded from moment to moment. The overall brain pattern that emerges varies greatly from time to time as circumstances change, so the phenomenological experience and intensity of emotions will also vary.

Emotions and Reason

Our brain is not a battleground between emotion and reason. The Triune Brain model that has been around for centuries is incorrect; that is, emotion and reason are not in different parts of the brain. The "neocortex" is not the slow, reasoning, part of the brain riding herd on the impulsive "reptilian brain." Many parts of the brain are involved in emotion and reasoning.

Our brain is constantly comparing our current experience to past experiences (memories) in order to generate a "concept" that explains our current experience. This process is essential to our survival and ability to reproduce.

Emotions to Behaviors

As our brain compares current experiences to past experiences, memories help us generate concepts (thoughts, narratives) that remove ambiguity and develop simulations that help us determine how to behave in order to survive. We imagine different actions we might take to deal with our current circumstances. This process increases our chances of behaving appropriately.

Our Brain Builds Stories

We create feelings as our emotions vary in response to our body's internal processes attempting to maintain homeostasis as we experience our current circumstances. We also create stories to explain what is happening. This process involves a complex interactional process within our entire brain as it in turn interacts with our body. We build or create our feelings. Keep in mind that notions of brain "parts" is largely a fiction left over from early anatomical studies (dissections) of the brain. Early anatomists did not have the sophisticated equipment that generate more complex images of brain anatomy possible today. Consequently, what looked like "parts" of the brain in the past are seen as integrated areas of the brain today.

Learning to Construct a New Story

As we become more aware of how our brain works, we can learn to construct a new story that can change how we feel as we modify our emotions, our physiological responses to our circumstance. This approach can be a component of what is coming to be known as "affective psychotherapy" and will be explored later in this paper.

In sum, Barrett and Panksepp have different views as to the nature of emotions, with Panksepp seeing them as emergent from complex neurological systems. He is not alone in this view. Barret's view that we construct stories is a component of some types of psychotherapy.

The Somatic Marker Hypothesis

Antonio Damasio (1991, 2000, 2010) has written extensively about somatic markers, physical signals generated within our body, that provide a "gut level" conscious feeling that guide sound decisions. These physical sensations alert us when our body is out of homeostasis; that is, some subsystem of our body is out of balance (e.g., hunger, thirst, lust, loneliness). This imbalance is uncomfortable, so we take action to get our systems back in balance and experience a state of pleasure. He further postulates the existence of a "protoself and mind". Biven (2022) summarizes Damasio's view: "The protoself creates maps about the homeostatic body. The mind creates maps about stimuli in the environment and in the body. We become conscious when protoself and mind maps combine. Consciousness involves three processes. First, the protoself feels pleasure, or pain that reflects homeostasis. Second, the protoself knows that a stimulus in the environment has caused the feeling of pleasure, or pain. The protoself acquires a sense of self."

Damasio goes on to argue that "an emotionally competent stimulus"; that is, a strong relevant stimulus from inside our body or from our environment, disrupts our homeostasis, which in turn activates our brain to initiate behavior that returns our body to homeostasis; e.g., take a drink, eat some food, talk to a friend. We can also experience "as-if loops"; our mind imagining an emotionally competent stimulus that can also initiate behavior. As-if loops take little energy and can be imagined quickly. As-if loops are a common part of social activity; that is, we imagine how various behaviors could help us maintain homeostasis within our relationships with others. This ability to imagine the effects of possible scenarios is a common theme in theories regarding human behavior.

Unlike Barrett, Damasio and Panksepp both see the brain stem components as important to emotions, consciousness and a sense of self. However, Panksepp argues that SELF is a primarily a motor function that does not require a homeostatic mechanism. In sum, he believes that organisms evolved the ability to move before senses emerged. This view is in contrast to most neuroscientists who see consciousness as a sensory process; that is, we sense our environment and react to it. Again, Biven (2022) details these differences clearly.

Neither Damasio or Panksepp can prove their point of view is correct and dismiss the other's theory. Both can cite research to support their theory and challenge the other's. Another way to handle this disagreement is to suggest that both have part of an overarching theory of how the brain generates a sense of Protoself or SELF. A desire to maintain homeostasis and instinctive emotional reactions to the environment may both contribute to consciousness. Being aware that the desire for homeostasis can motivate behavior, and that emotional responses to the environment may be hardwired and automatic, can help us decide how to help human beings as therapists. We shall do so later in this paper.

Why Therapists Should Study Neuroscience

Traditional "talk therapy", although helpful with many clients, is not adequate to deal with all aspects of difficult issues (e.g., Post Traumatic Stress Disorder, severe depression, personality disorders, conflict habituated couples and families).

Unconscious neurological systems (primary emotions) drive much of human behavior and cannot be directly changed by talking.

Strategies for changing primary emotions are needed to move psychotherapy beyond the limits of talk therapies.

A Caution to Avoid Getting "Lost in the Weeds" of Neurobiology

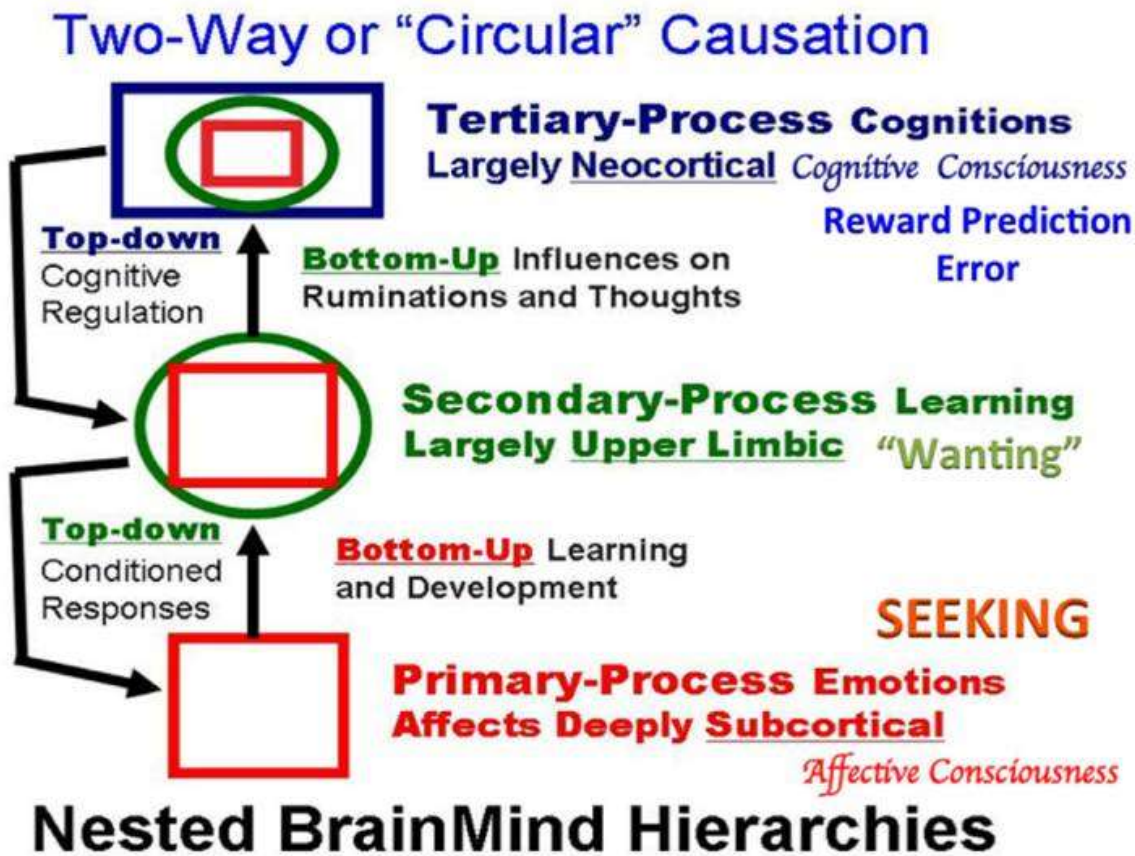
This next section of my paper is heavy-duty neuroscience and is included here for readers who have a neurobiological background and interest. It is a summary of extensive personal interviews with Dr. Douglas Watt who partnered with Jaak Panksepp for many years. Other readers can skip this section and go directly to t**he Areas of the Brain Involved in Love and SEEKING/EXPECTANCY PAS on page 23.**

Watt (2020) cautions that much is still unknown about how the neurocircuitry of our brain is involved in our behavior and our consciousness, what we commonly call our "mind." Neuroscience lacks the essential keystone in the arch – a neural theory of mind that is well validated and tested. The neural processes that cause consciousness to emerge are incompletely understood.

Watt posits that consciousness can be viewed as an emergent property of matter involved in ultra-complex signaling states within our brain. Consciousness somehow emerges from that other emergent property, life. Let us then start with a discussion of the nature of being regarding consciousness. We can think of a nested hierarchy of emergent properties that constitute the fundamental questions of science. First, there is the emergence of matter and the universe, then within that the emergence of life. Then, the emergence of mind. Since mind emerges from life and has no other known substrate, the antecedent discipline for psychology must be biology. Understanding what goes on at the psychological/biological interface is the essential work for those interested in how conscious and unconscious processes drive human behavior.

Watt also points out that everything we understand about these correlations among cognition, emotion, experiential states, behaviors and the brain suggests that what we're interested at a psychological level *"rests in the creation and activation of distributed networks"*, not in any version of a small group of systems in the brain, but more likely a group of fairly global networks. It is dynamic neural networks and not 'centers' in the brain that are the neural correlates for everything of interest regarding human emotion, cognition, and behavior. For example, the "amygdala is not the center of emotion in the brain". It's not even a 'center' for fear, as it's really a telencephalic structure that involves adaptively linking cognition to more ancient fear activating systems in the hypothalamus and periaqueductal gray (PAG). Consciousness appears to be some version of a global resonance, resting in transient alliances that run from the brainstem up to the thalamus, into the so-called 'limbic system' and into paleo and then neocortex. These global networks will be explored later in this paper.

Watt notes that it is important to emphasize these distributed network models to avoid a kind of neo-phrenology or simplistic localization in which function is attributed to an overly narrow group of systems and structures. All neuromodulators and neurotransmitters (See Appendix IV) have to be seen as gaining their functional roles by virtue of how they might signal in and alter the functional states of such distributed networks. Furthermore, secondary and tertiary chemical messengers inside of neurons need to be seen as cell signals that rebuild the network to adaptively respond better to those signals and associated challenges. For example, when people talk about the role of dopamine as though its adaptive function exists independent of a specified network, they're exposing their ignorance of these networks. Neuromodulators and neurotransmitters are an enormously diverse group of molecules and includes a vast array of molecules within neurons that all have a basic signaling function. Recent research has extended the list of macromolecules past traditional emphasis on amines and other small molecules like GABA and glutamate to a beginning appreciation of neuropeptides (e.g., endorphins and oxytocin). Further extensions would have to include hormones, cytokines, and perhaps other larger molecules yet to be discovered. It is also important to emphasize that neural signaling is probably an evolutionary extension of cell signals; that is, cells communicate with their somatic environment and have a rich repertoire of operating system responses that can be seen as analogous to behavior.



Graphic 1

Jaak Panksepp's concept of a tripartite system of levels for exploring emotion in the brain (Graphic 1) is useful in understanding complex brain networks.

In their paper What is Basic About Basic Emotions? Panksepp & Watt (2011) describe these levels: "Hierarchical controls are evident in brain regulation of emotionality. As a heuristic simplification, we prefer the following levels-of-analysis nomenclature: (a) *primary-process* core affects arise from ancient subcortical processes … (b) *secondary-process* elaborations—namely emotional learning—arise from Pavlovian/classical conditioning and instrumental/operant learning principles, and (c) *tertiary process* emotions—complex cognitive-affective amalgams, such as ruminations and affectively charged thoughts about ongoing emotional issues, which emerge via neocortical interactions with paralimbic and limbic structures. In the higher mind, these nested hierarchies interact with working-memory fields to plan alternative courses of action to cope with ongoing affective opportunities and challenges."

They point out that: "With the guidance of such evolutionary perspectives, we may eventually agree that *basic emotions* can only exist clearly at a primary-process level, namely before learning and higher order thoughts add rich developmental and cultural complexities. The general failure to recognize such "levels of control" continues to cause much mischief in modern emotion studies."

"Within nested BrainMind hierarchies, primary levels of affective experience guide what happens at secondary and tertiary levels developmentally. Eventually higher mind functions rule decision making, even in animals, but they collapse like a house of cards if the primary processes are severely damaged." (Watt & Pinkess, 2005)

"Emotional lives of mature individuals consist mostly of secondary- and tertiary-process emotional issues— "pure" primary-process emotions, unalloyed with complex cognitive attributions and appraisals, are almost theoretically impossible. But we should be clear that there is no evidence that neocortex can generate emotional feelings on its own (without accompanying arousals of paralimbic and subcortical emotional effector systems)."

Panksepp and Watt go on to describe how prototype affective systems interact with higher level processes: "From this point of view, anger provoking "irritation" becomes a low-level member of a RAGE/affective attack "family" of emotions, which can be further elaborated by cognitive/tertiary processes. Loneliness, sadness, shame, and guilt may all become cognitive/tertiary elaborations related to fundamental separation-distress (PANIC/ GRIEF) issues. Humor may be a cognized form of rough- and-tumble PLAYfulness. And so on for the other primes."

"In sum, with development and maturation, the MindBrain gets ever more complex, but that complexity is best approached by first outlining the most fundamental principles. That has generally not happened in psychology. At the highest level, we conceptualize our emotional lives in thoughts and words, but do such superordinate levels of organization really vastly modify how primary emotions feel? We don't know. But we do know these cognized tertiary emotional processes promote art, movies, music, poetry, rhetoric, theatre, etcetera. So, from a mature, fully resolved, MindBrain perspective, all emotions are not basic. But those that are become critically important components for the higher order complexities that arise from the developmental landscapes of individual lives and cultures.''

Watt continues by reminding us that in order to avoid confusion, we must be clear about what level of analysis of various brain systems we are discussing when examining human emotion. Are we talking about the prototype states SEEKING/EXPECTANCY, RAGE/ANGER, FEAR/ANXIETY, LUST/SEXUALITY, CARE/NUTURANCE, PANIC/GRIEF, LUST SEXUALITY, PLAY/JOY that Panksepp called the primary processing level? Or are we talking about "emotions", or better delineated as "feelings", particularly in adult humans, at the secondary learned associations and habits level? Or are we talking about tertiary level cognitive extensions of emotion that involve cognitive complexities. This interaction of levels of processing makes researching the neural correlates of emotion in adult humans an almost impossible task because we are required to include the telencephalon (cerebrum) and very global and highly distributed networks. This is particularly true because much of the technology for studying emotion in humans, i.e., functional imaging, primarily detects tertiary level cognitive activations, not with the underlying subcortical architectures that enable the primary process. For example, we experience an adaptive and cognitively extended form of rage when someone takes our parking space. We (hopefully) don't kill them (unless there is something really wrong with us!) but we might leave them a terse note explaining that this is not their proper territory. Such an experience reveals the functional/adaptive connection between our irritation and the RAGE system that of necessity defends supplies, territory, mates, and offspring.

To be clear, when Panksepp discussed secondary process, he was pointing to how prototype affective systems (primal emotions), could lead to behavioral learning. This behavioral learning is principally orchestrated by the basal ganglia which involves motor learning and control, emotion, executive functions and behavior, the amygdala, which involves emotional processing to be detailed later, and associated paleo cortical regions involved with our sense of smell. Feelings in humans no doubt typically involve both secondary level processes including learned associations to intrinsic rewards and punishments, but also cognitive extensions (the so-called tertiary process level). For example, shame and guilt might be viewed as tertiary cognitive extensions to separation distress (PANIC/GRIEF), and they require the capacity to create a self-image and to imagine a dynamic relationship with others. In shame we are exposed as defective and lacking in whatever it is necessary to secure esteem and love. It's very unlikely that a small infant mammal separated from its mother and siblings is capable of shame, but it is capable of a prototype state of separation distress. This example illustrates that when you discuss these things, you have to be careful to not conflate; that is, misidentify which of the three levels of emotional processing is involved, or to fail to identify an emotional circumstance in which more than one level of processing is involved. Not being careful can cause endless confusion because much of the time when people talk about emotion, they don't understand that they're talking about tertiary higher brain level cognitive emotional processing perceived as "feelings" in adult humans. There really is no primary process *per se* at that point because the primary affect produced at the lowest levels of the brain has usually been significantly modified at the secondary/limbic and higher cognitive levels of brain processing.

Not much is known about how much tertiary process there is in some more highly intelligent mammals. Mammals have both paleocortex and some neocortex, with neocortex expanding in primates, and then further expanding in hominid lines, especially modern humans. Furthermore, little is known about how cognitive processes interact with and activate primal, prototype affective systems. There are prototype elicitors for each of these prototype systems, and complex cognition may give us toolkits that allow us to recognize these systems when a more complex version of the original prototype elicitor comes along; such as in the parking example.

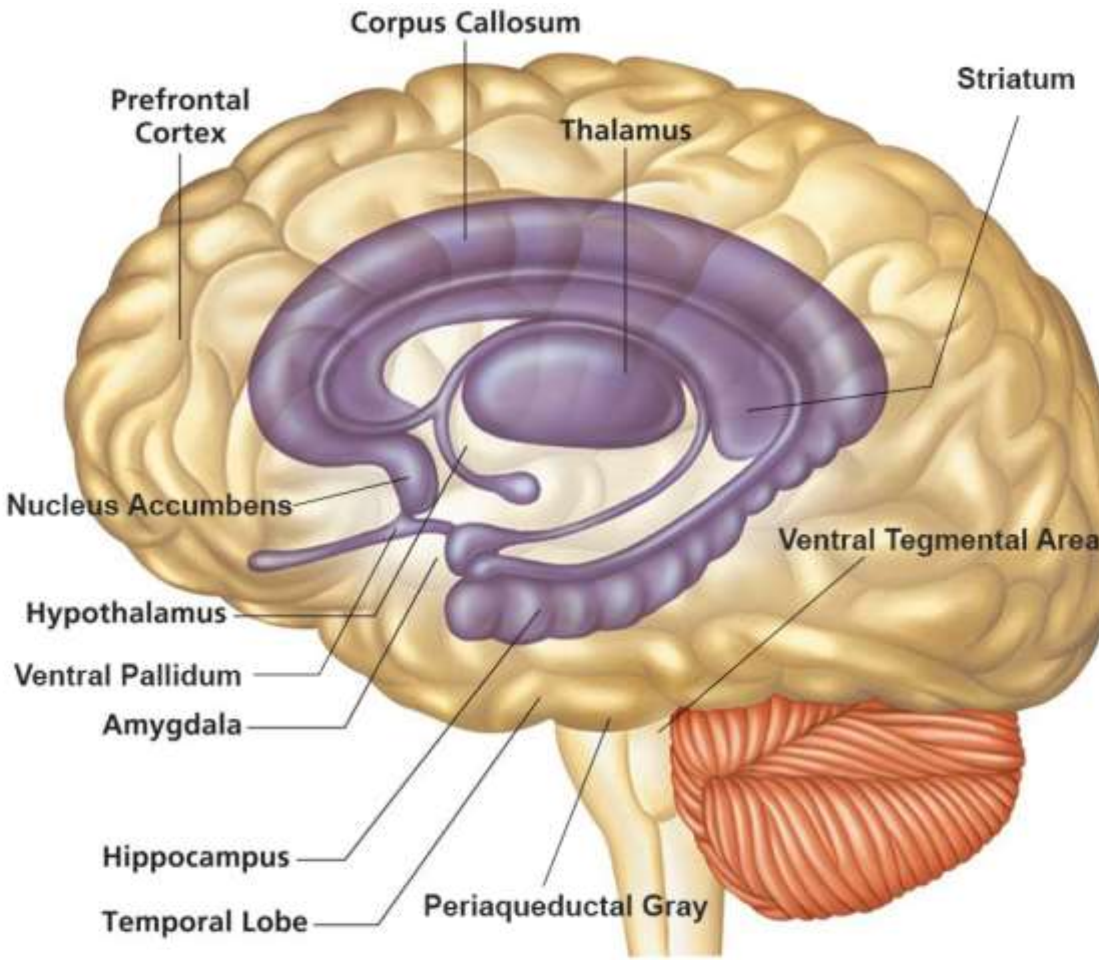
Another important issue to consider is the incredibly difficult problem of explaining valence, or the painfulness and pleasurableness of *certain states*. Valence, as used in psychology, means the intrinsic attractiveness (positive valence) or aversiveness (negative valence) of an event, object, or situation; the term is also used to characterize and categorize specific emotions.

An example of this mystery of valenced experience is pain. Pain signals a homeostatic/organismic threat, which is unpleasant. In other words, there is an inborn motivation to reduce the signal. When some homeostatic imbalance is occurring because some system in our body (thirst, hunger, loneliness) is not in the preferred range, we seek something to restore the balance (water, food, companionship). The relief of that imbalance is experienced as pleasurable. The most parsimonious way to make sense out of the intrinsically painful and pleasurable nature of core affective processes is that there is a conserved and intrinsic wiring of emotional systems such that certain types of stimulations within systems produce positive feedback, motivating systems to obtain more of what is needed to restore homeostatic balance. We describe this as liking something. We like pleasant tastes, sex, play, etc. There is a countervailing dislike of other types of signals. There is presumably an inborn wiring pattern that allows motivational systems to reduce the types of stimuli we dislike (e.g., pain, rage, fear, hunger). Common sense perspectives of human relationships map directly onto affective neuroscience. Relationships supply us with a constant stream of positive affects that counter the effects of negative affects.

Therefore, motivation and emotion have to be understood as containing these intrinsic dynamics of increasing the positives and decreasing the negatives. Additionally, there is probably some version of a central clearinghouse in which all of these imbalances compete; probably the paralimbic cortex and perhaps subcortical affective systems like the nucleus accumbens and even PAG may influence one another through *competitive lateral inhibition;* that is, these systems compete with each other for attention and at any given time, one of them dominates. Throughout our lifetime we chase these signals; pursuing the positives and shutting down the negatives. It is rather grandiose to think we are capable of doing anything without guidance from these basic affective signals. It is hard to identify a single motivated act that violates this principle. Deep lesions to PAG and other midline systems result in severe akinetic mutism – the global collapse of emotion and motivation. In that sense, the prototype emotional systems that Panksepp emphasized contain a set of *inborn compasses* that are continuously and adaptively extended and expanded by the secondary and tertiary processes, such that those higher-level systems continue to inform our behavior in much more complex environments. We can speculate on why the right hemisphere might take the lead in terms of its ability to see global social contexts in terms of their similarity to original activators of the prototype states. Again, as in the parking space example, we recognize a violation of territoriality. It is hard to conceive that we could build that bridge without the cortex; i.e., a bridge from rudimentary territoriality that a lower mammal might exhibit in defending a space, to moral outrage/sense of injustice at one's parking space having been stolen in a human.

As Panksepp emphasizes, there is a lot of modulation and inhibition brought to the table by cortex as well (presented in an understated way in Graphic 1). The first job of a highly evolved thinking creature is to clear the board of any pre-potent behavioral vectors (otherwise known as emotional flooding), integrate needs and presses with current environmental challenges, and formulate a plan that is likely to succeed. In that sense the prototype affective systems offer relatively "simple" prepackaged executive routines that are useful but that of course also have some rather harsh adaptive limits. The further processing of these systems by secondary and tertiary processes allows a much more graduated and vastly differentiated set of adaptive responses. In that sense it's useful to think in terms of the prototype states having prototype elicitors.

Areas of the Brain Involved in Love



Prototype Affective Systems (PAS; primal "raw" unprocessed emotions) are a proto-executive prepackaged set of executive routines originating early in the evolution of vertebrates and consist of a small number of affective behaviors. If you knock out this bottom of the system, the top of the system, despite having activating and inhibiting controls, no longer produces emotion and motivation. Higher order brain processing informs and transforms emotion and makes it something much more differentiated and complex than the prototype affective response itself. The overall brain processing system is dependent upon lower-level prototype affective systems. It is hard for an organism to recover from damage at the Protype Affective System level. Damage leads to permanent disability. The hierarchical and nested feedback loops that constitute the brain's processing of emotion blend lower-level PAS signals with higher order (more complex) processing that results in cognitive emotional awareness. We experience the nuances of the interplay of all orders of brain processing, not isolated PAS affects, feelings, or cognition. Evolution placed these PAS right next to brain stem motor systems so that these proto-executive systems (PAS) can tell motor systems when to turn on and perhaps to speed up the control process. If you lose these proto executive systems in the brain stem, the PAG and VTA, all the higher "fancy" cognitive systems cannot function.

The bones of this prototype affective system or "executive system" are the hypothalamus, the brain stem, and particularly the upper brain stem, including PAG, VTA, all of which provide innervations that arouse the forebrain and the superior colliculus. The neostriatum or paleo-striatum including the nucleus accumbens and the olfactory tubercle, as well as the amygdala are structures that contribute to secondary processing of emotion in the brain. These structures build associations to prototype affective states such as learning. To learn through classical conditioning that a tone means you are going to get a foot shock is one well-studied example of such PAS and secondary level interactive processing. Through evolution, these basic prototype affective systems, the VTA and other brain stem structures that form the ventral core of the SEEKING system, have come to depend on secondary systems for arousal. If part of the secondary processing structures such as the nucleus accumbens gets damaged, the VTA is not stimulated so these prototype affective systems do not become aroused. The nucleus accumbens and VTA are the most essential structures in the SEEKING system, and influence one another top down, and bottom up. The norepinephrine system also has a role in SEEKING, as does the serotonin system, the later system dampening and counterposing norepinephrine and dopamine. Dopamine circuits encourages us to "go get them", and norepinephrine circuits at a sensory level help us sort signal from noise to help us determine what is emotionally salient. The most essential proto-executive systems in the brain stem are the hypothalamus, all the amine cores (dopamine, serotonin, and norepinephrine), as well as some other midbrain nuclei, particularly the VTA and PAG. The secondary process includes the amygdala, the basal ganglia, and probably the paleocortex. The paleocortex becomes the great bridge among all those systems and the neocortex. The cingulate gyrus, especially the anterior cingulate gyrus, is classical paleocortex and is closely tied to SEEKING and basic motivation arousal. The cingulate gyrus is a curved fold covering the corpus callosum. A component of the limbic system, it is involved in processing emotions and behavior regulation. It also helps to regulate autonomic motor function.

The PAG is an ancient system. It does the final arbitration between pushes and pulls of prototype affective systems because they cannot all operate at the same time. At what might be called "emotional steady-state/rest," all of the prototype affective systems are in a relative counter-balanced state of even competition with one another, until something (e.g., an emotion-arousing event of some sort) tips the balance of the steady-state. With respect to functionality, the PAS—the proto executive systems are prepackaged programs. They have an "all in quality" when emotionally aroused; no shades of gray; this ability to rapidly "fire off" is related to the fact that appropriate emotional response in particular situations is often necessary for survival. For example, the cognition system blending with the PANIC/GRIEF (Separation Distress) system leads to more complex responses such as jealousy.

Most medial (center) and ventral (bottom) areas of the brain are ancient and involved in the most ancient functions of mind, e.g., homeostasis. Motion is also an ancient brain system and enables behavioral output enabling homeostasis. If brain areas are lateral (to either side) and dorsal (at the top of the brain), they evolved later and are largely associated with cognition. In his tripartite scheme Panksepp reminds us that nature never throws anything away but rather incorporates and adds to whatever is already in use. Consequently, brain areas that evolved later extend and expand upon the function of earlier areas and are connected with feedback loops that modulate and control earlier areas to some extent. Later brain areas are energized from below. Even though the brainstem is the most primitive, ancient and undifferentiated area of the brain, the brainstem has its own complexity because it has so many components and varied connectivity.

Panksepp and Watt (2011) tell us that "the underlying circuits for primary-process emotions were evolutionarily programmed/prewired, albeit also epigenetically "shaped." They are psychologically primitive and "building blocks" for higher emotions. Basic emotions are tools for living that are inherited potentials of the brain (i.e., SEEKING, RAGE, FEAR, LUST, CARE, PANIC/GRIEF, and PLAY, although there may be more). Including primary-process sensory and homeostatic affects, such as DISGUST and HUNGER, as basic "emotions" is unwise (i.e., may be category errors. They belong in "sensory" and "homeostatic" affect categories (see Panksepp, 2007a).

Evolutionary prewiring does not mean these functions are not further refined by experiences; e.g., epigenetic expansions of dendritic trees, induction of various trophic factors, and other complex housekeeping functions within the neuronal networks that constitute such systems. Plasticity is pervasive in brain development. The prototype affective networks supply motivational templates (raw affects that drive behavior to maintain homeostasis) and key control mechanisms for learning and the construction of "personality" and "temperament" (influences that may be monitored verbally; Davis, Panksepp, & Normansell, 2003).

Neuroscience evidence indicates that primary-process emotional systems engender "psychological primitives"—raw affects—that can serve as "building-blocks" and "fuel" for abundant higher MindBrain developments. This is truly remarkable! All of this entails experience-dependent neuroplasticity operating in widespread corticolimbic networks. We do not yet know how such higher integrations occur mechanistically, but we know that wherever brain stimulation evokes coherent emotional reactions, those stimulations serve as "rewards" and "punishments" in various learning tasks *(Ikemoto, 2010; Panksepp, 1971, 1982, 1998, 2005a, 2005b.*

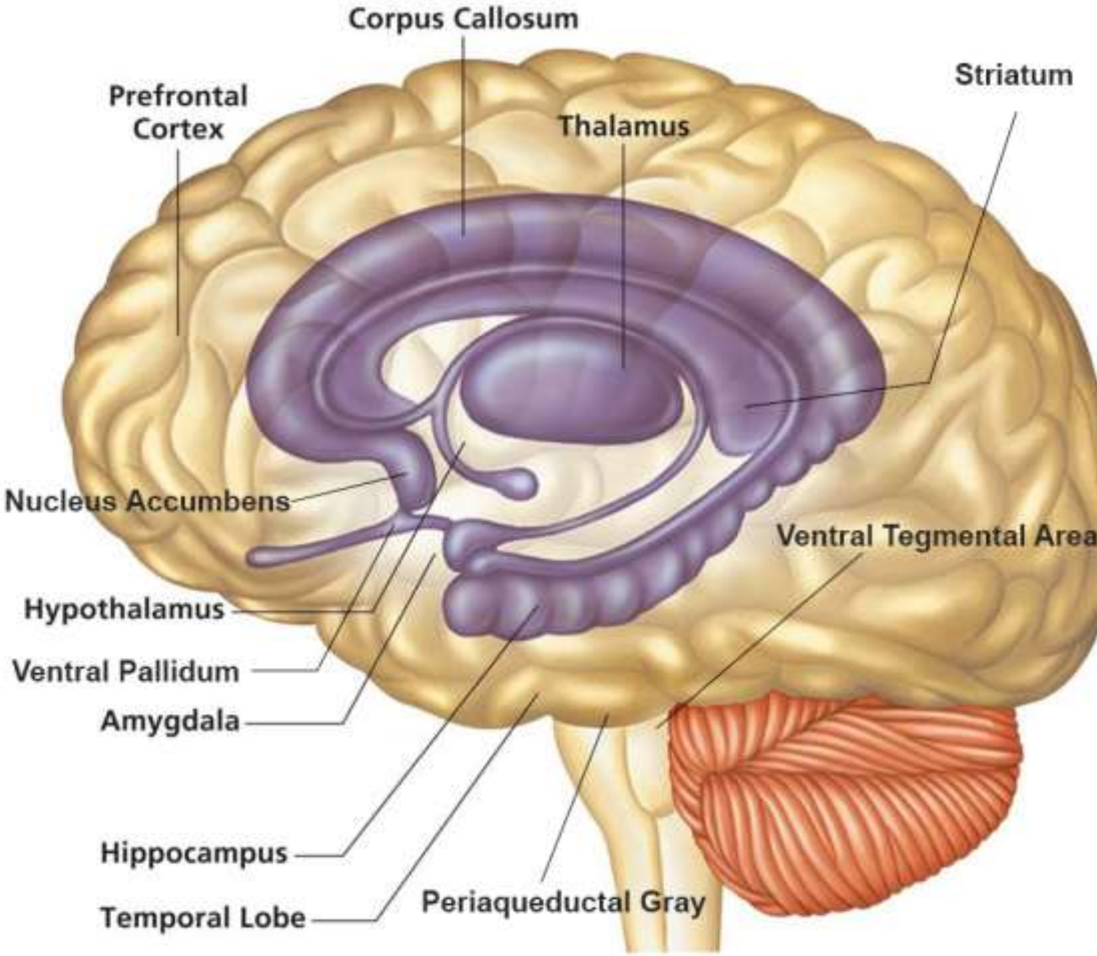
Primary-process emotions provide the materials and catalysts for the emergence of socially constructed emotions. Jealousy may coalesce and derive its nuanced affect from concatenations of mild FEARful, PANICked, LUSTy feelings (Panksepp, 2010a). Jealousy may emerge when one begins to PANIC that they will no longer have anyone to CARE for them (or share LUST with them), making them less happy/PLAYful, all of which promotes demanding SEEKING of reunion, commonly contaminated by RAGEful displays. Because of these affective cross-currents, one is often emotionally confused and ambivalent, with little fun left in life.

Some Editorial Observations about Consciousness and Brain Research

Consciousness involves the interaction of the tertiary affective processing level with primary and secondary processing levels described earlier. However, almost all of current neuroscience attention is focused on the cortex because of functional imaging (FI) and does not tell us how system integration, i.e., consciousness, is achieved. The most interesting question is how consciousness or mind emerges through the integration of many brain systems. Functional imaging does not tell us anything about that. Looking at the telencephalon (cerebrum) does not tell us about that. Using FI does not tell us what we need to know. Ventral thalamic systems and below are more important to achieving the dynamic integration that is necessary to create a mind. Brain areas above are getting networked in to help create the highly differentiated content that cognitive consciousness allows. This leads to fantastic refinement on many different dimensions; enhancement of sensory processing, enhanced motor processing in terms of motor skills, and complex ideas about what to do, the executive extension of the motor system. Every part of the system is enhanced by the telencephalon but it cannot do enhancement without preexisting creation of some kind of dynamic ventral brain system that lets us know that "somebody is in there." There is a purposeful active agent that does things that we can appreciate as deliberate and is coming from some behavior that has intention. If that is there, we can say there is a conscious actor. We are very far from understanding that process of global system integration. Extensive brain stem injury means "no one is there anymore." The brainstem is the most important functional unit in anatomical terms, yet the systemic exploration of its forty or more systems, the nuclei, is modest. These systems are not operating in isolation. The PAG is poorly understood. Mind is not limited to the cortex. The brain stem is responsible for sorting and processing complex stimuli that provides crucial information to the telencephalon, and possibly the claustrum and the nearby insular cortex which receive and transmit information from many brain areas and thus somehow construct a sense of our conscious selves. In sum, the whole brain in involved in the emergence of consciousness.

This completes my summary of interviews with Dr. Douglas Watt. Interested readers are encouraged to review published articles and books written by Watt and Panksepp that are included in the reference section of this paper. We will now return to a more general discussion emotions, feelings, thoughts, and human behavior.

Areas of the Brain Involved in Love



The SEEKING/EXPECTANCY Prototype Affective System

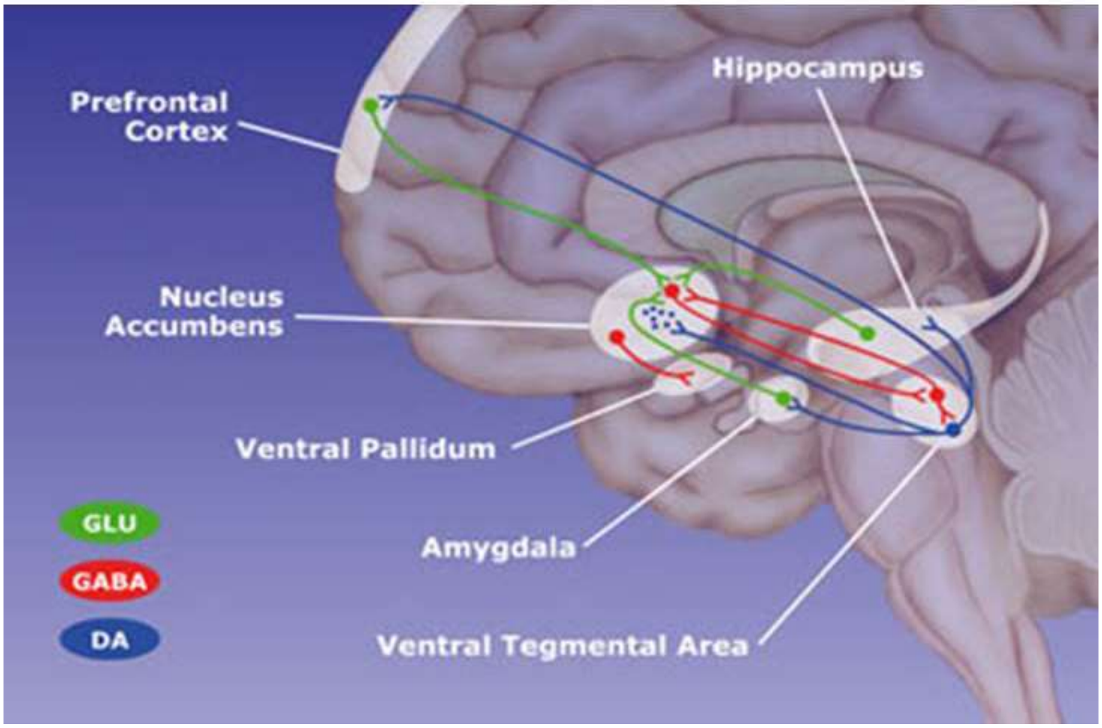
Of the seven **PAS**, SEEKING/EXPECTANCY is the most pervasive in that it supports and influences all other **PAS** and is fundamental to survival. It interacts with the CARE/NUTURANCE and PLAY/JOY systems (to be discussed later) to form a positive-affect group of systems (Davis et. al., 2003) involved in the development of love relationships in humans. It interacts with the FEAR/ANXIETY, RAGE/ANGER, and PANIC/GRIEF systems to form a negative-affect system that is activated when relationships are deteriorating (to be discussed in the Divorce and Death sections later).

SEEKING/EXPECTANCY is the most ancient PAS. All other PAS build on the SEEKING/EXPECTANCY system. Prototype Affective Systems are all specialized evolutionarily extended versions of SEEKING/EXPECTANCY. We seek safety when panicked, we seek reunion when separated and grieving. In PLAY/JOY we seek rough and tumble engagement. When enraged we seek to terminate whatever is bothering us. The SEEKING/EXPECTANCY system is the trunk line and everything else is extended from and subordinate to it. If the SEEKING/EXPECTANCY system is damaged, all the other prototype systems are also affected (Panksepp, 1998; Panksepp & Biven, 2012, Panksepp & Watt, 2011, Watt, personal communication, 2020).

SEEKING/EXPECTANCY evolved first, then organism defense systems (FEAR/ANXIETY, RAGE/ANGER), then social emotions (SEPARATION/ DISTRESS, CARING/NUTUREANCE, PLAY/JOY, LUST/SEXUALITY) in mammalian and avian lines. These systems evolved to support a bigger brain, which in turn lead to helping infants that needed to be cared for. Parent child bonds have to be strong so infants can be cared for and the species does not go extinct (Panksepp & Watt, 2011; Watt, personal communication, 2020).

Activation of the SEEKING/EXPECTANCY system is necessary to motivate any mammal including humans to want to do anything. If this system is not functioning well, a person may appear lethargic, and may indeed be, depressed. If this system is activated, the person is motivated to enthusiastically explore, seek out resources, and euphorically anticipate a reward. In fact, anticipation of a reward is the primary motivation that drives us to do something. Receiving the reward, e.g., food, water, sex, etc. is pleasurable because it returns our body to homeostasis (internal balance or the satiation of needs); but anticipating the reward is the initial driver, the so-called motivation. Consequently, calling the SEEKING/EXPECTANCY system the “reward system” is misleading. There are many affective reward systems in the brain. Unfortunately, the name “reward system” is still often used by individuals who are not aware of recent research which suggests that the “reward system” is not a single system, nor is it identical to the SEEKING/EXPECTANCY system as a whole, but rather just one major multi-faceted component of it.

Seeking/Expectancy (The Reward Circuit)

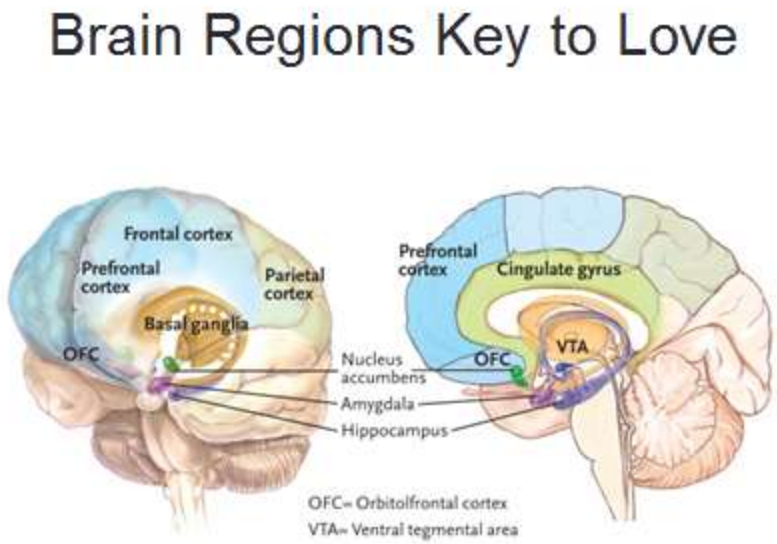


The SEEKING/EXPECTANCY system is necessary to motivate and guide our behavior as we look for and approach a potential mate; for example, when looking for a good restaurant to take a date. Without it we would not desire to be emotionally and sexually involved with another person. The LUST/SEXUALITY system by itself will not motivate us to mate. The two systems must coordinate to promote reproductive behavior.

Unpleasant states of homeostatic imbalance (e.g., hunger, loneliness, lust) will make the SEEKING/EXPECTANCY system more receptive to rewards and trigger activity to seek such rewards. This occurs when hormones generated throughout our body are processed by interoreceptors or "need receptors" (nerves cells sensitive to hormones) in the brain as described earlier. When a person is lonely, sexually aroused, or feels a need to play, stress hormones such as corticotrophin-releasing factor (CRF) and ultimately cortisol, or a dearth of endorphins (endogenous opioids) will be sensed by interceptors and they will seek another person to relieve the imbalance. The SEEKING/EXPECTANCY system provides a positive, enthused counterbalance to negative homeostatic states by motivating us to spend time with good friends or lovers and thereby reduce the level of stress hormones and raise the level of endorphins. Low doses of endorphins may suppress GABA neurons that normally inhibit the SEEKING/EXPECTATION system (Ikemoto, 2010). When GABA neurons are suppressed, the SEEKING/EXPECTATION system becomes more active and in turn tends to alleviate negative emotions such as those associated with the FEAR/ANXIETY system (Salamone, 1994) which makes it easier for us to approach another person.

The SEEKING/EXPECTANCY circuit runs from the ventral tegmental area (VTA) to three destinations: as part of the medial forebrain bundle, VTA axons travel to the lateral hypothalamus (MFB-LH), nucleus accumbens, and medial prefrontal cortex following the mesolimbic and mesocortical dopamine pathways, which also comprise component pathways of the medial forebrain bundle (Panksepp & Biven, 2012; see Brain Regions Key to Love and Areas of the Brain Involved in Love below). The VTA receives signals from the periaqueductal gray (PAG) in the midbrain which in turn receives inputs from the spinal cord, and the pons and medulla of the lower brainstem. It acts as an interface between the lower brainstem, the limbic system and ultimately the forebrain (prefrontal cortex). The PAG also receives information from the superior colliculus in the brainstem that helps integrate appropriate behavioral responses to external stimuli (e.g., orientation/attention to threat) as well as information from internal stressors (e.g., pain). It also sends information related to such experiences as sexual desire, fatigue, and hunger to the hypothalamus and amygdala (limbic system) for further processing (Panksepp & Watt, 2011; Watt, personal communication, 2020. In sum, the VTA receives messages from other parts of the brain and the body as to how efficiently basic human needs (e.g., sex, companionship) are being met. If needs are being satisfied, dopamine neurons alert the nucleus accumbens; dopamine levels increase, enhancing pleasurable feelings and thereby "rewarding" the behaviors through which the basic needs are met. The medial prefrontal cortex and MFB-LH coordinate their information processing to help devise strategies to get what we want out of life and avoid problems. Raw primal emotions connect to pleasure-producing portions of the brain that are informed by our "thinking" brain, so we follow the most productive course of action.

We humans become motivated to seek a relationship with other people when the SEEKING/EXPECTANCY system and the PANIC/GRIEF and/or the LUST/SEXUALITY systems are activated. The exact combination is determined by the nature of the relationship sought. To feel socially comfortable, we need other people to fulfill our desires for love and attachment. When we do not have someone to fill our social needs, we become lonely. If we can't find someone, we may exhibit varying degrees of panic or anxiety as we think about living alone. Or we might grieve if we lose someone we were attached to. When we do not have a sexual partner, we may become sexually aroused and seek another person to be physically involved with. Ideally that person will also be someone we care about. In sum, when we are lonely or anxious because we don't have a loved one or partner close, several of our prototype emotional systems become activated. All these behaviors occur when we desire to have other people in our lives to keep our bodies in a state of what might be referred to as "social homeostasis;" that is, to facilitate the restoration of our normal socially healthy comfort levels.



Early Stages of Intimate Human Relationships

Multiple parallel streams of brain systems are operating at the beginning of relationships; attraction occurs at multiple level. Sexual attraction is stimulated by features that predict reproductive fitness; e.g., the ratio of facial components such as narrow jaw in females and wide jaw in males are seen as more attractive. Similarly, hip to waist ratio influences how fertile a person looks to the opposite sex. This indicates that the LUST/SEXUALITY system is cued to features that predict a higher ability to reproduce successfully. Parallel to that, individuals must decide if they like this potential partner. People may not consciously ask themselves, "do I like him or her?" because their behavior is largely driven by their more unconscious LUST/SEXUALITY system. If someone finds the other person attractive but do not like them (an assessment that usually requires complex cognitive/tertiary processing), the chances of a successful relationship developing is lower. However, if someone sees the other person as attractive and likes them, the chances of a successful relationship increase. If one person sees the other as attractive, likeable, empathic, and caring, the relationship is reinforced and amplified in many additional ways. Parallel processes among brain systems may lead to repulsion or attraction to a potential mate (Panksepp & Watt, 2011; Watt, personal communication, 2020). In sum, because individuals are looking for a partner, are lonely, desire sexual intimacy, seek pleasure, and want someone to be concerned for them, the SEEKING, PANIC (Separation/Distress), LUST, JOY, and CARING systems are all running concurrently when couples begin a relationship. These systems interact with each other because they partially overlap and share much of the same circuitry. The balance among these systems determines if and how the relationship develops. For example, early in a relationship, both partners may probe one another to determine how caring or giving the other person tends to be. They may talk about earlier relationships to get some idea how nurturing each of them might be if their relationship continues. For a second or third date to occur, each person must feel safe (keep the FEAR/ANXIETY system relatively inactive or inhibited), be attracted to each other (LUST/SEXUALITY and PLAY/JOY systems activated), and have some reason to believe the other person will be concerned about their welfare (potential for CARE/NUTURANCE system activation). Also, each person's behavior must not activate the other person's ANGER/RAGE or PANIC/GRIEF (separation/distress) system. What is the point of continuing in a relationship if the person you are dating irritates you from the get go or has a history of ending relationships? All these proto-affective brain systems are operating constantly. What matters is the overall mix, not just one system's activity.

Lust

Fisher's first stage of love, the Lust or Sex Drive (Romance), is characterized by a craving for sexual gratification (Fisher, 2016). This should come as no surprise because humans, like all mammals, are driven to reproduce. Panksepp's LUST/SEXUALITY system and PANIC/SEPARATION systems are activated as humans initially approach each other seeking a mate. Our SEEKING/EXPECTANCY system motivates us to seek another person to fulfill this desire.

Humans, like other animals, display a rich assortment of "courting" behavior. We often flirt in a particular sequence. She smiles and lifts her eyebrows, raises her shoulders, arches her back, tosses her hair. He walks up to her, arches his back, and thrusts his upper body in her direction (Fisher, 2016). Such instinctive behaviors are common among mammals (Sapolsky, 2017). Like Sapolsky, my observations of human mating behavior in 27 different cultures and Sapolsky's and my observations of baboons in Kenya have shown similar recurring tendencies. All these behaviors are generated by the Primal Emotional systems described by Panksepp and are largely outside of our conscious awareness. Anthropologists, and relationship therapists are aware of these behavioral tendencies and use them in their professional work (Sapolsky, 2017; Joanning, Brewster, & Koval, 1984; Joanning & Keoughan, 2005, 2006).

We are usually unaware that such behavior is due to our genes, hormones, and nervous system driving us to reproduce. We may find someone attractive, interesting, and find ourselves pursuing them. When we interact with a potential love interest, phenylethylamine (PEA) in the ventral tegmental area (VTA) of our brain stimulates dopamine neurons that in turn increase dopamine levels in neural circuits of the nucleus accumbens (NA), an important brain area in forming memories of salient environmental stimuli, both positive and negative. In sum, the rise of dopamine levels in the nucleus accumbens helps us remember what environmental stimuli increase pleasure and what stimuli cause discomfort. Consequently, we seek a mate who we perceive to be a source of pleasure and avoid individuals who we perceive as causing pain. The same person can be seen as a source of pleasure (when courting) and a source of pain (when considering a divorce).

Phenylethylamine also helps to stimulate the production of beta-endorphins (endogenous opioids), which are our brain's collection of 'feel-good' neurochemicals. These endogenous opioids can give us a high like amphetamine. Some scientists believe that PEA is responsible for the giddy, intoxicating feeling we experience when falling in love (Fisher, 2016).

We are not aware of the activation of our LUST/SEXUALITY brain circuit, the flow of testosterone and estrogen through our blood stream and glands, or of the increase of dopamine in the SEEKING/EXPECTANCY system. None the less, our bodies are aware in the sense that the "feeling" center of our brain, the limbic system, is strongly activated and pushing us to engage in behavior that the rational part of our brain, the prefrontal cortex, may not perceive as rational. We all smile when we see lovers engaging in behavior that may seem charming, provocative, or silly to an observer. We engage in such behavior because our bodies are designed to do what is needed to reproduce. An amusing example of these behaviors is the television show, *The Orville*, a quirky science fiction parody of the Star Trek series in which the captain, a man, is attempting to deal with his first officer, a woman who happens to be his ex-wife. They are sexually attracted to one another, and so struggle to overcome their history as a couple.

When the lust system is activated, it produces feelings of sexual arousal; thoughts oriented toward sexual fulfillment urge us to engage in sexual activity. The evolutionary advantage of having a LUST/SEXUALITY system is to motivate organisms to reproduce.

Lust stems predominantly from the hypothalamus, a region of the brain that also controls basic desires such as hunger and thirst. The hypothalamus controls the endocrine system, ductless glands that release hormones that direct our body to respond to changes in our bodies and the environment. When we fall in love, the hypothalamus is actively influencing our thoughts and behavior by releasing dopamine that enhances testosterone release from testes, ovaries, and adrenal glands and promotes basic reproductive drive in both sexes.

The hypothalamus is a primary top-level controller of the autonomic nervous system that controls our heart rate and how fast we breathe. When men and women fall in love with someone our initial lustful feelings are promoted by testosterone, a long-acting hormone secreted from the testes in men and the adrenal gland in women, which stimulates the hypothalamus and produces a strong drive for reproduction in both men and women. This drive is enhanced by dopamine, a neurohormone produced by several areas of the brain including the VTA and the substantia nigra. This combination motivates us to seek sexual satisfaction. Once in our bloodstream, dopamine triggers a chain reaction within the nervous and endocrine system that eventually leads to testosterone feeding back to the hypothalamus once we have experienced sexual satiation, usually through orgasm. Specific receptors in the hypothalamus for testosterone let our brain know we have been sexually satisfied, which in turn stimulates more dopamine release (Panksepp, 2012). Activation of these dopamine circuits is experienced as pleasure. As we fall in love, we experience a highly sexual urge that is very pleasurable if we find the right partner and engage in sexual activity. The LUST/SEXUALITY system “jump starts” our relationship and sets the stage for the activation of other brain systems important to relationship development.

Men and women have somewhat different sexual neuro-circuitry that helps explain differences in sexual behavior (Panksepp, 2012). Our sexual interests and behavior as adults are developmentally the result of different experiences in our mother’s womb. All fetuses start as anatomically neutral, but male babies change structurally because of greater influence by testosterone during fetal development. Male fetuses have more testosterone receptors especially in the hypothalamus (specifically the anterior/front part, the preoptic area). This makes males very susceptible to surges of testosterone that occur during fetal development and again during puberty. Testosterone also activates vasopressin and nitric oxide. Certain vasopressin circuits promote sexual ardor, sexual bonding, inter-male aggression, and possibly jealousy; these circuits tend to make males more “pushy and competitive” (Taylor et. al., 2000). Males have twice as much vasopressin as females. Certain nitric oxide circuits heighten sexual eagerness and “offensive” aggression. This hormonal cocktail also promotes behavior associated with social dominance. Testosterone also sensitizes the RAGE/ANGER circuit. No wonder adolescent males at times engage in fierce competition for female attention.

Female fetuses are more influenced by estrogen which sensitizes oxytocin neural circuits in the female brain while testosterone increases vasopressin sensitivity in males. Oxytocin calms the brain and appears to facilitate positive social bonding in both men and women (Taylor et. al., 2000). Women have far higher estrogen levels than males. From an evolutionary perspective, greater estrogen production in females, in combination with oxytocin circuits, which facilitate social bonding with children and other women makes sense. When estrogen is combined with oxytocin, female-typical nurturing attitudes are enhanced, the tendency "to trend and befriend" (Taylor et.al. 2000). For hundreds of thousands of years proto-humans and modern humans survived in migrating small bands or clans with the women and children staying close to one another while men at times hunted. Not until the rise of agriculture approximately 11,000 years ago did that pattern change, a small period of time from an evolutionary standpoint. Women are neurologically wired to work together to raise children and promote survival of the species.

Like males, female sexual receptivity is governed by the hypothalamus, specifically the ventromedial hypothalamus. Human females do not produce much testosterone, so their hypothalamus is more influenced by estrogen and progesterone. Female testosterone is produced by the adrenal gland and has some influence on sexual receptivity especially when estrogen and progesterone levels are high during ovulation. Primary control of estrogen and progesterone is governed by the pituitary gland, a pea sized endocrine gland on a stalk just under the hypothalamus. The hypothalamus secretes gonadotropin releasing hormone (GnRH) during the menstrual cycle which in turn activates the release of two gonadotropins from the anterior pituitary-follicle stimulating hormone (FSH) and luteinizing hormone (LH). These two hormones travel via the blood stream and cause follicle/ovum development, as well as mature egg release at ovulation. FSH causes the egg-containing follicle in the ovaries to ripen and LH to release eggs as well as produce more estrogen and progesterone from the follicle during the second half of the menstrual cycle after ovulation, the peak of female sexual receptivity. These hormones in turn promote the release of oxytocin and make females' hypothalami more receptive to oxytocin. This hormonal cocktail makes females more trusting of and emotionally receptive to suitors they have already bonded with (Panksepp, 2012). Oxytocin reduces trust of unknown individuals and increases rejection of "suiters" who already have a partner (e.g., cheating husbands). However, there has been some research to suggest that women are more likely to cheat around ovulation, probably because estrogen and progesterone levels are high, and their bodies are in a state of sexual receptivity (maybe they dissatisfied with their husband so hook up with cheating husbands). Marriage counselors hear such stories in their consulting room (Joanning & Keoughan, 2006).

At a primary emotional level, attractiveness between the sexes is also neurologically programed. Men respond to a 0.73 waist to hip ratio, the classic hourglass figure, a sign of fertility recognized by wiring in the male visual system (Fisher, 2016). At a primal level, human females, like other primates are attracted to confident, dominant males with resources (though some scientists have challenged this belief, see comments at the end of this paragraph). Dominant, resource-rich males increase the likelihood that a female's children will be protected and have the resources needed to survive and thrive. At times human females can also be affected by testosterone as evidenced by mothers' fierce protection of their children, and anger with other women who attempt to seduce their mates. Social context and learning can modify our primal tendencies at a secondary (feeling) and tertiary (thought) level. Men may learn to treat women respectfully at a behavioral level and think of them as their equal, even though their primal urge may push them to be sexually dominant. Human females tend to exhibit more discernment than other primates and so may choose to not enter a relationship with a socially dominant, powerful, self-centered male even though he may offer social status and wealth (Fisher, 2016).

Sexually driven courting behavior is especially pronounced during adolescence because of the flood of sex hormones invading the bodies of young humans. Although the intensity of the LUST/SEXUALITY circuit's influence on our behavior diminishes with age, it never goes away. Even the "elderly" couples we have studied show activation of the LUST/SEXUALITY circuit especially if they are beginning a relationship (Joanning and Keoughan, 2005). Their bodies still want to reproduce even though they are not physically capable of doing so. And of course, oxytocin and endorphin release are still producing the rewarding emotions associated with establishment of a new, or reinforcement of a strong, existing bond.

Attempting to suppress the sex drive of adolescents is usually a futile effort because the LUST/SEXUALITY circuit is activated much of the time. The best we can hope for is to channel their sex drive in a productive direction by providing age-appropriate sex education including training regarding relationship development, e.g., guidance regarding sexual activity when appropriate as a relationship develops rather than an as end in itself.

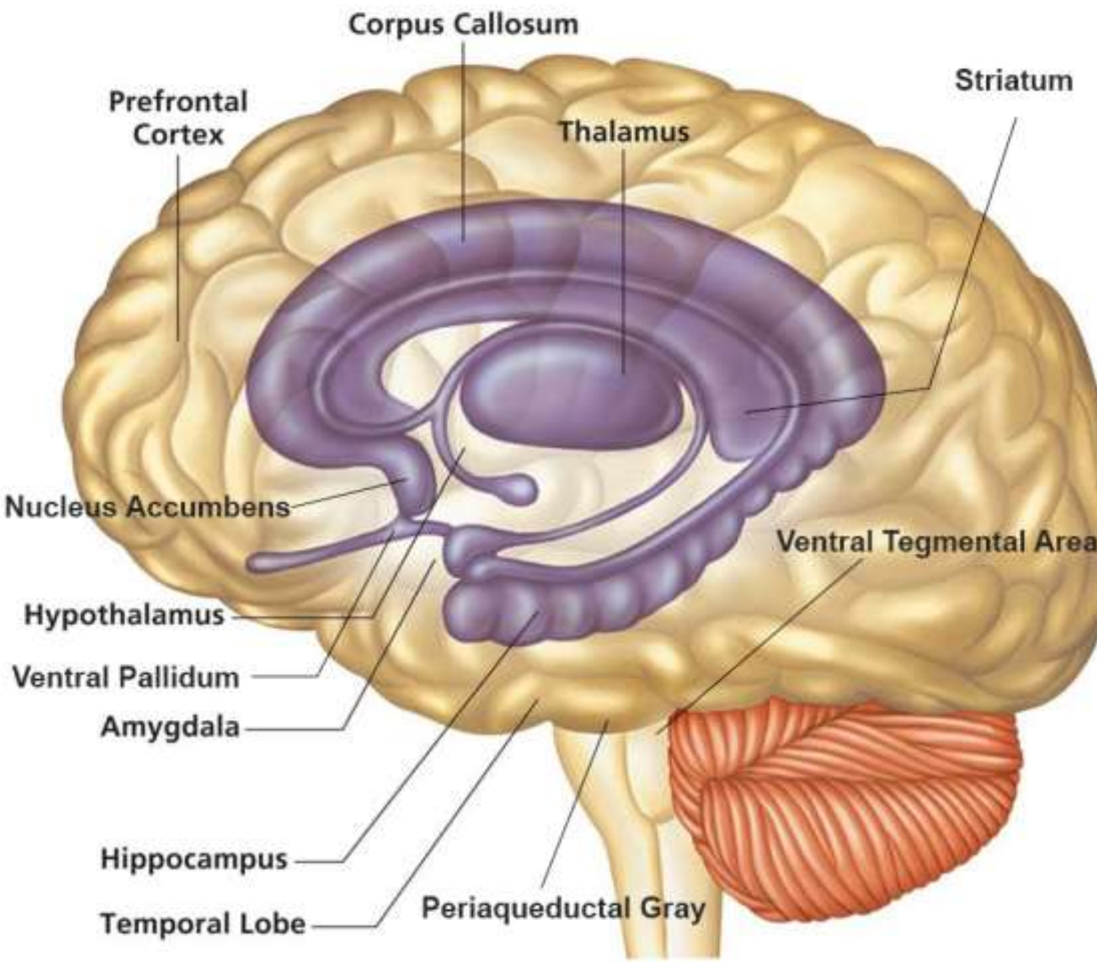
The LUST/SEXUALITY circuit stimulates sexual activity and social bonding because a bonded pair has each other to gratify sexual desire and to provide social support, which in turn stimulates beta-endorphin and oxytocin production. This process makes us feel calm and loved. However, oxytocin may not act alone but in a context of pleasant social interaction that enhances endogenous opioids (endorphins), the comfort and joy hormones. Feeling calm, loved, and comfortable with our partner leads to a satisfying sex life. A satisfying sex life promotes a competent immune system and increases our life span just like exercise; in fact, a satisfying sexual encounter is exercise. Well bonded, loving couples live longer because their bodies remain healthy longer. Sexual enrichment programs that emphasize couple closeness and sexually satisfying interaction enhance this effect (Joanning, H. & Keoughan, P., 2005; Nathan, E. & Joanning, H., 1985).

The other primal negative-affective brain systems will be covered later in this paper as we discuss relationship problems and divorce. Before beginning to explore the states of relationship development, a greater exploration of the limbic system that translates primal emotions into feelings will be helpful to help us better understand how brain systems interact.

Limbic System The stages of love and the brain systems involved with love are moderated by the limbic system, a part of the brain that evolved after the Primal Emotional systems identified by Panksepp and before the neocortex.

The limbic system affects mood, memory and hormone production. A primary part of the limbic system, the hypothalamus, controls the endocrine system and regulates temperature, hunger, thirst, sexual arousal, stress, and the sleep/wake cycle.

Areas of the Brain Involved in Love



Another part of the limbic system, the amygdala senses ambiguity in the environment and contributes to our sense of curiosity. If ambiguity is perceived as dangerous, the amygdala signals the hypothalamus to trigger the fight/anger or flight/fear response. These responses are involved with two of the brain systems identified by Panksepp, RAGE/ANGER and FEAR/ANXIETY. These systems will be described in more detail when we discuss stress responses during relationships, especially when couples move toward divorce or have a spouse die. If the amygdala compares new stimuli being perceived from the environment and senses no danger, the amygdala's activity decreases when we feel safe and allows the SEEKING/EXPECTANCY and LUST/SEXUALITY systems to operate. We become curious and seek a partner, an experience we will explore in more detail when we examine the Attraction Stage of love.

The amygdala attempts to make feelings congruent with and appropriate to the context of the event experienced. Ambiguity takes away our sense of security and predictability. Ambiguity is perceived as fearful, so the amygdala calls for more information by "turning up the volume" of hearing and increasing the sensitivity of all senses (Zerbi, V, et. al. 2019); it compares new stimuli to memories stored in the brain. If the ambiguity is resolved, it is typically because we consciously or unconsciously remember similar events that were not dangerous, and the amygdala stays calm. If the ambiguity is not resolved, the amygdala alerts the hypothalamus to take action to protect us from danger. The amygdala's default reaction is fear. For love to emerge, novelty is permissible as long as significant danger is not sensed, is minimal, or can be managed.

The amygdala is the "watchdog" or "early warning system" of our brain and nervous system. It reacts to the external and internal environment before our neocortex ("thinking brain") has time to react. A primary function of the amygdala is to keep us alive until we can "think through" what is happening to us.

An additional part of the limbic system that is involved in love is the hippocampus, a brain structure that contributes to memory formation, spatial memory, navigation and remembers prior sexual arousal especially in males. This is one of the first parts of the brain to be damaged by Alzheimer's disease causing the victim to be unable to form new memories. The hippocampus processes our experience of dealing with our partner and is critically involved in helping us "learn" how to relate to our partner. When an organism is highly stressed, this brain structure does not function properly. Neurons may die if stress is chronic/prolonged and sufficiently intense, making it difficult to process relationship issues. Relationship problems can be sufficiently stressful to lessen hippocampal functioning, at times causing one spouse to complain that the other is not remembering important relationship issues.

Attraction Fisher's second stage of love, Attraction, begins shortly after or concurrent with the LUST/SEXUALITY stage (Fisher, 2016). Attraction is characterized by increased energy, intrusive thinking about and craving for emotional union with a mate. In sum, our body is involved in an addiction-like process that takes over the SEEKING/EXPECTANCY system in the brain and occurs concurrently with activation of Panksepp's PLAY/JOY circuits.

As we continue to fall in love and the dopamine rush subsides, our developing love relationship is maintained by oxytocin and vasopressin, the same bonding, calming hormones that are secreted by the hypothalamus to promote lust. Some scientists point to a progression in a relationship. First lust (he or she is cute or sexy), then romance (I'll profess my love), then marriage (calmer and cozier). Sex, romance, and affection may dwindle but continue to interact (Fisher, 1998).

If the amygdala compares what we are experiencing in the here and now to memories stored in our brain and no ambiguity (danger) is sensed, it remains calm. The hypothalamus proceeds to instruct our endocrine glands to release hormones that produce pleasure (endorphins), bonding (oxytocin), and sexual desire (testosterone and dopamine) in response to our interaction with a potential lover.

During attraction, we become curious about our new partner and want to learn more about them. This curiosity is driven by Panksepp's SEEKING/EXPECTANCY system. When this system is active, people experience curiosity, interest, anticipation, craving, expectancy, engagement, excitement, eagerness, and directed purpose. It leads people to energetically explore their world and seek resources. It produces the invigorated feeling of anticipation we experience when actively seeking accomplishments and rewards.

The SEEKING/EXPECTANCY system is driven by dopamine, a hormone that causes a craving/desire feeling (Robinson & Berridge, 2008). Wolfram Schultz (2006) theorized that our dopamine neural circuitry compares anticipated or expected results with actual outcomes. If the outcome is better than we expected we get a dopamine surge; if worse, there may be a decline in dopamine release. It is possible that a combination of Robinson and Berridge's "incentive sensitization" view and Schultz's dopamine-as-mediator view gives us a moment-to-moment assessment of the value of a particular activity (with our partner) encoded in constantly changing dopamine levels (driven by our moment-to-moment interaction with our partner). Short-term changes are more congruent with the moment-to-moment reward prediction error view proposed by Schultz (i.e., I am getting my desires met or I am not) while longer terms changes involve motivational changes congruent with the incentive sensitization view (I crave my partner because she/he is a constant source of reward). A good and lasting relationship therefore satisfies a craving for the specific rewards I seek in a long-term relationship. Consequently, from an evolutionary perspective the SEEKING/EXPECTANCY system motivates us to learn how to interact with our partner to give us effective agency (a feeling of predictability and control) in our relationship. While falling in love, we use this system to learn all we can about our partner, and we feel vigorously motivated to do so. We experience a "love high." The SEEKING/EXPECTANCY system and the dopamine it is perceived as rewarding and motivates our behavior by satisfying our need for companionship and affirmation.

At the same time the SEEKING/EXPECTANCY system is activated, another system important to developing a love relationship is activated, the PLAY/JOY system. In the context of pair bonding this system triggers the urge to vigorously and spontaneously interact with another person. Like other pair bonding mammals, humans learn how to relate to other members of their species through play. Like kittens and puppies, human children use play to learn how to "get along" with others. Couples falling in love also use play to learn how to relate to one another. The accompanying emotions can be characterized by joy or delight, and associated thoughts are generally positive. From an evolutionary perspective, the play system triggers the release of hormones (oxytocin and vasopressin) that promote social belonging, pair bonding and monogamy. Oxytocin reinforces pair bonding and monogamous behavior while vasopressin can cause males to be very territorial and aggressive (i.e., possessive) regarding the woman they are attracted to. As relationships develop, vasopressin eventually drives individuals, especially women to be paternalistic and protective of their children. In combination with the SEEKING/EXPECTANCY system, the PLAY/JOY system motivates creativity and experimentation (learning to enjoy and explore one's relationship with a partner), and releases intrinsic healing properties of hormones (endorphins) that make us feel better.

During the attraction stage of love, we experience intense positive feelings and are drawn toward our partner because our relationship with him or her is the stimulus triggering our bodies to have these emotions that in turn stimulate feelings such as joy and enthusiasm. We seek our new partner like a drug addict seeks their desired drug. Fortunately, our bodies are designed to have a "love high" and we do not do physical damage to ourselves like we do when using street drugs to get high.

Hormones Before moving to the Attachment stage of love it will be helpful to describe the role of hormones in relationship development. Hormones are crucial to the function of brain systems and our bodies in general. Hormones come in a variety of "flavors" and functions. The following is a brief summary of the hormones already mentioned that are involved in sexual functioning, the key component of the Lust (Romance) stage of love and some additional hormones that are also important to the maintenance of relationships during the later stages of love. Chart 1 illustrates the endocrine glands directly involved with the stages of love. Chart two illustrates the hormones produced by each of our body's endocrine glands, some of which are directly involved in stages of love.

Chart 1

Endocrine Glands Involved in Love

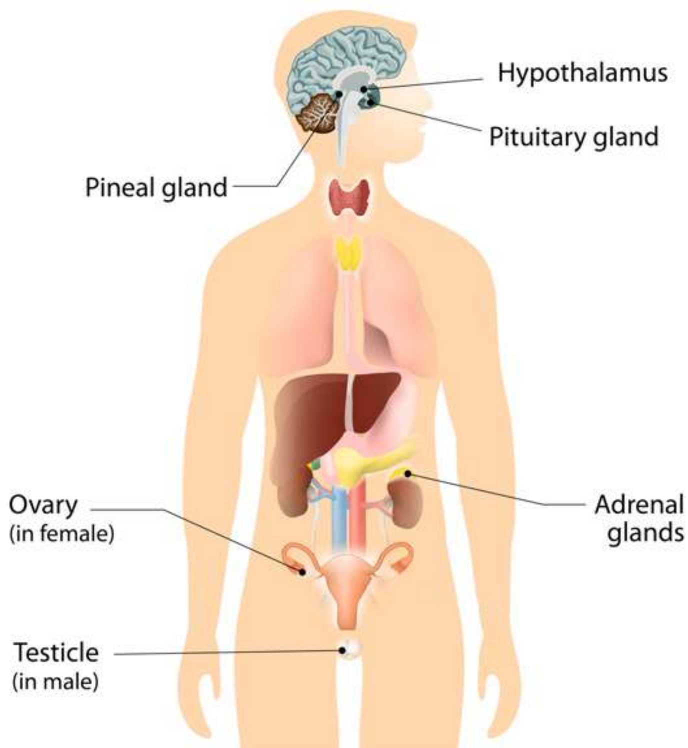
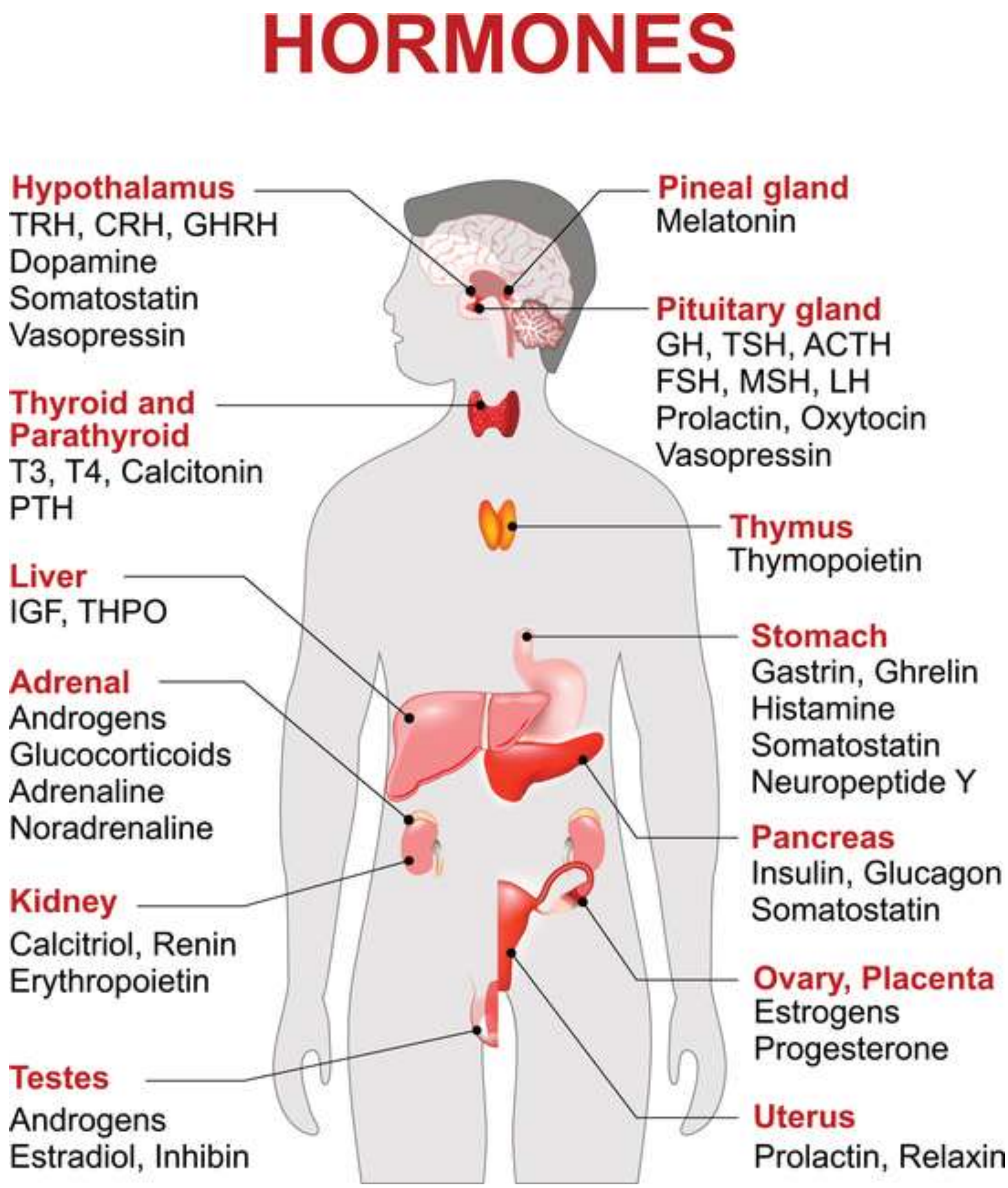


Chart 2

Hormones Produced by Endocrine Glands



Testosterone contributes to sexual urges (libido) and action; thus, it is critical to the sex drive of men and women, although men have much more of it than women, leading to the perception that men are more interested in having sex. However, interest in sexual expression is also moderated by age, health, quality of the relationship, stress levels, and attitudes about sexuality. The popular notion is that men are more sexual than women. Although young men may have a strong desire to have sex, that does not make women less sexual. Young men are simply more aroused in part due to high levels of testosterone in their systems. The picture changes as men and women age. Some men seen by sex therapists report a decrease in sexual urges as they grow older and some women seen by therapists complain that their partners can't keep up with their increasing sexual desire (Joanning & Keoughan, 2005). Sexual desire in couples may be more linked with women than men because testosterone tends to make men more sexually permissive in general, while changes in testosterone levels in women can lead to more drastic proportional changes in women's sexual behavior. In short, men usually have consistent levels of testosterone over time which leads to consistent sexual desire while women have more variable levels of testosterone leading to varying levels of sexual desire; for example, women are more sexually receptive around ovulation when testosterone operates in conjunction with other hormones.

Estrogen regulates reproductive cycles, menstruation, promotes wellbeing, keeps female genital tissues healthy, and promotes sperm production in males. Consequently, it is essential to keeping women's bodies sexually functional and capable of becoming pregnant before menopause. Estrogen supplementation may be helpful to maintain that functionality during and after menopause, but some concern exists regarding estrogen supplementation increasing the risk of breast cancer. Progesterone along with estrogen is needed to keep women's bodies fertile and facilitates enjoyment of sex. Women are advised to consult with their physician regarding the risks and benefits of hormone replacement therapy. Special attention should be given to the type of hormone replacement therapy. For example, estrogen patches on the abdomen that allow for estrogen absorption into the uterus and vagina are often preferable estrogen tablets that affect the entire body.

Oxytocin is a hormone secreted by the pituitary gland to reinforce attachment and trust, as well as to promote breastfeeding and childbirth. Oxytocin is referred to as the "cuddle hormone" because it strongly promotes bonding. It is expressed during nursing and surges during orgasm. It makes us feel bonded to our babies or to the person with whom we are having sex. It also is expressed if we hold or are held by a lover, parent, or caregiver. De Drew (2012) in a review article finds that oxytocin regulates cooperation and conflict among humans in three ways. First it enables social categorization of others into in-group versus out-group. Second, it dampens amygdala activity to enable the development of trust. Third, it up-regulates neural circuitries (e.g., inferior frontal gyrus, ventromedial prefrontal cortex, caudate nucleus) involved in empathy and other-concern. He goes on to state: "Consistent with an evolutionary perspective on the functionality of cooperation, it is concluded that oxytocin-motivated cooperation is mostly parochial—it motivates (i) in-group favoritism, (ii) cooperation towards in-group but not out-group members, and (iii) defense-motivated non-cooperation towards threatening outsiders. Thus, in addition to its well-known role in reproduction and pair-bonded formation, oxytocin's primary functions include in-group "tend-and-defend." In sum, not only does oxytocin promote pair bonding and within group cooperation, it also induces tribal behaviors that generate hostility toward outsiders.

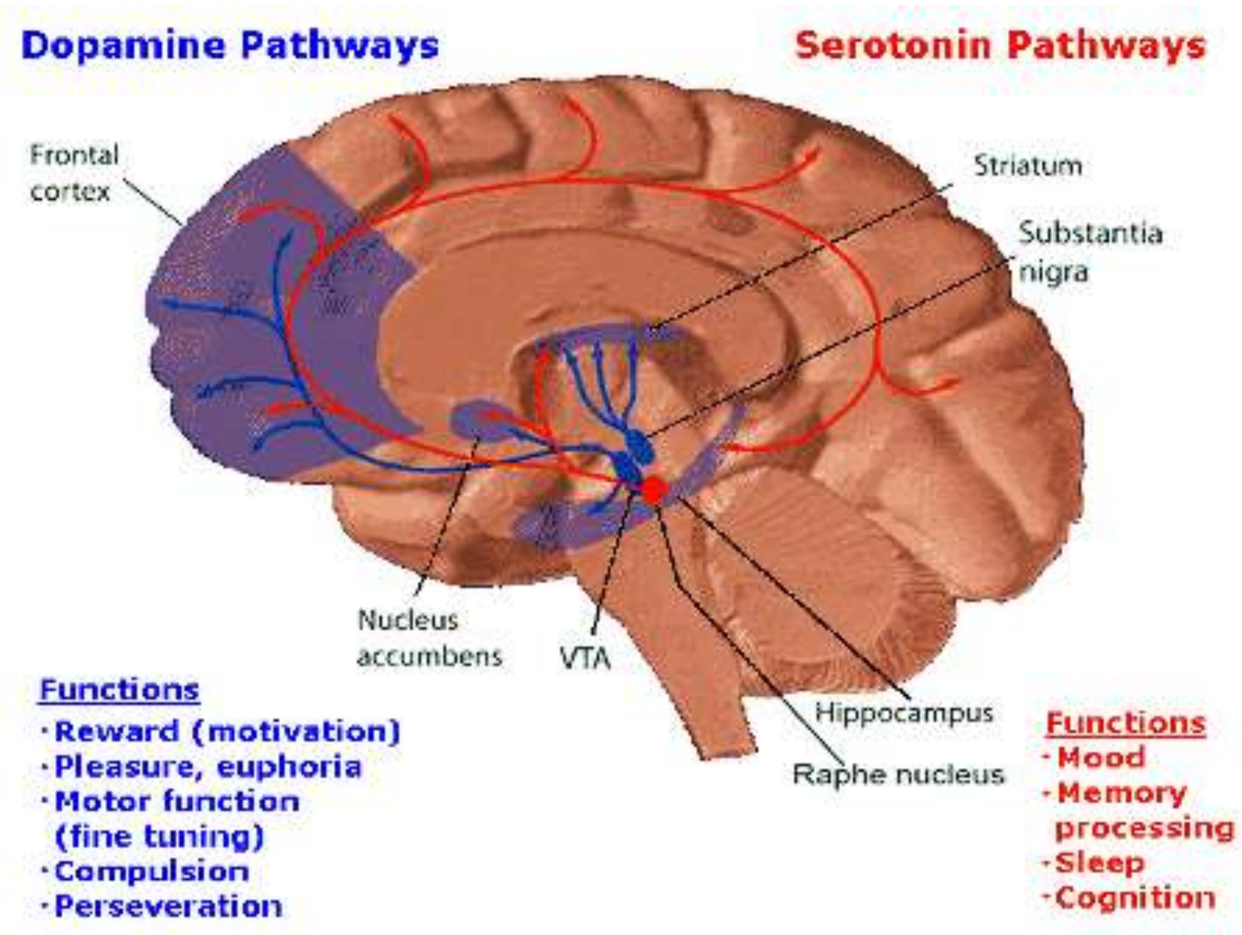
Vasopressin is a hormone similar to oxytocin that facilitates and coordinates reward circuits crucial for bonding. This hormone helps coordinate the closeness felt due to oxytocin with the good feelings generated by dopamine and endorphins.

Oxytocin and vasopressin are synthesized in the hypothalamus and secreted into the blood by the pituitary gland, a gland attached to the hypothalamus. These hormones are especially notable among monogamous pair bonded species as an evolutionary adaption for the long-term care of helpless infants. In short, we fall in love because our children need us! We will explore this notion when we describe parenting.

Endorphins are endogenous opioids that reduce pain sensation, increase feelings of comfort and surge with exercise, orgasm, and love. Non-endogenous opioids (such as street drugs) attach to the same receptor sites in the SEEING/EXPECTANCY reward circuit of the brain associated with pleasure and cause addiction and physical damage over time. As mentioned earlier, naturally occurring endorphins make us feel good while doing no damage because our brain is designed to be stimulated by this class of neurochemicals and because they are metabolized readily once their action is complete. Street drugs persist longer and lead to addiction and other harm because of prolonged and/or dysfunctional interaction mediated through endogenous opioid receptors. In sum, endorphins are good for us and street drugs damage our brain.

An increase in endorphins is also part of the placebo effect that needs to be controlled for in experiments. The placebo effect is real. If we take a pill or receive a treatment while being attended to by a person we respect and have them tell us the pill or their interaction with us will be helpful, endorphins are released into our bodies and make us feel better, at least for the short term. The placebo effect refers to the fact that this beneficial effect occurs even if the placebo pill or treatment has no actual physical/physiological efficacy. Believing it will have an effect triggers endorphin release. Having a lover who attends to us and tells us they love us also releases endorphins.

Dopamine is a hormone released in the mesocorticolimbic system which includes the motivation and reward pathways; specifically, the ventral tegmental to nucleus accumbens/ventral striatum, amygdala, hippocampus and prefrontal cortex pathway that promotes motivation and reward seeking behavior involved in promoting love (see the SEEKING/EXPECANCY: The Reward Circuit diagram). Dopamine attaches to receptor sites in the SEEKING/EXPECANCY reward circuit energizing our bodies and making us feel more effective. Again, the first stage of romantic love is like being high. Increased dopamine release is coupled with a decrease in serotonin; similar neurohormonal changes occur in individuals with obsessive compulsive disorders. We literally become obsessed with our beloved. Dopamine drives lust and triggers release of testosterone. Dopamine is also vital for voluntary movement, attentiveness, motivation and pleasure. Consequently, dopamine is a key player in addiction, ecstasy, and love.



Serotonin is a hormone that stabilizes mood and is involved in regulating memory, emotion, sleep, and appetite; too little leads to depression, too much lowers sexual desire. Antidepressant drugs affect serotonin levels by increasing activation of serotonin receptors or inhibiting it from being reabsorbed by our neurons. Previously it was thought that antidepressant drugs facilitate serotonergic mood circuitry by mimicking serotonin, or increasing serotonin release, or by inhibiting its reuptake and thus prolonging its synaptic action. More precisely serotonin has been thought to increase at serotonergic synapses with antidepressants (especially SSRIs, serotonin-selective reuptake inhibitors which block serotonin transporters/recycling). Now it is thought that since the most significant relief from depression occurs 6-8 or more weeks after taking a course of anti-depressant medication, it is not the changes in synaptic levels of serotonin, but rather new neurogenesis that occurs; that is, modification of neural circuitry is providing the primary beneficial anti-depressant effects. The relatively long-time course (weeks) involved in the development of a new romantic relationship fits with the neurogenesis model of serotonin's effects; that is, new neurons and new synapses are formed. Short-term effects might be associated with rapid changes in serotonin levels at the synaptic level (over minutes, hours or days), and may explain so called "love at first sight." In sum, falling in love alters our balance of dopamine and serotonin in a positive way. When we examine the effects of divorce or death of a spouse, we will see the opposite.

These hormones are expressed in the SEEKING/EXPECTANCY, or the so-called anticipation- reward circuit of the brain, and PLAY/JOY brain system, and these two systems in turn help to drive the Attraction and Attachment stages of love. All these hormones work collectively to move relationships from the reproductive Lust stage of love through the Attraction stage, the bridge to long term bonded commitment that emerges in the Attachment stage.

Readers interested in a summary of the basic functions of neurons and neurotransmitters are invited to read Appendix IV: Synapses, Neurotransmitters, Neuropeptides, Neuromodulators, Neurohormones, Hormones and Neuroreceptors.

Evidence Based Therapeutic Interventions for New Relationships

Communication Training and Premarital Therapy As couples move from initial Lust/ Romance through the Attraction stage of love, they may benefit from interventions designed to give them the tools needed to develop a healthy long-term relationship often involving marriage. Two interventions that have been shown to be effective are communication training (Joanning, 1982; Brock and Joanning, 1983) and premarital therapy (Bagarozzi, D. & Rauen, P., 1982).

Communication training focuses on specific skills shown to be helpful in sharing information necessary to maintain and improve relationships. These skills include speaking from self-awareness; that is, a) each partner using I statements to express what they see and hear their partner saying and doing; b) how that makes them feel about the relationship; c) what they desire from the relationship; d) what actions they are taking to maintain the relationship; and e) what they think is happening in the relationship. These "self-awareness" statements need to be accompanied by empathic "active listening" so that information can be shared accurately while the CARING/NURTURANCE and SEEKING/EXECTANCY brain systems are functioning. Counselors/therapists can train couples to use these skills effectively.

As couples approach marriage or decide to live together long-term, relationship therapy designed to focus on issues crucial to developing a long-term happy relationship can be very helpful. Such therapy is often provided by pastoral counselors but can also be provided by any mental health professional trained to work with couples. Premarital therapy should focus on characteristics of long-term happy marriages identified by past research. During premarital therapy, the therapist leads the couple through a discussion of these characteristics to determine if they already exist for the couple or could be developed. Therapy then focuses on characteristics that do not yet exist.

Long-Term Happy Marriages

"When you've been married to the best, it's hard to settle for less." This comment from the widow of my dad's best friend pretty much sums up the attitude I have encountered as I and my graduate student (Henrich, 1987) interviewed couples who stay together for at least 30 years and are very happy with their marriages. During this same time period I have worked with thousands of couples who have been very unhappy in their marriages. I have been curious as to why some couples do so well when 40% or more do so poorly that they divorce or stay in an unhappy marriage. Forty-eight years of research with these couples has given me some ideas of what makes the difference.

I started with older couples in rural west Texas: Southern Baptists, members of the Church of Christ, a few Catholic Mexican Americans and a few happy non-believers. I then moved to Iowa and again worked with older happily married rural couples of German Lutheran and German Catholic heritage. Later I worked with older dual career couples who were not only happy in their marriages but had fulfilling professional careers. I also have had an opportunity to interview older happy couples in Germany, England, Spain, Greece, Turkey, India, Hong Kong, Taiwan, and Japan. Although I noted some cultural differences, I was taken by the strong similarities among all these couples. This is a highly select group; at least 50 years old but usually in their 60's, 70's, or 80's. They are a resilient and up-beat bunch. They are survivors, children of the depression, in love with life and each other. They are not whiners or slackers. They have worked hard, most have raised a family, have persevered through adversity, and grown close to one another in the process.

I will highlight seven characteristics that appear common among this group. All the couples I have studied have been in relationships that are highly stable and highly satisfactory.

Most researchers have found that as the marriage lengthens, marital quality decreases. Marriage typically begins with a high level of satisfaction, declines as the first child is born, and increases again after the last child leaves home. However, many couples never again achieve the high level of satisfaction present early in their marriage. This is not the case for the couples I have studied. Their level of satisfaction may have lowered a bit when their children were young, but they report having the highest level of satisfaction in the later years of marriage. These couples tell me "…you work hard all of your life and at the end you should get your reward." The reward is high marital satisfaction. But how do these couples beat the odds?

These couples have told me "we really got to know each other, we learned to respect each other, things that troubled us earlier don't now, if you keep vintage wine it becomes better with age, the longer you're married, the closer you get." These couples learned what was important to one another and did things for each other just to make their partner happy. They talked about becoming "comfortable" with one another and becoming much more than two separate individuals. "We talk to each other about what happens during the day. When she's not home, I start to talk to her until I realize she's not next to me." One recent widower told me "I still talk to her even though I know she's gone; I don't want to break the habit."

These couples all went into their marriages with a very optimistic outlook of what their marriage would be like. They felt they would have no problems, and everything would work out for the best no matter what happened. They felt that love would carry them through any difficulties but soon found they were wrong. They learned it took hard work and dedication to make their marriage a success. Over the course of time they developed a "true definition of love."

I really pushed these couples to define "**true love**". They saw love as doing things to please their spouse. They wanted to do everything they could to make the marriage a success. They described their spouse as their best friend and their life's companion. They all wanted to give to their spouse without expecting a return. However, they all reported getting as much and usually much more back than they felt they had put into the relationship.

What these couples described to me is what family studies specialists describe as "multifaceted love;" the so-called four faces of love: romantic, sexual, companionate, and altruistic.

"Love is not passion, love is not sex or what you see on television, sex and passion are nice in the beginning but later in life it's giving without receiving, but yet you are receiving. Love is mutual respect, conducting yourself in such a manner that is pleasing to your spouse." "It's doing things for her that she could do for herself because she is special to me. It's having someone there who knows you and cares for you. It's living with my best friend."

Crisis: "Problems make you look at the bigger picture. Everything works together for the good, even the bad. Make the best of everything, look on problems as challenges. Problems help you become more united. You realize that there are things in life more important than money and material things. You turn a lot of cobs over on the fire at a time like that. A crisis helps you get your priorities in order. Turn a scar into a star."

Couples explained that moving to a "higher level of love" was through crises. Each couple had some trying time in their marriage. This trying time was a turning point, a time when they realized what is truly important in life. Each of these crises was threatening to one or both spouses or their family. The most common examples were severe physical illness, financial difficulties, long periods of physical separation usually due to war, and infidelity. Each of the couples looked on these crises in a positive way. They tried to find the good in the bad. They had the attitude that "it could have been worse, and it has brought us closer together." In sum the crisis was seen as a catalyst that helped the couple's marriage move to the high-quality state the couples were experiencing in old age. Without a crisis they felt they never would have obtained their "good" marriage.

Children were an important part of the lives of many of the couples I have interviewed. Raising a family did cause marital quality to decline initially. However, children were seen an asset not a liability. Couples saw raising a family as an opportunity to grow and develop as well as to receive pleasure from their children. They felt satisfied to spend their free time with their children. Again, these couples saw raising children as a challenge and an opportunity to grow together as a team.

Religion and Values are also key characteristics of long-term happy marriages. The rural couples were almost all religious as were many of the urban couples. A few rural couples and a significant proportion of urban and European couples were not religious. However, all these couples had one thing in common, similar values. Couples believed that having similar values made it much easier for them to make important decisions in their lives and helped them avoid arguments. For example, these couples usually agreed about how to raise their children, both how to relate to children and what values to instill. Disagreements about children are common among unhappy couples because children bring the parent's values differences into sharp focus. The couples I interviewed were spared this problem.

Living in a small community or having a supportive social group helped happy couples maintain their marriage. Again, common values come into the picture because the couples I interviewed could turn to the community or their social group for support. In small rural communities, people tend to have similar values that discourage divorce and promote marriage for life. Couples from small communities saw cities as places where marriage was not supported and divorce was allowed if not encouraged. However, my successful urban couples talked about being members of closely-knit social groups that promoted marriage by providing support to group members. This support took the form of companionship and fellowship as well as assistance in times of trouble.

Commitment is the final characteristic I want to highlight. The couples I have interviewed enter marriage with an unshakable belief that their marriage would last forever. These couples believe that "we no longer instill in our children the idea that when a couple is married, it's for life." They also believe that we "should take any negative situation and turn it to our advantage in some way or another." The key to success is having the desire to make the best of life's hard times. "Face life together. Commit to one another and life's challenges can be handled."

To review and summarize, the couples I have studied see their happy marriages as due to **highly stable and satisfying relationships, true love, having faced crises together, raising children, shared values, living in supportive communities, and a having strong sense of commitment to one another**.

The following is a case example that I feel is illustrative of this group of couples in general. In 1986 I spent 104 days at sea with 22 retired couples, 20 of whom were married 35 or more years, some as long as 60 years. All but two were very happy in their relationships. One couple was particularly interesting.

Irving was an 83-year-old retired appellate court judge. His "bride" Rosa belle was an 81-year-old homemaker who met Irving when she was 20 and married him two years later. When I met them, they had been married 59 years. They were both Jewish although they never mentioned it until I asked them about their religious beliefs. They were both raised in and have always lived in the same large southern city. When I watched them, they were like two teenagers on their third date, obviously in love and not ashamed to show it. Irving always referred to her as his "bride," Rosa belle always introduced him as her "Southern Gentleman."

As I got to know them, I was impressed by the intense emotional intimacy of their relationship. I asked them what made them so close. They told me of their desire to have a family. They had a son two years into their relationship. It was a difficult pregnancy and Rosa belle was told she would never have another child. To deal with their disappointment they put all their efforts into raising their son. He grew into a "fine young man who followed his father into the law." Unfortunately, their son suffered from biological depression and began taking anti-depressant medication in adolescence. At age 36 the depression worsened, and he committed suicide. The loss devastated the couple. They "turned to each other because our relationship was all we had left." Their commitment to each other as life companions allowed them to continue in the face of a tragedy that would have overwhelmed most couples.

One morning I went up to the top deck to lift weights with Irving. When I got to the weight room Irving was sitting on the bench press looking ashen and distressed. I thought he was having a heart attack. "Irving, are you alright?'' "Yes, yes, I'm just flustered." "About what?" I asked. "About 20 minutes ago I came up here (about 5:30 am) and started to walk out to the front deck and I saw a young couple, on the deck, you know, being intimate!" "What did you do?" "Nothing, I just watched, I had never seen anything like it." "I finally realized they might see me, so I stepped in here." "Irving, you mean you have never seen anyone having sex?" "No, of course not." "It must have been quite a shock." "Yes, it was."

Later that day I saw Rosa belle on the sun deck lying on a lounge chair. I asked her if Irving had gotten over his shock. "What shock?" "Oops." About this time Irving came walking over and Rosa belle asked him, "Irving, I understand you had a shocking experience, what happened." Now if I had been a gentleman I would have left at that moment. But my curiosity overwhelmed my usual gentlemanly instinct. I had to hear how this was going to turn out.

Irving turned bright red, hesitated, but finally told her. "Irving, you dear sweet man, we've been together sixty years and you still think I'm innocent." At that point she winked at me and I took my leave. I shared this example because it illustrates many of the key characteristics of long-term happy marriages.

Attachment Now that we explored the Attraction stage of relationships and therapeutic interventions designed to assist couples in that stage, we can move to Fisher's third stage of love. Attachment is characterized by forming close social contact with another person and experiencing feelings of calm, comfort, and emotional union with a mate. The brain systems already activated during the Lust (Romance) and Attraction stages of love continue to operate but are moderated by another brain system that begins to be activated during the Attraction stage and becomes dominant during the Attachment stage. This CARE/NUTURANCE system is crucial to the long-term survival of a relationship and is also critical to parenting. In short, this circuit is a major component of all types of love.

The CARE/NURTURANCE system produces spontaneous feelings of warmth, tenderness and concern for others, thoughts about the welfare of others, and urges individuals to act in nurturing ways toward others. The evolutionary advantage of this system is the protection of important relationships with others.

All the hormones described earlier continue to be active in our bodies if we maintain a close, loving relationship with our partner. Oxytocin ensures a feeling of closeness, dopamine a feeling of pleasure, serotonin a feeling of calmness, testosterone a feeling of sexual desire, and endorphins accentuate all these feelings. In sum, by the time the Attachment stage of love is fully achieved, the relationship becomes self-reinforcing, cognitively and emotionally. Couples are motivated to do what is necessary to keep these positive feelings flowing (Joanning, 1982).

Emotions and Feelings To highlight and review important concepts covered earlier in the paper, we often use these terms interchangeably in our daily lives. For the theory described in this paper, it is important to draw a clear distinction between the two. Primal Emotions are lower-level physical responses associated with Panksepp's Seven Executive Operating Systems of the brain. These Primal Emotions arise from biochemical reactions in and between our neurons and endocrine system. Primal Emotions are physical changes in our bodies, neurological and bodily reactions to stimuli in our environment. In sum, Panksepp, but not all neuroscientists, argues that Primal Emotions are purely physical responses-both visceral and behavioral. Affects or feelings are different in that they result from a higher order processing that occurs in the limbic system in cooperation with the neocortex. Figure 1 illustrates this difference and is explored next.

Primal Emotions (Figure 1) are bodily reactions activated by hormones and neuronal activity generated within our body as it reacts to our environment. Feelings (Secondary processes, Figure 1) emerge in our limbic system; especially in the amygdala and hippocampus described earlier. Thoughts (Tertiary processes, Figure 1) arise primarily in the ventromedial prefrontal cortices, which deal with conscious thoughts, reasoning, and decision-making. Thoughts originate in the neocortical regions of our brain, the outer layer of the brain that evolved most recently; thus the “neo” prefix. These thoughts include our personal “schema” about how the world works, grow out of our personal experiences, beliefs, memories, and thoughts linked to feelings and primary emotions. A feeling is our brain perceiving a Primal Emotion and assigning a meaning or label to it. The same emotion can generate different feelings depending on the context in which the emotion is experienced. Antonio Damasio (1999, 2010) has described feelings as mental experiences of a body state, the way in which our brain interprets emotions that are physical states arising from the body’s responses to external stimuli. For example: we are threatened (a man pointing a gun at us); we have a Primal Emotional reaction named FEAR/ANXIETY, and at a more complex level of processing, we cognitively label it as horror (because it is an appropriate label given the context of a gun pointed at us).

Primal Emotions are raw physical reactions common to human and other non-human mammals. Non-human mammals have at least rudimentary feelings but lack the symbolic representation ability of humans (i.e., language) to describe these emotion-relevant feelings the way humans do. This is because these secondary emotions or feelings arise in the limbic system, the paleo-mammalian brain, which non-humans also possess.

Feelings are interpretive labels used by humans to describe their experience of Primal Emotions. These more complex interpretations of primal emotions may involve both secondary feelings and even the more complex tertiary/neocortical interpretations that only the human brain can produce. FEAR/ANXIETY and SEEKING/EXPECTANCY are primal emotions. The specific Primal Emotional circuit that is activated is determined by how our limbic system, in interaction with our neocortex, is interpreting what is happening as we interact with our environment. If we are pushed out of an airplane because someone is trying to kill us, our FEAR/ANXIETY circuit is activated and we will feel terror because of how our limbic system is interpreting the event. If we are voluntarily sky diving, our SEEKING/EXPECTANCY circuit is activated and we feel exhilarated because we have chosen to do so and are relatively confident, we won’t die. The primal emotion activated within our body and our feeling label changes as the context changes. The same primal emotion can also induce different feelings if the context changes. For example, in close relationships, the primal emotion LUST/SEXUALITY could evoke a feeling of ecstasy if we are having sex with our lover, or guilt if we are masturbating while thinking of someone other than our lover.

Biologists and especially neuroscientists who study animal nervous systems and ascribe to evolutionary psychology, largely agree with Panksepp that emotions are primal; that is, rudimentary, basic or primary emotion "systems" (they debate the precise nature/meaning of "systems") are found to varying degrees throughout the vertebrates and that these are especially well-developed in mammals. It is most sociologists and many cognitive psychologists who are more reluctant to admit the existence of these primal forms of emotion and do so because they (arguably) don't take into adequate account evolutionary psychology. These naysayers of Panksepp view fall into the camps of the social constructivists (e.g., like Lisa Barrett (2006) or cognitive constructivists (Schacter & Singer, *et al*., 1962); both camps view emotions as being constructed and existing only at those higher brain levels (limbic and neocortical) rather than as more hard-wired into and arising from sub-cortical systems/circuits. They tend to deny that there is strong evidence for Primal Emotions as construed by Panksepp and other evolutionary neuroscientists or evolutionary psychologists who argue that if we evolved from lower animals, the rudiments of our emotions didn't pop into existence *de novo* but must have precursors that are ancient and found in common ancestors going back through mammals, birds, and reptiles at least. This author, who studies humans, and a colleague neuroscientist who studies simple organisms, subscribe to the general evolutionary view of our mental capacities and tend to agree with Panksepp and his colleagues. However, those of us who are interested in discrete and definable neural circuits tend to believe that Panksepp does overstep the evidence a bit when he talks about his seven systems as though they were discrete and precisely definable circuits. Panksepp talks about some massive areas of brain real estate (amygdala, hippocampus, midbrain) when he talks about these systems, even though he admittedly talks about subregions on occasion (e.g., periaqueductal gray or ventral tegmental area in midbrain.) Likewise, the neurotransmitter or neuromodulator systems he talks about (oxytocin, vasopressin, endorphins, dopamine, etc.) are very diffuse systems both anatomically and functionally. To his credit he says we need a lot more research to flesh out the details of these "systems" and that is a tremendous understatement. Lisa Barrett's 2006 review entitled "Are emotions natural kinds?" review takes the Primal Emotion system view to task for lack of definitive evidence and of course Panksepp (2007) defends his view with his "Neologizing the Psychology of Affects" response which says there is evidence for the Primal Emotions in non-human animals. That is where much of the debate really lies.

For purposes of this theory, we use Panksepp's Seven Executive Operating Systems as a theoretical framework for understanding how Primal Emotions might drive and explain the nature of close relationships. We have chosen Panksepp's systems as Primal Emotions because he has provided evidence of brain regions activated in humans and other animals when these emotions are experienced (although some social and affective psychologists may not be convinced that he has done so). For those interested in what parts of the brain are responsible for which Primal Emotions, we refer you to Panksepp's papers: The basic emotional circuits of mammalian brains: Do animals have affective lives? (Panksepp, 2011), and his books on the subject (Panksepp, 1998; Panksepp & Biven, 2012). Also, for purposes of this paper, we are using Panksepp's Seven Executive Operating Systems, as Primal Emotions not feelings, although people commonly refer to them as labels for feelings. Many feeling-related terms are used to describe meanings individuals attach to their subjective experience of Primal Emotions. We will continue to distinguish feeling labels from Primal Emotions as we discuss other stages of close relationships.

Evidence-Based Therapeutic Interventions to Help Couples

Maintain Satisfying Relationships and Deal with Relationship Problems

Relationship/Marital Therapy

As couples move through the Lust (Romance), Attraction, and Attachment stages of love, they often encounter issues such as differences of opinion or varying preferences that must be dealt with. If such issues are not resolved to mutual satisfaction, they may evolve into persistent problems and conflict about how to deal with them. Several models of relationship/marital therapy have been developed to assist couples. Three deal specifically with findings of affective neuroscience research regarding relationships: John Gottman's Sound Relationship House, Susan Johnson's Emotionally Focused Couples Therapy, and Brent Atkinson's Pragmatic/Experiential Therapy for Couples.

John Gottman (Gottman, 1999; Gottman & Silver, 1999) has researched couple interaction thoroughly in numerous studies and developed a theoretical model and approach to therapy outlined in his Sound Relationship House. Gottman acknowledges the role of neurological processes as part of this model.

Fig. 5.1 The Sound Relationship House

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Gottman outlines the basic assumptions of his approach in a short video The Easiest Way to Improve your relationship:"

https://www.youtube.com/watch?v=ib7Ain2aVR0

He summarizes the major threats to a relationship in a video entitled "The Four Horseman of the Apocalypse:"

https://www.youtube.com/watch?v=1o30Ps-_8is&list=PLXLZK-NAOX9d4MoKYmQ_fwK5KARVCshV9&index=2&t=0s

This second video shows behaviors that emerge as the CARING/NURTURANCE system shuts down and the RAGE/ANGER system is activated. It shows couples attempting to interact while angry with one another and illustrates each of the Four Horseman of the Apocalypse. This an excellent video to show couples involved in relationship/marital therapy.

Susan Johnson (Best, 2010; Johnson, S. M., 2020; Johnson, D. & Greenberg, L., 1994; Johnson, S. & Whitten, V., 2003) has based her couples therapy on attachment theory and neuroscience. She postulates that how we learn to bond as a child is related to how we bond with a partner as an adult. She also attends to the role of emotions in forming attachment bonds in childhood. As described later in this paper, the type of bond we form with our parents depends on the emotional context in which parenting occurs. Likewise, how we bond with a relationship partner in adult life depends on how we learned to bond as a child. Emotionally Focused Couples Therapy is designed to modify attachment bonds learned in childhood if they are incompatible with the secure attachment style preferable in adult relationships. Johnson incorporates some components of Panksepp and other affective neuroscientists' research findings. She focuses on the role of the amygdala and "primal fear" responses in relationships. Her therapy attempts to change the Primal Emotions of ANGER/RAGE ANDFEAR/ANXIETY. For more information on her work, please consult this link:
https://www.psychotherapy.net/video/emotionally-focused-couples-therapy

The following links related to the approach are available through university libraries using EBSCO. They illustrate Johnson's approach to therapy:

https://www.psychotherapy.net/stream/southala/video?vid=100

https://www.psychotherapy.net/stream/southala/search?q=sue+johnson

Brent Atkinson (2005) has based his couples therapy on the work of Jaak Panksepp and other affective neuroscientists as well as his own experience as founder and director of the Couples Research Institute in Geneva, Illinois. In his Pragmatic/Experiential Therapy (PET), he proposes that we can become programmed to engage in unhealthy patterns that play out with our partner. His model attempts to recalibrate the way that we interact with our lover in order to be capable of interacting in a different manner. Pragmatic/Experiential Therapy attempts to use emerging neuroscience findings about how the brain processes emotion into practical methods for improving relationships and increasing personal success. Dr. Atkinson pays close attention to Panksepp's model of brain systems driving human behavior. For more information regarding PET, contact:

The Couples Research Institute
www.thecouplesclinic.com
The Five Hundred Building
1250 Executive Place Geneva, IL 60134

Affect-Based Couples Therapy

Gottman, Johnson and Atkinson have started to move therapy in a direction informed by affective neuroscience research. However, more can be done. Research done by me and my colleagues at Iowa State University and the University of South Alabama suggest specific procedures that can be incorporated into couple therapy based on neuroscience findings. In addition to the couple communication training procedures described earlier in this paper, determining which brain systems are operating is key to determining how to intervene.

Observing couples' behavior and asking them about their feelings and thoughts can give indications regarding brain system functioning; that is, what primary emotions are driving second order feelings and tertiary thoughts. If couples' behavior reflects #1 or #2 communication as described in the Communication Rapid Assessment Scale (Joanning, Brewster, & Koval, 1984; See Appendix), they report "feeling" close and connected to their partner and their heart rates vary during their discussions as the intensity of the topic varies. Their CARING/NURTURANCE, SEEKING/EXPECTANCY and perhaps their PLAY/JOY and LUST/SEXUALITY systems are probably being activated. If, on the other hand, their behaviors indicate -1 or -2 communication behavior on the scale; they report "feeling" anxious, fearful, angry, and/or enraged; their heart rates are elevated and do not vary, their RAGE/ANGER, FEAR/ANXIETY, and/or PANIC/SEPARATION systems are probably being activated.

Our Neurobiology of Relationships research program at the University of South Alabama focuses on identifying physiological changes that occur as couples move across activation of primal brain circuits when interacting with one another. We are also attempting to develop physiological measures that can be simple to use in a clinical setting; e.g., wrist or hand monitors like devices used by athletes.

Knowing what brain systems are being activated is useful in developing appropriate therapeutic interventions. If a couples' SEEKING/EXPECTANCY and CARE/NURTURANCE systems are activated and they feel close and connected, the couple can simply be allowed to continue their conversation while the therapist monitors their activity, occasionally making suggestions or summarizing what has been discussed. If the couple reports feeling distressed and they are engaging in destructive communication behavior (-1 or -2 communication styles), the therapist can intervene to slow the interaction and "take it to a process level;" that is, have the couple focus on what each is doing that causes either or both to feel fear, anger, panic, or anxiety. Strategies described by Gottman, Johnson and Atkinson can be employed to guide the discussion.

Therapy for Common Relationship Problems

It is beyond the scope of this paper to give a detailed description of therapeutic interventions needed to deal with common problems couples encounter. However, some general information gleaned from clinical practice and couple research can be summarized.

Not surprisingly, when couples first get together, they tend to be on good behavior in order to favorably impress their potential lover. Early in courtship couples focus on one another, share stories about their past, engage in behaviors their partner finds pleasing, and tend to be kind and considerate. Such behavior stimulates the SEEKING/EXPECTANCY, LUST/SEXUALITY, PLAY/JOY, and ultimately, the CARE/NURTURANCE brain operating systems. However, overtime couples tend to shift to spending less time together, being less attentive to one another, desiring their preferences over those of their partner, and becoming less patient, considerate, and kind with their partner. These changes are easy to spot when each partner attempts to be "dominant" in one or more aspects of the relationship, often along traditional gender role lines. For example, women TEND to be more dominant when dealing with children and household matters. Men TEND to be more dominant in career and monetary matters. The last 50 years has seen a move toward egalitarian attitudes about these gender differences, however, they are issues still frequently seen by couple therapists. As couples attempt to deal with differences in attitude and preferences regarding these issues, they can become frustrated. Frustration can simulate the ANGER/RAGE, FEAR/ANXIETY, and/or PANIC/SEPARATION brain systems. When this happens frequently, couples may seek assistance from a relationship therapist. The partner more likely to seek such assistance is the female partner in a heterosexual relationship. The following are strategies for dealing with such couples as a therapist. These good-practice strategies have been gleaned by the me and my colleagues, especially those at Texas Tech and Iowa State University, over thirty years of work with couples in family therapy clinics designed to train couple and family therapists as well as conduct research on models of therapy.

1. If the "customer" is the wife (or female partner) who calls for an appointment, make sure you talk to and negotiate with the husband, so he comes with her to the sessions. Caution: seeing one partner alone to "talk about the relationship" greatly increases the chances of a divorce occurring because you can't "fix the relationship" if the "relationship" is not present. The attending partner will "dump" their frustration on the therapist and the therapist will "tend to side with the client." It takes "two to tango" and one partner is usually "not at fault for relationship problems." Relationships are complicated interactional processes that need to be observed in as much totality as possible to be understood.

2. Schedule the couple for a 90 minute to two-hour first session. The typical "fifty-minute hour" is just long enough to "get to the interesting stuff" and the session is over. Yes, insurance companies only want to pay for one-hour sessions so you will have to be creative to make it happen.

3. Begin the first session by asking the couple "What brings you by today?" Do not ask "What is the problem you are dealing with?" The second question assumes there is a problem and begins the therapeutic process on a negative note. The "What brings you by today?" question is neutral in valence and is considered to be a "Grand Tour Question" of the type used by cultural anthropologists when dealing with cultures they have not experienced and want to know holistically. As a therapist, you are venturing into "unknown territory" so "let the witness lead you" by asking this neutral, opened-ended question and listen to what they do with it. "Keep your mouth shut" during the first 30 to 60 minutes and let the couple "tell their story." It is important to make summary comments along the way so they know you are listening and understanding their story. Watch what they do and how they talk (use the Communication Rapid Assessment Scale as a guide; see Appendix) and make note of their behaviors. Only ask questions of clarification by putting a question mark after words they are using. For example; "What do you mean by 'We don't communicate well' or 'He never listens to me.'" This will give you clues about what brain systems are operating and what narrative(s) they use to make sense of their lives.

4. After the couple finishes "telling their story", ask them what they would like to have changed in their relationship and how they would know if the relationship had improved.

The process just described will help you get started with relationship therapy because you will have a "thick description" of the situation the couple is currently experiencing. Often the course of therapy will become obvious once this intake session is completed.

Parenting and Children

Women have a strong nurturance urge that is driven by the CARE/NURTURANCE primal emotional system. Men also have this urge although it is usually latent until it is stimulated as men interact with their infant children. The CARE/NURTURANCE system probably arises from the SEEKING/EXPECTANCY system that underlies all the primal emotional systems. The CARE/NURTURANCE system is driven by oxytocin and dopamine circuits. Oxytocin stimulates and maintains the desire to care and dopamine “rewards” caring behavior when infants and children respond favorably to their parents’ attention (Panksepp & Biven, 2012).

Consistency and quality of parental attention have a major impact on oxytocin production in the parent and the child. Oxytocin stimulates caring while vasopressin stimulates parental bonding with their child. This infant bond with a parent, their first primary caregiver, determines how well a child will relate to others during his or her lifetime. Oxytocin and vasopressin affect parents’ ability to attend to and bond with their children. The type of bond formed between parents and their children is the basis for categorizing the type of attachment style that a person will carry throughout their life (Panksepp & Biven, 2012).

Parents’ brains change while interacting with their children. Mom’s reward processing center is activated by seeing her baby’s face. Mom’s SEEKING/EXPECTANCY system (anticipation-reward center) is influenced by the emotions she sees in her baby. Abusive and neglectful mothers show less empathy and more aversion than nurturing moms. Empathy is a product of the CARE/NURTURANCE system interacting with the PANIC/GRIEF primary emotional system. The PANIC/GRIEF system in each parent is stimulated when their child cries. This leads the parents to protect the child in a caring manner which is necessary for survival. Most mothers can distinguish the cry of their baby from those of strangers(Panksepp & Biven, 2012).

Adult brains, even elderly adults, show more brain activity when viewing pictures of their parents, especially their moms, than pictures of any other humans. During stressful situations, adults touched by a woman in a supportive manner show brain reactions similar to babies touched by their mothers. The comforting response to mom’s touch becomes hard wired (Panksepp & Biven, 2012).

As pregnancy progresses, moms become better at discriminating emotions on the faces of others, especially fear, disgust, and anger. Animal studies with mice and primates show that fathers who interact with their offspring display brain changes like females, including greater sensitivity to oxytocin and vasopressin that facilitates bonding long-term with their children. Oxytocin stimulates contractions during labor and triggers letdown of milk when nipples are suckled. Oxytocin keeps the CARE/NURTURANCE emotional system active following delivery. Being cared for long-term gives infants and children a competitive edge in the battle for survival. The CARE/NURTURANCE system interacts with the LUST/SEXUALITY system to ensure reproduction and ultimately social attachments. Long-term bonding such as marriage increases the probability that parents will reproduce, continue their relationship, and help their children mature (Panksepp & Biven, 2012).

The CARE/NURTURANCE system is connected through the hypothalamus to the Ventral Tegmental Area (VTA), a dopamine-producing area of the brain. This connection stimulates the SEEING/EXPECTANCY system and in turn makes parenting rewarding. This connection also promotes goal-oriented maternal tendencies. If a baby cries, the PANIC/GRIEF system is activated, and parents protect their children which also reinforces a sense of reward in parents when the baby's distress is diminished. Oxytocin enhances learning by the CARE/NURTURANCE system that improves parenting skills. Oxytocin also enhances the effects of endogenous opioids, again leading the parents to feel rewarded by parenting.

Parents' brains become focused on the care and wellbeing of their offspring. Neurons in the part of the brain that regulate maternal behavior (medial preoptic area of the hypothalamus) grow impressively during late pregnancy preparing mom to respond to a baby with appropriate and sensitized impulses (Panksepp & Biven, 2012). Estrogen and progesterone help mom focus on cues and cries of her infant.

In sum, our experiences of parenting and our children's experience of being parented are greatly influenced by hormones generated within our bodies. The specific hormones released are in turn governed by the brain systems operating while we are parenting. To complete the cycle, hormones feed back to our brains to further regulate the neuronal/hormonal process driving our parenting. Nature has designed our bodies to ensure that the joys of parenting will outweigh the burdens. We have some conscious control of this process but much of what we do is driven by the emotions generated by interactions with our children. We can attempt to consciously reframe the feelings we experience in response to our body's primal emotional reaction to our children's behavior, but it is a difficult process, as any family therapist or parent will testify. The effects of hormones such as oxytocin on relational and parenting behavior suggest important future directions for mental health professionals, especially couple and family therapists, to attend to.

Psychotherapy with Children and Adult Survivors of Childhood Trauma How children develop emotionally, cognitively, and behaviorally is much dependent on how they are raised. Table 2 describes parenting styles and Table 3 how children react in terms of how they bond to parents or other caregivers (Bowlby,1988).

Permissive parents do not provide adequate structure, clear rules, and attentiveness. They may be so preoccupied with their own lives that they are not available to their children. Preoccupation may take the form of making their careers the primary focus of their lives, being addicted to drugs or alcohol, or simply being too immature to raise children. Whatever the cause, overly permissive parenting leaves children without proper guidance, nurturance and caring to develop into well-functioning adults. Permissive parents can produce children who display an avoidant attachment and/or disorganized attachment style because they have not learned to be emotionally close to others due to their parents' inattention or have not had enough guidance to learn how to cope optimally. In short, they had to learn to fend for themselves. These individuals tend to make poor relationship partners (Joanning & Keoughan, 2006).

Authoritarian parents represent the opposite extreme, being too controlling, arbitrary, and insisting their children follow inflexible rules with little or no age appropriate flexibility, relaxation, or negotiation of rules as the children reach adolescence and seek greater autonomy. This parenting style can produce children who are either meek and submissive or reactive and belligerent. These children can develop an ambivalent attachment style characterized by anxiety and/or intolerance of others. This author suspects that such children grow into adults with overly sensitive insulae, the part of the brain that contributes to the processing of disgust. Our neurobiology of relationships study is attempting to answer this question.

Table 2

Parenting Style	Jellyfish (Permissive Parents)	Dolphin (Authoritative Parenting)	Tiger (Authoritarian)
Drive in childhood	Drive dominated by child's demands.	Parent-guided drive of nurturing the child's nature.	Parent-driven pushing and/or hovering.
Autonomy	Too much autonomy too early.	Gradual increasing of autonomy with age.	Expectation of autonomy but it is unintentionally impeded by pushing and hovering.
Role-modeling	Non-purposeful	Purposeful use of role modeling for collaboration, balanced lifestyle, and core character values.	Non-purposeful or dominated by a narrow definition of success (financial or status oriented).
Instruction	Not enough or absent	Instruction when needed but focus is guidance including learning from trial and error.	Too much adult instruction leading to lack of opportunity for independent problem-solving.
Discipline	Avoidance of confrontation and few rules and consequences.	Collaborative discussion of rules and consequences. Parents maintain authority.	Parent-determined rules and consequences.
Goals	Not clear	Long term 21st century skills = creativity, collaboration, critical thinking, and communication (CQ)	Short-term performance or achievement.
Expectations	Not clear	Living a life of health, balance, meaning, and purpose.	Early performance and achievement with assumption this will lead to wealth, status, and thus happiness later in life.
Drive in adulthood	Not clear or random	Healthy, internal drive that is sustainable	Diminished and/ or dependent on external reward or pressure.

Table 3

Attachment styles	% of sample (also generalized to represent U.S. population)	The child's general state of being	Mother's responsiveness to her child's signals and needs	Fulfillment of the child's needs (why the child acts the way it does)
Secure Attachment	65%	Secure, explorative, happy	Quick, sensitive, consistent	Believes and trusts that his/her needs will be met
Avoidant Attachment	20%	Not very explorative, emotionally distant	Distant, disengaged	Subconsciously believes that his/her needs probably won't be met
Ambivalent Attachment	10-15%	Anxious, insecure, angry	Inconsistent; sometimes sensitive, sometimes neglectful	Cannot rely on his/her needs being met
Disorganized Attachment	10-15%	Depressed, angry, completely passive, nonresponsive	Extreme, erratic: Frightened or frightening, passive or intrusive	Severely confused with no strategy to have his/her needs met

Authoritative parents, in contrast to permissive and authoritative parents, are attentive to their children, impose clear but negotiable rules especially as children mature, and act as appropriate role models for their children. This parenting style produces adults who are altruistic and other oriented. Generally, authoritative parents have a functional happy marriage which their children emulate.

Loving, caring parents tend to produce children who are securely attached to their parents. Parents who begin with high structure and low autonomy for their children when they are infants but gradually reduce structure and encourage autonomy as their children grow to adulthood provide society with well-adjusted adults who can contribute to the good of society. Unfortunately, one third of children are treated harshly or raised by one or more anxious individuals who rear children to become less than optimally functioning adults. Such adults often develop psychological disorders that can cause themselves or others distress. If the distress is severe enough, these individuals may seek or be referred for mental health treatment. Throughout the rest of this paper, suggestions will be given for treating these problems based on what affective neuroscience is learning about how our bodies produce these effects.

If children are raised in a harsh or anxiety producing environment, their lives may give them limited opportunity for their PLAY/JOY primal emotional system to be activated, an important component of learning to interact with their social environment. If this is the case, children and adults may benefit from activation of this system of circuits, and in turn their SEEKING/EXPECTANCY system by play. For children, play therapy or access to children of a similar age in a safe environment can activate these systems and stimulate positive emotional growth. Play increases social learning and promotes a sense of fun and humor. Such an approach may be particularly helpful for attention deficit hyperactivity-oriented children or those with autistic tendencies. For adults, activities that are joyful such as social activities and dancing can activate these systems and possibly counter antisocial tendencies such as personality disorder or stress disorders resulting from childhood trauma. Therapies designed to engage adults in playful interactions and direct body work (e.g., family sculpting) may counter chronically activated RAGE/ANGER, FEAR/ANXIETY, or PANIC/GRIEF systems by stimulating hormone production (endorphins, dopamine) that suppress these systems. It is important that therapists guide patients toward positive emotional states so that hormone flow at a primal emotional level is stimulated; hormones that allow individuals to dampen negative primal emotional systems and enhance positive emotional states, along with positive feelings at a secondary level and positive thoughts at a tertiary level. This "bottom-up" approach contrasts with "top-down" approaches such as cognitive-behavioral therapy and mindfulness training. These approaches can still be used but in conjunction with primal affect-based approaches. Allowing clients to experience negative emotions in a safe context that also incorporates positive emotional experiences increases the range of emotional states available to them, and can help them learn to modulate their emotional state in a healthy way. Emotional arousal modifies how we think just as modifying how we think can modify emotional arousal. It is important to remember that emotions are primal and automatic while cognitions are primarily learned. It is also important to remember that we do have cognitive awareness of and response to many of our body states (e.g., hunger, nausea) and these can influence our emotional status from the primal to the feeling and to the cognitive/thinking levels. Therapists are advised to work from the "bottom up and top down" simultaneously to maximize the effectiveness of therapy.

The importance of early intervention must also be emphasized. Young children are particularly sensitive to environmental stressors because their brains are still developing, and their neurons and neural circuits are differentiating. The brain systems Panksepp has identified develop over time as a person's genetic disposition interacts with their environment. If the environment is harsh, young brains adapt to cope with the harshness, and this can produce lifelong negative results. One can speculate that children raised in such environments will tend to develop more active RAGE/ANGER, FEAR/ANXIETY and/or PANIC/GRIEF brain systems. However, young brains are also very plastic and thus resilient because new neurons develop rapidly (neurogenesis) as do new connections with other neurons (synaptogenesis), leading to modifications of the neural circuits that give rise to the various affective brain systems. If positive influences replace negative environmental stimuli, young brains can adapt in a positive manner. Just like young brains can learn multiple languages more easily than adult brains, young brains can overcome early harsh experiences if given the opportunity and potentially develop healthier, more adaptive and constructive emotional responses.

Teen Brains Yes, they do have one. Adults are often frustrated by their teenage children's behavior. There is a reason for their behavior; they think more quickly in specific areas but slower and less efficiently than adults in making complex connections. The teenage brain is still wiring up. Neurogenesis & synaptogenesis have a spurt at puberty so new neurons and new synapses are formed and then pruned throughout the teenage years (Strauch, 2003). In addition, another important change is occurring in the teen brain.

Myelination is the formation of a fatty sheath on the axon of neurons that occurs at different rates and time courses throughout life, but is especially prominent during adolescence. This process turns much of the brain (i.e., the axonal pathways connecting different brain processing regions) from gray to white. More precisely, myelin covers axonal "highways" that connect the gray matter processing areas of the cortex and deeper discrete processing areas (e.g., amygdala, basal ganglia and other brain nuclei), thus facilitating speed and improving coordination of processing for both short- and long-distance signaling. In a sense, myelination develops the connectivity that allows comparison of processed information from different brain areas. The adage applies here: "there is wisdom in a multitude of counselors." As the brain wires itself up during development, it enables its different processing areas (like "counselors") to provide their diversities of "wisdom" to the brain's decision-making centers in a coordinated way. Myelination contributes significantly to maturation. Myelination speeds up the conduction of nerve impulses up to 100 times faster than the unmyelinated gray matter of childhood (Giedd, 2015).

Myelination also accelerates axon recovery time between nerve impulses thus increasing information processing. Quicker recovery time allows up to a 30-fold increase in information transmission. Combining faster neuronal transmission with shorter recovery time provides a 3000-fold increase in computational power from childhood to adulthood (Giedd, 2015).

Increased speed and computational power increase the ability to learn. Inputs from nearby and distant neurons become able to arrive simultaneously at a given neuron allowing different parts of the brain to coordinate. Greater speed and coordination lead to better decision making.

Frequently used neural connections are strengthened and unused or maladaptive synapses are pruned. Gray matter decreases while white matter increases. More precisely, neurotransmitter receptors, transporters/uptake mechanisms (and many other neuroactive signals like the neurotransmitters, neuromodulators and neurohormones themselves) both increase and decrease in many different, but precisely localized neural circuits. At synapses, the synaptic plasticity and modulation can be up or down depending on the receptors and their upstream (e.g., genetic and second messenger) control. The neuromodulators are diffuse (redundant) with sites of occurrence and control throughout many different brain regions, but the receptor presence and absence are precisely controlled, and these changes can occur on the time scale of milliseconds.

Neurotransmitter receptor sites on neurons increase or decrease in functionally appropriate ways so dopamine, serotonin and glutamate have more effect and modulate neurotransmitter communication among neurons. As a general rule, neuromodulators and neurohormones tend to act by second messenger mechanisms that have slower and often prolonged actions (seconds to minutes or hours), in contrast to the actions of classical neurotransmitters (e.g., glutamate and GABA) that act very rapidly and transiently (milliseconds to a few seconds).

The combination of greater processing speed and specialization of brain function allows the prefrontal cortex to better organize, make decisions, plan, and regulate emotion. As the brain matures, individuals can make more accurate simulations of what will happen in the future if they behave and think in a particular way today. Thus, as an individual brain matures (due to the processes mentioned above) both short- and long-term consequences of particular decisions or actions are taken into account. It takes many years for maturation to occur. It is no wonder adults get frustrated with teens. While teenagers are planning to do something that is potentially dangerous, adults already know what might happen. But try telling that to a teen (Strauch, 2003).

The limbic system, the center for emotion and impulsive behavior, matures earlier and faster than the prefrontal cortex, the center for careful planning and decision-making (Strauch, 2003). Consequently, for at least ten years teens engage in novelty seeking, risk taking behavior and are more in tune with their peers than adults, unless the adults act appropriately. Adults need to "stand in" with mature, wise, consequential guidance when the teen brain cannot yet function.

In sum, a teenager's emotional brain is functioning well by the beginning of adolescence. Unfortunately, their prefrontal cortex-the planning, reasoning portion of the brain-is not well connected to the rest of their brain; thus, emotionally impulsive behavior emerges. Fortunately, by age 23-25, teen brains catch up with adults (Strauch, 2010). Indeed, we say the teen has "matured" and become (at least technically) an "adult." Of course, no adult is perfect and so there is still room for improvement ("wisdom"), the task of a lifetime.

Adults need to understand teen brain development. Respectful conversation between adults and teens led by adult example is crucial for monitoring and guiding teen behavior. Treat your teenage child like your best friend's child and you are more likely to get the desired response.

Evidenced-Based Therapeutic Interventions

to Help Families Deal with Parenting and Child Development Problems

Family Therapy As relationships progress, issues emerge that need to be addressed. Maintaining an intimate relationship with a partner can be stressful and parenting children is complex. Relationships can end because of stress. Consequently, couples and families often seek professional assistance to deal with relationship issues that have become problematic. Fortunately, a wide range of therapeutic modalities have emerged over the last century to deal with these issues (Nichols, M., 2017). It is beyond the scope of this paper to explore all these models of family therapy. However, two are worth mentioning because they relate nicely with the emerging findings of affective neuroscience. The reader is referred to the Nichols text for an in-depth review of these models. A brief overview of several is given below.

An early model of family therapy was developed by Murray Bowen, a psychiatrist who worked at the Menninger Clinic beginning in the 1940's and eventually moved to the National Institute of Mental Health. His model was an early attempt to deal directly with human emotions and their impact on complex human behavior. He postulated that emotions influence not only the current generation but that influence is passed from one generation to another. His therapeutic model was based on his background in biology and he paid attention to emotional processes such as anxiety. As we will see, anxiety can have a profound effect on human behavior.

A widely used modality of psychotherapy, Cognitive/Behavioral Therapy, has also been adapted to deal with couples and families. As the name implies, how we think affects how we behave, especially in intimate relationships. Our "cognitive schema," the set of our core beliefs about how relationships work, develops over our lifetimes but may be erroneous and therefore negatively affect our relationship. From an affective neuroscience perspective, these problematic core beliefs based on our experience as an organism, shape what we have learned and are stored in our cerebral cortex. When we have an emotional reaction to individuals with whom we are relating, these emotions are processed into feelings by our limbic system. Our limbic system relies on memories stored in our cerebral cortex to accurately interpret these primal emotions as feelings about what is happening. If our memories are distorted because our schema is inaccurate, we experience inappropriate feelings that lead us to behave inappropriately. Consequently, Cognitive/Behavior Family Therapy attempts to change cognitive schemas, so the feeling interpretations derived from Primal Emotions lead to appropriate behavior.

General Therapeutic Strategies for Dealing with Families

As we did earlier when we discussed interventions with couples, clinical researchers have developed general approaches for dealing with families who present for therapy. The interested reader should consult Nichols (2017) who in turn provides references to primary research studies regarding family therapy. Unpublished dissertation research conducted as well as clinical observations and data gathered from family therapy clinics at Texas Tech and Iowa State University has also suggested effective approaches to dealing with families. Although this is not published scientific research, the information gathered is based on careful records keep on thousands of couples and families seen at these clinics. The following is a brief overview.

1. When a parent calls for assistance with a family problem, take time on the phone to determine why they are calling. Use a question such as "What motivated you to call today?" This general question usually leads the caller to describe an incident or a repeated incident that is causing the parent or parents frustration. If "Dad" calls, the problem is usually extreme because men are usually more hesitant to call than women. They don't like other people to know they "can't handle family problems on their own." Make sure you spend enough time on the phone to determine who is involved in the problem that led to the call. The problem may involve nonfamily members such as the children's friends, uncles, aunts, grandparents, schoolteachers, bosses, co-workers, medical care givers, or law enforcement and social service agencies.

2. Structure the first session to include all relevant parties. For example, if Gramma sits with young children while the parents are working, she may be needed in the first session to get a complete picture of the problem. Don't allow a family member, especially a teenager, to skip the session because "they don't want to come." They may be the key person needed to understand and change the problem situation. Another example: if a child has been caught with drugs in their possession at school and the police have been contacted; it may be necessary to have the session conducted at school or a juvenile detention facility. In some cases, a school official or law enforcement officer may attend the session if asked. In sum, be sure to engage the "entire problem organized system" or you will not be able to intervene effectively.

3. As described when working with couples, schedule enough time for a first session with a family. Complex problems may require several hours to fully explore the situation with all involved parties.

4. When possible, use a room designed for family therapy. Clinics this author has designed have rooms that are 14 by 16 feet with a play therapy station along one side. Separate chairs with wheels are helpful.

5. Have the therapist "follow" the family members into the room. Allow each family member to choose their own chair. Watch how family members "align themselves." Family members will move the chairs to position themselves to reflect their emotional relationship with other family members. For example, problem teens tend to move away from other family members and turn their back to the mirror in rooms with a one-way mirror. Family members who are in a "coalition" will sit close to one another and face the "opposition."

6. Begin the session by asking the family and other participants, "What brings you by today?" as we described when working with couples. The parents have called because of a problem; however, don't begin by labeling someone as "the problem." Listen to their story and watch their interaction while minimizing your questions. Try not to "take charge of the session." Allow the session to unfold. Watch what each family member does and how other family members react. This will show you "how the system functions." Pay close attention to the "executive system;" that is, the parents if it is a two-parent family. What type of parenting team are they (recall our earlier discussion of parenting styles)? What type of attachment do the children display (recall our earlier discussion of attachment styles)? If the parenting team partners have different parenting styles, you may need to have a separate session with them to determine why. Often differing parenting styles correlate with marital/relationship problems. Parental relationship problems usually need to be dealt with before or concurrent with family problems. Family problems often grow out of parental relationship problems. When dealing with a single parent, therapy may need to focus on helping the single parent establish a support system. Single parents are often overwhelmed dealing with children and work.

7. As we described when discussing how to deal with couples in therapy, take time in the first session to let everyone "tell their story" and make sure they are allowed to do so. The "problem child," if there is one, may be hesitant to speak for fear of reprisal. It is often helpful for the therapist to simply roll his or her chair next to the child. This usually causes the parents to let the child "speak for themselves" especially if the therapist talks to the child rather than the parents.

8. At the end of the first session it is usually helpful for the therapist to "summarize what I have heard and seen today to make sure I got it right." This will help the family members feel "heard" and stimulate their SEEKING/EXPECTANCY brain system and suppress their FEAR/ANXIETY, RAGE/ANGER, and/or PANIC/SEPARATION brain systems. Further conversation and "homework" assignments can be designed to stimulate the CARE/NURTURACE brain systems.

9. In some cases, an "In-Home Family Visit" can be very informative and helpful. A good time for such a session is during "Hell Hour" from 5 to 7 pm on a weekday during the school year. The children are home from school, hungry, and would rather play than do homework.

The parents are just home from work, tired, and often "need a drink!" The therapist can simply sit in a corner and watch what goes on.

Relationships over the Long-Term Over time couples tend to bond or move apart depending on processes they develop to regulate their relationship. Loving couples tend to bond and develop styles of interaction that support continued bonding (Henrich, 1987). If a couple does not bond, they tend to develop interaction styles that negate love. They habitually respond to one another recounting perceived past transgressions. They complain about feeling stressed by their interactions (Joanning & Keoughan, 2006).

As couples continue in their relationship, the "real" self emerges; couples are constantly changed and shaped by life experiences. If the couple has developed a pattern of mutual respect, caring, communication, and problem solving, they can continue to enjoy the warm feelings that emerge as the LUST/SEXUALITY, PLAY/JOY, SEEKING/EXPECTANCY, and CARE/NURTURANCE systems function. Unfortunately, not all couples develop functional patterns of interaction (Gottman, 1999). Arguments become more frequent. Negative verbalizations take a huge toll on the couple (more potent than positive verbalization, Gottman, 1999). Partner support is not always well received. Sexual problems emerge probably because the CARE/NURTURANCE and SEEKING/EXPECTANCY systems are not functioning well. Difficulty with emotional regulation of the PANIC/GRIEF, FEAR/ANXIETY, AND RAGE/ANGER systems and hypersensitivity to negative emotions emerge. Gender differences become pronounced because men and women are socialized differently and have important differences in brain wiring (Panksepp and Biven, 2012). These changes are accompanied by stress responses that can become extreme.

> **"Sometimes I wonder if men and women really suit each other. Perhaps they should live next door and just visit now and then." -Katherine Hepburn**

Human Stress Response Certain stimuli conveying ambiguity or danger (e.g., your spouse's facial expression, tone of voice, or comments) feed directly into the amygdala. In humans the amygdala processes perceptions of ambiguity or danger that are transmitted to the neocortex for help in resolving the ambiguity and determining if danger really exists (Kurzweil, 2012).

In response to an ambiguous or threatening environmental or internal stimulus, the amygdala activates an increase in our sensitivity to stimuli, literally "turning up the volume" and making us more aware of visual, auditory, tactile, and olfactory stimuli occurring currently or in the near term (Zerbi, V. et. al., 2019). In short, the amygdala makes us more alert if ambiguous or threatening stimuli are sensed.

Once the amygdala does decide that ambiguity or danger is present, it signals the hypothalamus which in turn signals the pituitary or "master" gland to release a hormone, ACTH (adrenocorticotropin). This in turn triggers the release of the stress hormone cortisol from the adrenal glands (above the kidneys) which results in more energy being provided to your muscles and nervous system.

The adrenal glands also produce adrenaline (epinephrine) and noradrenaline (norepinephrine), which suppress your digestive, immune, and reproductive systems because they are of low priority in an emergency. Levels of blood pressure, blood sugar, cholesterol, and fibrinogen (which speeds clotting) all rise. Heart rate and respiration increase. Pupils dilate so you can see your enemy (e.g., angry spouse) and your escape route better (e.g., a way out of the room). In humans the "escape route" might become an excuse or a lie designed to placate a significant other. Our "old brain", (limbic system) and "new brain" (neocortex) come on-line and process Primal Emotions into secondary feelings and tertiary, cognitively labeled/identified higher level feelings. These secondary and tertiary feelings are interpretations of primal emotions within the person's current context.

Our old brain attempts to reduce fear and increase pleasure while our new brain attempts to determine whether fear or pleasure are appropriate given the circumstances. The new brain tries to control the old brain. The amygdala cannot evaluate ambiguity or danger on its own so it relies on the neocortex to help it to decide. When a person is experiencing PTSD, the amygdala over-rides the neocortical feedback that is trying to quell the amygdala's arousal. Fortunately, the neocortex can calm the amygdala in many circumstances if the person has learned that a situation or context currently being experienced is not a threat. If our lover is angry with us, the amygdala becomes aroused. When our lover is caring and supportive, our neocortex helps our amygdala stay calm.

When individuals are in contact with other individuals with whom they have an intimate relationship (e.g., spouses; parent and child) the amygdala is stimulated and seeks assistance from the hippocampus and neocortex, where memories are stored and processed, to determine if precedent can help it decide whether ambiguity or danger exists. Behaviorally, this process leads the individuals involved to attend very carefully to verbal and nonverbal cues consciously and unconsciously. This produces a strong emotional somatic marker (Damasio, 2000, 2010) that can make the situation stand out in our mind for future reference – a strong emotionally tinged memory.

Whether the individuals involved fight, flee, freeze, or "talk about it," their emotional cascade continues throughout their bodies. If they fight or attempt to flee, hormonal levels and physiological changes can escalate making it increasingly difficult for the neocortex to control the limbic system so the "old brain" goes into full "survival mode." To avoid defaulting to survival mode (e.g., bitter arguments or "stonewalling"), the people involved must slow down the cascade process by bringing the neocortex more fully on-line. Typically, this is done by "talking about it" slowly and deliberately (Joanning, 1982).

Males TEND to become "emotionally flooded" and try to escape. Females TEND to "push for emotional connection" and attack. These stereotypic responses are both biologically based and learned. Women are socialized to bond to support child-rearing while men are socialized to hunt silently with their pack to avoid detection by game or the enemy. These are ancient patterns. During conflict men TEND to be more reactive (high heart rate, tension) due to their evolutionary history as hunters leading them to shut down or stonewall. During conflict women TEND to be better able to soothe themselves during and following stress due to their evolutionary history as mothers (Sapolsky, 2017).

When humans are stressed, one or more of the brain executive operating systems Panksepp has identified are activated. These include the RAGE/ANGER, FEAR/ANXIETY, AND PANIC/SEPARATION systems.

Activation of the RAGE/ANGER executive operating system produces feelings ranging from frustration to intense anger (RAGE); thoughts that overflow with blame and scorn, and memories of past transgressions may drive us to strike at the offending agent. Nature evolved this system to enable us to protect ourselves. When dealing with a parent perceived as being unfair, children will become frustrated and express RAGE if their demands are not met; teenagers might rebel and run away from home. When a spouse learns that their partner has been unfaithful, they may become angry and consult a divorce attorney. In extreme cases one partner in an unhappy marriage may become so enraged that they harm the other partner physically. When activated, this system can lead to child or spouse abuse.

RAGE/ANGER is a primal emotional process that does not need an object**.** Jealousy and blame are examples of secondary feelings that emerge as the limbic system processes Primal Emotions within an environmental context. Secondary feelings have an object that grows out of our life experiences; e.g., our spouse if she or he has an affair, our enemy if they kill a friend. RAGE/ANGER can be particularly intense if someone "robs us" of someone we love. Divorce attorneys can attest to the venomousness of someone shunned. Humans may experience love as a limited resource and fight to protect it. In doing so we can experience secondary feelings such as blame or hatred, as our limbic system interacts with our neocortex to process what should be done, leading to tertiary thoughts such as what can we do to seek revenge that in turn may lead to action. These tertiary thoughts arise as we think about (neocortex) who or what is responsible for the ire we feel (a secondary feeling generated by the limbic system) as a result of our body's Primal Emotion of RAGE/ANGER.

When our SEEKING/EXPECTANCY system is looking for a lover and someone competes with us for this prize, our RAGE/ANGER system can drive us to behave in ways that may be unproductive and not socially sanctioned such as challenging or fighting with the competition. Any high school principal can tell stories of adolescents acting out when feelings of jealously emerge. Raw RAGE/ANGER is not cognitive; however, secondary and tertiary feelings have a cognitive component and emerge as we think about our body's reaction to our environment.

The neuro-circuitry of RAGE/ANGER runs between the periaqueductal gray (PAG) to the amygdala and hypothalamus. As mentioned earlier, the PAG is in the midbrain separated from the spinal cord by the pons and medulla of the lower brainstem. It acts as an interface between the lower brainstem, the limbic system and ultimately the forebrain (prefrontal cortex). The PAG helps integrate behavioral responses to external (e.g., threat) and internal (e.g., pain) stressors. It receives and sends information related to such experiences as sexual desire, fatigue, and hunger to the hypothalamus and amygdala (limbic system). The amygdala in turn senses something in the environment that could be a threat such as another man talking to my girlfriend and cooperates with the hypothalamus to prepare our body to react to the threat; we turn our body, focus on the other man, and signal for stress hormones. The PAG processes primal emotions in response to hormones and nerve impulses generated throughout our bodies. This information is sent to and then processed by the hypothalamus and amygdala. The amygdala and hypothalamus are also connected to the neocortex where memories of past experiences can be accessed to assist in determining if a threat exists and what should be done about it. The prefrontal cortex can also become involved to plan an appropriate course of action. The prefrontal cortex, hypothalamus, amygdala, and PAG are cross-innervated allowing constant monitoring of each component by the other components, thus operates through complex feedback loops.

Several hormones can promote activation of the RAGE/ANGER system, notably testosterone that in turn promotes social dominance. This is no surprise to anyone who has witnessed the response of young, sexually aroused male mammals (teenage boys) who are competing for girls; or girls who are competing for boys. Unfortunately, when primal emotional systems such as the RAGE/ANGER and LUST/SEXUALITY circuits are fully aroused, many areas of the neocortex shut down or are inadequate in the moment to control the Primal Emotional systems/circuits. No wonder adolescents may need an adult to monitor their behavior and intervene to limit problematic behavior.

Activation of the FEAR/ANXIETY operating system produces feelings ranging from anxiety to intense fright, thoughts on a continuum from worried to catastrophic, and motivation to escape existing circumstances. From an evolutionary perspective this system motivates organisms to escape danger. Without this system we would be helpless when confronted with life threatening circumstances. When dealing with our spouse, parent, or child, this system can become activated when we feel threatened by something they are doing; an angry spouse yelling at us, a child doing something dangerous, a parent beating us.

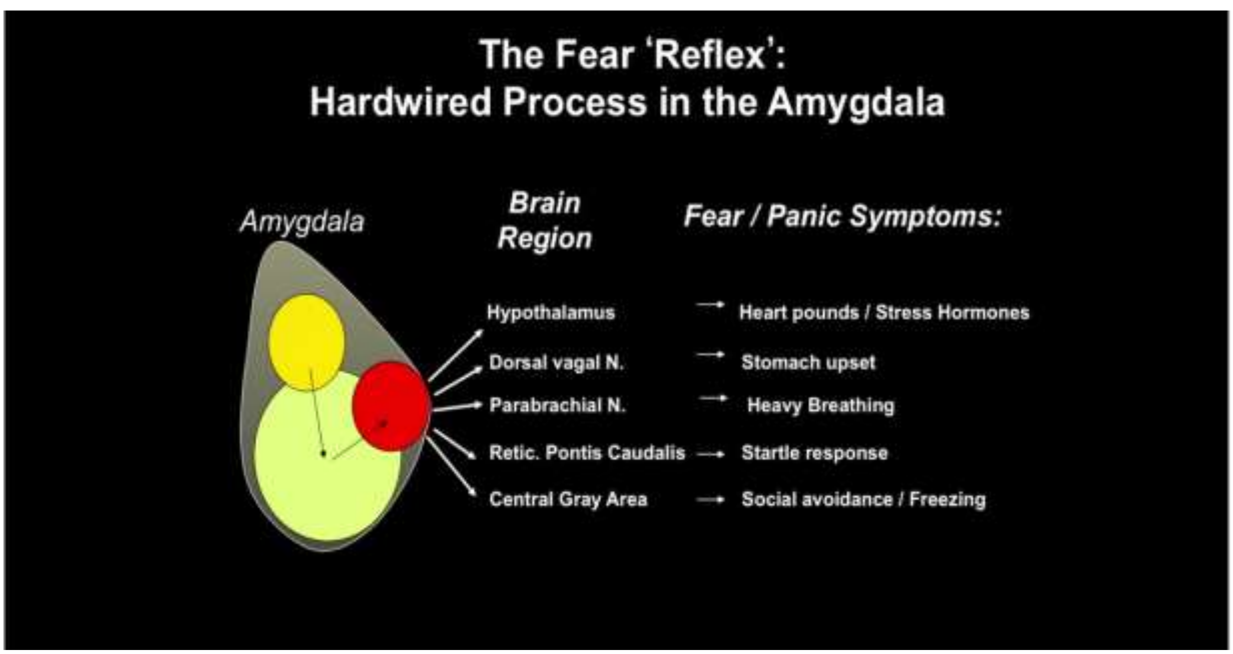
Although some triggers of FEAR/ANXIETY are instinctive (e.g., fear of falling, loud noises, pain, human infants feeling insecure when not being held), many are learned. Fear states promote learning because fear-producing events could cause us physical harm; events such as car crashes and being assaulted, or other events we can imagine that could cause us psychological distress; e. g., job loss or contraction of a fatal disease.

The FEAR/ANXIETY circuit includes processing by the PAG and the amygdala. The amygdala is in turn connected to the hypothalamus that it alerts if a threat is perceived. The hypothalamus triggers hormones that cause our heart to beat rapidly, our palms to sweat, and our bodies to freeze in place or try to run away. When the frightening stimulus is far away (an overbearing aunt who we will visit at Christmas) the higher cognitive parts of the brain such as the frontal cortex interact with the amygdala to keep us calm or cause us to freeze (hide, not return auntie's phone calls). If the frightful stimulus is close (a mugger coming toward us with a knife), the PAG takes over and pushes us to take flight, or turn and fight; e.g., if we are trapped and protecting our child. Finally, animals and people can experience free-floating anxiety states because we have an inherent, biologically hard-wired capacity to FEAR; that is; we have intrinsic emotional systems that cause us to experience FEAR/ANXIETY.

Paradoxically, primal pain (also processed by the PAG) can indirectly reduce our fear response by delaying or overriding our conscious awareness of pain so we can escape a dangerous situation. Pain stimuli from peripheral pain receptors travel the pain pathway in the spinal cord that ultimately goes to the PAG on its way to the thalamus and hence to the appropriate regions of the neocortex (i.e., the spinothalamic tract) directly triggering the release of endogenous opioids, endorphins and hormones that reduce the pain response. Consequently, someone hits us, but we run away before we realize that the assailant has broken our arm. We say "Alright" when our girlfriend says, "our relationship is over," we feel numb until we can seek our best male friend to commiserate about how cruel women can be. We tolerate pain until we can find a safe hiding place. These responses are hardwired so we can survive the vicissitudes of life.

Sometimes events are so fearful or anxiety-producing that we may escape the immediate threat, a firefight in combat, rape, or car accident, only to be haunted by the memory of the event. Our body continues to react to the threat, a condition known as Post Traumatic Stress Disorder (PTSD). Unfortunately, experiences such as physical, emotional, or sexual abuse by a relationship partner or parent can cause a spouse, partner, or child to experience PTSD. Family therapy clinics run by the author have had such clients referred by police departments or physicians. Such cases also present when a couple comes in for therapy and one of the partners has extreme difficulty dealing with sexual or trust issues. These problems can be the residual effect of past trauma.

Bremner, J. D. (2006) reports: "Brain areas implicated in the stress response include the amygdala, hippocampus, and prefrontal cortex. Traumatic stress can be associated with lasting changes in these brain areas. Traumatic stress is associated with increased cortisol and norepinephrine responses to subsequent stressors. Antidepressants have effects on the hippocampus that counteract the effects of stress. Findings from animal studies have been extended to patients with post-traumatic stress disorder (PTSD) showing smaller hippocampal and anterior cingulate volumes, increased amygdala function, and decreased medial prefrontal/anterior cingulate function. In addition, patients with PTSD show increased cortisol and norepinephrine responses to stress. Treatments that are efficacious for PTSD show a promotion of neurogenesis in animal studies, as well as promotion of memory and increased hippocampal volume in PTSD."



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The abnormal stress response continues automatically and chronically because the amygdala becomes more responsive (sensitized) while the medial prefrontal cortex becomes smaller and less responsive (less sensitized). The medial prefrontal cortex processes stimuli from the external environment and our body, and in turn interacts with our limbic system and PAG to generate appropriate emotions and feelings. In sum, FEAR/ANXIETY system is more intensely stimulated by the hypersensitized amygdala and the medial prefrontal cortex is less able to calm the amygdala. Treatment of PTSD requires shutting down this habitual reaction when a non-stress related environmental stimulus is present. Simply the memory of the event or the occurrence of a similar event can set off the intense FEAR/ANXIETY survival reaction. Treatment strategies such as cognitive/behavioral therapy attempt to calm the amygdala's habitual reaction to environmental stimuli reminiscent of the feared event. Vigorous exercise and laughter stimulate the medial prefrontal cortex to release beta-endorphins and neuropeptides that suppress pain. These and other stress-suppressing activities such as talking with friends also calm the amygdala and hippocampus which in turn diminishes the FEAR/ANXIETY response at a primal emotional level. Consequently, psychotherapies and/or physical and social activities that help us think differently and change our body's response while interacting with our environment can relieve stress and counter PTSD.

Medications can be used to suppress the FEAR/ANXIETY response in the short term. Benzodiazepines and brain norepinephrine inhibitors (beta blockers such as propranolol) can be used until psychotherapy can help clients establish emotion and cognition-based methods to replace inappropriate activation of the FEAR/ANXIETY system with activation of more positive Primary Emotional states.

The PANIC/GRIEF operating system involves processing in the anterior cingulate gyrus, dorsomedial thalamus, and the periaqueductal gray (PAG), (Damasio, *et.al.* 2000) and generates sadness, grief, and the urge to cry. It appears to have evolved from brain systems that mediate the intensity of pain and responds to social isolation. This system reacts to stress hormones released when mammals are isolated, and is calmed by brain opioids (endorphins), oxytocin, and prolactin produced when mammals are engaged in positive social activity. Prolonged intense activation of the system can in turn shut down the SEEKING/EXPECTANCY system and lead to depression as endorphin and serotonin levels fall or are depleted. This system is more sensitive in women when activated by separation and loss of attachment leading to higher rates of depression than in men (Panksepp & Biven, 2012). Some early studies suggest that buprenorphine, a relatively safe opiate receptor agonist/antagonist may be used to counter depressive symptoms by boosting endorphin levels rather than using standard anti-depressants (Panksepp & Biven, 2012). However, the FDA has not approved such usage in place of standard of care antidepressants. Some studies suggest that extreme arousal of the PANIC/GRIEF system may trigger panic attacks (Panksepp & Biven, 2012). Still other studies suggest over exposure of this system to endorphins may lead to autism as children become addicted to their own self-released opioids making them socially aloof. Much more research is needed to study the function and emotional/behavioral effects of this brain system (Panksepp & Biven, 2012).

PANIC/GRIEF is usually activated by separation from important persons or circumstances. Feelings associated with this neural command system include variations of loneliness, sadness, and disappointment. When the PANIC/GRIEF system is activated, it produces thoughts centering on the obtainment of social contact and urges us to move toward possible sources of comfort. This system evolved to motivate organisms to affiliate with and seek support from others. When a small child in a store is separated from her mother, she may wail and cry to try to find her parent.

When a couple is divorcing and has physically separated, the spouses often experience "separation shock," especially the partner less desirous of the divorce (Joanning & Keoughan, 2006). He or she may feel so alone and abandoned that they panic and pursue their partner, begging them to try again. Both partners need emotional support and can benefit from divorce adjustment therapy (Joanning & Keoughan, 2006).

Social support during times of crisis that stimulate the PANIC/GRIEF response can help calm this circuit by raising endorphin and dopamine levels. Having close friends interact with a person feeling distressed due to loss of a loved one stimulates the medial prefrontal cortex to release beta-endorphins that in turn calm the amygdala and hippocampus (Panksepp & Biven, 2012), enabling the person to feel more connected. This response is like that described for the treatment of PTSD.   Children raised by parents who have a good relationship tend to have better mental health in part because this brain system is rarely activated.

Panksepp pointed out that the PANIC/GRIEF system has a positive side in that when we are in contact with people we love and who care about us, this system is activated and beta-endorphins are released. One could argue that it might be referred to as the PANIC/GRIEF/AFFILIATION system. Also, clinicians note that PANIC comes on very quickly if a loved one is lost or unavailable; and that GRIEF tends to be long-term. If a loved one is killed in a car accident, PANIC is immediate and intense. Over time, PANIC subsides but GRIEF remains. When my wife began acting strangely and was diagnosed with Early Onset Alzheimer's Disease, I was overwhelmed by a feeling of PANIC that made it difficult for me to function. Overtime, the PANIC subsided as I figured out how to care for her, and replace her friendship with support from family and friends. However, my GRIEF over loosing her continues to this day, although at a less intense level.

Finally, affective support of individuals grieving the loss of a loved one boosts endorphin production and allows them to pass through the stages of grief without sinking into depression. Traditional cultures with close supportive communities have institutionalized this process. Sadly, modern cultures have moved away from long-term close support of grieving individuals making grief more stressful. Therapists can provide grief support by allowing clients to repeatedly talk about their lost loved one until they have externalized the lost individual without pushing the grieving person to achieve closure. Being an empathic listener provides a context that stimulates the production of endogenous opioids in the brain of the client (Joanning & Keoughan, 2006).

Bosch, Oliver J., & Young, Larry, J. (2018) have been studying social relationships of prairie voles that have potential applications for humans. They suggest that oxytocin (OT) plays an important role in the development of the capacity to form social bonds, the mediation of the positive aspects of early-life nurturing on adult bonding capacity, and the maintenance of social bonding. They have found that "OT facilitates mating-induced pair bonds in adults through interaction with the mesolimbic dopamine system. Variation in striatal OT receptor density predicts resilience and susceptibility to neonatal social neglect in female prairie voles. Finally, in adults, loss of a partner results in multiple disruptions in OT signaling, including decreased OT release in the striatum, which is caused by an activation of the brain corticotropin releasing factor (CRF) system. The dramatic behavioral consequence of partner loss is increased depressive-like behavior reminiscent of bereavement. Importantly, infusions of OT into the striatum of adults prevents the onset of depressive-like behavior following partner loss and evoking endogenous OT release using melanocortin agonists during neonatal social isolation rescues impairments in social bonding in adulthood. This work has important translational implications relevant to the disruptions of social bonds in childhood and in adults."

In sum, OT appears to facilitate social bonding, parenting, and resiliency in the face of partner loss. The clinical implication is that increasing OT levels can both improve relationship bonding and assist in recovery from partner loss. Clinicians already encourage couples to engage in behaviors designed to improve bonding and OT production (see Couple Communication above and below); and help individuals deal with loss by engaging in grief/bereavement counseling with clients. An interesting additional clinical intervention would be to introduce OT directly into the bodies of clients using nasal infusion. However, careful study is needed to ensure that such an approach is safe, effective, and ethical.

Couple Communication Revisited Couple therapists frequently hear client couples complain that they don't communicate with each other. Each person thinks their partner doesn't respect or care enough about their concerns to really listen and respond in a manner that pleases the speaker; "I say the same thing over and over again, but it doesn't get through." On the other hand, couples in satisfying relationships report feeling respected and understood by their partner. As discussed earlier, couples can be taught to communicate in a manner that improves relationship satisfaction (Brock & Joanning, 1983) and the effects of such training or the lack of it can be measured (Joanning, Brewster, and Koval, 1984). Couples can be taught specific skills that change the primary emotional responses their bodies generate and in turn the feelings they experience at the secondary level and the thoughts they have about their relationship at a tertiary level.

Specific skills that couples can learn that improve communication (Joanning, Brewster, and Koval, 1984) include:

-listening to their partner and paraphrasing what they have heard before responding

-ensuring that what is communicated is perceived as intended

-orienting their bodies to face their partner with hands in front extended toward their partner, holding hands if the topic is important or intense

-leaning toward their partner

-maintaining eye contact

-staying with an issue and discussing it until the issue is explored and understood by both partners

-each partner modulates their tone of voice to show interest in their partner's point of view

-each partner understands that agreement may not always be possible, but that creative alternatives or compromise may be achieved.

Couples in long term happy marriages display these behaviors (Henrich, 1987). Couples experiencing relationship difficulties tend to talk over one another, use a harsh or patronizing tone of voice, cross their arms or wave their arms in front of their bodies while talking, lean back away from their partner, change the topic or focus to defend their point of view, and make judgments about their partner's intent.

Couples who are in good relationships and communicate well report feeling calm, content, respected, understood by, and bonded with their partner. Descriptions of their thoughts and feelings indicate that their SEEKING/EXPECTANCY and CARE/NURTURING circuits are up and running most of the time they are together. Evidence of these circuits being engaged can be measured using EEG, EKG, and other biometric readouts and by observing how they interact while talking with one another about important issues in their relationship (Joanning, Shelly-Tremblay, Meyers & Overstreet, 2018). Couples in poor relationships display behaviors and report thoughts and feelings that indicate their RAGE/ANGER, FEAR/ANXIETY, and/or PANIC/SEPARATION circuits at times or frequently override their SEEKING/EXPECTANCY and CARING/NURTURANCE circuits.

Good communication appears to be a necessary condition to establish and maintain a good relationship. However, couples also need to be able to express affection, be physically and emotionally intimate as well as communicate to maintain a healthy, loving relationship. It would be interesting to give couples intranasal oxytocin as part of relationship therapy to see if such a move would "jump start" the SEEKING/EXPECTATION and CARE/NURTURANCE systems. In a similar vein, it is probably important for couples and therapists to exercise the "mirror neurons" of their sensory systems so their bodies can empathize with the emotional state of their partner or clients.

Divorce or Death of a Spouse When relationships deteriorate, the stress response described above sets in and couples go through a series of changes in their relationship (Joanning and Keoughan, 2006). The first change is "emotional erosion;" that is, positive feelings toward one's partner are replaced by negative feelings. The SEEKING/EXPECTANCY, LUST/SEXUALITY, PLAY/JOY, and CARE/NUTURANCE circuits dissipate and the RAGE/ANGER, FEAR/ANXIETY and/or PANIC/SEPARATION circuits become dominant. The intensity of feelings generated by one or more of the latter three circuits raise the stress hormone levels of one or both partners to the point that staying in the relationship becomes intolerable. Eventually the couple reaches the stage of "emotional divorce" and distance themselves emotionally. As this stage continues, the couple finally separates physically. This can set off "separation shock" mentioned above as their bodies adjust to absence of their partner. Even couples who mutually decide to separate can experience this "shock." After living together, sleeping together, being sexually intimate, couples have habituated to one another physically and emotionally. Severing that tie can produce unexpected effects such as arousal of the PANIC/SEPARATION circuit, especially for a partner who does not want the divorce to occur. Any therapist who has done divorce counseling has seen this phenomenon display itself as one or both divorcing partners engage in inappropriate behavior such as sexual promiscuity or exhausting their friends with complaints about their spouse. Some individuals contemplate suicide or causing harm to their partner. Divorce adjustment training can moderate these severe reactions and help individuals adjust more appropriately (Joanning, 1985).

Fortunately, after divorce, time can eventually remove stress as the RAGE/ANGER, FEAR/ANXIETY and PANIC/SEPARATION circuits dissipate and the SEEKING/EXPECTANCY, LUST/SEXUALITY, PLAY/JOY, AND CARE/NUTURANCE circuits are reactivated. Hopefully these changes occur as the partners go through the rebuilding and reestablishment stages of divorce; that is, they receive support from friends, establish a new intimate relationship, evaluate and change their behaviors (Fisher and Alberti, 2016).

Individuals who lose a partner to death also experience extreme stress especially if they had a close loving relationship with their spouse. The PANIC/SEPARATION circuit can become activated as they lose the close physical and emotional connection with their partner. This circuit is activated most severely if the partner dies suddenly because the surviving spouse does not have time to prepare emotionally. Widows and widowers also experience intense stress because of the loss of activation of the SEEKING/EXPECTANCY, LUST/SEXUALITY, PLAY/JOY, and CARE/NUTURANCE circuits stimulated by their partner. Grief counselors can help these individuals mourn the loss and take steps to reactivate these circuits by encouraging their clients to turn to friends and family for support and perhaps establish a new intimate relationship. Unfortunately for elderly women this can be difficult because of the limited number of same aged men. Some widows turn to female friends to fill the void in emotional support.

Suggestions for Mental Health Workers Enabling people to better understand how their brain systems operate may be therapeutic. For example, treating tinnitus (ringing in the ears) is best accomplished by first explaining what causes the tinnitus and how the brain's emotional reaction to phantom sound triggers a distress response (Tyler, 2006). This basic understanding of the process is an important step toward helping individuals learn to cope. Explaining the unknown by describing how emotional responses arise from deep in the brain can reduce the fear factor and change the Primal Emotional reaction, especially when coupled with behavioral and emotionally focused therapy. Our ongoing Neurobiology of Relationships Research Program in the Department of Psychology at the University of South Alabama is attempting to incorporate education regarding neurobiology into the therapy process. My colleagues, graduate students, and I routinely explain to couples how their brain, nervous system, and endocrine systems affect their behavior often at a subconscious level. Clients are "fascinated" by this information because it helps them develop a greater understanding of their own and their partner's behavior.

Further development of psychotherapeutic interventions may be facilitated by findings emerging from affective neuroscience. These interventions include direct brain stimulation such as transcranial magnetic stimulation, deep brain stimulation of the subgenual anterior cingulate for treatment resistant depression, and the development of pharmaceuticals that more precisely target specific brain structures, neurotransmitter and hormonal systems (Panksepp & Biven, 2012).

My colleagues and I have experimented with inducing emotionally based feelings at a secondary level attempting to directly stimulate Primal Emotional reactions. Examples include simply getting people to laugh, cry, or experience intense curiosity (Primal Emotional responses) using jokes, playing with a child or a dog, mental imagery, music, or engaging entertainment. I have used highly focused emotional experiences like those used during the "human potential movement" of the 1970's to attempt to stimulate Primal Emotional responses in my clients. I also suggest daily practice of positive emotional exercises to attempt to habituate individuals to gradually replace the negative effects of past stress and trauma. My wife, who is a professional stage director, uses such exercises to teach or assist actors to generate emotional responses needed to enhance their performance.

The personal characteristics of therapists are crucial to successful treatment. "Attention-Expectancy Effect," the impact of attunement to a client's emotional state while offering hope for improving that state is well known to researchers evaluating psychotherapeutic effectiveness. Therapists must be perceived as caring and able to offer helpful interventions. If a person is feeling bad and another person interacts with us in a caring, concerned manner we feel better. Such attention stimulates endorphin production and "eases the pain."

Caring attention to a client's emotional state can help change the primal emotional process that has "enslaved" the person's perceived feelings and higher cognitive functions. Creative caring, interventions that reframe a client's feeling and cognitive reaction to primal emotional processes can assist in changing those processes by reconsolidating memories in less troublesome forms. These emotion focused approaches to therapy access feelings emerging from primal emotional processes and change client reactions. Therapists tend to be a combination of social (helpers) and artistic (creative) personality types according to John Holland's Theory of Career Typologies (Holland, 1997). Who better to work with individuals wanting to change their emotional reaction to the vicissitudes of life?

Conclusion: The framework outlined here is an attempt to provide a conceptual schema to understand how complex patterns of behavior, feelings, and cognitions of love are driven by our biology. Although we may "think" we understand how we fall in love and maintain love, it is this author's contention that much of this lifelong process is outside our conscious awareness. A greater appreciation and understanding of the neurobiological correlates of affective responses, especially the non-cognitive, pre-linguistic primal emotional systems as elucidated by the life-long work of Jaak Panksepp might benefit our theoretical understanding of love and its many vicissitudes. It might also inform and improve counseling and psychotherapeutic interventions generally, if thoughtfully applied to other stages and circumstances of life, as this paper has attempted to do.

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APPENDIXES

APPENDIX I: COMMUNICATION RAPID ASSESSMENT SCALE VERBAL FORM

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COMMUNICATION RAPID ASSESSMENT SCALE VERBAL FORM

Joanning, Harvey; Brewster, James; & Koval, James (1984)

Instruction Form: Rate couple interactions using the 5-point scale below:

Rating	Scale Description
#2	Discussions that foster the relationship Couple stays with an issue Few if any interruptions Relatively equal speaking time or one person chooses to listen only Speaker's tone of voice conveys caring and interest Each person implies, "our opinions are simply different, not right or wrong!" Mutual personal information sharing and/or mutual problem solving Person speaking asks for information or a response from the person listening Each person shares his/her personal point of view (thoughts, feelings, intentions) Each speaker is tolerant of the other person's point of view and responds without judgement
#1	Discussions that foster the relationship Couple tends to stay with one issue but may stray to related issues Some interruptions Some inequality of speaking time but neither speaker dominates or forces partner to listen Tone of voice tends to sound caring and interested but sometimes sounds somewhat intolerant Some mutual personal information sharing and/or some mutual problem resolution Person speaking sometimes asks for information and a response form the person listening Each person shares some of his/her personal point of view (thoughts, feelings, intentions) Each speaker tends to be tolerant of the other person's point of view but sometimes sounds judgmental
0	Discussions focuses on non-relationship issues; casual social conversation No sharing of personal information Neutral communication (no impact upon the relationship) Avoid this category if borderline; go to #1 or -1 according to relationship impact
-1	Discussions that diminish the relationship Issues or topic discussed tends to vary Some interruptions Some "battling for air-time" or a tendency for one person to dominate Speakers tone of voice sounds somewhat harsh, irritated, and uncaring Limited mutual personal information sharing One person suggests a solution to the problem with minimal consideration of the other person's point of view (each person tries to tell the other person what to do or think) Each person is somewhat attacking and intolerant of the other person's point of view
-2	Discussions that diminish the relationship Issues or topic discussed may vary rapidly Many interruptions Virtual dominance of speaker time by one speaker or nearly constant "battling for airtime"; that is, speaker demands or forces the other person to listen Speaker's tone of voice sounds very harsh, angry, and uncaring Each person implies "I'm right and you're wrong" Virtual absence of mutual personal information sharing and/or mutual problem solving One person tries to force their solution to the problem on the other person with no consideration of the other person's point of view Neither person asks for information or responds to the other person in an intolerant, noncaring way Each person attacks the other person's point of view and is very judgmental

COMMUNICATION RAPID ASSESSMENT SCALE NONVERBAL FORM

Joanning, Harvey; Brewster, James; & Koval, James (1984)

Instruction Form: Rate couple interactions using the 5-point scale below:

Rating	Scale Description
	65-90% steady eye contact for both partners
	Speaker may maintain eye contact less often than the listener, but partners establish eye at least 65% of the time when they are listeners
	Numerous appropriate facial expressions by both partner (not exaggerated smiling/frowning and a congruence between facial expression and verbal content)
+2	Numerous positive head nods by both partners
	25% forward trunk lean by both partners
	Partners are 12-27 inches from each other
	Open, upright (no slouching) posture by both partners, generally shoulder orientation of 0% for both partners
	An absence of scratching, and face/hair touching for both partners
	Arms/legs of each partner are uncrossed
	Hand movements for both partners are appropriate and relaxed
	An absence of fidgeting in chair (chair swinging) for both partners
	50-64% steady eye contact for both partners, or one partner tends to consistently establish greater levels of eye contact
	Mainly appropriate facial expressions, but one or two exaggerations/incongruencies by one or both partners
	Some head nods by both partners, or one partner nods affirmatively significantly more often than the other partner
+1	Both partners have some amount of forward trunk lean (not more than 19%), or one partner Consistently has more facilitative forward lean than the other partner
	Partners are 28-40 inches from one another
	Shoulder orientation of less than 20% for one or both partners
	Some tenseness or exaggeration of hand movements by one or both partners
	Some instances of fidgeting on one's chair (one or two instances)
	Some torso slouching for one or both partners
0	Conflicting nonverbal cues (such as 65% eye contact by a 20% backward trunk lean, etc.) making it impossible to ascertain the impact of the couple's nonverbal interaction
	Large amounts of gaze avoidance (less than 50% eye contact but more than 10%) by one or both partners
	Large amounts of inappropriate (incongruent with verbal content) facial expressions by one or both partners
	Few head nods and mainly static head movements by one or both partners
	Backward trunk lean (less than 30%) by one or both partners
\	Partners are 41-60 inches from each other
	21-30% shoulder orientation from each other
-1	Significant amount of tense hand movements (fist, etc.) or exaggerated hand movements by one or both partners
	Large amounts of arm/leg crossing by one or both partners
	Large amounts of scratching, face/hair touching by one or both partners
	Large amounts of slouching torso by one or both partners
	Large amounts of chair fidgeting/swinging by one or both partners

COMMUNICATION RAPID ASSESSMENT SCALE NONVERBAL FORM CONTINUED

Rating	Scale Description
	Little (if any) eye contact (0-10%) by either partner, or a total stare (100% eye contact) by both Partners
	Much exaggerated use of smiles/frowns by both partners or very large amounts of incongruent facial expressions (incongruent with verbal content) by both partners
	A lack of head nods (static head movements) by both partners
	30% or more backward trunk lean by both partners
-2	Partners are over 60 inches (five feet) from one another
	More than 30% shoulder orientation for both partners
	Extremely slouched torso for both partners
	Excessive movement (crossing, uncrossing, fidgeting) of arms and legs by both partners
	Excessive scratching, face/hair touching by both partners
	Constantly tense hands (fists) or hand movements by both partners
	Excessive fidgeting/swinging in chair by both partners

INSTRUCTIONS FOR USING THE COMMUNICATION RAPID ASSESSMENT SCALE

Consider the couple's interaction as a whole; that is, do not allow one statement or behavior to be the basis of your rating. Rather, rate your impression of the overall segment of conversation you are rating. Try to be as consistent as you can and not mix categories, so that a rating category applies equally to all couples you rate and each segment of a particular couple's conversation.

For research purposes, we recommend rating the couple's interaction in 30 or 60 second intervals to give more data points that may indicate variation in communication quality over time. For research purposes we also recommend having the couple spend five minutes "Planning a pleasant activity you will engage in during your free time." This allows the couples to adapt to the process. Then have the couple spend 10 minutes discussing "The most difficult or important issue in your relationship." This discussion typically increases the stress level considerably and gives a good indication of how well the couple deals with issues on a daily basis.

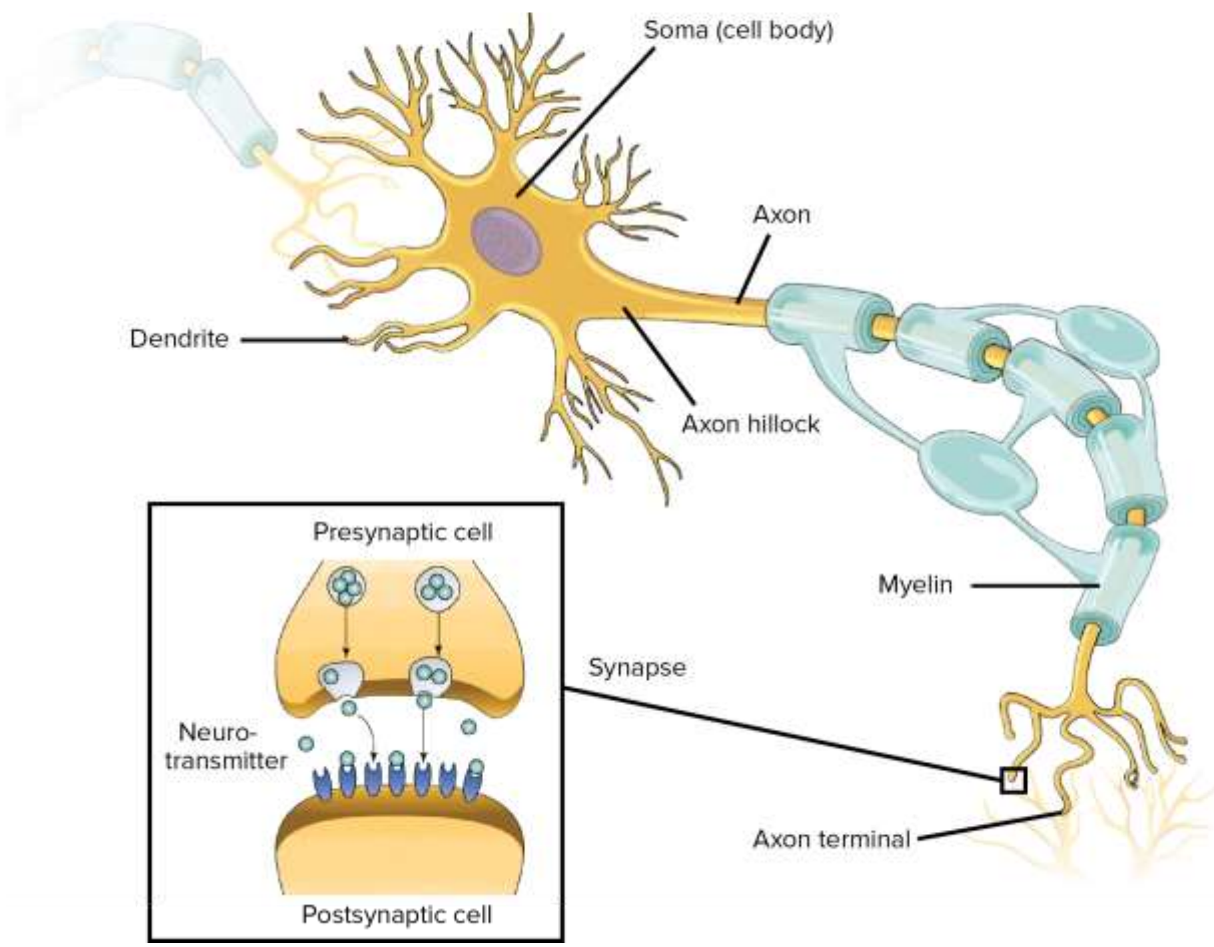
For clinical purposes, we recommend you have the couple engage in a conversation of important and/or difficult relationship issues toward the end of a first session or beginning in the second therapy session. You, as the therapist/counselor can listen to and observe the couple and rate their interaction using CRAS throughout the session. We recommend giving a rating every 3 to 5 minutes and recording your ratings in your case notes. Throughout the course of therapy, you can call attention to the difference between positive and negative communication. Give a copy of the CRAS to the couple, have them read it, and encourage them to emulate +2 communication as much as possible when discussing relationship issues. We have found the CRAS to be a highly "reactive instrument." That is, when couples read about the difference between positive and negative communication, they often spontaneously attempt to communicate in a positive manner. One couple commented, "Now that we have the roadmap, we know what to do!" Over the course of therapy, you can note whether the couple's communication quality improves. We strongly recommend sitting next to each partner as they attempt to learn to communicate more effective; in effect, coach them. If you have a co-therapist, it is helpful to have one therapist sit next to each partner and coach them.

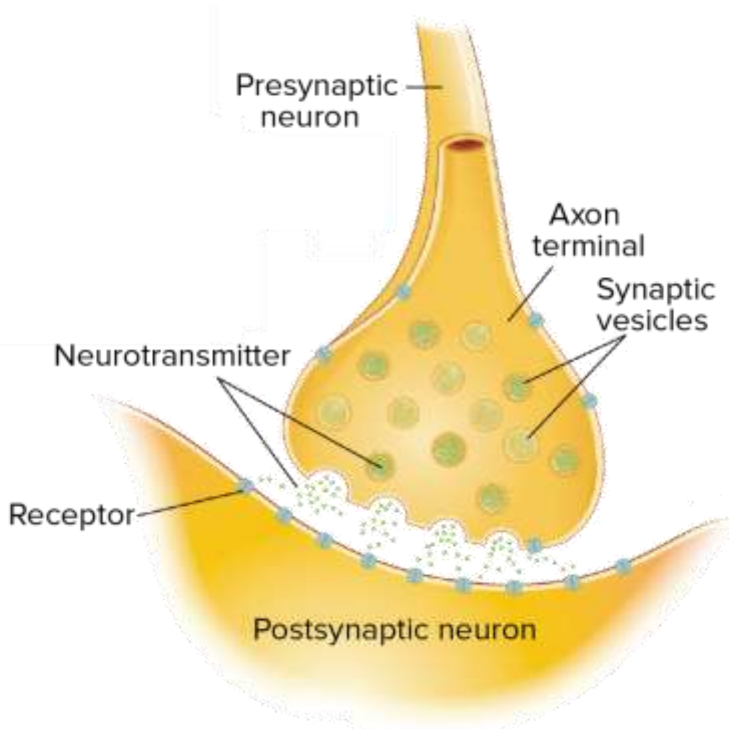
When rating, first decide if the conversation is neutral, no relationship impact. If so, give it a 0 rating. If the conversation segment has an impact on the relationship, decide if the overall impact is negative or positive and rate it – or +. Rate the degree to which the conversation segment is negative or positive using the category descriptions described above and give it a 1 or 2 rating.

Appendix IV: Synapses, Neurotransmitters, Neuropeptides, Neuromodulators, Neurohormones, Hormones and Neuroreceptors

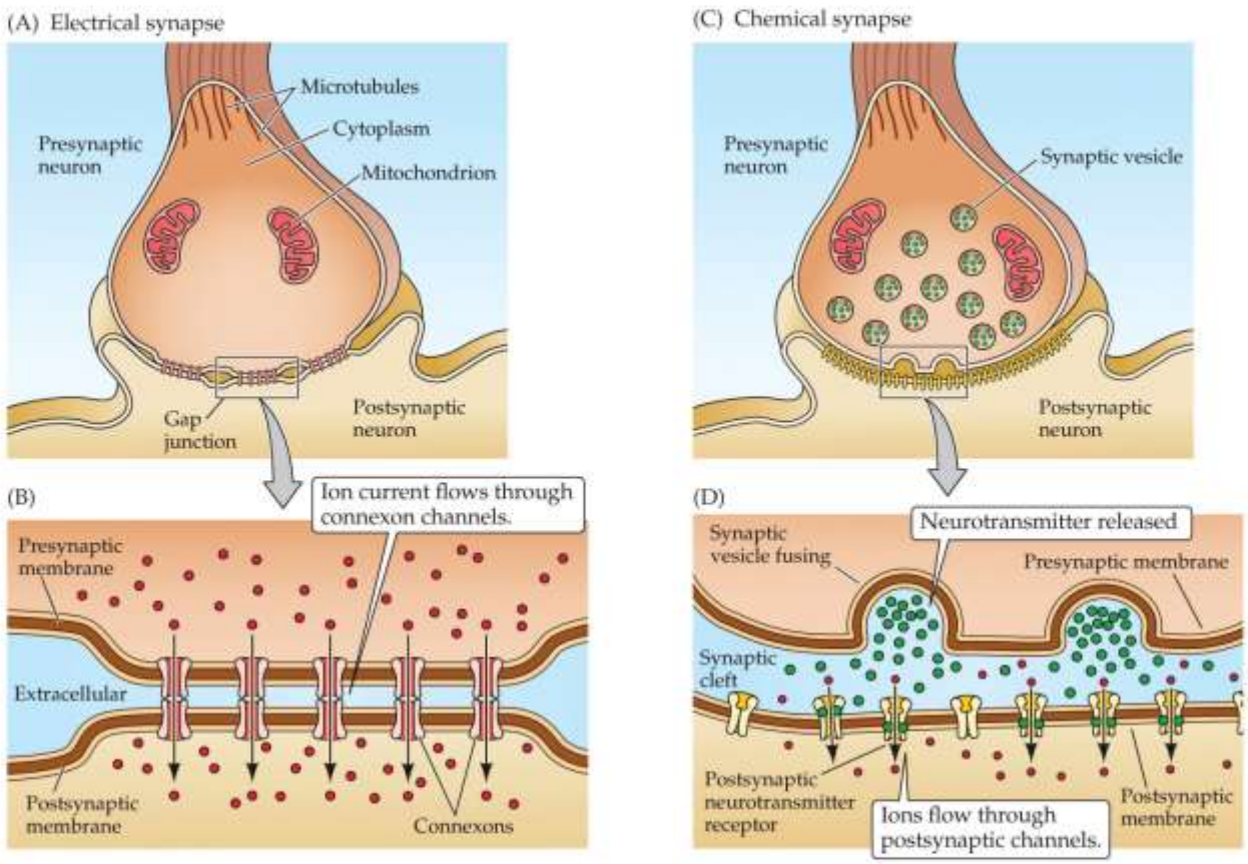
The following is an extremely simplified rendering of how our neurons function. Interested readers are encouraged to consult comprehensive texts such as Neuroscience (Purves et. al. 2017) for a more in-depth description of these processes.

Nerve Cell Structure





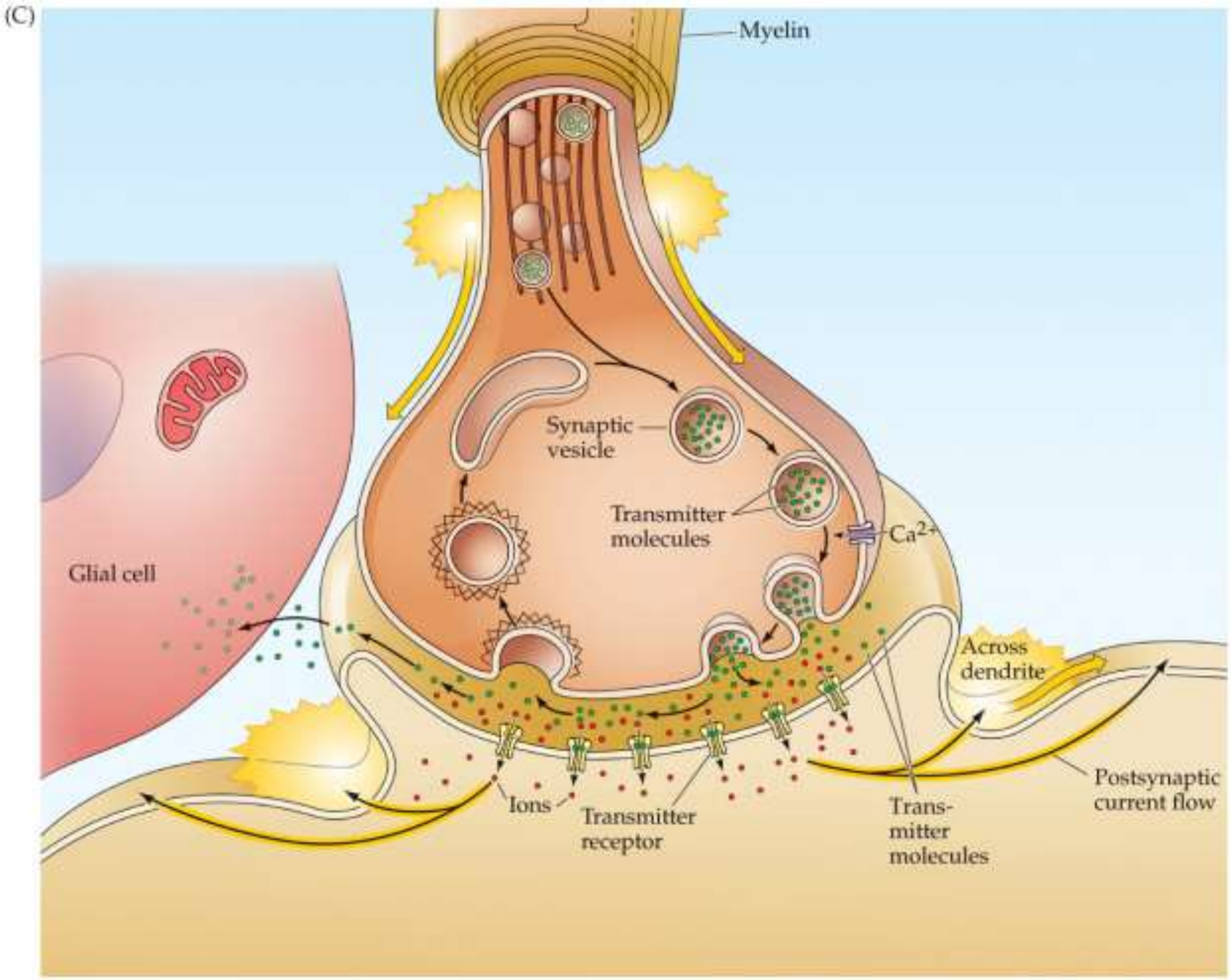
The relationships among synapses and the chemical messengers that influence them is complicated. I will attempt to provide a brief overview of each because they affect human behavior. I will also later describe how they affect intimate human behavior.



NEUROSCIENCE 6e, Figure 5.1

Synapses occur between the axon terminal of one neuron and the dendrite of another neuron. Synapses come in two types, electrical and chemical. Electrical synapses allow a direct flow of electrical current from one neuron to allow rapid synchronization of electrical activity in "interneurons;" specialized neurons that connect with one another. This near simultaneous firing of neurons is important in a variety of brain and organ activities. Chemical synapses involve chemical agents that carry messages between neurons. Unlike electrical synapses, chemical synapses do not involve direct transfer of electricity but rather transfer of chemicals in a complex series of steps that contribute to the brain's ability to "compute," that is, process information provided by our body and our senses to help us survive in our environment. Ultimately, these complex calculations generate emotions, feelings, and thoughts that I will describe in detail later.

Chemical Synapses



NEUROSCIENCE 6e, Figure 5.4 (Part 3)

Neuro-signal messengers come in a variety of types with different function. The most familiar are neurotransmitters, seven "small molecule" neurotransmitters (**acetylcholine**, **dopamine**, **gamma-aminobutyric acid (GABA**), **glutamate**, histamine, **norepinephrine**, and **serotonin**) and possibly an eighth (acid glycine) that do the majority of the work in the brain and nervous system. We will explore the function of six of these neurotransmitters that I have highlighted. Neurotransmitters are fast acting on a time scale of milliseconds that allow an organism to quickly response to internal bodily signals or environmental stimuli perceived by our senses. Small molecule neurotransmitters are synthesized in the nerve terminals found at the end of axons in neurons. However, the enzymes needed for the synthesis are produced in the cell body of the neuron and transferred down the axon along with the other major type of neurotransmitter, neuropeptides.

TABLE 6.1 ■ Functional Features of the Major Neurotransmitters

Neurotransmitter	Postsynaptic effect[a]	Precursor(s)	Rate-limiting step in synthesis	Removal mechanism	Type of vesicle
ACh	Excitatory	Choline + acetyl CoA	ChAT	AChE	Small, clear
Glutamate	Excitatory	Glutamine	Glutaminase	Transporters	Small, clear
GABA	Inhibitory	Glutamate	GAD	Transporters	Small, clear
Glycine	Inhibitory	Serine	Phosphoserine	Transporters	Small, clear
Catecholamines (epinephrine, norepinephrine, dopamine)	Excitatory	Tyrosine	Tyrosine hydroxylase	Transporters, MAO, COMT	Small, dense-core or large, irregular dense-core
Serotonin (5-HT)	Excitatory	Tryptophan	Tryptophan hydroxylase	Transporters, MAO	Large, dense-core
Histamine	Excitatory	Histidine	Histidine decarboxylase	Transporters	Large, dense-core
ATP	Excitatory	ADP	Mitochondrial oxidative phosphorylation; glycolysis	Hydrolysis to AMP and adenosine	Small, clear
Neuropeptides	Excitatory and inhibitory	Amino acids (protein synthesis)	Synthesis and transport	Proteases	Large, dense-core
Endocannabinoids	Inhibits inhibition	Membrane lipids	Enzymatic modification of lipids	Hydrolysis by FAAH	None
Nitric oxide	Excitatory and inhibitory	Arginine	Nitric oxide synthase	Spontaneous oxidation	None

[a]The most common postsynaptic effect is indicated; the same transmitter can elicit postsynaptic excitation or inhibition, depending on the nature of the receptors and ion channels activated by transmitter.

NEUROSCIENCE 6e, Table 6.1

Neuropeptides are made of small chains of amino acids, that is, proteins that are responsible for slow-onset, long-lasting responses in the nervous system and are involved in behaviors that last longer than those simulated by small molecule neurotransmitters.

Both types of neuro-signal messengers are “packaged” into vesicles in the axon terminal. The small molecule neurotransmitters are found in “small clear core vesicles” while neuropeptides are found in “large dense-core vesicles.” These vesicle names describe how these neurotransmitters appear when magnified. The packaging of vesicles is a complex process beyond the scope of this paper.

Neurotransmitters are released into the synaptic cleft between neurons when an “action potential,” an electrical current, is sent down the axon of the neuron if the cell body of the neuron has been sufficiently “excited” by nerve impulses received by the dendrites of the cell body from other neurons. The cell body compares the number of “exciting” and “inhibiting” signals it receives from other neurons. If the balance more sufficiently more exciting than inhibiting, the cell body will “fire” a signal down the axon to the axon terminal.

In addition to neurotransmitters, neurons also use neuromodulators and neurohormones to send messages to other neurons and parts of our body. Some neurons almost exclusively release neuromodulators that affect other neurons in their vicinity. Other neurons release both neurotransmitters from small clear vesicles and neuromodulators from dense-core vesicles. However, neurotransmitters containing vesicles are more numerous and tend to be released even when the neuron is firing less frequently. Neuromodulators are released when the firing rate of the neurons is rapid and more intense, probably because neuromodulator vesicles are fewer in number and placed behind neurotransmitter vesicles, so require more stimulation to move to the nerve’s terminal membrane. Neuromodulators are released by neurons into the space between neurons and have a “modulating affect,” on that area of the brain. They affect whether neurons will be excited or inhibited by neurotransmitters depending on which neural receptors are stimulated. Consequently, how neurons respond is a combination of the effects of neurotransmitters and neuromodulators. Neuromodulators can also affect muscle cells, endocrine glands, and many other types of cells. This interaction is very complex and a detailed discussion is beyond the scope of this paper. Again, the reader is encouraged to consult neuroscience textbooks cited in the Reference section of this paper (e.g., Purves et. al., 2017). Confusion can occur because, as you may have already noted, the term “neuromodulator” can refer to a chemical signal that is structurally either a small neurotransmitter-like molecule (e.g., dopamine, serotonin and norepinephrine), a larger neuropeptide (e.g., oxytocin, vasopressin), or even a larger, more complex neurohormone.

Neurohormones are released by neurons but enter the bloodstream and affect the body systemically as do hormones. Neurohormones are produced by neurons while hormones are produced by endocrine glands. Neurohormones are fast acting while hormones continue their affect long term. Neurohormones along with small molecule neurotransmitters help us act quickly (start running when we see a lion) while neuropeptides and hormones help us continue needed behavior for longer periods of time (keep running until we find a place to hide).

The distinction between neuromodulators and neurohormones can be difficult and confusing. Both are released from neurons. Generally speaking, neuromodulators have affects close to the releasing neuron while neurohormones have affects throughout the body.

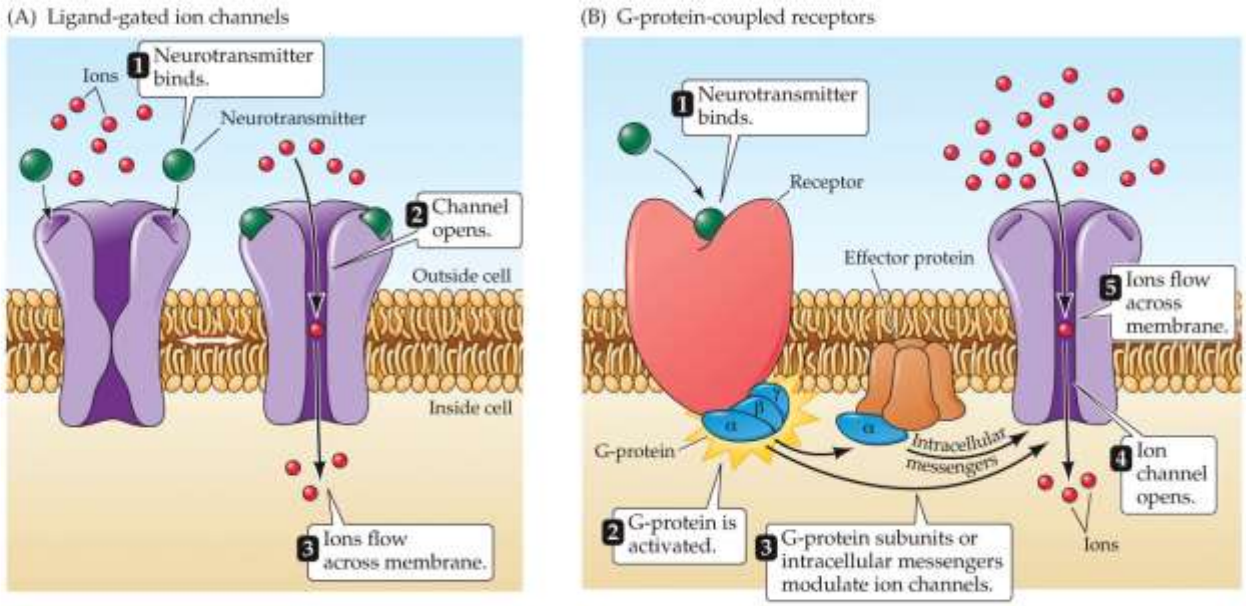
Hormones are produced and released by endocrine glands. Hormones can have the same chemical composition as neurotransmitters but they are released from different points of origins. Generally speaking, neurotransmitters are released by neurons and hormones are released by endocrine glands some of which are found in the brain.

Two analogies may help illustrate how neuromodulators and neurohormones/hormones differ. Neuromodulators are like letting your dogs into your fenced backyard. It is a limited area. If you let them out on a cool dry day, they are likely to chase each other, dig in your garden or bark at a squirrel teasing them from a tree. If you let them out on a hot, muggy day, they will likely take a nap in the shade. The temperature and humidity “modulate” your dogs’ behavior. Neurohormones and hormones are like letting dogs loose in the neighborhood unsupervised. You are likely to have neighbors and animal control calling you because your dogs are causing trouble throughout the town. Neuromodulators effect the local neuronal neighborhood. Neurohormones and hormones effect your whole body.

Another term often used by neuroscientists is “neurosecretory cell” or “neuroendocrine cell.” This refers to a cell that is a neuron/endocrine hybrid cell, most typically thought of as a neuron that releases either a neurohormone/neuropeptide, a hormone, or hormone-like signaling substance. The “secretory” part is purposely vague to allow for the diversity of functional substances that can be released depending on the particular neurosecretory cell involved. The consensus is that the hypothalamus, pituitary gland and pineal gland are clear examples of nervous tissues that involve neurosecretory/neuroendocrine cells. Neurosecretory cells are usually thought to be neurons that release into a nearby fluid, either a small capillary/blood vessel nearby (hence, hormonal release) or into fluid-filled spaces outside but near the neuron. These secretions have local distribution to nearby target neurons (or other target cells) with the appropriate receptors. Sometimes this is referred to as “paracrine” secretion. The three types of “-crine” secretion in this context are: “Paracrine signaling” that involves action on nearby cells, “endocrine signaling” that uses the blood stream/circulatory system to transport chemical signals to nearby and/or distant target cells, and “autocrine” signaling that acts on the presynaptic signaling cell itself (i.e., the cell releasing the substance – a sort of feedback mechanism so the releasing cell “knows” how its release is going and can monitor it in an on-going fashion).

Neuron receptors are found in the postsynaptic side of the synaptic cleft, usually on the tip of dendrites feeding into the cell body of a neuron. Like neurotransmitters, neuronal receptors come in different types.

Two Different Types of Neurotransmitter Receptors



NEUROSCIENCE 6e, Figure 5.14

Ligand-gated ion channels or ionotropic receptors (from ionic for electrically charged ions and from the Greek *tropos* for moves in response to a stimulus) are ion channels or gates that allow ions such as K+ (potassium), Na+ (sodium), Ca++ (calcium) or Cl- (chorine) to pass through the synaptic cleft into the dendrites of neurons. This passage of ions excites or inhibits neurons that share synaptic clefts thus sending a "message" from neuron to neuron. As mentioned earlier, the summative effect of exciting and inhibiting signals determines whether or not the receiving neuron will fire its axon. The more excited a neuron becomes the more frequently and intensely it will fire thereby increasing or decreasing the "loudness" of its message. Some of the neurons of an organism experiencing extreme arousal will have many neurons firing frequently thus stimulating the organism to action (e.g., flee, fight, freeze, or mate).

Metabotropic (from the word metabolic meaning a series of processes), also called G-protein-coupled channels, involve several steps needed to pass a signal through the "G-proteins" channel so operate more slowly than ionotropic channels. The combination of ionotropic and metabotropic channels give rise to postsynaptic actions that range from less than a millisecond to minutes, hours, or days. Ionic receptors generally mediate rapid postsynaptic effects ranging from one to tens of milliseconds. In contrast, metabotropic receptors typically produce much slower responses, ranging from hundreds of milliseconds to minutes or longer. A given neurotransmitter may stimulate both types of receptors. The net effect modulates how other neurons respond or how body systems such as muscles and organs react.

The collective effect of various neurotransmitters, neuromodulators, neurohormones, and receptor types allows for a wide variety of responses within our brain and throughout our body. In general, if our neurons are highly stimulated (a lion is chasing us), the more frequently and intensely our neurons will fire impulses down their axons, which in turn will increase the number of vesicles that bind with the presynaptic membrane and deposit neurotransmitters into the synaptic cleft. The more neurotransmitters in the cleft, the more stimulated the receptors become. Conversely, if our neurons are not be stimulated (we are taking a nap), the fewer neurotransmitters will enter the synaptic cleft and the less stimulation postsynaptic receptors will receive. In sum, our brain and nervous systems are capable of extremely complex computations that allow us to survive and thrive in response to how our bodies are experiencing their internal and external environments.