

Chapter 6

Fetal Pain

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Introduction

Discussion regarding the possibility of fetal pain began in earnest after it was discovered that the fetus will mount a hormonal stress response during invasive procedures (Giannakouloupoulos et al. 1994). The release of cortisol and β -endorphin following fetal tissue damage raised concern that the fetus may feel pain and generated considerable scientific and public debate. Scientific debate has largely focused on understanding the critical periods of change during fetal development that may bear on the experience of pain (Lee et al. 2005). Public debate has largely focused on the implications for abortion and the possibility (now a reality in large parts of America) that abortion should be restricted or regulated to prevent fetal pain (Brugger 2012).

In line with the dominant scientific debate, this review first focuses on the critical neurodevelopmental moments that are thought to be necessary for fetal pain experience. Serious limitations of this approach, however, will also be raised to explain why a neuroscientific answer to the issue of fetal pain remains inaccessible. Finally, it will be argued that fetal pain is an immensely provocative and thought-provoking issue that cannot be usefully used to guide clinical practice or policy.

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Approaches from Neuroscience

Probably the most audacious, and brilliant, attempt to end the fetal pain debate comes from the work of Mellor (2005). In 2005, Mellor published a comprehensive review documenting many decades of highly detailed observations of, mostly, fetal lambs. Those observations indicated that the fetal lamb rarely shows any behavioral signs of waking or alertness during gestation. In addition, the EEG pattern of fetal lambs indicates continuous sleep and that sleep pattern is not broken by hypoxic stress. Indeed, the EEG pattern shifts to a more quiescent state during periods of hypoxic stress (Hunter et al. 2003).

Based on observation and deduction, Mellor argued that the fetus is in a constant state of sedation or sleep throughout the whole of pregnancy, and never awakens. The environment of the womb is dark, quiet, warm, and buoyant, which places an emphasis on sleep. In addition, there is no avenue of escape or possibility of rescue from the womb, so there is nothing to be gained by expending energy on activity when under threat. Finally, the placenta provides a chemical environment, involving the release of adenosine, which maintains or enhances sleep.

The Mellor argument potentially ends the discussion about fetal pain because, regardless of any arguments about the neural or psychological readiness of the fetus, it is broadly accepted that feeling pain during sleep is not possible (Nofzinger and Derbyshire 2007; Wang et al. 2004). There are, however, important problems with Mellor's argument and, ultimately, the argument has failed to end the fetal pain debate. The failure is, however, highly interesting, and has important implications for all attempts to resolve the question of fetal pain using neuroscientific observations.

Problems begin with the interpretation of fetal EEG as "sleep" and "quiescence." When hypoxic stress is induced, the fetal lamb EEG shows a clear transition from a heightened state of activity to a reduced state of activity that can be viewed as a relative quiescence (Hunter et al. 2003). Within that relative quiescence, however, are various bursts and spikes of activity that are clearly not indicative of silence. The meaning of those bursts and spikes is uncertain, but they are not easily explained as "sleep." Furthermore, the normal EEG pattern of the fetus is not easily recognizable as a typical "sleep" pattern. In adult mammals, sleep is accompanied by characteristic stages of EEG wave patterns that are used to define the type of sleep that is occurring, such as dream sleep or deep sleep (Hobson 2005). These stages, however, are not apparent in the newborn neonate, which has essentially the same EEG pattern during waking and sleep (Weerd and Bossche 2003). Thus, it is not surprising that the EEG patterns observed in the fetus cannot be easily mapped onto the EEG patterns observed during sleep in the mature mammal. Although it is plausible that the fetus transitions from one state of sleep to a deeper state of sleep during stress, as Mellor argues, it is possibly more reasonable to state that the fetus transitions from one uncertain state of being to another uncertain state of being. The terms "sleep," "wakefulness," and so on imply a state of subjective existence that is not directly apparent in any of the EEG or other technical measures that might be made during gestation.

There is a difficulty in using terms that are, at least partially, subjective, such as “sleep,” in association with technical measurements, such as EEG. Technical measurements, such as EEG waveforms, are inherently precise and provide units that deliver exact information. In contrast, subjective states, such as wakefulness, are less precise. There is a tendency to read the technical precision into the subjective state, as if the technical measure *were* the subjective state or as if the subjective state has the same precision as the technical measurement. This problem is evident for all attempts to resolve the question of fetal pain with neuroscience as will now be explored in more detail.

Neurodevelopmental Stages Relevant to Pain

Several distinct stages in development have been identified as important for pain. The earliest gestational moment at which pain has been suggested is 7–8 weeks when the first reflex responses to touch appear (Humphrey 1964). At this point, there is evidence of free nerve endings in the periphery (skin) that are necessary for detecting stimuli in the noxious range. Reflex responses to touch demonstrate that there are connections from the periphery to the spinal cord and there is also evidence of further projections into the thalamus (Fitzgerald 1987).

Reflex responses mediated by the spinal cord, however, are not considered sufficient to support conscious pain experience. Indeed, spinal reflexes occur in mature adults and precede conscious experience; rapid withdrawal from an unexpected noxious stimulus occurs automatically, without conscious intervention (Petkó and Antal 2000). Although further projection from the spinal cord to the thalamus provides an additional neural basis for conscious experience, it should be noted that at 7–8-week gestation, the thalamus is profoundly immature. At this gestation, the thalamus lacks all evidence of the cellular structure associated with the more mature thalamus (Hevner 2000; Larroche 1981). Neuroscientists are yet to fully understand the precise relationship between structure and function; however, it is evident that some relationship exists. The stark immaturity of the thalamus at 7–8 weeks casts doubt on the likelihood of the thalamus delivering a mature function, such as would be necessary to generate an experience of pain.

In addition, however, at 7–8-week gestation the cortex is almost entirely absent and there are no thalamocortical projections. Although contentious, as discussed later, most neuroscientists view the cortex as necessary for pain experience (reviewed in RCOG 2010).

The next gestational moment that has been identified as important for pain occurs at 12–18 weeks when the subplate begins to form (Ulfig et al. 2000). The subplate is a developmental structure that forms underneath the cortical plate proper from 12-week gestation. Neurons destined for the cortical plate first migrate into the subplate where they wait until the cortical plate above is sufficiently mature, and then the neurons migrate to their mature position in the cortex. At 18-week gestation, there

are the first projections from the thalamus into the cortical subplate. As the neurons migrate, the subplate withers away and becomes the underlying white matter connecting cortical regions. This migration begins around 24-week gestation (Kostovic and Judas 2010).

There is evidence that the connections from the thalamus to the subplate are functional, and some have interpreted this functionality as sufficient for an experience of pain (Bhutta and Anand 2002). Similar to the immature thalamus, however, the subplate is not a mature structure. Typically, the subplate is understood as a developmental structure that is necessary for mature development (Ulfig et al. 2000). In itself, however, the subplate is not a mature structure capable of mature function such as the delivery of pain experience.

At 18-week gestation, it has been demonstrated that the fetus mounts a hormonal stress response (release of cortisol and β -endorphin) in response to noxious stimulation (Giannakouloupoulos et al. 1994). As mentioned earlier, this report largely began the current debate about fetal pain because the authors stated that “[the hormonal stress response of the fetus raises] the possibility that the human fetus feels pain in utero.” That statement, however, somewhat overstated what can be inferred from a hormonal stress response. While certainly consistent with an experience of pain, increases in cortisol and β -endorphin also occur when someone is anxious, exercising, or undergoing surgery with a general anesthetic (Mellor et al. 2005). Thus, the stress response cannot be equated with pain and is better understood as a generalized response mediated by brainstem circuits.

The next gestational moment that has been identified as important for pain occurs at 24–28-week gestation. By 24-week gestation, the cortical plate proper shows clear signs of maturity (including a laminar structure), and receives direct projections from the thalamus (Kostovic and Judas 2002). In addition, experiments with very premature infants at an equivalent age of around 24-week gestation show a clear cortical response following a standard heel lance procedure (Slater et al. 2006). Thus, by around 24-week gestation, there is good evidence of a complete connection from the periphery, through the spinal cord, into the thalamus and into the cortex. And there is also good reason to consider that connection functional and able to deliver nociceptive signals. Many have interpreted this moment as the point at which fetal pain is at least possible and, more typically, probable (Lee et al. 2005; RCOG 2010). If there is any consensus on the question of fetal pain, it is that fetal pain is unlikely before 24-week gestation, but increasingly likely afterwards. A committee of clinicians, academics, and medical professionals reporting on the possibility of fetal awareness for the British Royal College of Gynecologists (RCOG) summarized this consensus position:

In reviewing the neuroanatomical and physiological evidence in the fetus, it was apparent that connections from the periphery to the cortex are not intact before 24 weeks of gestation and, as most neuroscientists believe that the cortex is necessary for pain perception, it can be concluded that the fetus cannot experience pain in any sense prior to this gestation. (RCOG 2010).

Challenging the Neurodevelopmental Evidence

While a general consensus has emerged that fetal pain is not possible before 24-week gestation, a number of clinicians and investigators forcefully argue that fetal pain is possible well before 24 weeks (Anand 2007; Lowery et al. 2007; Merker 2007). There appear to be two dominant arguments within this position of dissent. The first is that the cortex is not necessary for pain experience and that pain can, instead, be supported by subcortical structures. The second is that observations of fetal behavior and facial expressions are sufficient to directly infer, or intuit, conscious states such as pain.

These arguments often run together. For example, Merker has reported that anencephalic infants, who survive with no, or highly minimal, cortex, go on to become infants with a clear emotional and conscious existence (Merker 2007). Merker bases his conclusion on observations of anencephalic infants who clearly laugh, show signs of upset, and generally display evidence of affective behavior. More anecdotally, obstetrician/gynecologist Stuart Campbell (personal communication) has observed the facial expressions of fetuses under 20 weeks with 4D ultrasound and claimed that the images indicate evidence of smiling and grimacing. More controlled examinations of 4D ultrasound images have provided similar, albeit more nuanced, interpretations (Reissland et al. 2011, 2013).

From these observations of apparent emotional responses, it is argued that the available underlying neural circuitry must be sufficient to support fetal experience, including fetal pain. The logic of the argument is compelling. Fetuses respond to a noxious event with a withdrawal, which at least demonstrates some capacity to detect damaging stimuli. The detection and withdrawal are dependent upon coherent activity within a signaling system, which is typically taken to be thalamic-brainstem-spinal circuitry. Although the consensus position is that the cortex is necessary for pain, there is no adequate explanation for how the cortex might directly give rise to pain. Consequently, it is difficult to explain why coherent activity within other parts of the nervous system cannot also give rise to pain. The argument is especially compelling because observation of the fetus gives a direct impression of pain; it just seems intuitively right that something akin to pain is being experienced.

The Argument from Intuition

In 1764, Voltaire issued a direct challenge to those, such as Descartes, who claimed that animals could not feel pain:

Answer me, machinist, has nature arranged all the springs of sentiment in this animal that he should not feel? Has he nerves, and is he incapable of suffering?

Here Voltaire argues from what appears to be intuitively correct. If the animal has a nervous system and responds as if it feels, how could it be that the animal does not feel? The position Voltaire adopts is one that many spontaneously feel is self-evidently correct. A similar position is adopted by many who argue that the fetus feels pain as soon as there is evidence of a behavioral reaction, which is before 10-week gestation.

Although this argument from intuition has some purchase, there are important limitations to an argument that relies on what “feels” right. The most important limitation is precisely that assumptions made based on observation and intuition can be incorrect. Cartoon characters can be observed to “emote” and “experience” but we know that the inference is incorrect and directly manipulated by the makers of the cartoon. Formal study has demonstrated that the inference of intention and feeling can be induced for colored shapes using relatively minor animations (Hamlin et al. 2007). If such an inference can be made with fairly crude images, then it is unsurprising that exquisite 4D ultrasound images have created quite powerful inferences about the experiences of the fetus.

To answer Voltaire, the cartoonist, for sure, has precisely “arranged all the springs of sentiment” without the cartoon feeling anything. The spontaneous feeling that objects and moving images are feeling is not accepted as indicating the true feelings of objects and moving images. Interestingly, prenatal health professionals also spontaneously ascribe feelings and thoughts to their fetal patients but when directly asked about the nature of those feelings and thoughts, the intuitions about fetal experience can diminish. Consider this comment from a midwife who was asked if the fetus could feel pain:

... it's most bizarre, now that you've asked me that question [can the fetus feel pain?], I kind of can't make the leap. (Williams 2005).

What this comment represents is a real tension between pain as a direct response to injury, which is apparently self-evident, and pain as a conscious experience, which is much less self-evident. Injury and behavior can be directly observed but experience cannot be. For older adults and infants, language is used to directly communicate experience. When used honestly, language provides an accurate portrayal of personal experience. In the absence of language, experience has to be inferred, and the process of inference is fraught with difficulty.

To summarize, direct empirical observation and intuition, either apart or combined, fail to adequately resolve whether the fetus feels pain. In light of these failings, the next section offers an alternate approach.

The Argument from “Reason”

A problem with both a pure empirical approach and an approach from intuition is the lack of any clear statement or investigation of the pain experience itself. The construct of pain is not examined and is, instead, presented as something

already known and understood. The problem with such an approach is that pain can be understood as something extremely complex or something relatively straightforward. The International Association for the Study of Pain (IASP), for example, defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey 1991). The definition goes on to explain that “pain is always subjective. Each individual learns the application of the word through experiences related to injury in early life.” Thus the IASP definition describes pain as multidimensional and subjective. The definition also implies that pain cannot be experienced before developmental processes that occur after birth.

In contrast, Anand and Craig (1996) have criticized the IASP definition as involving more complexity than necessary for an experience of pain that might be relevant to the fetus. Thus, the fetus may have a first-order, direct and immediate, painful experience without second-order reflection and knowledge of being in pain. A fetus gripped by forceps might just be “in pain” without an explicit recognition of being in pain or knowing that “I am in pain” (Tallis 2005).

The distinction between “being that” and “knowing that” might be useful in separating the IASP definition of pain from the definition provided by Anand and Craig (1996). Being in pain implies a direct apprehension of a stimulus without any comprehension. Direct apprehension might be something attributable to a fetus but not comprehension, which would involve knowledge such as the body part being threatened, identification of the sensation (crushing or stinging, for example), and reflection on the broader implications (fear of injury or death). Direct apprehension avoids attributing a level of knowledge that is implausible for the fetus. For a fetus to experience a crushing sensation in his or her leg, for example, the fetus would need some knowledge of what it is to be crushed—the difference between compression and torque—and knowledge of separate bodily appendages. These conceptual items of knowledge, however, will not be available to the fetus and so the IASP definition of pain cannot be easily mapped onto “fetal pain.”

From the above discussion, if the fetus does feel pain then it is a pain without the fear and sensory identity that is typical of pain experiences known to mature human beings. A pain without explicit localization, sensory components, and fear will, at least, lack some of the paradigmatic components of a typical pain experience (Corns 2014). Some of the negativity of pain is bound up in the threat to bodily integrity that is known to the injured subject and which cannot be easily reduced to measures of physical damage (Pustilnik, 2012). Human beings experience pain partly *through* the unpleasantness and anxiety that come from associating the outcome (a crushed limb) with concern for greater, more unpleasant outcomes (free movement, infection, death) (Derbyshire and Raja 2011).

In addition to the above limitations, it is unclear whether an “experience” of pain that is a pure immediacy and without comprehension is possible, or could ever constitute something deserving the term “experience.” At any given moment, many sensory neurons will be firing in response to different pressures, lights, sounds, smells, and so forth. Think right now of the many sensory neurons firing as you hold and manipulate this book. The sensory receptors in your hands, for example,

will fire as you adjust and relocate the book in your field of view. In general, however, you will not be aware of sensations associated with holding and manipulating the book. Your focus of attention, understanding, and experience will be dominated by the flow of understanding as you take in the words. Being aware of every sensation would drown out your ability to read and understand, because the cacophony of sensations would deliver a totality of being to your consciousness. You would, however, not be able to experience that totality because conscious beings experience specifics and not a totality. Human beings are “self-located” within experience. Viewing a Rothko canvas that includes 32 m of red, for example, may fill the viewer with an experience of red, but he or she will not become the experience red; they will remain self-located within the experience of red.

Some sort of conceptual apparatus is necessary to divide up the sensory world into that which fits together and requires attention, and that which can be ignored. A conceptual system that holds sensations together, *and* keeps sensations apart, seems necessary even for raw and immediate sensory experience. Such a conceptual apparatus is generally not considered to be available until sometime after birth (Hobson 2002; Vygotsky 1978).

Conclusion

Most discussion of fetal pain summarizes evidence from neuroscience. This approach is compelling and, to a point, highly persuasive. To the author’s knowledge, every commentary on fetal pain accepts that a minimum nervous system is necessary for pain (Anand and Hickey 1987; Brusseau 2008; Derbyshire 2006; Lee et al. 2005; Mellor et al. 2005; Vanhatalo and van Nieuwenhuizen 2000; Van Scheltema et al. 2008). That minimum nervous system includes peripheral nerve fibers that can detect noxious stimuli, and a central nervous system that can receive input from peripheral nerve fibers. The earliest that such a system is available in the human fetus is between 8- and 12-week gestation. Consequently, it is essentially agreed that pain is not possible until the latter part of the first trimester.

After 12 weeks, however, there is an intact peripheral and central nervous system that can, at least, process noxious stimulation in some fashion. Consensus over what experience might follow from this processing becomes much less clear. The majority of neuroscientists argue that the cortex is necessary for pain and, as the cortex is not a “functional unit” and is not connected to the periphery via the thalamus before 24-week gestation, pain is not possible until the third trimester (RCOG 2010). A significant minority of neuroscientists and clinicians, however, argue that subcortical circuitry, possibly combined with activity in the cortical subplate, is sufficient for fetal pain (Anand 2007; Lowery et al. 2007; Merker 2007). Thus, these authors suggest the possibility of fetal pain from 12-week gestation with increasing certainty from 18 weeks when the first thalamocortical fibers reach the subplate (Ulfig et al. 2000).

Rejecting this minority position on neuroscientific grounds alone is difficult. There is, currently, no comprehensive account of how neural activity gives rise to

pain experience or to any other experience. It remains highly uncertain exactly what neural activity means in terms of experience. Efforts to reject fetal pain on the grounds that the fetal EEG indicates “sleep” fail because it is not clear what “sleep” means for a fetus. Sleep can be described in terms of relative behavioral inactivity, reductions in electromyogram activity, changes in EEG activity, and changes in sensory and cognitive awareness (Hobson 2005). Physiological measurements of the fetus are generally consistent with the fetus being asleep but there are inconsistencies, including mobility in response to noxious stimuli, and EEG patterns that are not precisely consistent with known sleep stages (Hunter et al. 2003; Williams 2005). Most importantly, however, the very notion of “sleep” is a construction that arises largely from the subjective experience of a nightly fading consciousness combined with a loss of volitional control. All physiological measures are interpreted with reference to that construction of sleep but they do not bind or constitute sleep. Consequently, physiological recordings from the fetus cannot resolve whether the fetus is in a state of sleep or wakefulness. Fetal EEG recordings, for example, might not display patterns that are equivalent to mature states of wakefulness, but that does not mean the fetus lacks the capacity for some sort of wakefulness and, with it, some form of conscious experience, including pain (Van Scheltema et al. 2008). In essence, without a comprehensive understanding of how conscious states fall out of neural states, we have no principled position from which any fetal experience might be accepted or refuted.

Given this difficulty, some investigators and commentators have claimed that fetal experience can be accepted on intuitive grounds: there is a minimal nervous system present for the processing of noxious stimuli from at least 18-week gestation and, at the same gestation, the fetus will flinch, move away from a noxious stimulus, and show evidence of facial grimacing during noxious procedures (Reissland et al. 2011, 2013; Savell 2007; Williams 2005). When this evidence is taken together, it seems right to accept fetal pain.

The argument from intuition, however, fails for the same reason that it succeeds. When asked to rate the pain and distress of neonates under medical care, parents and health professionals can rate neonates as being “in pain” but not “in distress” (Elias et al. 2014). It is difficult to understand how a being might be in pain but not distressed. It is possible that healthcare teams make a distinction between pain in the sense of tissue damage, and pain in the sense of experience (Corns 2014). When pressed to describe pain in terms of experience, even those who work with fetuses and neonates in need of clinical care have difficulty in accepting the notion of fetal pain (Williams 2005). Thus, there may be a spontaneous intuition that fetal pain is possible but a more reflective intuition that the experience of pain imparts too much conceptual structure onto the fetus.

The lack of definitive answers from neuroscience and intuition suggests that the concerned putative parent and clinician must turn elsewhere to understand whether fetal pain is possible. Pain scientists long ago adopted a definition and understanding of pain as a multidimensional and subjective state that would appear to, *prima facie*, rule out the possibility of fetal pain (Merskey 1991). If pain is a highly

abstract, conceptual, subjective experience, then fetal pain is not possible; it is implausible to attribute so much conceptual and subjective experience to the fetus.

Opposition to this understanding of pain has led to suggestions that pain experience, for the fetus and neonate, might be more immediate, raw, and relevant to the needs and processing capacity of the more immature nervous system (Anand and Craig 1996). Thus, the fetus might experience something akin to pain without the self-reflective, explicit knowledge of *being in* pain (Derbyshire and Raja 2011).

While this distinction between a raw and more knowledge-based experience of pain looks like it may be useful and true, there remain considerable difficulties in explaining how the non-conceptual mind of a fetus might grab hold of any single experience amongst the cacophony of other possible experiences. The nervous system continuously receives an abundance of sensory input that could generate any number of experiences together. Consciousness experiences a singular stream of awareness, not a totality.

On balance, it is reasonable to conclude that the fetus cannot experience pain, at least not in any equivalent way to how mature infants and adults experience pain. An immediate, fleeting, experience, even if possible, will lack the precision and associated fear and dread of a more mature pain experience.

The above conclusion may provide sufficient reassurance for many clinicians and women seeking fetal procedures that fetal pain is not something for concern. It is, however, not possible to use fetal pain to provide a definitive guide for clinical practice or legal policy regarding the fetus. The fetal patient undergoing therapeutic surgery is not the same as a more mature infant who will self-explicitly report their feelings, distinguish the experience from other experiences, and remember the events of surgery. In the absence of a subjectivity to engage and without the possibility of a subjectivity that will be retained, the clinician can focus on other, measurable and objective, indicators of well-being. Rates of surgical complication, morbidity and mortality, unlike speculation about fetal pain, can provide a definitive guide to surgical practice (Anand et al. 1987). The later good that will accrue to the fetus from the minimizing of negative surgical outcomes provides sufficient moral justification for the followed procedures.

In the case of a woman seeking a pregnancy termination, there is no life to lead after the procedure and so there is no later good that will accrue to the fetus. The pregnant woman is precisely choosing to end her pregnancy, and while she may have concerns about the well-being of her fetus, that concern is obviously bounded by the greater decision to end the life of the fetus. Currently, the law in most countries recognizes that the definite subjectivity and personhood of the woman take precedence over the highly uncertain subjectivity, and not-yet personhood, of the fetus. Arguments about whether such laws are right or wrong cannot be resolved via the discussion of fetal pain (Derbyshire 2006).

In summary, assessing the evidence for and against fetal pain is not straightforward, and cannot be resolved with neuroscience or intuition. Whether the fetus can feel pain critically depends on what is meant by "pain." For the older infant and adult, pain is a multidimensional, subjective state that cannot be plausibly experienced by the fetus. By that account, fetal pain is impossible at any stage of gestation.

The younger infant and fetus, however, may experience a rawer, more immediate, “pain” that gradually matures into the multidimensional, subjective experience of older infants and adults. Even this experience, however, is not obviously plausible without a conceptual apparatus that can, at least, isolate one sensory state from another. The need for some psychological development to experience even the most basic of states seems necessary, and rules out fetal pain at any stage of gestation.

The vexed nature of the argument about fetal pain renders it an unsuitable grounding for deciding clinical practice or policy. Instead, therapeutic surgery for the fetus can be guided by objective measures of outcomes decided in clinical trials. Policy towards termination can be guided by democratic discussion of when society thinks it is acceptable for a woman to decide that she will not continue to be pregnant.

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