PREDICTORS OF CORTICOCORTICAL CONNECTIVITY

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Abstract

We tested two candidate predictors for connectivity among cortical areas, (i) proximity of the linked areas, measured by their border distance, as well as (ii) structural similarity of the areas, expressed through their type difference, Δ.
Analyses were based on extensive quantitative data about prefrontal projections in the rhesus monkey. Border distance as well as Δ predicted well if projections existed at all, and both were highly and inversely correlated with the density of existing ipsilateral- and contralateral connections. Structural type difference (Δ), however, was a superior predictor of projections to remote areas. Our findings permit the creation of new models linking cortical structure and connectivity, and may allow prediction of specific projections in the human cerebral cortex.

Description

What explains the intricate patterns of long-range connections among areas of the mammalian cerebral cortex? Previous hypotheses have suggested that connectivity is constrained by spatial proximity of the linked areas. We tested this idea and contrasted it with an alternative predictor of connectivity, structural type difference (Δ) between linked areas. We defined the number of borders intervening between two areas as a pairwise distance measure. We computed Δ by categorizing areas into five structural types (based on the number and density of neurons within cortical layers: lowest = 1, highest = 5), to determine the ordinal type difference of linked areas, as described previously (Barbas and Rempel-Clower, *Cerebral Cortex* **7**:635-646, 1997). Analyses were based on quantitative data about projections linking prefrontal areas of rhesus monkeys (164 ipsilateral and 85 contralateral projection sites among 21 areas, which were quantitatively characterized by 18 parameters based on structural features).

Border distance as well as Δ predicted if projections existed at all (rank order correlation, $p<0.001$). For existing projections, both measures correlated closely and inversely with relative projection density ($p<0.001$). These relations emerged for projections to ipsilateral as well as to contralateral cortices. While closely related to distance, Δ was a more powerful overall predictor of connections. The similarity of the two predictors may be explained by the fact that areas possessing similar type structure are frequently neighbors. However, there are also some distant areas with similar structure, resulting in the superiority of Δ for predicting remote connections.

We applied the structural concept to detailed, quantitative structural data for primate prefrontal cortices. Using multidimensional analyses of multiple structural features, prefrontal areas robustly clustered into two main groups, consisting of 'eulaminate' types (Δ values of 3-5) and 'limbic' types (Δ values of 1-2) of cortices. In line with the structural model (Δ) hypothesis, there were more connections within, than between, the two main groups of cortices, and connections running within the groups were significantly denser than those between.
The strong relationship between cortical structure and connectivity may be explained by temporal differences in the ontogeny of various cortical types.

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