This book revolves around two thematic lines of questioning. First, Cole is asking what is the role of culture in the mind. To attempt an answer, he explores the history of psychology. He discusses the process of division that the human sciences underwent at the end of the nineteenth century and the turn of the twentieth, and how the constitution of psychology as a science meant its divorce from history and culture. Cole traces various proposals for reconciling the experimental and historical sciences, discussing Mill's dual psychology, Volkerpsychologie, descriptive psychology, and Wundt's proposal for a dual psychology. He emphasizes Wundt's argument that once cultural history intertwines with individual experience, they can no longer be disentangled to be studied with experimental methods, and that genetic methods are needed to address culturally mediated psychological processes.

Cole's second axial line of questioning is, if one is a psychologist who believes that the role of culture in mind is significant, how does one conduct research while maintaining scientific credentials? To address this question Cole takes as a point of departure cultural-historical activity theory, and expands upon the basic principles laid out by Vygotsky, Luria, and Leontiev among others to formulate a more complex and nuanced understanding of the intertwining of the natural and cultural lines. Cole extends Vygotsky's insights to posit the co-evolution of the phylogenetic and ontogenetic. He stresses that adopting a cultural-historical approach does not answer the question of how to carry out analyses, and writes toward formulating a methodology that addresses the issue of describing and analyzing everyday life.