CONSCIOUSNESS AND ANESTHESIA: TOWARDS A NEW INTEGRATED PARADIGM

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Abstract

According to reported studies there is increasing evidence that an actual level of anesthesia may exist on a continuum between usual awareness and states of unconsciousness. Recent findings also indicate that levels of anesthesia may be related to specific disturbances in neural correlate of consciousness that is mainly based on large scale synchronization in the brain. Further research studies have also shown that these specific changes during loss of consciousness may be reflected in decreased large scale synchronization in the brain that is caused by decreased cooperation among simultaneously active neural assemblies. In this context, concept of cognitive unbinding has been proposed that is mainly caused by decreased synchronizaton and cooperation among neural assemblies, which leads to decreased level of consciousness and in the extreme case to global anesthesia. Several recent studies suggest that these findings could be very useful for detecting intraoperative awareness which may lead to serious adverse effects and symptoms of posttraumatic stress disorder (PTSD). According to these data episodes of intraoperative awareness could be detected by various techniques focused on detecting binding processes reflecting a level of dependence in neural activation.

Key words: General anesthesia; Cognitive binding; Anesthesia-related unbinding; Post Traumatic Stress Disorder; Intraoperative awareness

1. INTRODUCTION

In the history of anesthesiological research, mechanisms leading to analgesia or anaesthesia have been studied since the 19th century and according to various modern theories these mechanisms are mainly based on influences of various anesthetic drugs on receptors of neuronal systems (Scholz et al., 1999). According to recent evidence, mechanisms of consciousness and general anesthesia have common neural substrate, which is characterized by processes of cognitive and neural binding typically linked to conscious awareness, and on the other hand, by neural unbinding reflecting loss of consciousness in anestezia (Mashour, 2004, 2006). In this context, recent evidence indicates that cognitive processing and consciousness are formed through many interactions among functionally and spatially distributed neuronal populations that enable to synthesize and "bind" these widespread activities (Llinas, & Ribary, 1993; Von der Malsburg, 1994; Crick & Koch, 1995, 2003).

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2. NEURAL CORRELATES OF CONSCIOUSNESS: TARGETS OF GENERAL ANESTHESIA

Following these findings about neural binding and consciousness, Tononi conceptualized that critically important role in mechanisms of consciousness have processes of information integration and proposed theoretical model describing several specific processes how the neural systems may synthesize information (Tononi, 2004). Tononi proposed that consciousness reflects a higher capacity to integrate information processed in functionally specialized modules, which for example might be a reason why thalamocortical circuits seem to be more related to conscious processing than certain cerebellar circuits. In principle, the neural correlates related to various sensory modalities need to be combined with other sensory modalities to generate a unified perception connecting various sensory aspect of perceptual information and create unity of conscious experience (Von der Malsburg, 1981, 1996). This process of information integration is usually called "cognitive binding" and although its mechanism is unknown, several hypotheses describing integration of neural information have been proposed (Singer, 1996; Maunsell & Van Essen, 1983; Tanaka, 1993).

Important explanatory scheme for understanding of these processes was conceptualized as binding among various neural assemblies representing groups of interrelated neurons that synchronize their neural firing (Hebb, 1949; Gray, 1999; Joliot, 1994; Rodriguez et al., 1999; Rees et al., 2002). In addition there is an open question, whether several structures may have crucial significance for this mechanism of binding. For summary of some hypothetical proposals please see Table 1.

Table 1. Candidate structures proposed as the neural substrate of consciousness.

Proposed structures
<i>Extended reticular-thalamic activation system</i> (Newman & Baars, 1993)
<i>Intralaminar nucleus in the thalamus</i> (Bogen, 1995)
<i>Reentrant loops in thalamocortical system</i> (Edelman, 1989)
<i>40-Hz rhythmic activity in thalamocortical system</i> (Joliot, 1994)
<i>Neurons in the superior temporal sulcus</i> (Logothetis & Schall, 1989)
<i>Neural activity in visual area V5/MT</i> (Tootell, 1995)
<i>Neurons in the extrastriate visual cortex projecting to prefrontal areas</i> (Crick & Koch, 1995)
<i>Anterior cingulate system</i> (Cotterill, 1994)
<i>Recurrent processing from higher to lower cortical areas</i> (Cauller, 1991)

3. EFFECTS OF ANESTHETICS ON NEURAL CORRELATES OF CONSCIOUSNESS

General anesthetics most likely may generate unconsciousness by suppressing of activities related to neural correlates of conscious awareness at various levels of neural organization, as well as by disrupting processes of information integration. In this context, neural correlates of consciousness are modulated by general anesthetics and in general the process of anesthesia is related to disintegration of cognitive activity and mechanisms of neural binding in which various brain structures may have a specific role (Mashour, 2006)

3.1. Thalamocortical effects

According to recent data the thalamocortical system is thought to be critical for consciousness and several mechanisms of neural resonance in thalamocortical circuits have been proposed as "dynamic core" of consciousness (Edelman, 1989), which is in agreement with other findings

about cognitive binding and functional connectivity (Joliot, 1994; Bogen, 1995) and also with findings related to the “unified theory of narcosis” based on the evidence that thalamocortical circuits are disrupted under general anesthesia (Newman & Baars, 1993). It has also been demonstrated that Isoflurane and Halothane disrupt functional connectivity between the thalamus and cortex (Newman & Baars, 1993) and similarly Propofol has also been shown to induce a hyperpolarization block of thalamocortical neurons (Edelman, 1989).

3.2. Cortical and Corticocortical Effects

General anesthetics have been demonstrated to affect various brain regions and it has been found that multiple general anesthetics induce reversible inhibition of the medial orbital and dorsolateral prefrontal and frontal cortex, anterior cingulate cortex, and paracentral gyrus (John et al., 2001). In addition reported findings about frontal and cingulate cortex inhibition seem to be consistent with previously documented PET findings about propofol-induced anesthesia (Walling & Hicks, 2006).

It has also been found that *general anesthetics* of distinct pharmacological properties *affect EEG coherence* and this effect is typically related to actual levels of consciousness (John et al., 2001). Other findings show that rostrocaudal dissociation seems to be particularly linked to conscious awareness and anesthesia (Joliot, 1994), and effects of anesthesia on rostrocaudal processing have been studied also in animal models (Imas, 2005), which is consistent with data about neural correlates of recurrent processing of neural information (Cauller & Kulics, 1991). Other studies in humans have also shown functional uncoupling of neural regions in association with general anesthesia and for example Peltier et al. (2005) demonstrated loss of functional connectivity in the cerebral cortex during sevoflurane anesthesia, which also suggests that anesthetics typically *uncouple* neural activities in cortical regions.

3.3. Information Dissociation and Unconscious States

Based on the effect of anesthetic-mediated interruption of neural information synthesis, the “cognitive unbinding” paradigm of general anesthesia was postulated (Mashour, 2004, 2006). This concept explicitly states that anesthetics are mainly functionally based on interrupting various cognitive binding processes from cellular to global brain levels (John et al., 2001). In this context, practical applications of the concept of cognitive unbinding to general anesthesia, the so-called “anaesthetic cascade theory” was proposed by John and Prichep (2005). The proposed “anesthetic cascade” is mainly characterized by these processes:

1. Depression of the brainstem reduces the influence of the ascending reticular activating system on the thalamus and cortex
2. Depression of mesolimbic-dorsolateral prefrontal cortex interactions lead to blockade of memory storage
3. Further depression of the ascending reticular activating system leads to hyperpolarization of GABAergic neurons in the nucleus reticularis of the thalamus, which results in blockade of thalamocortical reverberations and the associated 40Hz gamma oscillations underlying perception.
4. Functional uncoupling of parietal-frontal cortical activity, thereby interrupting cognition, and finally reduced awareness and increase in frontal delta and theta band activity.

Important findings that support both these theories of cognitive unbinding and the anesthetic cascade reported Walling and Hicks (2006), who used phase-space analysis of EEG during sevoflurane anesthesia. In their research they observed that return of consciousness was characterized by a higher-dimensional phase space, reflecting a complexity of brain dynamics that could sustain consciousness. The phase space analysis have shown that the

fractal “strange attractors” were related to gamma band frequencies associated with consciousness, which authors linked to processes of “cognitive rebinding.”

This concept of anesthetic-induced unconsciousness as a consequence of information dissociation was supported also by recent studies of other types of unconscious states for example in brain-injured patients in vegetative states, who have fragmented cerebral activity (Schiff et al., 2002) and manifest loss of effective cortical connectivity (Laureys et al., 1999). It also has been suggested that vegetative states are related to “disconnection” syndromes (Laureys, 2005) and that neural regions mainly affected in vegetative states include the frontal cortex, cingulate cortex, association cortices, and thalamus, which also represent typical targets for general anesthetics (Laureys, 2005; Laureys et al., 2000). Nevertheless according to recent data there is no clear explanation how agents such as ketamine or nitrous oxide, which can lead to EEG activation rather than depression, fit within the proposed anesthetic cascade (Sakai et al., 1999; Yamamura et al., 1981; Rodriguez et al., 1999).

4. CONCLUSIONS

In summary, recent findings about consciousness and anesthesia, and their neural mechanisms present important conceptual consequences how to understand consciousness and its changes in unconscious states, including also various clinical problems that occur in anesthesiological practice. For example, at about 22% of patients have dreams during anesthesia (Leslie et al., 2007) and very serious problem represents intraoperative awareness with incidence at about 0.13% (Sebel et al., 2004), which may lead to serious psychological consequences and cause post-traumatic stress disorder (Osterman & van der Kolk, 1998; Samuelsson et al., 2007). These changes in awareness most likely might be detected using various methods that enable to detect neural binding which has very important consequences for anesthesiological practice. In this context, future investigation of general anesthesia and neural mechanisms of consciousness could provide applicable scientific understanding that may help to significantly improve intraoperative monitoring.

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