Anatomical Phenotyping and Staging of Brain Arteriovenous Malformations

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INTRODUCTION

- **Background:** Brain arteriovenous malformations (AVMs) are vascular anomalies that predispose patients to life-threatening intracranial hemorrhage.
- **Clinical need:** Clinical decision-making requires balancing the natural risk of hemorrhage against the risks of treatment. Yet, existing risk stratification relies on isolated imaging markers and fails to account for the dynamic spatiotemporal complexity of AVMs.
- **Hypothesis:** Building on our prior work, demonstrating how ontogenesis dictates the spatiotemporal organization and clinical outcomes of neuroepithelial tumors, we hypothesize that AVMs arise at distinct ontogenetic inflection points where morphogenesis deviates from its physiological trajectory. The timing and anatomical context of this disruption define a pathologically affected ontogenetic unit that determines the AVM's three-dimensional evolution and clinical behavior. **(Fig. 1)**
- **Aim:** To develop an integrative anatomical staging system to improve hemorrhage risk prediction.
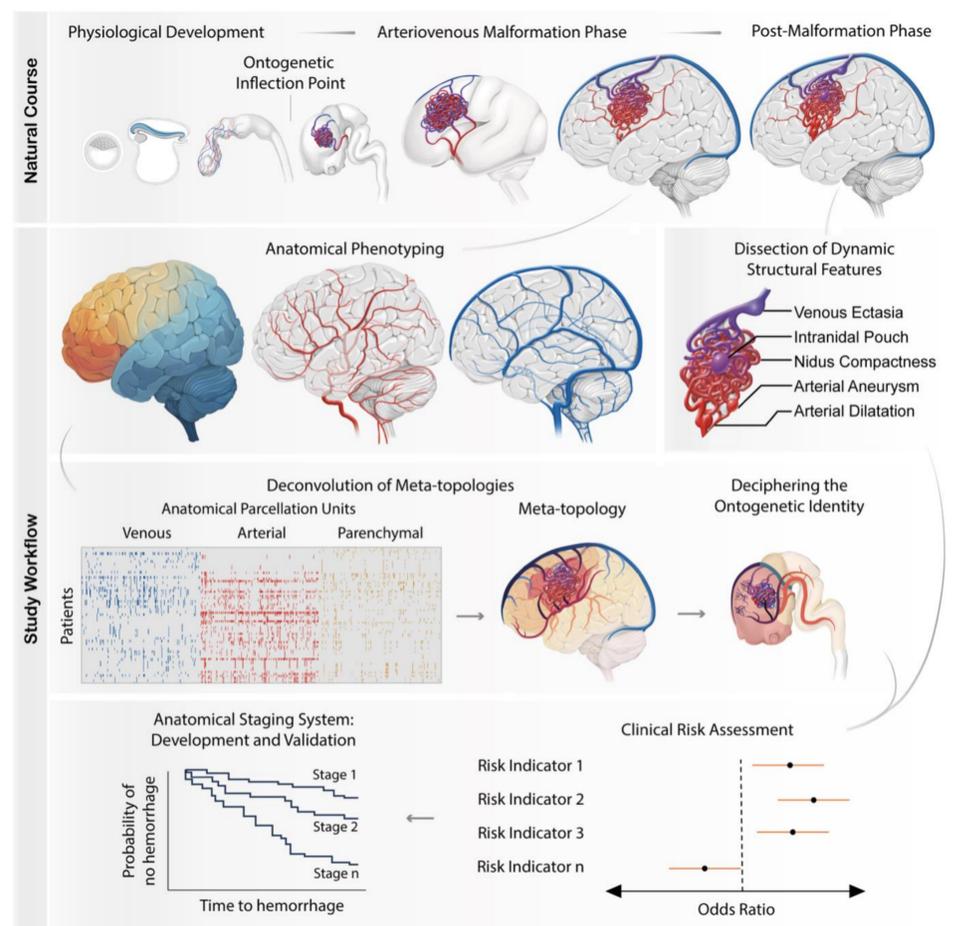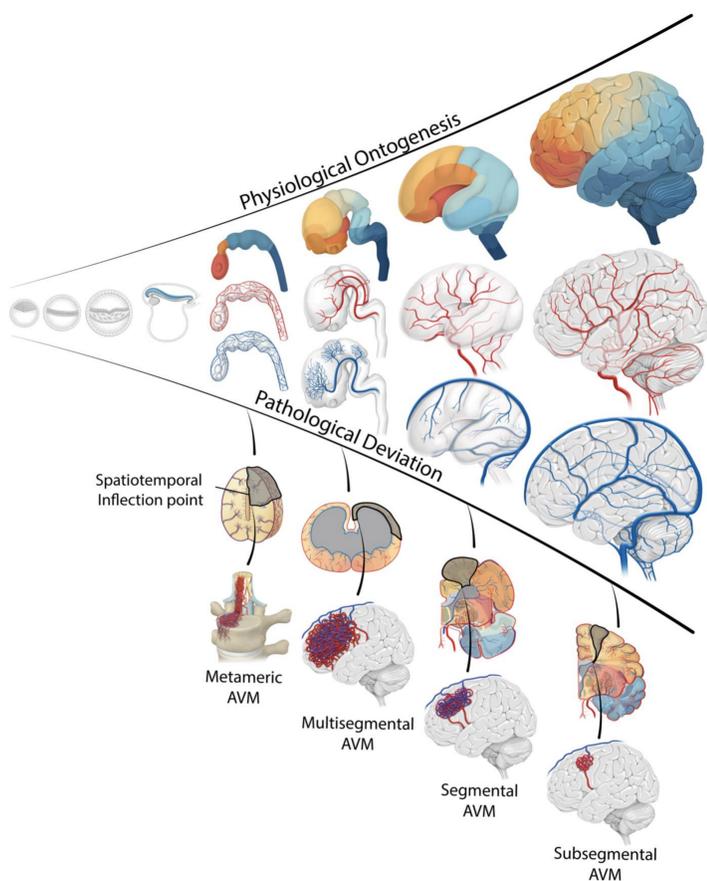

Fig. 1: Spatiotemporal Ontogenetic AVM Identity.

METHODS

This is a multicenter retrospective and prospective observational study with a sequential workflow **(Fig. 2):**

1. **Anatomical phenotyping** of parenchymal, arterial, and venous architecture.
2. **Unsupervised NNMF** to identify higher-order AVM meta-topologies.
3. **Ontogenetic mapping** of meta-topologies to embryological units.
4. **Integration of dynamic structural features** (e.g., aneurysms, nidus compactness, venous ectasia).
5. **Risk stratification** and **development of the anatomical staging system**.

Fig. 2: The Multidimensional Spatiotemporal Approach.

PILOT DATA

- **Anatomical phenotyping and ontogennetic mapping:** AVMs showed distinct parenchymal, arterial, and venous distributions with volume-normalized analyses demonstrating particularly high AVM localization to the central region cerebellar structures. Ontogenetic mapping revealed phase-specific developmental clustering, predominantly affecting prosencephalic and pallial derivatives.
- **Meta-topologies and risk assessment:** NNMF identified six biologically plausible AVM meta-topologies. Deep seated and infratentorial meta-topologies were associated with increased hemorrhage risk, whereas frontal meta-topologies showed a protective association.
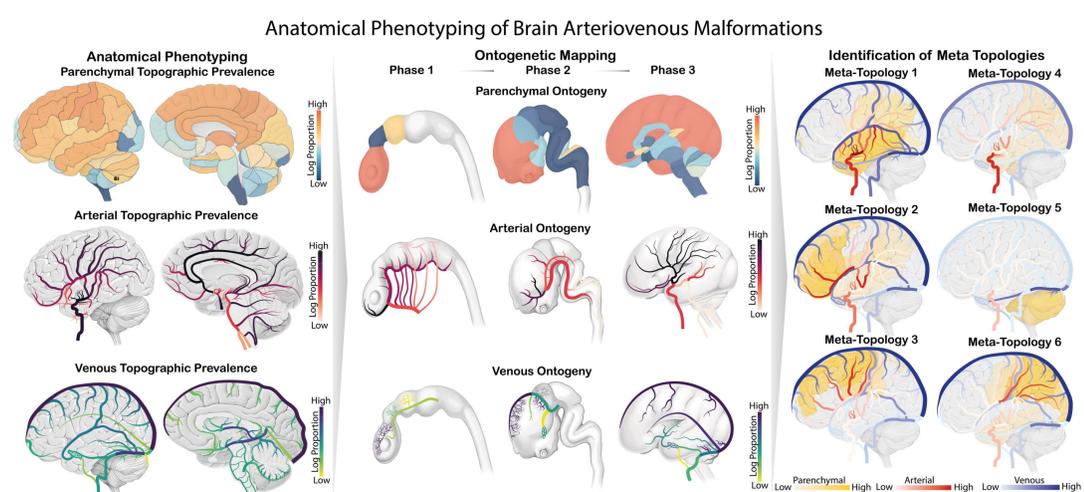

Fig. 3: Pilot Data Results

OUTLOOK

This study is designed as a multicenter effort with both retrospective and prospective enrollment, aiming for a total sample size of approximately 1,000 patients. This is essential to enhance the granularity, reproducibility, and clinical utility of the meta-topologies and the derived staging system.

REFERENCES

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