

# Expanding cerebellar horizons

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Anatomical connections must underly neuronal function. A new study by Middleton and Strick shows that the cerebellum projects to the dorsal prefrontal cortex of the monkey. This could provide the basis for cerebellar modulation of cognitive processes.

The cerebellum is something of a puzzle – its role has often been oversimplified and textbooks rarely mention anything more than its contribution to motor control, motor learning and motor coordination. But recently, some have suggested an intriguing and highly controversial hypothesis: in primates, the cerebellum may have a significant role in *cognitive* functions – traditionally, the domain of areas such as the prefrontal cortex<sup>1,2</sup>. The original argument put forward in support of this view is that, during evolution, the primate cerebellar hemispheres have expanded roughly in parallel with the great enlargement of the neocortex. In addition, clinical evidence suggests that cerebellar lesions result in impaired cognitive function<sup>3</sup>, and functional imaging studies have shown that the lateral cerebellum becomes active during cognitive tasks that are far removed from control of movement<sup>4</sup>. However persuasive these arguments may be, they remain indirect. Until now, they have not been substantiated by anatomical data that show how the cerebellum interacts with areas known to be critical for cognition. Therefore, the challenge has been to show that there are pathways in the primate brain through which the cerebellum can influence the prefrontal cortex.

Characterizing the connections of the cerebellum with the cerebral cortex has been difficult, for the simple reasons that cerebro-cerebellar connections involve more than one synapse (see Fig. 1) and that traditionally used tracers do not cross the synaptic cleft. Thus, injections of conventional retrograde tracers into the prefrontal cortex will label cells in the thalamic nuclei<sup>5</sup>, but one would then need to inject specific cell groups within the thalamus to see if they originated in the cerebellum. Recently, Strick and

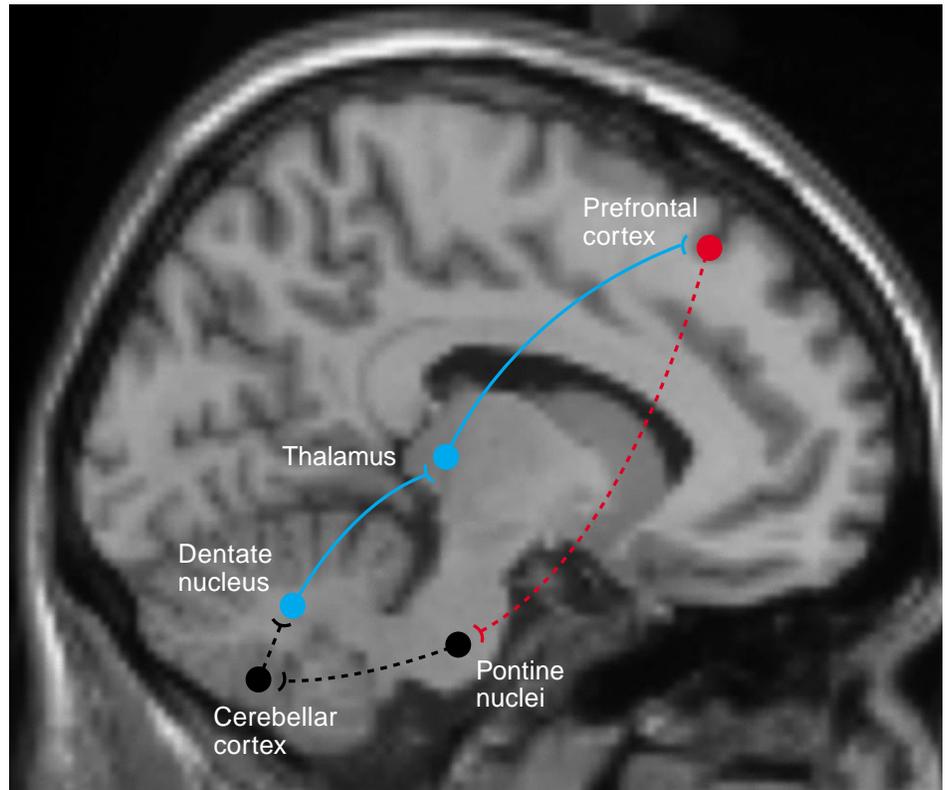


Fig. 1. Cerebro-cerebellar connections, showing projections from the cerebellar dentate nucleus to the prefrontal cortex via the thalamus (in blue). This pathway was identified using retrograde trans-synaptic viral tracers injected into the dorsal prefrontal cortex<sup>6</sup>. Projections from prefrontal cortex to the pontine nuclei (red) have been identified using conventional anterograde tracers<sup>8</sup>. Ponto-cerebellar and intrinsic cortico-nuclear cerebellar projections are shown in black.

colleagues have developed a method that can trace pathways using trans-synaptic tracers of viral origin. These can cross the synaptic cleft, and it has therefore become possible to explore the connectivity of the cerebral cortex one, two or more synapses away. The tracers appear to follow functionally specific pathways and are detected by antibodies to the virus. Therefore, tracts can be followed from the cerebral cortex to thalamus and then on to the output nuclei of the cerebellum, among other regions.

In the latest report from their extensive study in which conventional fluorescent dyes and the trans-neuronal tracer McIntyre-B herpes simplex virus type 1 were used to follow inputs to the prefrontal cortex of the *cebus* monkey, Middleton and Strick have fitted new pieces into the cerebellar puzzle<sup>6</sup>. Viral or conventional tracers were injected into

cortical areas 9, 46 and 12. The conventional tracers were used to examine the thalamic sources of input to each area and this confirmed the known distribution of inputs. The largest arose from thalamic regions receiving input from the basal ganglia, but with a substantial number of cells stained in the cerebellar-receiving nuclei of the motor thalamus (mainly MD and VLc, with a smaller number in area X).

When viral injections were made in the same prefrontal regions, two interesting features emerged. First, the prefrontal regions injected with tracer were found to receive heavy projections from a restricted portion of the ventral dentate nucleus of the cerebellum, and hardly any projections from the other cerebellar nuclei. Middleton and Strick report that each thalamic and prefrontal target seems to arise from slightly different

zones in the dentate nucleus, suggesting distinct cerebellar output channels. Second, only some areas of the prefrontal cortex examined were found to receive from the cerebellum. Injections into regions of the dorsal prefrontal cortex (upper bank of *sulcus principalis*, 46d, and area 9) resulted in significant labelling of the ventral dentate, but the number of cells labelled by injections into a region of the ventral prefrontal cortex (the ventral bank of *sulcus principalis*, 46v, and area 12) was negligible. This work brings the total volume of the dentate nucleus accounted for up to about 60% – the targets of the remaining 40% are still to be mapped.

Thus, an important finding of this study is that dorsal parts of the prefrontal cortex that are known to be important for functions such as working memory<sup>7</sup> and visuo-spatial attention can potentially be influenced by activity in the cerebellum. This is all the more interesting because traditional anterograde injection techniques have already been used to

identify projections from the dorsal prefrontal cortex to the pontine nuclei which provide inputs to the lateral cerebellum<sup>8</sup>. Projections from ventral portions of the prefrontal cortex to the pons are not seen. Thus, the general principle that cerebro–cerebellar connections are organized in anatomically segregated loops<sup>9</sup> applies to the dorsal prefrontal cortex and its connections to the cerebellum.

We can now see closed cerebro–cerebellar loops that include sensorimotor regions, oculomotor regions, and prefrontal regions. All we need do now is to work out what they are for!

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#### Journal Club

## Morphological tensions

Recent debates over language processing have centred on inflectional morphology, particularly the German plural system. Like the English past tense there are regular (e.g. play ⇒ played) and irregular forms (find ⇒ found) in German plurals. This fact has led to the suggestion by Steven Pinker and his colleagues that there must be a separate rule based route for recognising regular forms and an associationist route (a dual-route model) for recognising irregular forms<sup>1</sup>. However, previous connectionist models seemed to show that a single associationist route was sufficient at least for the English past tense. The importance of the German plural is that it is an example of 'minority default inflections'. The good performance of single-route connectionist models on, say, the English past tense is because of the high frequency of these forms (which is to say that the model is 'distribution dependent'). However, such a model should in principle be unable to handle the default, or regular form, when these are infrequent. The German plural is such a case.

In a new paper, Hahn and Nakisa address this issue using large-scale computer

simulations, directly comparing single-route and corresponding dual-route models<sup>2</sup>. The simulations reveal that dual-route models, and not just connectionist models, are distribution dependent. The assumption that minority default inflections are necessarily better handled by dual-route systems turns out to be false. This finding undermines the minority default argument that the mere existence of such inflectional systems is evidence for the dual-route account. The simulations involved large language samples and used a range of models. These models were chosen such that a range of potential confounds in the debate (specifically, connectionist/symbolic, single-route/dual-route, and similarity-based/frequency-based) could be separated. The simulations included a novel application of Nosofsky's well-known Generalised Context Model of categorisation, which has never been tested on large, naturalistic data sets before, nor been considered by linguists or psycholinguists. This model is tested together with a nearest neighbour classifier and a standard back-propagation neural network. Each model was tested in

single-route and dual-route versions, and for their ability to predict correctly the German plural forms of previously unseen words. In no case did the dual-route models achieve better performance than the single-route models. The authors also provide further experimental evidence supporting the single-route approach.

It would seem that the mere existence of languages with minority default inflections can no longer be argued to provide decisive evidence for a dual-route approach. Even more interestingly, it turns out that such languages appear to rely on the statistical distribution of morphological information to determine the form of a word.

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