Can fMRI Measures of Brain Motor Activation Add Significantly to Other Variables in the Prediction of Treatment Response?

Isabelle Loubinoux, PhD

See related article, pages 2108–2114.

This study is among the first to address the basic question of whether fMRI measures of brain motor activation can add significantly to other variables in the prediction of treatment response. The study attempts to use baseline variables in a cohort of 24 chronic stroke patients to predict response to a specific form of rehabilitation, 6 weeks of rehabilitation therapy that targeted arm motor function, especially distally. Patients were also randomized and either did or did not undergo motor cortex electrical stimulation, but the evaluation of this treatment was not the purpose of this study.

This work presents evidence of the use of fMRI as a useful tool to help predicting the responsiveness to an intervention aimed to improve arm motor function. It applies to patients able to mobilize the hand (active wrist extension of at least 5 degrees) and a measurable activation in the ipsilesional primary motor cortex (iM1). It is examining whether fMRI data can predict outcome, but crucially whether it can predict outcome over and above other scores. Only 2 variables out of 13 remain at the end of the analyses: degree of hand motor cortex activation and level of arm Fugl-Meyer score. Authors conclude that fMRI, in particular the degree of activation averaged in a region of interest encompassing the hand area, could help in the decision-making process for allocating patients to a therapeutic regime.

More precisely, the current results suggest that clinical evaluation of arm function predicts higher gain in less impaired patients. However, prediction is still difficult at the individual level. Then, adding a measure of brain function to clinical assessments improves ability to predict behavioral gains after a restorative therapy. It seems that there is a cutoff of $\approx 0.70\%$ of iM1 activation, above which no major gain is achieved with this set of data. Obviously, more patients are needed to validate a reliable cut-off or a more precise predictor. The results suggest that patients presenting activation near normal level (which is usually $\approx 2\%$ to $3\%$) would not be good candidates to enter a rehabilitative program. There would be an optimal level of motor cortex activation, with too much indicating maximal usage with no further reserve. However, below this cut-off, 2 outcomes were likely: significant gains or no significant gain. Because lower baseline motor cortex activation was also associated with larger increases in motor cortex activation after treatment, and because change in degree of iM1 activation was positively correlated with change in arm motor score after treatment, the authors interpret this result as a low baseline cortical activity that represents underuse of surviving cortical resources. Of course, this is a pilot study and such results need to be reproduced in a larger cohort to improve the accuracy of a prediction at the individual level. Because the literature is mixed and controversial with respect to motor cortex activity after stroke because multiple factors can influence findings, this study proposes a clear message. Moreover, it extends previous knowledge from the acute phase to the chronic phase because low baseline activity compared with normal in the acute phase of stroke recovery also has been shown to result in increased hand motor performance and increased activation 1 year after, suggesting that low M1 activation traduced as underuse of surviving cortical resources may predict further recovery. It should not be forgotten that low activation can indicate either room to increase activity or severe injury with little available resource to activate or improve.

Beyond this very informative analysis, there is not just one rule suggested by this set of data. It should be emphasized that “outliers” are present in this group of patients; for example, iM1 can remain still or even be further decreased, even in patients with iM1 stimulation and, yet, those patients improved. Thus, other routes than iM1 are likely to induce motor improvements in chronic stroke patients. This probably refers to individual brain strategies that are commonly observed. This also explains why correlations between clinical motor status and activation are not found in the chronic phase by the authors or others.1,2 In a statistical point of view, although it is clear that the degree of activation was the significant variable, its correlation coefficient was $\approx 0.45$. Squaring the coefficient gives a value of 0.20, which means that only 20% of the entire scatter in the change of motor Fugl-Meyer score can be accounted for by a linear relationship. Thus the 80% of the values has not been accounted for. The results should prove useful to future studies to determine what the other routes for subsequent recovery are. If group analyses are not able to evidence them, individual studies with techniques like inhibitory repetitive transcranial magnetic stimulation or transcranial direct current stimulation that induce temporary virtual lesions may be useful.

The opinions in this editorial are not necessarily those of the editors or of the American Heart Association.

From INSERM U225, Pavillon Riser, Purpan Hospital, Toulouse, France, and Université Paul-Sabatier, Toulouse, France.

Correspondence to Isabelle Loubinoux, INSERM U 825, Pavillon Riser, Hôpital Purpan, 31059 Toulouse, France. E-mail Isabelle.Loubinoux@toulouse.inserm.fr

(Stroke. 2007;38:2032-2033.)

© 2007 American Heart Association, Inc.

Stroke is available at http://www.strokeaha.org
DOI: 10.1161/STROKEAHA.107.488908
In the same line of the idea of individual strategies, the authors show that activation within iM1 may be displaced in any direction without one being more efficacious after treatment than the other at the group level.

At the group level, only iM1 gave a prediction of the outcome. It turns out that degree of activation in each of the other 4 areas examined (contralesional primary sensorimotor cortex, bilateral premotor cortex, and midline supplementary motor area) had no predictive value for treatment response. Again, this result is in accordance with results of the acute phase where the latter areas were not predictive of improvement.1 This means that iM1 activation is a very robust key, although not exclusive, actor of recovery. Further steps may be to explore other types of patients, possibly those who are not able to activate M1 and yet had recovered.

Disclosures
None.

References

KEY WORD: FMRI
Can fMRI Measures of Brain Motor Activation Add Significantly to Other Variables in the Prediction of Treatment Response?
Isabelle Loubinoux

*Stroke*. 2007;38:2032-2033; originally published online May 31, 2007;
doi: 10.1161/STROKEAHA.107.488908

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/38/7/2032

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/