# Effect of Dexmedetomidine on Postoperative Cognitive Dysfunction and Neuroprotection in the Elderly

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## Abstract


- Postoperative cognitive dysfunction (POCD) is a complication that has a reported incidence of 7% to 71% at 7-8 postoperative days, and 6% to 56% at 42-84 days [5] in elderly patients and predisposes adverse outcomes.
- Recently, dexmedetomidine, a highly selective alpha-adrenergic receptor agonist, has been shown to suppress the inflammatory response perioperatively and prevent cortical apoptosis.
- Evidence has demonstrated that the use of intravenous dexmedetomidine has decreased the incidence of postoperative cognitive dysfunction and improved outcomes following surgery in geriatrics.
- The mechanism of neuroprotection through the use of dexmedetomidine, may ameliorate cognitive dysfunction in elderly patients who have undergone general anesthesia.


## Objectives

- To evaluate whether the use of dexmedetomidine is associated with decreased incidence of postoperative cognitive dysfunction in geriatric patients undergoing general anesthesia for noncardiac surgery.
- To investigate the neurocognitive protection effects of dexmedetomidine.
- To consider the mechanism of neuroprotection with the use of dexmedetomidine in elderly patients.
- To determine whether the use of dexmedetomidine intraoperatively can shorten the recovery time from anesthesia and improve outcomes after surgery in the elderly.

## Methods

- Reviewed and analyzed scientific articles published until 2016.
- Inclusion Criteria: only evaluated studies that
  - Assessed the effects of intravenous administration of dexmedetomidine on incidence of POCD in comparison to a control group that received intravenous administered normal saline.
  - Used general anesthesia for noncardiac surgery.
- Exclusion criteria: ages <60 or >92, preoperative heart rate < 45 bpm, preoperative mean arterial pressure < 60 mmHg, sedatives or analgesics recently received, history of neurological disease, and ASA 4, 5, 6.
- Animal studies evaluating the protective effects of dexmedetomidine against POCD in aged mice and rats undergoing general anesthesia were reviewed to consider the possible mechanism of action of dexmedetomidine.

## Animal Model Studies

- POCD in aged rats was shown to be a result of increased expression of proapoptotic proteins and an increased release of proinflammatory factors.
- Administration of dexmedetomidine to rats resulted in decreased proapoptotic proteins (Fas, caspase-8, caspase-9), an increase in antiapoptotic protein Bcl-2 [6], and decreased release of proinflammatory factors (IL-1B, TNF-**α**) [4].
- Increased survival of hippocampal neurons decreased POCD occurrence.

## Retrospective Human Studies

- Inflammatory cytokines TNF-**α** and IL-6 levels were shown to be positively correlated with POCD occurrence.
  - Dexmedetomidine has shown to have anti-inflammatory activity and decrease levels of TNF-**α** and IL-6.
- It potentially works by decreasing inflammatory cytokine secretion through lipopolysaccharide-induced apoptosis by binding **α**2-adrenoceptors in presynaptic membrane and activating cholinergic anti-inflammatory pathways.
- Lower MMSE scores correlated with having POCD. Administration of dexmedetomidine correlated with higher postoperative MMSE scores and a decrease in POCD [1].
- Suppression of the inflammatory response by dexmedetomidine is suggested to be the reason for higher MMSE scores [3].

| | Cases size (n) | MMSE | | POCD (n, (%)) |
|---|---|---|---|---|
| | | Before surgery | After surgery | |
| Dex group | 87 | $28.24 \pm 5.18^{\#}$ | $25.86 \pm 4.10^{*,**}$ | $8\ (9.20)^{**}$ |
| Control group | 61 | $28.51 \pm 5.42$ | $23.29 \pm 4.59^{*}$ | 13 (21.31) |

$^{*}P < 0.05$ *vs* before surgery;
$^{**}P < 0.05$ *vs* control group;
$^{\#}P > 0.05$ *vs* control group.

**Table 1:** MMSE and incidence of POCD [2]

| quartile division | Cases size (n) | IL-6 (ng/L) | POCD (n (%)) |
|---|---|---|---|
| q1 | 22 | $57.96 \pm 10.16$ | 0 (0.00) |
| q2 | 22 | $65.27 \pm 10.62$ | 1 (4.55) |
| q3 | 22 | $70.34 \pm 11.82$ | 2 (9.09) |
| q4 | 21 | $83.24 \pm 14.82$ | 5 (22.73) |

**Table 2:** Relationship between POCD and the quartile divisions of IL-6 [2]

| | Cases size (n) | IL-6 (ng/L) | | TNF-α (ng/L) | |
|---|---|---|---|---|---|
| | | Before surgery | After surgery | Before surgery | After surgery |
| Dex group | 87 | $49.44 \pm 9.25^{\#}$ | $69.04 \pm 12.14^{*,**}$ | $45.28 \pm 8.99^{\#}$ | $64.82 \pm 9.71^{*,**}$ |
| Control group | 61 | $51.02 \pm 10.49$ | $86.48 \pm 13.51^{*}$ | $46.20 \pm 9.42$ | $75.74 \pm 10.39^{*}$ |

$^{*}P < 0.05$ *vs* before surgery;
$^{**}P < 0.05$ *vs* control group;
$^{\#}P > 0.05$ *vs* control group.

**Table 3:** Levels of IL-6 and TNF-a before and after surgery [2]

## Discussion

- The use of dexmedetomidine demonstrated neuroprotection by suppressing the release of proinflammatory factors and neuronal apoptosis.
- Conflicting results from human and animal studies on the mechanism of neuroprotection with the use of dexmedetomidine warrant further investigation into how this drug regulates the release of proapoptotic proteins and proinflammatory factors in order to better understand the apoptotic role in POCD.
- Despite this difference, literature still shows that continuous perioperative intravenous administration of dexmedetomidine decreases the incidence of POCD in aged patients undergoing general anesthesia, thereby resulting in improved postoperative outcomes.
- Incidence of POCD varies with existing literature because of multiple associated risk factors promoting POCD related to patient comorbidities, duration and invasiveness of surgery, and anesthesia. These factors permit further investigation in their role in POCD [5].
- More consistent post-op testing with MMSE, or other neurological testing, is advised in order to differentiate POCD from delirium.

## References


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