Postoperative Cognitive Dysfunction in Older Adults

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Surgery in Individuals Age 65+
- Surgery is common in older adults:
  - ~50% of all surgeries are performed on pts over the age of 65
  - Half of all individuals ≥ 65 years will have at least 1 surgery in the remainder of their lifetime
  - By 2040, people >65 will constitute nearly ¼ of the population

Possible Benefits
- Surgery can be very beneficial:
  - Can Reduce Pain
  - Can Reduce Medication & Side Effects
  - Can Save Lives
  - Can Improve Quality of Life

Possible Risks
- Surgery can have risks:
  - Death
  - Disappointment
  - Cognitive Deficits
    - Postoperative Cognitive Dysfunction (POCD)
  - Loss of Quality of Life

What is POCD?
- POCD defined as:
  - Reported cognitive decline
  - Corroborated by formal testing
  - Onset shortly after surgery
  - Can be short-term
  - Can be chronic
  - Can be progressive

Potential Causes of POCD
- What specifically causes POCD?
POCD Due to Postoperative Recovery
- Postoperative recovery often involves:
  - Lingering effects from anesthesia
  - Pain medications
  - Infection from surgery
  - These known issues can cause immediate or semi-immediate cognitive difficulties

- When this occurs and it can cause abrupt and significant behavioral and cognitive changes:
  - Delirium
    - Possible Symptoms:
      - Significant fluctuations in alertness and clarity
      - Significant memory and thinking disturbances
      - Hallucinations
      - Delusions

Delirium
- Occurs in about 40% of older adults after surgery
  - Compared to:
    - ~30% middle age (40-59)
    - ~35% young adult (18-39)
  - Usually transient
    - Symptoms often resolve when underlying issue is resolved

Case Example 1
- A seemingly healthy 71-year-old female underwent knee surgery because it was limiting her ability to walk. She underwent anesthesia, there were no complications during the surgery, and the surgery was successful. After regaining consciousness after the surgery, the patient's family noticed a significant change in her. She was confused, she was talking to her deceased parents, she thought the nurses were trying to harm her, and she didn't seem to know her family. Over the next couple of days, there would be times where she would seem attentive and clear in her thinking but then there would be other times when she would be very confused and "out of it." A week later, however, her thinking returned to normal. Her thinking has remained normal since that time.

Case Example 2
- A seemingly healthy 59-year-old male underwent a surgery to remove a fairly large cyst from his body. He underwent local anesthesia, there were no complications during the surgery, and the surgery was successful. There were no immediate issues with his thinking or memory at all. About a week and a half later, though, he began becoming very confused and thinking that his wife was cheating on him. His wife took him to the hospital where it was found that he had an infection due to not caring for his surgical wound correctly. The infection was treated with an antibiotic and he was provided with adequate care for his wound. A few days later, he was acting and thinking normally again.

Summary
- Issues relating to postoperative recovery can cause:
  - Abrupt and significant changes in thinking and behavior
  - The changes are known/suspected to be linked to some physical source (anesthesia, medication, infection)
  - The changes often go away over a relatively short time period after treatment
POCD Due to Surgical Insult

- Surgery often involves:
  - Altering blood flow throughout the body
  - A loss of blood
  - Need for oxygen saturation

- If these issues occur during surgery, they can cause cognitive difficulties

POCD Due to Surgical Insult

- When this occurs and it causes rather abrupt and long-standing cognitive changes

- Symptoms:
  - Often less significant than with delirium
  - Hallucinations and delusions are unlikely
  - Often consistent, permanent difficulties
  - Cognitive difficulties are generally in:
    - MPS, Attn, Memory, Exec Fx

POCD Due to Surgical Insult

- Most Common after Cardiac
- Also Common after Other Major Surgeries

- Can occur in up to 25%
  - Frequency is not significantly more likely to occur in older adults than younger adults
  - But older adults are more likely to have these surgeries

- Again, often stable and permanent

Case Example

The patient was a 70-year-old male who underwent heart surgery. He underwent anesthesia, there were no complications during the surgery, and the surgery was successful. After regaining consciousness, the patient seemed to be fairly clear in his thinking and was discharged home soon after. Since that time, though, he has noticed that he has had difficulty paying attention consistently, finding words when talking, and thinking quickly (his wife, in particular, indicated that he seems to stare at her for a few seconds before responding). This hasn’t gotten any better over time but it hasn’t gotten any worse either. The patient is still able to do things around the house, he is just slower, less detail focused, and makes more errors.

Summary

- Issues relating to surgical insults can cause:
  - Abrupt changes in thinking
  - Often less significant than with delirium but still noticeable
  - The changes often stay permanently
POCD Due to Other Factors

- Unlikely POCD due to Postoperative Recovery
  - Sudden changes that go away rather quickly
  - Can occur in any age group
  - Delirium
- Unlike POCD due to Surgical Insults
  - Sudden changes that permanently stay
  - Can occur in any age group
  - Stroke, Hypoxic Brain Injury, etc.
- POCD due to Other Factors is often different
  - A decline that worsens over time
  - Only occurs in older adults!
  - ~10% of the time
  - Dementia

What are these Other Factors?

Thought to possibly be:

1. Anesthesia
2. Systemic Inflammation
3. Genetic Predisposition
4. Exacerbation of Pre-Existing Cognitive Deficits

POCD Due to Other Factors

- Some evidence that anesthesia can negatively affect the release of certain neurotransmitters including acetylcholine
  - Acetylcholine is important for memory, and acetylcholine levels severely decline with Alzheimer’s dementia
  - Even outside of dementia, though, acetylcholine levels naturally decline with aging
  - So, if anesthesia affects acetylcholine, especially in individuals with low levels already, you might see memory decline

POCD Due to Other Factors

- Research has also suggested that anesthetics can increase β-amyloid protein in the brain
  - Excessive β-amyloid protein has been found to play a fundamental role in Alzheimer’s disease
  - 90% of all AD patients have excessive β-amyloid
  - Excessive β-amyloid protein is thought to be a cause of AD
  - So, if anesthesia causes increased β-amyloid, it might be contributing to the onset of AD

POCD Due to Other Factors

1. Anesthesia

Caveats:

- The anesthesia in the research generally refers to high doses of powerful anesthetic agents
  - As opposed to small doses of milder forms
  - Additionally, the longer the anesthesia duration, the great the risk is thought to be
POCD Due to Other Factors

Anesthesia can also:
- Reduce cerebral blood flow
- Reduce oxygen delivery to the brain
- Alter cerebral metabolism
- Thus, causing an insult to the brain, which could exacerbate an emerging dementia

POCD Due to Other Factors

- So anesthesia might reduce acetylcholine, increase β-amyloid, or cause insults to the brain.
- However, there are indications that anesthesia might not be the culprit (or the only culprit)

2. Systemic Inflammation
- Inflammation involves:
  - a release of bodily chemicals
  - that helps to eliminate an injurious agent and to remove damaged tissue components
  - so that the body can heal
- This occurs naturally after surgery, infections, injuries, etc.

POCD Due to Other Factors

- Unfortunately, when the body has excessive inflammatory chemicals, the chemicals can affect the brain and negatively impact memory
- Animal studies have found that neuroinflammation due to trauma leads to prolonged sickness behavior and cognitive decline in aged mice
- A human study found that elevated levels of inflammatory markers in CSF after coronary artery bypass surgery predicted cognitive decline

POCD Due to Other Factors

- Furthermore, researchers examined the impact of inflammation from pneumonia on cognition
  - Outside of surgery
  - They found:
    - Pts with pneumonia were more likely to cognitively decline and eventually develop dementia

POCD Due to Other Factors

- However, there are indications that inflammation might not be the culprit (or the only culprit)

3. Genetic Predisposition
- Studies have examined APOE E4 allele (a gene associated with AD) and it's association with POCD
  - Studies have been mixed but the largest found no significant association
  - More studies are recommended

POCD Due to Other Factors

- However, the current evidence for a genetic predisposition is small

4. Exacerbation of Pre-Existing Cognitive Deficits
- It is thought that the individuals who develop POCD might have a very early dementia that is either not yet behaviorally expressed or is not yet recognized by others
- Very few studies and the results are mixed
**POCD Due to Other Factors**

- What is known about this form of POCD is that:
  - Only occurs in older adults
  - Likelihood is ~10%
  - The reason for it is unclear but anesthesia, inflammation, a genetic predisposition, and a very early dementia might all contribute to various degrees
  - A consistent risk factor is increasing age

**Case Example 1**

The patient was an 88-year-old male who did not appear to have any significant cognitive difficulties prior to undergoing hip surgery. During his surgery, he underwent anesthesia, there were no complications, and the surgery was successful. After regaining consciousness, the patient was very confused but this confusion improved over time. Unfortunately, the patient did not return to his presurgical cognitive baseline. Additionally, over time, the patient's memory continued to decline. Three years after the surgery he was formally assessed for dementia and the results were consistent with AD. He, unfortunately, continued to experience progressive cognitive decline going forward.

**Case Example 2**

The patient was a 73-year-old male who had mild memory difficulties prior to undergoing back surgery. During his surgery, he underwent anesthesia, there were no complications, and the surgery was successful. After regaining consciousness, the patient was not confused but his memory seemed to have declined further than what it was. Neuropsychological testing was consistent with AD. An MRI of the brain did not show a stroke or any other kind of insult. Unfortunately, he continued to experience progressive cognitive decline going forward.

**Overall**

- **POCD due to Postoperative Recovery**
  - Sudden changes that go away rather quickly
  - Can occur in any age group
  - Happens ~40%
- **POCD due to Surgical Insults**
  - Sudden changes that permanently stay
  - Can occur in any age group
  - Happens ~25%
- **POCD due to Other Factors**
  - A dementia that worsens over time
  - Only occurs in older adults
  - Happens ~10%
- **No Long-Standing POCD**
  - Happens ~75%

**“It appears that a subset of the elderly population stands at the top of a “slippery slope,” vulnerable to prolonged or permanent cognitive decline after surgery. It is not currently possible to identify which patients are at particular risk, or which elements of the process of hospitalization, anesthesia, surgery, and postoperative care may be precipitating the deterioration. At present it is incumbent upon anesthetists, surgeons, and all involved in the perioperative care of elderly patients to consider the risk of POCD whenever surgery is contemplated and to discuss the issue with patients and their families. For some patients and some procedures, consideration of these risks may “move the goalposts” such that they no longer consider the proposed operation to be in their best interests.”**

-Tsai et al. (2010). An Update on Postoperative Cognitive Dysfunction. Advanced Anesthesia

Thank you!