Mood and Motivation in Parkinson’s Disease

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Learning objective:

• What is mood and the biology of mood.

• Changes in mood and motivation in Parkinson’s disease

• Treatment of mood disorders in Parkinson’s disease.
The Clinical Spectrum of Parkinson’s disease

**Motor Symptoms**
- Tremor
- Slow movement
- Muscular stiffness
- Problems with gait and balance
- Loss of facial expression
- Problems with speech and swallowing

**Non motor symptoms**
- Changes in mood and motivation
- Problems with memory and thinking
- Hallucinations
- Impulse control disorders
- Constipation
- Urinary problems
- Dizziness when standing
- Insomnia
- Acting out of dreams

Parkinson’s disease
What is Mood?

• Mood – a state of mind or feeling that is appropriate to the situational stimuli.

• Mood is a transient process and changes based on the stimuli and the situation.

• Mood disorder – mood that is persistently inappropriate or extreme in relation to the situational context.
The Biology of Mood

Chemical:

- 3 main neurotransmitters involved
  - Dopamine
  - Serotonin
  - Norepinephrine

- Regulate mood, motivation and reward, appetite, sex drive, sleep, arousal and physical symptoms associated with mood.

- Other chemical involved:
  - Acetylcholine – attention and working memory
  - Glutamate – excitatory neurochemical involved in stabilization of cell energy

Structural:

- Amygdala – understanding the emotional significance of different stimuli and experiencing emotions
- Prefrontal cortex – regulating and controlling emotions
- Ventral striatum – motivation, reward and learning
Other factors that can affect mood:

- Genetic vulnerability
- Stress
- Traumatic life events
- Inflammation
- Other medical problems – thyroid disease, anemia, low sodium or vitamin B12 deficiency, chronic infections.
- Medications – anti-seizure medications, blood pressure medications, sedatives, PD medications

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Changes in mood and motivation in Parkinson’s disease

- Transient anger, frustration, irritability, demoralization are common feelings in Parkinson’s disease.

- Disorders of mood and motivation, such as depression, anxiety or apathy may be more common in those with PD than with other medical conditions.

- Can occur at any stage – at diagnosis or as symptoms progress. Can also be a symptoms of medications wearing off. Predate motor symptoms in about 20-30% patient with mood disorders.

- Mood disorders associated with increased disability, worse quality of life and caregiver distress.
Changes in mood and motivation in Parkinson’s disease

• Depression and anxiety can be an emotional response to diagnosis and living with PD.

• Mood disorders also thought to have a biological basis:
  
  ➢ Reduction in levels of dopamine, serotonin, norepinephrine and their metabolites in the brain.

  ➢ Impaired activation and connectivity between prefrontal cortex, amygdala and ventral striatum on resting state fMRI
Depression

• Most common psychiatric disorder in PD (25-50% of PD patients)

• Depression can overlap with other symptoms of PD – psychomotor slowing, loss of facial expression, insomnia, loss of energy.

• Increased risk:
  – Women > men
  – Advanced stage of PD
  – Patients with cognitive problems

• In most mild to moderate depression. < 20% have severe depression.

• Non motor symptom most correlated with poor quality of life.

• Can affect long-term outcomes by causing social withdrawal, lack of exercise, more reluctant to seek care.
Symptoms of depression (DSM-5 criteria)

- Persistent sadness
- Feelings of hopelessness or pessimism
- Feelings of guilt, worthlessness or helplessness
- Loss of interest or pleasure in daily activities
- Diminished ability to concentrate or indecisiveness
- Psychomotor agitation
- Significant change in weight (loss or gain)
- Insomnia or excessive sleeping
- Recurrent thoughts of death or suicide

*Symptoms present for at least 2 weeks and are a change from previous functioning*
Anxiety

• Occurs in 20-40% of PD patients.

• Often occurs together with depression but can occur in isolation

• Can manifest in several ways:
  - Generalized anxiety
  - Panic attacks – unprovoked or during periods of medication wearing off
  - Agoraphobia
  - Social phobia

• Can worsen motor symptoms such as tremor
Symptoms of Anxiety

• Excessive feelings of fear, nervousness or worry associated for at least 6 months associated with at least 3 other symptoms:
  ➢ Restlessness or frequently feeling on edge
  ➢ Easily fatigued
  ➢ Difficulty concentrating
  ➢ Frequent irritability
  ➢ Increased muscle tension
  ➢ Sleep disturbance

• Patient may also experience physical symptoms such as unexplained bouts of nausea, shortness of breath, racing heart or sweating that occur for no reason

• Symptoms cause distress or impairment in functioning

• Not attributable to other condition or medication
Treatment of depression and anxiety in PD

• Adequate treatment of motor symptoms of Parkinson’s.

• Medications – antidepressants, anxiolytics

• Therapy or counseling – i.e. talk therapy

• Lifestyle changes – regular exercise, social activities, support groups

• Other interventions – relaxation techniques, biofeedback, meditation, massage, acupuncture, aromatherapy
Medications:

- **Tricyclics – 1st generation**
  - Nortriptyline, doxepin, desipramine, imipramine
  - May be slightly helpful in tremor. May help sleep
  - Potential side effects – dry mouth, urinary retention, constipation, sedation and confusion, lowering of blood pressure
  - Avoid use if cardiac problems, narrow angle glaucoma
  - Highly lethal in overdose

- **Selective serotonin reuptake inhibitors (SSRIs)**
  - Increase serotonin levels
  - Sertraline (Zoloft), citalopram (Celexa), escitalopram (Lexapro), paroxetine (Paxil), fluoxetine (Prozac)
  - Possible side effects – nausea, may aggravate tremor, changes in weight, sexual dysfunction.

- **Selective norepinephrine reuptake inhibitors (SNRIs)**
  - Increase both serotonin and norepinephrine
  - Venlafaxine (Effexor), duloxetine (Cymbalta)
  - Also help with neuropathic type pain
Medications:

• Other atypical antidepressants:
  - Bupropion (Wellbutrin) – increases norepinephrine and dopamine activity. Most activating antidepressant. Least likely to cause sexual side effects.
  - Mirtazapine (Remeron) – enhances release of norepinephrine and serotonin by different mechanism. Can stimulate appetite and improve sleep

• Other treatments for anxiety:
  - Buspirone (Buspar) – directly stimulates serotonin receptors
  - Benzodiazepines –
    - Alprazolam (Xanax), lorazepam (Ativan), clonazepam (Klonopin), diazepam (Valium)
    - Stimulate inhibitory GABA receptors in the brain
    - Fast-acting, good for episodic anxiety
    - Drawback – tolerance, dependence, sedation. Long-term may be associated with dementia.
MAO-B Inhibitors and SSRIs

- MAO-B Inhibitors – selegiline, rasagiline
- Labeling on MAO-B inhibitors stress caution when combining with antidepressants.
- Potential risk of serotonergic syndrome (serotonin excess)
  - Agitation and restlessness
  - Confusion
  - High blood pressure and rapid heart rate
  - Diarrhea
  - Muscle twitching, worsening tremor
- Pooled analysis of 8 studies:
  - no cases of serotonin syndrome > 1,500 patients taking rasagiline and SSRIs
  - 11 cases of serotonin syndrome in > 4,500 patients taking selegiline and SSRIs

Non-Pharmacological Approach

• Psychotherapy - Cognitive Behavioral Therapy (CBT):
  - Helps people better understand their illness
  - Helps you recognize patterns of negative thoughts
  - Teaches coping skills and how to think positively

• Complementary Therapies:
  - Meditation and mindfulness
  - Music therapy
  - Massage therapy
  - Light therapy
Exercise and mood

• Robust efficacy in the treatment of mood symptoms in the general population.

• Moderate aerobic activity and resistance training shown to significantly improve depression and anxiety in Parkinson’s.

• Also improves sleep and appetite.

• Improves concentration and memory.

• Lowers stress and inflammation
The Gut Microbiome and Mood

- Bi-directional communication between the gut and the brain

- In animal studies, transplantation of gut bacteria from animal expressing depressive behavior into normal animals produced similar behavior.

- In humans, severe interventional trials have shown that a mainly plant-based diet or Mediterranean diet has shown improvement in depression.
Other FDA Approved Therapies

• Electroconvulsive Therapy:
  ➢ Electric current applied through the scalp
  ➢ Effective in severe or refractory depression
  ➢ May also help motor symptoms
  ➢ Drawbacks – requires general anesthesia, temporary confusion and/or short-term memory problems.

• Repetitive transcranial magnetic stimulation (rTMS)
  ➢ Non-invasive coils to produce magnetic pulses that stimulate specific brain regions

• Vagus nerve stimulation (VNS)
  ➢ Surgically implanted pacemaker-like device that electrically stimulates the vagus nerve in the neck
  ➢ Not an immediate effect
Pseudobulbar Affect

• Described as brief episodes of emotional lability that do not match a person’s feelings or situation.

• Uncontrollable or inappropriate laughing or crying

• Frequently mistaken for depression

• Damage to brain areas that control normal expression of emotion.

• Can cause stress or frustration or avoidance of social interaction due to lack of emotional control.

• Nuedexta – only FDA-approved therapy
Apathy

• Greek phrase meaning “without passion”

• A state of indifference, characterized by lack of interest or motivation in the world around oneself.

• In contrast to depression, a person with apathy lacks emotion. No feeling of sadness, guilt or hopelessness.

• Apathy can occur on its own or can co-exist along with depression or cognitive problems.
The different dimensions of apathy

• **Cognitive/Behavioral:**
  - Little or no-goal directed behavior, inability to “get up and go”
  - Trouble initiating activities/tasks, needs to be prompted
  - Loss of curiosity in learning new things

• **Emotional:**
  - Emotional indifference or inability to express emotion
  - Lack of passion related to activities or situations that previously provoked emotion
  - Less empathy toward feelings of others

• **Social:**
  - Less interest in participating in social or leisure activities
  - Less interest in family or interest in meeting new people
  - Less participation in conversation
  - Reduced spontaneous interactions with others
The Effects of Apathy

• On the patient:
  - Can have negative effects on physical and mental health
  - Lack of motivation to participate in exercise or rehab
  - Withdrawal from hobbies and social activities
  - Lack of self-awareness therefore do not seek help or understand why those around them are frustrated

• Family and caregivers
  - Can put a strain on relationships
  - A person with apathy may be thought to be lazy, defiant, unwilling/not wanting to help themselves.
  - Sensation that patient does not want to spend time or care about their feeling
Treatment of Apathy

• No approved therapies

• Medications that may be helpful:
  - Dopaminergic therapy – levodopa, dopamine agonists
  - Rivastigmine
  - Antidepressants that activate dopamine and enhance cholinergic function

• TMS
Coping with Apathy – non-pharmacological approaches

• Maintain a regular schedule of structured activities:
  ➢ Focus on more relevant activities first – medical and therapy appointments
  ➢ Chores, household duties
  ➢ Keep a calendar and check tasks off as they are done

• Avoid isolation:
  ➢ Schedule time with family and friends
  ➢ Support groups

• Tips for caregivers:
  ➢ Be patient
  ➢ Provide positive feedback when goals are reached.
In Summary

• Mood is a state of mind associated with environmental situations.

• Regulation of mood is a complex interplay of brain chemicals and connections.

• Mood changes are common in Parkinson’s disease.

• Mood disorders can be a reaction to the diagnosis and living with Parkinson’s disease but is thought to have a biological basis.

• Treatment option for mood disorders include medications, psychotherapy, lifestyle changes, complementary therapies.

• Other procedures are FDA approved for severe or refractory depression.