are kept separate throughout the processing chains that support choice and monitoring under this framework.

An intriguing alternative suggestion put forward by the authors is that accuracy is inherently valuable. Because confidence predicts accuracy, then confidence itself is also valuable. This alternative model accounts for the data by assuming that the VMPFC signal is simply reporting value, as previously thought, but that this value signal reports the sum of the true internal value and the value that is derived from participants' confidence. Such a model raises questions about how the brain can integrate two such different sources of value into a common scale, but it predicts subtle relationships between confidence and choice that might be further tested.

Despite the clear differences between these two ideas, there are important similarities. Both argue that the confidence signal computed in VMPFC has functional consequences in downstream regions, either as its own signal or in a compound value representation. This view is markedly different from ideas in which similar signals that arise in VMPFC during binary decisions have been described as the consequence of the neural dynamics[3,5,12]. In binary choice, signals are often found to reflect the difference in value between chosen and unchosen items—a signal that could be interpreted as the participants' confidence in the choices that they have made. However, it has been possible to predict the dynamics of these signals using neural network models that do not explicitly compute value difference or choice confidence at any stage. The different internal network dynamics on trials that subjects find easy versus difficult are sufficient to account for the signal. Thus, even though such confidence-like variables affect the measured content of the neural signals, it is not necessarily the case that they have any functional downstream consequences, and it remains a possibility that confidence is not computed explicitly in the VMPFC.

Despite these open questions, there are several important triumphs in the current report: a new and robust dimension to one of the most influential signals in human neuroscience, evidence of such decision-related activity even in the absence of value, and an elegant mathematical treatment in which to frame these effects. Neuroeconomists across the world will be dusting off the archives and retrieving their old data to have a look.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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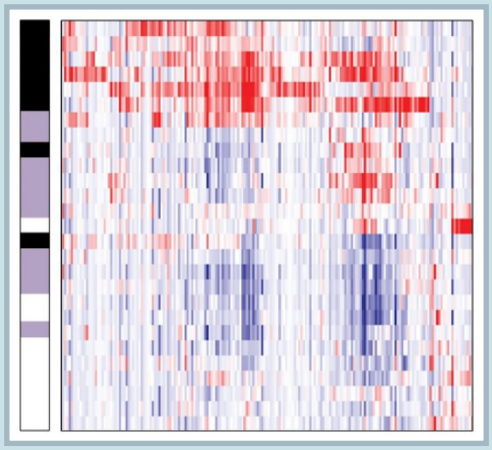
The RNAs of ALS

There has been accumulating evidence over the last decade that the etiology of amyotrophic lateral sclerosis (ALS) involves alterations in RNA processing and metabolism. Recently, a mutation that consists of the expansion of a hexanucleotide repeat in the *C9orf72* gene was found in ALS families (c9ALS). The abnormal repeat leads to the accumulation of *C9orf72* transcripts and the generation of dipeptide-repeat protein (DPRs), both of which are thought to be neurotoxic. Interestingly, many RNA-binding proteins form aggregates in c9ALS, and DPRs are thought to affect RNA biogenesis. These findings suggest that RNA metabolism could be affected on a large scale in the disease, but the extent of such changes is currently unknown.



On page 1175 of this issue, Petrucelli and colleagues report their analysis of brain transcriptomes in c9ALS and sporadic ALS (sALS) patients. Using RNA sequencing on cerebellar and frontal cortex samples, the authors found hundreds of genes that were differentially expressed in patients and healthy individuals. Twice as many genes were dysregulated in c9ALS than in sALS, but, surprisingly, only a small fraction of changes occurred in the same genes in the two patient groups. The authors also identified distinct coexpression network modules in c9ALS and sALS and found that alternative splicing (AS) and alternative polyadenylation were higher in c9ALS than in sALS samples, with only a small fraction of AS events shared across the two groups. The picture shows hierarchical clustering of individuals based on the pattern of differentially expressed genes in frontal cortex (red and blue tick marks in the square indicate up- and downregulated genes, respectively). The bar on the left shows individual controls in white, sALS cases in purple and c9ALS cases in black. Note the segregation of the two patient populations into distinct clusters, pointing to the transcriptomic divergence between c9ALS and sALS.

This exploratory analysis of the transcriptional landscape in ALS reveals widespread changes in RNA expression and processing and further anchors the RNA-centric view of ALS. However, the modest overlap in the changes in RNA expression and processing between c9LAS and sALS suggests an important divergence in the molecular presentation of the disease in these two patient populations and possibly predicts a more general heterogeneity of the disease. Although it is currently unclear which of these RNA changes relate to the neuropathology of the disease or how, this study represents an important step in our understanding of the molecular etiology of ALS. Public access to these data will hopefully seed many future mechanistic studies that will bridge the genetics of the disease to the biology underlying its pathogenesis.

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