Procedural Sedation and Analgesia in Children

An Essay

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- **AAP**: American academy of pediatrics
- **ACC**: Anterior cingulate cortex
- **ASA**: American society of anesthesiologists
- **BP**: Blood pressure
- **cGMP**: Cyclic guanosine monophosphate
- **CGRP**: Calcitonin gene related protein
- **CNS**: Central nervous system
- **COX**: Cyclo-oxygenase
- **CT**: Computed tomography
- **ECG**: Electrocardiography
- **GABA**: Ɣ-aminobutyric acid
- **GIT**: Gastrointestinal tract
- **HR**: Heart rate
- **IC**: Insular cortex
- **ICU**: Intensive care unit
- **IV-PCA**: Intravenous patient-controlled analgesia
- **LDT**: Laterodorsal tegmental nucleus
- **MOAA/S**: Modified Observer Assessment Sedation Score
- **MRI**: Magnetic resonance imaging
- **NMDA**: N-methyl-d-aspartate
- **NO**: Nitric oxide
- **NREM**: Non rapid eye movement
- **NRM**: Nucleus raphe magnus
- **NRS**: Numerical rating scales
- **NSAIDs**: Non steroidal anti inflammatory drugs
- **OAA/S**: Observer's Assessment of Alertness/Sedation Scale
- **PACU**: Post-anesthesia care unit
- **PAG**: Periaqueductal gray
- **PICU**: Pediatric intensive care unit
- **PO**: Per os (By mouth)

- **PPT**: Pedunculopontine tegmental nucleus
- **PRIS**: Propofol infusion syndrome
- **PSA**: Procedural sedation and analgesia
- **REM**: Rapid eye movement
- **RSS**: Ramsay Sedation Scale
- **SpO_2**: Saturation of peripheral oxygen
- **TCE**: Trichloroethanol
- **TMN**: Tuberomammillary nucleus
- **VAS**: Visual analogue scale
- **VLPO**: Ventrolateral preoptic nucleus
- **VPL**: Ventroposterolateral
- **VPM**: Ventroposteromedian
- **VRS**: Verbal rating scale
- **WDR**: Wide dynamic range

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Procedural sedation and analgesia (PSA) can be defined as the use of sedative, analgesic, or dissociative drugs in order to provide anxiolysis, analgesia, sedation, and motor control during painful or unpleasant diagnostic and therapeutic procedures.**(Krauss and Green, 2006)**

During the past 20 years, PSA has evolved into a distinct skill set with a growing number of indications and practice settings. Given the logistical and economic advantages of not requiring the operating theatre, procedures once restricted to the theatre are now done by many different practitioners (cardiologists, dentists, emergency physicians, gastroenterologists, intensive care doctors, oncologists, plastic surgeons, and radiologists) in inpatient and outpatient settings. The rapid growth of procedural sedation and analgesia has been fuelled by new drug and monitoring technology, expanded practitioner skills, the need to shift procedural work to outpatient settings, and widespread acceptance of the ethical imperative to treat pain and anxiety in children.**(Krauss and Green, 2006)**

Since anesthesiologists cannot cover the growing demand for PSA, non-anesthesiologists have organized their own PSA strategies. Historically, this resulted in a wide range of drugs and techniques for use in pediatric PSA, involving a large variance of sedation levels, sedation level predictability, effectiveness, and associated risks. However, by the end of last century, PSA by non-anesthesiologists was increasingly criticized by anesthesiologists for neglecting transparency and standard safety precautions. There are strong

indications that within this criticism, a source could be found for PSA-related accidents.**(Ratnapalan and Schneeweiss, 2007)**

In order to prevent PSA-related tragedies, there are guidelines that specify safety precautions that include the assessment of the risk of sedation prior to PSA, informed consent, guidelines on proper fasting status, appropriate monitoring, recovery standards, appropriate rescue facilities, and specific professional skills and competence. Generally recommended skills and competence are: the ability to perform a preprocedural risk analysis, practical knowledge and experience of applied sedatives, the ability to implement the necessary monitoring and surveillance, the ability to recognize and interpret sedation levels, and the ability to immediately recognize and adequately treat any unwanted side effects or complications, particularly hypoventilation and airway obstruction. These recommendations are mainly based on indirect evidence, expert opinion, "common sense", and widely accepted safety rules for general anesthesia. The adoption of a uniform and systematic practice is associated with a significant reduction in adverse events during anesthesia.**(Polaner et al., 2001)**

The practice of pediatric sedation and pain control has significantly evolved with new pharmacologic agents, painless interventions, improved continuous monitoring, and safety protocols. Despite such advances, clinicians can still be reluctant to use sedation and analgesia with pediatric patients. The emergency physician should have a firm understanding of the available modalities for treating pain and must be able to provide sedation

for painful or anxiety-provoking procedures in the emergency department.**(Alexander and Manno, 2003)**

The main aim of this essay is to discuss the guidelines of PSA including their types, techniques, possible risks and safety precautions during painful or unpleasant diagnostic and therapeutic procedures in pediatrics age group.

Alertness and associated forebrain and cortical arousal are mediated by several ascending pathways with distinct neuronal components that project from the upper brain stem near the junction of the pons and the midbrain. One pathway innervates the thalamus, and the second extends into the posterior hypothalamus and forebrain. Key cell populations of the ascending arousal pathway include cholinergic, noradrenergic, serotoninergic, dopaminergic, and histaminergic neurons located in the pedunculopontine and laterodorsal tegmental nucleus (PPT/LDT), locus coeruleus, dorsal and median raphe nucleus, and tuberomammillary nucleus (TMN), respectively. Projections from these various cell groups fire in a characteristic pattern to promote arousal. However, every 24 hours the arousal system is inhibited during sleep by sleep-active γ-aminobutyric acid (GABA)-ergic and galaninergic neurons of the ventrolateral preoptic nucleus (VLPO). The interaction between the VLPO and the branches of the ascending arousal pathway is mutually inhibiting, functioning much like an electrical "on-off" switch, enabling the body to maintain a stable state of wakefulness and sleep. Normally, this "sleep-wake switch" design ensures stability between sleep and wakefulness while promoting rapid transitioning between the two behavioral states.**(Fuller et al., 2006)**

The Ascending Arousal System Induces Wakefulness

In 1930, Von Economo reported that a viral disease known as encephalitis lethargica was caused by lesions of the posterior hypothalamus and rostral midbrain. Consequently, he assumed that wakefulness is mediated by an

ascending arousal system that begins in the brainstem, which remains active following midbrain interruption of the classical sensory pathways.**(Von Economo, 1930)**

Nearly two decades later, Moruzzi, Magoun, and colleagues confirmed that waking behavior is maintained by an "ascending reticular activating system," originating in the upper brainstem adjacent to the junction of the pons and midbrain and continuing on to the diencephalon, where it splits into two branches. It is now known that the ascending arousal system contains two major branches, each comprising discrete cell populations and neurotransmitters (Fig. 1). The first branch innervates the thalamus, activating relay neurons and reticular nuclei essential for thalamocortical transmission. Two cholinergic structures in the brainstem and basal forebrain serve as the origin of these projections to the principal thalamic nuclei – the PPT/LDT nuclei. PPT/LDT neurons are most active during wakefulness and rapid eye movement (REM) sleep and discharge more slowly during non-REM (NREM) sleep, a period when cortical activity is reduced. Transmission to the reticular nucleus of the thalamus is of particular importance, as the site functions as a gating mechanism that can block the generation of thalamocortical rhythms and promote a state of excitability and wakefulness. Other projections from the upper brainstem to the midline and intralaminar thalamic nuclei, which include the reticular formation, the parabrachial nucleus, and the monoaminergic systems, are also believed to be involved in cortical arousal.**(Saper et al., 2005)**.

The second branch of the ascending arousal system projects into the lateral hypothalamus, basal forebrain, and the cerebral cortex. It comprises a

number of monoaminergic cell populations, including noradrenergic neurons of the locus coeruleus, serotoninergic dorsal and median raphe nuclei, dopaminergic neurons of the ventral periaqueductal grey matter, and the histaminergic TMN. Several additional cerebrocortical afferents have been identified: lateral hypothalamic peptidergic neurons, which contain melanin concentrating hormone or orexin/hypocretin, and basal forebrain nuclei, which contain acetylcholine or GABA. Neurons in these monoaminergic systems have broad action potentials, discharging most rapidly during wakefulness, slowing during NREM sleep, and showing little activity during REM sleep. A similar pattern was reported in orexin/hypocretin neurons of the lateral hypothalamus. In contrast, melatonin-concentrating neurons, which play an important role in REM homeostasis, are strongly active during REM sleep, and cholinergic neurons of the basal forebrain discharge at maximal rates during both REM sleep and active waking.**(Mileykovskiy et al., 2005)**.

In sum, cholinergic neurons, monoaminergic cell populations, and orexin/hypocretin nuclei of the lateral hypothalamus located along the two branches of the ascending arousal system, discharge in a stereotypical and coordinated manner to promote cortical arousal, with each making unique, though overlapping and redundant, contributions to achieve and sustain wakefulness. During sleep, these circuits are blocked by neurons of the VLPO.**(Jonathan et al., 2008)**

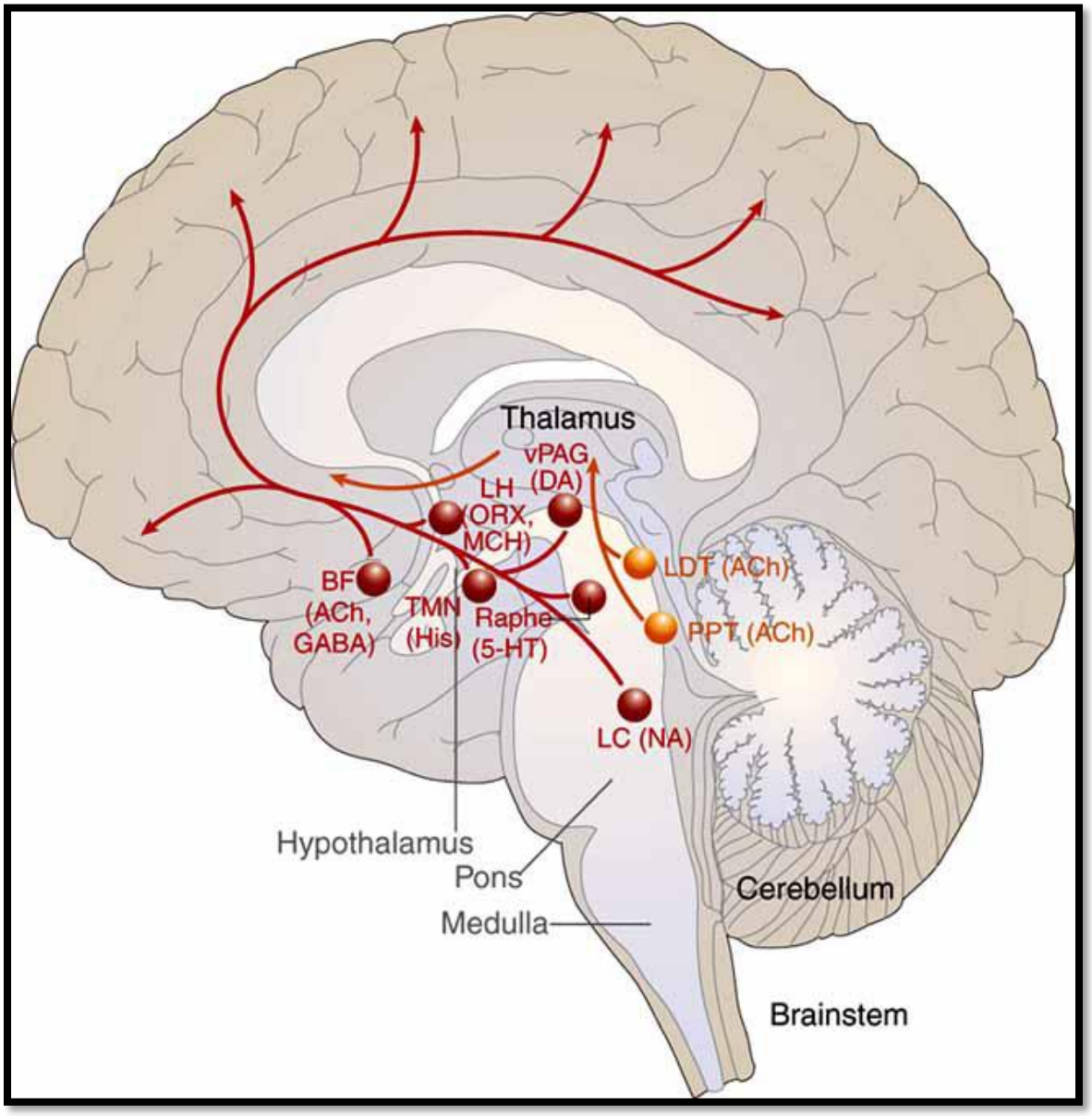

Fig. 1: A schematic drawing showing key components of the ascending arousal system. (**Quoted from Saper et al., 2005)**