To err is human...: can the methods of cognitive neuroscience contribute to our understanding of errors in anaesthesia?

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When future generations look back and describe the development of anaesthesia one of the key themes from our time will be that we formalized the importance of learning from our errors. Indeed, there is currently great interest in the evaluation of human error in anaesthesia, with a focus on promoting training and research into ‘human factors’. However, by turning to cognitive neuroscience, it may be appreciated that there is a rich literature exploring the neural underpinnings of human error, and its complex relationship with behaviour.

Cognitive neuroscience

Cognitive neuroscience is grounded in the philosophical and psychological traditions of exploring how complex mental functions enable high-level human thought. During the 20th century, the fields of cognitive psychology and neuropsychology became particularly influential, and there was obvious benefit to be gained from integrating these disciplines with neuroscience which focused on brain anatomy and physiology. Since the 1990s (declared as the ‘Decade of the Brain’ in the USA) the newly developing field of cognitive neuroscience has benefitted worldwide from increasing recognition. In particular, there was improved access to neuroimaging techniques and with it the promotion of cross-discipline expertise: medical imaging, neurophysiology, clinical psychology, computer science, to name a few. In short, cognitive neuroscience had set-forth to integrate knowledge from multiple-related disciplines in order to improve understanding of structural and functional relationships in the human brain. Of interest to anaesthesia currently, some of this attention was directed towards understanding the anatomy of human error.

Performance monitoring

At any one time behaviour reflects the integration of ‘bottom-up’ sensory information (incoming stimuli), ‘top-down’ executive pathways (attention allocation and decision-making), retrieval from memory and filing of newly learned information (updating experience), and initiation of a response via the appropriate modality be it speech or motor (action). In order for this system to run successfully the brain must monitor performance on a moment-by-moment basis so that when there is a mismatch between intention and action it may be recognized and responded to. Within this system there is
scope for error, be it because of knowledge failure, mistakes and/or momentary slips in attention. The former may be remedied through education and experience. Cognitive neuroscientists studying performance monitoring have been particularly interested in the latter (slips in attention), which relates to errors occurring in online tasks. For example, responding incorrectly to certain stimuli when under pressure of time, or, in an everyday example, that moment at which you put your ‘coffee in the cornflakes’ as well-described by one group of researchers.1 Two components of error processing have been described: a ‘monitoring system’ to detect errors, and a ‘remedial action system’ to compensate for errors.2 In this view, a comparator mechanism in the monitoring system identifies instances of mismatch between what response should have occurred with what response actually occurred. The remedial action system may then intervene to correct and/or compensate for the error. Immediate self-correction of errors was described by Rabbitt and Rodgers,3 who posed the now classic question: what response actually occurred. The remedial action system mechanism in the monitoring system identifies instances of mismatch between what response should have occurred with what response actually occurred. The remedial action system may then intervene to correct and/or compensate for the error. Immediate self-correction of errors was described by Rabbitt and Rodgers,3 who posed the now classic question: what does a man do after he makes an error? Our understanding of such speeded responding was enhanced by the work of De Jong and colleagues4 who identified that incorrect motor commands initiated by the brain in stimulus-response tasks may be terminated before being carried-out but only within a certain timeframe. For example, if the comparator realizes soon enough that a wrong button is about to be pressed it intercepts the first motor signal with a new instruction to press the correct button instead, but should a critical time threshold have passed then the original erroneous motor plan will be carried-out as it has gone ‘beyond the point of no return’. Similarly, compensation may take the form of slowing down,4 which is a more conscious response to making an error, with the premise that slower could then facilitate being surer.

This cognitive framework could be applied to ‘slips’ occurring in the everyday practice of anaesthesia from the harmless to more severe. For example, turning one knob on the anaesthetic machine when it was actually intended to turn a different knob, but then immediately correcting the choice before too much thought was given to what had occurred. More serious failure of this system could mean that the error is not recognized and thus there is no potential for self-correction or slowing down to prevent further errors. Perhaps, for example, explaining errors with initiating gas and/or inhalation agent supply on patient transfer to theatre.5

The cognitive neuroscience methodology to understanding human errors

Cognitive neuroscientists have explored changes in the brain associated with such errors by utilizing mainly electroencephalography (EEG) and magnetic resonance imaging (MRI) methods. EEG is particularly useful in that it allows us to look at aspects of online performance monitoring within the millisecond timeframe. Event-related potentials (ERPs) are short sections of the EEG that are time-locked to the occurrence of a particular stimulus or response, for example the point at which you press the button after being directed to do so by a stimulus. For the purpose of analysis, we can divide and then average the sections of EEG (ERPs) according to whether they were associated with a correct or error response. For each of the averaged ERP waveforms: ‘correct’ and ‘error’, we can then calculate the size of negative and positive deflections in the waveform (‘component magnitude’: μV) and the latency (ms) at which these components occur. Differences between ERP component magnitude and latency between conditions (error/correct) and between groups of people can then be analysed statistically. Furthermore, ERP components may be compared with behavioural performance on the same task (e.g. response time, error rate, self-correction rate, post-error slowing, or with performance on neuropsychological tests). Traditionally, EEG is viewed as having very good temporal resolution (which suits analysis of errors occurring in the millisecond timeframe) but less good spatial resolution, with MRI techniques offering the opposite, namely better spatial than temporal resolution. In brief, cognitive neuroscience techniques offer the opportunity to build-up a more complete picture of what happens when we make an error.

An example of an objective measure of error processing: the error related negativity

In 1991, Falkensteink6 described a negative waveform (‘Ne’) that consistently appeared in the EEG trace following an error in a choice response task. This was also observed by Gehring and colleagues7 who called it the error-related negativity (ERN): see Figure 1 for an example of an ERN waveform.8 Importantly, a similar waveform did not appear or was much reduced after a correct response suggesting that the ERN reflected the brain’s recognition of error. The ERN is seen within ~200 ms of an error occurring and is therefore likely to be pre-attentive; although a longer latency positive waveform (‘Pe’) that follows the ERN was predicted to reflect more
conscious post-error processing and perhaps also the initiation of remedial actions after an error.\(^2\) Indeed, increased magnitude of the Pe has been associated with decreased error rate overall, and more efficient performance on subsequent correct trials.\(^10\)

The ERN appears maximally over the frontal-central scalp (FCz in the standard 10–20 system of EEG lead placement), indicating to early researchers that the signal was likely to be generated from within the frontal lobes. It is not surprising that the frontal lobes are involved in producing the ERN. The function and structure of the frontal lobes have been closely scrutinized by cognitive neuroscientists who have long-since recognized their supervisory role, particularly in monitoring activity in complex and/or novel tasks in order to facilitate optimum allocation of attentional resources. Source localization studies suggested that a potential generator of the ERN was the anterior cingulate cortex (ACC) in the medial aspect of the frontal lobes.\(^11\) A number of studies incorporating MRI techniques\(^12\) and studies of patients with lesions located in this area of the brain\(^14\) have since added weight to the view that distributed frontal lobe neural networks, particularly those incorporating the dorsolateral prefrontal cortex, supplementary motor cortex, and medial (ACC) areas, underpin a performance monitoring system that allows for the detection of errors as and when they occur. Within this network, the ACC may signal to recruit additional fronto-parietal brain areas when there are competing demands on attention:\(^15\) perhaps allowing us to pay more attention when a problem is recognized. This could involve recruitment of dorsolateral prefrontal cortex for cognitive control and more ventral areas of the prefrontal cortex for decision-making elements of the task at hand.\(^16\) Thus, the identification and study of the ERN has provided impetus to learn more about the performance monitoring system as a whole, and how this system relates to brain structure and function.

**Wider implications of an error-processing system**

The knowledge that frontal lobe networks are also involved in other aspects of behaviour including affective state prompted cognitive neuroscientists to investigate the effect of mood on performance monitoring. Indeed, it has been found that the magnitude of the ERN is increased even with subclinical anxiety,\(^10\) with sense of failure/helplessness,\(^17\) and can apparently predict the up-regulation of defensive mechanisms.\(^18\)

Moreover, fatigue, a state which will also be familiar to all anaesthetists, has been shown to reduce the size of the ERN.\(^19\) Thus, both increased and decreased ERN magnitude could reflect influences on current performance monitoring capacity.

Aspects of personality have also been explored. It was acknowledged that individuals vary greatly in the degree to which they show cognitive control, which may in turn influence how they process and respond to errors.\(^20\) Related to this, others considered if the ERN reflects ‘fast-guessing’ or other forms of impulsive behaviour where a response is made before all information has been adequately processed.\(^2\) It has since been demonstrated that the ERN is increased in those who self-rated themselves as having greater cognitive control (are less impulsive),\(^20\) which was the opposite of what might have been expected. However, the results with regard to personality traits in general are heterogenous, with high ‘emotionality’ and ‘openness’ also resulting in increased ERN magnitude, whereas decreased ‘social orientation’ results in reduced ERN magnitude.\(^20\) In another study, extraversion was also associated with reduced ERN magnitude, but mostly in association with social stimuli (facial expression).\(^21\) The authors suggested that extroverts either engage less in performance monitoring or find errors less salient, perhaps related to greater underlying confidence in social interaction.

Associated as it is with anxiety and other aspects of behaviour, it may come as no surprise that autonomic nervous system arousal has been investigated in relation to the ERN. Post-error heart rate deceleration, skin conductance, and pupil-size changes have been demonstrated, and shown to be sensitive to the ERN/Pe complex, more so for subjectively perceived compared with un-perceived errors.\(^22\) Similarities between the timeframe and scalp distribution of the Pe potential and components associated with a more basic ‘startle/orienting’ response (such as the ‘P300’ potential) have been noted\(^22\) and could reflect acute refocusing of attention with activation of a state of readiness to respond physically.

Research into the ERN/Pe extends far beyond this necessarily brief overview. However, we have highlighted that there are many potential influences on error processing, reflecting the fact that it is a high-level function that is complex and dynamic. The ERN/Pe provides a fascinating, objective manifestation of this system, demonstrating thus far that it reliably appears at the point of making an error, is influenced by both external and internal influences on mood state, reflects the degree to which errors/conflict are consciously perceived by the individual and is associated with remedial and physiological changes.

**Relevance to anaesthesia**

Most anaesthetists would agree that their everyday practice requires a good deal of online performance monitoring of the type described above; also, that slips of attention can occur on a daily basis particularly during critical periods of induction and reversal of anaesthesia. They may also already appreciate that this function could be negatively affected by common scenarios including mood change and mental fatigue. So what specifically can we learn from cognitive neuroscience?

First, we note that there has recently been great focus on drawing from the experience of other disciplines, particularly the aviation industry, in order to try and limit mistakes in anaesthesia. We highlight the considerable progress that has already been made by cognitive neuroscientists working in affiliated academic and medical settings in understanding what underlies human error-processing. Cognitive neuroscience offers our profession an indication of what happens internally when we make an error and how remedial actions are generated.
Importantly, understanding this may allow us to harness mechanisms to improve error recognition and response, particularly when respondents have to be fast. By incorporating cognitive neuroscience techniques such as ERN/Pe recording, rate of error self-correction and degree of post-error slowing (in the context of wider ‘biofeedback’) into simulation training it may be possible to help individuals improve their internal and situational awareness of how errors occur and how we can learn from them. Improvement in performance monitoring with training in anaesthesia and with increasing levels of simulated conflict may reflect dynamically in errors processing variables, further reinforcing the importance of awareness of this system.

Secondly, there are times of recognized action-density (e.g. induction and emergence) when performance monitoring might come under particular challenge irrespective of experience in anaesthetic practice. Objective demonstration that external, competing influences on our attention at these times can interfere with our ability to recognize and respond to errors could help emphasize the importance of limiting interruptions, particularly in the anaesthetic room at point of induction, and while transferring patients into theatre: what is the effect of receiving a bleep or being aware of this system.

Thirdly, it has been shown that ERN generation can be activated simply by watching those around you make an error, confirming that we monitor the actions of others and our own performance. Knowing that an individual’s performance monitoring may at times be subject to interference from external (competing demands on attention) and internal (mood and motivation) factors, it is reassuring that we might rely on those around us to help recognize errors even when they are not directly involved in the task at hand. This could be investigated in simulations which simultaneously record potentials in task performers and observers, and could provide observers with powerful reassurance as to the importance of ‘speaking-out’ for patient safety.

In practical support of these suggestions cognitive neuroscientists are exploring the means by which ERP components may be studied in more naturalistic working environments. Perhaps, therefore it is not so much a question of can cognitive neuroscience tell us anything about errors in anaesthesia, but how we can make this happen.

Declaration of interest

None declared.

References


5 Nickalls RW, Mahajan RP. Awareness and anaesthesia: think don’t, think data. Br J Anaesth 2010; 104: 1–2


Thrombocytopenia is encountered not infrequently in the critically ill patient. Determining the cause is vital to ensure that the patient gets the right treatment at the right time. Heparin-induced thrombocytopenia (HIT) is one of the differential diagnoses requiring treatment rapidly because it is a prothrombotic condition compared with the other causes of thrombocytopenia. An anticoagulant useful in HIT has recently been introduced in the UK but has been used in many other countries for many years. After a brief introduction to HIT, we discuss the value of this ‘new’ agent and other licensed alternatives along with the barriers put in its way to impede its introduction when other potential treatments disappeared.

HIT exists in one of two forms, type I (non-immune) or type II (immune). Type I can also be described as heparin-associated thrombocytopenia, typically occurs within the first 5 days of heparin treatment, it results in minimal reduction in platelets (unlikely <100,000 mm$^3$), and is thought to be a result of a direct non-immune interaction between the surface of platelets and heparin.$^1$ No treatment is necessary and heparin should be continued.$^7$ Conversely, type II (which is the form of HIT we are now concentrating on in this editorial) has a much more progressive thrombotic profile. It results from a stimulation of the immune system leading to the formation of IgG antibodies against platelet factor 4 (PF4) and heparin complex. IgG binds to PF4–heparin complex, leading to platelet activation, thrombosis, and thrombocytopenia.$^3$ $^4$ There are a number of separate risk factors for HIT. At a structural level, porcine, rather than bovine sourced, is less likely to lead to HIT. Low molecular weight heparin when used for thromboprophylaxis is also less likely than unfractionated heparin to lead to HIT.$^5$ Overall, the incidence is higher in surgical rather than medical patients, and cardiac and orthopaedic patients are the most at risk. Curiously, women have double the risk of men.$^6$ Calculating the overall incidence of HIT is difficult due to the requirement to delineate the studies between simply the presence of antibodies, antibodies with thrombocytopenia, and antibodies with thrombosis.

Diagnosing HIT relies on a combination of both a high clinical pre-test probability score and an assay.$^7$ The probability scoring system most commonly used is the ‘4T’ score, composed of Thrombocytopenia, Timing of onset of thrombocytopenia, presence of Thrombosis, and oTher possible causes of thrombocytopenia being ruled out. A low score in the ‘4T’ scoring system has a high negative predictive value for the presence of HIT.$^8$ A clinician has to strike the balance between waiting for the assay confirmation and continuing or stopping heparin in the meantime. An alternative anticoagulant could be used pending the results of the assay; however, they are more expensive, unfamiliar to staff, and often are difficult to source immediately. The laboratory tests can either be a platelet activation assay or be an antigen assay, both are highly sensitive, with a negative test therefore making HIT unlikely.$^4$ However, the specificity is not as high resulting in overtreatment of patients who do not have HIT.$^8$ On diagnosis of HIT, type II heparin should be discontinued. The aim is to stop the prothrombotic cycle that can lead to catastrophic venous and arterial thrombotic events.$^9$ Although the platelet count may be low, prophylactic platelets are not indicated in patients not bleeding as they potentially increase the thrombotic risk. However, platelet transfusion may have