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The role of predictive coding in the pathogenesis of delirium

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ABSTRACT

Delirium and dementia represent an emerging global crisis in healthcare. Attempts have been made to identify the pathognomonic feature that would make delirium stand out from dementia but unfortunately the global neural dysfunction of both disorders has made the establishment of a direct measurement difficult. Modern conceptualisations of delirium have been influenced by the assessment tools used to assess, detect, and analyse its complex and transient nature. Recent publication of the DSM-V criteria for delirium has marginally altered the previous DSM-IV criteria with a focus upon inattention with vague terms such as consciousness downplayed. Such an alteration has been found to be restrictive and thus impact upon delirium case identification. Although these findings are approximating the empirical state of delirium as measured by validated instruments, a more refined neuroscientifically informed phenomenological framework is required in order to enhance the theoretical understanding of delirium assessment and resolve these challenges. One such application is the predictive coding (PC) model, also known as the hierarchical Bayesian inference model, to interpreting delirium pathophysiology. Therefore, the aims of this paper are to 1) propose the hypothesis that delirium pathophysiology can be explained in terms of the PC model, 2) support this hypothesis by applying this model to current methods of assessing delirium phenomenology, particularly attention, and 3) outline a future programme of research to test many of the parameters of this application.

Introduction

Delirium and dementia represent an emerging global crisis in healthcare [1,2]. Historically delirium has been described as a disorder of consciousness with patients experiencing a ’clouding of consciousness’, and has been contrasted to the typical retention of lucidity in dementia [3–5]. However, contemporary attempts have been made to identify the pathognomonic feature that would make delirium stand out from dementia but unfortunately the global neural dysfunction of both disorders has made the establishment of a direct measurement difficult [6,7]. The robust rating scale for delirium phenomenology, the Revised Delirium Rating Scale-Revised-98 (DRS-R98), combined with longitudinal and factor analytical methods have been used to confirm the hypothetical existence of a three domain theory for the phenotype of delirium. This three domain theory has been conceptualised as being composed of 1) general cognition, 2) higher level cognition and 3) circadian integrity Fig. 1 [9–11]. However, disparities of up to a third of delirium status attribution, namely full syndromal delirium (FSD) or subsyndromal delirium (SSD), by validated instruments such as the Confusion assessment method (CAM) and the DRS-R98 have indicated that the neurobehavioural interface of what can be diagnosed as delirium requires more focused research [12]. Moreover, recent publication of the DSM-V criteria for delirium has marginally altered the previous DSM-IV criteria with a focus upon inattention with vague terms such as consciousness downplayed [13]. Such an alteration has been found to be restrictive and thus impact upon delirium case identification. Indeed, recent work using pooled data sets and retrospective study designs have indicated that there is a varied concordance (30–89%) between DSM IV and DSM-V attributed cases. Such a discrepancy was due to challenges in interpreting key phenomenological features such as orientation, acute onset and fluctuating course [12]. Although these findings are approximating the empirical state of delirium as measured by validated instruments, a more refined neuroscientifically informed phenomenological framework is required in order to enhance the theoretical understanding of delirium assessment and resolve these challenges. One such application is the predictive coding (PC) model, also known as the hierarchical Bayesian inference model, to interpreting delirium pathophysiology. The PC model has been applied to neurocognitive disorders including schizophrenia, as well as global brain states such as waking consciousness and dreaming in an effort to expand their respective theoretical frameworks [13,14]. According to the PC model, perception and attention are bound together with neural networks that integrate top down processing connections (execu-

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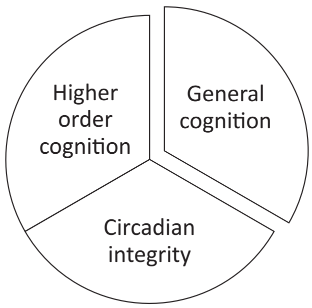

Fig. 1. Three domain theory of delirium phenomenology.

tive cognition) with bottom up sensory input. The hierarchical neural network in which perception results from is the interface between sensory driven analysis and top-down expectation to produce prediction errors Fig. 2. The errors then serve as part of the process to update and enhance the conditional expectations, in an effort to reduce the gap in predictive errors [15,16]. In a state of health, the brain/psyche optimises this complex interface in order to minimise prediction error and ensure that the subject remains orientated and operating at an appropriate cognitive functioning level. In contrast to this state, features of neurocognitive failure e.g. inattention, disorientation, delusions, and hallucinations dominate and are the result of the breakdown in the integrity of this critical system [13,17]. Such domains are integral features of the phenomenology of delirium [7]. Therefore, the aims of this paper are to 1) propose the hypothesis that delirium pathophysiology can be explained in terms of the PC model, 2) support this hypothesis by applying this model to current methods of assessing delirium phenomenology, particularly attention, and 3) outline a future programme of research to test many of the parameters of this application (see Table 1).

Overview of the predictive coding model of the brain/psyche

The PC model of CNS activity has been proposed to be congruent to more far ranging theories of physics, namely the free energy principle, which when applied to biological systems enables them to resist the otherwise inevitable trajectory towards disorder [18]. In the context of the brain/psyche, the improbability of sensations in conflict with the model of the environment generated by the brain is referred to as surprise or also known as self-information.

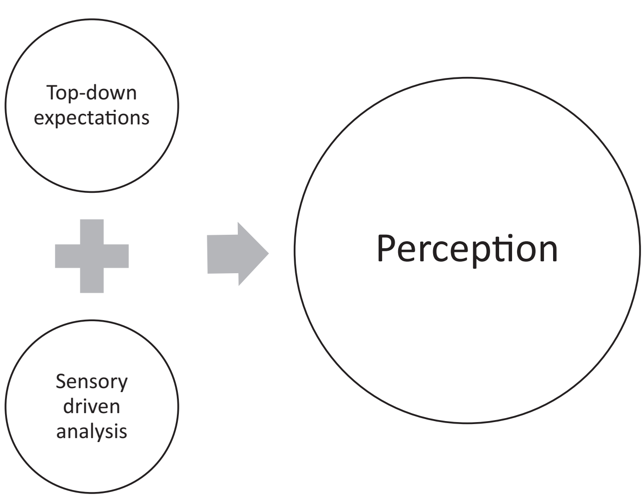

Fig. 2. Perception as interface between top-down expectations and sensory driven analysis.

Surprise averaged over time is believed to be congruent with entropy, and by minimising this, biological systems such as the brain can resist the restraints of the second law of thermodynamics. The brain can measure free energy in terms of sensory driven analysis and interoceptive mechanisms. Therefore, by resisting the impact of free energy, the organism can operate within the world in an organised and typical manner. Updating prior beliefs into posterior beliefs through minimising prediction error (free energy), the brain can minimise this by changing predictions to match sensory driven analysis or vice versa [see Fig. 3] [16]. This operation is a dimension of the common feature of all biological systems, namely homeostasis [18].

When applied to schizophrenia and psychotic features, the PC model highlights how false inferences are at the core of inappropriate perceptions and beliefs [13]. Such disorders in cognitive processing are congruent with the neuromodualtion of excitation at post synaptic sites particularly situated in cortical lamina [19,20]. Cortical pyramidal neurons have been proposed to be critical to the encoding of the predictive error modulatory process, with superficial neurons signalling predictive errors via extrinsic feedforward ascending connections and deep neurons signalling predictions via intrinsic feedback descending connections towards the superficial pyramidal neuronal population [15,16]. There is also the relative influence of predictive errors to consider, both in terms of their respective gain and weight. This aspect is attributed to the intrinsic connectivity that orchestrates the gain of neuronal groups involved in signalling prediction error. This output is then proposed to correspond to mathematical models of precision and hence confidence regarding to the information processes within the PC system (see Fig. 1). Precision in this sense is attributed to the optimal signalling of prediction errors by the post synaptic gain of neurons involved in this process. This process is a key component of attention and sensory processing, wherein the selectively enabled convection of precise information is performed [16,21]. More generally it has been proposed that attention is the inference about precision (the uncertainty) of the causes of sensory input, while perception is the inference about the causes themselves [16].

Delirium and phenomenology

Delirium is a complex phenomenological entity that is as unique as the psyche that experiences it. Investigating the phenomenology of delirium is based upon a wide variety of perspectives from quantitative (e.g. DRS-R98) to qualitative (e.g. semi-structured interviews), and from objective (e.g. bioelectronics detection and neuroimaging) to observer rated scales and clinical interviews with the patient. Not surprisingly there is immense overlap between these categories of investigation. For example, in semi-structured interviews of the delirious experience, patients consistently report disturbed features of reality including, blurring between the boundary of reality and dreaming, reversal of daytime and night time, clouding of consciousness, and a feeling of disintegration [22]. In *The phenomenology of perception*, Merleu-Ponty explains that experience of the external world is not merely a result of perceived images (called "*perceptum*," "what is seen") and thus based solely upon sensory detection. The subject that perceives these images is bound with the experience (called "*percipiens*," "he who is seeing"). The *perceptum* and *percipiens* are both aspects of the same seamless phenomena, due in part because the construct of subject is based upon sensation, perception and the cohesion of the experienced body i.e. the ego [23]. The human ego is an agency that gives coherency and masks the underlying fragmentary nature of the body [24]. This phenomenon can be identified with the individuals' experience as resulting from the multitude of underlying neuropsychological processes that exist