

Legal and animal welfare implications of when consciousness first appears in developing young and of the potential for delayed onset of increased pain sensitivity

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Introduction

During the recent past the extent to which mammalian foetuses may experience sensations, including pain, has been re-evaluated. The conclusion, based on integrating previously uncollated high quality scientific evidence widely distributed in the literature and on our own more recent research, is that conscious experience of sensations does not normally occur until after birth in any mammalian young observed to date ((Mellor and Gregory, 2003; Mellor and Stafford, 2004; Lee et al., 2005; Mellor et al., 2005; Mellor and Diesch, 2006, 2007; Diesch et al., 2008). A rather similar, but qualified, conclusion has been drawn regarding the possibility that consciousness may not occur until after hatching in domestic chickens (Mellor and Diesch, 2007), but this will not be addressed here. Such conclusions have relevance to the definition of 'animal' in those animal welfare laws which focus on the possibility of an organism suffering through the conscious perception of noxious stimuli (e.g. feeling pain). That is because those definitions usually exclude developmental stages when, at the time the legislation was framed, the young were presumed to lack the capacity for conscious perception. For instance, mammalian foetuses are protected under the New Zealand Animal Welfare Act 1999 after the first half of pregnancy has elapsed, and marsupial pouch young are protected from immediately after birth.

The purposes of the present paper are, first, to briefly summarise the main conclusions about the onset of 'awareness' or consciousness during development of mammalian young and the timing of that in relation to birth. The second is to evaluate the possibility that invasive stimuli applied before the onset of conscious perception could subsequently increase an animal's sensitivity to pain and suffering after the capacity for

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consciousness has developed. Finally, consideration will be given to the potential impact of these insights on the utility and appropriateness of some facets of the current definition of 'animal' in welfare legislation, principally the New Zealand Animal Welfare Act 1999 (Anonymous, 1999).

As most of the ideas presented here on the onset of consciousness have been published in the reviews noted above only the major points are summarised and the reader is referred to these original publications.

Developmental pattern of the mammalian nervous system

The general pattern of neurological development appears to be rather similar in most mammals, irrespective of when the capacities for sensory perception and conscious awareness first appear in relation to the timing of birth.

Neuroanatomically, there is a progression in all cases from rudimentary neural structures towards increasing size, complexity and maturity such that peripheral, visceral, spinal and brain nerve tracts and related neural aggregations and tracts develop, proliferate, interconnect and grow. Associated with this neuroanatomical development is a functional maturation that is reflected in changes in behaviour and in the electrical activity of the brain.

Behaviourally, initial 'startles' or jerky whole-body movements progress through individual limb, neck or head movements to later apparently purposeful and eventually well-coordinated limb movements or changes in body position within the uterus or pouch (in marsupials).

Neurophysiologically, a progression of electrical states in the brain parallels these behavioural changes. Electrical activity in the cerebral cortex is of particular note because functional maturation of the cortex is considered to be an essential prerequisite of conscious awareness. Pre-cortical and cortical structures are electrically silent initially – i.e. there is no activity in the electroencephalogram (EEG). The EEG then exhibits sporadic spikes, which evolve into short periods of sustained activity against a background of electrical silence. Continuous mixed sleep-like EEG activity then appears and this subsequently matures into differentiated and alternating rapid-eye-movement (REM) and non-REM sleep-like patterns. Finally, EEG patterns indicating repetitive sleep-wake cycles are the last to appear, and, as we shall see, this usually occurs after birth.

Relation between neurological development and states of unconsciousness

During the early stages of electrical silence and sporadic short epochs of EEG activity the cerebral cortex does not have the functional capacity to support any states resembling consciousness. Likewise, unconsciousness is likely to continue during the subsequent stage of continuous undifferentiated sleep-like EEG activity. However, once REM-non-REM differentiation occurs the functional capacity of the brain may have matured sufficiently to support conscious awareness, because it is at this stage that neural connections, which are essential for consciousness, become well established between sub-cortical brain structures and the cerebral cortex. This is indicated by the example of human infants who are born prematurely at 28-30 weeks after conception (full-term is at about 40 weeks), because they exhibit the capacity for conscious awareness during wakeful phases of their repetitive sleep-wake cycles. As we shall see, however, whether or not conscious awareness appears at the stage the brain first develops the capacity to support it very much depends on when birth occurs in relation to that.

Onset of consciousness in relation to birth

This general pattern of neurological development appears to be common in different mammals, but the stage when birth occurs during this developmental path depends on the species and obviously determines the neurological maturity of the young at that time (Ellingson and Rose, 1970; Tyndale-Biscoe and Janssens, 1988). We may illustrate this by comparing young that are neurologically extremely immature, moderately immature or mature at birth.

Extremely immature at birth

Newborn marsupial joeys are neurologically exceptionally immature, and most development occurs postnatally while they are in their mother's pouch (Tyndale-Biscoe and Janssens, 1988). They do not appear to show clear behavioural or EEG evidence of conscious awareness for at least the first one-third to one-half of pouch life, which in the Tammar wallaby (*Macropus eugenii eugenii*), for example, has a total average duration of about 250 days (Tyndale-Biscoe and Janssens, 1988; Diesch et al., 2008). Clearly the marsupial joey is insensate before birth.

Moderately immature at birth

The newborns of a number of other mammals (e.g. cat, dog, mouse, rat, rabbit) are also neurologically immature, but markedly less so than are marsupial joeys. Their EEGs variously exhibit the following characteristics at birth (Ellingson and Rose, 1970): electrical silence or very low voltage; or intermittent activity or continuous and undifferentiated activity. Only after 3-14 days does REM-non-REM differentiation occur, and EEG evidence of conscious wakefulness does not appear before this. The obvious conclusion to be drawn from these observations is that the young of these species are unconscious before birth and therefore cannot experience pain or any other sensations until the capacity for consciousness develops after birth.

There are implications of these observations for the acceptability or otherwise of conducting invasive procedures on such newborns without using anaesthesia or analgesia. As noted above, the absence of sensory perception during unconscious states precludes suffering, and as unconsciousness in these newborns is due to neurological immaturity, potentially noxious stimulation could not arouse them to conscious wakefulness. However, once sleep-wake cycles become established pain relief would be required if the invasive procedure is severe.

Mature at birth

Neurologically mature newborns include lambs, kids, bovine calves, fawns, foals, piglets, guinea-pig pups and human infants (Ellingson and Rose, 1970; Mellor and Gregory, 2003; Mellor and Stafford, 2004; Lee et al., 2005; Mellor et al., 2005; Mellor and Diesch, 2006, 2007). Most published information refers to fetal and newborn lambs and human infants, but sufficient is known about the other species for some cautious inferences to be made about them as well.

Using REM-non-REM differentiation and the establishment of neural connections between the sub-cortical and cortical brain regions as primary criteria, the fetal brains of animals that are neurologically mature at birth appear to develop the capacity to support conscious awareness after about 80% of pregnancy has elapsed. It is not surprising, therefore, that such newborns usually become conscious within the first few minutes to hours after birth. However, although the first appearance of consciousness may occur quite rapidly after birth (i.e. within a few minutes), it probably is not an “off-on” phenomenon like switching on a light; rather, it appears to be more gradual, like slowly increasing the light intensity using a “dimmer” switch.

Once consciousness appears after birth the young will perceive by their senses and will therefore be able to experience pain and, potentially, suffer from it. There is some evidence, however, that during the first few days after birth the young may be less sensitive to painful stimuli. Thus, changes in the EEG that are considered to indicate the intensity of perceived pain are much lower in lambs that are castrated using rubber rings during the first day or two after birth than subsequently (Johnson et al., in press). It is suggested that this may be due to a slow waning of the pain-relieving effects of substances with known anaesthetic, sedative and analgesic actions that are synthesised before birth by the fetal brain (Mellor and Diesch, 2006).

As the onset of consciousness soon after birth indicates that the capacity for consciousness is present in such newborns before birth, this raises the question of whether or not neurologically mature fetuses are in fact conscious before birth. This question will be addressed below.

The consciousness status of neurologically mature fetuses

We have already seen that mammalian embryos, fetuses and newborns are most unlikely to be consciously aware when their EEG is electrically silent, intermittent or continuous with mixed sleep-like patterns, and that it is only after REM-non-REM differentiation occurs that consciousness is likely to be possible. We have also seen that such EEG differentiation occurs before birth only in those mammals that are neurologically mature at that time. Thus, the question of whether or not prenatal consciousness exists is probably relevant only to those fetuses that are neurologically mature at birth.

Three lines of evidence, *taken together*, provide strong support for the view that neurologically mature mammalian fetuses do not normally exhibit conscious awareness before or during birth (Mellor and Gregory, 2003; Mellor et al., 2005, Mellor and Diesch, 2006).

First, fetal EEG patterns and fetal behaviour demonstrate that sleep-like states of unconsciousness are continuously present throughout the last half of pregnancy. This is because the continuous undifferentiated EEG patterns and the differentiated and alternating REM-non-REM patterns, which appear later and are indistinguishable from those seen during postnatal sleep, are all incompatible with consciousness. In addition, during labour there is a shift in the balance between the REM and non-REM states of unconsciousness towards the deeper non-REM state.

Second, at least eight fetal, placental and uterine factors with well-demonstrated inhibitory effects on the fetal EEG apparently operate throughout the last half of pregnancy. They are adenosine, allopregnanolone, pregnanolone, prostaglandin D₃, at least one placental neuroinhibitory peptide, warmth, cushioned tactile stimulation and buoyancy. These observations show that mature fetal cerebrocortical function occurs in an inhibitory physiological environment that is unique to prenatal life.

Third, the neurologically mature fetus is not arousable from non-REM or REM sleep-like states to conscious wakefulness by potentially noxious stimulation such as occurs during induced hypercapnia (high carbon dioxide), exposure to sounds loud enough to cause intense auditory pain and surgical manipulations causing tissue damage. This contrasts strikingly with the situation after birth where these are potent stimuli that arouse sleeping young to conscious wakefulness.

This non-responsiveness to potentially noxious stimulation of the fetus is a further indication of the unique inhibitory functional environment of the fetal brain. The contrasting high responsiveness of the newborn to the same stimuli suggests that expulsion from the uterus at birth would lead to a marked reduction in overall neuroinhibitory influences on the brain. In fact this does seem to occur because immediately after birth the major neuroinhibitors are substantially withdrawn and are replaced by a range of potent neuroactivators that support the onset of conscious awareness (Mellor and Diesch, 2006, 2007).

Potential for pre-conscious induction of greater post-conscious pain sensitivity

Although the pre-conscious organism is not able to *experience* pain, invasive procedures will stimulate nociceptors and thereby cause impulse barrages in those nociceptive nerve tracts that have developed at the time the procedure is conducted. These impulse barrages cause withdrawal reflexes and other behavioural responses, stress hormone release and changes in the rates of blood flow to the brain and other organs during and shortly after invasive procedures (Lee et al., 2005; Mellor et al., 2005). However, none of these responses requires an intact cerebral cortex as they are elicited by neural mechanisms below the level of the cerebral cortex (Lee et al., 2005; Mellor et al., 2005; Mellor and Diesch, 2006, 2007). Nevertheless, they raise the possibility that noxious fetal stimulation might initiate responses in the developing nervous system resulting in long term changes that persist until after the onset of

consciousness. There is an increasing body of evidence in the human literature that children subjected to noxious stimulation as pre-term infants or during the early postnatal period in full-term infants may demonstrate increased perception of pain lasting for many months or years (Taddio et al. 1997, Grunau 2000, Buskila 2003, Grunau 2006). A recent study in our laboratory has suggested that such lasting hyperalgesia might also occur in sheep exposed to the noxious stimulus of castration within 12 hours of birth (McCracken et al. 2006). Whilst as yet unproven, the possibility of such long-term hyperalgesia warrants further study.

Implications for legal definitions of ‘animal’

The New Zealand Animal Welfare Act 1999 has as one of its major purposes the protection of animals from human actions that cause unreasonable or unnecessary pain, distress or other harm (Anonymous, 1999). The definition of ‘animal’ in the Act is framed around this purpose and includes, among other animals, any mammal, bird or reptile at any age apart from the earliest developmental stages. Thus, the definition excludes the first half of gestation or development in the case of mammalian fetuses or avian or reptilian pre-hatched young, respectively, or the developmental stage up to and including birth, before the joey’s entry into the maternal pouch, in the case of marsupials. This was because of the presumption, at the time the Act was framed, that young beyond these stages have the potential to be conscious and experience pain and distress. The observations outlined here cast serious doubt on this presumption with regard to mammalian young. The situation is clearly more complex than was previously envisaged, but the current restrictions have merit, in a precautionary sense, in ensuring that mammalian young are protected before there is any likelihood that they have reached a developmental stage when suffering could occur, or where treatment during pre-conscious stages might eventually be shown to result in greater sensitivity to painful stimuli subsequently, once the capacity for consciousness has developed.

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References

- Anonymous (1999). Animal Welfare Act 1999. Pp 5-6 and 48-67. New Zealand Government Printer, Wellington, NZ.
- Buskila, D., Neumann, L., Zmora, E., Feldman, M., Bolotin, A. and Press, J. (2003). Pain sensitivity in prematurely born adolescents. **Archives of Pediatrics and Adolescent Medicine** **157**, 1079-1082.

- Diesch, T.J., Mellor, D.J., Johnson, C.B. and Lentle, R.G. (2008). Responsiveness to painful stimuli in anaesthetised newborn and young animals of varying neurological maturity (wallaby joeys, rat pups and lambs). **AATEX Journal 14**, Special Issue, 549-552
- Ellingson, R.J. and Rose, G.H. (1970). Ontogenesis of the electroencephalogram. In: *Developmental Neurobiology*, Ed Himwich. Pp 441-474. W.A. Charles C Thomas Publisher, Springfield, Illinois, USA.
- Grunau, R.E. (2000). Long-term consequences of pain in neonates. In: *Pain in Neonates*. Eds Anand, K.J.S., Stevens, B.J., McGrath, P.J. Elsevier, Amsterdam, The Netherlands.
- Grunau, R.E. (2006). Long-term consequences of pain in human neonates. **Seminars in Fetal and Neonatal Medicine 11**, 268.
- Johnson, C.B., Sylvester, S.P., Stafford, K.J., Mitchinson, S.L., Ward, R.N. and Mellor, D.J. Effects of age on the electroencephalographic response to castration in lambs anaesthetised using halothane in oxygen from birth to six weeks old. **Veterinary Anaesthesia and Analgesia** (in press).
- Lee, S.J., Peter Ralston, H.J., Drey, E.A., Partridge, J.C. and Rosen, M.A. (2005). Fetal pain: a systematic multidisciplinary review of the evidence. **Journal of the American Medical Association 294**, 947-954.
- M^cCracken, L., Waran, N., Mitchinson, S. and Johnson, C.B. (2006). Does age of castration influence post-castration hyperalgesia? (Abstract). **Proceedings of IX World Congress of Veterinary Anaesthesiology**, p165.
- Mellor, D.J. and Diesch, T.J. (2006). Onset of sentience: the potential for suffering in fetal and newborn farm animals. **Applied Animal Behaviour Science 100**, 48-57.
- Mellor, D.J. and Diesch, T.J. (2007). Birth and hatching: key events in the onset of 'awareness' in lambs and chicks. **New Zealand Veterinary Journal 55**, 51-60
- Mellor, D.J., Diesch, T.J., Gunn, A.J. and Bennet, L. (2005). The importance of 'awareness' for understanding fetal pain. **Brain Research Reviews 49**, 455-471.
- Mellor, D.J., Diesch, T.J., Gunn, A.J. and Bennet, L. (2008). Fetal 'awareness' and 'pain': what precautions should be taken to safeguard fetal welfare during experiments? **AATEX Journal 14**, Special Issue, 79-83.
- Mellor, D.J. and Gregory, N.G. (2003). Responsiveness, behavioural arousal and awareness in fetal and newborn lambs: experimental, practical and therapeutic implications. **New Zealand Veterinary Journal 51**, 2-13.
- Mellor, D.J. and Stafford, K.J. (2004). Animal welfare implications of neonatal mortality and morbidity in farm animals. **Veterinary Journal 168**, 118-133.
- Taddio, A., Katz, J., Ilersich, A.L. and Koren, G. (1997). Effect of neonatal circumcision on pain response during subsequent routine vaccination. **Lancet 349**, 599-603.
- Tyndale-Biscoe, C.H. and Janssens, P.A. (Eds) (1988). *The developing marsupial: models for biomedical research*. Springer-Verlag, Heidelberg, Germany.