# This Week in The Journal

## Cerebellar Role in Language Prediction

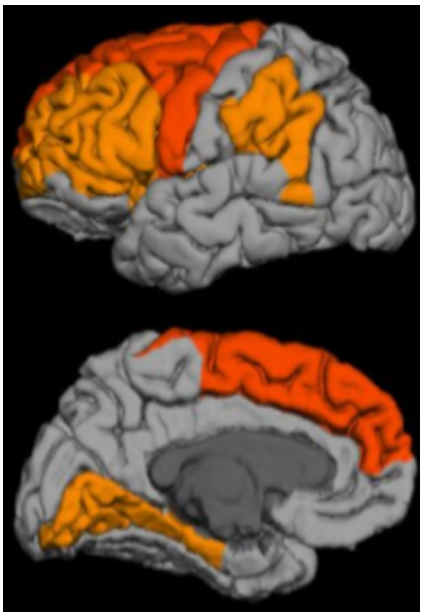
Elise Lesage, Peter C. Hansen, and R. Chris Miall

(see pages 6231–6241)

The cerebellum is thought to contribute to motor learning and coordination by creating internal models that predict the sensory effects of motor commands and by modifying commands when predictions are violated. These functions rely on reciprocal connections between the cerebellum and motor cortex. Because the cerebellum makes similar reciprocal connections with many other cortical regions, including prefrontal and posterior parietal cortex, the cerebellum may have similar roles in nonmotor function. Indeed, functional magnetic resonance imaging indicates that the cerebellum is activated during many nonmotor tasks, including language comprehension (Moberget and Ivry 2016 Ann NY Acad Sci 1369:154). Whether the cerebellar role in language involves prediction has been unclear, however.

To address this question, Lesage et al. examined cerebellar activity as volunteers read sentences. Participants viewed a sentence that set a context, followed by a sentence fragment with the final word omitted. On some trials. the final word was highly predictable from the context and stem sentences (as indicated in a separate experiment, in which most participants chose the same word to complete the sentence); on other trials, the final word was less predictable. After a pause, participants saw the final word and judged the plausibility of the sentence. Consistent with previous work, a broad region of the posterolateral cerebellum and cerebellar vermis were activated as subjects read. Importantly, while subjects read incomplete stems, activity levels in a subregion of right posterolateral cerebellum was correlated with the predictability of the final word. When the final word was shown, activation in this same subregion was inversely correlated with plausibility: activity was greater when the outcome was rated unlikely. Additional tests showed that while the cerebellar area activated generally during reading was also activated during phonological, orthographic, and semantic processing tasks, the subregion linked to predictability was significantly engaged only during the phonological processing task.

These results suggest that the cerebellum has a predictive role during sentence processing and that it generates a prediction error when an unexpected word appears. The fact that the subregion involved in prediction is also engaged during phonological processing indicates that word prediction during reading might be related to the motor predictions involved in articulating sentences. More studies will be needed to determine whether the cerebellum also engages in semantic prediction.



Regions in which cortical thickness is lower in 22q11.2 duplication carriers than in deletion carriers (light and dark orange; FDR-corrected, $q < 0.05$) and where thickness is lower in duplication carriers than controls (dark orange, uncorrected, nominal $p < 0.05$). See Lin et al. for details.

## Contrasting Effects of 22q11.2 Deletion and Duplication

Amy Lin, Christopher R.K. Ching, Ariana Vajdi, Daqiang Sun, Rachel K. Jonas, et al.

(see pages 6183–6199)

Human chromosome 22 is highly susceptible to homologous recombination and thus to deletion or duplication of a segment (22q11.2) containing 40–50 genes. 22q11.2 deletion, one of the most common human copy number variations, produces a wide range of phenotypes, typically involving abnormal development of the heart, facial structure, and/or brain. People with 22q11.2 deletions frequently have intellectual disabilities, and many have autism spectrum disorders. Additionally, 22q11.2 deletion is the strongest known genetic risk factor for schizophrenia. In contrast to 22q11.2 deletion, duplications in this region generally produce a mild phenotype, often going undetected. Nonetheless, 22q11.2 duplication, like deletion, has been linked to intellectual disability and autism. Unlike 22q11.2 deletion, however, duplication appears to reduce schizophrenia risk.

Because 22q11.2 deletion and duplication have similar effects on autism risk but opposite effects on schizophrenia risk, comparing the anatomical and physiological effects of deletion and duplication may offer insight into the etiology of these diseases. Several studies using magnetic resonance imaging have indicated that gray and white matter volume are lower in people with 22q11.2 deletions than in controls, and similar results have been found in mouse models. Lin et al. complement these studies by comparing brain structure in people with typical chromosome 22 to those with 22q11.2 duplication or deletion.

Consistent with previous reports, total gray and white matter volume and regional surface areas were lower in 22q11.2 deletion carriers than in controls. But cortical thickness was greater in several cortical regions in deletion carriers. For the most part, differences between duplication carriers and controls were not statistically significant after corrections for multiple comparisons. Nonetheless, thickness of the left caudal and superior frontal gyrus and the right precuneus was significantly lower in duplication carriers than in controls.

These results confirm the pronounced effects of 22q11.2 deletion on cortical volume, thickness, and area, while suggesting that 22q11.2 duplication has opposite, but less widespread effects than deletion. Future studies with larger samples may detect additional structural differences between duplication carriers and controls. Generation of mouse models of 22q11.2 duplication should further elucidate the effects of this mutation and may provide clues about how this duplication reduces schizophrenia risk while increasing autism risk.

*This Week in The Journal was written by Teresa Esch, Ph.D.*