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Editorial

# The Wada test: the best steam engine on the tracks

In 1953, the Roanoke Shops of the Norfolk and Western Railroad built a steam locomotive, No. 244, an 0-8-0 switcher ("shunter" in British parlance), the culmination of more than a century of technology development. Just after five years, the N&W scrapped it. Following the industry's shift to diesel-electric power, No. 244 was the last steam locomotive made in the United States (Rosenberg and Archer, 1973).

Since the introduction of the Wada test in 1949, it has undergone extensive validation and refinement. The Wada Test has three functions: lateralization of language, assessment of the risk of memory loss after epilepsy surgery, and prediction of localization and surgical outcome. When I met Juhn Wada during the 1998 American Epilepsy Society meeting, he told me one factor leading to his development of the intracarotid amobarbital test (Wada, 1949) was amobarbital's easy availability. It is no small irony, therefore, that amobarbital's worldwide shortage has triggered validation of alternative sedatives. This switch may mark a time when, like the peak of steam power, a different technology altogether takes over.

The experienced and busy pediatric epilepsy surgery program at the Hospital for Sick Children in Toronto reports its findings of the safety and reliability of the etomidate speech test (EST) (Gulati et al., 2019). Twenty-one patients (12% of 172 consecutive patients who underwent functional magnetic resonance imaging (fMRI) between 2013–2017) underwent the EST after fMRI failed to provide language lateralization. Of these, 18 patients underwent bilateral and 3 unilateral EST. All right-handed patients (n = 14) had left-hemisphere dominant language. Of the 5 left-handed patients, 2 (40%) had right-hemispheric dominant language. Thus, of the pool of 21 patients with ambiguous lateralization from fMRI, about 10% had the suspicion of right hemispheric language dominance confirmed (only about 1% of the total pool of 172 fMRI patients). No patients experienced complications such as hemorrhage or stroke.

But, given the low incidence of right-hemispheric language lateralization, the difficulty in testing the lateralization of memory in the pediatric group (not attempted in these patients), and the plasticity of language in the pediatric brain, when do Wada tests remain clinically appropriate and valuable? Is a 1% confirmation rate worth the risk and expense?

In short, opinions differ.

Haag et al surveyed 26 clinicians in Europe during a retrospective case series of Wada test use (Haag et al., 2008). Surveyed clinicians rated the Wada test as having good reliability and validity for language but questionable for memory lateralization. Nevertheless, the authors concluded that "clinicians currently do not want to rely solely on noninvasive functional imaging in all patients." (Haag et al., 2008). Tobias Loddenkemper, in the accompanying editorial, noted the declining use of the Wada test in the Cleveland Clinic practice (Loddenkemper, 2008) and wondered if there were any clear indications for continued use of the Wada test. Despite evidence of decreasing enthusiasm for the Wada test, a survey of 78 clinicians in 2015 found that positions had hardened (Quigg, 2015). For example, respondents diverged on the frequency of use of the Wada test. About 1/3 of subjects used the Wada for "all or nearly all" surgery candidates; almost the same proportion cited the risk of the procedure as the main reason why it was avoided. Respondents disagreed on indications for postsurgical memory risk and prediction of outcome; equal numbers of respondents ranked memory lateralization and prediction as first – or last –as primary indications to perform a Wada test. The conflict continued in what physicians choose to do with the findings of poor memory contralateral to the side of proposed surgery (specifically in the case of mesial temporal lobe epilepsy), the so-called "Wada failure". More than 15% advised pressing forward with surgery despite the potential of memory loss. A near similar proportion – 14% – advised the opposite; in their view, patients should decline surgery since the risk of severe memory loss was too great.

Haag et al found that small variations in the Wada protocol were the norm rather than the exception (Haag et al., 2008), and one can speculate that this variability is more a sign of adaptability and robustness rather than weakness. Risks are rare. Gulati et al reported no complications (Gulati et al., 2019). In our experience at the University of Virginia, we have conducted > 400 Wada tests in subjects > 14 years old, and only one patient (˜0.25%) experienced transient neurological deficits (that patient required emergent intraarterial clot lysis). Haag et al reported a complication rate of 1.09% in 1373 tests (Haag et al., 2008).

Nevertheless, despite its gold standard status and low risk, a newer technology has swept the industry. In 2017, the American Academy of Neurology published guidelines that summarized the validity of fMRI in the presurgical evaluation of patients with epilepsy (Szaflarski et al., 2017). The panel concluded that fMRI was appropriate for use in language lateralization in lieu of the Wada test save for temporal neocortical or tumor-associated epilepsy (neither of which had insufficient evidence). Given that fMRI is noninvasive, it's only a matter of time before evidence accumulates in these two areas.

The gist from the range of findings, opinions, and recommendations is that physicians in epilepsy programs feel most comfortable with what works, and as Gulati et al demonstrate, etomidate works great in their pediatric epilepsy patients (Gulati et al., 2019). By extension, etomidate should work great in other centers as an amobarbital replacement. But, as in the case of the last steam engine, the admirable refinements represented in the etomidate speech test may represent the peak after which noninvasive methods completely take over.

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