

Collaborations in Stroke Genetic Discovery, Part 1: Standardizing phenotypic data collection in the International Stroke Genetics Consortium

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Goals of Manuscript

Provide the international stroke community with consensus from the ISGC regarding phenotypic data collection for studies of stroke genetics

Topics Covered

- Study Design – Choosing the Population
- Demographics
- Vascular and Other Risk Factors
- Stroke Phenotyping
- Severity Measures
- Neuroimaging Protocols
- Ethics Specific to Stroke Genetics Studies

Study Design – choosing the population

- Case-control or cohort
- Must define cases & controls clearly
- Definition of stroke:
 - sudden onset of neurologic symptoms
 - imaging-based (AHA recommendation) vs. not (creates bias)
- Controls: stroke-free, from a comparable population, matched on age, sex, and race.

Demographics

- Case-control status
- Date of biosample draw
- Year / month of birth
- Age at recruitment, age at stroke
- Sex
- Whether stroke is first, or recurrent
- Race / ethnicity

Vascular & Other Risk Factors

- Use recognized definitions (PhenX)
- Minimal: Clinician-diagnosed HTN, DM, Afib, dyslipidemia, prior stroke, pregnant state
- Optimal: PVD, coronary artery disease, obesity, valvular disease, family history
- Tobacco use, alcohol use
- Baseline functional status, SES
- Record as dichotomous (yes/no) vs. real data (continuous) - % stenosis, LDL, BMI, pack-year history

Ischemic Stroke Phenotyping

- AIS:
 - Minimal: mechanistic method (TOAST)
 - OCSP (anatomic) concurrent if done
 - Preferred: CCS
- TIA: symptoms resolved
 - Imaging-negative vs. imaging not required
- Severity: NIHSS, SSS (appropriate language)

ICH Phenotyping

- Exclude traumatic forms
- Define location
- Much discussion about whether to include etiology and mechanism
- Severity: use standard scales (GCS, FUNC, ICH score)
- Size: ABC/2, direct, ordinal

SAH Phenotyping

- Define etiologically (aneurysmal, ICAD, perimesencephalic, undetermined)
- Severity: H&H, WFNS
- Other: aneurysmal rupture status, delayed ischemic injury, treatment, additional aneurysms, family history

Neuroimaging

- Record MR parameters
- Prefer centrally-adjudicated imaging data
- CT: minimum for major stroke types
- MRI: preferred for AIS, WMH
- Timing matters – CT ok for ICH if within a week; otherwise MRI for ICH

Outcomes

- Time points: early (24 hrs, 7d) and late (3 or 6? mo)
- Minimal: death
- Optimal: neurologic deterioration, recurrent stroke, BI, GOS, FIM, mRS
- Related factors: education, social support, acute therapies

Ethics

- Strongly encourage ethically enrolling those with reduced decisional capacity – typically by surrogate
- Include data element as to who consents
- Informed consent should include:
 - Data repositories / sharing
 - Future uses
 - Returning of main or incidental findings

Conclusions

- We hope to encourage more prospective studies that are:
 - of high quality using at least minimal standards
 - that can be harmonized with existing studies
 - that allow for data sharing and future uses
 - and are ethically conducted

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- And we hope this paper comes to a newsstand near you soon