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### Table 1
Comparison of Select Features of Depression and Dementia

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Depression</th>
<th>Dementia</th>
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</thead>
<tbody>
<tr>
<td>Mood</td>
<td>Develop a persistently sad mood over a period of weeks</td>
<td>Usually normal but can become transiently unhappy in reaction to events</td>
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<tr>
<td>Sense of Guilt or Worthlessness</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Suicidal Thinking</td>
<td>Common</td>
<td>Rare</td>
</tr>
</tbody>
</table>
| Anxiety/Agitation                | - Can develop over weeks  
                                 | - Often worse in the morning                                              | - Seen as dementia progresses  
                                 |                                                                          | - Often worse in latter part of the day (sundowning) and in unfamiliar surroundings  |
| Cognition                        | - Problems with concentration and focus that develop over weeks  
                                 | - Indecisiveness and anxiety about making mistakes                      | - Progressive, gradual decline in memory and other domains  
                                 |                                                                          | - Concentration normal early on                                                  |
| Concern about Cognitive Deficits | - Seem to exaggerate severity  
                                 | - Preoccupied with deficits                                              | - Show little concern  
                                 |                                                                          | - Minimizes and often denies                                                     |
| Interest in Hobbies and Other Pleasurable Activities | Loss of interest in hobbies and formerly pleasurable activities over weeks | Gradual loss of interest and initiative over years                       |
| Physical Symptoms                | - Changes in appetite over weeks — weight can be up or down  
                                 |                                                                          | - Gradual loss of weight over years                                       |
                                 | - Over weeks can see either more or less sleep than usual  
                                 |                                                                          | - Gradual disruption of normal sleep-wake cycles                          |
                                 | - Frequent complaints of fatigue and, if depression is severe, can become “slowed down” (psychomotor retardation) | - Often less active but rare to see psychomotor retardation until dementia is advanced |
depression “helps” in dementia

INSISTS YOU FORGOT SOMETHING

REFUSES TO TELL YOU WHAT IS IT
DEPRESSION

WHAT CAUSES IT?
Like anxiety, a family history of depression may increase the risk. In addition, physical/emotional abuse, certain medications (e.g., Accutane), traumatic life events, substance abuse and social isolation can make someone more vulnerable to clinical depression.

SYMPTOMS:
- concentration difficulties
- feelings of worthlessness, and helplessness
- fatigue and decreased energy

HOW COMMON IS IT?
3% of the population has been diagnosed with depression.
Anatomy of Free Will

Researchers get their first glimpse at the human...
Depression has other pathways that are leading to dementia too.

- HPA axis dysfunction
- Chronic inflammation
- Neuretrophin signaling

- Glucocorticoids
- Pre-inflammatory cytokines
- BDNF TGF-β1

Increased vulnerability to Aβ toxicity and hippocampal atrophy

Cognitive deficit

Alzheimer’s disease
depression can lead to “dementia like” situations and dynamically is related with our immune status
Various mechanisms are leading to dementia or to “dementia like” situations, which are dynamically connected and related.
In mourning it is the world which has become poor and empty;

..in melancholia it is the ego itself....”
with stages of mourning and grief also related with PTSD and Losses
Depression is linked to autoimmunity
**TOLERANCE**
- Environmentally induced cell stress or chronic inflammation

**HOST DEFENSE**
- Failure to clear cell debris
- Loss of appropriate negative regulation
- Retroviral activation or DNA damage

**AUTOIMMUNITY**
Autoimmunity leads to the process of neuro inflammation.
Auto Abs play an important role in the final formation of AD’s Lesions
LACK OF THE CONTAINER IN CHILDHOOD

CRH & cytokine production

CRH added to primary cultures of PBMCs

- IL-6 (Th2-type immunity) release
- IFN-γ (Th1-type immunity) levels in a dose dependent manner

HPA Axis
Hormones, stress and sleep
How hormones affect sleep through our stress levels

The adrenal glands, located just above the kidneys, produce hormones that are related to stress such as adrenaline, cortisone and cortisol.

During periods of long lasting stress, the adrenocorticotropic hormone (ACTH) within the pituitary gland triggers the release of cortisone and cortisol.
CRH, stress and reproduction: effects in the development of the offspring

Vrekoussis et al. 2010

Intra-uterine CRH/stress

Fetal programming
BRAIN PLASTICITY

BRAIN PLASTICITY IS THE CAPACITY OF THE BRAIN AND OF THE NERVOUS TISSUE TO BE SHAPED, INTEGRATED AND MODIFIED, IN A STRUCTURAL AND FUNCTIONAL LEVEL, ACCORDING TO THE STIMULI OF THE HUMAN’S BODY AND ITS ENVIRONMENT.

CHANGES OF THE BRAIN’S PLASTICITY CORRESPOND TO THE DYNAMIC PROCESS OF NEURAL COMMUNICATION OF THE HUMAN’S BEING WITH ITS INTERNAL AND EXTERNAL ENVIRONMENT.

IT IS DETERMINED BY THE DYNAMIC NETWORK OF THE NEURONIC ADAPTIONS AND SYNAPSES THAT IS TIMELESS MODIFIED THROUGH THE DENDRITIC ENDS OF THE NEURONS WHICH MANY OF THEM INCREASE THUS MAKING NEW ADAPTIONS, OTHER DECREASE GIVING END TO THE COMMUNICATION.
LEVELS OF BRAIN PLASTICITY

A NEW BRAIN NETWORK EMERGES ACCORDING TO THE MODEL OF THE GROUP MATRIX THAT IS IN A CONTINUING SITUATION OF CHANGE CALLED PLASTICITY

- Brain Plasticity
- Cellular Plasticity
- Neuron Plasticity
- Synaptic Plasticity

SOCIAL BRAIN IS FORMED FROM ITS EXPERIENCES AND ACTIVITIES THROUGH ITS ACTIVATION OF THE NEURON SYNAPSES ACCORDING TO THEIR USE.
A network of facilitated synapses in a synchronous and dynamic activation corresponds to a specific representation of the external reality....

Formation of new representations of the external reality can be resulted by a selected neuron group activation.

(Mela,. C .1999)

> Memory explicit -> Cortex -> Conscious
> Memory implicit -> Limbic system -> Unconscious
> Cellular & immunologic memory -> Pregnancy
> Emotional memory
TRAUMA & THE WAYS OF FUNCTIONS OF MEMORY
(with an analogue or not to the cellular one)

IMPLICIT: Unconscious process sited in areas of the limbic system (amygdala) that encapsulates the memory of the traumatic event. It becomes conscious by a violent way (outburst, neuron discharge: eg in epilepsy \{Mela, C, “Forum Journal”1999\} or during a social conflict)

• EXPLICIT: Conscious process, related with Cognition. It is sited on the Brain Cortex.

• Memory in the endometrium life related with mother's experiences and the Social Unconscious is an Immunologic Memory and not a Brain Function (\textit{Mela et al 2012})
Left brain

Right brain
lesions in the neocortex and hippocampus
PTSD

WHAT CAUSES IT?
PTSD is an anxiety disorder. People with Post-Traumatic Stress Disorder have persistent symptoms that occur after experiencing a traumatic event such as war, rape, child abuse, natural disasters, or being taken hostage.

SYMPTOMS:
- vivid flashbacks
- nightmares & disturbed sleep
- using alcohol or drugs to avoid memories

HOW COMMON IS IT?
3% of the population has been diagnosed with post-traumatic stress disorder.
Normal brain  PTSD brain

"What happened to you wasn't even that bad"

PTSD
Figure. Interplay between cognitive and negative valence systems as relevant to violent behavior.
Comprehensive map of primate brain development reveals what makes human brains different.
Cytokine’s answers deregulates immune response

- Promotes allergic disease
- Reduces protective type 1 immunity
- Mobilizes immunosuppressive macrophages in tumours
- Antagonizes antitumour cytotoxic T cell responses
- Induces fibrosis
- Activates anti-helminth immunity
- Augments barrier defences
- Regulates tissue repair and regeneration
- Neutralizes toxins
- Suppresses type 1 autoimmune disease
- Maintains metabolic homeostasis
the suffering you see

the suffering that's never talked about
Chemical dynamics in toxicity

Chemical dynamics of Psychoneuroimmunology

Stress
Anxiety

Noradrenalin
Dopamine
Serotonin

Depression/sickness
behaviour
Immuno-suppression
Hippocampal Toxicity

Pro-Inflammatory
Cytokines

Cardiac
Inflammation

Diabetes
Osteoporosis
Balance of emotional and immune states and the common parameters
This immune and emotional link can also influence the brains’ process of ageing.
The trauma related consequences on Brain

- Delirium
- Amnesia
- Dysexecutive Syndrome
- Saliency Network
- Default Mode Network
- Central Executive Network
trauma’s neuro-degenerating consequences on synapses
The immune memory: Trauma and cellular memory (B and T cells)
Inhibition of neurotransmission in acute stress
Fig. 2. Schematic representation of the key steps in the molecular mechanisms mediating long-term potentiation in neurons. AA = arachidonic acid; NO = nitric oxide; NOS = nitric oxide synthase; AC = adenylate cyclase; RE = endoplasmic reticulum; mGluR = metabotropic glutamate receptor; PKA = protein kinase; MAPK = mitogen-activated protein kinase; PKC = protein kinase C; TyrK = tyrosine-specific protein kinase; PI3K = phosphoinositide-3 kinase.
Scheme showing the relationship between neuronal activity and neuroplasticity in the brain.

Neuronal Stimulation ➔ Neuronal Activity ➔ Synaptic Transmission ➔ Neurotrophic Factor ➔ Modulation Synapse ➔ Neuroprotection ➔ Plasticity ➔ Morphology, Number, Strength, Efficiency
Synaptic Strengthening: Long-Term Potentiation

A

B

C

D

LTP in the dentate gyrus

LTD in area CA1

LTP and heterosynaptic LTD in DG
Synaptic strength measured using the AMPAR/NMDAR ratio.

a Basal/control state

AMPAR/NMDAR ratio = 0.4

b LTP

AMPAR/NMDAR ratio = 1.0

+40 mV

AMPAR EPSC  NMDAR EPSC
Well-described forms of LTP and LTD.
Patient-Analyst’s Relationship = A Strong Predictor of Response to any Therapy
What psychotherapy offered to these patients?

1. The psychotherapeutic sessions have created a new and a safe container where anxiety, stress and distress have been managed >> HPA axis, CRH, Levels of cortisole and ILs

2. During the psychotherapeutic sessions they felt that they have finally found in life the space to express their selves, to create and also the place to share their feelings.

3. The psychotherapeutic sessions provided a new orientation to time, place and persons thus functioning as a “restart” in their brains’ function and orientation according to the “here and now” situation, in treatment.

4. Corrective Emotional Experience >> synaptic strengthening / synaptic plasticity / neuroprotection

5. Working with past traumatic experiences and painful memories, implicit memories became explicit and conscious, thus bringing information to a conscious or pre-conscious level by dreams and many emotions >> “a trip from amygdala to the cortex”

6. The creative components of a Psychotherapeutic session such as sensibility and Flexibility, Adaptation and Reciprocal Trust lead not only to a Social Positive Learning but also to a somatic relaxing feedback.
Window of Tolerance

Hyperarousal Zone

2. Sympathetic “Fight or Flight” Response
Increased sensations, flooded
Emotional reactivity, hypervigilant
Intrusive imagery, Flashbacks
Disorganised cognitive processing

Window of Tolerance
Optimal Arousal Zone

1. Ventral Vagal “Social Engagement” Response
State where emotions can be
tolerated and information
integrated

Hypoarousal Zone

3. Dorsal Vagal “Immobilisation” Response
Relative absence of sensation
Numbing of emotions
Disabled cognitive processing
Reduced physical movement

Adapted from Ogden, Minton, & Pain, 2006, p. 27, 32; Corrigan, Fisher, & Nutt, 2010, p. 2
The new real time brain-feedback, during Psychotherapy, reduces lapses of attention.
“talking therapies” not only ameliorate MCI’s symptoms
Small Worlds from Large Networks

Waves of electrical activity sweep across the brain, even when it is at rest. A number of studies now try to map these neural patterns because they may play a critical role in mental life. Patric Hagmann of the University of Lausanne in Switzerland and Olaf Sporns of Indiana University have charted the brain with a technique called diffusion tensor imaging. They found that the dense network of connections (left) has a few well-connected hubs (red dots) through which many links pass (below). Such "small-world" networks of hubs may help our brains process information more rapidly and allow the organ to maintain its structural integrity efficiently.
4 SPECIFIC THERAPEUTIC FACTORS
(Eve Lewes, 1944) RECOVERY FROM ORGANIC TRAUMA.

1. The group situation fosters Social Integration and Relieves Isolation: neuron and synaptic reparation

2. “Mirror Reaction”: visual brain pathway

3. “Resonance”: acoustic brain pathway

4. Activation of the Collective Unconscious: from amygdala to cortex

5. Exchange between the members of the Group: selected neuron activation and reconnection
IMPORTANT REMARKS

PSYCHOTHERPY HELPS FEELINGS TO BECOME CONSCIOUS:

- The asymmetry of the hemispheres of the brain in structure and during its function is determinant to the establishment of the communication, in a qualitative and quantitative analysis and modification.

- The conscious mechanisms foster communication.

- *The Corpus Callosum* creates is the link of the hemispheres (known as the “center of the soul”)*
Clear memories can re-shape brain’s better connectivity
Various forms of despair as seen on the 3rd May 1808 in the painting by Xavier de Salas Goya.
Thus “protecting” brain from trauma and PTSD related consequences.
Phases of medical traumatic stress*

Three stages of response with different implications for intervention.

I. Peri-Trauma
- Potentially traumatic event
  - OBJECTIVE
- Perception of event
  - SUBJECTIVE
- Address child’s experience of event

II. Early (Evolving) Responses
- Acute traumatic stress
  - Pain
  - Uncertainty
  - Loss
  - Others’ reactions...
- Address immediate needs
  - Reduce distress
  - Prevent PTSD symptoms

III. Long-term
- Persistent PTSD symptoms and other distress
- Treat PTSD and other ongoing distress

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Breakdown in communication in mind or from mind to mind (isolation)
Cut in neurons’ communication
(resignation)
Resulting an influence on our immune homeostasis and tolerance
And on brains’ architecture
Matrix is an analogue of the neuron web (S.H Foulkes)
Abnormal relationships deregulation
• Introjection of new relationships ↔
  selective neuron
group stimulation
“talking therapies” not only ameliorate MCI’s symptoms
But can modify our brain plasticity
By creating new wired brain circuits
Like dopamine’s and serotonin’s secretion
Thus modifying neurotransmission too
By inaugurating new paths of intervention by selected neuron group stimulation
Where Psychotherapy could more intervene..
This illustration depicts areas of the brain that are activated in children when they listen to stories. The brain areas in blue are activated in sighted children. They include the prefrontal cortex and lateral temporal cortex. Orange is the part of visual cortex that responds to language only in blind children.
THANK YOU FOR YOUR ATTENTION!