Can the Wada test be replaced by fMRI and other techniques?

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The Wada test is typically used for identification of the language- and memory-dominant cerebral hemisphere. The test is considered the "gold standards"—a term implying that the evidence it furnishes is trust worthier than evidence from other methods. The advent of noninvasive functional neuroimaging now raises the possibility of replacing this "gold standard" pro-vided it offers equally trustworthy results. It will be argued here that these methods, namely functional magnetic resonance imaging fMRI, magnetoencephalography (MEG), and transcranial magnetic stimulation (TMS) do provide equally trustworthy results, and that therefore they may replace the Wada test in many if not most cases.

The compatibility of the language lateralization results of the Wada and the fMRI procedure has been shown in a number of studies reporting perfect concordance or high concordance equally high is the compatibility between the results of the Wada and MEG with respect to language lateralization. Fewer studies, however, report comparisons of laterality estimates for memory between fMRI and Wada, with some reporting high and others also low concordance raising the questions as to which method is to be trusted.

Given that the degree of concordance between the Wada and the noninvasive methods is not perfect (and sometimes low as in the case of memory lateralization) the question becomes: The results of which method is to be considered valid? On the basis of the assumption that the Wada is the "gold standard," the tendency is to consider discordant estimates as failures of the neuroimaging methods. However, when that assumption is put to the empirical test it becomes obvious that the results of the Wada should not be considered any more valid than the results of the noninvasive methods. For example, the efficacy of the Wada procedure is lower than would be expected for a gold standard procedure for predicting the likelihood of postoperative language and memory deficits. In contrast, fMRI has shown better predictive efficacy than the Wada. In addition, many studies are conducted every year for the purpose of fine tuning the noninvasive methods in revealing with increasing reliability brain regions involved in different aspects of memory and language performance using fMRI, MEG and, lately, TMS and verifying the validity of the findings, mainly against prior knowledge gained from lesion studies.

Therefore, given that the validity of the data of the Wada is limited, there is no justification in considering them more trustworthy than data supplied by neuroimaging, in those few cases that the results are in fact discordant.

The practical question of course remains: Given that both types of methods are suboptimal, which type should be used preoperatively? But, given the compatibility of the two sets of methods, both in terms of their concordance in most cases and their imperfections in few cases, the noninvasive methods should be used as a matter of course because, in case their results are ambiguous, testing can be repeated and the results of the different ones cross-validated (e.g. of fMRI or MEG against TMS for expressive language; MEG and fMRI for receptive language, and so on). And only if the ambiguity is still not resolved should the Wada test be performed in the hope that they may resolve it.

Moreover, although both types of methods have limitations, the following ones, specific to the invasive but not to the non-invasive methods, render the latter preferable. First, the Wada is associated with appreciable morbidity, ranging between 3 and 5%. Second, it is associated with

patient discomfort. In contrast, no morbidity and only minor discomfort is associated with neuroimaging. Third, the results of the Wada procedure may not suffice for assessing memory laterality because delivery of the sodium amobarbital to the hippocampal formation is not always possible and because the structure of the Wada protocol does not allow for separate estimation of hemispheric dominance for verbal and for nonverbal encoding, although there is evidence of stimulus modality–specific encoding in the left and the right hippocampus. Needless to say, fMRI can discern the involvement of all brain structures associated with memory, both neocortical and paleo-cortical, and because it can be repeated, it can identify distinct components of the memory-specific brain circuitry.

A fourth and a fifth limitation of the Wada test are due to the narrow time window in which it must be performed and its repetition for establishing reliability of the results is impractical. Moreover, the Wada may not probe for the mechanisms of a host of different cognitive operations that are subsumed under "language" and "memory." Yet, the neuronal networks of such operations can be assessed separately in the context of several neuroimaging sessions.

A seventh problem, also reducible to the time constraints, is the inability to control for situational variables that may corrupt the integrity of the data. Attention lapses on the part of the patient in the crowded Wada suite where a number of tasks have to be done under time constraints may well produce misleading data.

Eighth, the Wada test cannot supply information about the primary visual and auditory cortex that both MEG and fMRI can readily supply. Finally, the Wada test requires alertness and cooperation on the part of the patient. Thus it cannot be used with patients with attention deficit and hyperactivity problems, patients in a state of confusion, patients with encephalopathies, or patients who are very young. None of these limitations apply to neuroimaging, where localization of sensory, motor, and even receptive language cortex can be accomplished with the patient under sedation.

For all the preceding reasons it is proposed that the Wada may be replaced as the methods of choice in many if not most cases where the non-invasive methods are available.