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MINI REVIEW

Markers of consciousness in infants: Towards a 'cluster-based' approach

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Abstract

As recently as the 1980s, it was not uncommon for paediatric surgeons to operate on infants without anaesthesia. Today, the same omission would be considered criminal malpractice, and there is an increased concern with the possibility of consciousness in the earliest stage of human infancy. This concern reflects a more general trend that has characterised science since the early 1990s of taking consciousness seriously. While this attitude shift has opened minds towards the possibility that our earliest experiences predate our first memories, convincing demonstrations of infant consciousness remain challenging given that infants cannot report on their experiences. Furthermore, while many behavioural and neural markers of consciousness that do not rely on language have been validated in adults, no one specific marker can be confidently translated to infancy. For this reason, we have proposed the 'cluster-based' approach, in which a consensus of evidence across many markers, all pointing towards the same developmental period, could be used to argue convincingly for the presence of consciousness.

Conclusion: We review the most promising markers for early consciousness, arguing that consciousness is likely to be in place by 5 months of age if not earlier.

KEYWORDS
biomarkers, consciousness, foetus, infant, neonate, neuroimaging

1 | INTRODUCTION

We are now living in what might be regarded as a 'golden age' of consciousness research. While most of the 20th Century was chilled by a long 'consciousness winter'[1] during which the scientific study of consciousness was largely taboo, theories of consciousness and empirical studies into both ordinary and altered states of consciousness have flourished since the early 1990s.[2,3] But despite current advances, one frontier area of consciousness research has remained largely unstudied with few exceptions[4]: infant consciousness, the very beginning of human experience.[5–9] We define consciousness as subjective experience. Specifically, we favour Thomas Nagel's[10] definition of consciousness: '[A]n organism has conscious mental states if and only if there is something that it is like to be that organism—something it is like *for* the organism. We may call this the subjective character of experience'. In other words, if it feels like something to be an infant, than an infant is conscious, regardless of whether the infant

Abbreviations: DMN, default mode network; EEG, electroencephalography; ERP, event-related potential; fMRI, Functional magnetic resonance imaging; MEG, magnetoencephalography; NICU, newborn intensive care units; PCI, perturbational complexity index.

has the capacity for self-awareness, introspection, etc. Although self-awareness and the capacity for introspection characterise ordinary waking consciousness as it occurs in older children, it seems unlikely that these features will also characterise the earliest states of human consciousness.

The ontogeny of consciousness is not merely interesting from a philosophical and scientific perspective — it also has a vitally important clinical dimension. No paediatric surgeon today would consider operating on an infant without anaesthesia, though this was not uncommon during the 1980s.[5,11] Nonetheless, as recently as the turn of the millennium, newborns in the NICU were routinely subjected to many relatively minor albeit potentially painful procedures (such as intubation) without analgesics or anaesthetics.[12] Clinicians must weigh the potential for pain and suffering that newborn infants might experience against the potential harms caused by common anaesthetics and analgesics.[13,14] Thus, there is a pressing need to know when and in what form consciousness might first emerge.

Unfortunately, we cannot ask infants if they are conscious, nor can we ask them to follow simple commands that might reveal conscious understanding. However, this absence of evidence is not evidence of absence; many adults diagnosed with disorders of consciousness are later discovered to have a rich, internal life that is masked by a cognitive-motor dissociation.[15] In the case of infants, experience might very plausibly be masked by immature cognitive development and motor control. In response to these problems, we recently proposed a 'cluster-based' approach[16] for inferring when consciousness first emerges [see also[17]]. If markers of consciousness which have been validated in adults appear in a developmental cluster, that is, emerge together at a similar age, then we can reasonably infer the presence of consciousness at that age. Because the approach appeals to a variety of markers, it need not assume the reliability of any particular marker of consciousness. The cluster-based approach also avoids favouring any particular theory of consciousness; we believe this is a prudent approach, given that the science of consciousness has not yet converged on a single theory.[16] While the cluster-based approach may incorporate markers that are inspired by particular theories, such as global prediction errors[18] [inspired by the global workspace theory] or the perturbational complexity index [inspired by the integrated information theory[19]], the diverse aggregate of markers included by this approach does not collectively learn towards any particular theory.

2 | WHICH MARKERS CONSTITUTE A CLUSTER?

Markers in a cluster need not be obtained from the same methodologies; in fact, a cluster-based case for consciousness is strengthened if its members involve a diverse array of methods (e.g. behavioural, electrophysiological and neuroimaging markers). That said, we focus here on neural markers. Behavioural responses that are reliable indicators of consciousness (such as those that involve intentional agency) tend not to be available in young children due to their immature motor development, while behavioural responses that are available in young children (such as looking and crying) tend to be uncertain indicators of consciousness. If a marker is present in a cluster, then its specificity is key – our cluster ought to be composed of markers that are unlikely to appear in the absence of consciousness. Conversely, if a marker is absent in a cluster, then its sensitivity is key – we need not worry about the absence of markers such as verbal reports, which are known to miss consciousness in a substantial proportion of cases. Below, we highlight four markers of consciousness that can be found by 5 months of age—and in some cases substantially earlier. This list is by no means exhaustive, and we strongly advocate for future work that might not only identify additional markers that might contribute to this cluster but also provide guidance as to how to weight markers (see 'Future directions').

Although an interest in pain is often central to questions about when consciousness first emerges, we see no easy way of addressing pain from the perspective of the cluster-based approach. This is because we do not yet have well-confirmed ways of distinguishing pain as such – that is, an unpleasant sensory or emotional experience associated with, or resembling that associated with, actual or potential tissue damage– from mere nociception (i.e. the neural representation of noxious stimuli) in foetuses or young infants [although see Salomons and Iannetti[20]]. Indeed, attempts to identify when in development the capacity for pain (as opposed to mere nociception) is acquired need to be informed by a more general account of when the capacity for consciousness as such first emerges.

Key notes

- Inferring the developmental onset of consciousness is highly relevant for neonatal care, especially where analgesics and anaesthesia are concerned.
- Infant consciousness might be inferred from the aggregate of many diverse neural and behavioural markers without relying heavily on one specific theory of consciousness.
- This 'marker-based' approach already includes evidence from functional connectivity networks, global prediction errors, attention and multisensory integration.

2.1 | Network markers

There is compelling evidence that the capacity for consciousness requires large-scale networks in the brain.[21] A key network here is the default mode network (DMN), so-named because the brain defaults to this mode of activity, which includes mind-wandering and self-referential processes,[22] in task-free resting states. Although consciousness can occur in the absence of DMN activity, the recovery of consciousness following anaesthesia and severe brain damage in adults is associated with the re-emergence of reciprocal modulation between the DMN and fronto-parietal brain networks.[23,24]

Although an early study failed to detect the DMN in infants as young as 5 months of age,[25] later work reported the 'primitive and incomplete' DMN in 2-week-old newborns.[26] This view was challenged just 2 years later by a study of 9-month old infants which reported that 'cortical hubs and their associated cortical networks are largely confined to primary sensory and motor brain regions in the infant brain'.[27] Although networks continue to mature through infancy and childhood due to neuronal maturation, synaptogenesis and axon myelination, we now know that many networks are present no later than full-term birth, albeit often in rudimentary form.[28–34] A recent study with a large sample of newborns by Hu et al.[29] is particularly striking. This work found evidence of reciprocal modulation between the DMN and the dorsal attention network at full-term birth in nearly 300 neonates (or term-equivalent age in 73 preterm neonates),[29] suggesting that key features of the neural circuitry associated with consciousness are in place by (or soon after) birth.

2.2 | Attentional markers

Attention is plausibly regarded as another marker of consciousness. According to some theorists, not only do all forms of consciousness involve attention, but attention also involves consciousness.[35] If attention were sufficient for consciousness, then we could use data about the onset of attention in infancy to guide ascriptions of consciousness. However, it is controversial whether all forms of attention involve consciousness, and data from both normal vision and blindsight suggest that certain forms of bottom-up attention might operate outside of consciousness.[36] If that conclusion is right, then the presence of bottom-up attention from birth would not necessarily show that consciousness is also present from birth. That said, a recent fMRI study of bottom-up attention in infants showed that these attentional effects can be seen to recruit fronto-parietal networks from 3 months of age.[30]

More compelling with respect to consciousness is the attentional blink, which is widely taken to involve conscious processing. When two stimuli are presented in succession, the second is often prevented from entering conscious awareness due to the fact that the first monopolises attention. The attentional blink can be seen in infants from 5 months, but it is much longer in infants than it is in adults. A paradigm that produces an attentional blink of 200ms in adults (and 3-year olds) produces an attentional blink of 1,200ms in 5-month olds.[37] Also related to consciousness is endogenous ('internally directed') attention, which emerges at around 4 months of age.[38] For example, 4 month olds can inhibit a pre-potent response to orient towards a peripheral cue when they have learned that an attractive display will appear at a location other than that which has been cued.[39]

2.3 | Multisensory integration markers

A third marker of consciousness involves multisensory integration. Although certain forms of multisensory integration appear to be possible independently of consciousness,[40,41] a review concluded that 'the more complex or novel the stimuli, the more likely consciousness will be needed for integration to occur'.[42] In particular, consciousness appears to be required for the McGurk effect (in which presenting an auditory /ba/ with the lip movements for/ga/ produces a percept of the phoneme/da/), for the effect disappears when flash suppression is used to prevent the visual stimulus from reaching awareness.[43] Consistent McGurk-type effects can be found consistently from 5 months of age[44] and less consistently from 4 months.[45]

2.4 | The local–global effect

Perhaps the most direct, albeit preliminary, evidence for thinking that consciousness is in place soon after birth (if not earlier) involves an auditory oddball paradigm known as the 'local-global effect'. First developed in connection with post-comatose disorders of consciousness,[18] the local-global effect exploits a late cortical response associated with surprise and the re-orientation of attention. Although P300 responses to first-order (local or within trial) oddballs do not appear to be indicative of consciousness, P300 responses to second-order ('global' or between-trial) oddballs generally occur only when consciousness is present.[18] Thus, there is some reason to treat the presence of global oddballs (the 'local-global effect') as a marker of infant consciousness. An early event-related potential (ERP) study found evidence of the local-global effect in 3-month olds,[46] while a more recent magnetoencephalography (MEG) study found evidence of the local-global effect in newborns.[47] A P300-like response to global oddballs has even been found in foetuses 35 weeks and older.[48] However, as Dehaene-Lambertz[6] has noted that finding is arguably not best described as a local-global effect, for the P300-like response to global oddballs was not accompanied by a similar response to local oddballs, and it may be that the foetuses had fused the regular stimuli and the local oddball into a single stimulus, thus (in effect) treating global oddball trials as local oddballs trials.

3 | WHEN DOES CONSCIOUSNESS BEGIN?

We do not yet know when the first spark of consciousness appears in human development. However, we are beginning to form increasingly more informed guesses. Although influential articulations of the view that consciousness is not present before 12 months of age were published as recently as the early 2000s,[49,50] even more recent discussions of the topic are sympathetic to the possibility that newborns,[51,52] or even late term foetuses,[48,53] are conscious. Within the past several years, most consciousness researchers surveyed have viewed infant consciousness as either likely or certain.[54]

Additionally, recent interest in 'exotic' or otherwise non-ordinary states of consciousness,[55] such as non-egoic, non-cognitive and non-sensory 'pure consciousness',[56] has also opened speculative discussions of foetal consciousness.[53] While some experts[57] have argued that consciousness might even begin as early as the second trimester, such an early estimate seems incompatible with a common view that the thalamocortical system is the neural substrate of consciousness,[58] for thalamocortical synapses which transmit sensory afferent signals do not form until the final days of the second trimester.[59] Indeed, spinal anaesthesia which blocks sensory afferents in young infants induces a sleep-like state characterised by spindles and slow waves,[60] suggesting that the young developing brain depends on afferent drive to maintain consciousness. In this light, it seems infeasible that the even less mature brain of a second trimester foetus could maintain consciousness without afferent input from thalamocortical fibres.

In our opinion, evidence from intrinsic connectivity networks recorded with fMRI[28,29] lends plausibility to the view that infants might have at least brief periods of consciousness from (or soon after) birth, though behavioural markers in the cluster-based approach have yet to be observed at birth (see Table 1). Of course, it is possible that some form of foetal consciousness might emerge between the formation of thalamocortical connections and birth, but as yet that possibility remains speculative. Evidence from foetal MEG[48] has been used to argue for consciousness during the third trimester, but see recent scepticism.[6]

4 | FUTURE DEVELOPMENT OF NEURAL COMPLEXITY MARKERS

One additional marker which we are particularly eager to see explored in infants is perturbational complexity. In adults, the perturbational complexity index (PCI)[19] is an extremely accurate marker of consciousness across many states, such as wakefulness, sleep, general anaesthesia and disorders of consciousness. However, PCI relies on transcranial magnetic stimulation, which should not be applied to very young, developing brains for ethical reasons. We recently introduced a roadmap for the development of an alternative, infant-friendly version of PCI that uses sensory stimulation.[58] While this variant of PCI – which we have labelled sensory PCI or 'sPCI' – has yet to be properly implemented using multivariate M/EEG recordings of perinatal evoked sensory responses, investigations in this area are currently underway.[61] Furthermore, several studies have measured spontaneous (i.e. unperturbed) neural complexity in infants, which is also associated with consciousness in adults and children.[62–64] These studies, while rarely conducted with the goal of inferring perinatal consciousness, nonetheless demonstrate a broad stratification of infant sleep. Quiet sleep, analogous to non-rapid eye movement (NREM) sleep in adults, generally shows lower spontaneous complexity in infant EEG recordings, whereas active sleep, analogous to rapid eye movement (REM) sleep in adults, shows generally higher spontaneous complexity.[65–68] This observation fits with the tendency for REM sleep to be richer in phenomenological content, at least in adults who can report their dreams; however, it is unclear

TABLE 1 Key evidence for a nascent cluster of early markers.

Study	Subjects	Main Finding
Hu et al. (2022)[29]	Newborn infants	Default mode, dorsal attention and executive control networks are present at birth (or term-equivalent age), and there is a functional relation between the default mode and dorsal attention networks.
Thomason et al. (2015)[34]	Foetuses	Default mode network synchronisation present at 37 weeks gestation
Sylvester et al. (2023)[28]	Newborn infants	Functional connectivity is present in the default mode, fronto-parietal and dorsal attention networks at birth
Ellis et al. (2021)[30]	3–4-month-old infants	Stimulus-driven attention recruits frontoparietal and cingulo-opercular networks, as in adults
Burnham & Dodd (2004)[44]	5-month-old infants	McGurk effect present, suggesting consciousness-involving multisensory integration
Basirat et al. (2014)[46]	3-month-old infants	P300-like response to global auditory oddballs
Moser et al. (2020)[47]	Newborn infants	P300-like MEG response to global auditory oddballs
Moser et al. (2021)[48]	Foetuses	P300-like MEG response to global (but not local) auditory oddballs present beginning at 35 weeks gestation

whether infants dream, as the rapid eye movements characteristic of active/REM sleep are not generally taken as sufficient evidence of dreaming.[69] Infant EEG studies of neural complexity also suggest that spontaneous neural complexity,[67,70] including measures that account for spatial integration or synergy,[68,71] gradually grows more pronounced during the perinatal period, which is consistent with a gradual emergence of consciousness soon after birth. However, this interpretation is complicated by the curious fact that auditory-evoked neural activity, unlike spontaneous activity, actually shows diminishing neural complexity with gestational age during the perinatal period, particularly in male foetuses, though these results from MEG were limited to one-dimensional signals,[61] that is, the univariate data were not sufficient for estimation of PCI. Clearly, further studies are needed to resolve this discrepancy and determine how neural complexity markers may fit into the cluster-based approach.

5 | OTHER FUTURE DIRECTIONS

Task-free (or 'passive') behavioural responses may also provide valuable measures of infant consciousness. For instance, a 'sniff test', in which odorant-dependent sniffing is used as a biomarker of consciousness, has been proposed for use in adults with disorders of consciousness.[72] It is conceivable that a similar approach, for example, based on the preference that newborns show for maternal breast odours,[73] could offer insight into infant consciousness. The sniff test could even be combined with a PCI approach by using olfactory stimuli as cortical perturbations[58] and recording both behavioural (sniff) and neural (complexity) responses. Given the promise of attentional markers of infant consciousness,[30] neonatal eye-tracking or pupillometry studies may also contribute to the cluster-based approach using passive behavioural paradigms. In utero, ultrasound recordings of eye movements or gross head movements may also yield relevant insights regarding markers of consciousness. For instance, recent work using ultrasound to explore foetal reactions to complex visual stimuli, for example, face-like patterns projected into the womb using red light emitting diodes,[74] might lead to future markers with relevance for consciousness in foetuses.

6 | CONCLUSIONS

The question of when and in what form consciousness first emerges is of both clinical and scientific importance. Although it is daunting, we have suggested that it is best addressed by adopting a cluster-based approach. This approach does not hinge on any particular marker, nor does it assume the framework of any particular theory of consciousness. While many markers of consciousness that have high specificity in adults (such as the capacity to produce verbal reports) are absent in infants, this is inconsequential so long as the absent markers lack sensitivity—for example, we know that consciousness can and often does occur in the absence of verbal report. We strongly advocate for future work that will test further markers and determine whether they contribute to a nascent cluster pointing towards an early emergence for consciousness sometime near birth.

AUTHOR CONTRIBUTIONS

Joel Frohlich: Conceptualization, Methodology, Writing – Original Draft, Writing – Review & Editing. **Tim Bayne:** Conceptualization, Methodology, Funding Acquisition, Writing – Original Draft, Writing – Review & Editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no interests to declare.

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