

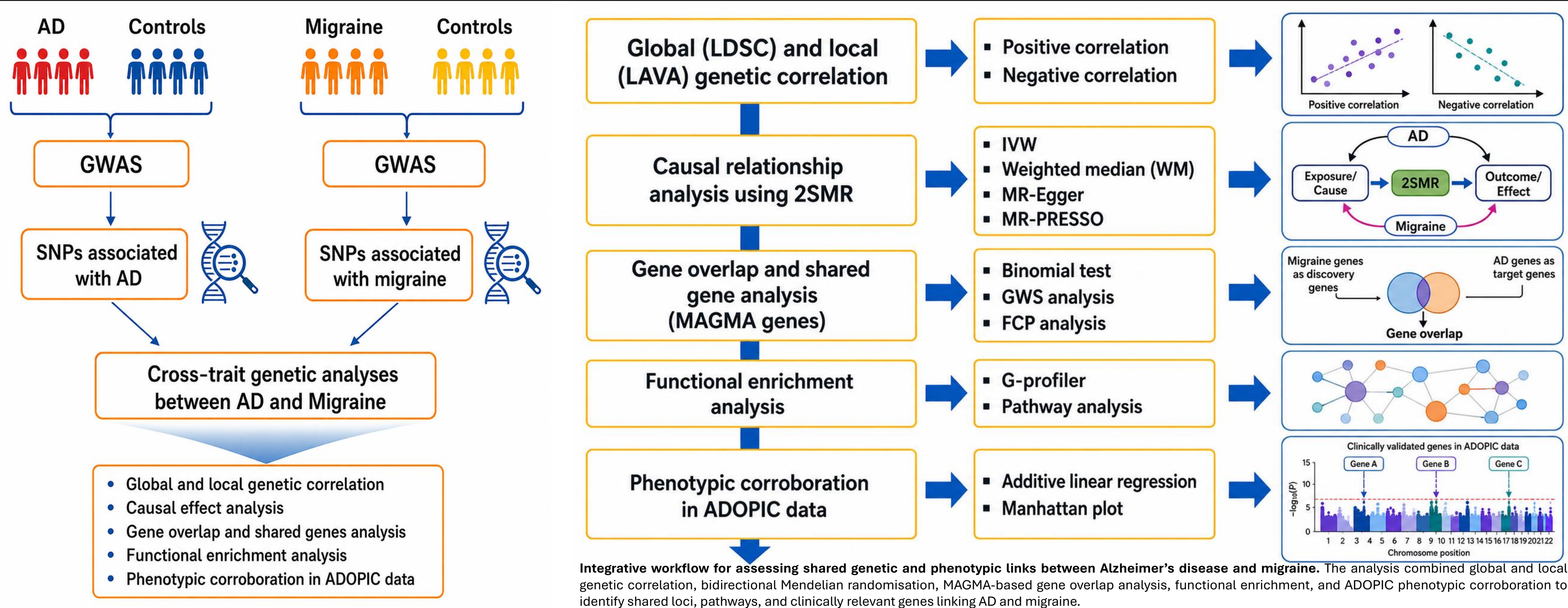
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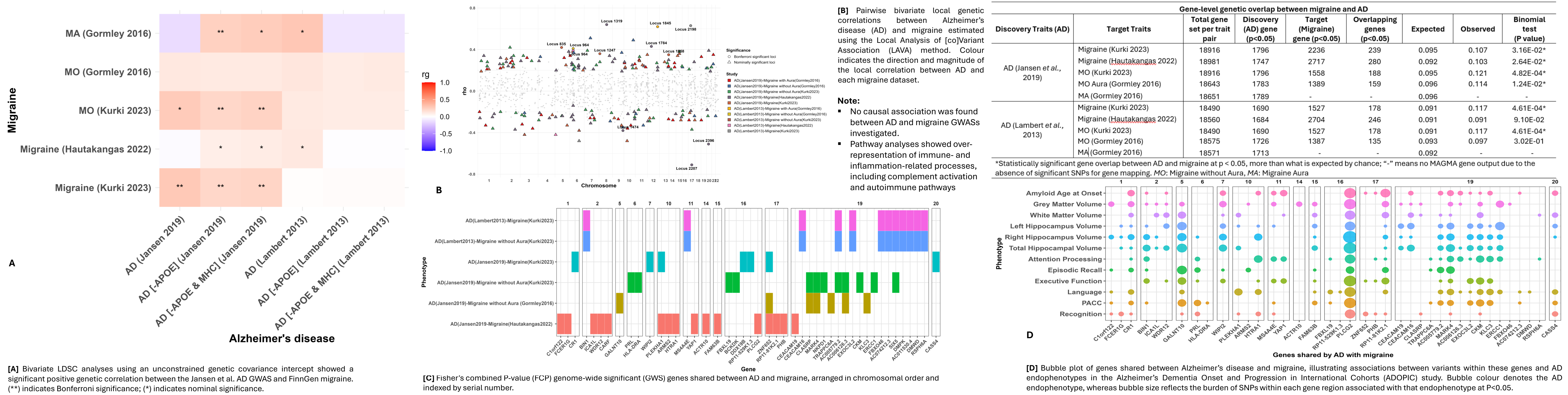
Introduction

- Alzheimer's disease (AD) and migraine are common neurological disorders with overlapping inflammatory, vascular, and neurobiological features.
- AD is characterised by pathological processes that include extracellular amyloid plaque deposition, intracellular neurofibrillary tangle accumulation, neuroinflammation, synaptic dysfunction, and progressive cognitive decline.
- Similarly, migraine involves complex neurovascular mechanisms, including trigeminovascular activation, cortical hyperexcitability, and increasing evidence of neuroimmune signalling (Biscetti *et al.*, 2023).
- Epidemiological studies suggest a possible association between migraine and later-life cognitive decline or dementia risk (Kim *et al.*, 2023; Lee *et al.*, 2021; Islamoska *et al.*, 2020), while meta-analyses have reported elevated dementia risk among individuals with a history of migraine, with some evidence of stronger associations for migraine with aura (Wang *et al.*, 2022; Jiang *et al.*, 2022; Zhu *et al.*, 2025).
- Despite these observations, it remains unclear whether the genetic and molecular overlap between AD and migraine reflects shared heritability, causal links, or convergent neurovascular and neurodegenerative mechanisms.
- Understanding this overlap may reveal convergent biological pathways and identify genes relevant to AD pathogenesis, risk stratification, and therapeutic discovery.
- Integrative genetic analyses using complementary analytical and computational approaches can therefore help clarify the shared genetic architecture between AD and migraine and provide insight into their overlapping biological mechanisms.
- Accordingly, this study investigated the genetic relationship between AD and migraine using integrative genomic approaches to identify shared loci, potential causal effects, overlapping genes, enriched biological pathways, and candidate targets for functional validation.

Methods



Results



Conclusions and Future Directions

- AD and migraine share significant global and local genetic architecture without evidence of direct causality.
 - Convergent immune- and inflammation-related pathways provide biological insights into their co-occurrence, suggesting possible shared mechanisms and implications linking biomarkers/therapeutics more cautiously to the pathway findings.
 - Phenotypic corroboration provides clinically relevant phenotypic associations between variants within shared genes and AD endophenotypes.
- Future Direction:** Functional validation of the shared genes identified between AD and migraine is recommended using experimental and single-cell approaches to confirm their mechanistic roles and clarify their cell-type-specific contributions to disease biology.

References

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