The 9th International Symposium on Memory and Awareness in Anesthesia (MAA9) was held in Tokyo, Japan on June 20–23, 2014, attracting over 70 delegates from around the world. It was chaired by Jiro Kurata, from the Tokyo Medical and Dental University, and was jointly sponsored by the British Journal of Anaesthesia to support research activities in the fields of awareness during anaesthesia, neurobiological mechanisms of general anaesthesia, consciousness, and memory. This topic complements the recently published National Audit Project NAP5 survey of accidental awareness under general anaesthesia conducted in the UK in 2012 and published in the British Journal of Anaesthesia last year.1–3 The present British Journal of Anaesthesia special issue on Memory and Awareness in Anaesthesia was planned by Hugh Hemmings, a co-organizer of MAA9, to present the most current findings and views on topics from selected presentations during the meeting, in addition to submissions in response to an open call for papers. All the MAA9 abstracts are also included in this special on-line-only issue. Details of the MAA9 programme can be found at the conference website (http://maa9.umin.jp/).

The scope of previous MAA symposia has ranged from the neuroscience of anaesthetic action, memory, and consciousness to the clinical aspects of awareness during anaesthesia. The MAA9 followed this tradition, while emphasizing the clinical aspects: epidemiology, diagnosis, prevention, and treatment of intraoperative awareness, with a conference slogan of ‘Minding the Mind of Subconscious Self’. Although anaesthesiology has devoted tremendous efforts to studies of anaesthetic pharmacology and the mechanisms of anaesthetic-induced unconsciousness, which can be approached in a relatively direct manner through behavioural analyses, it has paid much less attention to subconscious processes of mind. At least part of memory is formed in the subconscious domain of mind,4 and for this reason could be resistant to clinical ranges of general anaesthetics aimed to produce elimination of conscious behaviour. The MAA9 was programmed to propose that anaesthesiology should now approach the next stage, the care for the subconscious mind.

Detection of intraoperative awareness during anaesthesia has historically been a major focus of research and technology development in anaesthesiology. Currently, there are several kinds of anaesthetic depth monitors, in addition to real-time or simulated monitors of anaesthetic concentrations, available in most operating theatres. Behaviour-based standardization of mathematically processed EEG, cortical evoked potentials, or both has attempted to turn ‘probability of awareness’ into an anaesthetic depth index, or a ‘vital sign for consciousness’. In recent years, such indices for anaesthetic depth have been tested for efficacy in detecting intraoperative awareness compared with anaesthetic concentration monitors, which is summarized in the review by Mashour,2 along with some of the controversial and established aspects of intraoperative awareness. Despite such efforts, titrated administration of anaesthetics, using either an anaesthetic depth or a concentration monitor, has not been successful in decreasing the incidence of intraoperative awareness with recall. No single reliable anaesthetic technique or monitor is yet available to eliminate awareness with recall during general anaesthesia.
A significant concern is the increasing reliance on EEG-based monitors of anaesthetic depth to titrate administration of anaesthetic agents. Some of the issues with using processed indices of the EEG rather than the raw waveform are addressed in the review by Hagihira, along with editorial commentary by Veselis. Purdon and colleagues report profound age-dependent changes in the EEG that also have important implications for depth-of-anaesthesia monitors relying on processed EEG signals. Greater sensitivity to anaesthetics evident in the increased susceptibility to burst suppression in the elderly is supported by animal studies that demonstrate delayed emergence and increased sensitivity to anaesthetics in old rats. This is highlighted in an editorial by Hudson and Proekt. Age-dependent changes in the EEG response to anaesthesia also occur in children, as demonstrated for sevoflurane by Akeju and colleagues; this phenomenon has implications for EEG-based monitors of anaesthetic depth in both the young and the elderly. The impact of the unique pharmacological profile of ketamine on its EEG signature is described in a study by Pal and colleagues, who show that ketamine, like other general anaesthetics, suppresses high-frequency activity and promotes a breakdown in cortical coherence.

Reasons for failure of general anaesthesia in suppressing memory and awareness could include technical problems or mishaps, such as an inadvertent discontinuation or a low concentration of general anaesthetic agent. Neuromuscular blocking agents, which are non-hypnotics, could also conceal conscious behaviour and affect reliability of EEG-based depth-of-anaesthesia monitors. These issues are highlighted in two studies by Thomsen and colleagues from a Danish registry of patients with documented butyrylcholinesterase (plasma cholinesterase) deficiency, showing that prolonged paralysis due to impaired elimination of esterase-dependent neuromuscular blockers (succinylcholine or mivacurium) markedly increased the likelihood of awareness during emergence from anaesthesia, particularly when neuromuscular function monitoring was not used. The importance of not withholding neuromuscular function monitoring when paralytic drugs are used during anaesthesia is highlighted in the editorial by Avidan and Stevens. An important limitation of EEG-based depth-of-anaesthesia monitors is described by Schuller and colleagues in a fascinating study of volunteer anaesthetists who underwent intentional awake paralysis using the isolated forearm technique to show that the bispectral index monitor itself cannot always distinguish ‘anaesthesia’ from paralysis, the implications of which are highlighted in an editorial by Schneider and Pilge. Use of the isolated forearm technique as a monitor of depth of anaesthesia and as a research tool into mechanisms of anaesthesia is presented in a thought-provoking debate and review by Pandit and colleagues.

Not all known cases of intraoperative awareness with recall, however, can be explained by such ‘logical’ causes. Should we now question the ability of general anaesthetics to produce unconsciousness and amnesia reliably? Targeting only conscious behaviour might not necessarily provide reliable protection of patients from traumatic memory of physical or psychological injuries during surgery and anaesthesia. The mechanisms of memory formation are reviewed by Veselis, while Pryor and colleagues used functional magnetic resonance imaging to show that propofol suppresses emotional memory formation through a hippocampal mechanism. Implicit memory formation during anaesthesia remains understudied and poses a significant problem that could be relevant to post-traumatic stress disorder, and possibly, postoperative delirium and cognitive dysfunction. A report from the Anaesthesia Awareness Registry of the American Society of Anesthesiologists indicates that explicit recall of intraoperative awareness can have significant negative psychological impact on patients, which suggests that a more systematic response and follow-up care are necessary.

Amongst the irreplaceable roles of the MAA conferences has been, and hopefully will continue to be, an investigation into subconscious processing of information during anaesthesia. Now that we have abundant, if not sufficient, evidence for anaesthetic-induced unconsciousness, we should investigate further the science of subconsciously. The next meeting, MAA10, will continue this conversation around the clinical and basic science of memory and awareness in anaesthesia, to be chaired by Professor Sinikka Münte in Helsinki, Finland in 2017. Until the details of MAA10 are officially announced, the MAA9 facebook page (http://www.facebook.com/maa9.jp/) will remain a source of information on the development of MAA10. Please leave a comment on this page if you have suggestions or would like to be included in the mailing list for MAA10.

We sincerely hope that this special issue, marking the up-to-date knowledge and insights on memory and awareness in anaesthesia, will help to promote further scientific inquiries and technological development to eliminate the most dreadful complication of general anaesthesia: intraoperative awareness. Caring for the whole human existence, conscious and subconscious, should continue to be the core mission of anaesthesiology. Finally, we would like to thank all the authors of these excellent articles, all the attendees, support staff, and sponsors of the MAA9, and Oxford University Press for realizing this special issue.

**Authors’ contributions**

Wrote, edited, and approved the final version; contributed equally to the work: J.K. and H.C.H.

**Declaration of interest**

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**References**

What about $\beta$? Relationship between pain and EEG spindles during anaesthesia

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The prodigous children of the EEG frequency spectrum these days are $\theta$ and $\gamma$.1–3 As we wrestle with weighty concepts of consciousness, memory, and anaesthetic effects thereon, the first objective measure of brain activity is being scrutinized more closely for clues about the underlying machinery. The most basic grammar used to communicate in ‘EEG language’ refers to the different frequencies in the EEG signal. This has its roots in the historical order of interest in different EEG oscillations, documented as letters from the beginning portion of the Greek alphabet.4 Rhythms of different frequencies were noticeable to the naked eye in analog EEG signals, and those most noticeable attracted our interest first. This is somewhat akin to contemporary astrophysicists still using references to the constellations. There is nothing inherently wrong with this, as long as one is aware of the history and is careful to avoid imbuing mechanisms of action too closely to descriptive labels.

One important caveat with this analogy is that whereas the borders between constellations are well defined, they are not so with EEG frequencies. The frequency at which $\alpha$ becomes $\beta$, the border of which embodies sleep spindles, is somewhat ill defined. Thus, one person’s (fast or high) $\alpha$ might be another’s (slow or low) $\beta$. Current interest in $\theta$ rhythms centres on memory processes, but it should be remembered that $\theta$ has been related to many other aspects of cognition (including movement) in the past.5 Likewise, $\gamma$ is studied to understand the processes of consciousness, closely related to information transfer in the brain.5,6 Thus, $\gamma$ is of interest in how anaesthetics affect consciousness, or in other words, how anaesthetics ‘work’.7 In fact, the definition of $\gamma$ has been extended to higher frequency bands to capture more of the EEG bandwidth as recording methods and capacity for data storage and analysis improve.8 As with $\gamma$, $\beta$ (a) has been subdivided into various frequency bands, with ‘sigma’ a less frequently used term basically analogous to ‘sleep spindles’. Both refer to similar frequencies in the EEG, approximately 12–14 Hz, though, again, these boundaries are porous.9,10 Greek letter labels may be good shorthand, but the underlying principles of communication, network activity, and information content, and the underlying neurobiology that produces these oscillations are really the important principles to focus on.