Antinociception versus neurocognitive effect of biased mu-opioid receptor oliceridine versus morphine – Utility Function Analyses

1. Morphine and oliceridine have different molecular effects despite both acting at the mu-opioid receptor:
   1. Morphine activates TOLL-like receptor 4 on microglia cells, causing a proinflammatory response, possibly causing neurocognitive effects. Oliceridine has a lesser effect at these receptors.
   2. Oliceridine, but not morphine, is biased towards the G-protein intracellular pathway, causing less respiratory depression (See diagram 2).

2. Utility Function Analyses

Utility = \( P(B) - P(H) \)

3. The utility function of antihypertensive therapy

- motor instability (inability to mobilize or a high likelihood of falling)
- dizziness/lightheadedness
- memory loss and confusion
- delirium
- progression of already existing cognitive impairment

4. Opioid-induced neurocognitive dysfunction is an important opioid adverse effect

Conclusions: These utility data indicate that over the clinical concentration range, oliceridine is an analgesic with a favorable safety profile over morphine when considering analgesia and neurocognitive function.