Cluster correction and graphical user interface for support vector regression lesion-symptom mapping

Andrew DeMarco[1] and Peter Turkeltaub[1,2]

[1]Georgetown University Medical Center, Washington, DC, [2]MedStar National Rehabilitation Hospital, Washington, DC

Background

- Traditional VLSM (Bates et al., 2003) assumes voxelwise independence, but this is unwarranted given autocorrelation inherent to neuroimaging data non-random lesion distribution (Husain & Nachev, 2007).
- Recently, such a multivariate method, support vector regression (SVR-LSM), has outperformed traditional VLSM (Zhang et al., 2014)
- But limitations in usability, e.g., requires scripting, third-party SVR package (Chang & Lin, 2011), no cluster correction (Eklund et al., 2016)
- Lesion volume a confound in LSM analysis, but unclear when or how best to address it

1. We address these limitations and wrap the existing software in a graphic interface and improve usability
2. We explore lesion-volume as a confound for LSM and test the value of lesion-volume control methods

New Software Application

Adaptation of Zhang et al. (2014), with new features:

- Clusterwise FWE correction via permutation testing
- Flexible covariate handling via nuisance models
- Computation completely within MATLAB
- Load/save config files, parallel processing, output summary, model diagnostics
- github.com/atdemarco/svrlsmgui

DOWNLOAD SOFTWARE

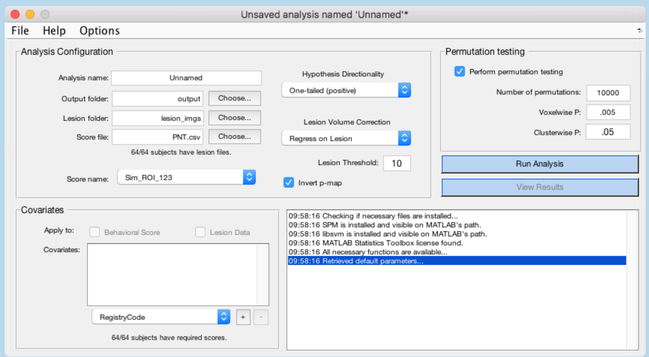

Fig 1. Screenshot of MATLAB-based graphical user interface for SVR-LSM.

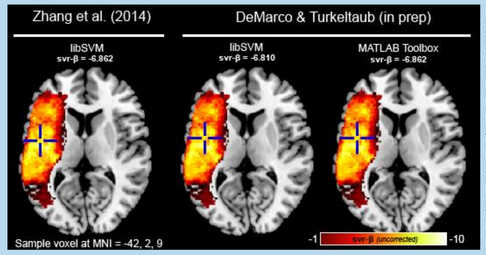

Fig 2. Uncorrected SVR-β output for original SVR-LSM, new implement-tation using libSVM and MATLAB's SVM functionality; individuals with chronic left-hemisphere stroke (N = 48) modeling WAB Repetition.

- New SVR-LSM implementation replicates previous implementation, MATLAB SVR highly similar

Lesion Volume Control Methods

- Software permits four methods to control for lesion volume as a confound, in addition to no control
- Optimal application of correction not clear

#	Method	Corrects behavior	Corrects lesion data
1	No correction	✗	✗
2	dTLVC (Zhang et al., 2014)	✗	Partial
3	Regress on Behavior	✓	✗
4	Regress on Lesion	✗	✓
5	Regress on Both	✓	✓

Where Is Lesion Volume A Problem?

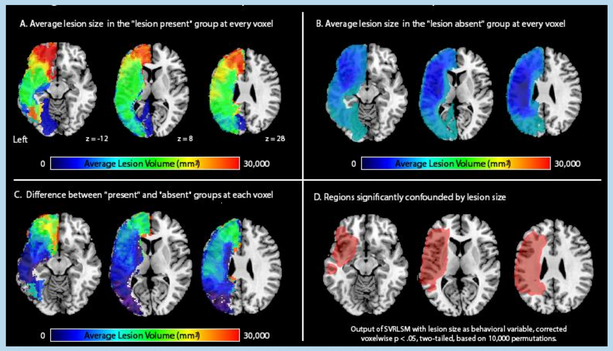

Fig 3. Regional bias of lesion size in individuals with left-hemisphere stroke (N = 48). Maps of average lesion size in (A) "lesion present" group, (B) "lesion absent" group, (C) difference between lesion size in A and B, and (D) regions where lesion size is significantly different (red outline), voxelwise, $p < .05$ (two-tailed), based on 10,000 permutations

- Bias contributed by lesion volume as a confound evident throughout entire left-hemisphere, and statistically significant in much of MCA territory

Volume Control Methods Compared

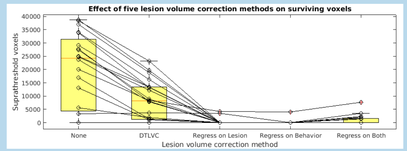

Fig 4. Spaghetti plot of effect of 4 lesion volume correction methods on 20 behaviors in individuals with left-hemisphere stroke (N = 49), voxelwise $p < .005$, clusterwise $p < .05$, 10,000 perms.

- Many results with no correction, dTLVC more modest. Regression methods most conservative, Regress on Both most sensitive (Fig 4)

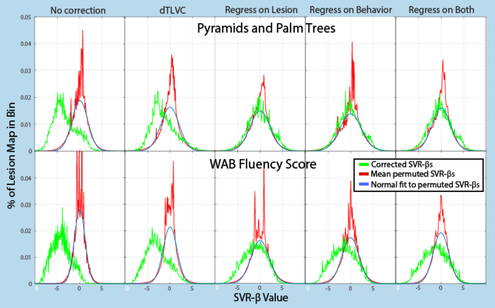

Fig 5. Histograms of uncorrected βs after correction (green) for two behaviors, Pyramids and Palm Trees (top), WAB Fluency (bottom), and average histogram of 1000 permuted SVR-β maps (red).

- Bias evident in uncorrected and dTLVC histograms, but eliminated in regression methods (Fig 5)

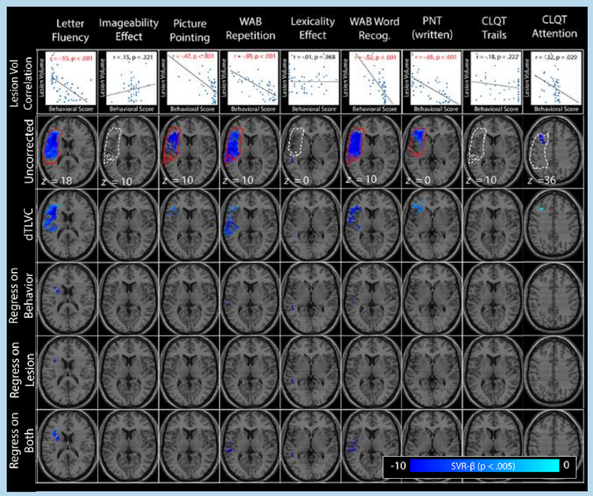

Fig 6. Lesion size correlations for nine behaviors measured in left-hemisphere stroke survivors (N = 48); thumbnails of suprathreshold SVR-β values (voxelwise, p < .005)for five lesion correction methods. Top row depicts significant correlation (p < .05) with lesion volume (red outline) and not (dotted white outline).

- Many findings similar to lesion bias confound in uncorrected and dTLVC images (Fig 6) when behavior correlated with lesion volume
- With Regression, these findings eliminated

Effects of Correction on Localization

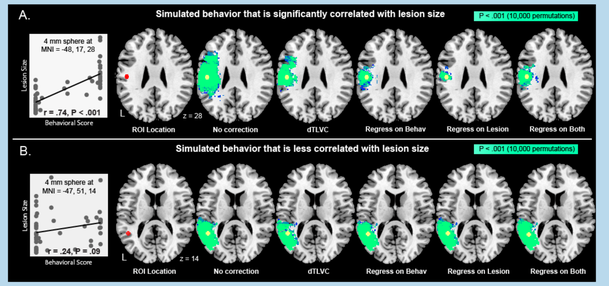

Fig 7. Effect of lesion size corrections on localization for (A) simulated behavior correlated with lesion size and (B) simulated behavior less correlated with lesion size. Behaviors simulated by counting lesioned voxels in 4mm sphere (red) placed based on correlation with lesion size, voxelwise p < .001 on 10,000 perms (green).

- Improved spatial specificity for behavior correlated with lesion volume, no qualitative differences in behavior less correlated with lesion volume

When To Correct for Lesion Volume?

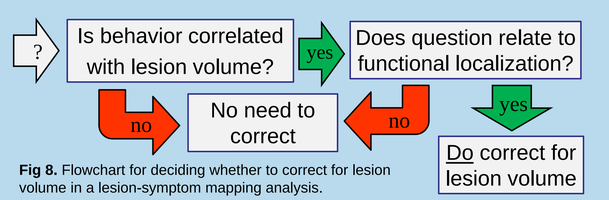

Fig 8. Flowchart for deciding whether to correct for lesion volume in a lesion-symptom mapping analysis.

Conclusions

1. This new release of SVR-LSM enables easier, flexible multivariate lesion-symptom mapping
2. Lesion volume bias is widespread; correction via regression can improve spatial specificity; Regress on Both Behavior and Lesion most sensitive

Acknowledgments

We thank Ze Wang for providing the SVR-LSM software. We also thank Elizabeth Lacey, Zainab Anbari, Mackenzie Fama, and Kate Spiegel for data collection. The research was supported by the Doris Duke Charitable Foundation (grant #2012062), NIH/NCATS via GHUCCTS (KL2TR000102 and TL1TR001431), and by the NIDCD (R01DC014960).

SELECTED REFERENCES

Zhang, Kimberg, Coslett, Schwartz & Wang (2014). *Human Brian Mapping,*
Mah, Husain, Rees, & Nachev (2014). *Brain*, 137(9): 2522-2531.
Husain & Nachev (2007). *Trends in Cog Neurosci*, 11(1): 30-36.
Chang & Lin (2011). *TIST,* 2(3): 27.
Eklund, Nichols, & Knutsson (2016). *PNAS*, 113(28): 7900-7905.
Bates, Wilson, Saygin, Dick, Sereno, Knight, & Dronkers (2003). *Nature Neurosci, 6(5):* 448-450.