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

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The prodigy children of the EEG frequency spectrum these days are $\theta$ and $\gamma$. 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. 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. Likewise, $\gamma$ is studied to understand the processes of consciousness, closely related to information transfer in the brain. Thus, $\gamma$ is of interest in how anaesthetics affect consciousness, or in other words, how anaesthetics ‘work.’ 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.

As with $\gamma$, $\beta$ ($\alpha$) 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. 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.
But, what about β? This frequency band is faster than θ and slower than γ. β frequencies have been described as the least understood of the EEG frequencies, and classically, have been conceptualized as closely related to motor activity.11 β is very close to and somewhat faster than the resting α rhythms, which occur in the occipital area when eyes are closed. Many well-informed people are familiar with this ‘rhythm of meditation’. The α-β region of the EEG spectrum notably captures the bi-phasic EEG response to anaesthetics, most evident with GABAergic i.v. agents, such as thiopental, propofol, and the benzodiazepines.12 13 This same frequency region embodies the closely studied α-anteriorization, where occipital α at rest becomes frontal α under lower doses of many, but not all anaesthetics.14–17 This EEG region also expresses activity of thalamocortical loops, most noticeable during sleep and thus termed sleep spindles. These oscillations wax and wane over short time periods, producing a very noticeable ‘spindle’ appearance on the analog EEG. These oscillations have had their physiology well defined, the iconic work being that of Steriade and colleagues,18 among others. The interaction of thalamus, cortex, sleep, and anaesthesia is irresistible for closer examination. One seeks mechanistic explanations of anaesthetics in this region of EEG as one might look into the heart of Sagittarius for clues about our home galaxy.

Much important scientific discovery starts with an astute observation of a phenomenon that is, hopefully, reported anecdotally. One purpose of this early communication is to stimulate further critical inquiry. Often this forum exists in case reports, but for observations not amenable to this format a conference of experts might fit the bill. The article by Hagihira19 in this special issue of the British Journal of Anaesthesia lies somewhat above this mark, because the original observations have been reported previously.20 What Hagihira19 proposes is that by measuring the bicoherence of EEG signals, especially in the α-β-spindle–sigma range, one can more objectively titrate analgesia during anaesthesia.

When one considers the potential implications of the work, it is surprising that not a lot of follow-up has occurred. The physiology underlying Hagihira’s observations is presented in somewhat more detail in the current manuscript than previously. He proposes that thalamic processes may be indexed by measuring ‘high’ and ‘low’ bicoherence frequency values (pBIC in their terminology). As inhalational anaesthetic concentration increases, power spectrum values segregate into two distinct peaks, and low and high pBIC are measured at these peaks values, approximately 4 and 10 Hz. In the present manuscript,15 isoflurane data were used, but similar effects occur with sevoflurane. The ‘high’ pBIC seems to have value in titration of analgesics, with a seemingly consistent response to fentanyl, as reported in a small number of subjects. All subjects demonstrated the same changes in pBIC with skin incision and fentanyl administration. When compared with other common measures derived from the EEG, these changes were more consistent. As mentioned, initial reports of this observation have been made, with details of how EEG signals were analysed reported there.20 The present manuscript15 highlights this most interesting observation from a subset of the initially reported data, those where isoflurane was administered at 1.0% and where fentanyl was administered after surgical incision. The author does highlight in the present report15 his success in its use for thousands of patients since then. Additionally, the author points out that pBIC seemed to work best in patients where spindle activity was noticeable in the EEG, which did not occur in a minority of patients. Even a remote possibility of an objective measure useful to titrate intraoperative analgesic medications needs to be investigated more thoroughly. Our poor ability to titrate intraoperative analgesia is evidenced by the number of quality improvement measures that revolve around pain soon after our anaesthetics.21 A monitor, closely related to the widely available bispectral index monitor but with open access, could revolutionize our thinking about intraoperative analgesic management.

Although the present report15 is useful, it must be regarded as a starting point, or perhaps more accurately, as pointing to a starting point. With the recent emphasis on the issue of reproducibility, it is imperative that these most interesting results are replicated in a larger patient population with more diverse anaesthetic techniques.22 The initial studies of small numbers of patients from a single institution need to be expanded to different opioids and other potent analgesics in a wider patient population. Additionally, Hagihira19 proposes that his metric reflects underlying neurobiology, specifically influences of thalamic reticular nuclei and the membrane potentials of thalamocortical relay neurons. Thus, a series of animal studies spring to mind which could support or refute, or more importantly, point to new directions to investigate this phenomenon.

It would be very fruitful if a neurobiological construct were developed to explain pain modulation of EEG spindles during anaesthesia. The fact that these EEG frequencies also express the activity of basal ganglia cortical loops may point to a link between anaesthetic effects on consciousness (depth of anaesthesia) and on pain, which possibly would be expressed as motor activity.23 24 Some have suggested that motor activity (e.g. frontalis muscle tension or grimaces) could act as a measure of intraoperative analgesia. Also, a decrease in β activity occurs with novel motor movement, representing a change in the current motor set or ‘status quo’.1 Thus, pain during anaesthesia may be associated with new motor activity in the facial muscles, which may be detectable by pure EEG measures, as opposed to measures of EMG. This may be very difficult to sort out, because EEG and EMG frequencies overlap greatly.25 Again, animal studies delineating the underlying neurobiology could be helpful to understand mechanisms. Another issue that needs to be considered is whether β during anaesthesia is representative of GABAergic effects modulating cortical interneuronal activity rather than indexing deep brain structures affected by anaesthetics. It is clear that spindles arise from the thalamus, and these seem to be a major component of the pBIC. However, both β and γ rhythms arise from different layers of cortical neurons, and they modulate each other.26 Thus, there could be many different neurobiological sources for the pBIC signal, and the mechanistic interpretation may be difficult to sort out.

As with other anaesthesia monitors, the first step is to document clinical utility, and that is why a carefully designed pragmatic trial should be the next step from anecdotal observations. Once clinical applicability is established, the underlying neurobiological mechanisms should be delineated, which would add great validity to the use of the monitor. The fact that Hagihira19 has reported great success in clinical use is most encouraging, and thus there is reason to hope that subsequent studies will be fruitful . . . but the proof, as it is said, is in the pudding.

Declaration of interest

None declared.

References

Some heightened sensitivity

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With the progressive ageing of the population, anaesthetists are increasingly faced with geriatric patients. As our patient population grows, there have been regular calls to limit anaesthetic exposure in older patients out of fear of overdose. The current concern regarding postoperative cognitive dysfunction weighs heavily on some patients’ minds, while anaesthetists ponder the significance of the ‘triple low’ as a predictor of morbidity and mortality.1 2 Anecdotally, elderly patients take a variable, but prolonged, amount of time to recover from anaesthesia relative to younger patients. The open question remains, how and