

## **Title page**

The Development of Measures of Consciousness in Delirium

Consciousness in delirium

Eamonn Eeles [1,2], Donna Pinsker [1], Renee England [3], Hana Burianova [4],  
Greg Watson [5], Sarah Ward [6]

[1] Internal Medicine Service, The Prince Charles Hospital, Brisbane QLD 4032  
Australia

[2] School of Medicine, Northside Clinical School, The Prince Charles Hospital QLD  
4032

[3] School of Historical and Philosophical enquiry, The University of Queensland, St  
Lucia QLD 4072 Australia

[4] Swansea University School of Health and Human Sciences

[5] Royal Brisbane and Woman's Hospital Health Service District, Psychiatry,  
Herston, QLD, AUS

[6] Redcliffe Hospital, Redcliffe, QLD, AUS

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Corresponding author: [eamonn.eeles@health.qld.gov.au](mailto:eamonn.eeles@health.qld.gov.au)

Eamonn Eeles MBBS MRCP MSc FRACP

Internal Medicine Services

The Prince Charles Hospital

Rode Road

Brisbane

Australia

4032

phone+61731395686

fax+61731394923

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## **Abstract**

### Background

Delirium is a common disorder in hospitalized older adults and has been defined as a disturbance of consciousness. Unfortunately, there is no testable measure of consciousness as pertains to its 'clouding' in delirium and rates of recognition of delirium suffer. A greater understanding of consciousness, and its disruption in delirium, may help us to develop clinical tools to aid diagnosis.

### Methods

Our group have set out on this quest to help generate measurable facets of consciousness whose disturbance could signal delirium and pave the way for better diagnostics. Based upon existing literature in the field of consciousness we have explored pre-reflective state, experiential awareness and reflective versus the task positive state.

### Results

From these states of consciousness, we have derived a set of potential questions that could be used to interrogate consciousness integrity.

### Conclusions

Candidate questions can be used to measure state of consciousness that may have utility in the diagnosis of delirium

Key words: delirium, attention, consciousness

## **Introduction**

Delirium is a common disorder in hospitalized older adults and has been defined as a disturbance of consciousness.<sup>1</sup> Just how consciousness is impacted in delirium remains uncertain, however, as is reflected in the diverse iterations of diagnostic criteria over recent decades. Unfortunately, there is no testable measure of consciousness as pertains to its 'clouding' in delirium. This would matter less if clinicians were adept at detecting delirium, which, by and large, they are not. In fact, up to 60% of delirium cases are missed.<sup>2</sup> A greater understanding of consciousness, and its disruption in delirium, may help us gain a more robust conceptual foothold into this disorder.<sup>3</sup> Our group have set out on this quest to help generate measurable facets of consciousness whose disturbance could signal delirium and pave the way for better diagnostics.

The conventional pathway to arriving at a clinical diagnosis of delirium currently relies on more tangible facets of the disorder. In particular, the so-called sentinel gate of delirium, attention and its disturbance is central to the clinical diagnosis. An impaired ability to focus, sustain, or shift attention has spawned the use of bedside cognitive tests, incorporating measures, such as the ability to recite months of the year backwards.<sup>4</sup> While this approach is feasible in practical terms, there are problems with being overly reliant on attention in the diagnosis of delirium. For instance, there are some candidate neurological territories responsible for attention, such as sensory cortices, during bimodal selective attention.<sup>5</sup> However, widespread cortical and cerebellar connectivity required during tasks of attention make it difficult to easily reduce to a single neurobiological substrate even when a specific mode of attention is

being targeted.<sup>6</sup> Attention can also be difficult to measure in a standardised manner across a range of intellectual and educational , and in the setting of cognitive impairment.<sup>7</sup> Additionally, there is a mounting argument that the inattention may be somewhat superfluous,<sup>8,9</sup> insufficiently precise or sufficient, in and of itself, to make a diagnosis of delirium.<sup>10</sup> More fundamentally, it would seem that while inattention is an important part of the syndrome of delirium it may not be central to the biological mechanisms.<sup>11</sup> Ultimately, whilst attention and consciousness are coupled,<sup>12,13,14</sup> they remain distinct entities.<sup>15</sup> Thus, we need to more fully explore how consciousness might pertain to delirium.<sup>8,11</sup> This is where we stumble across our first obstacle as the absence of clinical tools renders this problem academic.<sup>16,17</sup> In order to shine a light on the ‘hard problem’ of consciousness<sup>18</sup> we have brought together some accepted concepts in this field of study and considered relevance to delirium. In so doing we hope to expand on ways in which we might be better able to diagnose this otherwise seemingly elusive and yet tragic condition. What follows is an attempt to explore the entity of consciousness and present some of these candidate questions that may test its integrity.

\* One of the most commonly and intensively researched screening tools has one of its four question relating to altered level of consciousness.<sup>19</sup>

## **Materials and Methods**

We first set out the states of consciousness as described between the schools of neurology, neuropsychology, psychiatry and philosophy.

### **Phenomenal me-ness or the pre-reflective state**

There is bountiful evidence to suggest that consciousness comprises a number of different states that exist as experientially distinct but interchangeable phenomena.

Perhaps the most rudimentary of these is the pre-reflective state. Pre-reflective consciousness is a state of awareness prior to contemplation.<sup>20</sup> Together, an implicit and first order sense of ownership and agency form part of the embodied subject of experience<sup>21,22</sup> upon which other levels of selfhood are constructed.<sup>20</sup> Pre-reflective thought is perceived by the conscious subject as part of the mind, i.e. it is recognised as a part of conscious experience that is always there, though we do not normally attend to it.<sup>23</sup> In evolutionary and adaptive terms, the pre-reflective state allows us to 'take in' before we 'take stock'.<sup>24</sup> Some authors debated whether pre-reflective state incorporates a first person dimension<sup>25</sup> and posit that it may be divested in a feeling of self.<sup>26</sup> For the purposes of inclusivity, however, we shall assume for the purposes of our argument that first person mineness is part of pre-reflective consciousness. Neurophysiologically, the pre-reflective self is characterised by activation of distinct regions that receive visceral and somatic afferents, such as the insula, somatosensory cortex<sup>27,28</sup> and subcortical-cortical midline structures.<sup>29</sup>

Related to pre-reflective consciousness is the concept of minimal self, or the most fundamental level of the self.<sup>20</sup> In the field of psychiatry the minimal self relates to an individual as aware of being the 'immediate subject of experience'.<sup>30</sup> Interference in this sensed experience is linked with psychopathologies.<sup>31</sup> For instance, the minimal self of pre-reflective consciousness is perceived to be weakened in schizophrenia and psychosis.<sup>32,33,34</sup> Symptoms of this aberrancy include delusions such as thought interference whereupon thoughts or ideas manifest seemingly outside of the self.<sup>35,36</sup> The ipseity-disturbance model proposes that heightened awareness of some of the pre-reflective properties become interposed with a fading of the perception of self.<sup>33,34</sup> What results is a difficulty in demarcating self from non-self,<sup>37</sup> which is reflected in first-hand accounts including such features as 'alienation from surroundings'.<sup>38</sup> Such

delusions have been attributed to aberrant cerebro-cerebellar and prefrontal cortical dynamic network connectivity<sup>39,40</sup> including reduced activity in the cognitive evaluation network.<sup>41</sup>

Correspondingly, there is an argument that both schizophrenia<sup>42</sup> and delirium are disorders of consciousness<sup>43,44</sup> as they share many clinical features that potentially impinge on the notion of minimal self.\*\* Rates of delusions (80%) and perceptual disturbance of are observed in delirium and certainly chime with what is observed in schizophrenia.<sup>45</sup> If such first rank symptoms derive from disruption in pre-reflective consciousness and disturbance in the coherence of minimal self, then this is likely also to be impacted in delirium. Clinical tools in schizophrenia have exploited impairments in the minimal self, such as the Examination of Anomalous Self-Experience (EASE) checklist<sup>46</sup> which has in two of its five domains comprising traits of demarcation and self-awareness. Therefore, it is reasonable to derive clinical tools which may test these pre-reflective components of consciousness in delirium.

\*\*Among other theories such as neurodevelopmental, salience and glutamate theory.<sup>47</sup>

### **Consciousness-experiential awareness**

It is the nature of the sensed experience that represents an emergent feature of complex system features of consciousness (the phenomenon cannot be predicted by the sum of the parts)<sup>48,49,50</sup> Or, to borrow from the experientialist philosopher David Hume, it has been asserted that all knowledge of the physical world is acquired through the senses.<sup>51</sup> Again, there is debate concerning the ability to operationalize of consciousness with respect to the senses.<sup>52</sup> Nevertheless, there remains ample grounds to continue to examine the relationship between sensory modalities and consciousness. It is not only knowledge that may be gained but also feelings that are informed. For instance, the sound of waves in the ocean may be calming, seeing an

old friend may be uplifting, and the touch of a spider may cause panic.<sup>53</sup> At its most rudimentary, awareness of the environment through multisensory processing is an integral part of consciousness.<sup>54,55</sup> The sensed experience may go beyond modulation of the qualia of a moment but interfere with the very state of consciousness.<sup>56,57</sup> The neurophysiological correlates of multisensory sensory processing include but are not confined to superior parietal, temporo-parietal, and ventral premotor areas.<sup>58</sup> When it comes to the experience of delirium it would seem to be a distinctly and universally unpleasant one, driven largely through corruption of the senses through perceptual distortion.<sup>59</sup> So, it makes sense that a measure of awareness of the surrounding as part of the construct of consciousness should be grounded in an evaluation of perception and the senses. In addition to an experience being grounded in a medium, of taste or touch for instance, it is encountered within the dimension of time, or at least time perception [60].<sup>60</sup> One such theory is the internal clock model based upon the number of impulses accumulated during an epoch of focussed attention.<sup>61,62</sup> This perception can be distorted by illness, such as schizophrenia, ADHD and Parkinson's disease.<sup>63</sup>

### **Consciousness - the reflective versus the task state**

Hughlings Jackson in his treatise on the dissolution of the mind alluded to and perhaps founded an understanding of consciousness based upon hierarchies of mental processes.<sup>64</sup> At the risk of injustice to this seminal work we can consider that as consciousness lifts itself out from a pre-reflective (and passive sensory state) it enters a higher cognitive moiety. This cognitive state comprises but is not confined to either one of creative thinking or a planning and doing state. The creative thinking, imaginary or reflective state is subserved through the default mode network (DMN).<sup>65</sup> For example, the DMN is active when picturing oneself in a daydream. When the DMN is engaged in daydreaming, there is a reciprocal reduction of task engagement,

purportedly controlled by the task positive network, or TPN.<sup>66</sup> The TPN enables engagement with the outside world and is active during attention-demanding tasks.<sup>67</sup> It is argued that It is this interplay between the DMN and TPN that results in much of conscious thought.<sup>67</sup>

Studies, employing functional neuroimaging, have demonstrated that the brain regions of the DMN include the anterior medial prefrontal cortex, posterior cingulate cortex, precuneus, angular gyrus, and lateral parietal cortex.<sup>68,69</sup> Distinct areas encompassing the TPN include the intraparietal sulcus, frontal eye field, and the middle temporal region.<sup>68,69</sup> The DMN and TPN are functionally anti-correlated but not entirely mutually exclusive. The degree of independence between these paired networks varies depending on the nature of the cognitive operation/s being performed at any given time.<sup>70</sup>

Resting state, or default mode connectivity, has been shown to be disrupted in brain injured patients with associated disorders of consciousness.<sup>71</sup> Additionally, and specifically, it has been shown that pathological co-activation of the TPN arises in delirium.<sup>72</sup> Therefore, clinical instruments that can examine the type of thinking that is representative of these distinct paired networks may guide us towards a useful tool.

## **Results**

### **Derivation of a set of consciousness tests**

Using the descriptions pertaining to each conscious milieu, we derived a set of candidate tests from first principles. There were no operationalized criteria against which the tests could be developed, as is the limiting factor for any instrument that purports to measure the content of consciousness. Accordingly, a blue -sky methodology or curiosity-driven approach, was used to generate a series of potential

tests. An iterative method among a multidisciplinary team comprising a geriatrician, psychiatrist, philosopher, neuropsychologist, neurobiologist, physician, and neurologist was used to refine the questions until a consensus amongst all parties was reached.

### **Candidate tests of consciousness that could apply to delirium**

#### **Test of phenomenal me-ness**

The questions developed involved a personal experience either as of the self or of the non-self. Phenomenal me-ness would be demonstrated by a congruent answer e.g. question 1 below if the person seemed very happy and they articulated that they also felt very happy at the time of enquiry then that would be a correct response.

1. Before you uttered your first word today, what did you do? Can you express how you felt at that time in terms of an emotion; happy, sad, indifferent?
2. Did you have a break at any time today? Where were you? Did you have a conversation? Who shared the most personal thoughts in conversation?
3. (Interoception:) Are you hungry or full? If I gave you a large tasty meal would you eat it all? Do you prefer being hungry or full?
4. (Mineness:) What is the first thing you heard today? Did you make the noise or did it come from elsewhere? Have you ever made that noise?
5. Did you have any thoughts today that were not your own?

#### **Tests of sensed experience**

Test items involved a recalled experience of each of the senses, which could be reasonably verifiable by an independent rater. Presentations of a multiple choice was included to reduce the likelihood that subjects would pass the test simply through

superficial knowledge or platitudes. A correct answer for the purposes of the test would be one that was reasonably verifiable by a next of kin. Each sensory test may require a brief screen to assess integrity prior to commencement. Similarly, for some of the tests long term memory memory, high frequency object naming and gnosia would be assumed. Failure in the test may require testing of the individual domains to exclude a focal neurological problem.

Object identification; Object description of sensed experience, affinity for the experience, how the experience informed consciousness +-false dichotomy, objective verification from a loved one. Impairment in sensed consciousness would be registered upon a disparity between the subject and loved one's interpretation of their answer e.g. 'I like chalk.' vs 'He/she would have hated the feel of chalk.'

Touch: What is this (touching chalk with eyes closed)? Describe it? Is it nice, bad or neutral? How does it make you feel (good, bad, indifferent)? Is it used to tell the time?

Informant question (IQ): *Would your loved one like or dislike this on a good day?*

There could also be a pleasant, or at least less noxious alternative question, such as 'what type of fabric do you like to wear? Could you make a table out of it?'

Smell: What is this (smell of cinnamon)? Describe the smell... Is it sweet or spicy? Is it nice, bad or neutral? How does it make you feel (good, bad, indifferent)? Is it used to flavour food or drinks? IC: *Would your loved one like or dislike this on a good day?*

Sound: What is this (sound of kitten purring)? Describe the sound? Do you like it (good, bad, neutral)? How does it make you feel? (good, bad, indifferent). Can this animal bark? IQ: *Would your loved one like or dislike this on a good day?*

Sight: What is this (visual clown)? What do you think he is trying to do? Do you like it (good bad neutral)? How does it make you feel? (good, bad, indifferent) Are his shoes too small? IQ: *Would your loved one like or dislike this on a good day?*

Taste: What is this (taste of salt)? Describe the taste. Is it nice, bad or neutral? How does it make you feel (good, bad, indifferent)? Is it sweet? IQ: *Would your loved one like or dislike this on a good day?*

Time perception: Is it day time or night time? Do you feel time is passing slowly in hospital? How long do you think you have been here (hours, days or weeks)? Are you a morning person or a night person? IQ: *Would your loved one describe themselves as a morning or night person? Would you like to be woken up at this hour (picture of someone asleep with the moon out)?*

These are all tests that may rely on procedural memory and conditioned reflexes and so, to further evaluate the experiential sense, a further layer of complexity is added to the event to make it sufficiently probing: We have named these tests of putting the experiences together-conflicting multidimensionality. Failure on testing of conflicting multidimensionality would be incurred when a subject is anchored to the object (the clown) rather than the action of the object (anger of a clown) see table 1.

### **Memory based upon sensed experience**

The questions targeted past experiences involving each of the senses that could be reasonably verifiable by an independent rater. Again, a false dichotomy was included in an effort to reduce the likelihood of subjects passing the test through superficial knowledge or platitudes. Again, Impairment in sensed experience would be registered upon a disparity between the subject and loved ones interpretation of their answer e.g. swimming in the sea 'I loved swimming in the sea' vs 'he hated swimming in the sea'

Object identification, Object description of sensed experience, affinity for the experience, how the experience informed consciousness +-false dichotomy.

Do you remember a time you went swimming in the sea? (y/n) Where was it? If yes, was it warm or cold? Was it nice, bad, or neutral? How did it make you feel? (good, bad, indifferent). IQ: *Would your loved one like or dislike this on a good day?* Is a fridge warm/ Is an oven cold?\*

Name a subject that was taught at school? What was it about? Did you enjoy it? Was it nice, bad, or neutral? How did you feel during the class? (good, bad, indifferent). IQ: *Would your loved one like or dislike this on a good day?* Is mathematics the same as art? Are science and physics related?

Name your favourite dessert? Do you enjoy it? Is it nice, bad, or neutral? How does eating your favourite dessert make you feel? (good, bad, indifferent). IQ: *Would your loved one like or dislike this on a good day?* If it were here now would you put gravy on it?

What is your favourite smell? Do you enjoy it? Is it nice bad or neutral? How does smelling this make you feel (good bad indifferent)? IQ: *Would your loved one like or dislike this on a good day?* If you could smell it now would it make you think of a flower?

Name some music that you like? Do you enjoy it? Is it nice bad or neutral? How does listening to this make you feel (good bad indifferent)? IQ: *Would your loved one like or dislike this on a good day?* Does loud music help you sleep?

Can you remember a time when you visited somewhere new? Can you recall something that you saw there? Did you enjoy seeing it? Was it nice bad or neutral? How did seeing it make you feel (good bad indifferent)? IQ: *Would your loved one*

*like or dislike this on a good day? Do you tend to see more things when travelling by day or by night?*

### **Reflective thinking versus the task engagement in the task positive state**

As we have discussed, functional network co-operation between the DMN and TPN is required for the realisation of full consciousness. In order to tap into these states, questions were developed that harnessed reflective thought and an executive planning task that related to it.<sup>67</sup> The planning task is designed to be an externally verifiable aspect of the self-referential thought. A scenario was created that was thought likely to represent these cognitive proxies for the respective networks. In this instance, a world map was decided upon as it provides a template for imagining of self in another dimension (place) but with easily verifiable facts relatable to that location (see figure 1).

(i) First question. Point to where we are now. Show me a place you would like to visit.

(ii) Second question. A reasonably well-known fact related to the geography.

North America: Is this where the Statue of Liberty is located? Is this where cowboys came from? Was George Washington a president?

South America: Are there are rainforests here? Does South America have seas or oceans around it? Is the Amazon River in South America?

Antarctica: Is the weather generally warm here? Would you expect to see snow/ice here? Would you expect to see a camel here?

Europe: Is Germany in Europe? Are there any castles in Europe? Is the Eiffel tower somewhere in Europe?

Asia: Are chopsticks used in parts of Asia? Is the Great Wall of China somewhere in Asia?

Africa: Are there lions in Africa? Are there deserts in Africa? It is generally cold in Africa?

**Other candidate cognitive proxies for the Default Mode/ Task positive states:**

Could you be dreaming right now? (y/n) How could you show that this isn't a dream?  
e.g., pinch yourself

Who was your best friend at school? Name something that you liked doing together. Name a subject that you were better at?

Do you remember the last time you swam in the sea? Do you remember a time you bathed in water? Was it warm or cold? Is a fridge warm/ Is an oven cold?

Are you a night owl or a "morning person"? Is being a morning person better for working late? Is being a night owl better if you want to see the sunrise?

Do you ever dream about driving? (y/n) Would it be safe to dream and drive at the same time?

Do you like dessert? Name your favourite dessert? If it were here now would you put gravy on it?

Neil Armstrong was the first man on the moon. Would you like to visit the moon? Is the moon more visible by day rather than night?

Can you swim? Does a person need gills to swim?

Are you right or left handed? (if R) Can you feel your right thumb? Is your right thumb important for writing with a pen?

Do you like the taste of coffee? Is it generally drunk hot or cold? Is coffee sweetened with salt?

Do you prefer small or large gatherings of friends? A small gathering would always be noisier than a large one?

## **Discussion**

A framework for consciousness, from the foundational pre-reflective state to experiential awareness up to higher order thinking involving paired functional networks are established concepts. Understanding consciousness in this way can help devise tests of measurement in each facet of consciousness; disturbance therein can help provide a rationale for clinical tests in the area of delirium. A multiprofessional team derived a number of candidate tests for each facet of consciousness thus described alongside pre-defined criteria from first principles. What was developed were easily testable series of questions. The pre-reflective questions incorporated enquires with respect to the embodied self and ownership of thought, experiential questions invoked the senses and congruence with state of mind and reflective thinking questions drew on a scenario that was thought likely to evoke default mode and task positive thinking respectively. When there are currently no measures of consciousness used in the identification of delirium it seems an earnest beginning. Field testing these questions on healthy individuals may help develop normative values and establish how they can be used in combination. These questions can then be tested in the clinical arena as a potential screening tool to potentially more accurately diagnose delirium.

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List of figure legends:

Table 1 showing tests of the sense experience as part of consciousness

Figure 1 showing the sort of world map that could be presented to an individual with default mode/ task positive questions to follow



Kitten							Kitten catching bird
Clown							A clown being angry
Salt							Salt being poured into a cup of tea
Time							Would you like to be woken up at this hour?

Figure 1 showing the sort of world map that could be presented to an individual with default mode/ task positive questions to follow