

Supplementary

The rationales for the biomarkers selected

1. The rational for the choice of TNF- α

Surgery activates the innate immune system resulting in release of proinflammatory mediators (TNF- α , IL-1 and IL-6). However, ketamine could suppress nuclear factor- κ B expression involved in the transcription of genes encoding the proinflammatory cytokines tumour necrosis factor (TNF- α). [1]

2. The rational for the choice of BDNF

BDNF has a role in increasing synaptic plasticity and synaptic function. Reviews have suggested that brain-derived neurotrophic factor (BDNF) improved memory function, reversed age-related changes in brain and prevented cell death. [2] Furthermore, ketamine requires brain-derived neurotrophic factor (BDNF) signals to exert antidepressant effects. [3]

3. The rational for the choice of acetylcholine

Acetylcholine is thought to be involved in the neuroplasticity, and is present in several neural pathways responsible for arousal, attention and memory. [4] However, ketamine could increase cholinergic tone that may contribute to the improvement of cognition. [5]

References

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- [5] Hambrecht-Wiedbusch VS, Li D, Mashour GA. Paradoxical Emergence: Administration of Subanesthetic Ketamine during Isoflurane Anesthesia Induces Burst Suppression but Accelerates Recovery. *Anesthesiology.* 2017;126(3):482-494.