TECHNICAL COMMENTS

# Response to Comments on "Detecting Awareness in the Vegetative State"

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*Science* 02 Mar 2007:
Vol. 315, Issue 5816, pp. 1221
DOI: 10.1126/science.1135583



## Abstract

Additional data, supported by relevant functional neuroimaging literature, confirm that the "normal" patterns of brain activity reported in a patient who was clinically diagnosed as vegetative could not have occurred "automatically" in the absence of conscious awareness. The most parsimonious explanation remains that this patient was consciously aware despite her diagnosis of vegetative state.

The crux of the arguments set forth by both Nachev and Husain (*1*) and Greenberg (*2*) is that the words "tennis" and "house" may have automatically triggered the patterns of activation observed in the supplementary motor area (SMA), the parahippocampal gyrus (PPA), the posterior parietal lobe (PPC), and the lateral premotor cortex (PMC) in our patient (*3*) in the absence of conscious awareness. We know of no data supporting the inference that such stimuli do unconsciously elicit sustained hemodynamic responses in these regions of the brain, yet considerable data exists to suggest that they do not.

For example, although it is well documented that words such as "tennis" and "house" can, under certain circumstances, elicit wholly automatic neural responses in the absence of conscious awareness (*4*), such responses are typically transient (i.e., lasting for a few seconds) and, unsurprisingly, occur in regions of the brain that are associated with word processing. In our patient, the observed activity was not transient but persisted for the full 30 s of each imagery task—far longer than would be expected, even given the hemodynamics of the blood oxygen level–dependent response. In fact, these task-specific changes persisted until the patient was cued with another stimulus indicating that she should rest. Such responses are impossible to explain in terms of automatic brain processes. In addition, the responses in the patient were observed, not in brain regions that are known to be involved in word processing but, rather, in regions that are known to be involved in the two imagery tasks that she was asked to carry out. Thus, in one condition ("tennis") a sustained response was observed in the SMA, a region known to be involved in purposefully imagining coordinated movements, and in the other condition ("house"), a response was observed in the PPA, a region that is frequently activated during real or imaginary spatial navigation. Again, sustained activity in these regions of the brain is impossible to explain in terms of unconscious responses to either single key words or to short noninstructive sentences containing those words and, to our knowledge, no data supporting this has been reported.

Nachev and Husain state that "the presence of brain activation is not sufficient evidence for the associated behavior…unless one has also shown that the same activation cannot occur without it" (*1*). This statement is, of course, nonfalsifiable (it would require an infinite number of experiments) and is therefore of little relevance to empirical research. On the other hand, Greenberg (*2*) suggests a clear empirical test of the alternative hypothesis. He asks whether noninstructive sentences ("Sharleen was playing tennis") would have produced the pattern of activation observed in our patient.

To answer this question, we have supplemented the main figure from our original study (*3*) to show how a volunteer, prompted with such noninstructive sentences (including the words "tennis" and "house") responds when no previous instructions are given about using these words to guide imagery (see **Fig. 1**). When modeling for a 30-s sustained response, in exactly thesameway as we did with the patient, no activity was observed in the SMA, the PPA, or any of the other areas that were activated both in the patient and in the healthy volunteers who were asked to do the mental imagery tasks (**Fig. 1C**). This was true even when the unthresholded data were examined. In contrast, significant sustained activity was observed in these regions in our patient (**Fig. 1A**) and in each of the healthy volunteers who were asked to perform the mental imagery tasks in our original study (**Fig. 1B**) [for single-subject data, see the Supporting Online Material (SOM) in (*3*)].

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**Fig. 1.**

(**A**) SMA activity during tennis imagery, and PPA, PPC, and PMC activity while imagining moving around a house in the patient described in (*3*). (**B**) Statistically indistinguishable activity in all four brain regions in a group of 12 healthy volunteers (controls) asked to perform the same imagery tasks. (**C**) The result when one healthy volunteer underwent exactly the same functional magnetic resonance imaging procedure as the patient described in (*3*), except that noninstructive sentences (e.g., "The man played tennis,""The man walked around his house") were used. Using an identical statistical model to that used with the patient, we observed no significant sustained activity in the SMA, PPA, PPC, PMC, or any other brain region. All results are thresholded at $P < 0.05$, corrected for multiple comparisons. *X* values refer to the distance in millimeters from the midline in stereotaxic space [see SOM text in (*3*)].

In short, the argument that our stimuli may have automatically elicited the responses that we reported in our patient is supported neither by a direct test of this hypothesis nor by relevant literature in this area. The most parsimonious explanation therefore remains that this patient was consciously aware and purposefully following the instructions given to her, despite her diagnosis of vegetative state.

## References and Notes

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Vol 315, Issue 5816
02 March 2007
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