INTRODUCTION: Intramyocellular lipid (IMCL) droplets, principal repositories of the intramuscular triglyceride used as metabolic fuel during exercise, are dynamic complex organelles with vital roles in regulating the synthesis, utilization, and trafficking of lipids [1-4]. The involvement of IMCL droplets in the pathogenesis of insulin resistance in obesity and type 2 diabetes is an area of intense investigation [5, 6]. The IMCL droplet is composed of a relatively homogeneous lipid ester core and a phospholipid monolayer [1, 7, 8], presenting a spatially restricted environment for lipid molecular diffusion (Fig. 1). MR diffusion studies offer a potential means of probing lipid droplet microstructures in vivo by characterizing the diffusion behavior of lipid protons. In this study, the restricted diffusion behavior of IMCL was characterized by examining the IMCL apparent diffusion coefficients (ADC) with DW-MRS sensitized to the very slow diffusion of lipid molecules. MR results were compared with histological analyses of lipid droplet size using transmission electron microscopy (TEM). To determine the sensitivity of IMCL ADC to lipid droplet size changes in vivo, IMCL ADC were examined in rodent hindlimb muscles under normal feeding condition, after 60-hr fasting, with streptozotocin (STZ)-induced diabetes, and with high-fat-diet (HFD)-induced obesity.

METHODS: Animal Preparation: Adult SD rats were divided into four groups. The control group (n=14) were examined under normal feeding condition. The fasting group (n=6) were examined after 60-hr food deprivation. The obese group (n=11) were first given high-fat diet starting from postnatal day 25 and then examined at 7 weeks later. The diabetic group (n=6) were first injected intravenously with streptozotocin (100mg/kg) and then examined at 7 weeks later. During MR experiments, animals were positioned in a pair of unipolar diffusion gradients along the x-axis. For diffusion-weighted (DW) MRS, a STEAM based single-voxel MRS sequence was implemented by adding a pair of unipolar diffusion gradients along the x-axis. For diffusion-weighted (DW) MRS, a STEAM based single-voxel MRS sequence was implemented by adding a pair of unipolar diffusion gradients along the x-axis. IMCL ADC were examined in rodent hindlimb muscles under normal feeding condition, after 60-hr fasting, with streptozotocin (STZ)-induced diabetes, and with high-fat-diet (HFD)-induced obesity.

RESULTS AND DISCUSSION: As shown in Fig.2, monoexponential diffusion decays were observed for IMCL. More importantly, IMCL ADCs decreased markedly with diffusion time, confirming the spatially restricted diffusion of lipid molecules within IMCL droplets. Furthermore, IMCL ADC was sensitive to metabolic alterations, decreasing in the 60-hr fasting and diabetic groups while increasing in the obese group. These findings indicated that the IMCL droplet size decreased following 60-hr fasting and in STZ-induced diabetes but increased in high-fat-diet-induced obesity. IMCL droplet size as determined by TEM was closely correlated with ADC and droplet diameters estimated from ADC measurements (Figs. 3 and 4).

CONCLUSION: Our results clearly demonstrate the feasibility of MR diffusion characterization of IMCL droplet microstructure and provide evidence of the sensitivity of this method to metabolic alterations. The use of diffusion MR methodology in vivo promises to provide new biophysical insights in the investigation of droplet dynamics and lipid metabolism in both animal models and human subjects. The diffusion MR results may help contribute to an improved understanding and diagnosis of obesity, diabetes, and other metabolic disorders.