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Commentary

Finding the Stripes: Distinguishing Bipolar Disorder From Major Depressive Disorder

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"When you hear hoof beats, think of horses not zebras" (Sotos, 2006). This aphorism was coined by physician Theodore Woodward of the University of Maryland School of Medicine in the 1940s. The aim was to help medical students learn to differentiate between the common and the rare as these have implications for treatment and outcomes. While major depressive disorder is more common and bipolar disorder more rare, distinguishing the two is clinically difficult as they share many common features, especially during depressive episodes (Phillips and Kupfer, 2013). Indeed, a recent study by Holmskov et al. (2016) found that 1 in 5 participants in clinical trials for antidepressants underwent a diagnostic conversion from unipolar depression to bipolar depression over time. This means that a substantial number of people with bipolar disorder were actually misdiagnosed, sometimes for years. Further to this, a survey of patients with bipolar disorder in 2000 found that for over a third of patients, an accurate diagnosis took over a decade (Hirschfeld et al., 2003). This is troubling as data has shown a 10% less likelihood of recovery for each year treatment is delayed for bipolar disorder (Lish et al., 1994). Time is simply not a luxury found in treating bipolar disorder. Another potential cost to getting diagnosis wrong is that antidepressants carry the risk of triggering mania, and may increase the rates of cycling between mood states (Baldessarini et al., 2010). This means making the right diagnosis is critical for a more positive outcome.

Given these circumstances, accurately distinguishing between the relative zebra (bipolar disorder) and the horse (major depressive disorder) is important. The question is, since this is so difficult to do clinically, are there other approaches that show potential?

In this issue of *EBioMedicine*, Niu et al. (2017) used magnetic resonance imaging (MRI) to compare regional cortical thickness in both major depressive disorder and bipolar disorder in a rare head to head contrast. Their approach used high quality MRI data, substantial and well characterized samples, along with a relatively objective image analysis approach. As expected, given the symptom overlap, some regions show deficits in both groups (i.e., left inferior temporal cortex) while others distinguished the two (i.e., left rostral middle frontal cortex). The bipolar disorder group showed abnormalities in the frontal pole that were associated with clinical variables like age of onset. In keeping with the metaphor, this approach is allowing researchers to pick out the stripes of the zebra.

Other researchers have used a similar approach to hunt for differences between closely related diagnostic groups using MRI (Langevin et al., 2015; MacMaster et al., 2014; Fallucca et al., 2011). MRI is well tolerated, widely available, and has a minimum risk associated with it. As a tool for the identification of potential biomarkers, it has remarkable potential. A biomarker is an objectively measured and evaluated characteristic that acts as an indicator of diagnostic status or response to intervention. To be applied as a surrogate clinical measure, biomarkers must have a strong evidence base, including likely biological relationships and prognostic value. For biological relationships to symptoms, the inferior temporal cortex and rostral middle frontal cortex both play a critical role in mood regulation. The initial stage of biomarker research involves exploration and validation at single sites. This is followed by characterization and surrogacy in a multi-site collaborative study. Such validation studies appraise the performance of the proposed biomarkers, ensuring construct validity. The next step needed to build on the work by Niu et al. (2017) would be to validate and replicate their findings.

To truly transform mood disorders, diagnostic biomarkers are needed. While some could argue that the cost of MRI data acquisition and subsequent analysis is high, the cost of getting the diagnosis wrong is potentially even higher, especially for those afflicted. The work by Niu et al. (2017) in this issue may be the first step in the development of a diagnostic biomarker for distinguishing bipolar disorder from major depressive disorder. If pursued and validated, this approach would fulfil one of the major promises of brain imaging to psychiatry.

Disclosure

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References

Baldessarini, R.J., Vieta, E., Calabrese, J.R., Tohen, M., Bowden, C.L., 2010. Bipolar depression: overview and commentary. Harv. Rev. Psychiatry 18 (3), 143–157.

Fallucca, E., MacMaster, F.P., Haddad, J., Easter, P., Dick, R., May, G., et al., 2011. Distinguishing between major depressive disorder and obsessive-compulsive disorder in children by measuring regional cortical thickness. Arch. Gen. Psychiatry 68 (5), 527–533.

Hirschfeld, R.M., Lewis, L., Vornik, L.A., 2003. Perceptions and impact of bipolar disorder: how far have we really come? Results of the national depressive and manic-depressive association 2000 survey of individuals with bipolar disorder. J. Clin. Psychiatry 64 (2), 161–174.

Holmskov, J., Licht, R.W., Andersen, K., Bjerregaard Stage, T., Morkeberg Nilsson, F., Bjerregaard Stage, K., et al., 2016. Diagnostic conversion to bipolar disorder in unipolar depressed patients participating in trials on antidepressants. Eur. Psychiatry 40, 76–81.

Langevin, L.M., MacMaster, F.P., Dewey, D., 2015. Distinct patterns of cortical thinning in concurrent motor and attention disorders. Dev. Med. Child Neurol. 57 (3), 257–264.

Lish, J.D., Dime-Meenan, S., Whybrow, P.C., Price, R.A., Hirschfeld, R.M., 1994. The National Depressive and Manic-depressive Association (DMDA) survey of bipolar members. J. Affect. Disord. 31 (4), 281–294.

MacMaster, F.P., Carrey, N., Langevin, L.M., Jaworska, N., Crawford, S., 2014. Disorder-specific volumetric brain difference in adolescent major depressive disorder and bipolar depression. Brain Imaging Behav. 8 (1), 119–127.

Niu, M., Wang, Y., Jia, Y., Wang, J., Zhong, S., Lin, J., et al., 2017. Common and specific abnormalities in cortical thickness in patients with major depressive and bipolar disorders. EBioMedicine 16, 162–171.

Phillips, M.L., Kupfer, D.J., 2013. Bipolar disorder diagnosis: challenges and future directions. Lancet 381 (9878), 1663–1671.

Sotos, J.G., 2006. Zebra Cards: An Aid to Obscure Diagnoses. Mt. Vernon Book Systems, Mt. Vernon, VA.