From Fat Location to Fat Function:
Using MRI to Examine the Links Between Body Fat and Metabolic Outcomes

Despite the well-known links between obesity and metabolic diseases, and the increased obesity and metabolic diseases among certain ethnic groups, the mechanisms of these observations remain elusive. Several putative explanations exist for why fat affects metabolic health and how this might vary by ethnicity. One such theory is based on the anatomic location of fat deposition. Current literature suggests that visceral, liver and skeletal fat accumulation affect organ function and contribute to the development of insulin resistance, fatty liver, and the metabolic syndrome. However, even in individuals matched for body fat and fat distribution, significant differences can exist in metabolic outcomes. In addition, ethnic differences in fat distribution and ectopic fat deposition do not explain ethnic disparities in metabolic diseases. Visceral fat has long been hypothesized to be one of the major factors linking increased obesity to increased disease risk. However, this hypothesis leads to an ethnic paradox, because African Americans, who are at increased risk for obesity-related diseases, especially cardiovascular disease, have lower visceral fat beginning early in life. More recent studies have also shown that ectopic fat deposition varies by ethnicity in the same way as visceral fat. Studies consistently show that Hispanics have a much higher prevalence of fatty liver disease than African Americans, also beginning early in life. Part of this ethnic difference is driven by a genetic contribution from PNPLA3, and in part driven by higher sugar consumption. Pancreatic fat fraction is also higher in Hispanics than African Americans, and the magnitude of this difference increases with age. There is also some evidence to suggest that ethnic differences in body fat pattern and accumulation may result from fundamental differences in adipose tissue biology and that adipose tissue biology itself drives metabolic disease risk. The increase in body fat content with obesity can occur by either an increase in adipocyte cell size or number, or by the spillover of triglycerides to ectopic tissues as described above. When adipocyte cell size increases with progressing obesity, it is an indication of the inability of adipocytes to expand in number to accommodate the extra tri-glyceride accumulation. Furthermore, it is now also evident that adipose tissue can become infiltrated with macrophages and this inflammatory profile drives metabolic risk. Given these observations, the disparities in metabolic diseases among ethnicities and cultures may be explained by the degree of chronic low-grade inflammation of adipose tissue. Therefore, targeting adipose tissue inflammation has become an important new strategy in treating the metabolic conditions typically associated with obesity and further studies are needed to examine these hypothesis across ethnicities and cultures that vary in the link between obesity, diabetes and metabolic risk.