

REVIEW ARTICLE

Interpretations of responses using the isolated forearm technique in general anaesthesia: a debate

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Abstract

The isolated forearm technique (IFT) enables an otherwise paralysed patient to communicate awareness to the anaesthetist. We present a debate that focuses on how best to interpret IFT responses. On one side, Pandit argues that there is a range of response types from none through to movement initiated by the patient to alert the researcher. He also presents a *de novo* numerical scale by which IFT responses could be classed. Each response type reflects the underlying mental state (degree of unconsciousness), and he concludes that the effect of general anaesthesia on patients is not binary but heterogeneous. There can be mental states resulting from anaesthesia that produce adequate levels of conscious impairment sufficient for surgery to proceed, but in which a degree of wakefulness, including a capacity for later recall, is retained (a state previously termed 'dysanaesthesia'). A literature review of IFT (31 trials) is presented to support this assertion. In rebuttal, Russell and Wang argue that IFT response types are not so discrete, and that the IFT technique precludes higher levels of response. They argue that overinterpretation of IFT responses might in fact result in a greater risk of accidental awareness; a binary interpretation of the IFT response is the safest option. All authors agree that the IFT has a role in clinical practice and the study of anaesthetic mechanisms.

Key words: depth of anaesthesia; mechanisms; monitoring; unconsciousness

Editor's key points

- The isolated forearm technique (IFT) allows otherwise paralysed patients to respond with hand movement.
- Differences exist in the interpretation of IFT responses: either a graded response reflecting multiple mental states, or a binary response (conscious or unconscious).
- The IFT could be useful both as a tool for monitoring and for understanding the mechanisms of anaesthesia.

This article is based on a debate between Pandit, Russell, and Wang that took place at the 9th International Symposium on Memory and Awareness, in Tokyo, Japan in September 2014. Pandit offered a novel and nuanced way of interpreting the hand

movements observed during the isolated forearm technique (IFT). Russell and Wang argued that a positive IFT response represents full consciousness, requiring more anaesthetic. An informal 'vote' taken at the end of the debate overwhelmingly supported the interpretation of Russell and Wang (by ~80:20). This result may reflect clinical pragmatism, but nevertheless the onus here is upon Pandit to convince the reader of any new interpretation. Here, we present a common Introduction, followed by the respective sides of the debate, ending with concluding remarks that seek to outline common ground and identify areas for future research.

The IFT is an elegant and potentially valid solution to the dilemma of how to ascertain that a paralysed patient is 'conscious'. The definition of consciousness has historically challenged both philosophers and scientists. Consciousness is generally regarded

Accepted: March 1, 2015

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as a subjective experience, but definitions based wholly on introspection allow limited access to another person to gain insight in an objective way into underlying mechanisms. Aspects of brain function, such as memory, language, or emotion, are regarded as important to the conscious state, but views differ on the extent to which they are central.^{1–5} Pragmatically, consciousness is a mental state in which the person engages in coherent cognitive activity and is aware of themselves and their surroundings. Groundbreaking work in minimally conscious patients challenges many assumptions.⁶

Consciousness in another person is normally determined by their responsiveness to stimuli or interrogation. Thus—as in the Glasgow Coma Scale (GCS)—when a person demonstrates impaired responsiveness it is generally concluded that they are in a reduced or impaired state of consciousness.⁷ Likewise, questions about orientation in time, place, and person indicate impaired mental capacity in delirious or confused patients. However, motor responsiveness can be impaired in ways other than those that affect mental state alone. During anaesthesia, if responsiveness is abolished by neuromuscular block (NMB), the patient can appear unconscious but is in fact only paralysed. This state can arise when, for example, NMB is mistakenly administered before any anaesthetic agent in a drug error; the patient is as awake as before the drug error, but is unable to communicate their predicament.

The use of NMB appears to lie at the root of the problem of accidental awareness during general anaesthesia (AAGA). The 5th National Audit Project (NAP5) of the Royal College and Association of Anaesthetists found that reports of AAGA are virtually confined to patients who receive NMB (incidence of reports ~1:8000).^{8–11} In the absence of NMB, AAGA very rarely occurs (~1:136 000) and elicits only vague recollections with little or no longer-term psychological harm. These overall incidences of reports of AAGA are several orders of magnitude lower than incidences obtained in studies where all patients were subjected to one or more follow-up ‘Brice’ interviews.^{12–15} Given that NAP5 methodology did not include such follow-up, but relied instead on patient self-reporting,⁸ it is not known how NAP5 data compare with previous studies. It is also not fully established whether the large differences of incidence between paralysed and unparalysed patients also apply to Brice methods.

The IFT was introduced by Tunstall¹⁶ and then refined and championed by, amongst others, Russell and Wang. It involves first, inducing anaesthesia. Then, a cuff is inflated on one (usually the dominant) arm, to isolate it from the circulation. Then NMB is introduced i.v. via the other arm such that the patient is now paralysed, except for the isolated arm. If the patient were to awaken accidentally, they retain motor capacity in this isolated arm to communicate their predicament (see the study using the IFT published in this issue by Schuller and colleagues). There are important technical details that have been discussed elsewhere.^{17 18} A nerve stimulator should be used to confirm that the isolated arm is not paralysed. Cuff inflation should not be prolonged (e.g. <20 min is suggested), but it can be re-inflated at intervals before each top-up dose of NMB is administered. The patient is given a command at regular intervals to move their unparalysed hand or arm (e.g. ‘[patient name], this is Dr Y; please open and close the fingers of your [dominant] hand’).

It has been widely accepted that any patient response to this command signifies ‘consciousness’ (or, as Tunstall preferred to call it, ‘wakefulness’, because the event was not generally recalled afterwards). Debates about the IFT were nevertheless vigorous,^{19–21} and centred around its utility in clinical practice rather than how to interpret the responses. The ethics of whether it is

sufficient only to prevent bad memories (as opposed to inducing unconsciousness) has been discussed elsewhere,^{22 23} and some anaesthetic techniques appear (at least in retrospect) to create a state in which patients are paralysed but conscious during surgery, but with subsequent amnesia for intraoperative events.²⁴ In such a technique, the incidence of intraoperative IFT responses was high, but postoperative recall low. Russell¹⁷ has reasonably argued that it was unethical to rely purely on amnesia when the IFT responses indicated that patients were wakeful (let alone in pain) in this way during surgery. In a recent ‘pro con’ debate in the literature, Sleight¹⁸ questioned whether the relatively cumbersome nature (his view) of using the IFT made it a distraction and also argued that there was no randomized controlled trial evidence of utility. In response, Russell¹⁷ listed and countered 14 fallacies, arguing in favour of the clinical utility of IFT.

In contrast to these earlier debates, the present discussion is not about clinical utility. The authors agree that the IFT is useful and has a place in modern anaesthetic practice. The NAP5 Report makes a specific recommendation that the IFT should be taught and should enter the UK anaesthetic training curriculum.^{8–10} Rather, this debate revolves around an analysis of possible patient responses during IFT and what proper meaning to apply to those responses.

Pandit: isolated forearm technique responses are graded, and this reflects graded levels of consciousness

The conventional interpretation of any positive IFT response to command is that it signifies ‘consciousness’ or ‘wakefulness’. Elsewhere, Russell and Wang^{17 22} have argued that this is so because in order to respond to a given command, the patient must be able to hear the instructions, comprehend the words as a command, choose to respond, and finally, execute a motor response. As they wrote: ‘it seems perverse not to associate [these] processes with consciousness’.²²

Superficially, this approach is pragmatic in clinical practice, or a good method to quantify behaviour. However, a simple binary interpretation of the IFT result (i.e. patient awake or asleep) may not represent the complete picture. The IFT paradigm offers an opportunity to investigate what otherwise would be difficult to do in clinical practice; that is, observing and quantifying different qualities of consciousness that may be a particular expression of neurobiology unique and relevant to anaesthesia.

An *ab initio* scale of responses reflecting consciousness as a graded phenomenon

A binary view of anaesthesia was presented by Prys-Roberts,²⁵ who argued that there cannot be degrees of anaesthesia or variable depths of anaesthesia. More recently, Sleight²⁶ opined that ‘the [anaesthetized] patient is not like a submarine’. Sleight was alluding to the possibility (or fact) that there is greater complexity to anaesthetic drug effects than merely descending or ascending in a ‘linear’ manner. There is little argument that in an EEG, burst suppression represents a ‘deeper’ form of anaesthesia than slow-wave activity. Furthermore, some brain functions contributing to consciousness may have inertia in their responses with respect to dose, such that transitions from one state to another are not apparent and come across as binary at a phenotypic level. It is already very well established in clinical practice and neuroscience that consciousness and unconsciousness can be graded phenomena. Certainly, there is some point in severe brain injury or anaesthesia when there is complete mental oblivion, but before

that point is reached, the patient may appear to be in a mental state of oblivion but in fact may not be.

In relation to brain pathology, the GCS is used to reflect the principle that a patient's response to a stimulus or command can be used to reflect the degree of underlying mental and neurological capabilities.⁷ Thus, patients who are 'unconscious' in fact encompass a range of GCS scores. Likewise, an anaesthetized patient can be viewed as having disrupted or changed neurological and mental capability induced by the drugs (the very purpose of anaesthetic agents is to alter or disrupt mental state). The IFT offers the opportunity for responses to be assessed, and these, suitably graded, could be used to quantify the degree of impairment in more than a binary way. Perhaps Wilson²⁷ was among the first to recognize that a 'response' during IFT is not a singular or binary entity and could be graded. He identified from careful observation at least three types of IFT response: no response, movement with tactile stimulus (e.g. intubation or surgery), and movement to verbal command (which can then be supplemented with choice or conditional logic 'if . . . then' questions).²⁷

Wilson's ideas were never developed or adopted, but Table 1 is an extension of his logic to a more complete range of five possible responses. Purely designed from first principles (*ab initio*), it does not presuppose or represent any underlying neuroscientific model, nor is it based on any existing experimental evidence. The scale is proposed merely as a working hypothesis.

The possible responses in the scale are ordered *a priori* to reflect logical ascending stages of conscious abilities. At the highest level, the patient is able to initiate movement, without prompting, which is judged by the observer to be an attempt to communicate. We might expect a patient to respond in this way after accidental injection of NMB before anaesthetic. Progressive impairments of consciousness in turn limit the patient to responding only to verbal command, only to tactile or painful stimuli, or to making random, reflex-type movements unrelated to stimulation. At Level 0, there is no response or movement. This proposed scale could be applied to a group of patients under study or to the same patient over time during the course of an anaesthetic, as their conscious level may fluctuate. The underlying assumption inherent in this scale is that, like the GCS, the degree and type of motor response can, at least in part, reflect the underlying mental state.


At what level on the isolated forearm technique scale do patients generally show responses?

It is apposite next to consider the types of responses or movements according to this scale observed when the IFT is used. This might provide insight into the effects of anaesthesia on underlying mental state. Ideally, a large, prospective observational trial of many hundreds of IFT patients might provide the best evidence, but this is not available. The IFT is rarely used in practice. The NAP5 Baseline^{28 29} and Activity Surveys^{11 30} established that merely 14 senior anaesthetists in the UK use it with any regularity (~0.03% of all general anaesthetics), while it is not used at all in Ireland.

Instead, for the purposes of this article, I applied the scale retrospectively to describe the results of published studies based on a literature review. The words 'isolated forearm technique', 'IFT', 'depth of anaesthesia monitoring', 'anaesthesia depth', 'memory', 'anaesthesia wakefulness', and 'anaesthesia awareness', separately and in combinations, were used as search terms in PubMed. The publications of authors of retrieved papers were searched in turn. Papers were accepted if they used the IFT during anaesthesia and stated a denominator number of patients and a numerator for patients responding or not to command. Letters, abstracts, and full papers were potentially included where they offered numerator and denominator data and a clear description of IFT responses. Papers were excluded if not in English (none were found), or where IFT was used solely to monitor emergence from anaesthesia (when, of course, it can be expected that all patients would test positive). Where verbal command was issued repeatedly and different proportions of patients responded over the time course of anaesthesia, the highest proportion quoted was used. Some older studies used anaesthesia techniques no longer commonly used. Nevertheless, these data were included as being techniques acceptable at the time, and a sensitivity analysis was conducted to assess any change in trends over time.

There were a total of 116 papers initially retrieved, of which 57 were excluded because they did not use IFT (e.g. the search method yielded several orthopaedic publications where the forearm vasculature was occluded for surgery). Of the 59 remaining papers, 28 were excluded because they did not meet the criteria listed above or were correspondence items about papers that were

Table 1 Isolated forearm technique response scale proposed by Pandit. An *ab initio* scale; the types of movement response are shown that might indicate levels of intellectual and mental capacity in a patient with unimpaired motor capacity in the muscle groups or limb(s) used to communicate the responses

| | | |
|---|-----------------------------------|---|
|  | Increasing level of consciousness | Level 0 |
| | | No response or spontaneous movement |
| | | Level 1 |
| | | Random, spontaneous movement, not associated with any stimulus, where the movement does not localize a stimulus; difficult to identify as a meaningful attempt at communication and is possibly even a reflex |
| | | Level 2 |
| | | Movement in response to tactile stimulus, including painful stimulus (2a, non-localizing movement; 2b, movement that localizes the stimulus) |
| | | Level 3 |
| | | Movement response to direct verbal commands (e.g. 'squeeze hand', 'move your fingers') |
| | | Level 4 |
| | | Movement response to choice questions or conversation (e.g. 'Do you want to be more/less asleep?', 'Are you comfortable?') |
| | | Level 5 |
| | | Spontaneous, purposeful movement initiated by the patient that indicates a desire to communicate; associated with Level 3 or 4 responses when the appropriate questions are asked (e.g. waving arm or hand to indicate distress or seek attention to initiate questioning as above) |

included. This left 31 papers suitable for analysis, and from these,^{31–61} the number of patients responding was extracted, and response type was classified according to the IFT scale in Table 1.

There were limitations of this retrospective approach. Original studies were undertaken for a variety of different reasons, using a range of techniques. Anaesthesia was not standardized, and clearly, involved very different 'depths of anaesthesia'. The administration of IFT was not standardized. For example, while the majority of studies regarded as positive any response to command, Schultetus and colleagues³⁷ required the patient to squeeze the experimenter's hand twice (and did not report how many patients responded only once, whom they regarded as negative). Millar and Watkinson³⁴ simply played an audio tape to patients through closed headphones and did not speak directly with them, so they were only able to observe hand movement if it occurred and could not clearly determine whether this was contiguous with a command through the headphones. They also included a 'control' group who received only white noise via the headphones; these patients exhibited movement to 'white noise command' at a rate similar to those receiving genuine commands (35%). This suggested that the responses marked as Level

3 in the test group according to the IFT scale may, in fact, have been Level 1 or 2. The description of IFT responses in the published papers often lack detail. A striking example of this was the (excluded) study of Breckenridge and Aitkenhead.⁶² Published only as an abstract, it was impossible to determine from the description how many patients responded, let alone at what likely level of response. In other articles, quantification of Level 4 responses proved especially difficult, because some articles stated that they presented patients with choice or conditional logic questions (e.g. 'if you are comfortable, then squeeze . . .'), but then did not go on to state how many patients responded to the choice, or if so, whether to express satisfaction or dissatisfaction.

Given these limitations, this analysis is not designed robustly to test a given hypothesis in relation to IFT. Rather, it illustrates the range of IFT responses that might be obtained when general anaesthesia is intended. Nevertheless, it is clear from Table 2 that the range of responses is not binary. About half of all patients (the majority) exhibited no response, Level 0. Where there was a response, the commonest form was response to an instruction to squeeze the hand, Level 3 (32%). Incidentally, a previous smaller review analysing only 13 IFT trials reported a similar proportion.⁶³

Table 2 Types of responses (Table 1 scale) during isolated forearm technique recorded during trials. Studies are identified by first author and reference. The total (third column) refers to the total number of patients subjected to the isolated forearm technique, regardless of how many subgroups there may have been in the trials being compared. Level 4 responses are shown (8th column; no Level 5 responses were identified), where patients clearly responded to confirm either they were or were not in pain. The last column shows the number of patients exhibiting postoperative recall, usually on direct questioning. The percentages in the last row do not sum to 100% because within trials some patients exhibited more than one level of response at different times. * This was a single patient who wished to remain in her Level 3 state during Caesarean section and exhibited a Level 4 response; † in children; ‡ as a percentage of total n; ¶ as a percentage of Level 3 n; § as a percentage of Level 3 n

| Paper | Year | Total n | Level 0 n | Level 1 n | Level 2 n | Level 3 n | Level 4 n | Postoperative recall n |
|-----------------------------|------|----------|-----------|-----------|-----------|-----------|-----------|------------------------|
| Tunstall ³¹ | 1979 | 32 | 1 | 0 | 31 | 23 | 1 | 0 |
| Tunstall ^{32*} | 1980 | 1 | 0 | 0 | 0 | 1 | 1 | 1 |
| Wilson ³³ | 1980 | 40 | 1 | 0 | 25 | 14 | 7 | 0 |
| Millar ³⁴ | 1983 | 27 | 8 | 15 | 9 | 9 | 0 | 0 |
| Russell ³⁵ | 1985 | 23 | 5 | 0 | 18 | 11 | 0 | 1 |
| Russell ³⁶ | 1986 | 55 | 24 | 16 | 15 | 13 | 0 | 0 |
| Schultetus ³⁷ | 1986 | 36 | 13 | 0 | 17 | 12 | 0 | 3 |
| Watanabe ³⁸ | 1988 | 10 | 2 | 0 | 0 | 8 | 0 | 0 |
| Tunstall ³⁹ | 1989 | 113 | 49 | 17 | 0 | 47 | 0 | 0 |
| Thornton ⁴⁰ | 1989 | 7 | 1 | 2 | 0 | 4 | 0 | 0 |
| Baraka ⁴¹ | 1989 | 50 | 0 | 0 | 0 | 18 | 0 | 2 |
| Baraka ⁴² | 1990 | 20 | 17 | 0 | 0 | 3 | 0 | 0 |
| Bogod ⁴³ | 1990 | 74 | 15 | 30 | 0 | 29 | 0 | 0 |
| King ⁴⁴ | 1993 | 30 | 1 | 0 | 0 | 29 | 24 | 0 |
| Russell ⁴⁵ | 1993 | 33 | 4 | 5 | 0 | 28 | 20 | 3 |
| Gaitini ⁴⁶ | 1995 | 50 | 29 | 3 | 0 | 18 | 0 | 0 |
| Byers ^{47†} | 1997 | 41 | 33 | 0 | 0 | 8 | 0 | 0 |
| Russell ⁴⁸ | 1997 | 68 | 58 | 10 | 0 | 0 | 0 | 1 |
| St Pierre ⁴⁹ | 2000 | 30 | 13 | 0 | 0 | 17 | 0 | 1 |
| Russell ⁵⁰ | 2001 | 40 | 33 | 0 | 0 | 7 | 1 | 0 |
| Kerssens ⁵¹ | 2002 | 56 | 15 | 4 | 0 | 37 | 0 | 8 |
| Schneider ⁵² | 2002 | 20 | 12 | 0 | 0 | 8 | 0 | 0 |
| Slavov ⁵³ | 2002 | 41 | 31 | 0 | 10 | 0 | 0 | 0 |
| Ge ⁵⁴ | 2003 | 14 | 14 | 0 | 0 | 0 | 0 | 0 |
| Russell ⁵⁵ | 2006 | 12 | 0 | 0 | 0 | 12 | 0 | 3 |
| Kocaman Akbay ⁵⁶ | 2007 | 51 | 42 | 0 | 2 | 7 | 0 | 0 |
| Andrade ^{57†} | 2008 | 184 | 181 | 1 | 0 | 2 | 0 | 0 |
| Linstedt ⁵⁸ | 2012 | 67 | 6 | 31 | 18 | 12 | 0 | 0 |
| Russell ⁵⁹ | 2013 | 34 | 23 | 0 | 0 | 11 | 0 | 0 |
| Russell ⁶⁰ | 2013 | 22 | 8 | 0 | 0 | 16 | 0 | 2 |
| Zand ⁶¹ | 2014 | 61 | 24 | 7 | 0 | 30 | 0 | 0 |
| Total | | 1342 (–) | 663 (49%) | 141 (11%) | 145 (11%) | 434 (32%) | 54§ (12%) | 25 (2%‡; 6%¶) |

A minority (12%) of patients were documented additionally to provide coherent responses to choice questions relating to their comfort (Level 4). Generally, these patients indicated dissatisfaction or pain (47/54; 87%). However, as the trial protocols of many studies appeared reasonably to require that anaesthesia was promptly deepened on obtaining a Level 3 response, before any further questioning was posed, the true number of potential Level 4 responders (and those in pain or distress) may have been higher.

Responses confined to a motor response to stimulus such as laryngoscopy or surgery (Level 2) did occur, but rarely (in only 11% of patients; i.e. these did not exhibit Level 3 responses or higher). A similar proportion showed only spontaneous movement not regarded as relating to stimulation or communicating awareness, Level 1. Notably, in none of these trials did the anaesthetist feel the patient was spontaneously and volitionally using their isolated forearm movements to initiate communication and signify that they were awake (i.e. Level 5 responses were absent). The one possible exception is a patient, described in detail by Tunstall in 1980,³¹ who awoke unexpectedly during her Caesarean section but then chose to remain awake, seemingly engaging in a 'conversation'.

It might be anticipated that the increasing Levels of IFT response are related to the prevailing anaesthetic concentration, such that increasing concentration should smoothly change the Level from 5 to 0. This is not quite the case. The two commonest responses are none (Level 0), or response to command only (Level 3); other types are relatively uncommon (Fig. 1A). This suggests the following two possibilities (which are not mutually exclusive): (i) a highly specific effect of anaesthetic on the brain that produces certain mental states (i.e. those associated with Level 0 and 3 responses) more than others; and (ii) that the proposed IFT scale is non-linear with respect to anaesthetic effect on mental functions (Fig. 1B).

Figure 2A shows that there is no effect of year of publication on the rate of Level 3-positive IFT responses. Thus, although some of the older studies used anaesthetic techniques that could now be criticised as failing adequately to prevent AAGA, this does not seem to affect overall IFT response rate. Study size yields a statistically significant relationship (Fig. 1B), but the small magnitude of r^2 (0.19) suggests a trivial influence.

The high incidence of Level 3-positive motor response (32%) must be viewed as surprisingly high; however, the rate of explicit recall was low (2% of all studied patients; 6% of Level 3-positive patients). This may be because anaesthesia was often promptly deepened, before the experience became imprinted in explicit memory, or because patients are experiencing amnesic concentrations of anaesthetic drugs during the commands. Regardless, when recall was present it was largely confined to vague memory of the verbal command (in 18 of the 25 patients, 72%); recall of other events directly related to surgery or anaesthesia was rare.

Table 3 summarizes some insightful comments made by patients at the time of IFT responsiveness. The striking aspect of this qualitative reporting is the sense of neutrality or even detachment conveyed ('floating dispassionately', 'closed in and awkward', 'trouble understanding it was about me', and 'searching for body'). Extreme distress or alarm is generally absent, although there seems some sense of concern expressed by patients who realize they are not in their 'normal' awake mental state.

This qualitative aspect of patient reports after IFT is also characterized in many of the vignettes reported in NAP5.^{9,10} Although NAP5 did not use IFT, about half of the total number of AAGA reports were expressed in neutral ways by patients. Similar phrases arose in the neutral NAP5 cases as in Table 3, which convey the same sense of detachment, albeit with a similar level of realization that this was not a normal mental state: 'I was floating', 'I felt alive only in my head', 'in the back of my mind, I thought I could

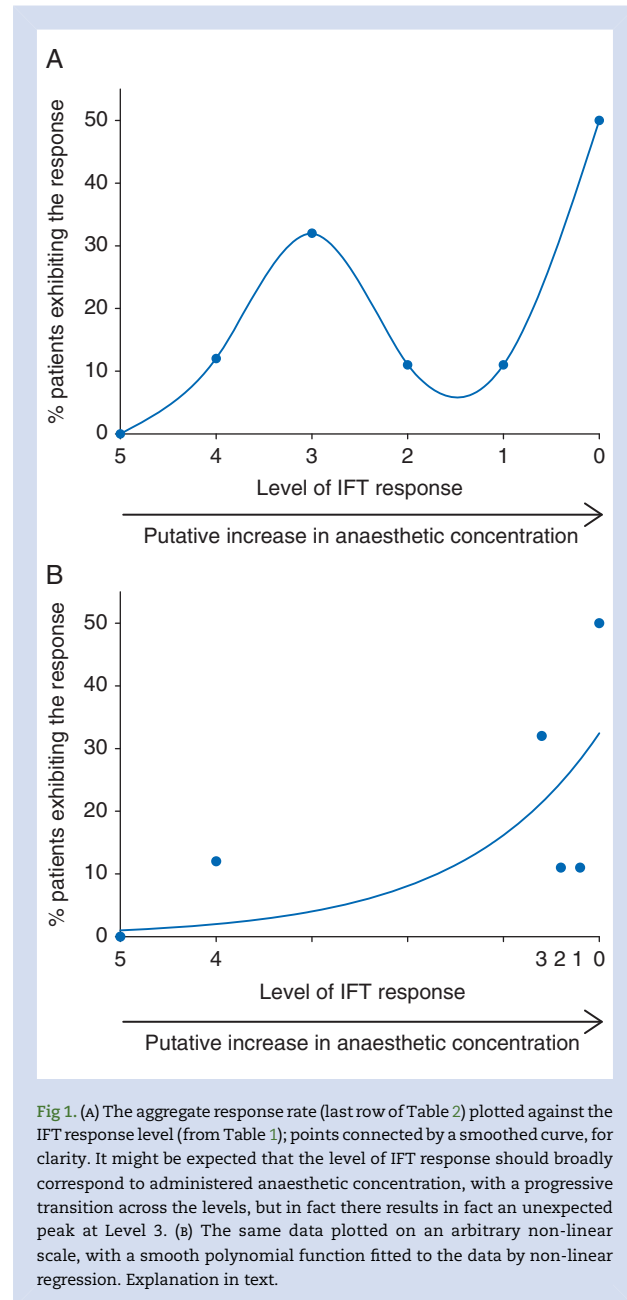


Fig 1. (A) The aggregate response rate (last row of Table 2) plotted against the IFT response level (from Table 1); points connected by a smoothed curve, for clarity. It might be expected that the level of IFT response should broadly correspond to administered anaesthetic concentration, with a progressive transition across the levels, but in fact there results in fact an unexpected peak at Level 3. (B) The same data plotted on an arbitrary non-linear scale, with a smooth polynomial function fitted to the data by non-linear regression. Explanation in text.

feel the surgery', 'it was like I dreamed the whole operation', 'I dreamt I was having surgery, which was nice', 'I had a vision of hanging upside down and people talking', 'I heard distant voices but gave it no serious thought', and 'I heard staff talking and was frustrated I was not asleep'.

Two key questions

We learn little or nothing about anaesthetic mechanisms or the nature of consciousness from those patients who do not respond or who recall nothing. We learn much more from the fewer who respond or have some recall, because these patients provide information for analysis. This is not to suggest that memory and recall are the same as 'consciousness' but merely to acknowledge that our methodologies rely heavily upon there being a patient story to discuss.

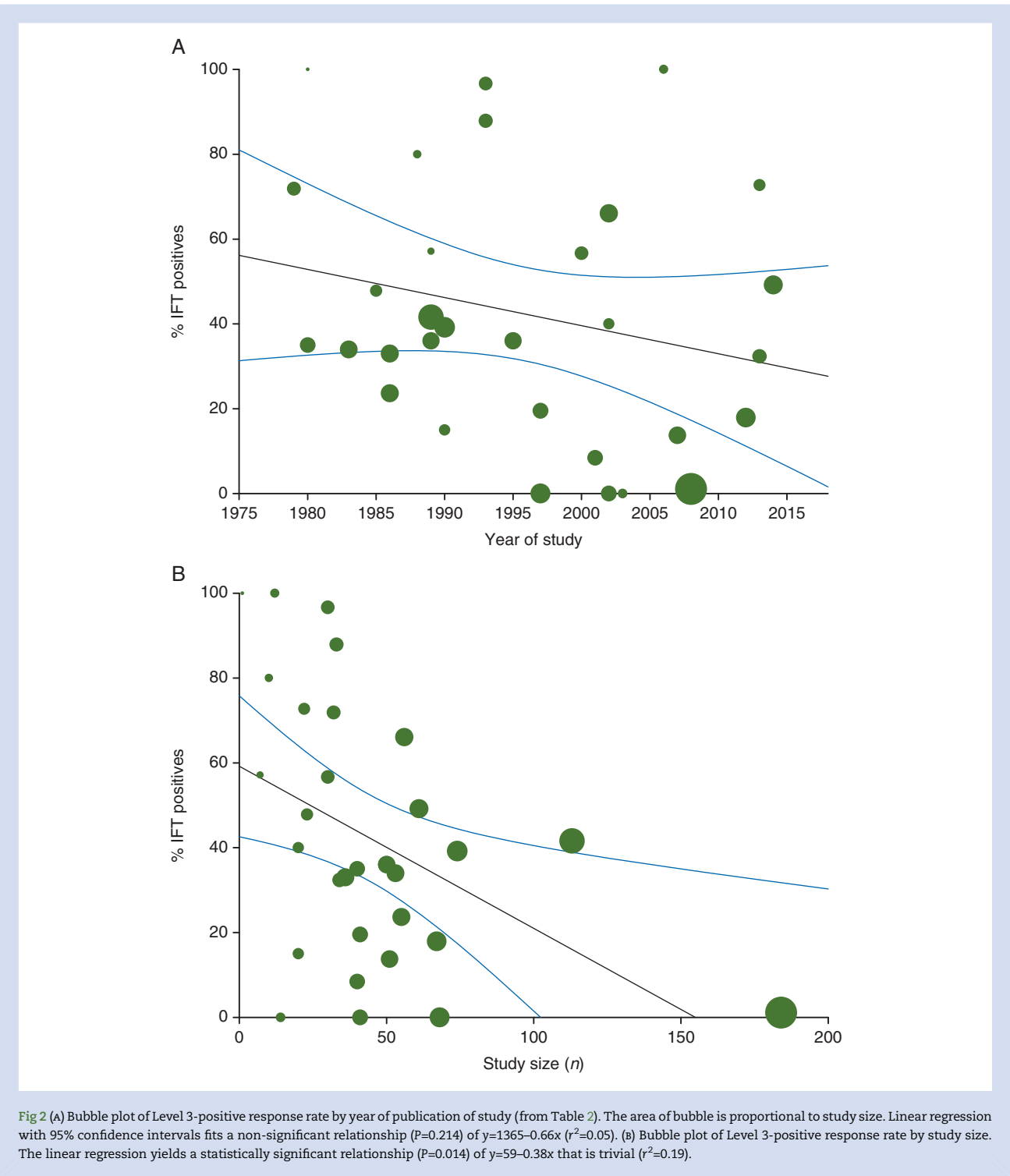


Fig 2 (A) Bubble plot of Level 3-positive response rate by year of publication of study (from Table 2). The area of bubble is proportional to study size. Linear regression with 95% confidence intervals fits a non-significant relationship ($P=0.214$) of $y=1365-0.66x$ ($r^2=0.05$). (B) Bubble plot of Level 3-positive response rate by study size. The linear regression yields a statistically significant relationship ($P=0.014$) of $y=59-0.38x$ that is trivial ($r^2=0.19$).

Having established the nature of the range of IFT responses (Table 2), my argument now rests upon resolving two key questions:

1. Why is there such a striking disparity between the rate of Level 3 (32%) and Level 2 (11%) or Level 5 (0%) responses? In other words, why do so few patients respond spontaneously if aware of the surgery but so many respond to a direct command to move?

2. On the few occasions that Level 3-positive patients have recall, why do so few recall the surgery (8%) but so many recall the command to move (72%)?

A conventional response to the first question, articulated by Russell and Wang^{17 24} previously and below, is that patients are comfortable and have no reason to move spontaneously during surgery even if they awaken. I am surprised by this view. Certainly, analgesia is an aim of the anaesthetic technique, and given

Table 3 Salient patient reports from the trials in Table 2 (and two other sources that later commented on these trials) of descriptions of recall. Many patient reports (not listed here) simply recalled the anaesthetist giving the command to move. Only one patient of the 25 who were recall positive in Table 2 (other than the patient listed below) vaguely remembered the surgery

Russell³⁵

- Patient reported that she ‘floated dispassionately up in the air viewing herself below, all alone on earth, frightened, and with no one to talk to’.

Russell and Wang⁴⁸

- Patient 1: aware of someone opening her eyelid and the anaesthetist’s command very soothing; also a buzzing noise.

Kerssens and colleagues⁵¹

- Patient 1: ‘[I heard] my name [and being asked to] squeeze my hand. I wanted to talk but couldn’t. I wasn’t afraid but felt closed in and a little awkward.’
- Patient 2: ‘[I heard] my name [and being asked to] squeeze hand. I had trouble to understand it was about me . . . I tried to respond but was not sure whether I succeeded. It felt all right’
- Patient 3: ‘[I heard being asked to] squeeze hand. No sense that I squeezed but understood that I succeeded. Not frightened.’
- Patient 4: ‘You called out but I couldn’t respond. I wanted to, but my arm didn’t go. Later I sensed that it moved and then I fell asleep.’

Russell⁵⁵

- Patient 1: ‘This is [the anaesthetist] speaking . . . remembers some pain in her abdomen at this time but does not know when/where this was . . .’

Russell¹⁷

- ‘[The patient] described searching for their body when given the command to move’

that analgesics are very powerful, patients may not feel pain. I therefore agree that pain should probably be discounted as a common trigger for movement. However, when patients are informed that they will undergo general anaesthesia and give consent for it, they naturally expect to be unconscious. If, during surgery, the patient becomes unexpectedly conscious, then I would anticipate that they would use any motor capacity they possess (e.g. as provided by IFT) to signify their new-found awareness (regardless of analgesia). That they generally do not do this, to my mind, warrants a specific explanation not involving lack of pain. Furthermore, I find relevant the reported feelings of ‘searching for their bodies’ or ‘floating’, etc.

Another explanation for the disparity offered by Russell and Wang is a technical one. They argue that verbal command is provided too frequently to allow detection of a spontaneous response. Therefore, any movement that occurs is probably always in temporal association with a command. This may well be true of the experiments conducted by them. However, the majority of IFT studies (20 of 31) were undertaken by researchers other than Russell, Wang and Tunstall (11 of 31), and it is clear that in these studies there was plenty of time for patients to demonstrate spontaneous movement in between commands; hence, I do not believe that the technical argument explains the disparity.

I propose an alternative explanation for these two questions and seek to frame this explanation in the context of some wider theories. In doing so, I refer to a novel and specific idea of the nature of consciousness, as it is relevant to anaesthesia, presented elsewhere.^{64 65}

Sensory–perceptual uncoupling: dysanaesthesia

I have previously presented a model that exploits many of the established ingredients of the nature of consciousness that are consistent with neuroscientific and philosophical consensus. In brief, the model first outlines those elements of consciousness that are uncontentious. Then, it proposes that the loss of consciousness induced by general anaesthesia is a disruption of these essential ingredients, in whole or in part. These uncontentious requirements for consciousness can be summarized as follows:

1. all senses are relevant inputs into the system (e.g. touch, hearing, vision, pain, and temperature) and contribute to the conscious state. The more sensations that are lost, the greater is the potential for consciousness to be altered or reduced.⁶⁶ This is not say that a person suddenly struck blind is in a reduced conscious state. Rather, it is to acknowledge that increasing sensory deprivation makes it more likely that a reduced conscious state will result.^{66 67}
2. specific to each sensation is an important step (translation) of the sensory input into a perceptual experience. The difference between ‘sensation’ and ‘perception’ is readily accepted philosophically as ‘qualia’,^{68 69} and in neuroscience when distinguishing ‘nociception’ from ‘pain’,⁷⁰ or in the visual sciences when experimenting with optical illusions.⁷¹ Uncoupling perception from sensation can, in the widest sense, disrupt consciousness, in the same way as uncoupling pain from nociception is a proposed analgesic therapy.⁷⁰
3. all the perceptual experiences at any given time are bound into a single, coherent, indivisible experience.⁷² Walking in a park is experienced as a holistic event and not a constellation of separate experiences that require effort to combine. The more this binding is disrupted, the greater is the potential for conscious level to be reduced.

Note that none of these steps alone is key; each only makes its contribution to the conscious state. Within this scheme, consciousness can theoretically be impaired by several manipulations, as follows:

1. obtunding the sensations (e.g. by analgesia or locoregional anaesthesia), which impairs the associated perceptions. Sensations that are not obtunded persist, along with their associated perceptions.
2. uncoupling perceptions from sensations, predicted to result in a neutral, emotionally detached, bland experience of the sensation(s) uncoupled.
3. unbinding the perceptual experiences, resulting in a fragmented experience, where different sensations and perceptions normally matched become disintegrated.

Thus, each of these steps, perhaps achieved using different drug combinations, will impair consciousness in specific and graded ways, and not in the manner of an all-or-nothing 'switch'. Of these steps, I have proposed the term 'dysanaesthesia' to describe the step of uncoupling of perception from sensation,^{64 65} characterized by a sense of emotional detachment from the surroundings.

Consequently, I argue that patients in this state have no motivation spontaneously to respond to the events of surgery, even when they retain motor capacity to do so; IFT reveals this state. When sensations persist in the absence of perceptions, patients are merely technically or neutrally aware of events. Amnesia for some or all events of surgery arises because these neutral, emotionally bland experiences do not command attention and are therefore less likely to be recalled compared with events that evoked a strong emotional response. The link between explicit memory and attention is well established.^{5 73}

Accordingly, a patient in a dysanaesthetic state would retain the ability to respond by movement to a verbal command during IFT, but in an automatic way (Level 3 response), akin to jumping when hearing a noise or the 'cocktail party' effect on hearing one's name. The auditory sensory pathway is intact, and words—especially simple instructions—can be understood in this mental state (and patients may have been primed by preoperative instructions). The tactile or auditory sensations from surgery (regardless of pain or nociception) are also transmitted as sensory information to the brain, but in contrast are not perceived with emotional content. These tactile and auditory sensations provide no specific instruction to move, whereas the verbal directive is a specific personal instruction and therefore results in a higher level of attention. This could explain why the verbal command is: (i) more likely to evoke a response than is surgical stimulation or awareness of surroundings; and (ii) more likely to be recalled later than is the surgery. Even then, recall of instructions is commonly described in a detached or distant way ('I did not know it was about me', 'I searched for my body', etc.; Table 3). It is natural that those patients who remember might find this dysanaesthetic state uneasy (using terminology such as 'awkward' or 'alive only in my head'; Table 3). However, this sense of unease is not sufficient to compel them to move the unparalysed arm spontaneously to attract attention. In some respects, this is similar to patient reports after neurolept anaesthesia (droperidol or fentanyl only).⁷⁴

The dysanaesthesia hypothesis also explains IFT patients' response to choice questioning ('if in pain, then . . .') and why some patients indicate in response to the choice that they are uncomfortable, although they did not move spontaneously to indicate this in advance of questioning. Patients are, in fact, probably not in 'pain' (a perception), so they do not spontaneously alert the anaesthetist (i.e. Level 5 IFT responses are absent) and there is no imprinting of painful memory. However, nociceptive input (the sensation) may remain intact and can be recognized as such. Therefore, if directly asked during surgery, 'Are you in pain?', patients may be triggered to 'search their sensations' and recognize some inputs as nociceptive. They therefore make a truthful Level 4 IFT response to the question but, lacking emotional content, it is not something that appears to have adverse consequences.

In these ways, sensory-perceptual uncoupling (dysanaesthesia) provides an explanation for all aspects of the IFT response patterns. Initially proposed as a macroscopic model with no basis in neurophysiological pathways, the concept has received support from recent brain imaging work that has identified such an uncoupling is possible. Ní Mhuirheartaigh and

colleagues⁷⁵ described an experiment using very slow induction of anaesthesia with propofol, with simultaneous functional magnetic resonance imaging and EEG recordings. They identified a state associated with loss of responsiveness when the thalamocortical network became isolated from sensory stimuli.

Summary of Pandit's argument

In summary, I propose an *ab initio* scale of responses observable in IFT patients. A strikingly high proportion of IFT patients exhibit a positive response to a direct instruction to move. Equally striking is the fact that spontaneous movement is relatively uncommon; this disparity of incidence of responses requires explanation. Also uncommon is a recall for events. Strikingly, where there is recall it is focused on the verbal command rather than on the surgery itself. This disparity also requires explanation. Many patient descriptions use phraseology that indicates a sense of neutrality and detachment.

I propose that IFT has revealed, through the range of specific response types it elicits, a highly graded range of conscious levels that can arise during otherwise apparently satisfactory clinical anaesthesia. Some of these are compatible with surgery, at least in the superficial sense that although patients demonstrate responses (Level 3 and 4) they do not suffer adverse consequences. Figure 3 illustrates the proposed relationships between anaesthetic concentration, IFT responses, and mental states. I have proposed elsewhere a macroscopic model that explains these observations and that has some neurophysiological basis in recent experimental observations. Although this model challenges a conventional notion that all IFT-positive patients are 'conscious' in a binary (awake or asleep) sense, it does not challenge the notion that the IFT remains a clinically useful technique. The IFT can clearly identify patients who are fully conscious and awake (i.e. those exhibiting Level 4 and 5 responses). The IFT can also reliably confirm that a patient is fully anaesthetized (Level 0 response). Pragmatically, whenever any IFT movement response is obtained, it is wise to assume that this reflects a risk of inadequate level of unconsciousness and, along with verbal reassurance, the anaesthesia, analgesia, or both should be increased.

Finally, the IFT reveals subtle states of mind that could provide insights into how anaesthetics act on the brain.

Russell and Wang: isolated forearm technique responses are unambiguous and best interpreted as binary

Just as Pandit accepts the potential utility of the IFT in clinical practice, we also accept the broad proposition that there are levels of consciousness and that general anaesthesia is not an all-or-nothing phenomenon. In contrast to Pandit, however, we view the IFT primarily as a practical tool for monitoring depth of anaesthesia, hence, as an aid to clinical decision-making. Furthermore, in our view the IFT is the only direct measure of consciousness available to the anaesthetist when using NMB. The response to choice or conditional logic questioning is a precise reflection of the state of mind such that we learn what the patient feels or desires. In contrast, the EEG may be a direct measure of brain electrical activity, but that is one or more levels removed from the state of mind (so at best, indirect).

Whilst it is interesting to speculate about the nature of consciousness, we think that what the anaesthetist primarily needs help with is the answer to a simple binary question: 'is my patient adequately anaesthetized'? We argue that if a

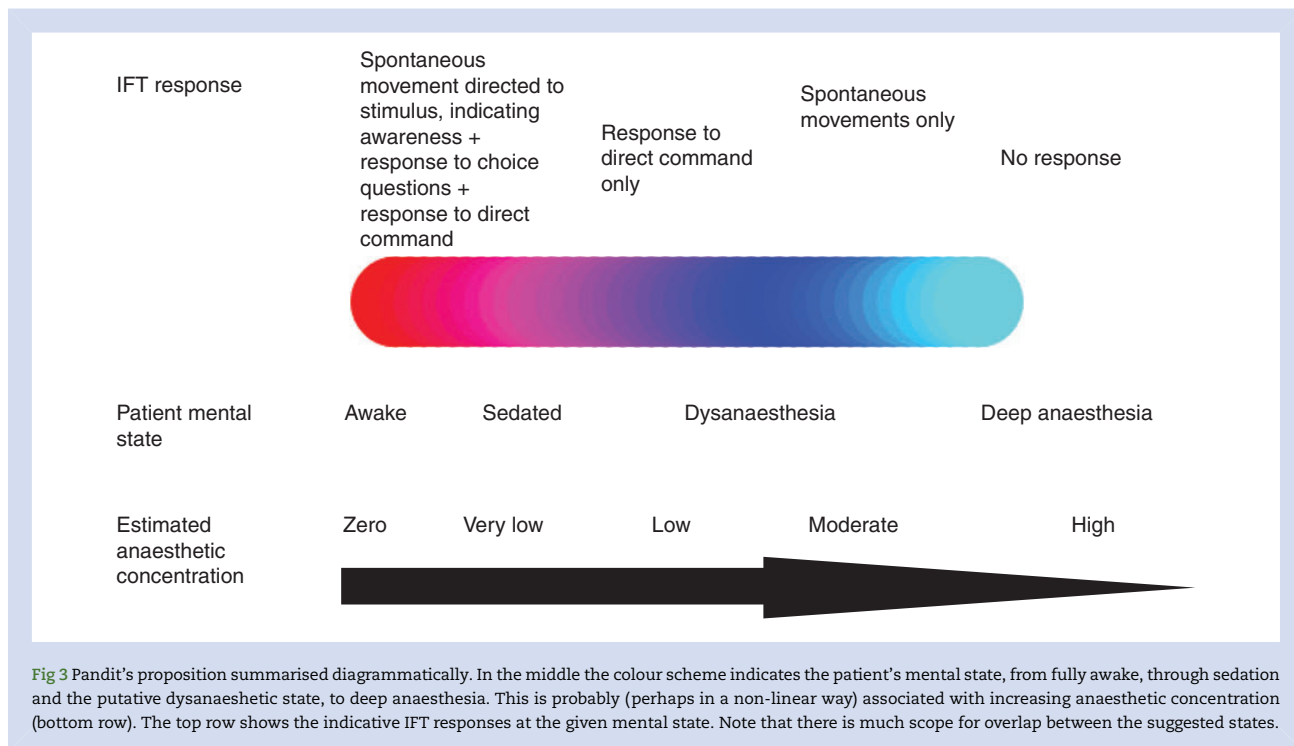


Fig 3 Pandit's proposition summarised diagrammatically. In the middle the colour scheme indicates the patient's mental state, from fully awake, through sedation and the putative dysanaesthetic state, to deep anaesthesia. This is probably (perhaps in a non-linear way) associated with increasing anaesthetic concentration (bottom row). The top row shows the indicative IFT responses at the given mental state. Note that there is much scope for overlap between the suggested states.

patient is able to respond to command, as revealed by the IFT, then the answer is that they are not adequately anaesthetized, and more anaesthetic should be administered. We do not believe that practising anaesthetists (or their patients) are generally concerned about sophisticated models of consciousness; they simply want to know when to deepen (or possibly lighten) the anaesthetic. A discussion about models of consciousness might have a place somewhere, but not in the realm of clinical practice. We address our rebuttal in two parts: first, a critique of Pandit's analysis of IFT studies; and second, a critique of his hypothesis of dysanaesthesia.

Critique of Pandit's analysis of isolated forearm technique studies

One stated justification for developing an *ab initio* scale for measuring IFT responses is that scales such as the GCS⁷ have established the general principle of relating patient responsiveness to underlying neurological state. It is not clear to us that such other scales are relevant guides or even that pathological coma is akin to 'unconsciousness' in the sense used in relation to anaesthesia, which we think a unique state. Rather, the GCS assesses whether or not there is any response (if not then there is complete unconsciousness), and if there is a response then there is a condition of something less than unconsciousness (e.g. severe functional impairment, which may not preclude some consciousness). In NAP5, for example, there were several instances of patients reporting AAGA who had suffered cardiac arrest and had relatively low GCS at the time, and also patients who had episodes of AAGA whilst in critical care, with life-threatening illnesses including neurological impairment or head injury.^{9,10} It is therefore entirely possible to be assigned a very low GCS yet be sufficiently conscious later to report AAGA.

Pandit suggests it was Wilson²⁷ who first proposed there was more than one response type with IFT, but in fact this was implicit in one of Tunstall's³¹ early papers. We previously proposed a

scale extending Wilson's and simpler than that in Table 1, which in contrast to Pandit, does not imply a given mental state underlying each response.⁷⁶ In our scheme, Grade 0 (no movement) and Grade 1 (spontaneous movement not contingent on command) are similar to Pandit's. Our Grade 2 indicates a response to a simple instruction (but not conditional command) or response where full instructions are not followed (e.g. squeezing once and not twice). Our Grade 3 is a response to conditional questioning.⁷⁶ Thus, the higher the level of response, the more brain mechanisms are 'engaged'. Pandit was unaware of this scale because it appeared only in conference proceedings.⁷⁶ We suggested that any response in our scale indicates 'consciousness' because in a dynamic situation even a putatively 'reflex' response should be viewed seriously and every effort made to question the patient to exclude higher grades of response. In contrast to Pandit (Table 1), we are not persuaded that someone responding only to tactile stimulus is necessarily in a lesser state of consciousness than someone responding only to verbal stimulus. However, our limited IFT literature review in that chapter broadly agrees with Pandit's estimate of the proportion of patients responding.⁷⁶

Thus, in our view, hand movement contingent on command during IFT should be a signal to the anaesthetist to: (i) reassure the patient by talking to them; and (ii) increase the anaesthetic dose.

We agree with the limitations and uncertainties he offers in relation to his analysis of trials, but we would go further and suggest that Pandit has 'read too much' into the evidence. It is reasonable to attempt to learn something from the rather disparate literature, and Table 2 offers a useful and comprehensive database. However, the evidence is not sufficiently strong to allow any general conclusions. To distinguish between the response categories that Pandit presents in Table 1 would require that all patients who made a 'random' movement were questioned promptly to exclude a Level 3 (his scale) response. This is not always possible, and careful reading of the primary literature shows that this simply did not happen. Thus, Table 1 presents a rather artificial scale; if applied prospectively, we feel there

would be some ethical dilemma created by using it in full measure. For example, unless pain was inflicted, how would one know that a Level 2 or 5 response (Table 1 scale) had been excluded?

Pandit's interpretation of the IFT responses rests largely upon the fact that spontaneous IFT movement (interpreted to alert the experimenter that the patient is awake, Level 5) is rarely if ever observed. However, we feel this information (absence of such movement) cannot be gleaned from the studies reviewed because such a category of response was not always recorded or included. Historically, the Breckenridge and Aitkenhead⁶² abstract was arguably the single most influential publication on IFT in its day and probably did most to curtail the clinical use of IFT. We agree that the article was flawed; Pandit excludes it from analysis. Nevertheless, they clearly describe spontaneous movement in which patients repeatedly attempted to remove the surgeon from the operative field! Breckenridge and Aitkenhead regarded this as good reason to dismiss the IFT as a viable technique, perhaps because these patients did not technically 'respond' to a verbal command (although in the circumstances this aspect seemed irrelevant). In contrast to Pandit, we feel this is strong evidence of a Level 5 response.

Furthermore, in his finding of a zero incidence of a Level 5 response, Pandit fails to take account of the circumstances of those trials in which a tape is running continuously with repetition of commands every minute and the voice of the anaesthetist saying 'if you can hear my voice, open and close your fingers'. We do not believe that in this situation a patient would be motivated to do anything else spontaneously unless they were in pain or acute distress (and we know this is rarely the case because of effective analgesia). Our expectation is that the patient is hearing the voice of the anaesthetist talking to them as if they are conscious, so would not think it necessary to alert the anaesthetist to their conscious state other than to respond as requested.

The state of mind envisaged by Pandit that, in his view, should motivate spontaneous IFT movement also involves anxiety. Indeed, anxiety is described by many patients who have experienced AAGA; its potential cause is concern that something has gone wrong and that they must alert the theatre staff. Normally, we agree that this might cause the patient to try to move, but a response to command with IFT is not the same as AAGA, and hearing the anaesthetist's voice directly speaking to them in the former instance will, we think, allay all such worries and there will be no spontaneous movement. The general lack of anxiety after IFT is confirmed at interviews after the operation.

Our experience in conducting many IFT trials leads us to argue that Pandit's analysis as summarized in Table 2 is presented more in hope than in expectation. Thus, he includes Millar and Watkinson,³⁴ but in our view it is very difficult to conclude anything from that paper. Certainly, about one-third of their patients responded to command (included as Level 3 responses in Table 2), but Millar and Watkinson³⁴ also included a control group who were played 'commands' that were in fact white noise, to which as many patients 'responded' as did the patients who responded to real commands. This would seem to invalidate the fact that the responses to real commands in the test group were genuine. Likewise, Bogod and colleagues⁴³ asked patients to open and close the hand if they would rather be more asleep, but there was no option to indicate that they were comfortable and happy to stay as they were. Thus, a 'no movement' response to the question may in fact have been a positive sign of a Level 4 response rather than zero Level 4 response rate.

There are major differences between Pandit's expectations and ours of how a patient would react if unexpectedly awake but not in pain or discomfort. He expects them to move

spontaneously; we do not. Patients who are comfortable with regional anaesthesia and sedated do not jump around, even when they feel something other than pain, and even when they did not expect to do so. They do move vigorously or attract attention if in pain. Although Pandit largely dismisses the role of pain and analgesia in the overall response type, we think it is of central importance. A patient in pain will not only respond to command but also exhibit reflex responses and purposeful movement to remove the stimulus, which may be difficult to classify according to the scale in Table 1. Furthermore, we argue that if one cuts a patient's leg, the patient will try to move the leg, not the isolated forearm. However, the leg is paralysed and the patient has no way of inherently knowing that the only part of their body not paralysed is the isolated forearm. However, if the patient is instructed to move the isolated forearm, they respond accordingly. This also explains the general lack of spontaneous movement vs the high rate of movement to command.

Critique of dysanaesthesia

Our main concern with regard to Pandit's concept of 'dysanaesthesia' is a pragmatic one; because the theory appears to suggest a third state of mind that is neither consciousness nor unconsciousness, it may be viewed by anaesthetists as an acceptable end point for general anaesthesia. Indeed, the title of one of his articles alludes to a putative state where the patient is 'acceptably aware'.⁶⁵ We do not agree. In anaesthesia for, say, neurosurgery or scoliosis surgery where the patient is not uncommonly woken during surgery, or for sedation procedures as for endoscopy, a great deal of care should be taken to explain to patients that they will experience a range of mental states. Without such careful explanation, there is a risk of psychological trauma. While it is self-evident that some patients who become accidentally aware during anaesthesia and most who respond during IFT fail to suffer adverse consequence, we fear that those who fail to read beyond the title or who misread the contents of what is undoubtedly a complex paper may be misled into practice that might be considered both unethical and dangerous. This criticism also applies to similar (but distinct) theories of 'disconnectedness'⁶³ or 'unbinding'⁷² that have been proposed by others.

There are many personal accounts of AAGA; amongst them, we urge readers to consult the brief account by Whitaker⁷⁷ (a surgeon), who conceded some sensation of detachment ('It was not so much terrifying as unnerving. . . thinking it was a dream but knowing it wasn't. . .'). Yet his account is telling: 'months following this unfortunate incident I recalled those few seconds of awareness repeatedly and tried to analyse my feelings about the event. The overriding impression was one of impending death and as I am not normally a remotely depressive sort of person the taste of the event remains bitter.' Dysanaesthesia, if seen as an acceptable end point for general anaesthesia, runs the risk of justifying awake paralysis.

As described, dysanaesthesia encompasses a range of mental states in between consciousness and the oblivion of complete general anaesthesia (Fig. 3). Yet, ascribing it a single term gives the impression of a single mental state (see press reaction to Pandit's article describing 'a third state of consciousness'; <http://www.bbc.co.uk/news/health-24357476>). A patient undergoing regional anaesthesia with sedation will commonly describe experiences of the type presented in Table 3. There would therefore seem to be considerable overlap between the various states in Fig. 3, from which dysanaesthesia could be removed.

Pandit argues that the absence of extreme distress in the retrospective reports of IFT patients who had recall is supportive

of his hypothesis of dysanaesthesia. However, this interpretation fails to take account of an important aspect integral to the conduct of IFT. There is great reassurance provided by constant verbal communication with the patient. Typically, the distress of AAGA is compounded by a feeling that no one else is aware of the patient's predicament. This can lead to catastrophic interpretations by the patient. Communication with the anaesthetist, even if only in the form of relatively simple IFT commands, normalizes the patient's perception of their condition and reduces their anxiety.¹⁰ Also, many of the components of the anaesthetic cause sedation if not unconsciousness. We would dispute the need to posit a new state of (un)consciousness (dysanaesthesia) to describe this state of mild sedation.

Summary of Wang and Russell's argument

The IFT is at once sophisticated and crude. As a means of directly interrogating mental state in the presence of otherwise complete bodily paralysis, it is difficult to envisage any more sophisticated a method. As a means to determine mental state, it is very crude.

The task of moving one limb in response to an auditory command represents a basic level of mental capacity. However, response to conditional commands ('if you are comfortable, squeeze your hand twice') or choice questions can indicate a higher level of cognitive processing. The reason why some patients exhibit the former but not the latter is because the higher (executive) brain centres may be obtunded by anaesthetic, preventing responses to complex conditional commands but leaving intact the ability to respond to simple command. This would be consistent with an extensive body of work on how anaesthetics might work by disrupting connectivities between critical brain regions.⁷⁸ We consider that this represents increasing levels of consciousness without necessarily specifying any underlying model of consciousness.

If we have any starting assumption, it is simply that consciousness is independent of perception and memory. Thus, in our view, it is perfectly possible to be conscious with no perceptual input;⁷⁹ equally, it is perfectly possible to be conscious at a given time with no subsequent memory or recall.⁸⁰

There is a great deal of evidence from the clinical, psychological and experimental literature to support our views. Thus, the phenomenon of inattention blindness (the inability to perceive things that are in front of one's eyes)⁷⁹ is demonstrated most strikingly in the 'invisible gorilla' experiment (see <https://www.youtube.com/watch?v=vjG698U2Mvo>).⁸⁰ People who fail to see the gorilla do not have impaired consciousness. The celebrated case of H.M., who lost the ability to form new explicit memories after extensive hippocampal surgery, shows that it is entirely possible to have no memory yet be conscious.⁸¹ Given that, in the administration of general anaesthesia, we feel it is amongst the responsibilities of the anaesthetist to ensure unconsciousness (in addition to providing analgesia), particularly to avoid the psychological trauma of awake paralysis as identified in NAP5, we argue that the detection of consciousness, at any level, should trigger a response to increase the dose of anaesthetic. In Russell's⁵⁹ study, the median end-tidal value of isoflurane at which a positive IFT response occurred was ~0.3%, which suggests that there generally is little danger of anaesthetic overdosage should anaesthetic concentration be increased.

Concluding remarks

Jointly, we encourage readers to contribute to this debate about the IFT (and also use it in their practice to gain experience).

There are clear areas of agreement above, namely that: (i) the IFT has utility as both a clinical monitoring technique and a research tool; (ii) the IFT should be used to calibrate other putative monitors for 'depth of anaesthesia', such as EEG-based technology^{59 60}; (iii) consciousness and unconsciousness are graded phenomena and not binary all-or-nothing entities; (iv) being awake, sedated, and anaesthetized represent a continuum and not discrete steps; (v) IFT responses are varied and not only of one type (e.g. response to command vs response to choice questions); (vi) a scale (as in Table 1 or as previously presented)⁷⁶ can suitably describe the range of responses observable; and (vii) when any response to IFT command is elicited, it is wise to deepen anaesthesia.

However, the areas of disagreement and debate include the following: (i) whether the different types of IFT responses in Table 1 can be regarded as representing discrete underlying mental states that are less-than-complete anaesthesia; (ii) whether IFT patients generally exhibit (or can be expected to exhibit) spontaneous movement that alerts the researcher or anaesthetist that they are awake, even if they are not in pain; and (iii) whether, within the spectrum from awake to sedated to complete anaesthesia, there exists a discrete mental state with defined characteristics (e.g. dysanaesthesia,^{64 65} or as proposed by others, disconnectedness,⁶³ or unbinding⁷²).

The answers to these questions are unlikely to be settled by further debate, but instead by more research. Most centrally, a prospective trial involving the use of a modified form of questioning during IFT might assess whether response types (Table 1) exist as discrete entities.

One prerequisite to obtaining clearer answers from future research might be to agree on standardized commands for the IFT, where each command is recognized to gain access to a discrete neural network underlying the response. Consensus might be easy to attain because relatively few research groups use the IFT. However, any consensus should not be regarded as premature or a constraint to the design of studies. Standardizing the reporting of the conduct of the study is also important, because subsequent meta-analyses are likely. Specifying details of the questions asked during commands and in what order, the timing, and the nature of the postoperative interviews, etc., would assist future systematic reviews to draw more robust conclusions. The ethical dimensions of IFT studies themselves raise several issues for debate. For example, given that many patients can have dim recollections of IFT, what is the appropriate form of consent for any study?

Then, the answers to several questions might inform future discussion. If IFT-positive patients (Level 3 response) are 'asked' at the time why they did not move spontaneously to the surgery, what is their answer? Do completely unparalysed patients respond in the same ways (or at all) if they are asked to squeeze their hand? Will partly paralysed respond to command, and if so, how many will respond? If temporary paralysis is used (e.g. single dose of suxamethonium and no further NMB), is the rate of response the same as with IFT with full paralysis? Is the specific rate of IFT (Level 3) response dependent on the anaesthetic drugs used? It has been suggested that dexmedetomidine may reduce⁸² or indeed increase⁸³ the response rate. Others are using β -blockers with IFT to test a similar hypothesis⁸⁴ (see <https://clinicaltrials.gov/ct2/show/study/NCT01377636>). Is memory (i.e. recall) related to the level at which the patient responded during IFT (e.g. is a Level 4 or 5 response associated with a higher rate of recall than, say, Level 1 or 2)? In planning such research, the relatively high rate of overall response during IFT (~50%; Table 2) suggests that the sample sizes required to test any of

the above hypotheses should be achievable. However, this same positive response rate does raise the concern that perhaps many more of our paralysed patients are wakeful than we might suppose.

Authors' contributions

J.J.P. devised the scale presented in Table 1 and conducted the analysis of literature that is the basis of Tables 2 and 3. All authors wrote and revised the manuscript.

Declarations of interest

J.J.P. was Clinical Lead of the 5th National Audit Project (NAP5) of the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland 2011–4. M.W. was a panel member and co-author of the NAP5 Report. M.W. has received honoraria and travel funding for overseas lectures from Abbvie/Abbott. He has been loaned two BIS monitors by Covidien for use in an intensive care unit research project on implicit memory. M.W. was a member of the National Institute for Health and Clinical Excellence's Diagnostics Advisory Committee on depth of anaesthesia monitoring. The views expressed are their own and not those of these organizations. This article is based on a lecture entitled 'The case for dysanaesthesia: the uncoupling of sensation from perception', organized as a debate with I. F. Russell and M. Wang on the interpretation of the isolated forearm technique, given at the 9th Meeting on Memory and Awareness in Anaesthesia (MAA9), Tokyo, Japan, September 2014. Although the article is arranged as a two-part debate, readers should understand that Russell and Wang extensively contributed to the part written by Pandit, and conversely, Pandit contributed to large parts of the section attributed to Russell and Wang. This was therefore truly a collaborative effort.

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Handling editor: H. C. Hemmings