# NEUROBIOLOGY for CLINICIANS

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## THE BRAIN

- IS NOT RATIONAL
  - IT MAKES DECISIONS THROUGH EMOTIONS
  - IF LOSE CAPACITY TO HAVE EMOTIONS CAN NOT EVEN INITIATE A TASK (ANTONIO DAMASIO)
    - MIGHT STARE AT TOOTHBRUSH WITH TOOTHPASTE
       ON IT
- DOES NOT MULTITASK
  - DELUSION IS WE WILL GET MORE THINGS DONE IF WE DO MORE THAN ONE THING AT A TIME

## THE BRAIN

- DOES NOT MULTITASK (CONTINUED)
  - MAY FLIP BACK AND FORTH BETWEEN TWO THINGS BUT STILL MISS MORE THAN WE WOULD IMAGINE
- IS A PATTERN-MAKER NOT A TRUTH-MAKER
  - TRIES TO FIT EVERYTHING INTO RECOGNIZABLE PATTERNS
  - SEEKS WHAT IS KNOWN AS OPPOSED TO WHAT IS UNKNOWN

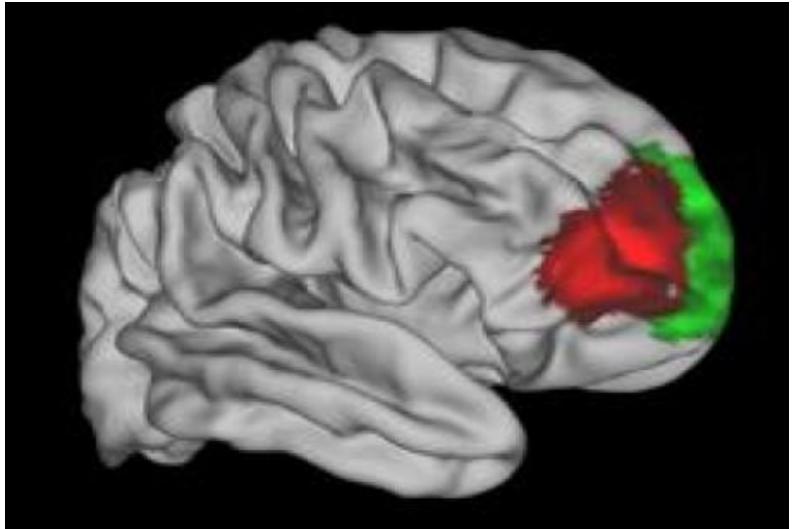
## THE HUMAN BRAIN

- The brain is a mosaic of interlinked areas. We wanted to look at this very important region of the frontal part of the brain (*ventrolateral frontal cortex*) and see how many tiles there are and where they are placed.
- The connections of each tile -- how they are wired up to the rest of the brain -- as it is these connections that determine the information that can reach that component part and the influence that part can have on other brain regions.
- From the MRI data, the researchers were able to divide the human *ventrolateral frontal cortex* into 12 areas that were consistent across all the individuals.

#### THE HUMAN BRAIN

- Each of these 12 areas has its own pattern of connections with the rest of the brain, a sort of "neural fingerprint,"
- The researchers were then able to compare the 12 areas in the human brain region with the organization of the monkey prefrontal cortex.
- Overall, they were very similar with 11 of the 12 areas being found in both species and being connected up to other brain areas in very similar ways.
- However, one area of the human ventrolateral frontal cortex had no equivalent in the macaque -- an area called the lateral frontal pole prefrontal cortex.

#### THE HUMAN BRAIN RED=LATERAL FRONTAL POLE PFC



#### THE HUMAN BRAIN

 This ventrolateral frontal cortex area of the brain is involved in many of the highest aspects of cognition and language, and is only present in humans and other primates. Some parts are implicated in psychiatric conditions like ADHD, drug addiction or compulsive behavior disorders. Language is affected when other parts are damaged after stroke or neurodegenerative disease.

## THE HUMAN BRAIN

- The brain area pinpointed is known to be intimately involved in some of the most advanced planning and decision-making processes that we think of as being especially human.
- Being able to plan into the future, be flexible in our approach, multi-tasking and learning from others involves this brain area

Franz-Xaver Neubert, Rogier B. Mars, Adam G. Thomas, Jerome Sallet, Matthew F.S. Rushworth. **Comparison of Human Ventral Frontal Cortex Areas for Cognitive Control and Language with Areas in Monkey Frontal Cortex**.*Neuron*, 2014; 81 (3): 700 DOI: <u>10.1016/j.neuron.2013.11.012</u>

# MINDSET INDUCTION

- Telling people that hard work trumps genes causes instant changes in the brain and may make them more willing to strive for success
- Telling people that intelligence is genetically fixed may inadvertently hamper learning

Hans S. Schroder, Tim P. Moran, M. Brent Donnellan, Jason S. Moser. **Mindset induction effects on cognitive control: A neurobehavioral investigation**.*Biological Psychology*, 2014; 103: 27 DOI: <u>10.1016/j.biopsycho.2014.08.004</u>

# NEUROBIOLOGY

- NEUROPLASTICITY
- EPIGENETIC CHANGES
- CENTRAL NERVOUS SYSTEM (CNS) ANATOMY
- BRAIN DEVELOPMENT
- LEFT AND RIGHT HEMISPHERES
- CONSCIOUS AND UNCONSCIOUS ASPECTS
- LEARNING AND MEMORY

- HUMANS CREATE NEW NEURONS IN AREAS
   OF THE BRAIN INVOLVED IN NEW LEARNING
  - AMYGDALA
  - HIPPOCAMPUS
  - CORTEX
- THE CORTEX IS FIRST ORGANIZED BY OUR EXPERIENCE AND THIS ORGANIZES OUR INTERACTIONS WITH THE WORLD

- BRAIN AT ALL AGES IS RESPONSIVE TO ENVIRONMENTAL STIMULI
- SYNAPSES CAN CHANGE IN MINUTES WHEN STIMULATED
- NEUROPLASTICITY IS MODULATED BY
  - GENETIC FORCES
  - EPIGENETIC FORCES
- THESE FACTORS INFLUENCE THE EXPRESSION OF GENES WITHOUT CHANGING THE DNA SEQUENCE

- EPIGENTIC CHANGES ARE POTENTIALLY REVERSIBLE
- BRAIN IS VERY SENSITIVE TO SOCIAL STIMULI
- SOCIAL STIMULI (PARENTING, STYLE, EARLY STRESS, ETC.) CAN EPIGENTICALLY MODIFY THE EXPRESSION OF GENES THAT INFLUENCE BRAIN STRUCTURE AND FUNCTION (INCLUDING SENSITIVITY TO STRESS)

- PREVENTION BASED ON IMPROVED PARENTING STYLE REDUCED RISK OF SUBSTANCE ABUSE IN ADOLESCENTS WITH A PARTICULAR VARIANT OF A GENE THAT RECYCLES SEROTONIN BACK INTO THE NEURON
  - THIS VARIANT IS VERY SENSITIVE TO SOCIAL ADVESITY

- BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF)
  - WHEN AN ACTIVITY REQUIRES SPECIFIC CONNECTIONS BETWEEN NEURONS, BDNF CONSOLIDATES THE CONNECTION
  - BDNF PROMOTES THE MYELINATION OF NEURONS
  - DURING CRITICAL PERIODS BDNF TURNS ON THE NUCLEUS BASALIS, A PART OF THE BRAIN THAT FOCUSES ATTENTION AND KEEPS IT FOCUSED THROUGHOUT THE ENTIRE CRITICAL PERIOD

- BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF)
  - THE NUCLEUS BASALIS IS THE MODULATORY CONTROL CENTER FOR PLASTICITY
    - EXAMPLE-LANGUAGE HAS A CRITICAL PERIOD FROM INFANCY TO 8/PUBERTY. DURING THIS PERIOD LANGUAGE IS EASY TO LEARN. AFTER THE CRITICAL PERIOD IT TAKES SOMETHING NOVEL, IMPORTANT, SURPRISING OR IF ONE MAKES THE EFFORT TO PAY CLOSE ATTENTION
  - BDNF HELPS CLOSE DOWN THE CRITICAL PERIOD ONCE THE MAIN NEURAL CONNECTIONS ARE IN PLACE (STABILIZES SYSTEM)

#### • BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF)

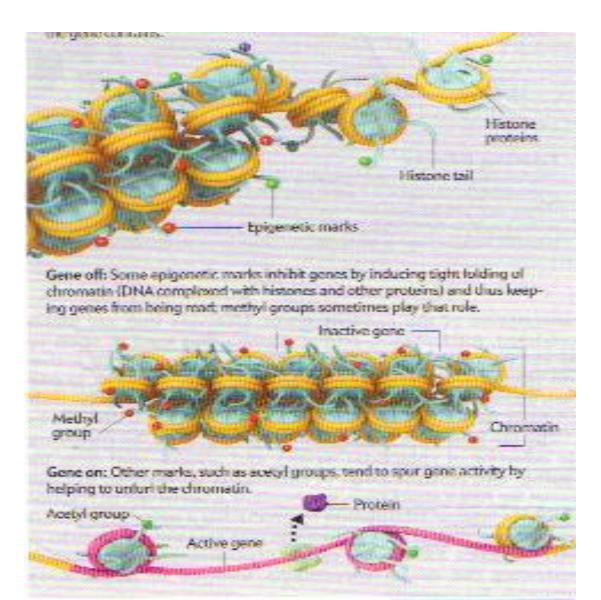
- THERE HAS BEEN AT LEAST A THREE FOLD INCREASE IN AUTISM IN THE LAST 15 YEARS ESPECIALLY IN CHILDREN EXPOSED TO A LOT OR CONSTANT WHITE NOISE (AIRPORT, SUBWAYS, INNER CITY TRAFFIC)-THESE CHILDREN ALSO HAVE LOWERED IQ
  - DURING AUDITORY CRITICAL PERIOD TOO MUCH STIMULATION CAUSES INCREASED BDNF RELEASE SHUTTING DOWN THE CRITICAL PERIOD AND LEAVING BRAIN MAPS POORLY DIFFERENTIATED
  - AUTISTIC CHILDREN DO PROCESS SOUND IN AN ABNORMAL WAY-THE UNDIFFERENTIATED MAP GETS TURNED ON BY ANY FREQUENCY CAUSING EXTREME SENSITIVITY TO SOUND AND POSSIBILITY OF EPILETIC SEIZURES
  - THE SAME PROBLEM MAY BE RELATED TO ATTENTIONAL DISORDERS

- Do not "mutate" genes
- Mark genes in ways that alter how active they are
- Can last up to a lifetime
- Changes caused by drug use or chronic stress can change the way the brain responds to experience
  - Priming brain for resilience or to succumb to addiction

- Psychiatric disorders are precipitated in genetically susceptible individuals by environmental inputs (nature and nurture)
- Neurotransmitters can activate or inhibit nerve cells and switch "on" or "off" responsive genes
  - This helps determine how a nerve cell will respond and ultimately shapes behavior

- How gene activity is regulated
  - A gene is a stretch of DNA that specifies the make-up of a protein
  - Proteins carry out most processes in cells and this controls all cell behavior
  - DNA is wrapped around clusters of proteins called *histones* and further bundled into chromosomes

- The packaging of DNA helps regulate gene behavior
  - Tight packing tends to keep gene in an inactive state
  - When gene is needed it unfurls making the DNA available for transcription of DNA into RNA
    - RNA serves as a template for producing the encoded protein
  - Whether relaxed or tight is influenced by genetic markers (chemical tags attached to a histone or DNA)



- Epigenetic modifications are made by a variety of enzymes
  - Some of the enzymes add chemical tags and other enzymes remove tags
    - Called "writers" and "erasers"
  - Environment can influence gene activity by regulating the behavior of the "writers" and "erasers"
    - Addiction works in this manner

- Drugs of abuse usurp the brains reward center
  - A single dose of cocaine switches on nearly 100 genes
  - Chronic use causes some genes to go silent (desensitization) but a much larger number have their levels boosted even higher (sensitized)
    - This "primes" the gene allowing them to remember rewarding effects (a set-up for relapse)
      - This loosens the structure of DNA so it is more prone to activity (i.e. increased sensitivity)

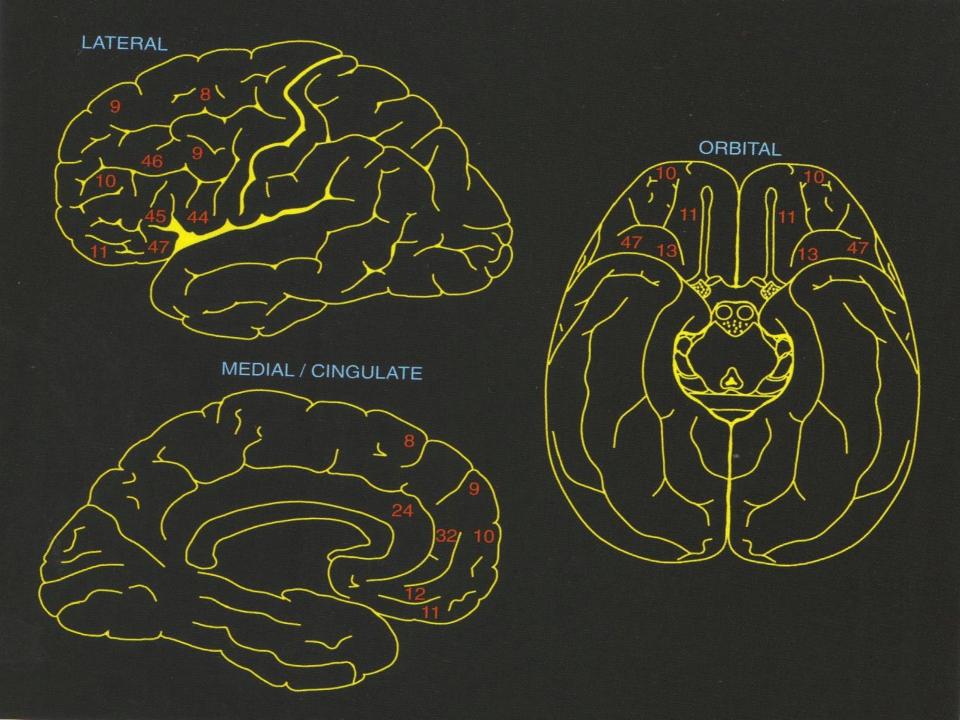
- Drugs of abuse usurp the brains reward center (continued)
  - The loosened structure in addiction is caused by
    - Reducing activity of certain "erasers" that remove acetyl groups on histone
    - Reducing activity of certain "writers" that add inhibitory methyl groups
    - When more acetylated and less methylated the structure remains in a more open and relaxed state amenable to activation

- Neural adaptations in depression
  - Mild mannered mice paired with more aggressive mice (social defeat model)
  - After 10 days of being bullied the docile mice develop many signs of human depression (no enjoyment of sex or sweets, more anxious and withdrawn, listless)
  - Epigenetic modifications noted in around 2000 genes in the reward center
    - More histone methylation repressing gene activity

- Neural adaptations in depression (continued)
  - Depression may shut down genes important to activating reward center
  - Many of the changes can be reversed with an antidepressant (imipramine)
  - About one-third of male mice who were in the social defeat situation appeared to be resistant to depression
  - This suggests that an alternate pattern of epigenetic modification takes place that is positive (resilience)

## **CNS ANATOMY**

- CORTICAL AREAS
  - FRONTAL LOBE
    - PREFRONTAL CORTEX
  - OCCIPITAL LOBE
  - TEMPORAL LOBE
  - PARIETAL LOBE
- LIMBIC STRUCTURES
- BRAIN STEM
- CEREBELLUM
- MOTOR CORTEX
- WHITE MATTER
- SYMPTOMS RESIDE IN NEURAL CIRCUITS



# **OCCIPITAL LOBE**

 Pathways from the occipital lobes reach the temporal and parietal lobes and are eventually processed consciously. Two important pathways of information originating in the occipital lobes are the dorsal and ventral streams. The dorsal stream projects to the parietal lobes and processes where objects are located. The ventral stream projects to structures in the temporal lobes and processes what objects are.

#### **TEMPORAL LOBE**

- The temporal lobes contain a large number of substructures, whose functions include perception, face recognition, object recognition, memory acquisition, understanding language, and emotional reactions.
- Deep stimulation of the temporal lobe has been shown to produce *profound religious and out-ofbody experiences*
- Damage to the temporal lobes can result in neurological deficits called <u>agnosias</u>, which refer to the inability to recognize specific categories (body parts, colors, faces, music, smells).

## PARIETAL LOBE

- The parietal cortex plays an important role in integrating information from different senses to build a coherent picture of the world. It integrates information from the ventral visual pathways (which process what things are) and dorsal visual pathways (which process where things are). This allows us to coordinate our movements in response to the objects in our environment.
- Spatial orientation

# LIMBIC STRUCTURES

- AMYGDALA
  - PROCESSING EMOTIONS AND FEAR LEARNING
- HIPPOCAMPUS
  - MEMORY FORMATION AND STORAGE PLACE FOR LONG TERM MEMORY
- HYPOTHALAMUS
  - CONTROLS AUTONOMIC FUNCTIONS AND GLANDULAR ACTIVITY (PITUITARY)

# LIMBIC STRUCTURES

• THALAMUS

 The thalamus is heavily involved in relaying information between the cortex and brain stem and within different cortical structures. The thalamus contributes to many processes in the brain including perception, attention, timing, and movement. It plays a central role in alertness and awareness.

- ACTS LIKE A WAY STATION

## **BRAIN STEM**

- The brain stem consists of a group of structures that lie deep within the brain, including the pons, medulla oblongata, and midbrain. It plays an important role in maintaining homeostasis by controlling autonomic functions such as breathing, heart rate, and blood pressure.
- The locus coeruleus is a noradrenergic area associated with alcohol and drug acute abstinence syndrome

#### CEREBELLUM

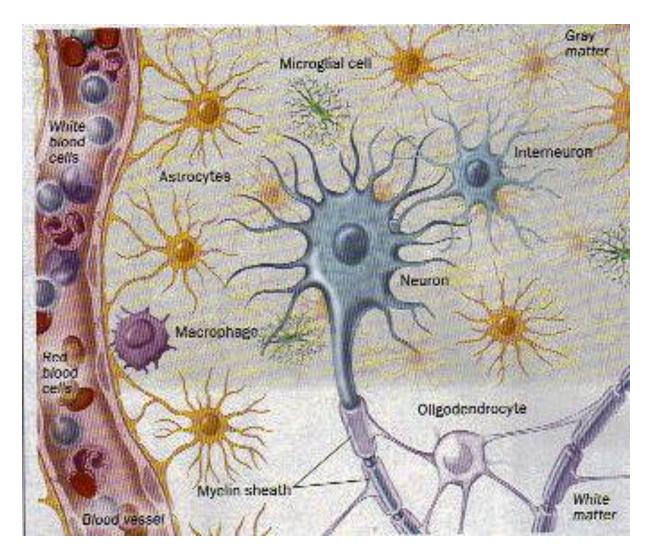
- The cerebellum monitors and regulates motor behavior, particularly automatic movements. The cerebellum is important to the timing of rhythmic movements.
- Some recent studies have associated the cerebellum with cognitive functions, such as learning and attention.

# **MOTOR CORTEX**

 The primary motor cortex is critical to initiating motor movements. Areas of the motor cortex correspond precisely to specific body parts (HOMUNCULUS). For example, leg movements map to the part of the motor cortex closest to the midline. Not all body parts are equally represented by surface area or cell density – representations of the arm hand motor area occupy the most space in the motor cortex

# WHITE MATTER

- White matter is composed of bundles of myelinated axons
- White matter is often called the wiring of the brain because it connects individual neurons and groups of neurons together
- Amyloid plaques in white matter involved in neurodegenerative diseases
- Myelin degeneration found in Multiple Sclerosis
- Axonal shearing may be reversible



- NEURON DOCTRINE IS FLAWED
- SOME INFORMATION BYPASSES NEURONS COMPLETELY FLOWING WITHOUT ELECTRICITY THROUGHT NETWORKS OF GLIAL CELLS
- GLIAL CELLS INTERACT WITH NEURONS AND
   CONTROL THEM
- BRAIN IS COMPOSED OF 85% GLIAL CELLS
   AND 15% NEURONS

- ASTROCYTES
  - FERRY NEUROTRANSMITTERS, FOOD AND WASTE
  - CONTROL SYNAPTIC COMMUNICATION
- OLIGODENDROCYTES
  - WRAP THEMSELVES AROUND NEURONS LIKE SHEATHS (MYELIN) AND SPEED CONDUCTION BY UP TO 50 X'S
- MICROGLIA
  - FIRST RESPONDERS TO INJURY AND DISEASE KILLING INVADING GERMS AND INITIATING REPAIR

- NEURONS ARE DEPENDENT ON GLIA TO FIRE ELECTRICAL IMPULSES AND TO PASS MESSAGES ACROSS SYNAPSES
- GLIA HAVE SAME NEUROTRANSMITTER (NT) RECEPTORS AS NEURONS
- WHEN NEURONS RELEASE NT SO DO GLIA
- GLIA NT RELEASE IMPACTS IMMEDIATE AND
   DISTANT SYNAPSES

- GLIAL SIGNALING OCCURS IN DEGREES AND
   OCCURS SLOWLY
- ARE INVOLVED IN SYNAPTIC PLASTICITY DETERMINING WHERE AND WHEN NEW SYNAPSES FORM
  - THE PROTEIN THROMBOSPONDIN-ACTIVE DURING BRAIN DEVELOPMENT AND AFTER INJURY-IS RELEASED BY ASTROCYTES TO ACTIVATE SYNAPSE FORMATION

- DEMENTIA OF ALZHEIMERS COULD BE A DIRECT OUTCOME OF MICROGLIA THAT HAVE LOST THE ABILITY OT CLEAD WASTE
  - NORMALLY MICROGLIA DIGEST PROTEIN THAT FORM AMYLOID PLAQUES
- MICROGLIA INVOLVED IN SOME CHRONIC PAIN PATIENTS WHERE PAIN DOES NOT RELENT AFTER HEALING
  - MICROGLIA AND ASTROCYTES RELASE CHEMICALS THAT PROMOTE HEALING
  - THESE CHEMICALS STIMULATE NEURONS
    - INITIALLY BENEFICIAL BECAUSE INCREASED PAIN AND SENSITIVITY CAUSE US TO PROTECT INJURED AREA
    - IN CHRONIC PAIN MICROGLIA DO NOT STOP RELEASING THESES CHEMICALS

- INVOLVED IN DEMYELINATING DISORDERS SUCH AS MULTIPLE SCLEROSIS
- MICROGLIA RELEASE CYTOKINES LINKED TO OCD
  - HOXb8 GENE ASSOCIATED WITH COMPULSIVE GROOMING AND HAIR REMOVAL IN MICE SIMILAR TO HUMAN OCD
  - ONLY CELLS IN BRAIN THAT HAVE THIS GENE IS MICROGLIA

- POSTMORTEM BRAIN TISSUE ANALYSIS LINKS
   OLIGODENDROCYTES AND ASTROCYTES TO
   DEPRESSION AND SCHIZOPHRENIA
  - SEE REDUCED NUMBERS CONFIRNED BY MRI FINDINGS
  - ALL HALLUCINOGENIC DRUGS (LSD, PCP, ETC.)
     PRODUCE THEIR EFFECTS BY ALTERING LEVELS OF
     NTs IN SPECIFIC CIRCUITS
    - ASTROCYTES REGULATE NT LEVELS AT SYNAPSES

- ASTROCYTES HAVE A PRINCIPLE ROLE IN WORKING MEMORY
  - MARIJUANA IMPAIRS WORKING (SHORT TERM) MEMORY
    - EXAMPLE-LOOSE TRAIN OF THOUGHT IN MID-SENTENCE
    - DISCOVERED BY REMOVING CB1 RECEPTORS FROM ASTROCYTES LEAVING NO SHORT TERM DEFICIT BUT REMOVIMG CB1 RECEPTORS FROM NEURONS CREATED FORGETFULLNESS IN MICE THE SAME AS WITH RECEPTORS
    - "WHAT MARIJUANA REVEALS ABOUT MEMORY" SCAMMIND. JULY/AUGUST, 2012, PG. 10.

- ASTROCYTES INGEST WEAK, EXTRANEOUS AND REDUNDANT SYNAPSES DURING BRAIN "PRUNING"
- WITHOUT THESE STAR-SHAPED CELLS SYNAPSES FAIL TO SEND STRONG SIGNALS
- WITHOUT THE ASTROCYTES, NEURONS ARE NOT AS GOOD AT CREATING NEW SYNAPSES
- MICROGLIA ALSO DIGEST CERTAIN SYNAPSES

BRAIN IN THE NEWS. Vol. 21 No.1, January 2014

# **GLIAL CELLS AND DEPRESSION**

- One type of non-neuronal brain cells, called microglia, underlie the depressive symptoms brought on by exposure to chronic stress
- In experiments with animals, the researchers were able to demonstrate that compounds that alter the functioning of microglia can serve as novel and efficient antidepressant drugs

# **GLIAL CELLS AND DEPRESSION**

 Comprising roughly 10% of brain cells, microglia are the representatives of the immune system in the brain; but recent studies have shown that these cells are also involved in physiological processes not directly related to infection and injury, including the response to stress.

 The idea that the balance between excitatory and inhibitory inputs depends on astrocyte signals gains strong support with this new study and suggests a pivotal role for astrocytes in the development of neurological disorders involving impaired inhibitory synapse transmission

Flávia Gomes et al. Astrocyte Transforming Growth Factor Beta 1 Promotes Inhibitory Synapse Formation Via Cam Kinase II Signaling. *Glia*, July 2014 DOI: <u>10.1002/(ISSN)1098-1136</u>

- When something captures your interest, unique electrical rhythms sweep through your brain.
- These waves are called gamma oscillations and they reflect a symphony of cells -- both excitatory and inhibitory -- playing together in an orchestrated way

- Though their role has been debated, gamma waves have been associated with higher-level brain function, and disturbances in the patterns have been tied to schizophrenia, Alzheimer's disease, autism, epilepsy and other disorders.
- Astrocytes may in fact be major players that control these waves.

- We have been able to do a causal experiment, where we selectively block gamma oscillations and show that it has a highly specific impact on how the brain interacts with the world."
- New evidence suggests that astrocytes are actively supplying the right environment for gamma waves to occur, which in turn makes the brain more likely to learn and change the strength of its neuronal connections.

 The recognition system is hugely important. It includes recognizing other people, places, facts and things that happened in the past. With this new discovery, scientists can begin to better understand the role of gamma waves in recognition memory.

Salk Institute. "Memory relies on astrocytes, the brain's lesser known cells: supportive cells vital in cognitive function." ScienceDaily. ScienceDaily, 28 July 2014. <www.sciencedaily.com/releases/2014/07/140728154036.htm>

### **GLIAL CELLS-EPIGENETIC CHANGES**

- Activated through permanent stress, immune cells will have a damaging effect on and cause changes to the brain. This may result in mental disorders
- A certain type of phagocyte, microglia, under normal circumstances repair synapses between nerves cells in the brain and stimulate their growth. Once activated, however, microglia may damage nerve cells and trigger inflammation processes

### **GLIAL CELLS-EPIGENETIC CHANGES**

- The more frequently microglia get triggered due to stress, the more they are inclined to remain in the destructive mode -- a risk factor for mental diseases such as schizophrenia.
- Researchers demonstrated as far back as the 1950s that children born of mothers who contracted true viral influenza during pregnancy were seven times as likely to suffer schizophrenia later in life

# **GLIAL CELLS-EPIGENETIC CHANGES**

 The embryo undergoes some kind of immune response which has far-reaching consequences and presumably shapes the future immune system

Ruhr-Universitaet-Bochum. "Mental disorders due to permanent stress?."ScienceDaily.ScienceDaily,21November2014.<www.sciencedaily.com/releases/2014/11/141121082907.htm>.

# SUPRACHIASMATIC NUCLEUS

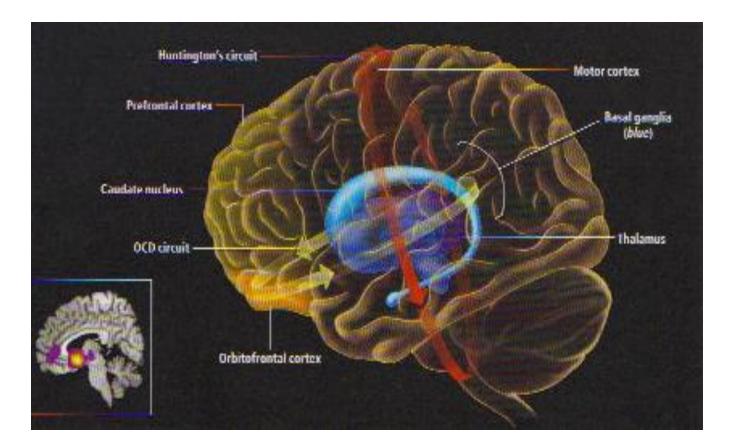
- BRAINS MASTER CIRCADIAN CLOCK
- FOUND IN HYPOTHALAMUS
- CONTROLS SLEEP-WAKE CYCLE
- SCN CELLS ACTIVE DURING THE DAY AND SILENT AT NIGHT
- BEGINS TO DECLINE IN MIDDLE AGE
  - REDUCED ACTIVITY DURING THE DAY AND INCREASE DURING THE NIGHT
    - REDUCED AMPLITUDE

# SUPRACHIASMATIC NUCLEUS

- BEGINS TO DECLINE DURING MIDDLE AGE (CONTINUED)
  - DIFFICULTY SLEEPING
  - DIFFICULTY ADJUSTING TO TIME ZONES
  - DIFFICULTY WITH SHIFT WORK
  - REDUCED ALERTNESS WHEN AWAKE
    - IMPACTS MEMORY AND METABOLIC PROCESSSES

# SYMPTOMS RESIDE IN CIRCUITS

- Problems occur when networks do not communicate properly
  - Neurotransmitters
  - Transporters or vesicles
  - Reuptake pumps
  - Receptors
- Neural circuits in depression



- ORBITOFRONTAL CORTEX-A DECISION MAKING HUB
- BASAL GANGLIA-MEDIATES REWARD
   FEELINGS AND INITIATES BEHAVIOR
- THALAMUS-STIMULUS FILTERING
- ANTERIOR CINGULATE-MONITORS MISTAKES
   AND FOCUSES ATTENTION

- INVOLUNTARY MOVEMENTS ORIGINATE IN THE BASAL GANGLIA, A GROUP OF STRUCTURES INVOLVED IN INITIATING AND COORDINATING BASIC MOTOR ACTIONS
- THE CAUDATE NUCLEUS OF THE BASAL GANGLIA IS A PART OF THE BRAIN CIRCUIT THAT DRIVES OCD ALONG WITH THE ORBITOFORNTAL CORTEX, A REGION CRITICAL TO DECISION MAKING AND MORAL JUDGMENT AND THE THALAMUS WHICH RELAYS AND INTEGRATES SENSORY INFORMATION
- OCD SUFFERERS SHOW HYPERACTIVITY IN AREAS OF THE FRONTAL CORTEX AND THE BASAL GANGLIA

- WHEN SYMPTOMS IMPROVE-EITHER BY PSYCHOTHERAPY OR MEDICATION-A DECREASE IN ORBITOFRONTAL CORTICAL ACTIVITY IS OBSERVED
- IN NON-RESPONSIVE PATIENTS DISCONNECTING THE ORBITOFRONTAL FROM THE CAUDATE NUCLEUS REDUCES SYMPTOMS IN SEVERE OCD

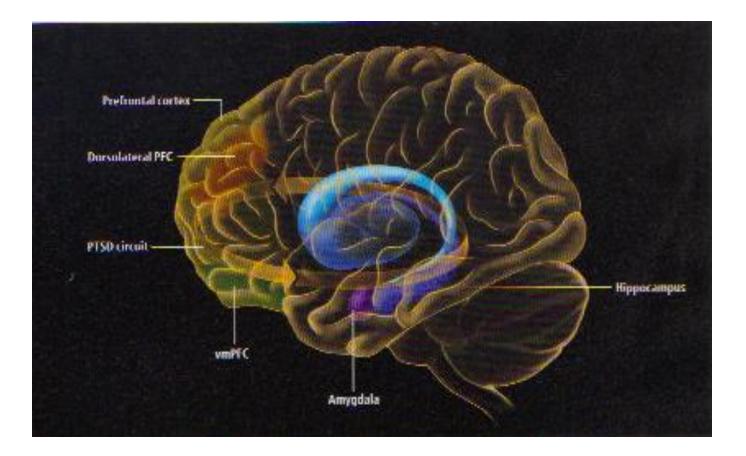
- NORMALLY WHEN WE MAKE A MISTAKE
  - WE GET A "MISTAKE FEELING"-A NAGGING SENSE SOMETHING IS WRONG
    - OFC DETECTS MISTAKE
    - THE MORE ACTIVE THE OFC THE MORE OBSESSIVE THE PERSON IS
  - NEXT WE BECOME ANXIOUS-THIS DRIVES US TO CORRECT THE MISTAKE
    - ANTERIOR CINGULATE TRIGGERS THE ANXIETY THAT SOMETHING BAD WILL HAPPEN IF MISTAKE IS NOT CORRECTED
    - AC SENDS SIGNALS TO THE HEART AND GUT

- NORMALLY WHEN WE MAKE A MISTAKE
  - WHEN THE MISTAKE IS CORRECTED AN AUTOMATIC "GEAR SHIFT" ALLOWS US TO MOVE ON-THE "MISTAKE FEELING' AND ANXIETY DISAPPEAR
    - CAUDATE NUCLEUS IS THE "GEAR SHIFT"
    - IN OCD THE PAGE IS NOT TURNED AND THE "MISTAKE FEELING" AND THE ANXIETY INCREASE BECAUSE THE CAUDATE IS "STICKY"
    - ALL THREE AREAS BECOME HYPERACTIVE-A FORM OF "BRAIN LOCK"

- MAY CONSIDER GETTING THE PERSON WITH OCD TO RELABEL WHAT IS HAPPENING
  - NOT AN ATTACK OF GERMS OR AIDS BUT AN EPISODE OF OCD
  - THIS CREATES SOME SEPARATION BY REMINDING THEMSELVES IT IS A FAULTY CIRCUIT
  - NEED TO DISTINGUISH BETWEEN THE FORM OF OCD (WORRISOME THOUGHTS AND URGES) AND THE CONTENT OF THE OBSESSION (DANGEROUS GERMS)
    - THE MORE ONE FOCUSES ON THE CONTENT THE MORE THE SYMPTOMS INCREASE

- THEN HAVE THE PATIENT REFOCUS ON A POSITIVE, WHOLESOME IDEALLY PLEASURABLE ACTIVITY
  - EVERY MOMENT YOU THINK OF THE CONTENT YOU STRENGTHEN THE CIRCUIT
  - EVERY TIME YOU DO SOMETHING DIFFERENT YOU STRENGTHEN A DIFFERENT CIRCUIT
    - "the more you do it the more you want to"
    - "the less you do it the less you want to"

#### POST-TRAUMATIC STRESS DISORDER CIRCUIT



### POST-TRAUMATIC STRESS DISORDER CIRCUIT

- MALFUNCTIONING OF THE VENTROMEDIAL PREFRONTAL CORTEX (vmPFC) IS THOUGHT TO INCREASE VULNERABILITY BECAUSE IT MODULATES THE AMYGDALA, A DRIVER OF FEAR AND ANXIETY
- NORMALLY EXTINCTION REPLACES A FEAR RESPONSE WHEN A NEUTRAL RESPONSE IS LEARNED BY THE HIPPOCAMPUS AND THE DORSOLATERAL PREFRONTAL CORTEX
- THE vmPFC IS BELIEVED TO SERVE AS THE CRITICAL LINK BETWEEN THE DORSOLATERAL PFC AND THE AMYGDALA ALLOWING EXTINCTION LEARNING TO QUIET THE AYGDALA

### POST-TRAUMATIC STRESS DISORDER CIRCUIT

- SYMPTOMS SUCH AS DISTURBED SLEEP AND INCREASED VIGILANCE ARE EXPECTED IMMEDIATELY AFTER A TRAUMATIC EVENT
- PTSD DEVELOPES WEEKS, MONTHS AND YEARS LATER IN ABOUT 20% OF TRAUMA VICTIMS
- EXTINCTION CAN OCCUR VIA REPEATED EXPOSURE TO A PARTICULAR TRAUMA-RELATED MEMORY OR CUE
- THE FEAR RESPONSE IS REPLACED BY A NEUTRAL RESPONSE. PTSD CAN BE CONSIDERED A FAILURE OF EXTINCTION

- EVIDENCE SUGGESTS A DYSFUNCTIONAL CIRCUIT MAKES EXTINCTION HARDER TO ACHIEVE
- KEY BRAIN HUBS FOR FEAR ARE THE AMYGDALA AND A GALAXY OF ADJACENT CELLS CALLED THE BED NUCLEUS OF THE STRIA TERMINALIS
- THESE TWO AREAS DRIVE VIRTUALLY ALL SYMPTOMS OF FEAR INCLUDING RACING HEART, INCREASED SWEATING, FREEZING AND EXAGGERATED STARTLE RESPONSE

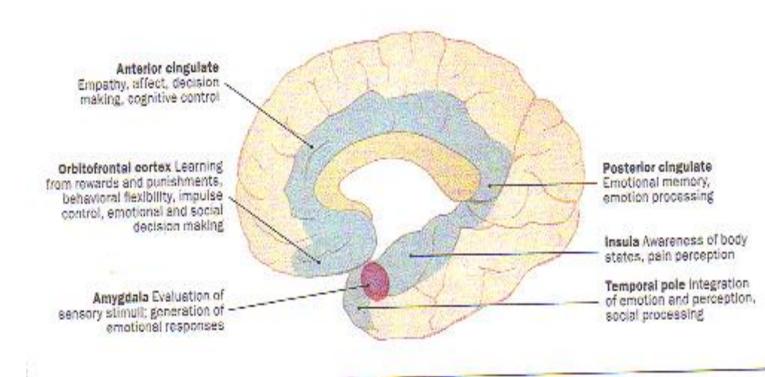
- IF AMYGDALA IS THE ENGINE OF FEAR, SOMETHING SHOULD BE RESPONSIBLE FOR TURNING IT OFF
- GREG QUIRK AT THE UNIVERSITY OF PUERTO RICO SHOWED A TINY AREA IN THE PREFRONTAL CORTEX OF RODENTS CALLED THE INFRALIMBIC REGION IS CENTRAL TO FEAR EXTINCTION
- ACTIVITY IN THIS AREA INCREASES DURING EXTINCTION SERVING AS A BRAKE ON THE AMYGDALA WHILE BLOCKING THE INFRALIMBIC REGION IMPAIRS EXTINCTION

- IN PTSD, NEUROIMAGING SHOWS REDUCED ACTIVITY IN vmPFC WHICH IS COMPARABLE TO THE RAT'S INFRALIMBIC REGION
- THE PATIENTS ALSO HAD SMALLER vmPFC RELATIVE TO TRAUMA –EXPOSED CONTROLS
- EXTINCTION INVOLVES INCREASE IN vmPFC ACTIVITY AND REDUCED FIRING OF PFC

- IN COGNITIVE-BEHAVIORAL THERAPY IMAGING SHOWS THE IMPORTANCE OF THE HIPPOCAMPUS FOR ASSESSING CONTEXT AND THE DORSOLATERAL PFC FOR LEARNING TO TOLERATE AND OVERCOME FEAR
- THE DORSOLATERAL PFC DOESN'T DIRECTLY CONNECT TO THE AMYGDALA
- THE vmPFC IS THOUGHT TO BE THE CRITICAL LINK BETWEEN THE DORSOLATERAL PFC AND AMYGDALA ALLOWING COGNITIVE TREATMENT TO PRODUCE NEW LEARNING AND RECOVERY

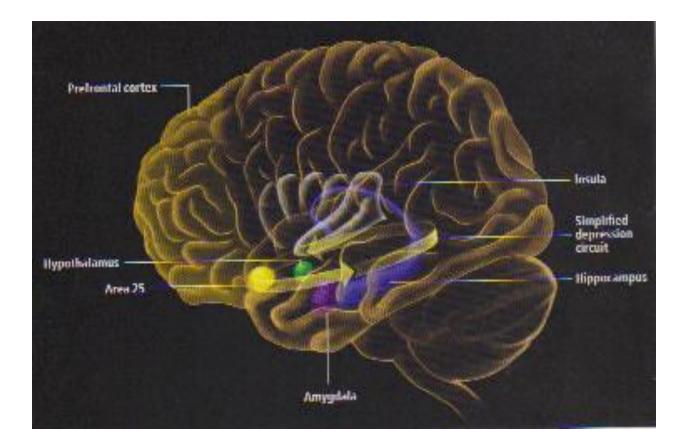
INSEL, THOMAS. "FAULTY CIRCUITS". SCIENTIFIC AMERICAN. APRIL 2010, PPGS 44-51.

- PARALIMBIC SYSTEM IS A CIRCUIT OF INTERCONNECTED BRAIN REGIONS THAT MAY WELL BE THE AREA OF MALFUNCTION IN ASPD
- THESE INTERCONNECTED BRAIN REGIONS REGISTER FEELINGS AND OTHER SENSATIONS AND ASSIGN EMOTIONAL VALUE TO EXPERIENCES, AS WELL AS, BEING INVOLVED IN DECISION MAKING, HIGH LEVEL REASONING AND IMPULSE CONTROL
- AREA IS UNDERDEVELOPED IN ASPD AND DAMAGE TO THESE AREAS CAN CREATE PSYCHOPANTIC TRAITS



- OFC INVOLVED IN SOPHISTICATED DECISION-MAKING TASKS THAT INVOLVE SENSITIVITY TO RISK, REWARD AND PUNISHENT
- LEADS TO PROBLEMS OF IMPULSIVITY AND
   INSIGHT AND LASH OUT IN RESPONSE TO
   PERCEIVED AFFRONTS
- THESE WERE GAGES'S PREDOMINANT SYMPTOMS ALTHOUGH HE STILL POSSESSED EMPATHY

- THE ANTERIOR CINGULATE REGULATES EMOTIONAL STATES AND HELPS PEOPLE CONTROL THEIR IMPULSES AND MONITOR THERIR BEHAVIOR FOR MISTAKES
- THE INSULA PLAYS A KEY ROLE IN THE RECOGNITON OF VIOLATION OF SOCIAL NORMS, AS WELL AS, THE EXPERIENCING OF ANGER, FEAR, EMPATHY AND DISGUST
- INSULA ALSO INVOLVED IN PAIN PERCEPTION AND PSYCHOPATHS ARE STRIKINGLY UNFAZED BY THREAT OF PAIN



- BRODMANN AREA 25 ACTS AS A HUB OF THE DEPRESSION CIRCUIT
- AREA 25 CONNECTS DIRECTLY TO THE AMYGDALA WHICH MEDIATES ANXIETY AND FEAR, AND THE HYPOTHALAMUS INVOLVED IN STRESS REPONSES
- THESE REGIONS EXCHANGE SIGNALS WITH THE HIPPOCAMPUS, A CENTER OF MEMORY PROCESSING, AND THE INSULA WHERE SENSORY PERCEPTION AND EMOTIONS ARE PROCESSED
- A SMALLER AREA 25 IS SUSPECTED OF CREATING A HIGHER RISK OF DEPRESSION IN PEOPLE WITH A GENE VARIANT THAT INHIBITS SEROTONIN PROCESSING

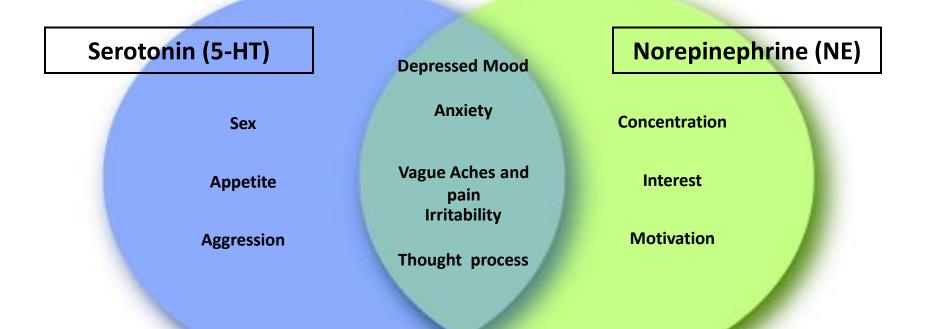
- HELEN MAYBERG AT EMORY HAS SHOWN AREA 25 IS OVERLY ACTIVE IN DEPRESSED PATIENTS AND SYMPTOM IMPROVEMENT IS CORRELATED WITH REDUCED ACTIVITY
- AREA 25 IS EXCEPTIONALLY RICH IN SEROTONIN TRANSPORTERS AND THOSE WITH A SHORT VARIANT OF THE SEOTONIN TRANSPORTER GENE HAVE A RELATIVE "UNCOUPLING" WITH SUBCORTICAL AREAS AND ALSO CONNECTION WITH FRONTAL CORTEX THATDISTURBS INSIGHT AND SELF-ESTEEM. CAN LEAD TO DISTORTED ASSESSMENT OF THE INTERNAL AND EXTERNAL WORLD

- "UNCOUPLING"CAUSES DISRUPTED CONNECTIONS WITH...
  - HYPOTHALAMUS
    - CHANGES IN APPETITE
    - CHANGES IN SLEEP
    - CHANGES IN ENERGY
  - AMYGDALA AND INSULA
    - ANXIETY
    - MOOD CHANGES
  - HIPPOCAMPUS
    - MEMORY PROCESSING
    - ATTENTION

#### Depression. It's not only a state of mind. The symptoms of depression

Emotional Symptoms Include:	Physical Symptoms Include:
Sadness	Vague aches and pains
Loss of interest or pleasure	Headache
Overwhelmed	Sleep disturbances
Anxiety	Fatigue
Diminished ability to think or	Back pain
concentrate, indecisiveness	Significant change in appetite
Excessive or inappropriate guilt	resulting in weight loss or gain
guit	

#### There are at least two sides to the neurotransmitter story Functional domains of Serotonin and Norephrephrine<sup>1-4</sup>



 Both serotonin and norepinephrine mediate a broad spectrum of depressive symptoms

# **Suffering and Misery**

- Psychological pain uses many of the same neural pathways as emotional pain
  - Not abstract or conceptual as you feel it in your body
  - Body mechanisms are involved
    - SYMPATHETIC NERVOUS SYSTEM
    - HYPOTHALAMIC-PITUTIARY-ADRENAL AXIS

# **Suffering and Misery**

- Let's start with a real or perceived threat
  - The amygdala reacts sending signals to:
    - Thalamus
      - To brain stem to increase norepinephrine (NE) throughout the brain
    - Sympathetic Nervous System (SNS)
      - Sends signals to major organs and muscle groups
        - » "Flight or Fight"
    - Hypothalamus
      - To pituitary releasing stress hormones
        - » Epinephrine (increases HR and dilates pupils)
        - » Cortisol

# **Suffering and Misery**

- Cortisol
  - Suppresses immune system to reduce inflammation
  - Continues to stimulate the amygdala
  - Suppresses hippocampal activity which normally inhibits amygdala leading to more cortisol
  - Remember amygdala hardwired to focus on negative
  - PFC is overridden pushing its appraisal in a negative direction

#### Mental Consequences of SNS/HPAA Activation

#### • ANXIETY

#### If amygdala gets neurosensitized causes

- Rapid arousal of "state" anxiety (based on specific situations)
- Helps form implicit memories and shades these memories with fear thus intensifying "trait" anxiety (free floating)
- With frequent SNS/HPAA activation hippocampus wears down impacting explicit memories (clear record of what actually happened)
  - Cortisol inhibits new neuronal growth and weakens existing synaptic connections in hippocampus
  - May help explain dissociation
    - » "Know something happened, don't exactly know what happened but feel really upset"

#### Mental Consequences of SNS/HPAA Activation

- **DEPRESSION** 
  - When norepinephrine is reduced may feel flat or even apathetic with poor concentration
  - Over time glucocorticoids (cortisol, etc) reduce dopamine causing loss of feeling of well-being and enjoyment of life
  - Constant stress reduces serotonin levels
    - The most important neurotransmitter for maintainig good mood state

#### Mental Consequences of SNS/HPAA Activation

- Psychotherapy
- Pharmacotherapy
- Activation of parasympathetic nervous system
  - Responsible for steady-state
  - Produces feelings of relaxation
    - Touching lips
    - Breathing
    - Forms of meditation and relaxation

## Memory

- Explicit and implicit memories when made only key features are stored
- When brain retrieves it is not like a computer that pulls up the whole file
- Brain rebuilds memory from key features

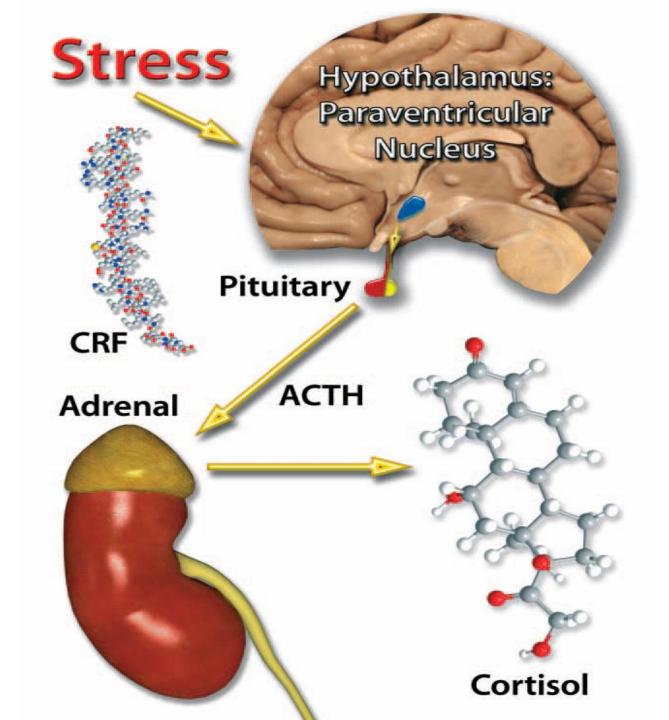
   Simulation
- Each recollection is shaded by the emotional state especially if unpleasant or pleasant

## Memory

- Amygdala and hippocampus will associate them with neural patterns
- When recollection take place it is now with these associations
  - Example-If increasingly associate negative feeling states with memory it will become more negative.
     On the other hand, if add positive meaning and feelings to the memory you start to build a more positive view (positive feelings also increase immune and cardiovascular functioning and lift mood)

## Hypothalamic-Pituitary-Adrenal Axis (HPA)

- HPA is an integral part of the stress response, as is the sympathetic nervous system, both also affect the immune system
- Studies of early life trauma
  - Some studies show blunted HPA response in adults and others show hyperresponsive HPA
  - Reduction in hippocampal volume
  - Increase in autoimmune disorders



# Autonomic Nervous System (ANS)

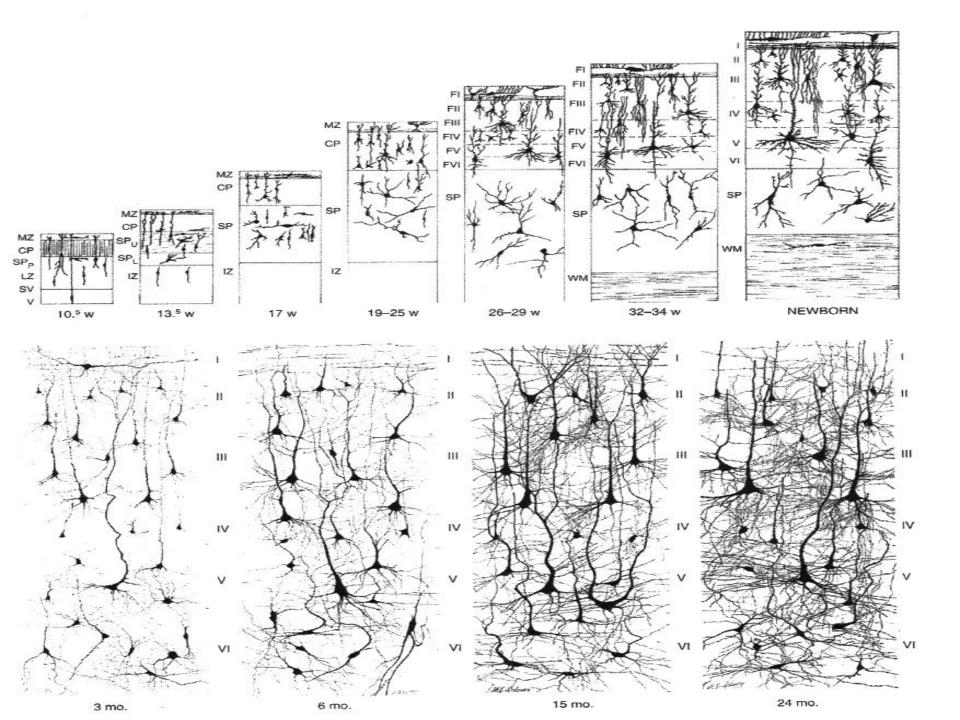
- Alterations in cardiovascular response with history of early life trauma
  - Heart rate and blood pressure elevations
    - Stress excites the locus coeruleus-norepinephrine system
  - Greater incidence of ischemic heart disease (IHD)
    - Depression also associated with increase in IHD
      - Increased risk of depression in early life trauma survivors
  - General increased risk of heart disease

### **Other Manifestations**

- Increased rates of obesity and eating disorders
- Increase in many psychiatric disorders
- Low cognitive functioning and/or poor attention
  - Neurodevelopmental possibilities

# **BRAIN DEVELOPMENT**

- Lower brain mostly born intact
- Prefrontal Cortex (PFC) plastic especially between 0-5 and 10-20 years of age
- PFC takes up to 25 years to develop
- Developmental delays occur secondary to early life trauma and early onset alcohol/drug abuse.
- PFC CRITICAL TO BECOMING RESILIENT



# **RESILIENCE AND THE PFC**

• WHAT CAN WE TREAT?



# Affect

# PEER AND PARENTAL RELATIONSHIPS

#### Preadolescence & Adolescence Neurobiology Themes

- Brain cells, connectivity, receptors and neurotransmitters peak in childhood and are reduced during adolescence
- Connectivity among brain regions increases
- Balance between frontal (executive control) and limbic (emotional) systems changes

#### Brain Cells, Connectivity, Receptors and Neurotransmitters

- Plasticity
- Competitive elimination
- Gray matter volume increases during childhood, declines through adolescence, level off during adulthood and then declines later in life

#### Connectivity Among Brain Regions Increases

- Cognitive advances due to faster communication and increased integration
- Myelinated axons transmit impulses up to 100 times faster and decrease recovery time allowing a 30 fold increase in frequency
- Roughly equivalent to a 3000-fold increase in computer bandwidth

### Balance Between Frontal and Limbic Systems Changes

- Prefrontal Lobe circuitry increases
  - Some ability to delay gratification
  - Initial development of executive functioning
    - Problem solving
    - Abstraction
    - Conceptualization
    - Judgment



#### **Modulation Ratio**

• IN ORDER TO USE THE COGNITIVE AND BEHAVIORAL STRATEGIES WANT STUDENT TO HAVE:

## INHIBITION EXCITATION

#### What Changes Modulation Ratio and Increases Risk of Anger and Aggression?

- Anything that excitation in the lowers areas of the brain (brainstem and diencephalon)
- Anything that inhibition in the areas of higher brain function (neocortex and limbic system)

## **LEFT AND RIGHT HEMISPHERE**

- Right Hemisphere-Parallel Processor
- Left Hemisphere-Serial Processor
- Communicate through the Corpus Collosum

   300 million axonal fibers
- Each hemisphere thinks differently and care about different things

## **RIGHT HEMISPHERE**

- The Present Moment-Right here and now
- Thinks in pictures and symbols
- Receives sensory information that allows us to understand what the moment feels like, smells like and tastes like

- Sensory collage

- Connects to the energy all around us
- We are energy beings connected to everything through the consciousness of our right hemisphere

# LEFT HEMISPHERE

- Linear and methodical
- All about the past and the future
- Takes the collage of the present moment and categorizes and organizes the informational details
- It then associates this information with what we have learned from the past and projects it into the future

# **LEFT HEMISPHERE**

- Thinks in language
- It is the ongoing chatter in the brain
- It is calculating intelligence (survival and gain)
- It says, "I am"
  - This separates us from everything else
- The "Experiencer"
  - Ego
  - Animal brain heritage

# **LEFT/RIGHT BRAIN**

- If disconnected from the brain chatter that connects us to the outer world the mind is silent
- Lose the complications of the past and future and become overwhelmed by the peacefulness of the moment
- The more time we spend in the inner circuitry of our right hemisphere the more peace we project into the world

- Kight hemisphere (RH) processes only what it receives and nothing more
- XLeft hemisphere (LH) appears to make elaborations, associations and searches for logical patterns even when none are present
- **XRH retains veridical (**actual; genuine) representations of each to-be-remembered item and tends to accurately recognize previously viewed items and reject new items even when they are similar (Turk et al, 2003)

- ★LH tends to elaborate and make inferences about the material presented often at the expense of veracity (Metcalf, 1995, Phelps & Gazzaniga, 1992)
- XLH also attempts to assign a coherent explanation to events or behavior even when none is present (Wolford, 2000)
  - +Described as the LEFT HEMISPHERE INTERPRETER Turk et al, 20030

- Interpretive function of the LH takes available information from the distributed self-processing networks and creates a unified sense of self from the input
  - +I AM
  - +Dualistic EGO
- Interpretive function tries to make sense out of incomplete or ambiguous data

- The LEFT HEMISPHERE INTERPRETER seems to be the link between trying to make sense of the world and the perception of self in the LH
- \*This might explain why everyone's reality and perception of the world are different and an illusion as described by spiritual traditions such as Buddhism and Hinduism

# **LEFT/RIGHT BRAIN**

- LEFT HEMISPHERE
  - CONSCIOUS
  - SERIAL
  - INFORMATION PROCESSING
- RIGHT HEMISPHERE
  - UNCONSCIOUS
  - NONVERBAL
  - EMOTIONAL PROCESSING

# **RIGHT HEMISPHERE**

- EARLY DEVELOPMENTAL UNCONSCIOUS
- EMOTIONAL "SELF"
- 80-90% IS UNCONSCIOUS
- THE ABOVE DRIVES OR MOTIVATES HUMAN EMOTION
- HUMAN EMOTION IS THE DRIVING FORCE
   BEHING COGNITION AND BEHAVIOR
- EMOTION IS MEDIUM IN WHICH PRIMARY
   INTERPERSONAL INFORMATION IS
   TRANSMITTED

- RECOGNITION AND EXPRESSION OF
   EMOTION
- NONVERBAL EMOTIONAL EXPRESSION
- RH TO RH AFFECTIVE COMMUNICATION EQUALS THE RELATIONAL UNCONSCIOUS
- UNCONSCIOUS RH IMPLICIT SELF CONTINUOUSLY APPRAISES LIFE EXPERIENCES AND RESPONDS ACCORDING TO ITS SCHEME OF INTERPRETATION

- ONE UNCONSCIOUS MIND COMMUNICATES
   WITH ANOTHER UNCONSCIOUS MIND
- RH RESPONDS QUICKLY TO ALL STIMULI
- IMPLICIT LEVEL OF THE THERAPEUTIC ALLIANCE (BENEATH THE EXPLICIT COGNITIONS AND LANGUAGE) ARE THE CORE OF THE CHANGE MECHANISM AT THE UNCONSCIOUS LEVEL

# **RIGHT HEMISPHERE (RH) RIGHT HEMISPHERE LEFT HEMISPHERE** LANGUAGE **IMAGES** LIMBIC SYSTEM **MOTIVATION & EMOTION BRAIN STEM ANS, AROUSAL & PAIN**

- INVOLVES CO-CREATION OF AN INTERSUBJECTIVE CONTEXT THAT FACILITATES THE PROCESS OF CHANGE (ATTACHMENT COMMUNICATION)
- ATTACHMENT COMMUNICATION REPRESENTS RH TO RH TRANSACTION THAT FACILITATE THE EXPERIENCE DEPENDENT MATURATION OF RH

- EMOTIONAL AVAILABLILITY OF CAREGIVER IN INTIMACY SEEMS TO BE THE CENTRAL GROWTH PROMOTING FACTOR IN EARLY REARING EXPERIENCE
- CAREGIVER MAXIMIZES POSITIVE AFFECT
   AND MINIMIZES NEGATIVE AFFECT
- PROMOTES INCREASED TOLERANCE FOR POSITIVE AND NEGATIVE AFFECT (AFFECTIVE RANGE)

- THE BROADER THE RANGE OF EMOTIONS THAT A CHILD EXPERIENCES THE BROADER WILL BE THE EMOTIONAL RANGE OF THE SELF THAT DEVELOPES
- THERAPEUTIC ALLIANCE
  - THERAPIST'S FACILITATING BEHAVIORS COMBINE WITH THE PATIENTS CAPACITY FOR ATTACHMENT TO PERMIT DEVELOPMENT OF ALLIANCE (PRIMARY COMPONENT OF EMOTIONAL BOND)

- THERAPEUTIC ALLIANCE (CONTINUED)
  - KEY IS HOW TO BE SUBJECTIVELY WITH PATIENT ESPECIALLY DURING AFFECTIVELY STRESSFULL MOMENTS
    - UNCONSCIOUS INTERSUBJECTIVE PROCESSES INCLUDE EMPATHY, IDENTIFICATION WITH OTHERS AND SELF-AWARENESS
  - FACIAL EXPRESSIONS CAN BE APPRAISED BY THE RH WITHIN 30 MILLISECONDS
    - MAY TAKE HOURS TO DAYS TO GET INTENSE REACTION BACK TO BASE LINE

- MUST BE ATTENTIVE TO LH PATIENT VERBALIZATIONS IN ORDER TO OBJECTIVELY DIAGNOSE AND UNDERSTAND PATIENTS DYSREGULATED SYMPTOMS
- BUT ALSO ATTENTIVE INTERSUBJECTIVELY TO RELATIONAL TRANSACTIONS (REFLECT EMOTIONS SUCH AS APPROVAL/DISAPPROVAL, SUPPORT, HUMOR AND FEAR)
  - FACIAL EXPRESSIONS
  - BODY POSTURE
  - TONE AND TEMPO OF VOICE

- RIGHT SIDE OF FACE (LH)-SOCIALLY CONSCIOUS CONTENT, SOCIALLY APPROPRIATE CLUES
- LEFT SIDE OF FACE (RH)-HIDDEN PERSONALIZED FEELINGS, IMPLICIT UNCONSCIOUS CONTENT
- IN HEIGHTENED AFFECTIVE MOMENT THE EMPATHIC THERAPIST'S RH CAN REGULATE PATIENTS DYSREGULATED RH

• CARL ROGERS (1986)

"AS A THERAPIST, I FIND THAT WHEN I AM **CLOSEST TO MY INNER, INSTINCTIVE SELF,** WHEN I AM SOMEHOW IN TOUCH WITH THE UNKNOWN IN ME, WHEN PERHAPS I AM IN A SLIGHTLY ALTERED STATE OF CONSCIOUSNESS IN THE RELATIONSHIP, THEN WHATEVER I DO SEEMS FULL OF **HEALING.**"

- LEFT TO RIGHT HEMISPHERE
- AT LOW LEVELS OF CONSCIOUSNESS
  - FAST FLOW TO AMYGDALA AND EMOTIONAL BRAIN
- AS LEVELS OF CONSCIOUSNESS INCREASES
  - FAST FLOW TO PREFRONTAL CORTEX
  - DEVELOPMENT OF ETHERIC BRAIN (ENERGY BRAIN) AND "THIRD EYE"
  - KUNDALINI ENERGY

- POSITIVE EFFECTS OF MEDITATION AND CONTEMPLATION
  - STIMULATES ANTERIOR CINGULATE GYRUS
    - COMPASSION
    - MAINTAINS BALANCE BETWEEN THE FRONTAL LOBES (INITIATE THOUGHTS AND BEHAVIORS) AND LIMBIC SYSTEM (PROCESSES FEELINGS AND EMOTIONS)
    - ANTERIOR CINGULATE
      - EMOTIONAL REGULATION
      - LEARNING
      - MEMORY
      - PLAYS ROLE IN LOWERING ANXIETY AND IRRITABILITY
      - COUNTERS DEPRESSION
      - ENHANCES SOCIAL AWARENESS

- SPIRITUAL VALUES CAUSE INCREASE IN BLOOD SUPPLY TO FRONTAL CORTEX AND ANTERIOR CINGULATE AND REDUCED BLOOD FLOW TO LIMBIC AREAS (AMYGDALA)
- ANGER CAUSES JUST THE OPPOSITE REACTION
- MEDITATION/CONTEMPLATION ENHANCES
   ACTIVITY OF THE PREFRONTAL-ANTERIOR
   CINGULATE-BASAL GANGLIA-THALAMUS PREFRONTAL CIRCUIT

#### PREFRONTAL-ANTERIOR CINGULATE-BASAL GANGLIA-THALAMUS-PREFRONTAL CIRCUIT

- THIS CIRCUIT CONTROLS:
  - CONSCIOUSNESS
  - CLARITY OF MIND
  - REALITY FORMATION
  - ERROR DETECTION
  - EMPATHY
  - COMPASSION
  - EMOTIONAL BALANCE
  - SUPPRESSION OF FEAR AND ANGER

NEWBERG, ANDREW. HOW GOD CHANGES YOUR BRAIN.

- FRONTAL LOBES
  - -SELECTIVE ATTENTION
  - -EXPECTATION
  - -OPTIMISM
  - -INTENTION
- KEYS TO BELIEF THAT ONE'S ACTIONS CAN MAKE A SPIRITUAL DIFFERENCE IN SELF AND THE WORLD

#### CONSCIOUS AND UNCONSCIOUS ASPECTS

- CONSCIOUS MIND OR BRAIN
  - PREFRONTAL CORTEX
  - ALSO CALLED THE SOCIAL BRAIN
- UNCONSCIOUS MIND
  - GENETIC AND SPECIES SPECIFIC
  - SURVIVAL ORIENTED

#### Unconscious Homeostasis Stereotypic Movements Learned Movements Neurotransmitter and Hormone Release Autonomic Regulation Responds to Generalized Features of objects Responses are fast

#### Conscious

Novel Movement Sequences Can assume Voluntary control of some unconscious Processes Neurotransmitter and Hormone Release

> Autonomic Regulation

Can address Specific Detail

Responses can be slow

- Coordinate the many brain activities needed to utilize:
  - Executive Functions
    - Set goals
    - Make plans to attain those goals
    - Organize steps to carry out the plans
    - Ensure that desired outcomes are achieved
  - Conscience
  - Pursue Reward Within the Law

- The *orbital and medial prefrontal cortex* is primarily connected with
  - Thalamus
  - Hypothalamus
  - Amygdala
  - Hippocampus
  - Temporal lobe
- Involved with *emotion* and *instinctive* and *affect-modulated* behavior

- The *lateral prefrontal cortex* is primarily connected with...
  - Thalamus
  - Caudate nucleus
  - Neocortex
- Constitutes the substrate for *executive functioning*

- Anterior Cingulate Cortex
- Orbitofrontal Cortex
- Dorsolateral Prefrontal Cortex

• Therapist task-optimize plasticity

#### **DORSOLATERAL PREFRONTAL CORTEX**

- Entry point for verbal psychotherapy
- Essential for advanced reasoning
- Modulation of behavior thru use of words

# DORSOLATERAL PREFRONTAL CORTEX

DORSOLATERAL PREFRONTAL CIRCUIT

- Modulates Executive Functions

- Organization
- Problem Solving
- Working Memory
- Memory Retrieval
- Self-directedness
- Ability to address novelty
- Use of language to guide behavior

#### **Executive Functions**

- Abstract Thinking
  - Discerning relationships
  - "Seeing the forest for the trees"
- Attention Shifting
  - Ability to shift attention when needed
- Information Manipulation

Manipulate information in short-term memory

### **Executive Functions**

- Planning And Foresight
  - Forming a mental model of a future event or situation
- Monitoring And Error Correction

   Engaged when results do not match intentions
- Decision Making
  - Weigh options, arrive at a decision and see it through

## **Executive Functions**

• Inhibition

Ability to inhibit impulses and delay gratification

• Social Functioning

- Appropriate processing of social cues

### DORSOLATERAL PREFRONTAL CORTEX AND ADHD

- It is the dorsolateral prefrontal cortex that most groups find is different in kids with ADHD. It's a bit smaller in volume. If you look at cortical thickness, it tends to be a bit thinner.
- The amygdala is very much associated with emotional processing. Some people have found differences, some haven't.

### DORSOLATERAL PREFRONTAL CORTEX AND ADHD

- One particularly interesting recent finding was that the connections between the amygdala and the frontal parts of the brain might be different in kids with ADHD.
- One particularly interesting study actually found that the hippocampus was bigger in kids who had ADHD. And, the fewer symptoms they had, the bigger the hippocampus, which might suggest that the hippocampus getting bigger is compensating for the symptoms.
- DRD4 gene-associated with brain development

- ANTERIOR CINGULATE CIRCUIT
  - Motivates goal-directed behavior
  - Conflict monitoring
  - Component of reward circuitry
  - Emotional-cognitive integration
  - Plays a part in experience of empathy
- If damaged-Apathy

- Coordinates
  - Maternal behavior
  - Nursing
  - Play
- Monitors personal, environmental and interpersonal information
- Helps regulate emotion and pain
- Allocates attention to whatever is most salient

- Cocaine craving
  - Increases activation of the Anterior Cingulate which controls
    - Maternal behavior
    - Nurturance
    - Bonding
- Substance abusers may seek to satisfy intimacy needs by manipulating the neurobiology of attachment

- Detection of errors
- Adjustment of response according to new information
- Clients with alexythymia (inability to experience or express feelings) have smaller anterior cingulate cortices
- Larger anterior cortices associated with worry and fearfulness
- Anterior cingulate has overlapping functions with other prefrontal cortices

## **SPINDLE CELLS**

- IN ANTERIOR CINGULATE AND INSULA
- Spindle cells (VON ECONOMO CELLS) appear to play a central role in the development of *intelligent behavior* and *adaptive response to changing conditions* and <u>cognitive dissonance</u>. They become widely connected with diverse parts of the brain, indicating their essential contributions to the superior capacity of hominids to focus on difficult problems.
- Spindle cells emerge after birth and are experiencedependent
- Early neglect and abuse negatively impact development causing deficits in anterior cingulate abilities

### **SPINDLE CELLS**

- AUTISM
  - INVOLVES THEORY OF MIND WHICH EMERGES AROUND 4 YO
  - IF CANNOT FIGURE OUT OTHER PEOPLE SOCIAL INTERACTIONS ARE BAFFLING
  - DON'T LOOK AT THE OTHERS FACE, DON'T COPY. DON'T MIMIC AND DON'T YAWN WHEN OTHERS AROUND THEM DO

## **SPINDLE CELLS**

- AUTISM
  - AREAS OF THE INSULA AND ANTERIOR CINGULATE WHICH ARE ACTIVATED BY SOCIAL INTERACTION ARE RELATIVELY INACTIVE IN AUTISM
  - MAY INVOVLE SPINDLE NEURONS WHICH ARE
     FOUND ONLY IN THE TWO ABOVE AREAS
  - THESE NEURONS KEEP TRACK OF SOCIAL EXPERIENCES AND PROVIDE BASIS FOR INTUITIVE SOCIAL LEARNING WHEN WE WATCH AND COPY OTHERS
  - Scientific Am Mind. March/April 2011, pg 16-17.

# **ANTERIOR CINGULATE DEFICITS**

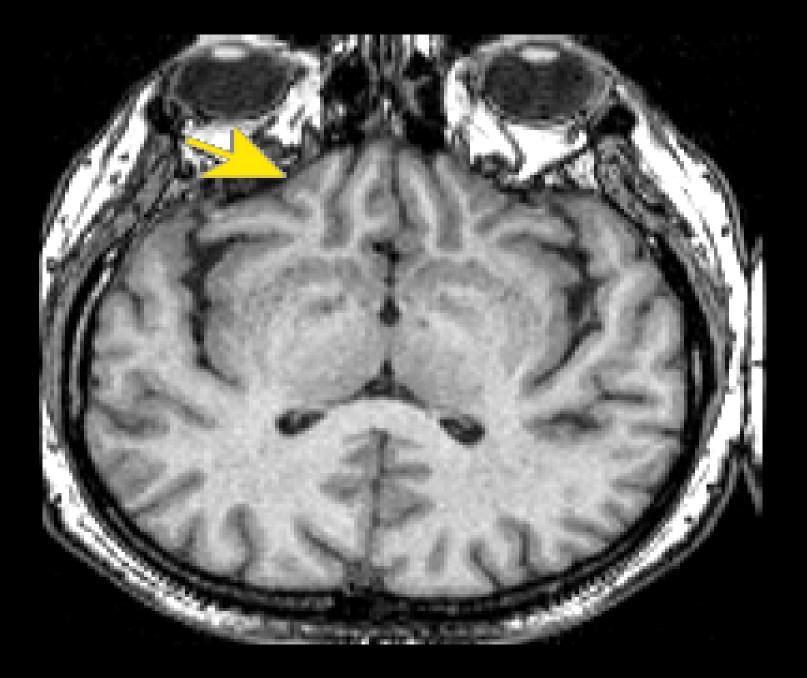
- Decreased maternal behavior
- Decreased empathy
- Decreased emotional stability
- Disruption of Autonomic Nervous System (ANS) and Hypothalamic-Pituitary-Adrenal (HPA) functioning
- Increased response to stress
- Decreased expressiveness
- Inappropriate social behavior
- Impulsiveness

# **Empathy Also...**

- Requires
  - Conceptual understanding
  - Emotional attunement
  - Ability to regulate affect
- Damage to Orbito Frontal Cortex
  - Impairs emotional resonance
- Damage to Dorsolateral PFC
  - Loss of cognitive flexibility
- Acquired Pseudopsychopathic Personality

#### ORBITOFRONTAL CIRCUIT

- Modulates pursuit of reward
  - Risk
  - Context
  - Potential consequences
- In conjunction with amygdala can stimulate or inhibit ANS
- If damaged-impulsivity, social inappropriateness, disregard for rules and consequences



- Senior Executive of the emotional brain
- Regulates interpersonal and social behavior
- Directly connects to all areas of the brain
  - Brain stem
  - Limbic system
  - Cerebral Cortex
    - Right hemisphere specializes in inhibitory control

- Modulates instinctive behavior and internal drives
- Processes face and voice information for appraisal of external environment
- Therefore, integrates external and internal environment
- Early developmental trauma has negative impact on OFC

#### • CONNECTS TO:

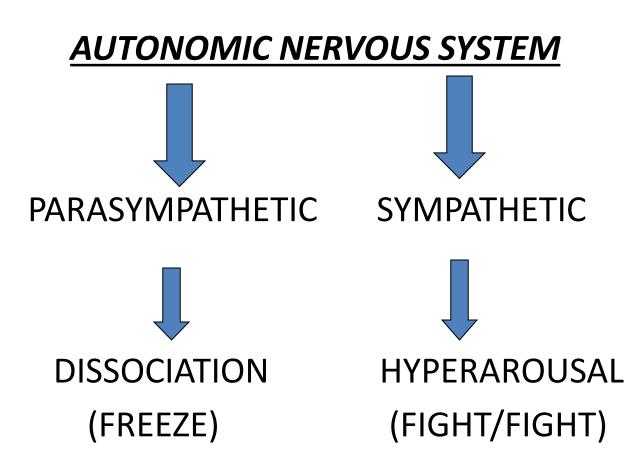
#### - Hypothalamus

- Head ganglion of ANS & locus of drive
- Pituitary
- The hypothalamus is one of the most important parts of the brain, involved in many kinds of motivation, among other functions. The hypothalamus controls the "Four F's": fighting, fleeing, feeding, and mating.

#### – Amygdala

#### – Reticular Formation

• Brainstem regulation of arousal



## Parasympathetic Nervous System

- Conservation/Withdrawal
- Shame (Blushing)
- Repetitive Dissociative Symptoms
  - Tics
  - Stuttering
  - Poor eye contact
  - Somatic complaints

# Sympathetic Nervous System

- Fight or Flight
- Increased Cortisol
  - Insomnia
  - Increased serum lipids
  - Promotes obesity (abdominal area)
  - Diabetes
  - Hypertension
  - Atherosclerosis
  - Suppresses immune system
  - Peptic ulcerations
  - Atrophy of Hippocampus

## **Face Appraisal**

- Inner Images are important source of emotional self-regulation
- Without internalized Right Brain parental strategies for self-soothing become stress vulnerable
  - Negative Look
    - Increases Cortisol stops DA and endorphin release

# **Face Appraisal**

- Positive Look
  - Increase B-endorphin release
    - » Helps neurons grow by regulating glucose and insulin
  - Increases Dopamine
- Disapproving look can cause shift from sympathetic to parasympathetic arousal creating effects often called SHAME
  - Reduced BP
  - Shallow breathing

# Face Appraisal

- Facial Expressions
  - Reading of facial expressions are genetically encoded
  - Fusiform face area helps determine identity and links faces to memories
  - Amygdala and orbitofrontal cortex-negative faces
  - Striatum and orbitofrontal cortex-attractive faces
  - Orbitofrontal and anterior cingulate-make social and moral judgments

### FACE APPRAISAL

- Our findings suggest that the brain automatically responds to a face's trustworthiness before it is even consciously perceived
- In the first experiment, the researchers examined amygdala activity in response to three levels of a face's trustworthiness: low, medium, and high. In the second experiment, they assessed amygdala activity in response to a fully continuous spectrum of trustworthiness.

### FACE APPRAISAL

 Across the two experiments, the researchers found that specific regions inside the amygdala exhibited activity tracking how untrustworthy a face appeared, and other regions inside the amygdala exhibited activity tracking the overall strength of the trustworthiness signal (whether untrustworthy or trustworthy) -- even though subjects could not consciously see any of the faces.

New York University. "Our brains judge a face's trustworthiness, even when we can't see it." ScienceDaily. ScienceDaily, 5 August 2014. <www.sciencedaily.com/releases/2014/08/140805220718.htm>.

## **UNCONSCIOUS MIND**

"The unconscious handles a variety of important tasks that are best accomplished automatically, with great speed and no opportunity for deviation, or, in other words, no room for choice."

Viamontes and Beitman, "Mapping The Unconscious in the Mind". Psych Annals. 37:4, April 2007, pg. 250.

## **UNCONSCIOUS MIND**

- All input and output categories of the unconscious are genetically determined and species specific
- It is possible to learn how to reclassify stimuli
  - Children dislike the taste of coffee (bitter)
  - Many learn to reclassify coffee as a "liked" flavor because it induces a body state interpreted as "good" or "pleasant"

## **Unconscious Circuit Responses**

- Neurotransmitter or hormone release
- Activation of genetically encoded behavioral sequence
- Modification of ANS tone
- Activation of learned behavioral sequences

- Level 1: Organize homeostatic functions, automatic actions and stereotypic behavior
  - Neurological Systems
    - Brain Stem
    - Basal Forebrain
    - Hypothalamus
  - Involves anxiety, fear and anger
    - Inappropriate activation can cause pathological statesanxiety, fear and anger

- Level 2: Intensity of engagement with environment
  - Brain stem arousal and sleep centers
  - State of DA, SER, NE and Acetylcholine receptors throughout brain
  - Modulation of corresponding neurotransmitters
  - Brain energy modulation
    - Reduced ATP causes increased adenosine creating lethargy

-Caffeine blocks adenosine receptors

- Level 3: Interactions with primary rewards and punishers encoded in genes
  - Amygdala and orbitofrontal cortex
    - Both modulate HTH autonomic center
    - Both act as "couplers" that tie recognition of the primary reinforcer to the genetically programmed response
      - Primary reinforcers are certain tastes and smells, pleasant touch and probably smiling faces
      - Primary punishers include unpleasant taste and odors, painful somatosensory stimuli and probably loud voices and angry/threatening faces

- Level 3: (continued)
  - Stereotyped behaviors
    - Example-Put bitter taste in mouth and it is immediately 'spit" out
  - The basic states that are induced in encounters with primary rewards and punishers are the foundation for the development of EMOTIONS

- Level 4: Define unconscious reactions to secondary rewards and punishers that have been learned
  - Amygdala and orbitofrontal cortex mediate response to simple objects that become associated with reward and punishment
    - Example- "craving"
  - Often found in certain anxiety disorders like phobias, OCD

#### • <u>Level 4:</u>

- Many categories of psychopathology involve learning of inappropriate responses to previously neutral stimuli
- Involves attaching the somatic state pattern that normally accompanies a primary reinforcer to a previously neutral object

#### • <u>Level 4:</u>

#### – Intervention often involves:

- Perceived object
- Unconscious processing
- Prepares body

•

**Conscious processing** 

• Can precipitate maladaptive response

- Level 5: Mediate social functioning
- Significant impact on behavior and psychopathology
  - Facial expressions
    - Amygdala appears to have prewired programs for recognition of negative facial expressions
  - Theory of Mind

## **THEORY OF MIND**

- Ability to think about what another is thinking
- Starts as visceral-emotional sense of others gained from "mirror" neuron system
- Key component of social interaction
- Involves
  - Right Orbitofrontal Cortex
    - Decodes mental states
  - Left Orbitofrontal Cortex
    - Reasoning analysis of mental states

# **THEORY OF MIND**

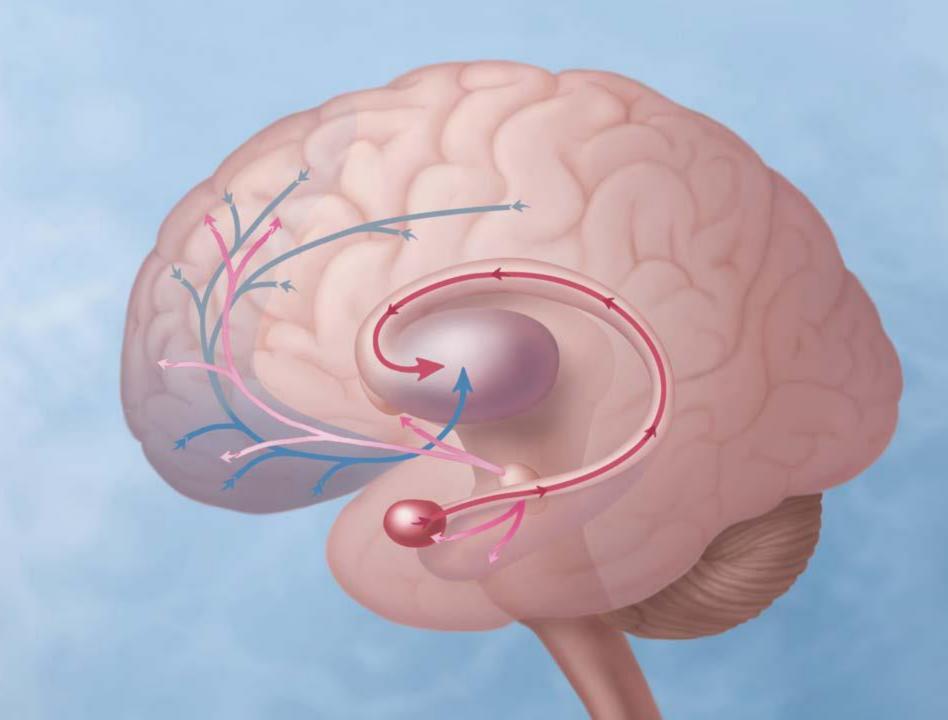
- Involves (continued)
  - Amygdale
  - Insula
    - Experience of self
    - Ability to distinguish self from other
  - Anterior Cingulate
    - Pair-bonding
    - Nurturance

# **THEORY OF MIND**

- Involves (continued)
  - Dorsolateral Prefrontal Cortex
    - Executive functions
      - Actions
      - Goals
      - Abstractions

### "IMPULSIVE" & "REFLECTIVE" SYSTEMS

- "SHOULD I" OR "SHOULDN'T I"
- DETERMINATION RESTS ON THE INTERNAL STRUGGLE BETWEEN THE "IMPULSIVE" SYSTEM (IN RED) AND THE "REFLECTIVE" SYSTEM (IN BLUE)
- WHICHEVER SYSTEM PREVAILS DETERMINES
   OUTCOME



# **"IMPULSIVE" SYSTEM**

- PIVOTAL STRUCTURE IS THE AMYGDALA
  - RECOGNIZES ENVIRONMENTAL FEATURES THAT ARE POTENTIAL SOURCES OF PLEASURE OR SATISFACTION OF NEEDS AND TRIGGERS EXCITATORY RESPONSES IN OTHER BRAIN AREAS
  - THESE RESPONSES FAVOR FEELINGS OF DESIRE, ANTICIPATION, MUSCULAR TENSION AND URGES TO ACT

## **"REFLECTIVE" SYSTEM**

- KEY STRUCTURE IN THE "REFLECTIVE" SYSTEM IS THE ORBITOFRONTAL CORTEX OR VENTROMEDIAL PREFRONTAL CORTEX (VMPC)
  - VMPC INTERPRETS SAME ENVIRONMENTAL FEATURES AS AMYGDALA BUT DOES SO WITH INPUT FROM BRAIN STRUCTURES THAT STORE RECOLLECTED OR IMAGINED ASSOCIATIONS FROM PAST EXPERIENCE

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# LEARNING AND MEMORY

- NEUROBIOLOGY OF MEMORY AND BELIEF
- ASSOCIATIVE MEMORY
- INTUITIVE INSIGHT
- LEARNING AND MEMORY
- ADDICTION: DYSFUNCTION IN LEARNING
   AND MEMORY

- RIGHT PREFRONTAL CORTEX (PFC) PLAYS A CRUCIAL ROLE IN INTEGRATING...
  - PERCEPTIONS
  - IDEAS
  - MEMORIES
- DISRUPTED FUNCTION
  - RIGHT PFC CAN CAUSE STRANGE AND UNUSUAL BELIEFS
  - LIMBIC SYSTEM CAN CAUSE LOSS OF ABILITY TO SUPRESS FANTASIES THAT DO NOT PERTAIN TO ONGOING REALITY

- IMAGINARY MEMORIES AND REALITY-BASED MEMORIES ARE STORED DIFFERENTLY IN THE BRAIN
- DISRUPTED FUNCTION
  - MAY LOSE THE ABILITY TO DISTINGUISH BETWEEN FACT AND FANTASY
    - ANTIANXIETY DRUGS (ATIVAN, XANAX, VALIUM, ETC.) CAN IMPAIR CONSCIOUS RECOLLECTION OF TRUE MEMORIES BUT NOT FALSE MEMORIES
      - » PROBABLY DUE TO HIGHER LEVEL OF NEURAL ORGANIZATION CREATING GREATER CHANCE OF DISRUPTION

- MEMORIES ALSO EFFECTED BY STRESS
  - ALTERS BOTH MEMORY FORMATION AND RECALL
  - MAY INTERFERE WITH LAYING DOWN OF MEMORY TRACES FOR INCIDENTS OF CHILD ABUSE AND CAN LEAD TO LONG-TERM DISTORTION OF FACTS OR EVEN AMNESIA
  - HIGHLY EMOTIONAL AND TRAUMATIC EXPERIENCES SEEM TO ENHANCE MEMORY STORAGE BUT IN A FRAGMENTED WAY

- MEMORIES ALSO EFFECTED BY STRESS (CONTINUED)
  - SUBJECT TO SPATIAL AND TEMPORAL DISTORTION
  - THIS CAUSES LEFT HEMISPHERE TO COMPENSATE FOR INCONSISTENCIES IN RECALL BY CONSTRUCTING ALTERNATIVE SCENARIOS TO BUILD A CONSISTENT STORY

- SUMMARY OF RESEARCH PERTAINING TO ACCURACY OF MEMORY AND BELIEFS
  - ALL MEMORIES AND BELIEFS ARE SUBJECT TO CHANGE AND DISTORTION OVER TIME
  - CONSCIOUS BELIEFS AND MEMORY RECALL ARE HIGHLY DEPENDENT ON LANGUAGE, EMOTION, AND SOCIAL INTERACTION; AS THESE VARIABLES CHANGE, SO DO OUR MEMORIES AND BELIEFS
  - CHILDREN'S MEMORIES AND BELIEFS DISTINGUISH POORLY BETWEEN FANTASY AND FACTS

- SUMMARY OF RESEARCH PERTAINING TO ACCURACY OF MEMORY AND BELIEFS (CONTINUED)
  - THE OLDER A MEMORY, THE MORE DIFFICULT IT IS TO ASCERTAIN ACCURACY.
  - AUTOBIOGRAPHICAL MEMORIES ARE PARTICULARLY PRONE TO INACCURACY
  - TRAUMATIC EVENTS EMBED MEMORIES IN A POWERFUL BUT SOMETIMES FRAGMENTARY WAY

- SUMMARY OF RESEARCH PERTAINING TO ACCURACY OF MEMORY AND BELIEFS (CONTINUED)
  - NEUROLOGICAL DISORDERS AND DRUGS CAN DISRUPT THE BRAIN'S ABILITY TO DISTINGUISH BETWEEN TRUE AND FALSE MEMORIES AND BELIEFS
  - BELIEF SYSTEMS TEND TO DEVELOP IN WAYS THAT PARALLEL THE BRAIN'S OWN BIOLOGICAL DEVELOPMENT AND ACQUISITION OF KNOWLEDGE AND SOCIAL SKILLS

NEWBERG, WHY WE BELIEVE WHAT WE BELIEVE, PG. 114.

## **INTUITIVE INSIGHT**

- ARCHIMEDES IN THE BATH (CALCULATE DENSITY AND VOLUME)
- DESCARTES IN BED WATCHING FLIES ON CEILING (COORDINATE GEOMETRY)
- NEWTON WHEN HE SAY AN APPLE FALL (LAW OF UNIVERSAL GRAVITY)
- "AHA" OR EPIPHANY

#### "AHA" OR EPIPHANY

- A SUDDEN COMPREHENSION THAT ALLOWS YOU TO SEE SOMETHING IN A DIFFERENT WAY
- REQUIRES MORE NEURAL RESOURCES THAT
   METHODICAL THINKING
- FACILITATED BY A POSITIVE MOOD
- DAYDREAMING

#### DAYDREAMING

- ONE-THIRD OF THE TIME
- INVOLVES SEVERAL NEURAL AREAS
   ASSOCIATED WITH COMPLEX PROBLEM
   SOLVING
- ONLY TIME THESE AREAS WORK IN UNISON

# INSIGHT (INTUITIVE)

FLASH OF GAMMA WAVES EMANATING
 FROM RIGHT HEMISPHERE

- HANDLES ASSOCIATIONS

- ASSEMBLES ELEMENTS OF A PROBLEM
- BRAIN BROADCASTS THE SIGNAL ONE-THIRD
   OF A SECOND PRIOR TO CONSCIOUS
   MOMENT OF INSIGHT

# INSIGHT (INTUITIVE)

- PATTERNS OF HIGH FREQUENCY NEURAL ACTIVITY IN RIGHT FRONTAL CORTEX THAT IDENTIFIES WHO WILL SOLVE PROBLEM BY INSIGHT AND WHO WOULD NOT
- INSIGHT FAVORS A PREPARED MIND
- CREATIVE THOUGHT IS A PRODUCT OF NEURONS AND NERVE CHEMISTRY OUTSIDE OF AWARENESS AND BEYOND ONES DIRECT CONTROL

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