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PSYSCAN

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Functional MRI connectivity accurately distinguishes cases with psychotic disorders from healthy controls, based on cortical features associated with brain network development

Sarah E Morgan* (sem91@cam.ac.uk, Cambridge University, UK), Jonathan Young*, Ameera X Patel, Kirstie J Whitaker, Cristina Scarpazza, Therese van Amelsvoort, Machteld Marcelis, Jim van Os, Gary Donohoe, David Mothersill, Aiden Corvin, Celso Arango, Andrea Mechelli, Martijn van den Heuvel, René S Kahn, Philip McGuire, Michael Brammer†, Edward T Bullmore†

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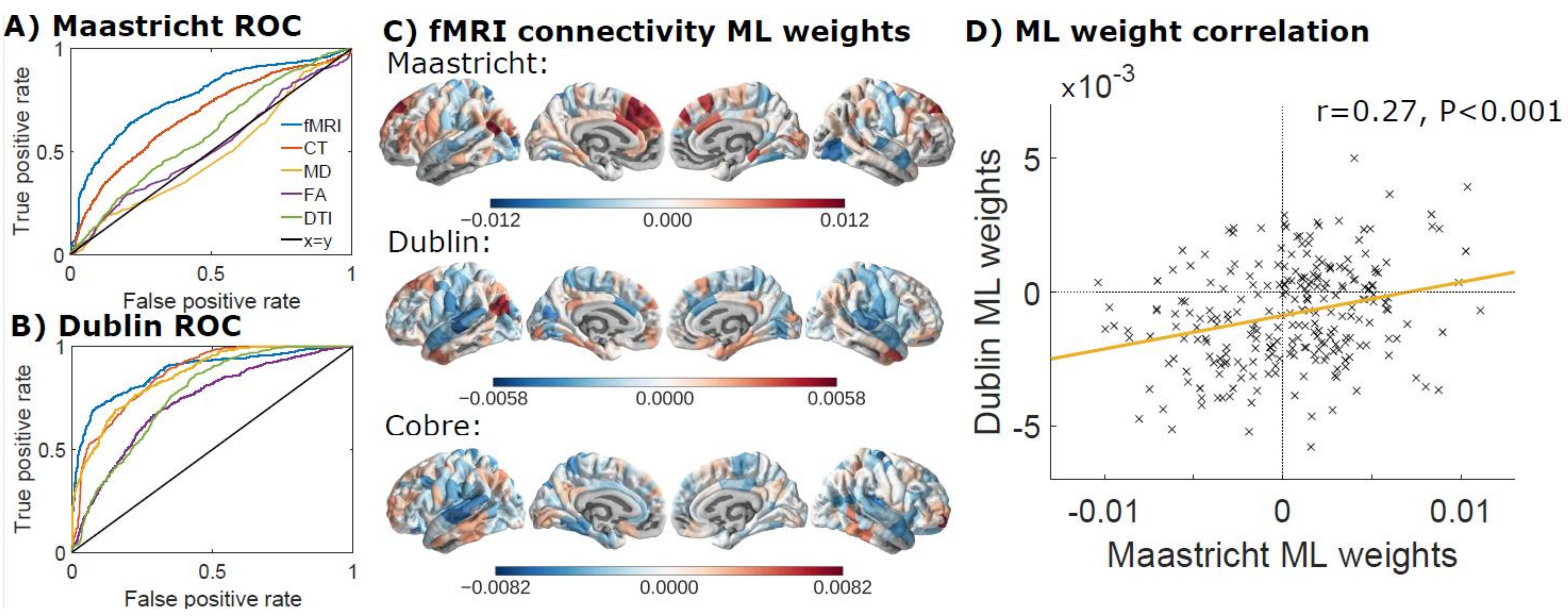
In brief:

KEY POINTS

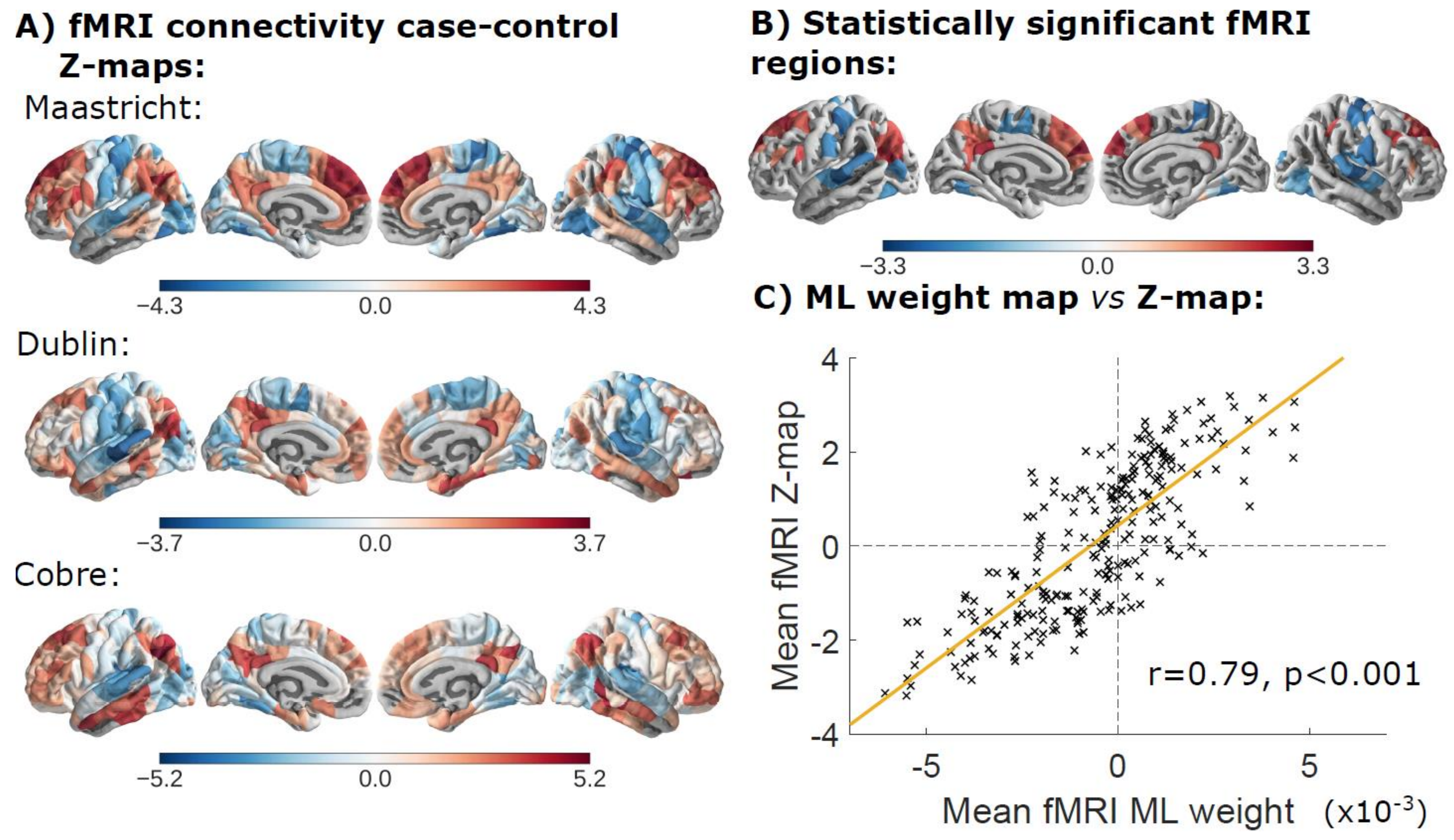
- ✓ Machine learning (ML) can distinguish cases with psychotic disorder from healthy controls based on MRI data but it is not yet clear which MRI metrics are the most informative for case-control ML, or how ML algorithms relate to the underlying biology.
- ✓ We analysed multi-modal MRI data from two independent case-control studies of psychotic disorders (in total, ***n* = 93 cases** and ***n* = 139** healthy controls) and compared ML accuracy across 5 selected MRI metrics from 3 modalities.
- ✓ In both principal studies, the most informative metric was fMRI connectivity: the areas under the receiver operating characteristic curve were 88% and 76%, respectively.
- ✓ The cortical map of diagnostic connectivity features (ML weights) was replicable between studies ($r = 0.27$, $P < 0.001$); correlated with replicable case-control differences in fMRI degree centrality, and with a prior cortical map of adolescent development of functional connectivity; predicted intermediate probabilities of psychosis in non-psychotic siblings of cases (***n* = 64**); and was replicated in a third case-control study (cases, ***n* = 67**; controls, ***n* = 81**).
- ✓ Overall, ML most accurately distinguished cases from controls by a replicable pattern of fMRI connectivity features, highlighting abnormal hubness of cortical nodes in an anatomical pattern consistent with the concept of psychosis as a disorder of network development.

1. fMRI connectivity accurately distinguished patients with schizophrenia from healthy controls, based on a replicable cortical pattern:

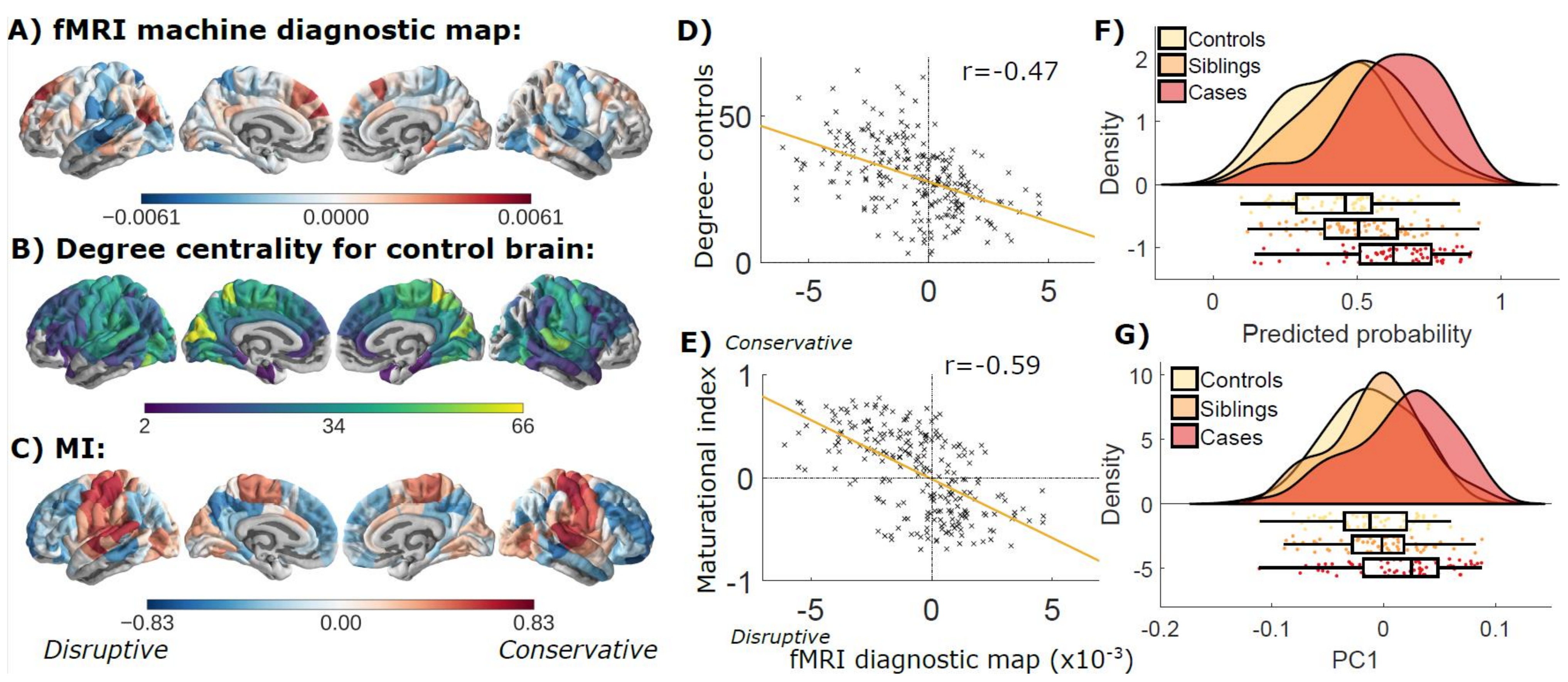


- We analysed two case-control studies, from Maastricht and Dublin, which were collected independently and subsequently collated as part of the PSYSCAN programme.
- Cortical thickness, mean diffusivity and fractional anisotropy were estimated at each of 308 cortical regions, as well as functional (fMRI) and structural (DTI) connectivity between each pair of regions.
- fMRI connectivity informed the most accurate machine learning case-control classification, in both datasets (AUC=0.88 in Dublin, AUC=0.76 in Maastricht); see **Figures 1 A** and **1B**.
- The feature weights from the ML algorithm trained on fMRI data were mapped onto a cortical surface to form a diagnostic feature map for each study (**Figure 1C**). fMRI ML feature weights for the Maastricht and Dublin datasets were correlated (r=0.27, P<0.001).
- Results replicated in the openly available Cobre dataset (AUC=0.75 for case-control classification based on fMRI connectivity).

2. The cortical map of fMRI ML feature weights was correlated with statistical case-control differences in functional connectivity:



3. The cortical map of fMRI ML feature weights was correlated with degree centrality and a prior map of brain network development during adolescence:



Maturational index (MI) maps the brain regions which are most active during adolescent development (Vasa et al, PNAS 2020)

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