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REVIEW ARTICLE

The Emergence of Human Consciousness: From Fetal to Neonatal Life

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ABSTRACT: A simple definition of consciousness is sensory awareness of the body, the self, and the world. The fetus may be aware of the body, for example by perceiving pain. It reacts to touch, smell, and sound, and shows facial expressions responding to external stimuli. However, these reactions are probably preprogrammed and have a subcortical nonconscious origin. Furthermore, the fetus is almost continuously asleep and unconscious partially due to endogenous sedation. Conversely, the newborn infant can be awake, exhibit sensory awareness, and process memorized mental representations. It is also able to differentiate between self and nonself touch, express emotions, and show signs of shared feelings. Yet, it is unreflective, present oriented, and makes little reference to concept of him/herself. Newborn infants display features characteristic of what may be referred to as basic consciousness and they still have to undergo considerable maturation to reach the level of adult consciousness. The preterm infant, *ex utero*, may open its eyes and establish minimal eye contact with its mother. It also shows avoidance reactions to harmful stimuli. However, the thalamocortical connections are not yet fully established, which is why it can only reach a minimal level of consciousness. **(*Pediatr Res* 65: 255–260, 2009)**

Consciousness in general and the birth of consciousness in particular remain as key puzzles confronting the scientific worldview (1). According to Searle (2) it can be defined as "inner, qualitative, subjective states, and processes of sentience or awareness." This includes "one's autobiography and mental time" together with the capacity to introspect and report about one's mental state by verbal and nonverbal means. Consciousness emerges from special neuronal features in the brain or "neuronal correlates" of consciousness according to Koch (1). Tononi and Edelman (3) propose that there is a dynamic core of several neurons distributed across many brain regions. Merker (4) claims that conscious function cannot be confined to the thalamocortical complex alone, but also to lower structures, which is of particular interest from a developmental point of view. We deliberately restrict our discussion to a "global neuronal workspace" (GNW) model (5), or metaphorically "a theater of mind" according to Baars (6). In the GNW, multimodal perceptions, emotions and feelings (present), evoked memories (past), together with anticipations of actions (future) become subjectively integrated in a continuously changing and dynamic "flow of consciousness" (7–9). This then leads to the distinction between the states of consciousness (wakefulness, sleep, coma, general anesthesia) and the content of the conscious experience. The states of consciousness are under vertical control of the brain stem and diencephalic subcortical structures and mediated by the corticothalamic relationships (10). The content of conscious experience (11) is then viewed as being processed through a recurrent horizontal network of cortical pyramidal neurons with long-distance connections assembling thalamocortical regions, particularly prefrontal and higher association areas, parietotemporal and cingulate cortices (12) referred to here as GNW circuits (8,9). This model has been corroborated by neural network simulations and experimental evoked response potentials recordings showing reverberating activity within the GNW circuits as corresponding to consciously reportable states. Our working hypothesis will thus be that such mobilization of the GNW circuits constitutes an objective sign of access to consciousness (8). This is in contrast with the subliminal mobilization of underlying automatic and nonconscious processors (Fig. 1) (5).[1]

The question then becomes as follows: where and when do these objective signs of consciousness appear during development? As presented in this review, analysis of human brain development from early fetal stages *in utero* up to the adult state offers original insights into the neural bases of the access to consciousness. We argue that consciousness is a progressive, stepwise, structural, and functional evolution of its multiple intricate components (7–9).

DEVELOPMENT OF THE NEURAL CIRCUITS OF CONSCIOUSNESS

At birth, the newborn brain is in a "transitional" stage of development with an almost adult number of neurons (with the exception of adult neurogenesis) but an immature set of

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Abbreviations: fMRI, functional MRI; **GNW,** global neuronal workspace; **REM,** rapid eye movement

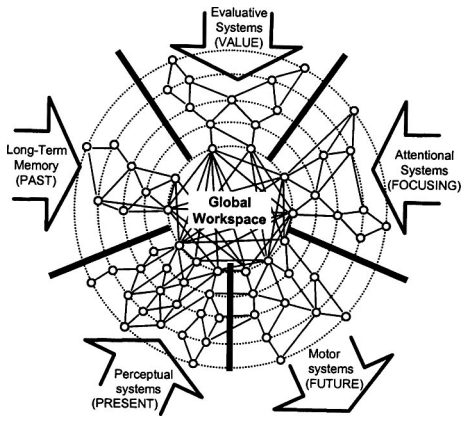

Figure 1. Schematic representation of the Global Neuronal Workspace (GNW) hypothesis. The model distinguishes five relatively autonomous and specialized autonomous processors involved in perception, motor activity, attention, evaluation, and long-term memory connected throughout the brain by long-axon neurons of the GNW. Reprinted from Dehaene *et al*., Proc Natl Acad Sci USA 95:14529–14534, Copyright © 1998 The National Academy of Sciences USA, with permission.

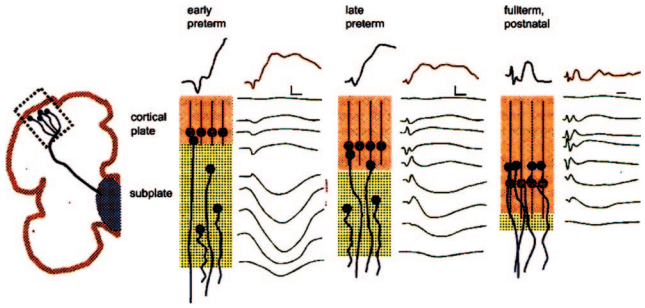

Figure 2. Comparison between the maturation of thalamocortical-cortical connections and somatosensory evoked potentials (SEP). In the early preterm infant (<24–25 gestational weeks), thalamic axons establish a dense synaptic network in the subplate. After approximately 25 gestational weeks thalamic fibers make synapses in the deep cortical layers. In the full-term infants, the thalamic fibers have reached their final destination in layer IV of the cortex. This is reflected by the SEP responses. In the early preterms, the evoked responses consist only of long depolarizations of the deep layers. A delayed cortical activation can be seen. When the thalamic-cortical fibers extend to the cortex, faster cortical responses are seen, paralleling the accumulation of synapses in layer IV. Reprinted from Vanhatalo *et al.,* Semin Fetal Neonatal Med 11:464–470, Copyright © 2006 Elsevier Ltd., with permission.

connections (13). During the few months after birth, there is an overproduction of synapses accompanied by a process of synaptic elimination and stabilization, which lasts until adolescence (14). Myelination begins prenatally, but is not completed until the third decade in the frontal cortex (15) where the highest executive functions and conscious thoughts take place (1,9).

Thalamic afferents to the cortex develop from approximately 12–16 wk of gestation, reach the cortical subplate, but "wait" until they grow into the cortical plate (16). At this stage, only long depolarization of the deep layers may reach the cortex (17) (Fig. 2). After 24 wk, thalamocortical axons grow into the somatosensory, auditory, visual, and frontal cortices and the pathways mediating pain perception become functional around the 29–30 wk (18). From approximately 34 wk, a synchrony of the EEG rhythm of the two hemispheres becomes detectable at the same time as long-range callosal connections, and thus the GNW circuits, are established (18–20). From the 26th wk, pyramidal neurons in the primary visual cortex of humans develop dendritic spines (19). At birth, the dendritic spines have not reached the adult density, but suffice for the detection of visually evoked potentials. The connectivity of the cerebral cortex particularly in the prefrontal area, mature later than the subcortical structures. However, the fusiform area for face recognition (21) and the left-hemispheric temporal lobe cortices for processing speech stimuli (22) function already in the newborn. Moreover, the main fascicles of myelinated long-range connections such as the corpus callosum, cerebellar peduncles, corticospinal tract, spinothalamic tract are unambiguously identified at the age of 1–4 mo (23). In short, the vertical brain stem, diencephalic, and thalamocortical pathways, which regulate the states of consciousness, become established before their connection with the horizontal GNW cortical circuits yielding, in the newborn, plausibly functional, though still immature, neural dispositions for access to a conscious content.

The neurochemistry of the developing brain reveals that γ-aminobutyric acid (GABA) is the dominant excitatory neurotransmitter during fetal life (20,24,25). Soon before or around birth depending on the brain area, GABA becomes the main inhibitory neurotransmitter. This is a consequence of the expression of the $K+/Cl-$ cotransporter KCC2 that creates a low intracellular $Cl-$ concentration. Then glutamate and aspartate become the major excitatory amino acids (20,24). In addition, a transient switch in GABA signaling from fetal excitatory to inhibitory is elicited by maternal oxytocin release upon delivery (26).

Neuromodulators, like noradrenaline and acetylcholine which regulate sleep–wakefulness cycles develop progressively before and after birth (24). Also the supply from the mother's blood of neuromodulators like serotonin is probably important for the normal development of the brain (27). The rich dopaminergic innervation of the prefrontal cortex (28) accompanies the cognitive advances in infants between 6 and 12 mo.

Well-defined sleep states appear at approximately 32 gestational weeks in the human fetus (29,30) or preterm infants (31). By ultrasound recordings, active sleep can be identified by rapid eye movements, breathing, swallowing, and atonia, whereas apnea, absence of eye movements and tonic muscle activity occur during quiet or nonrapid eye movement sleep. This spontaneous activity is interpreted as an early "inner stimulation" which could anticipate the sensorimotor experience of the newborn with the outside world and regulate thalamocortical development (32). At approximately 35 wk, spontaneous electrical activity transients become synchronous across hemispheres as callosal connections develop suggesting a possible role in the maturation of the GNW circuits (33).

SENSORY PERCEPTION

The newborn brain is not "blank." Spontaneous resting activity can be identified in five cortical areas, as revealed by functional MRI (34). The primary visual areas, the somatosensory and auditory cortex are active indicating that sensory auditory and visual impressions are processed in the newborn cortex (Fig. 3).

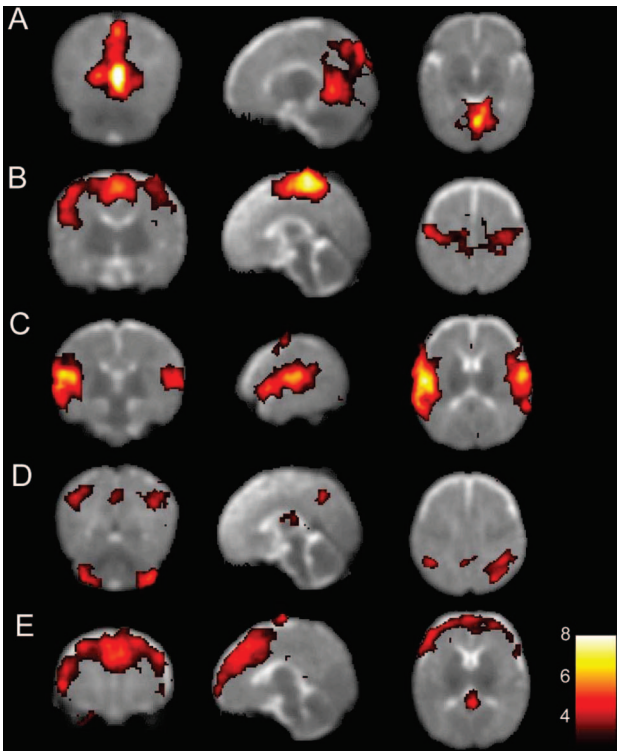

Figure 3. Functional MRI used to map the resting state activity of the brain of lightly sedated preterm infants born before 27 gestational week and scanned at term age around 40 gestational weeks. Several unique resting-states networks are revealed that encompass: (*A*) Primary visual areas; (*B*) Somatosensory areas and motor cortices; (*C*) Temporal areas including primary auditory cortex; (*D*) Parts of parietal cortex; (*E*) Medial and lateral sections of the anterior prefrontal cortex. Reprinted from Fransson *et al.*, Proc Natl Acad Sci USA 104:15531–15536, Copyright © 2007 The National Academy of Sciences of the USA, with permission.

There are several indications that various sensory modalities are processed in the developing brain befor birth (35–38).

Pain. Nociceptive reactions such as withdrawal reflexes can be recorded from the 19th wk (35). By the 20th wk, fetuses were found to increase the levels of cortisol, beta-endorphin, and noradrenaline in umbilical blood when a needle was inserted into the abdomen (38). Facial expressions similar to adults experiencing pain can be seen in preterm infants after 28 wk (18). Painful stimulations by either venipuncture or heel lances of preterm infants of 25–45 wk produced an increase in hemodynamic response in the somatosensory cortex revealed by real-time near infrared spectroscopy (39,40) either bilaterally and/or over the contralateral areas. Interestingly, the cortical responses to noxious stimulation were found to be greater in awake than in sleeping infants (39). Moreover, the bilateral activation noticed in the Bartocci *et al.* (40) study was suggested to include the S_2 cortex, anterior insula, ventral premotor area, and anterior cingulate cortex which belong to the GNW circuits.

Olfaction. The behavior of alert newborn infants appears to be influenced by olfactory cues mainly originating from the intrauterine environment (41,42). For instance, they seem to be more attracted by the smell of amniotic fluid than by other odors. Exposure to amniotic fluid and other maternal odors were found to have a soothing effect in newborns. Clear behavioral responses to smell can be recorded in preterm infants from approximately the 29th wk of gestation and the fetus can probably smell from approximately the 20th, the time at which the epithelial plugs blocking the nostrils disappear (41). Near infrared spectroscopy recordings in the left anterior orbitofrontal gyri of newborns (from 6 to 192 h) in a quiet awake state show increased hemodynamic response during exposure to smells like that of colostrum or of vanilla compared with water (43). Conversely, a decreased response, which was significantly greater in the right than in the left side, was noticed when the babies were exposed to the smell of a disinfectant or of a detergent (44).

Vision. Visual acuity in the full-term newborn infants is only 1/40 visual acuity in the adult but newborns can process complex visual stimuli, recognize faces, and imitate (21). They have developed preferential looking *i.e.*, they look longer at patterned field stimuli than at gray fields. The ability to recognize different colors, as well as other features of visual perception, develops later. Infants at birth prefer images of attractive faces, are sensitive to the presence of eyes in a face, and have a preference to look at faces that enjoy them in eye contact (21). Such face detectors preferentially mobilize a subcortical route that seems more developed than the cortical route at birth. In any case, these experiments require the infant not only to be awake and attentive but also to be sensitive to a "social" eye-contact relationship.

Hearing. Responses to low frequency noise can be recorded from approximately the 16th wk in the fetus brain (45). The cochlea is probably structurally developed from around the 18th gestational week to provide auditory input. However, the auditory cortex does not respond to hearing until around the 26th wk in preterm infants. At this age, brainstem auditory evoked responses can be first observed, although they may not be reliable until the 28th week (46). In a recent study, cortical activation to sound was detected in the fetus from the 33rd wk of gestation (47).

Memory. If a 22–23 wk human fetus is exposed to a repetitive stimulus, such as the vibration of an electric tooth brush, it reacts by movements; after multiple stimuli it does not react any longer, it habituates (48). Newborn infants remember sounds, melodies, and rhythmic poems they have been exposed to during fetal life (49,50). However, short-term memory is rather limited in newborn infants, retention of visual objects lasts only for a few seconds. A 2-mo-old baby remembers a soother or a face which suddenly disappears (51) but working memory is not fully efficient before 7 mo (49). Long-term memories disappear during early childhood (infant amnesia) and full declarative memory develops only after 3 y (49).

Language. Infants display elaborate capacities for oral language perception that are rapidly modified by their linguistic environment (52). As early as a few days after birth, babies can discriminate between speech excerpts from language belonging to different rhythmic families, but prefer to listen to their native languages even when speakers are unknown (53,54). Exposure of the mother speech *in utero* during the last week of fetal life, under sleeping "unconscious" conditions, may explain why neonates react to the maternal voice (52).

The left hemisphere of the newborn brain was found to be more activated than the right during human speech, as shown

by an optical topographic study (55). Furthermore in 3-mo-old awake infants, functional MRI recordings reveal an activation of the Broca's area (before the babbling stage) together with an additional activation in the right dorsolateral prefrontal cortex by speech stimuli with a significant advantage for the native language (22) thus revealing an active mobilization of a long-distance temporofrontal GNW circuit by speech stimuli (56).

THE FIRST ACCESS TO CONSCIOUSNESS

The fetus is mainly asleep, although it shows vigorous continual activity, including breathing, eye openings, and facial expression (30). Yet, most of these preprogrammed movements are from subcortical origin. Attempts to "wake up" the fetal sheep by noxious stimuli, such as pinching, cause inhibition instead of arousal (57). Furthermore, the fetus is sedated by the low oxygen tension of the fetal blood and the neurosteroid anesthetics pregnanolone and the sleep-inducing prostaglandin D2 provided by the placenta (36). The most parsimonious, yet challenging, interpretation of these data are that *in utero* the fetus is mostly in a state of "unconsciousness."

Upon delivery, the newborn baby arouses and stays awake for approximately 2 h. The eyes are wide open with usually large pupils and it may cry. After a couple of hours it usually falls asleep again, being awake the following days for only short periods of time (58). The delivery from the mother's womb thus causes arousal from a "resting," sleeping, state *in utero*. After birth, electrophysiological signs on EEG scalp recordings indicate an intense flow of novel sensory stimuli after birth (20). In addition, arousal is enhanced by the release from endogenous analgesia possibly caused by removal of the mentioned placental "suppressors" which *in utero* selectively inhibit neural activity of the fetus (36). The catecholamine surge triggered by vaginal delivery may also be critical for the arousal at birth (59). In the rat fetus, a 2- to 3-fold increase of noradrenaline turnover has been demonstrated in the newborn rat brain, probably mainly reflecting the activation of the locus coeruleus at birth (60).

During the stress of being born the cholinergic system may be activated as well. Indeed, blocking the activation of the cholinergic system in rodent pups blunts the arousal response to hypoxia and increases mortality (7). Mice missing the β2-containing nicotinic acetylcholine receptors lack the ability to arouse to the same extent as wild-type mice, and a similar phenotype is observed in newborn pups after chronic exposure of the pregnant mother to nicotine (61). These mice may offer useful models of the sudden infant death syndrome.

Birth may also release an inborn "positive emotion," a "motivation" oriented toward the outside world and in particular toward the feeding mother. It is interesting to note that in many species this first arousal drives the newborn to spontaneously explore the world, in particular to look for food (62). The infant affective display then becomes part of a conscious intercommunication system with the caretaker.

SELF-AWARENESS, CRYING, AND SOCIAL INTERACTIONS IN THE NEWBORN

The newborn infant at birth already reacts differently to tactile stimulation by the mother as compared with a self-stimulation which he/she does not respond to (63). The newborn infant is known to imitate certain body movements. For instance, tongue protrusion by an adult will produce tongue protrusion in a newborn (64), even though this does not actually mean an authentic self-recognition.

An almost unique feature of the human newborn is crying. It produces characteristic sounds and grimaces with vigorous body movements (65) to the extent that crying may be viewed as a distinct state of consciousness interpreted as an "honest signaling of need or vigor" to obtain vital care from his mother (66). Newborns distinguish their own cry from the cry of another newborn. They respond significantly more with crying when hearing another newborn crying than when hearing their own cry (66). As a consequence of affect sharing, emotional contagion is already developed in the newborn. Emotion recognition and sharing emerge in the newborn much earlier than "theory of mind." EEG brain activity in crying infants reveals a right frontal activation asymmetry already in 1-mo-old infants related to more frequent sad and precry faces (67). Infants who cried in response to maternal separation had greater right frontal asymmetry compared with infants who did not cry during the preceding baseline period (68). Interestingly, the right frontal activation associated with negative emotions was not observed in infants who had received a sucrose solution (69), and may thus be interpreted as an early sign of mobilization of the GNW circuits.

The hunger for air that emerges at birth can be called a primordial emotion (62). This first arousal drives the newborn to spontaneously explore the world, particularly to search for food in the mother's breast. The neural correlates for a "conscious" social communication of the newborn with his/her caretaker through crying become accessible to scientific investigation.

CONCLUSION

A first conclusion of this ongoing research is that the fetus *in utero* is almost continuously asleep and unconscious partially due to endogenous sedation. In particular, it would not consciously experience nociceptive inputs as pain. Conversely, the newborn infant exhibits in addition to sensory awareness specially to painful stimuli, the ability to differentiate between self and nonself touch, sense that their bodies are separate from the world, to express emotions, and to show signs of shared feelings. Moreover, "objective signs" for the mobilization of the GNW circuits are being detected in awake infants at the level of the prefrontal cortex in sensory processing, in responses to novelty and to speech and in social interaction. Yet, its capacities for internal manipulations in working memory are reduced, it is unreflective, present oriented and makes little reference to concept of him/herself. Newborn infants display features characteristic of what may be referred to as basic or minimal consciousness (7,9,70). They still have

to undergo considerable maturation to reach the level of adult consciousness (70).

The preterm infant *ex utero* may open its eyes and establish a minimal eye contact with its mother. It also shows avoidance reactions to harmful stimuli. The connections with the GNW circuits are not yet fully established. Our view is that it has reached only a lower level of minimal consciousness analogous (though, of course, not identical) to that of a rat/mouse (7,9). A pending question is the status of the preterm fetus born before 26 wk (<700 g) who has closed eyes and seems constantly asleep. The immaturity of its brain networks is such that it may not even reach a level of minimal consciousness. The postnatal maturation of the brain may be delayed (71) and there are indications that the connectivity with the GNW will be suboptimal in some cases (72) as indicated by deficient executive functions (73). Therefore, the timing of the emergence of minimal consciousness has been proposed as an ethical limit of human viability and it might be possible to withhold or withdraw intensive care if these infants are severely brain damaged (74,75).

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