General anaesthesia: from molecular targets to neuronal pathways of sleep and arousal.



General anaesthesia



Loss of consciousness in humans occurs over a very narrow range of anaesthetic concentrations and correlates with loss of the righting reflex in rodents



Schema: left-1 subunit of GABA A receptor, right-5 subunints simmetrically surrounding the channel, passing Cl into the cell.



## Schematic representation of the structure of a two-pore K+ channel.



The NMDA receptor is one of the main mediators of excitatory neurotransmission. The binding of both glutamate and glycine activates this receptor. The receptor is a ligand gated ion channel, which permits the movement of calcium, sodium and potassium across the postsynaptic membrane. The NMDA receptor is composed of the main NMDAR1 sub-unit and four additional sub-units - NMDA-R2A, NMDA-R2B, NMDA-R2C and NMDA-R2D sub-units.



Three key molecular targets and some known determinants of their anaestethic sensitivities

## a Awake versus minimally conscious



c Propofol LOC



**b** NREM sleep



d Sevoflurane LOC



Functional brain imaging reveals similarities between anaesthetic-induced loss of consciousness and deep natural sleep.



Expanded trace of oscillatory activity of thalamocortical neurons and the proposed currents that largely mediate it.



Figure 4 Thalamic oscillations

## Thank you for the attention!!!