Raising standards of accuracy in deep brain stimulation requires consistent definitions and unbiased reporting

Dear editor

We read with interest the novel systematic review and meta-analysis of the relationship between targeting accuracy and motor outcome in subthalamic nucleus (STN) deep brain stimulation (DBS) presented by Kremer *et al*.[1] Efficacy of DBS is purported to be dependent on accurate placement of electrodes in target structures and, as the authors highlight, a tolerance of 2 mm from a desired target has gained informal traction in clinical practice. The authors' rigorous approach reveals several shortcomings to reviewing peer-reviewed published data to test the validity of the '2 mm rule'. As pointed out in the paper, the studies included in their meta-analysis demonstrate generally accurate electrode placement and reveal publication bias towards series with greater accuracy. Some of the included studies even cited electrode misplacement as an exclusion criterion from their series, thus further reducing the range of accuracies available for meta-analysis. One might expect outliers in targeting accuracy to inform us most about how electrode placement affects clinical outcome. Furthermore, despite over 160 000 patients having been implanted with DBS systems worldwide, mostly for Parkinson's disease, individual patient data were available for only 206. Although the available data do not refute the '2 mm rule', these issues raise the question of whether meta-analysis of published data is an appropriate method for examining its applicability in the real world.

Key to reporting of targeting accuracy are consistent definitions of how accuracy is measured. The common definition relates to error in the stereotactic method, that is, the discrepancy between intended and actual electrode placement. Kremer *et al* describe two variations of this error: the radial error and the three-dimensional (3D) error. Their figure 1 is ambiguous regarding how these measures are illustrated. Radial error represents the two-dimensional discrepancy between the target and the point at which the electrode crosses the axial plane containing the target and can be expressed as a scalar distance and/or its vector components in the X (mediolateral) and Y (anteroposterior) directions. There is no 'perpendicular distance' in this axial plane as given in the figure caption. In contrast, 3D error appears to describe the discrepancy between the target and the point on the electrode which was intended to pass through the target on the preoperative plan, and can similarly be represented as a scalar distance and/or its vector components in the X, Y and Z (superoinferior) dimensions. Other 3D definitions of error include the trajectory error which describes the shortest perpendicular distance and its component vectors between the target and the implanted electrode, and the tip-to-tip error (or Euclidean error) describing the discrepancy between the tip of the implanted electrode and where the tip was intended to be placed (figure 1A).

When examining the dimension of targeting error, Kremer *et al* show in their supplementary analysis at study level only a positive correlation between Z-error magnitude and motor improvement. However, not only the dimension but also the direction of error can determine clinical outcome. It is well known that stimulation outside of the boundaries of the STN can have different consequences

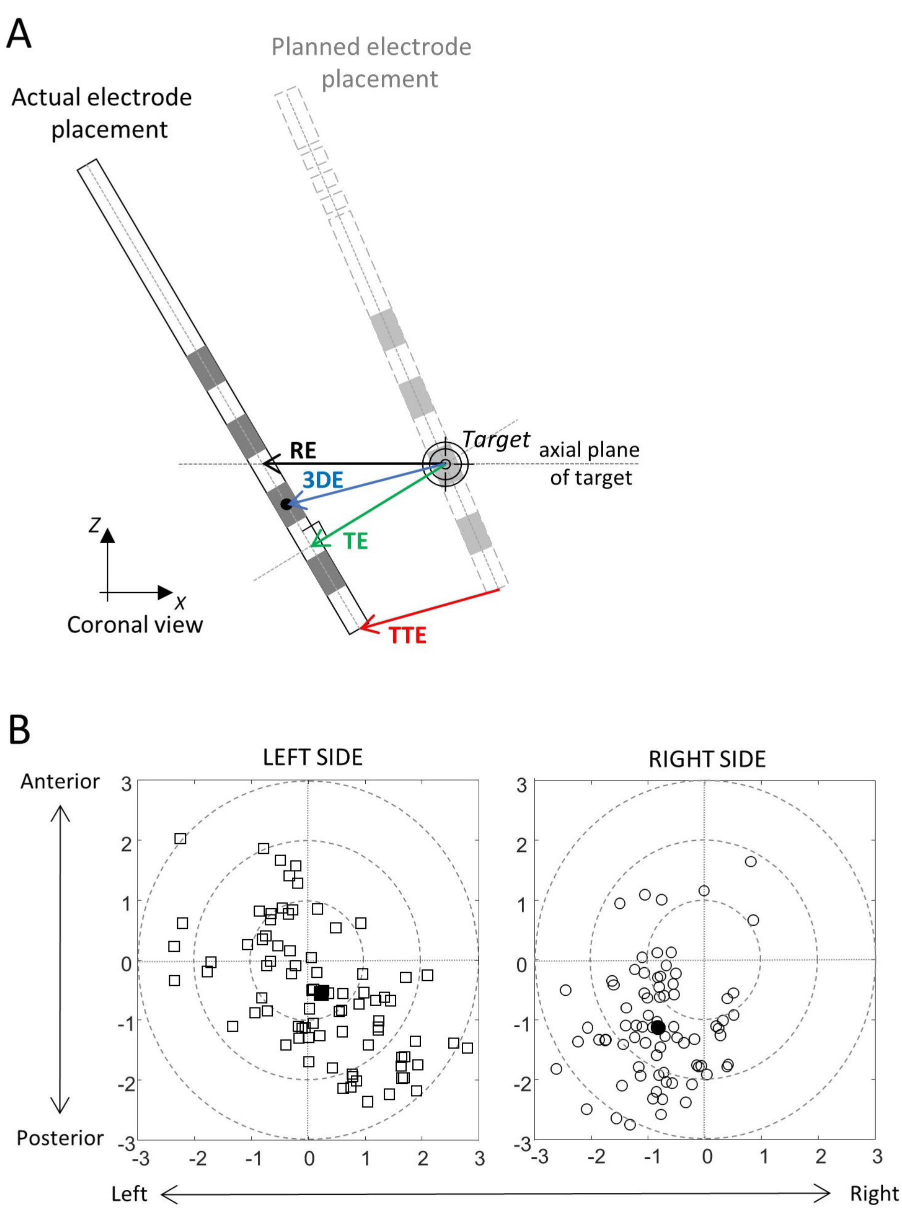

Figure 1 (A) Schematic illustration of definitions of DBS targeting error in coronal view: radial error (RE), three-dimensional error (3DE), trajectory error (TE) and tip-to-tip error (TTE). (B) graphical representation of radial error showing points at which electrodes traverse the axial plane of targeting relative to the target (at the origin) for 164 DBS electrodes implanted in 84 patients in the left (square markers) and right (circle markers) hemispheres. Solid markers represent the mean radial error for each side. Axis scales are in millimetres. Concentric dashed circles represent radii of 1, 2 and 3 mm from target. DBS, deep brain stimulation.

for treatment efficacy depending on the direction of deviation. Our own audit of DBS targeting accuracy reveals a systematic tendency to err posteromedially from the target (figure 1B). In STN DBS, this results in a propensity to deviate towards the posterior subthalamic area or caudal zona incerta, stimulation of which remains beneficial in treating the symptoms of Parkinson's disease.[2] This may be better tolerated than, for example, a laterally directed error which results in undesirable capsular side effects.

A different approach to looking at electrode location and clinical outcome examines electrode placement relative to defined anatomical structures. This approach allows one to assess targeting accuracy independently of surgeon variation in target definition, rather than evaluating precision of the surgical method in isolation, and facilitates pooling of datasets. This could be done, for example, using registration to a standard space and a group-defined atlas.[3] However, this creates the potential for errors due to registration and failure to capture individual anatomical variation in target nuclei. Alternatively, one can use segmentation at the individual level.[4] However, these methods are not yet universally defined, do not readily allow functional subsegmentation of targets and still require registration for group comparisons.

These issues highlight the need for standardised, objective and automated reporting of real-world targeting accuracy and clinical outcome data. This should ideally be on a national or international level, for example, through the use of registries and will facilitate better understanding of the acceptable tolerance limits of electrode placement in DBS and the likelihood of treatment failure being a result of suboptimal placement in relation to different targets. It has further important roles in evaluating factors affecting accuracy,[3] benchmarking of individual surgeon or unit practice for clinical governance purposes and clinical negligence litigation. The need for this is highlighted by a North American database review of 28 000 DBS patients, which found that up to a third of operations were revised, almost half because of electrode misplacement or lack of efficacy.[5]

Standardised universal reporting of consistently defined measures to prospective registries should shed more light on the relationships between DBS targeting accuracy and its determinants, electrode position and clinical outcome in the real world than meta-analysis of selective published case series. We hope to stimulate further exploration of this important topic to establish clear standards for DBS electrode placement.

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