COMMENTARY

Dying to know the truth: visions of a dying brain, or false memories?

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The nature of mind-brain relationships and the possibility of life-after-death are some of the most profound issues relating to mankind's place in the universe. The report in today's *Lancet* by Pim van Lommel and colleagues of near-death experiences (NDEs) in survivors of a cardiac arrest provides intriguing data that are relevant to these issues. Theirs is the second prospective study of this type, the first being a smaller-scale study done in Southampton by Parnia and colleagues.[1] Both groups of researchers think that their findings indicate a need for radical revision of current assumptions about the relationship between consciousness and brain function. van Lommel and colleagues ask, "How could a clear consciousness outside one's body be experienced at the moment that the brain no longer functions during a period of clinical death with flat EEG?". But the truth is that nobody knows when the NDEs reported by these patients actually occurred. Was it really during the period of flat EEG or might they have occurred as the patients rapidly entered or gradually recovered from that state?

Elsewhere, Parnia and Fenwick have reviewed NDEs during cardiac arrest and have considered the latter possibility.[2] They think that such an explanation is unlikely, mainly because of anecdotal reports of patients accurately recalling events that took place during the actual cardiac arrest, apparently during the out-of-body experience (OBE) phase of the NDE. An OBE can be defined as an experience in which a person seems to perceive the world from a location outside the physical body. One such anecdote was reported to van Lommel and colleagues during the pilot phase of their study by a coronary-care-unit nurse. Unfortunately, they do not report whether any attempt was made to corroborate details with the patient. On many previous occasions such attempts at corroboration have revealed that the evidence was not as impressive as it initially seemed.[3] Blackmore[4] lists several alternative non-paranormal explanations as to why people may sometimes seem to accurately describe events occurring during their NDEs. These include "information available at the time, prior knowledge, fantasy or dreams, lucky guesses, and information from the remaining senses. Then there is selective memory for correct details, incorporation of details learned between the NDE and giving an account of it, and the tendency to tell a good story".

Having said that, the OBE component of the NDE offers probably the best hope of launching any kind of serious attack on current concepts of the relationship between consciousness and brain function. Parnia and colleagues[1] had hidden targets on boards suspended from the ceiling of the wards used in their study, in the hope that if any patient reported an OBE during their cardiac arrest, they would subsequently be able to identify the targets. Unfortunately, none of the four patients who experienced an NDE in the study experienced an OBE as part of the NDE. However, if reports of veridical perception during OBEs were to be forthcoming in future studies, they would represent a very strong challenge to any non-paranormal explanation of the NDE.

van Lommel and colleagues' report raises the possibility of a new potential artefact in such studies. It seems that at least some NDEs may be the result of false memories, of the mind trying to retrospectively "fill in the gap" after a period of cortical inactivity. The investigators report that, at the 2-year follow-up, four of 37 patients contacted to act as controls (ie, people who had not initially reported an NDE) reported that they had had one. Although these patients represent fewer than 1% of the total sample, they represent over 10% of the 37 patients interviewed with a view to acting as controls. If this subsample is at all representative, it implies that around 30 patients from the sample of 282 who initially denied an NDE would, if they had survived for another 2 years, be claiming that they had had one. van Lommel and colleagues suggest that these patients may have been unwilling or unable to describe their NDEs in the first interview, but no attempt seems to have been made to corroborate these possibilities with the patients themselves. It seems likely that at least some patients, on hearing about other survivors' NDEs, would start to imagine what it would have been like if they had had the same experience. Recent psychological studies have shown conclusively that simply imagining that one has had experiences that had in fact never been encountered will lead to the development of false memories for those experiences.[5–7] Interestingly, susceptibility to false memories correlates with tendency to dissociate,[8,9] which in turn correlates with the tendency to report NDEs.

Perhaps the switching of classification of patients represents nothing more than changes in definition of NDE at different stages of the study. This possibility may receive some support from the fact that, at the 2-year follow-up, over a third of the 17 patients who had originally reported superficial NDEs were then deemed to not have had NDEs at all. Another possibility is ordinary forgetting. Such problems must be rectified in future studies because their overall effect would be to blur the distinction between NDE and non-NDE-patients. This overlap would make it much more difficult to identify possible physiological and psychological differences between the groups. Nevertheless, the prospective nature of the studies by van Lommel and

colleagues and Parnia and colleagues is to be welcomed as a major advance over previous retrospective approaches.

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Microchimerism: expanding new horizon in human health or incidental remnant of pregnancy?

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Bidirectional traffic between mother and fetus is now well documented. Foreign DNA has been detected and quantified with PCR-based techniques, and foreign cells have been identified with fluorescence in-situ hybridisation (FISH).[1] Transferred cells have been found to persist for years in the new host, probably for the host's lifetime. HLA molecules have an important role in the definition of "self", are associated with autoimmune diseases, and are key determinants of transplantation success. These observations, when considered together, led to the hypothesis that persistent microchimerism deriving from pregnancy and the HLA relationships between host and non-host cells are involved in the pathogenesis of autoimmune disease. Initial studies in scleroderma, primary biliary cirrhosis, and Sjögren's syndrome have both lent credence and raised doubts about this hypothesis.

Thyroid tissue that is microchimeric with fetal cells is of especial interest because of the high frequency of subclinical thyroiditis postpartum.[2] In this issue of *The Lancet*, Bharath Srivatsa and colleagues report their study of thyroid specimens obtained from women at surgery or necropsy. The investigators used FISH with probes to the Y and X chromosomes to identify male, presumably fetal, cells. Male cells were found significantly more often in specimens affected by disease than in normal specimens. Earlier this year Klintschar and colleagues[3] reported that microchimerism was commoner in thyroids affected by Hashimoto's disease than in nodular goitre. They had extracted DNA from thyroids from women and used PCR to identify male DNA. The two studies lend support to the idea that microchimerism with fetal cells can affect the health of the mother's thyroid, but both groups of researchers readily acknowledged that microchimerism could be a secondary event. The relative frequencies of microchimerism differ in the two reports, but the two studies are not directly comparable because they used different techniques and because the summary provided by Klintschar and colleagues was for all women tested, not just those with sons. The frequency of microchimerism may also depend on the extent of sampling and whether the organ is being examined early or late in the course of a disease.

Srivatsa and colleagues found microchimerism not only in autoimmune thyroiditis but also in various other thyroid diseases, a finding analogous to that in liver disease, in which microchimerism is common in primary biliary cirrhosis as well as in non-autoimmune liver disease.[4] It is important to remember that microchimerism with fetal cells is commonly detected in the peripheral blood of healthy parous women. Persistence of maternal cells in the offspring has also been frequently reported in healthy individuals.[5] In other words, microchimerism arising from pregnancy is common. Yet existing data lend themselves to two very different interpretations. One is that microchimerism is an incidental byproduct of pregnancy without ancillary biological significance. Alternatively microchimerism could have far-reaching and diverse implications for health, including beneficial effects. Nonetheless, some individuals could be adversely affected by microchimerism given appropriate disease triggers in the context of particular HLA genes of mother and/or child and the HLA-relationships between host and non-host cell populations.[6,7]

Srivatsa and colleagues' careful studies provide evidence of an overall difference between diseased and healthy thyroid tissue in whether or not there is microchimerism. However, identification of fetal cells in the mother on the basis of a sex difference provides only presumptive evidence of microchimerism, as the investigators point out. Confirmation of the source of cells could be obtained by pursuing converging lines of evidence—for example, by examination for genetic polymorphisms unique to the child. In four cases male cells were found in women without a male birth. Although not formally proven, miscarriage, reported in one woman, is an assumed alternative source of fetal cells. The simplest explanation for the others is an unrecognised miscarriage. Other possibilities include early unrecognised loss of a twin brother, undisclosed induced abortion, transfer via the maternal circulation of cells from an older brother, or possibly from sexual intercourse.

There are technical and clinical issues to consider in the interpretation of results from studies of michrochimerism. Contamination can occur with PCR-based techniques and with DNA extracted from paraffin-embedded tissues since pathologists do not routinely change paraffin baths between samples. The particular Y-chromosome sequence used can be important. Some Y-chromosome sequences cross-react with autosomal sequences. Multiple-copy sequences have greater sensitivity than single-copy sequences (eg, SRY), but some vary in copy number from individual to individual (eg, DYZ1) and could give spurious results in quantitative assays. Overlapping cells in histological sections can produce artefacts when FISH is used to study tissues, and only cells with two signals in a well-defined nucleus should be counted. Clinical variables are equally important in interpretation. Some reports lack