

Neuromaturation and the Moral Status of Human Fetal Life

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Fetal personhood: an intrinsic property or a matter of multiple attributions?

THE QUESTION "When does human life begin?" has become the well-known and controversial encapsulation of a central issue in the conflict over abortion--the moral status of embryonic/fetal life. From one perspective the question as put is thought to frame the issue adequately. In this view personhood is a matter of natural objectivity; we are simply *presented* with the fact of full humanness or personhood--an *intrinsic* and *scientifically discoverable* property emerging during the course of a continuous ontogenetic process. However, there is a problem with this notion of intrinsic personhood, and it is deciding which of several different suggested properties is the one "real" answer to when a particular and personal human life has begun. Is it possession of the unique human genome achieved after fertilization, loss of embryonic ability to twin (i.e. developmental individuality) roughly two weeks later, appearance of fetal motility at six to seven weeks of gestation, emergence of unmistakably human form a few weeks later still, first awareness, or birth? In deciding, one must give reasons for one's choice and thereby necessarily introduce "extra-biological" dimensions as part of the choosing. As a result, the biological indicators come to serve as little more than the material referents for these reasons. The recognition that reasoned choices among contending properties must be made has led many to focus precisely on those reasons, and to claim that the properties whereby we understand and value prenatal personhood are not those discoverable by science but those *constituted* within a social fabric, and most properly by those who are directly involved with the fetus before and after its birth (Solomon, 1983, p.220).

Harrison (1983), for example, claims that our evaluation of embryonic and fetal human life is a complex exercise of moral agency in the face of a precise moral question: "When shall we predicate full human value to developing fetal life?" Such predication or attribution is clearly a socially constitutive act *extrinsic* to the fetus. It is not, however, an act unconcerned with the changing nature of the fetus or its intimate and dependent relation to the woman nurturing it. Thus, as we exercise this moral agency we are counselled to take into account "developmental criteria for stipulating the degree of similarity to existing human beings required for counting fetal life as *a* human life" while

attending to "the moral reasons for and against viewing prenatal life as morally continuous or discontinuous with existent humanity" (Harrison, 1983, pp. 208-209). That is, we are to *look for developmental differences which make a moral difference*.

Given the view expressed by Harrison, how do we engage in the process of predication? If we cannot begin with scientific facts about prenatal ontogenesis, if the meaning or definition of personhood is simply not something arrived at empirically, then it must be decided upon. The justification for a choice of developmental criterion must originate elsewhere and earlier, within our moral communities. Thus, we look toward the embryo or fetus from the vantage point of existent humanity, having already chosen one or more criteria--about ourselves--as anchors of a possible moral continuity with the developing fetus. These prior choices of criteria thereby condition the nature of our moral gaze.

While several such criteria have been suggested (and noted above), perhaps the most compelling of prenatal criteria are those related to the central nervous system (CNS). This is so because the CNS materially underpins the development of several capacities we socially construe as of moral importance to us: (1) awareness (especially of pleasure and pain); (2) a discrete and sustainable bodily existence achieved through birth which enables a transition in the manner of nurturance and occasions "a covenant of caring" that *creates* personal existence"; (Harrison, 1983, p.223;) (3) a rich meshwork of neocortical circuitry whose post-natal "remodeling" (see below) may in part reflect the neuro-embodiment of an emerging personal existence lived in interaction with others; and finally, those Engelhart (1983, p.184) associates with persons in the strict sense (i.e. persons of the sort we hopefully are): (4) sense of self, (5) ability to exercise rationality, and (6) capacity to choose freely and responsibly. Thus, our moral sensibilities turn our gaze to a collection of important, neurally-enabled capacities warranting attention. It is at that point scientific methodologies and tools can sometimes be used to tell us *when* there emerges a nervous system of sufficient material complexity to embody those capacities (already) judged as morally pertinent. Knowing when, we are (perhaps) better prepared to fashion the bridge of moral continuity spoken of by Harrison.

A brief chronicle of human embryonic/fetal neuromaturation: knowing when integrative transitions occur

Although the process of human development from newly fertilized ovum to birth is properly considered a continuum of change, it is an uneven continuum. There are periods of developmental transition during which integrative functions appear and increasingly complex embryonic and fetal properties emerge. This general observation is true of neuromaturation as well. Thus, if we adopt the position that the integrative activities of the prenatal CNS are an important consideration for our possible ascription of moral standing, we must ask *which* integrative functions are of moral significance and *what degree of neural development* must be evidenced before we are advised to "draw the line" that encompasses particular fetal lives within our moral communities and protects them from harm?

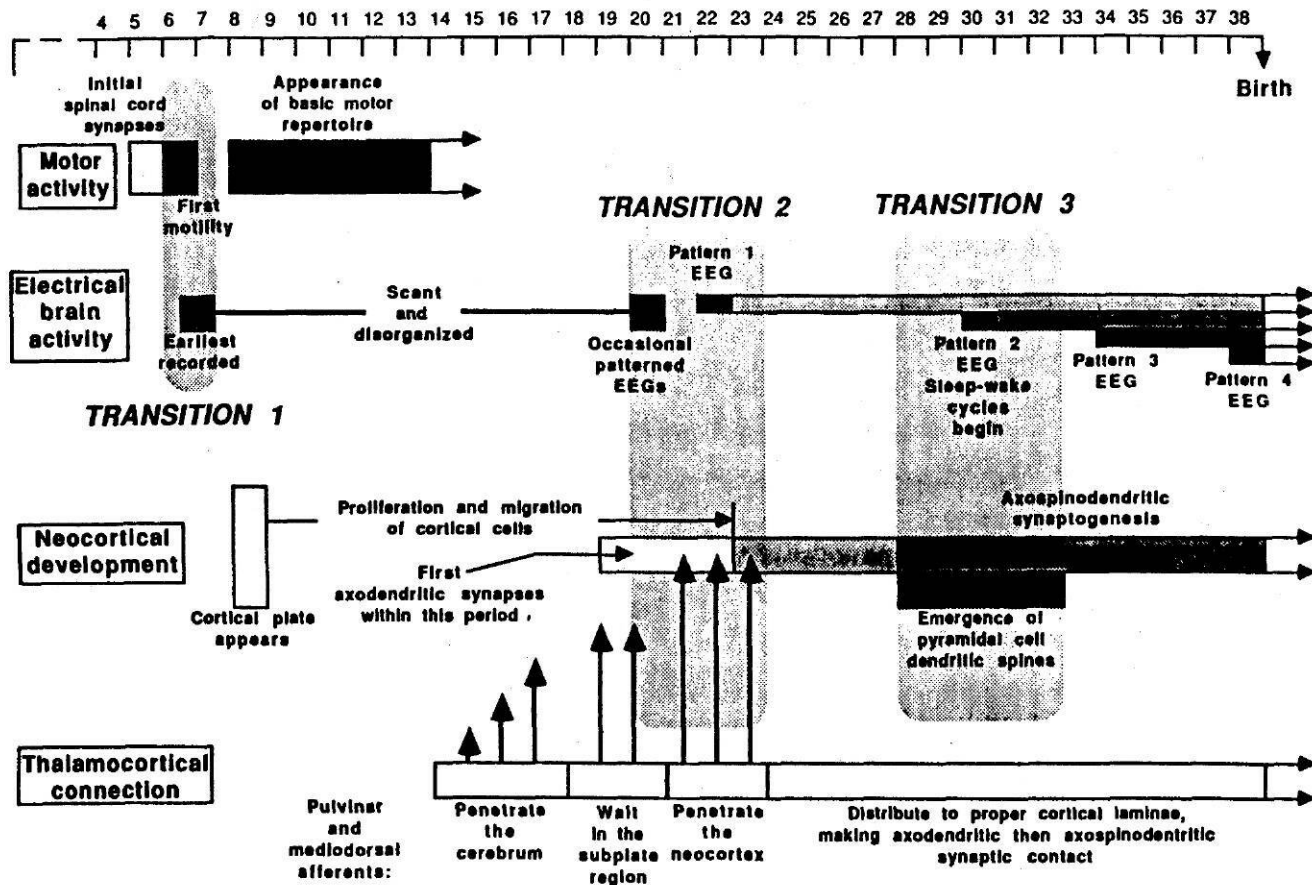


FIGURE 1. Neuromaturation Processes During Fetal Human Life

First, it is important to understand that the development of the nervous system can be followed as a sequence of processes (Flower, 1985), not all of which may be of comparable moral significance. The earliest developmental event is the appearance of *unspecialized* (or *presumptive*) neural cells; these are different from other embryonic cells in that only they are destined to produce the CNS as ontogenesis proceeds. There then follow two further changes, developments which begin at different times and proceed at different rates in various parts of the CNS (a circumstance that makes it difficult to speak about neuromaturation of the fetal CNS as a whole). First, presumptive cells begin preparing to function as nerve cells; they *differentiate* by changing their morphology and biosynthetic activities. This differentiation enables the second major change, a *cooperative assembly into supercellular arrays*. Neural cells synapse ("hook up") with one another, producing information-carrying circuits. As is probably obvious, the last of these developmental processes will eventually come to interest us most, for it is neural circuitry that makes possible the integrative function of the nervous system.

However, it is useful to look first at earlier events and then proceed in the direction of greater complexity. As the human embryo develops, when is there first "something neural" to observe, characterize, and talk about scientifically? During the third week of human development it is already possible to identify that portion of the embryo which is the presumptive or rudimentary forerunner of the future CNS; at this time, however, there are no functional nerve cells. In the fifth week (Figure 1), maturing neurons can be found in the cervical (neck) region of the embryonic spinal cord (Okado, 1981, pp.212, 215); they are sufficiently specialized that the simplest sort of supercellular circuits (reflex arcs) can be established soon thereafter, serving to support rudimentary fetal motility. At this time, also, there are undoubtedly differentiating neurons in the developing brainstem region (Humphrey, 1978). However, if we look for the neocortex we will not find it even in rudimentary form. It is put in place by processes of cellular proliferation and migration that do not begin until the eighth week and last through the fifth month of development. And even when most of the neocortical cells are in their proper place at five months, the multicellular assemblage does not yet constitute a functioning cellular array, for these neocortical cells have yet to fully differentiate. For instance, if we look for indications of neocortical cellular specialization (evidenced morphologically by the production of long cellular extensions known as axons and dendrites, and by the appearance of multiple synaptic targets or "spines" on the latter) we will find relatively few before 20 weeks. Many weeks later, with the relatively sudden emergence of these specialized cellular morphologies and synaptic points-of-contact, a rapid and quantitatively enhanced formation of complex neocortical circuitry is enabled.

Looking at specific neuromaturational processes

The Earliest Events

If at three weeks of development there are no functional nerve cells, how much time passes before neural function (of some sort) appears? We can ask when electrical activity is first detectable and when there first appear

functions (such as motility) known to be dependent on neural maturation. In both cases the answer is the same: about the sixth-to-seventh week (Figure 1). As was noted earlier, there is not even the hint of a neocortex at this time; thus, the electrical activity observed (Borkowski and Bernstine, 1955) does not indicate higher brain function. However, such activity may be a manifestation of early embryonic brainstem function.

What of prenatal motility? What degree of neuromaturation is required to support it? Very little, as it turns out. When observed ultrasonographically, the late-stage embryo of six weeks can be seen to exhibit occasional and "just discernible movement"; a week later, a "startle" response emerges. Over the next six to seven weeks a relatively complex repertoire of spontaneous motor activities emerges (de Vries *et al*, 1982); the fetal limbs and head move about, breathing movements occur, and swallowing and sucking are observed. The "control" of this activity might conceivably reside in the relatively simple neural circuitry of the spinal cord, as Robertson (1985) has suggested in his account of the later cyclic motor activity of post-mid-gestation fetuses. However, as the development of younger fetuses proceeds, the various motor activities exhibit temporal patterns of expression which differ one from the other (de Vries *et al*, 1985), possibly indicative of some measure of modulatory influence "higher" than the spinal cord. It has been suggested (Flower, 1985) that the earliest modulator of such activity is the brainstem (serving, for example, to integrate rudimentary sensory input from such sources as fetal muscle "stretch receptors," small "sensors" embedded in muscle tissue and triggered by muscle contractile activity to send electrical impulses to the CNS). This suggestion of a general integrative function (Transition 1 in Figure 1) is made more reasonable by the recent observations of Visser and colleagues (1985). They found that anencephalic fetuses lacking the brainstem region exhibited considerable *but abnormally patterned* motility when compared to that of anencephalic fetuses with intact brainstem. They also noted that substantial motility (though again unorganized) was possible even in anencephalics in which only abnormally situated nests of spinal cord neurons were present. Thus, little neural circuitry was necessary for movement, but an intact brainstem was associated with normal *patterns* of fetal activity.

Of what significance is this putative brainstem integrative function? Is it, if real, in any way an attractor of our moral concern? At this very early time do we have morally justifiable reasons for establishing a moral bridge expressed through an imputation of some form of fetal personhood? In virtue of what actions on our part would we define the imputation? As the brainstem is not the same thing as the neocortex we can be certain that the patterned changes in fetal motility are not the result of intention; they are not indicative of any sort of conscious awareness and need not draw our moral attention for that reason. However, are there other reasons to attend to a fetus of this stage? At least one philosopher thinks so. Tauer (1985, p.258-259) has argued that "...if integration through the brainstem is a valid hypothesis...it seems reasonable to describe the late first trimester fetus's relationship to tactile stimuli and to its own movements...as fetal 'experience'." While such experience is not conscious as we have noted, Tauer suggests (p.259) that "it is comparable to other nonconscious experience in its significance for psychological life." This is so for Tauer because she counts the foundations of later personal traits (self-consciousness,

rationality, and self-determination) as begun when integrative brain pathways are first established, including those of the brainstem. In other words, Tauer advances a "whole brain" conception of personal prenatal becoming. She suggests (citing Mittelman, 1960, p.104-105) that "intrauterine events may be 'physiological antecedents of later happenings...traces that in some way are equivalents of later memory traces...'" If such speculative traces do exist and if they influence (even in part) later neural capacities of moral significance then one can understand why Tauer would attribute to fetuses older than six weeks a status she calls the *psychic sense of person*. For Tauer, an integrative foundation is being laid down, one that in some (undoubtedly indirect) way may affect the person-to-be. But what kind of respect does she argue is due a fetus with such a status? Or asked differently (to emphasize the constitutive nature of status-giving), what actions of ours would realize that status in practice?

Crucial for the attribution of psychic personhood is the *realized* potential of such fetuses to become persons in the strict sense. The status of psychic personhood is morally relevant only if fetal "experience" is continuous with and determines the development of personal psychological characteristics of a person like you and me--that is, only if a full pregnancy is anticipated and completed. Thus, *Tauer's argument for psychic personhood* (as she recognizes) *is not one on the basis of which we would proscribe abortion during the first trimester*. Instead--and certainly of importance--Tauer's argument for attributing psychic personhood to a human life during its seventh week of prenatal development is relevant to the question of--and is constituted by--the care and nurturance necessary to protect the normal integrative embodiment of a CNS crucial for continued creation of a personal existence. That is, even if the speculative claims of (later-effective) "memory trace-like" experience as early as six to seven weeks of gestation can be sustained, the notion of psychic personhood instructs us only as to our proper relationship to a fetus that will develop to birth: we ought to avoid injurious intervention (e.g. experimentation or traumatic therapeutic measures) and to care for the fetus's normal development through proper maternal nutrition, avoidance of undue stress, harmful chemicals and the like, thus protecting a future person. Of course, such a concern for protective behavior would come into play before six to seven weeks of gestation because *earlier* processes of CNS (and other organ-system) development are subject to developmental mishap as evidenced by such abnormalities as anencephaly and spina bifida. While Tauer would surely be concerned about such outcomes and the avoidance of conditions producing them, her arguments concerning psychic personhood--as we have seen--are directed to those processes of CNS emergence involving the formation of integrative pathways which might exert some type of "memory" effect. Such concern surely entails not only responsible maternal care but also an *enabling societal concern*, one that ensures the availability of proper prenatal services to all women seeking to care well for the fetal lives their bodies sustain. Thus we find, perhaps surprisingly, that the early events of human neuromaturation--as stated thus far--may have much to do with how we view and support full-term pregnancies while having nothing to do with the morality of early abortions.

Emergence of the neocortex: As noted earlier, neocortical development requires many months. The cells of the neocortex are produced by a zone of proliferative cells located some distance from the site of neocortex formation,

thus prospective neocortical cells must actively migrate to their final position--a process that begins at about 52-54 days of embryonic development (Molliver et al, 1973, p.406; Marin-Padilla, 1983, p.34). Continuing for more than three months, this process of cell proliferation and migration produces a succession of neocortical cell layers within which neurons of different function specialize and begin forming synapses, the interconnections that produce a supercellular form of organization: neocortical circuitry. The first of these synapses are formed some time between 19 and 22 weeks of development (Molliver et al, 1973, p.404), although most neocortical synaptogenesis occurs over an extended period of time beginning at about the 28th week (Purpura, 1975, p.45-46, examining the visual neocortex), a time after which the key neuronal classes of the neocortex exhibit on their dendritic extensions the tiny projections or spines which are the necessary "targets" for establishing neocortical circuitry which is *morphophysiologicaly equivalent* to that of a full-term neonate.

Of greater importance for our purposes here, perhaps, is Purpura's observation that such dendritic spine development "does not represent a continuous process traceable to early fetal phases of dendritic differentiation." Thus, for example, while neocortical cells of 24 to 27 week fetuses have already begun formation of dendritic extensions, they possess no dendritic spines (Purpura, 1975, p.46). Rather, they begin to appear "suddenly" at around the 28th week. This rapid appearance of dendritic spines is an example of what was earlier termed an "uneven continuity," a developmental transition (Transition 3 in Figure 1) occurring over a relatively short time period (in this case, the seventh month of pregnancy). This observation should not be taken to mean that prior to 28 weeks the visual region of the neocortex is inactive. In fact, preterm infants exhibit electrical activity in the visual neocortex (visual evoked responses or VERs) as early as 24-25 weeks of gestation (i.e. after the time of appropriate thalamocortical connection to be noted below). In the particular situation studied by Purpura and his colleagues, the transition in synaptic capability (and thus supercellular circuit-forming capacity) was associated with a qualitative change in this functional VER activity to that characteristic of a full-term neonatal VER (i.e. attainment of morphophysiological equivalence as an outcome of neuromaturational events of the seventh gestational month).

In short then, at least one region of the neocortex, that one processing visual information, exhibits a rather sharply-bounded developmental emergence of dendritic spines that in turn enables a quantitative leap in synaptic connectivity. Whether other regions of the neocortex follow a similar time-course of synaptic transition--that is, whether this time period might reflect a nearly *qualitative* shift in over-all neocortical capability--is not known with certainty. However, recent observation of simultaneous or *isosynchronous* synapse production in *diverse* regions of the cortex of non-human primates at a stage of neuromaturation comparable to that studied by Purpura is suggestive of this possibility (Rakic et al, 1986). If fetal humans exhibit this self-same isosynchronous synaptic transition then we might expect that Transition 3 (Figure 1) leads to a neocortex exhibiting qualitative different capabilities.

What sensory input is there for the neocortex to process?

It would hardly be controversial to argue that we are most likely to attend to fetuses whose level of neuromaturation supports (we suspect) some determinable form of awareness. After all, aware is how we are (if not asleep, anaesthetized, or in a coma). And to be aware--unless there is some form of awareness that is subcortical--there must be a synaptically interconnected neocortex and sensory input to it. How and when is the latter achieved?

Nearly all input to the neocortex passes through the thalamus, an important multi-component structure that modulates qualitatively different "types" of sensory input prior to passing them on to appropriate regions of the sensory neocortex. Without functional thalamocortical connections, the neocortex is nearly isolated and, in any case, not in receipt of the sort of neural information which when processed is represented as sensation. Thus, we can change the question posed above: do we have any knowledge of the developmental time-course over which thalamic neurons send out extensions to and connect with the neocortex? Studies by Kostovic and Goldman-Rakic (1983) and Dostovic and Rakic (1984) indicate that two regions of the thalamus (the pulvinar and mediodorsal) produce fibers that penetrate the neocortex at least as early as the 22nd or 23rd week (Transition 2 in Figure 1) but probably not much earlier. It is possible that the first neocortical synapses detected by Molliver and co-workers (1973) number among them initial contacts between neocortical cells and sensory-input fibers--although at present there is no evidence that this is (or is not) the case. It is possible that other regions of the thalamus send extensions toward the forming neocortex at earlier times. If they do, however, any synaptic interconnection could not involve the neocortex proper (for, as we have just seen, no neocortical synapses are seen earlier than 19 weeks of gestation). The thalamocortical axons might target cells which lie "beneath" the overlying neocortex (the so-called subplate region) as the former "await" maturation of their eventual targets in the neocortex itself--a situation suggested to occur in the maturation of the neocortex of other mammals (Chun, Nakamura and Shatz, 1987). As indicated above, most of neocortical synaptogenesis--including the bulk of those thalamocortical connections linking the "sensory outside" to the neocortical neurons which underpin a possible "awareness within" --are established many weeks later. Thus, beginning at perhaps 21 to 23 weeks of gestation there is a transition to a neocortex potentially in receipt of sensory input.

Neocortical Activity At and After Mid-Gestation

In spite of the evidence we have just examined, we cannot as yet define what degree and kind of neocortical synaptogenesis is necessary and sufficient to support particular complex CNS functions, including some degree of awareness. We can, however, follow the emergence of increasingly complex electroencephalograms (EEGs) as well as the behavior of premature fetal-infants, and note the "resemblance" of both to those of older infants.

Prior to mid-gestation, the electrical activity associated with brain function is relatively unorganized and does not exhibit patterns suggesting the

type of activity characteristic of much older fetuses or newborn infants. After mid-gestation, however, a series of increasingly complex EEG pattern changes occur. Thus, Transition 2 is characterized not only by initial neocortical synaptogenesis and arrival of sensory input channels but by the first manifestation of patterned (but intermittent) brain waves as well. Gertler (1986) has recently suggested that this first appearance of neocortical activity constitute what he terms "brain birth." However, what sort of brain birth is this? Normal postnatal brain function is characterized by *continuous* electrical activity. An activity pattern of this sort is not present from the time the first neocortical cells begin making synaptic contact; rather, the change in EEG pattern to one of continuous electrical activity occurs at about 30 weeks of gestation--the period designated here as Transition 3. Furthermore, this latter EEG pattern marks the distinction between fetal wakefulness and sleep (Spehlmann, 1981). It is maybe significant that this latter activity transition occurs as the number and type of neocortical synapses changes between 28 and 32 weeks of development, perhaps representing the functional outcome of the suggested isosynchronous shift in pattern of neuronal connectivity noted earlier.

This period of transition is highlighted by other observations as well. Premature fetal-infants of 28-32 weeks gestation have been characterized (Gesell, 1971) as "loosely articulated and flaccid mannikins"; they are limp and torporous if stimulated. Only several weeks later does this torpor give way to a genuine wakefulness when the newborn is stirred to activity, just about the time (roughly 34-36 weeks of gestational age) EEG patterns change once again and there emerge so-called "behavioral states"--stable, synchronously recurrent constellations of activities (motility, breathing and heart rate) that had previously changed independently of one another (Prechtl and O'Brien, 1982; Nijhuis *et al*, 1982).

Looking at what has been said, *it seems we may have the greatest difficulty deciding what to make of the period of time from 20 to 30 weeks*, the interim between Transitions 2 and 3. At the outset of this time period the neocortex is a collection of individual neurons; at the "end," an interconnected collective exhibiting continuous electrical activity and participating in cycles of fetal sleep and wakefulness. If we are wont to speak seriously of fetal personhood, we will surely focus on this time period, a time frame which brackets the second-to-third trimester "division." Of crucial importance, of course, is whether we look to the earliest events and talk of a personhood-entitling "brain birth" as Gertler has suggested, or whether we turn our attention to the (perhaps) qualitative shift in neocortical connectivity and emergence of sleep/wake cycles occurring near this period's end, thereby requiring as a developmental difference which makes a moral difference a fetal neocortex exhibiting morphophysiological properties similar to those of full-term infants. Whatever tentative choice we might make as between Transitions 2 and 3, it is clear the course of fetal ontogenesis bracketed by these transitions is one about which we need much more information.

The "Finishing Touches" of Neuromaturation

Neuromaturation is not a process ending at birth. For example, Huttenlocher (1979) and Huttenlocher *et al* (1982) have followed the process of

neocortical synaptogenesis from the 28th week of gestation to early adolescence. They found that the number of synapses increases rapidly during the last weeks of prenatal development and up until about one year of age after which time there is a gradual loss of synapses (especially during early childhood), with the synaptic number characteristic of adults reached by early adolescence.

What does such a decrease represent?

In other organisms, a comparable "paring back" of synaptic connections in some regions of the neocortex has been interpreted as an *activity-or experience dependent* stabilization or "tailoring" of some neural pathways at the expense of others. If a similar neurodevelopmental plasticity is the case in humans as well, one might consider the eventual "fine-tuning" of neocortical connectivity during childhood as a "lived accomplishment." If fine-tuning does occur, it would be unlikely the experiential dimension is the whole story. Thatcher and colleagues (1987, pp.1110-1113) have recently demonstrated age-dependent changes in neocortical EEG activity from birth through adolescence. From these observations they conclude (p.1113) that during human cortical development "there is a genetically programmed unfolding of specific corticocortical connections at relatively specific postnatal ages." Combining these views, one could say (not at all surprisingly) that as each of us lives our early years, the experiencing of our world "shapes", at least in part, the neocortical pathways so crucial to developing personhood. Neuromaturation and emergent personhood are thus as inextricably intermeshed as are the myriad neuronal circuits that comprise the human central nervous system.

Where has our investigation of embryonic and fetal neuromaturation led us?

Observations of neuromaturation suggest the possibility of three significant integrative transitions during ontogenesis of the prenatal human CNS. The first appears to involve the brainstem's modulatory effect on patterns of fetal motility emerging during the first trimester. It has been argued here and by Tauer (1985), however, that this integrative function is not one which would lead us to predicate a sort of fetal personhood barring abortion in the first trimester. The second transition is undoubtedly more complex. It includes the arrival in the neocortex of sensory-input fibers from the thalamus--a minimal requirement for establishing even the possibility of awareness at the neocortical level. The third transition is marked by the emergence of continuous EEG activity and wake/sleep cycles; it may also be characterized by a rather abruptly initiated period of dendritic spine formation, thereby providing the capacity for a type of synaptogenesis characteristic of more mature neocortical circuitry and (perhaps) establishing the first material possibility of neocortical functions comparable to those of normal, full-term infants--including, one might presume, the first manifestation of awareness. Thus, if we return to those neocortical capacities most likely to engage our moral attention as we prepare to ascribe a protected status of fetal personhood (i.e. possible awareness and/or a discrete and sustainable bodily existence regularly achieved through birth), we might be led to conclude that it is probably not until after 28 weeks of gestation that the fetal human attains a level of neocortex-mediated complexity sufficient to enable

those sentient capacities the presence of which might lead us to predicate personhood of a sort we attribute to full-term newborns.

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