Author's response to reviews

Title: Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome?

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Dear Editor,

We hereby resubmit for publication the revision of our consensus paper entitled “Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome ?”. We thank the reviewers for their constructive comments and have made all their proposed changes; hence, hoping the paper will now be accepted for publication in your journal.

In response to Reviewer 1:

1. When Brian Jennett coined the term „persistent vegetative state“ in 1972, he regarded this term as preliminary. He expected a discussion within the neurological community about what would be the better name for the syndrome as similar but yet different from coma. Ironically, the MS of Laureys et al is proposed almost four decades later, and it is still a “debate paper”. From the said above it should be clear that I find the idea presented in the MS, in general, very good, but probably not sufficient. In other words, I believe that the European Task Force is on a right way, but that it is going this way too slowly. Particularly, I agree completely that the term „vegetative“ is regarded by many lay persons as pejorative.

We thank the Reviewer for considering the ideas presented in the MS as “very good” and “agreeing completely that the term „vegetative“ is regarded by many lay persons as pejorative”. As pointed out by the reviewer, we consent that they may for some not yet be sufficient and occurring too slow but consider this MS as an important first step in the right direction, accepting that different scholars may have different opinions on this matter, hence our “debate-consensus” paper.

2. However, not only names of concepts make concepts pejorative, but also vice versa. It is possible, as the authors correctly state, that we can disregard the human value of these patients BECAUSE the term we use has pejorative “vegetable” connotations. But it is also possible, that if we continue to disregard their human value, ANY term we introduce will get pejorative connotations. An example: it is not the word “nigger” that produced the racist ideology, but it was the racist ideology that was manifested in the denigrating word. I feel that the authors underestimate this feedback principle. Perhaps for the same reason the authors confound two albeit related but nonetheless distinct issues: the one is the issue of the appropriateness of the term PVS (in which, I repeat, I fully agree with the authors), and the other is the issue of diagnostic errors (and the possible role of non-clinical techniques such as fMRI and ERP in reducing the error rate).

We have stressed both confounders (appropriateness of the term and risk of diagnostic errors) as requested.

It now reads in the revised abstract. “Given these concerns regarding the negative associations intrinsic to the term “vegetative state” as well as the diagnostic errors… we here propose to replace the name “
3. This confounding is reflected in the term proposed by the Task force, Unresponsive Wakefulness Syndrome. “Unresponsive” means the lack of responses, but the critical question is, WHICH responses are lacking? The authors know even better than me that many PVS (now: UWS) patients exhibit a range of quite intriguing EEG and BOLD responses. By unresponsiveness we mean absence of voluntary motor responses as they can be assessed at the bedside and, as also requested by Reviewer 2, have stressed this in the revision. It now reads: “behavioral signs of consciousness” in the abstract and “…who sometimes never recover any voluntary responsiveness” in the discussion (also see comment 3 – Reviewer 2)

4. A minor point: the outdated term “apallic syndrome” is mentioned only on p.8. From the viewpoint of the history of medicine, it would be better to begin with this term, because this was the first scientific description of the condition we are working with.

The term “apallic syndrome” is mentioned in the title and early in the MS (background section 7 line) as requested: “In Europe, this clinical syndrome was initially termed “apallic syndrome” [2] ...”.

In response to Reviewer 2:

1. The authors are to be commended for proposing to replace the term “vegetative state” in a strong and convincing way through this coordinated multinational effort. Only time will tell if their proposal succeeds, but the attempt is worth the effort. I have only a few suggestions for strengthening the manuscript. The comparison with brain death on pp. 8-9 could be fine-tuned, if it is really necessary at all. Although absent blood flow to the entire brain surely guarantees permanence of whole brain failure, it remains to be established that “arteriography, echo Doppler or nuclear imaging” have the requisite sensitivity to distinguish truly absent flow from very low flow (in the ischemic penumbra range, insufficient for function but barely sufficient for tissue viability) in all parts of the brain. Furthermore, “absent electrogenesis on EEG or ERP” surely does not confirm “whole brain failure” but only failure (and not even necessarily irreversible failure) of the portions of the neocortex adjacent to the skull (EEG) or of the specific sensory pathways studied by ERPs. (Cf. the recent critique of confirmatory tests by Wijdicks in Neurology 2010;75:77-83.) Even the assertion that whole brain failure establishes “the absence of life” is becoming increasingly debated. The gratuitous taking of sides on an issue that has nothing to do with the topic of the paper (apart from serving as an analogy) runs the risk of distracting, if not detracting, from the authors’ message, notwithstanding that they assume the mainstream majority view. This paper (and this review) are not the proper venue for delving into the controversies surrounding brain death, and I would recommend avoiding wording that appears to take for granted what is in fact controversial about something not directly related to the proposed change of terminology for “vegetative state.”

We thank the reviewer for his positive comments and have removed the comparison to brain death in the revision as requested.

2. Another controversial issue that is simply taken for granted is that
“awareness of environment and self” requires “higher neocortical integrative”
brain functions (p. 9). To be sure, such awareness requires integrative brain
functions, but the authors’ insightful reasons for insisting on the descriptive term
UWS without implications regarding subjective consciousness also apply to the
evidence (or lack thereof) that subjective consciousness is generated from
integrative activity specifically of the “higher neocortex.” (Cf. Merker B.
Consciousness without a cerebral cortex: a challenge for neuroscience and
medicine. Behav Brain Sci. 2007;30:63-81.) If there is no evidence of awareness in
someone who is globally aphasic and can’t understand commands, and is agnostic
and apraxic for what little movement remains possible within the confines of
spastic quadriplegia, that doesn’t ipso facto prove that the person has no primary
sensations, no capacity to suffer pain and discomfort, and no awareness of self.
Again, I would urge sticking with the theme of the paper and avoiding side
assertions that lack evidence, even though they may be popularly held, and are
really unnecessary for the authors’ purpose.

We have removed the reference to “higher neocortical integrative brain
function” and have added the specific challenge of possible aphasia, agnosia and
apraxia in these patients as requested. It now reads: “This situation is further
complicated when patients with such disorders of consciousness have underlying
deficits in the domain of verbal or non-verbal communication functions, such as
aphasia, agnosia or apraxia [32, 33].”

3. The authors draw attention to the multiple lines of evidence that a subset
of UWS patients do have inner cognitive functioning and subjective awareness. But
in two places the wording contradicts this important point. E.g., Abstract, end of
the Discussion paragraph: “(who sometimes never recover consciousness...),”
implying that all such patients were in fact unconscious. It would be more
consistent with the paper’s title and thesis to state: “(who sometimes never recover
responsiveness...).” The same inconsistency occurs on page 7, third line of
Discussion: “who sometimes never recover consciousness...”

We have changed the wording in both abstract and discussion as requested.
It now reads:
“...recover behavioral signs of consciousness” and
"...who sometimes never recover any voluntary responsiveness"

4. A few very minor stylistic suggestions or typos:
Abstract Summary: “If after 35 years...” # “Since after 35 years...”
Abstract Summary: “... we think it is be better...” # “... we think it would be
better...”
Page 7, line 4: “misdiagnosis chronic patients” # “misdiagnosis of chronic
patients”
Page 7, penultimate line of first paragraph: “...(ERP) have shown...” # “…(ERP)
studies have shown...”
Page 7, last line of first paragraph: “careful to make” # “careful about making”
or “careful before making”
Page 7, first line of Discussion: “inherent to” # “inherent in”
We thank the Reviewer for these stylistic corrections and have made all
requested changes in the revision (highlighted).

5. Discretionary revisions: Page 5, line 11: “preserved vegetative
(autonomous) nervous functioning”. “Autonomous” from what? Does the inclusion
of this parenthetical term contribute anything? I find it confusing. We have deleted “(autonomous)” as requested.

Thanks for your time and effort in considering this revision. 
Steven Laureys