Facilitating neuroimaging marker discovery and validation: The predictive mapping approach

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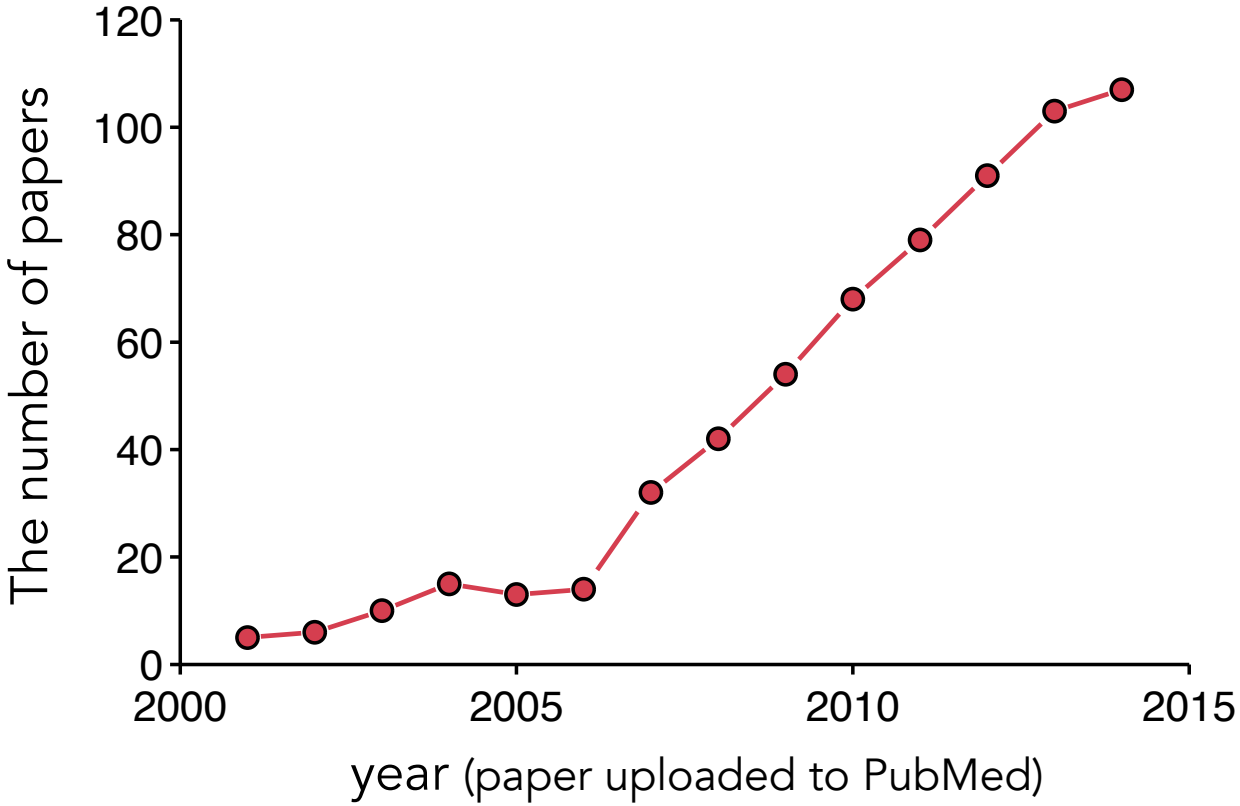
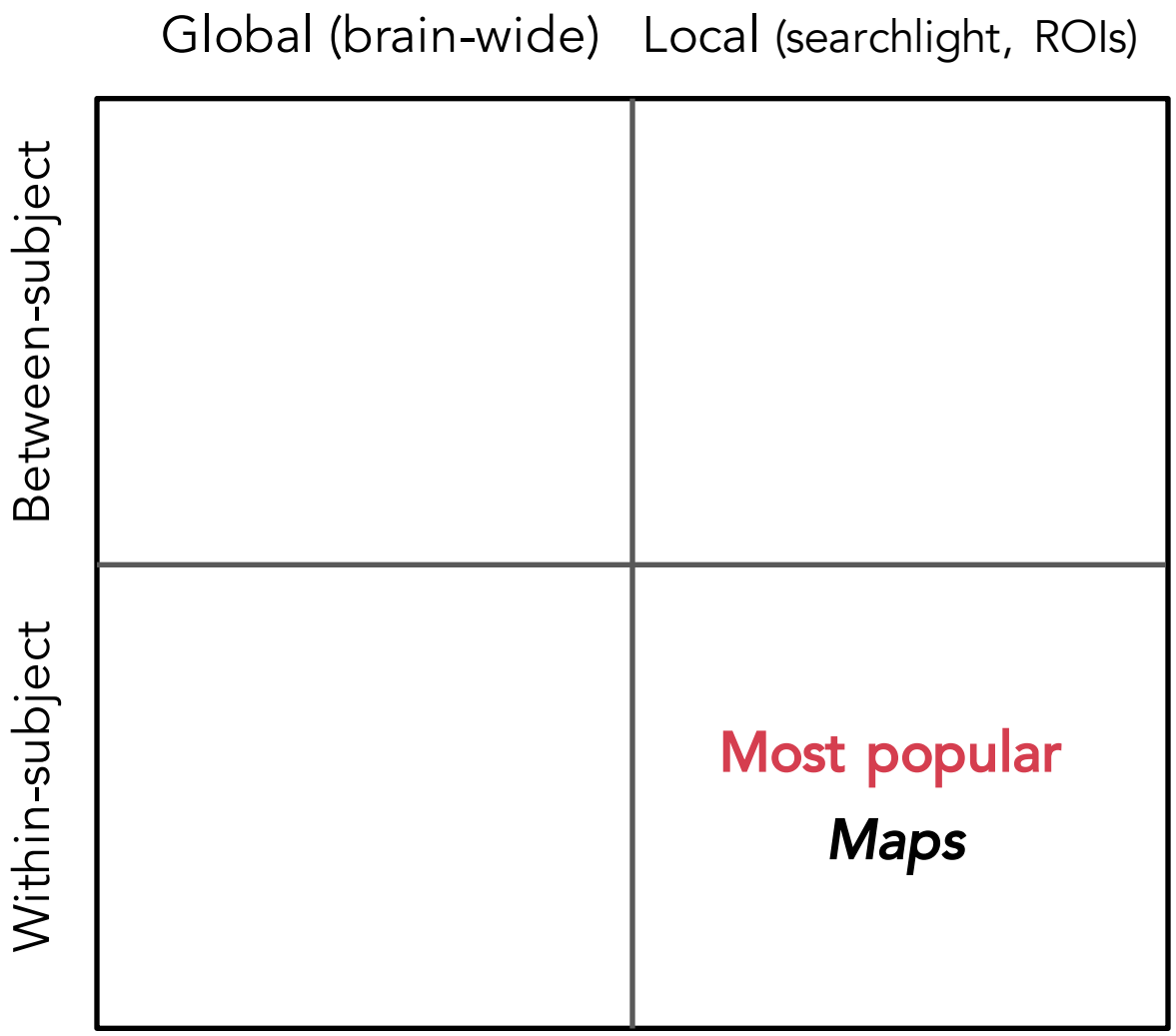
Multivariate pattern analysis (MVPA) has become very popular!

- PubMed search: (multivariate pattern analysis) AND (fMRI)



There are different MVPA approaches



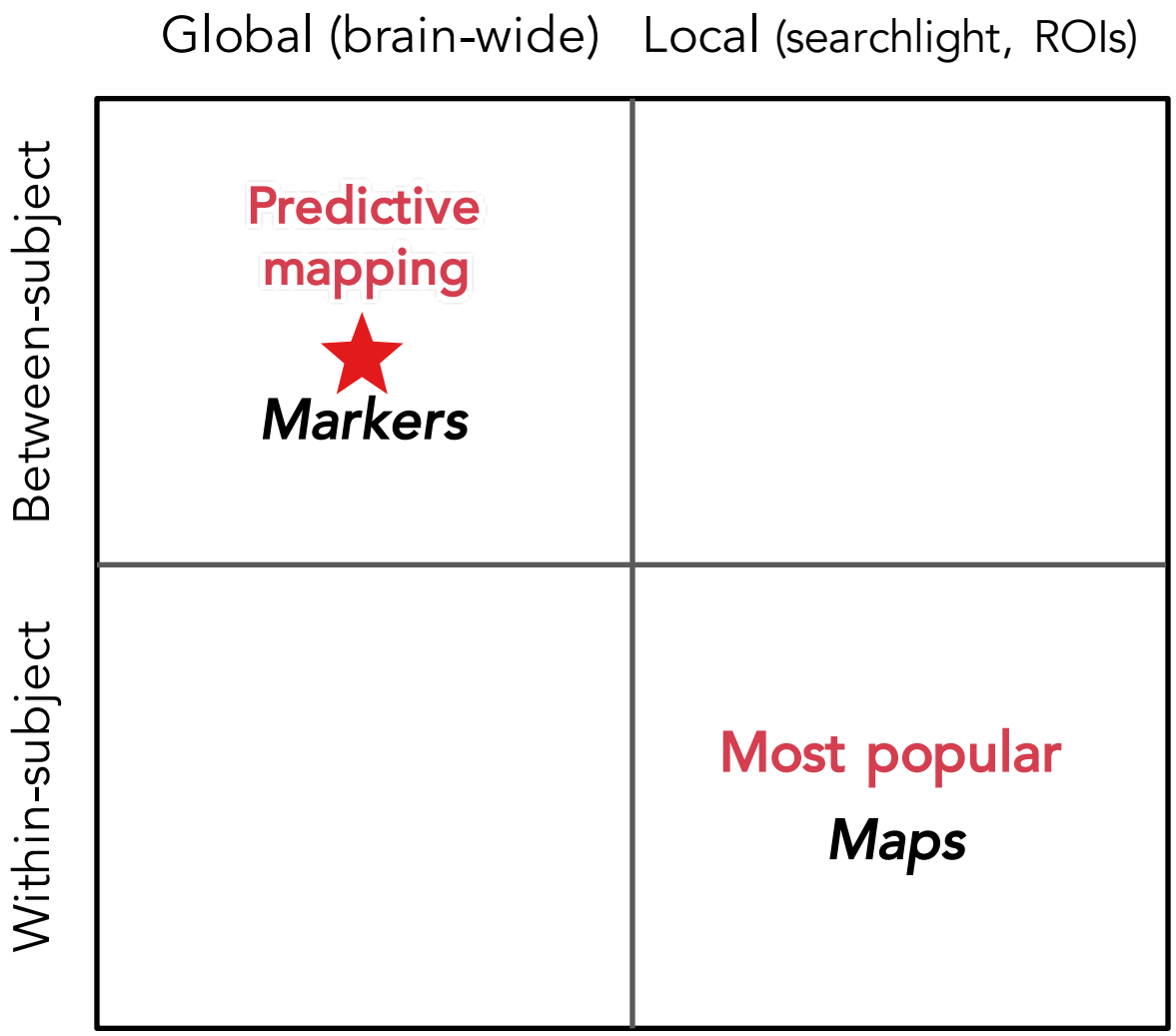
studies

	G	L
B	29	6
W	12	83

Figure 3

"Identifying anatomical regions associated with particular mental processes"

There are different MVPA approaches



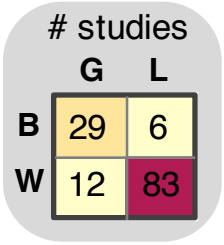
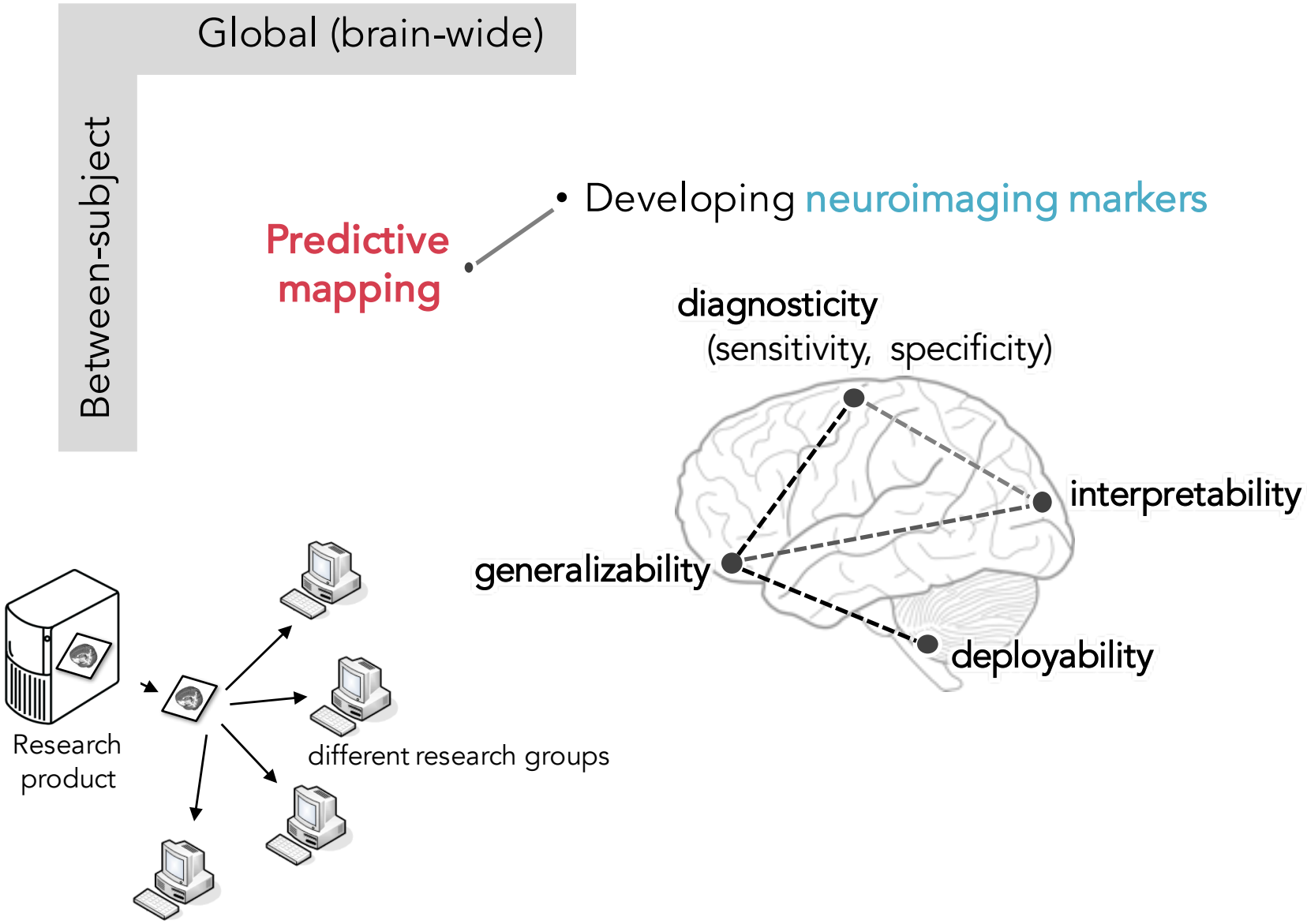


Figure 3

"Identifying multivariate patterns of brain activity optimized to be predictive of, and sensitive and specific to, a particular type of mental process"

There are different MVPA approaches



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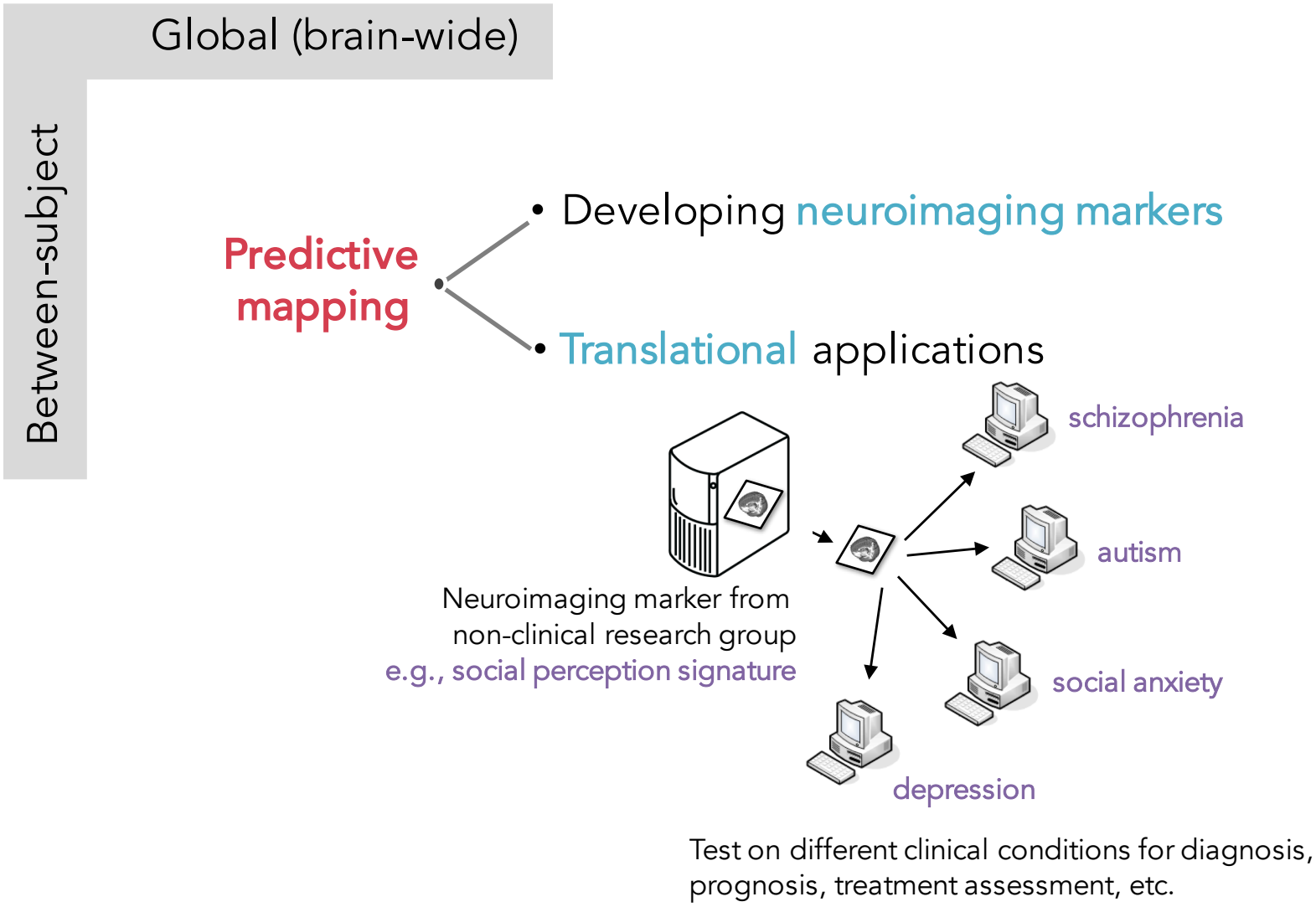
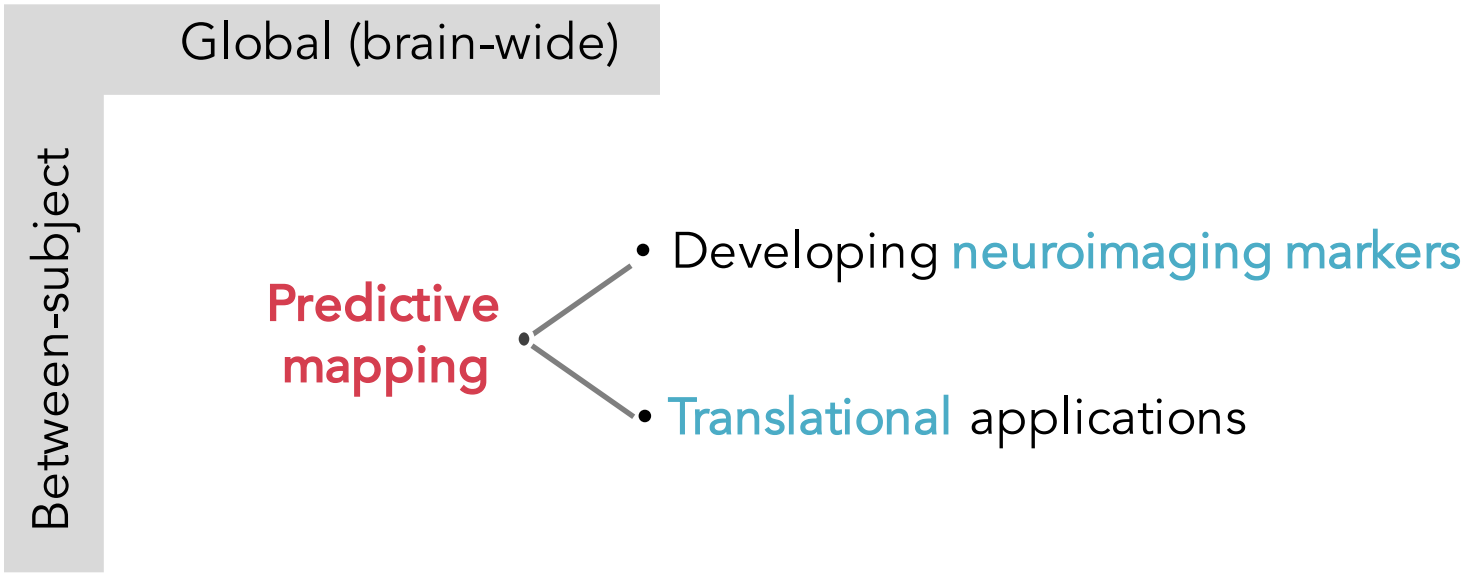
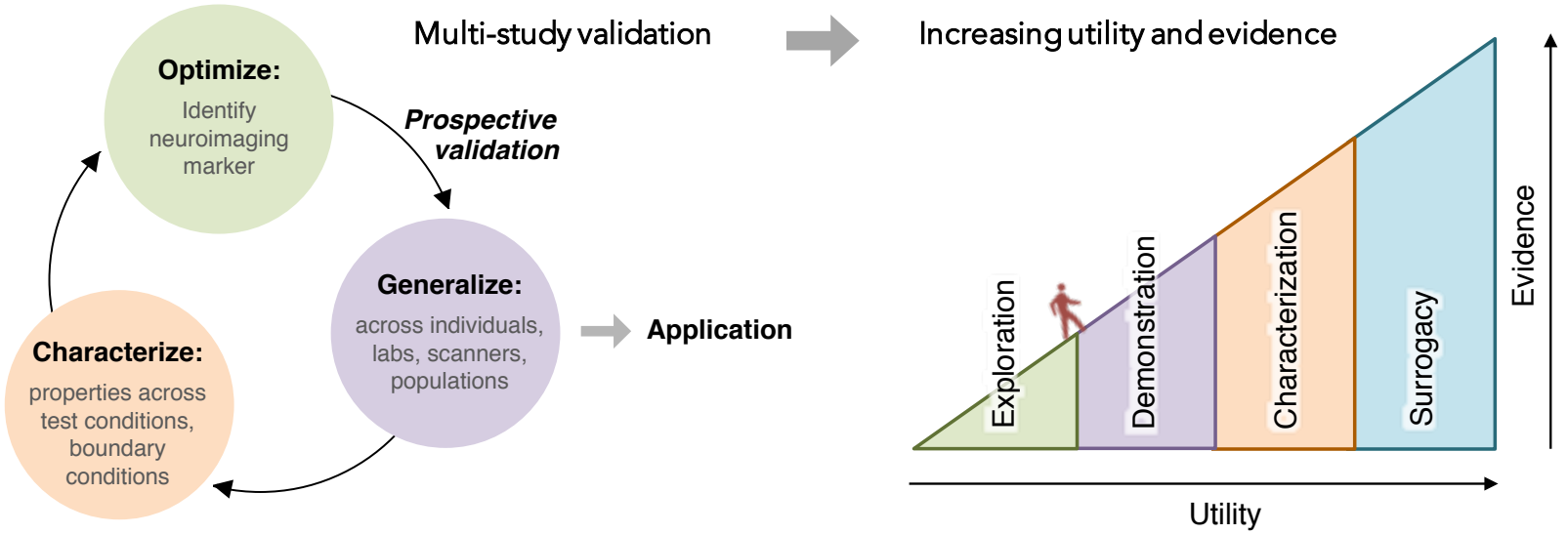


Multi-study validation of neuroimaging markers





Review paper summary

- Introduced the predictive mapping approach (basic concepts)

  Predictive mapping: a type of multivariate pattern analysis (MVPA) combined with experimental designs optimized for marker development

  It aims to develop multivariate, system-level predictive models that are sensitive and specific to particular outcomes of interest and can be prospective tested on new individuals and new study samples.

Review paper summary

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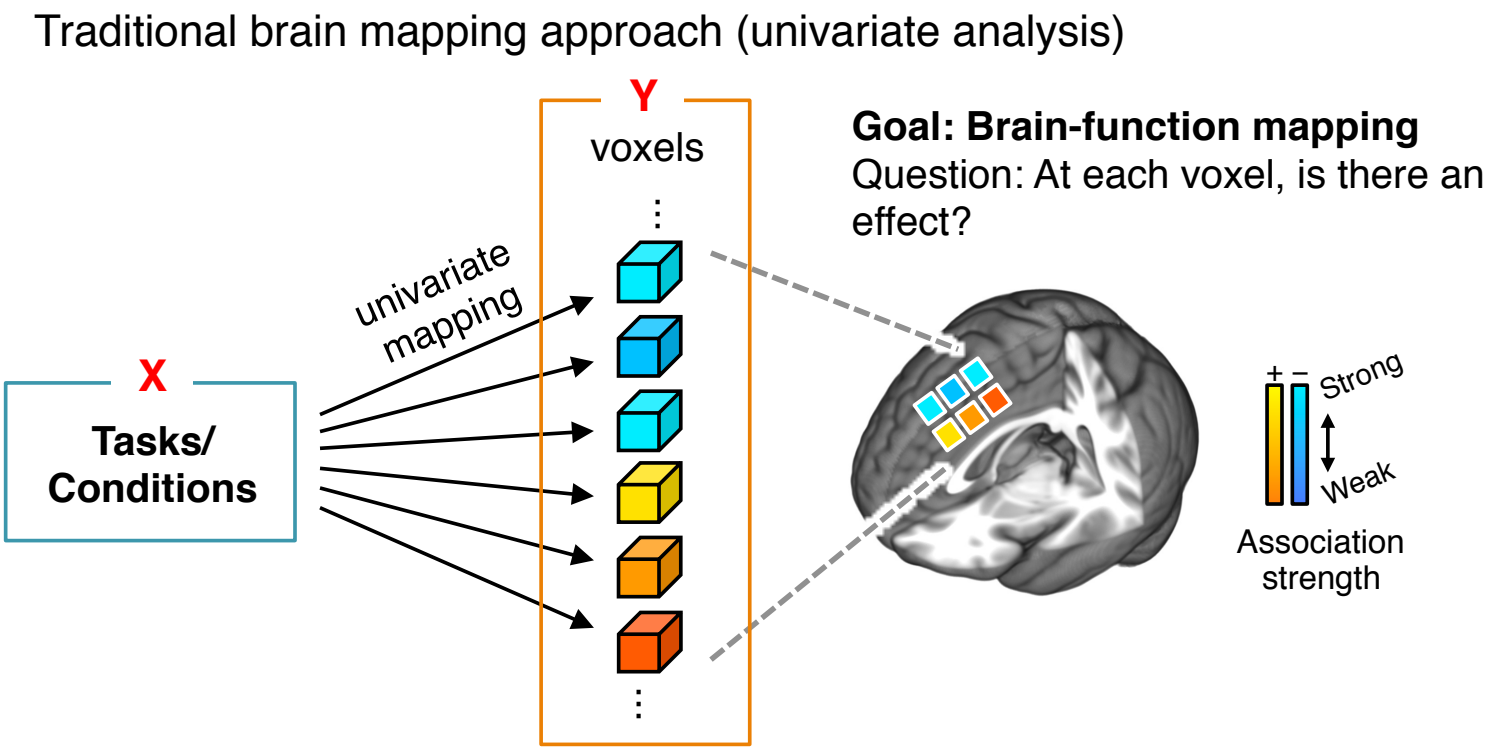
- by contrasting it to traditional mapping (univariate analysis) and information-based mapping



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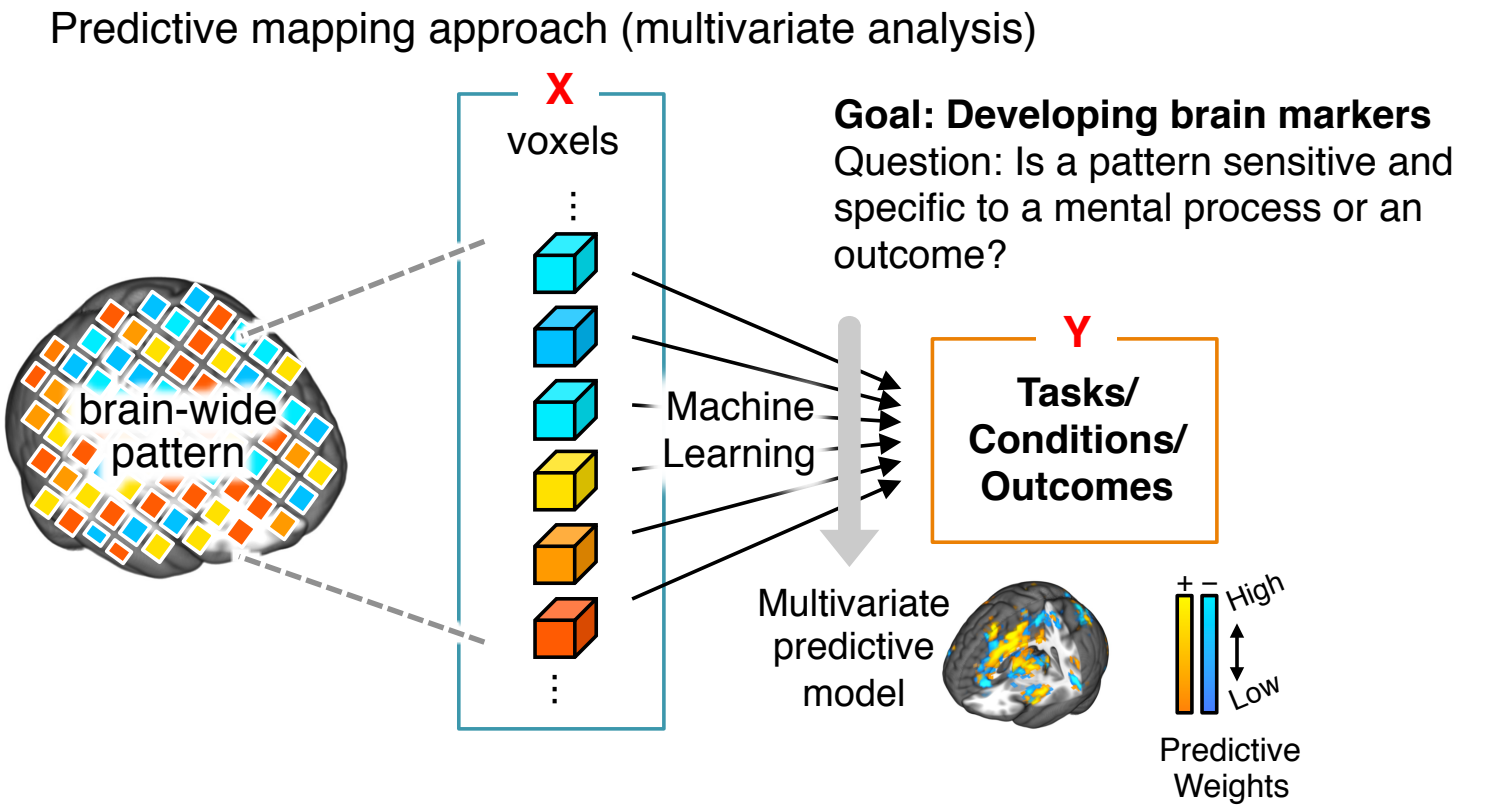

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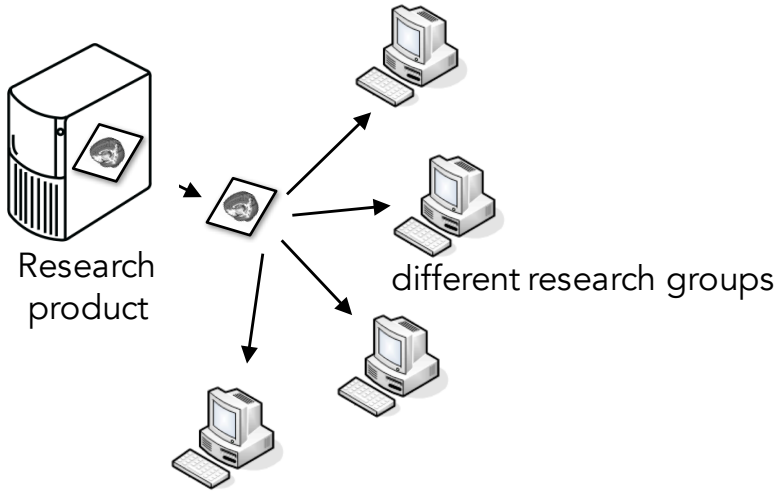

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Development Stages	Criteria	Definition	Test setting
Discovery	1 Diagnosticity	Sensitivity: positive results when a target psychological or behavioral process is engaged	Positive control
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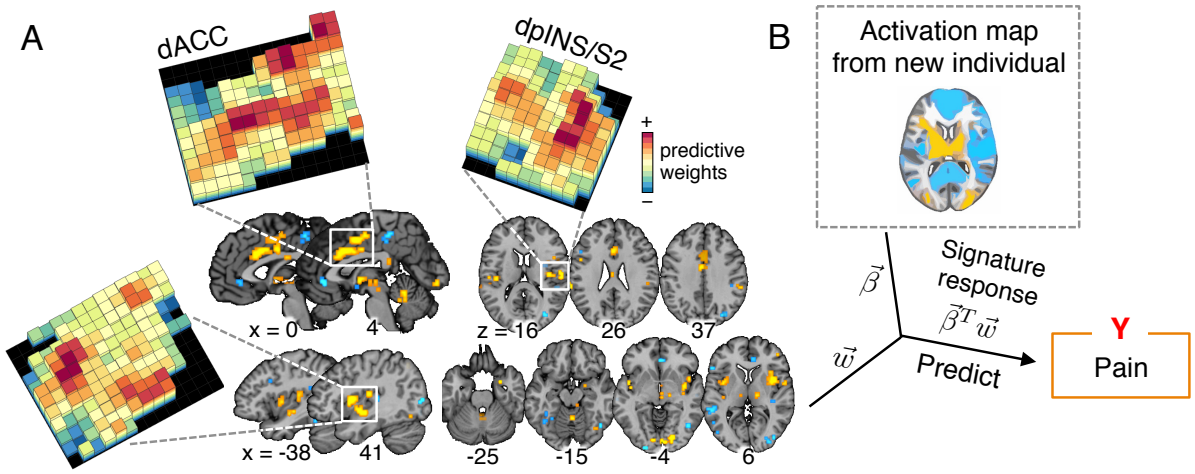
Figure 7



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- Presented literature survey results and discussed broader implications and recommendations

Figure 1

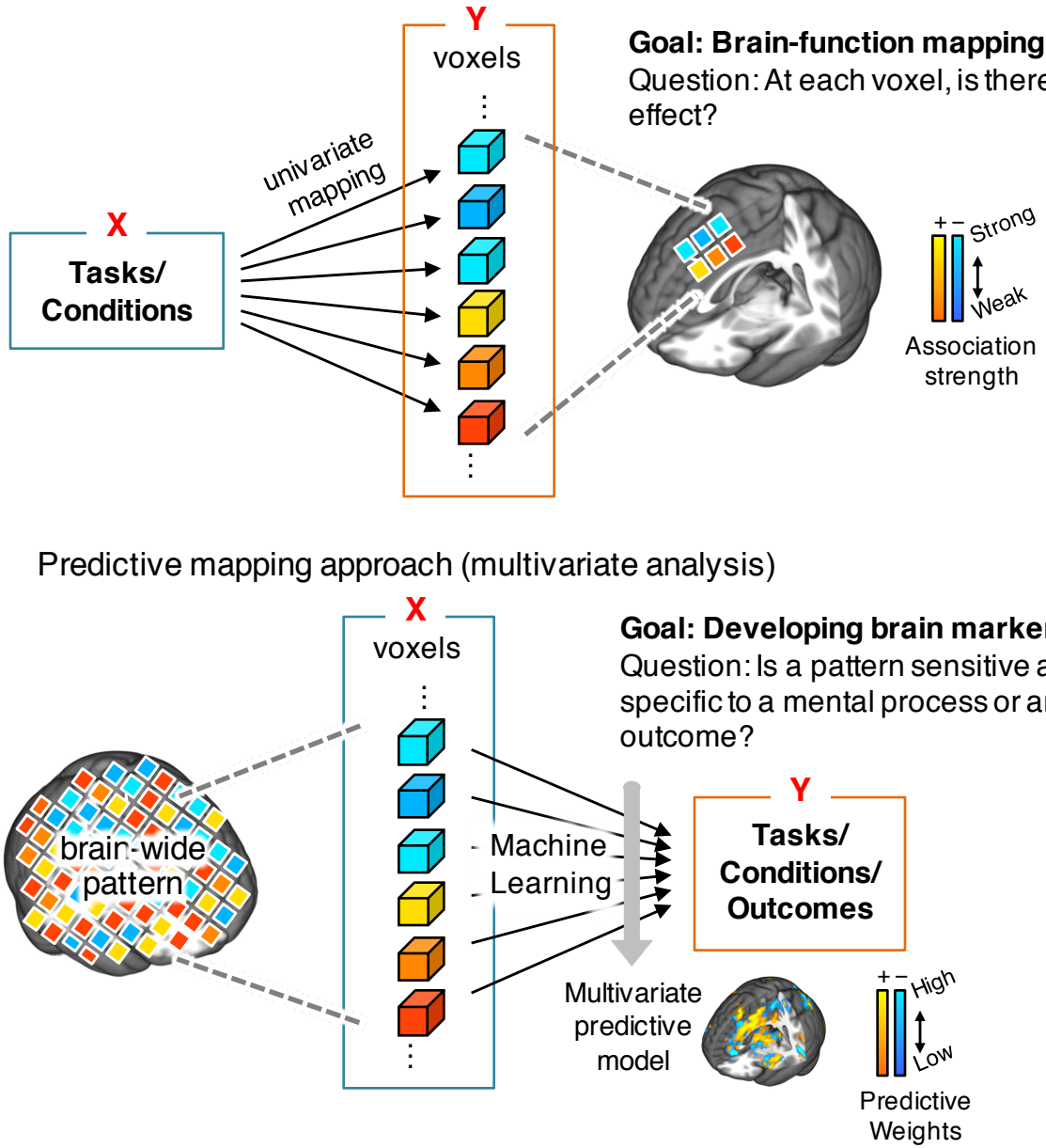

Figure 1. Traditional versus predictive mapping approach. A. Traditional mapping (univariate analysis) aims to obtain the functional architecture of the brain by localizing the effects in the brain. This approach is often suffers from low sensitivity and specificity. **B.** The predictive mapping approach aims to develop a multivariate, brain-wide prediction (decoding) model that is sensitive and specific to the outcomes-of-interest.

Figure 2

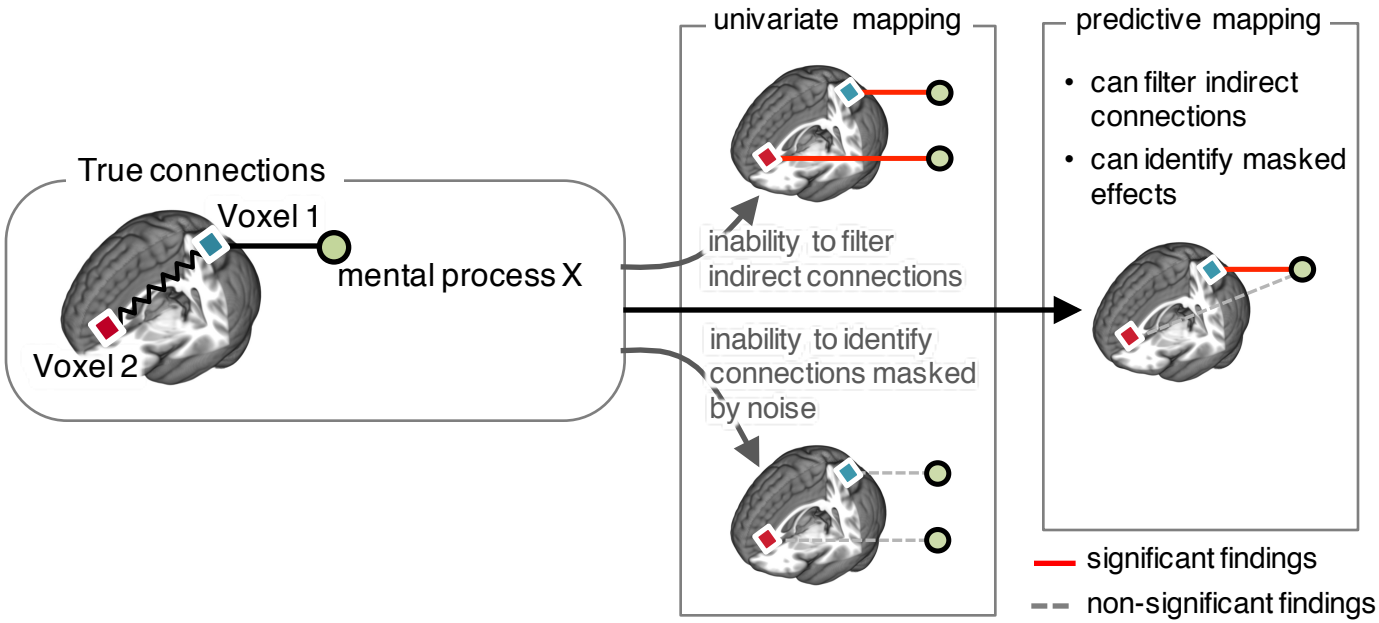

Figure 2. Benefits of predictive mapping. There are a number of scenarios under which predictive mapping yields higher power and more accurate representation of brain-outcome relationships than traditional (univariate) mapping. We illustrate one such scenario here, in which there is a direct relationship between Voxel 1 and the outcome (mental process X), and a correlation between Voxel 1 and Voxel 2 that reflects a common source of noise unrelated to the outcome. In the top panel, univariate mapping may identify significant effects in both voxels, as it cannot separate regions with indirect connections to X from those that have more direct relationships. The predictive mapping approach controls for Voxel 1 when assessing the effects of Voxel 2, and so will not spuriously identify Voxel 2 as significant. In addition, controlling for Voxel 2 can remove some of the noise in Voxel 1, which may otherwise mask the relationship between Voxel 1 and X and prevent it from reaching significance (bottom panel). For both reasons, under this scenario, the predictive mapping approach has a greater chance of identifying the true relationships.

Figure 3

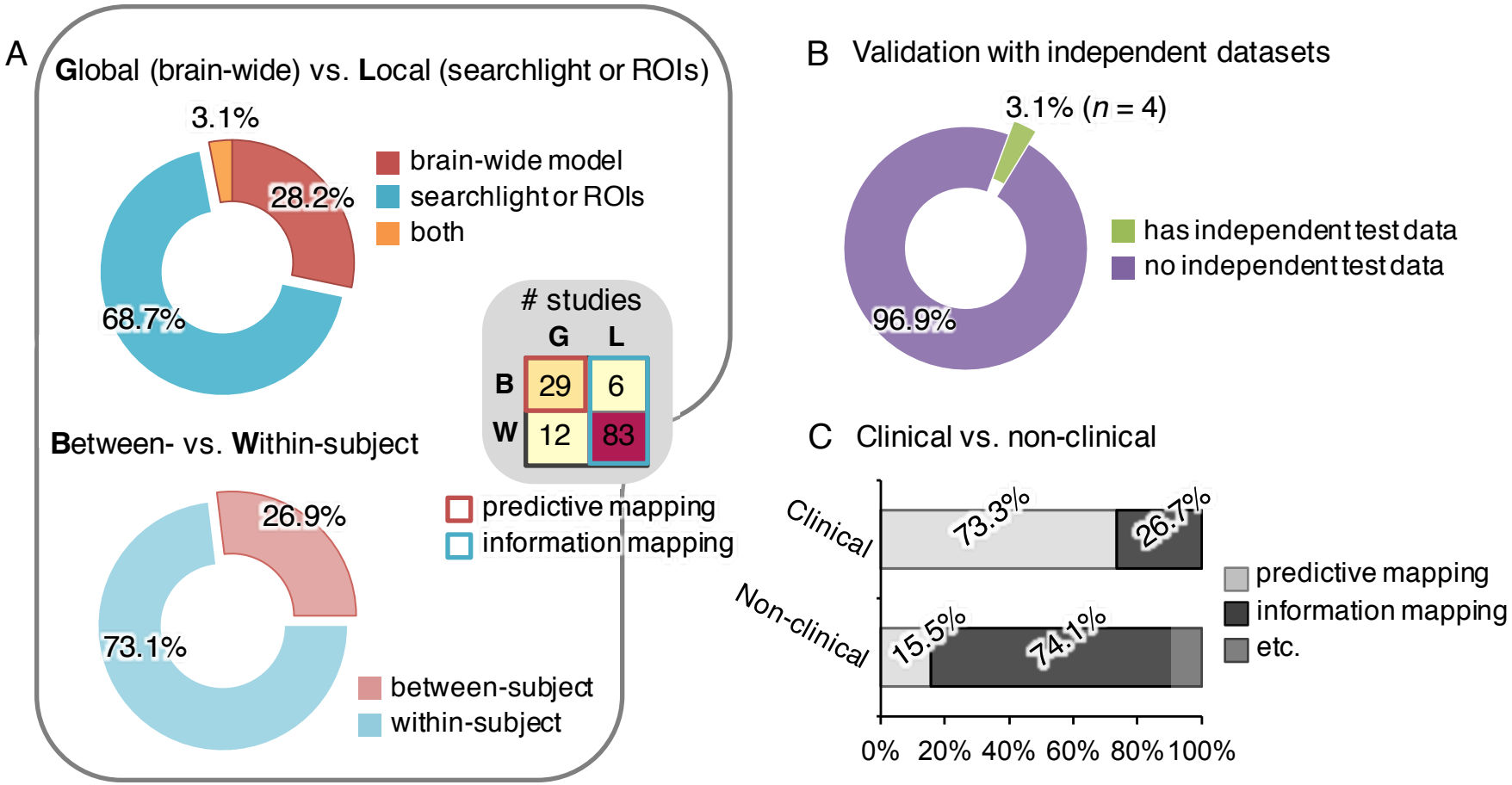

Figure 3. Survey results. We conducted a literature survey of recent fMRI studies that used multivariate pattern analysis (N = 131 studies published between Jan 2014 and Jun 2015). **A.** The proportion of studies using brain-wide vs. local region information (top) and between- vs. within-subject information (bottom). The table in the middle panel shows the number of studies for each combination of conditions. The cell within the red outlined box indicates predictive mapping (global and between-subjects), while the cell within the blue outlined box indicates information mapping (local). **B.** The proportion of studies that have independent test datasets. **C.** The proportion of studies using the predictive mapping approach for clinical vs. non-clinical (basic) studies.

Figure 4

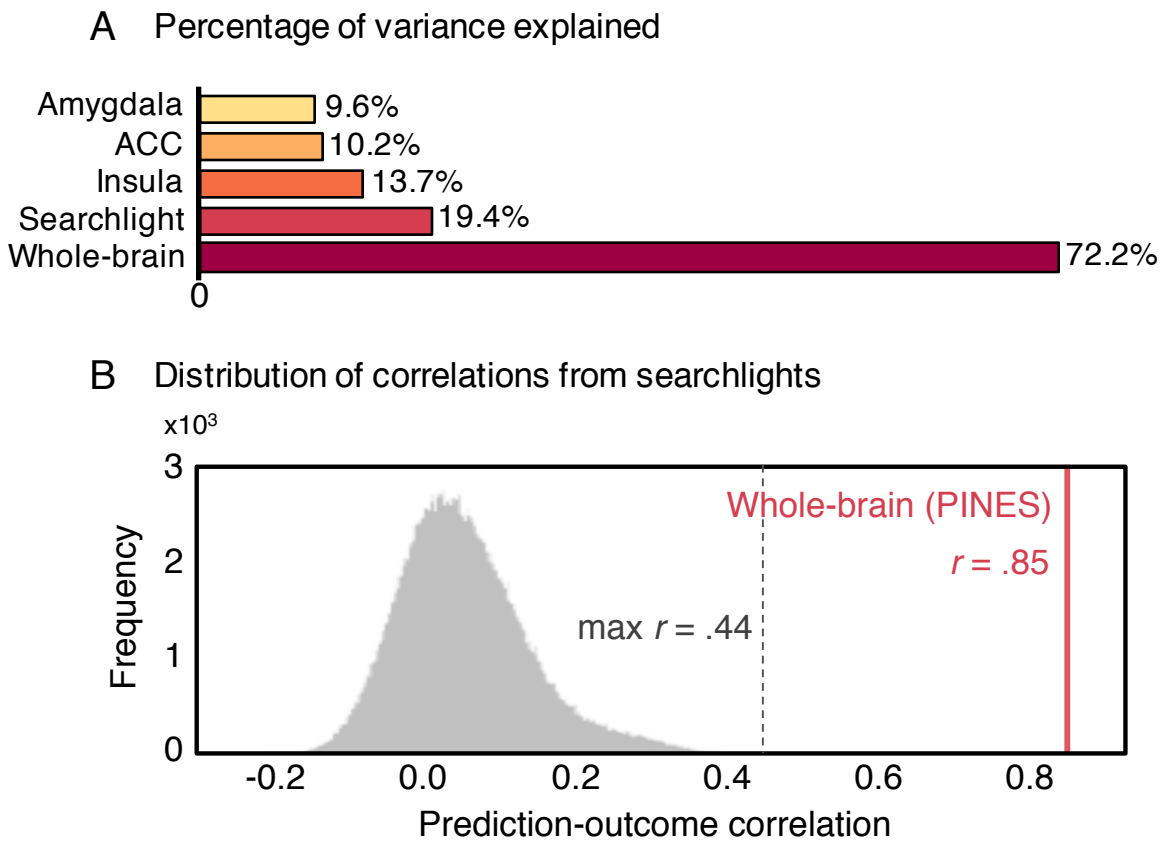

Figure 4. An example of predictive performance with the whole brain versus local regions (Reproduced from [21]). **A.** The percentage of variance explained by predictive models based on local regions vs. the whole brain when predicting negative emotion ratings induced by aversive pictures. Local regions include amygdala, anterior cingulate cortex (ACC), insula, and searchlights (sphere with 5 voxel radius). **B.** Distribution of prediction-outcome correlations from searchlights. The dashed line represents the maximum correlation when searchlights used, and the red line shows the prediction-outcome correlation with the whole brain.

Figure 5

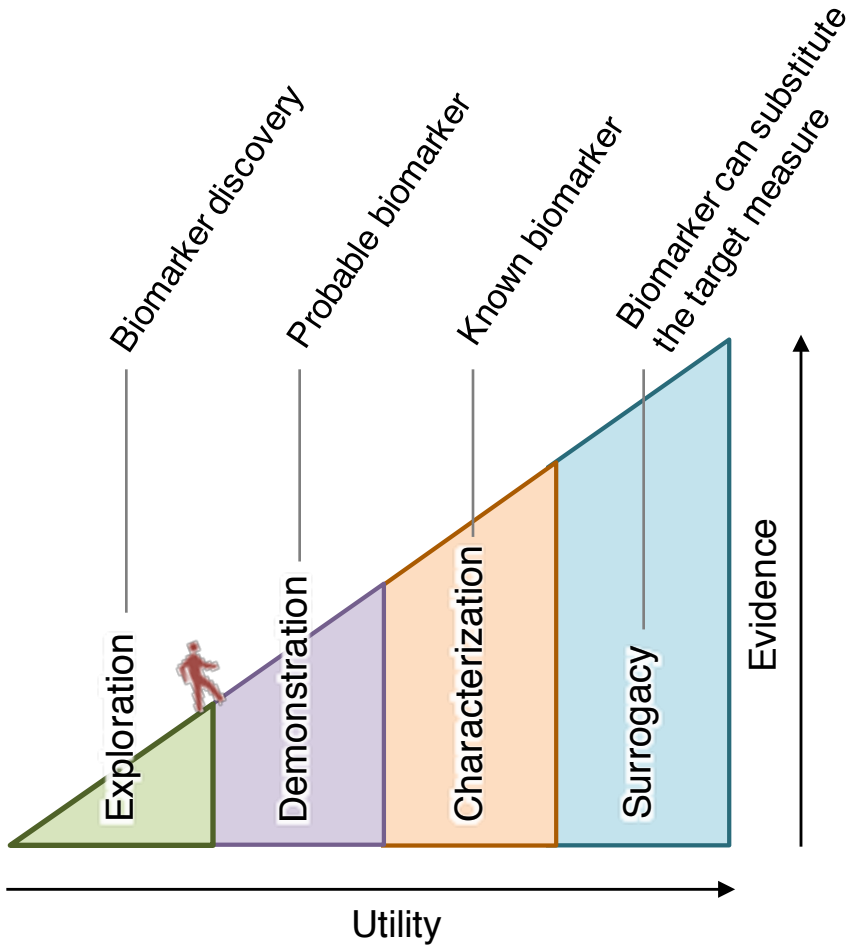

Figure 5. To be a useful neuroimaging marker, it needs to demonstrate increasing levels of supporting evidence and generalizability through multiple stages. Therefore, establishing neuroimaging markers requires a long development and validation process supported by multi-study and multi-site efforts (Reproduced from [35]).

Figure 6

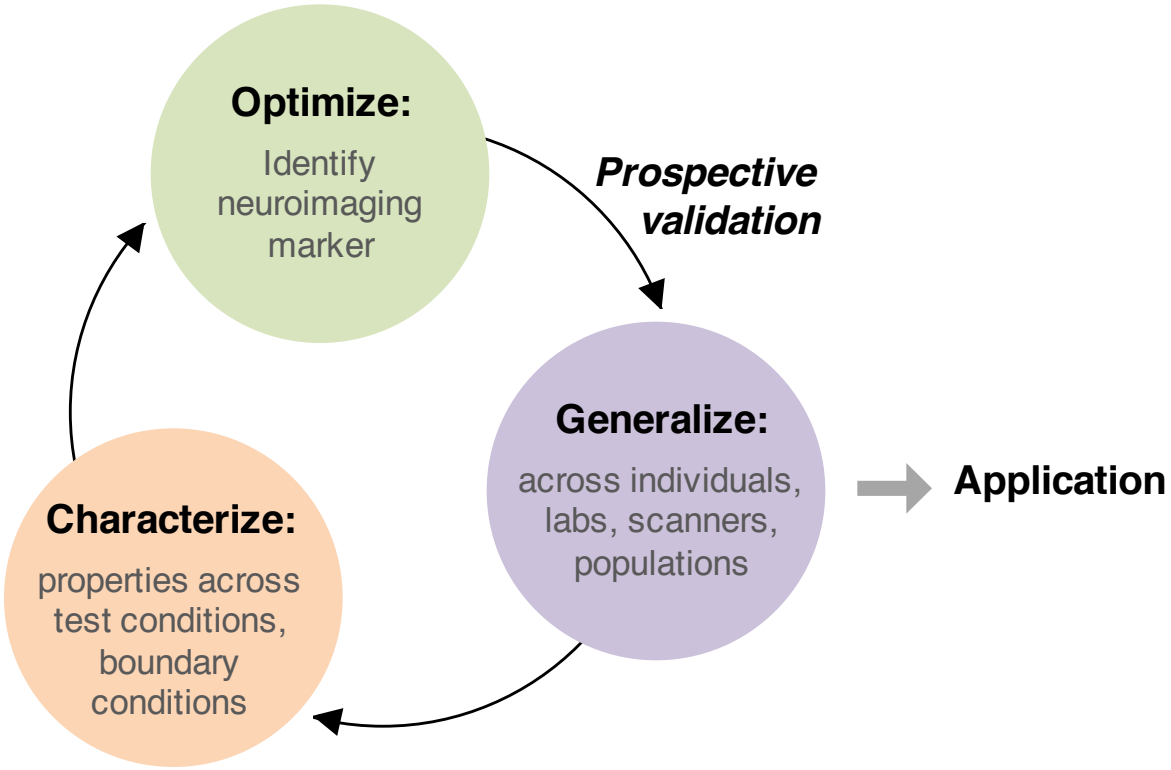

Figure 6. Neuroimaging marker development and validation process. This process can be described as an iterative process of optimization, generalization, and characterization (for details, see text).

Figure 7

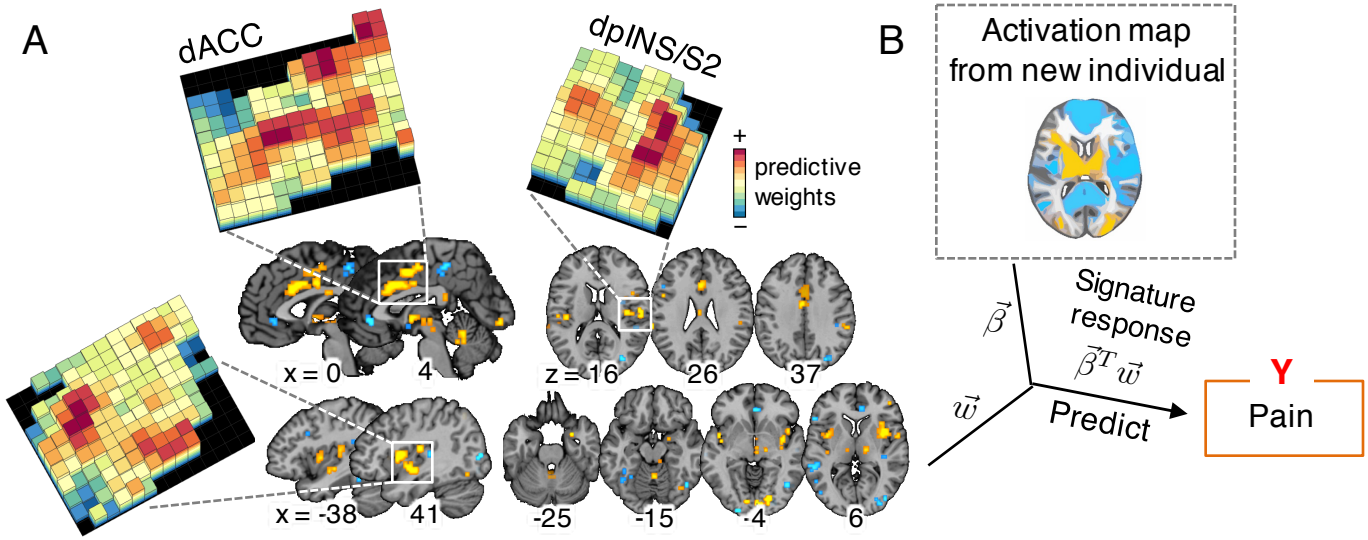

Figure 7. The Neurologic Pain Signature (NPS). The NPS is defined by brain-wide, meso-scale patterns of fMRI activity across multiple pain-related regions, and can be prospectively tested on new individuals and datasets. The brain map shown here is the thresholded pattern map ($q < 0.05$, false discovery rate [FDR]) for display only. All voxels within NPS should be used to predict pain in new individuals. Some examples of unthresholded patterns are presented in the insets; each 3-d bar represents one voxel. dACC, dorsal anterior cingulate cortex; INS, insula; dpINS, dorsal posterior insula; S2, secondary somatosensory cortex. Reproduced with permission from [20].

Figure 8

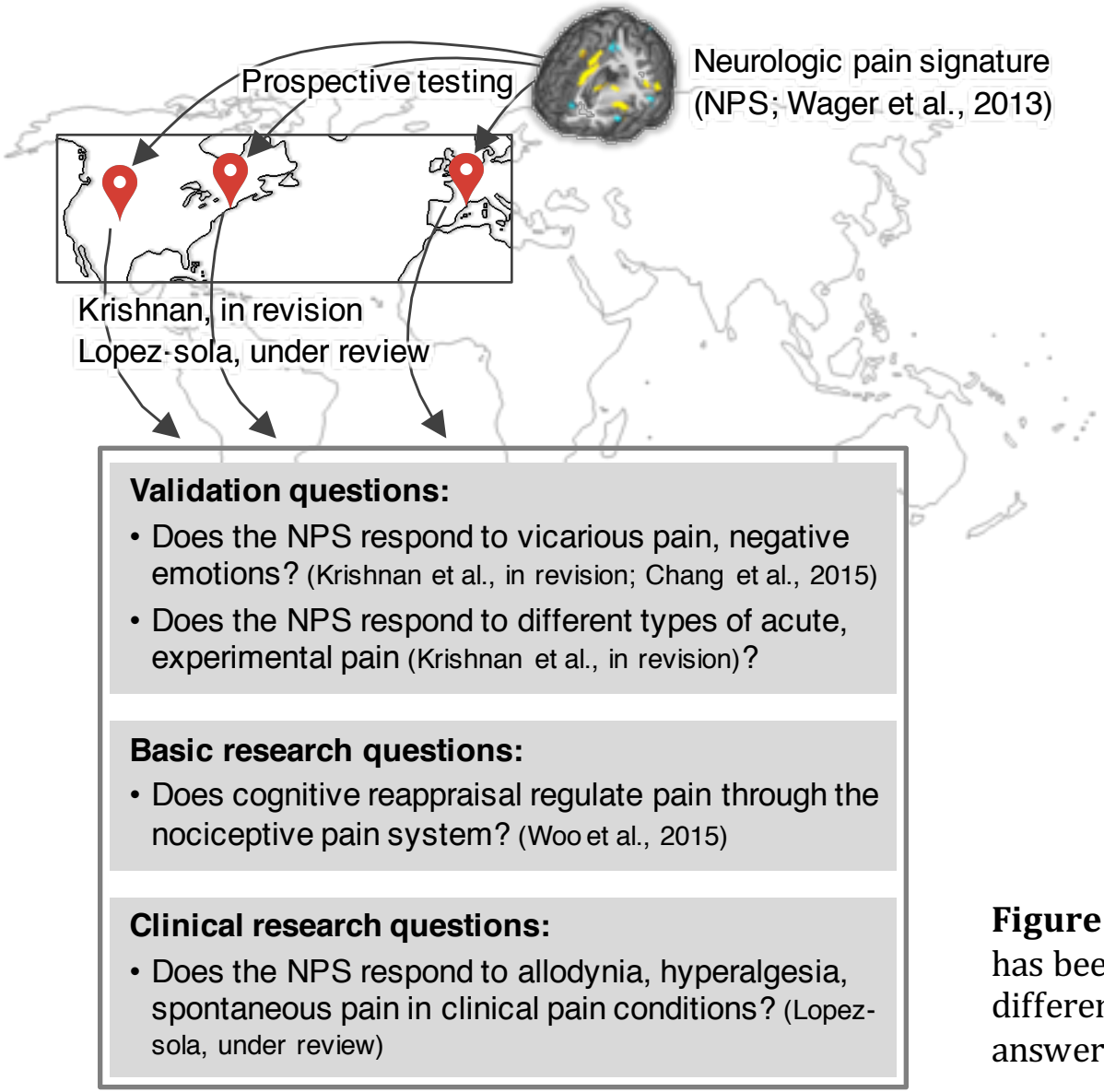

Figure 8. Deployability of the NPS. The NPS has been applied and tested on datasets from different laboratories around the world to answer different types of research questions.

Table

Table. Desirable characteristics of neuroimaging biomarkers

Development Stages	Criteria	Definition	Test setting
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