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Foreword

Blues' Clues

> I wanted only to try to live in accord with the promptings that came from my true self. Why was that so very difficult?
>
> —*Hermann Hesse: Demian (1919)*

Despite being all too common, depression remains a largely under-diagnosed and under-treated condition. This discrepancy is particularly true outside of specialized treatment centers, and even more so for children and adolescents caught under depression's yoke. Even when accurately identified in schools or primary care settings, a diagnosis of youth depression often leads to logistic and practical challenges. These include having few viable options for appropriate referral, and a recent and partly justified sense of skittishness among primary care clinicians about implementing treatment themselves–what with the dust over antidepressants and suicidality in this age group far from settled. Paradoxically, the controversy over suicidal ideation and its putative association with medications intended to ameliorate it has shifted attention away from the much larger public health concern: left untreated, depression can be a deadly disorder. Suicide remains a leading cause of mortality for this age group, and we have much to lose if our prescribing trepidations lead to communal therapeutic inaction.

Which should not imply that our treatments are as effective as we would have hoped for. Indeed, depression may prove to have been a better testing ground for the shortcomings and limitations of our psychotropic medications than for their touted benefits and initial promise. The enthusiasm over tricylic antidepressants fizzled under our repeated (and uniformly failed) attempts to extend their efficacy downward in age. The selective serotonin reuptake inhibitors—close suicidal scrutiny aside—remain ineffective in about a third of treated youths, and in several trials, are hard to distinguish from placebo, when differentiated at all.

But there is cause for optimism while we wait for the next generation of revolutionary compounds to emerge from drug development pipelines that have been dry for too long. For one, psychotherapy research has made exciting advances by developing and adapting treatment options for children and adolescents. Cognitive-behavioral and interpersonal forms of psychotherapy have a growing base of evidence to support their efficacy, and

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large-scale efforts are underway to move such gains from the clinical trial setting into the effectiveness realm of 'real world' implementation. And lest it be implied that talk therapy is superior to medication (or the other way around), it should be noted that in the field of youth depression we now have initial empirical evidence comparing and contrasting the two, which, unsurprisingly if reassuringly, shows that their combination is usually best.

Just as research on combination treatments has been fruitful, research investigating the combination of influences on etiology has been among the most elegant and heuristically important in pediatric mental health. The centuries-old debate pitting environmental against constitutional factors in the development of psychopathology has in recent years given way to a more productive line of inquiry about the interplay between the two. Paradigmatic of this approach, the work by Caspi and colleagues has explored the interaction between genetic and environmental factors (serotonin transporter polymorphisms and degree of childhood abuse, respectively) on the genesis of depressive outcomes later in life. With technological advances so near at hand, it stands to reason that however promising and exciting such single gene-environment interactions are today, they are likely to be supplanted by much more complex, if not genome-wide, quests for genetic causality, with an equivalent complexity in multi-determined environmental mediation.

Many of our better hopes for a deeper understanding of depression and other neuropsychiatric disorders of youth reside in the promise of genetics. Such hopes are not only about etiology and underlying mechanisms: they could have major treatment implications as well. For example, prediction of response (or of major adverse effects, such as induction of mania or suicidality by antidepressants) could plausibly be determined through genotyping. Whether pharmacogenetics will ultimately deliver on its promise remains to be seen. But the excitement of this line of biological work is palpable, as are so many other areas covered in this issue, notably in neuroimaging and our latest understanding of the HPA axis and its implications for the development of novel therapeutics.

The Western Psychiatric Institute and Clinic in Pittsburgh has long held a peerless command on child and adolescent depression research. The seminal contributions by the late Joaquim Puig-Antich have blossomed into a veritable center of excellence, where so many of his colleagues and students have carried on his formidable tradition. David Brent has been a central figure within it, and through his contributions to psychotherapy and suicide prevention (to name but two) has advanced the field of child and adolescent depression like few others. I am grateful to David for joining in the coordination of this issue, which my good friend Gil Zalsman so steadily spearheaded. After completing postgraduate training at Columbia University (where he remains affiliated as a Research Scientist), Gil is back in his native Israel, where his energy and vision are helping seed, grow and transform his home institution, the Sackler Faculty of Medicine, Tel

Aviv University. Gil's original research contributions to the budding gene-environment interaction field provide a sense of the intellectual rigor and breadth of his scientific agenda. It is my hope that this aptly co-edited issue will prove useful to those caring for children and adolescents in North America, the Middle East, and well beyond.

The successful treatment of depression can reduce the likelihood of well-known adverse outcomes such as school drop-out, teenage pregnancy, substance abuse, or, the direst one, completed suicide. But there is more to successful treatment than what it can prevent. There is what it can confer and help reclaim: it is the mission of all of us working on behalf of children and adolescents everywhere to help them live fully and according to the promptings of their true selves.

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