

Suicide after successful deep brain stimulation for movement disorders

To the Editor: Burkhard et al.¹ report a high rate of suicide in patients who received deep brain stimulation (DBS) implants in four different targets for three different indications. The conclusion that patients treated with DBS have an increased risk of suicide appeared inadequately supported by the evidence provided and prompted us to review our own series collected at the Besta Institute (table). Our data showed that there was not a non-specific increase in the risk of suicide following DBS implants and suggest instead that psychiatric unwanted reactions occur following subthalamic nucleus, but not posterior hypothalamus implants.

Only four of Burkhard's patients had Parkinson disease (PD), and three of them had early-onset PD that was genetically determined in most instances. Early-onset PD has a strong impact on quality of life and a high incidence of depression (and possibly of suicides). Indeed, the early-onset PD patients of the Swiss series had depression and other signs of psychosis. Considering only PD patients included in the heterogeneous Swiss series, the rate of suicides is reduced to 2.8%, more than double that of another series of 77 PD patients treated in France with bilateral STN stimulation.²

There may be more than one reason why patients with movement disorders in southwestern Switzerland have a higher rate of suicide than expected. First, Switzerland has one of the highest suicide rates in Europe.³

Second, the patients enrolled in the Swiss study did not comply with current selection criteria for DBS, such as CAPSIT guidelines,⁴ which exclude PD patients with severe depression from undergoing surgical interventional therapies. All patients but one in the Swiss series had a previous history of severe depression, and two of them had suicidal ideations or attempts before undergoing surgery. A pre-morbid mood disorder is a predictor of lower outcome and of psychiatric complications following DBS in PD.^{2,5}

In the Swiss series, four of the six patients who committed suicide had two DBS implants, which involve three surgical procedures (implant-explant-implant) and an undisclosed number of surgical tracks in each hemisphere. It is doubtful that such multiple sequences are representative of standard clinical practice. A combination of microscopic lesions in strategic brain areas may have contributed to the observed suicidal behaviors. Furthermore, three patients had dementia. There is insufficient information on their cognitive dysfunction and on changes in medication that may have affected the patients' outcome.

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Reply from the Authors: We aimed to alert the medical community about DBS being a potential risk factor for suicide at a time when DBS is progressively becoming a routine procedure for advanced movement disorders, notably PD.¹ This concern is shared by many other groups which have observed similar cases in their DBS cohort^{2,6-8} and requires extensive pre-operative evaluation and intensive psychiatric support in at-risk patients.⁹

We were interested to learn that Albanese et al. might be one of the few groups spared by this complication. In our patients, all but one suicide occurred between 2 to 7 years after the DBS procedure, suggesting that the follow-up of patients of Albanese et al. (PD: 3 years, CCH: 2 years) may be too short for such a complication statistically to occur.

Furthermore, with an estimated prevalence of one every 25 patients in our cohort, it seems clear that their yet unpublished CCH group (16 patients) is too small to substantiate the claim that posterior hypothalamus DBS is safer than STN. Finally, Albanese et al. are purposefully mixing patients with CCH and PD, forgetting that the psychodynamics of these two unrelated conditions may be enormously different.

The correspondence by Albanese et al. contains several errors. First, none of our suicide patients was demented, neither before

Table Clinical variables of patients who received DBS implants for PD or chronic cluster headache (CCH) at the Besta Institute

Indication	PD	CCH
Target site	STN	PH
Patients, no.	72	16
Implants, no.	144*	18†
M/F ratio	1.7	7
Age at implant, y	56.2 ± 7.2	43.0 ± 12.9
Disease duration at implant, y	12.6 ± 4.2	3.3 ± 2.4
Follow-up, mo	34.2 ± 18.2	23.5 ± 14.5
Levodopa equivalents at implant	1150,5 ± 555,6	—
Levodopa equivalents at last visit	621,4 ± 428,2	—
Average voltage, V	2.94 ± 0.39	2.1 (0,5–3,2)
Average pulse duration, µs	63.5 ± 0.6	60.0 ± 0.0
Energy delivered at last visit, µW	1.78 ± 0.74	NA
Psychiatric side effects, patients	15‡	0
Transient increase of sexual desire	8	0
Transient manic psychosis	5	0
Transient depression	5	0
Transient psychic akinesia	3	0
Cognitive deterioration	3	0
Suicide attempts	0	0
Suicides	0	0

PD patients with less than a year follow-up are not included.

* All patients received a bilateral implant.

† Two patients received a bilateral implant.

‡ Six patients had more than one side effect.

CCH = chronic cluster headache; PD = Parkinson disease; STN = subthalamic nucleus; PH = posterior hypothalamus.

nor at the time of death. Three PD patients exhibited mild neuropsychological abnormalities consistent with the underlying pathology, but did not fulfill the DSM-IV criteria for dementia. Second, as we discussed, no changes of stimulation parameters or medications occurred at or near the time of suicide. Third, while most patients had a past history of depression, none was severely depressed when assessed pre-operatively and all had low scores on the Montgomery and Asberg depression rating scale.¹⁰ All cases fulfilled the CAPSIT-PD⁴ guidelines at the time of evaluation, as required by our DBS program.

We were particularly interested in the 11% rate of transient hypersexuality reported by Albanese et al. This was only rarely observed in our cohort. Whether this unexpected reaction reflects a cultural trait, a bias related to authors' domains of interest, or a true DBS-induced complication needs further investigation.

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Should thrombolysis be given to a stroke patient refusing therapy due to profound anosognosia?

To the Editor: We read the article by Katz and Segal with interest.¹ We agree that anosognosia due to acute stroke is common and can cause difficulty in the consent process. If the patient fails to perceive that a stroke has occurred, declining treatment is reasonable. We do not believe, however, that this refusal necessarily obviates the option of thrombolysis.

Valid consent requires “adequate decision-making capacity,” including the ability to understand pertinent information regarding her/his condition, to process that information, and to express a decision.² A person with anosognosia has limited capacity to provide valid consent because of the inability to recognize deficits. At our institution and many others offering thrombolysis as standard of care, individuals unable to provide informed consent and for whom no surrogate decision-maker is available, are treated based on presumed “consent” in a manner analogous to that used for emergency surgery. We understand the authors’ discomfort when applying this strategy to anosognosic patients who are alert and reasonable but nonetheless lack capacity.

While not cognizant of personal deficits, a person with anosognosia is not necessarily impaired in the ability to comprehend information about stroke and its treatment in general, nor in the ability to process this information and render an opinion regarding management. Preservation of reasoning is a leading theory for nearly invariable recovery from anosognosia.³

When faced with an acute stroke patient with anosognosia and no available surrogate decision-maker, one approach that we have used with success is to ask the patient to consider consenting to thrombolytic therapy if she or he were to have a stroke with deficits similar to those manifested, after providing adequate information to make this decision. This is akin to Fleck’s “advance directive” approach⁴ or allowing the patient to serve as her or his own surrogate decision-maker.

Thrombolysis is not without risk, but is proven therapy. Patients should be involved in the decision making process regarding its use. Difficulty obtaining consent is a barrier to delivery of acute thrombolysis in stroke.⁵ We agree that the issue of thrombolysis, consent, and anosognosia needs to be addressed, and that the AAN consider it in updating its position paper.

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Reply from the Authors: We thank Dr. Worrall et al. for their interest in our article. We acknowledge that our patient with anosognosia, while alert and reasonable, lacked capacity due to her inability to understand the nature of her illness. While her vehement objections did not entirely preclude therapy, we were uncomfortable in treating her against her will. Given this difficulty, we reiterate that the AAN consider updating its position paper to account for anosognosia.

Worrall and colleagues’ suggestion of using an “advanced directive” approach may provide an alternative solution. However, a patient’s response to a hypothetical situation may not accurately mimic their reaction to a real-time, clinical event. In an Italian survey⁶ describing the opinions of patients given such an option, only 59% responded favorably, while 19% refused therapy and 22% were unable to make a decision. tPA treatment in this study was described as an investigative therapy that “would reduce disability but carries a high risk of death.”

We should be aware that although we have a therapy with proven benefit, it is also potentially harmful. We cannot account for or make assumptions about individual patients’ desires or ignore issues such as possible cultural, religious, or educational biases.

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Efficacy of rapid IV administration of valproic acid for status epilepticus

To the Editor: We read the paper by Limdi et al. with interest.¹ It confirms that intravenous valproic acid (VPA) is efficacious in status epilepticus (SE), and well tolerated with respect to the cardiovascular system. As noted by the authors, similar safety was previously reported by others. Intravenous VPA has been used safely in critically ill hypotensive patients² and pediatric subjects.³ It is also efficacious in various SE forms including generalized convulsive,^{2,3} complex-partial,³ and myoclonic.⁴ Limdi et al. interestingly report very high VPA dosages (up to 78 mg/kg), used not only safely but “successfully” as defined by cessation of SE. However, a critical parameter in the evaluation of SE treat-

ment is the final outcome of the patients (i.e., mortality). Although many factors can contribute to a fatal outcome in this setting, it would be of interest to see how mortality in this fairly large series compares to studies using other antiepileptic drugs.

Another important issue is the possibility of inducing a VPA-hyperammonemic encephalopathy after rapid intravenous VPA loading. This may be important in clinical practice because this condition can be extremely difficult to differentiate from a prolonged postictal state or ongoing nonconvulsive SE.⁵

One of us recently observed two episodes of encephalopathy within 24 to 48 hours after intravenous VPA treatment of complex partial SE, despite VPA blood levels within the usual therapeutic range. The diagnosis was made by EEG analysis, showing monotonous background delta-theta slowing and determination of serum