and cognitive challenges faced by those with DM1, a novel method called Photovoice will be tested to explore the experience of individuals with DM1. To describe the experiences of individuals with DM1, to identify barriers and facilitors to their health, to assess the feasibility of using Photovoice with this population, and to develop a list of themes and health concerns that may be used to generate future research questions. Photovoice is a qualitative research method that gives participants cameras to document their experiences. Photovoice was developed based on concepts from feminist theory, documentary photography, and the work of educator Paulo Freire. The goal of Photovoice is to give those outside of the traditional power structure the ability to capture their experiences and share them with policy makers. Participants will be given cameras and asked to “take pictures of what it is like to live with DM1”. They will also be asked to take pictures of barriers and facilitators to their health. Their photographs will guide individual interviews and a focus group. There is a need to add patient-centered research to the DM1 literature while exploring new methods for data collection. In this study, we assume that those living with DM1 are experts about their condition, and that Photovoice may be an appropriate research method to use to capture their experiences.

Adipocytes represent a large pool of cells participating in glucose uptake, which depends on the presence and type of the insulin receptors (IR). The human IR is expressed in two isoforms: The A-isoform (IRA) lacks the exon 11 and binds both insulin and insulin-like growth factor-II, whereas the exon 11 containing isoform (IRB) only binds insulin. In adults, IRB is expressed predominantly in insulin-sensitive tissues: liver, muscle, adipocytes, and kidney. Altered expression of the two variants was recorded in adipocytes of patients with insulin independent diabetes mellitus that appears also in myotonic dystrophy type 1 (DM1). DM1 muscles contain lower levels of IR and display aberrant IR splicing associated with weaker metabolic response. Importantly, the primary determinant of pathogenic CUGexp foci formation – MBNL1 protein – seems to be responsible for IR splicing in DM1 myoblasts. Comparable splicing abnormalities occur in DM2 before muscle pathology develops. Our study demonstrates the presence of CUGexp and CUG/CUGexp nuclear foci in fat cells of both DM1 and DM2 patients respectively. We also show the expression and sequestration of MBNL1 protein in these foci, which indicates similar pathological processes as in the skeletal muscle could take place in adipose and other soft tissues. Therefore, an involvement of adipose tissue in DM1 could be explained by an aberrant IR splicing, which is indeed supported by our first results. This suggests a possible mechanism leading from RNAexp foci formation and MBNL1 sequestration to DM-associated disturbance of the insulin uptake in the fat cells. If further confirmed, these results correspond to the report that describes abnormal IR splicing in a DM mice. MB1a antibody supplied by Prof G. Morris, monoclonal antibody resource, Wolfson, RJAH Orthopaedic Hospital, Oswestry, UK. Supported by the NS/9877-3 (Ministry of Health of CR) and IAA50040802 (GAAV CR) grants.

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P5.5 Sequestration of MBNL1 protein by mutant ZNF9 RNA in lymphocytes of patients with myotonic dystrophy type 2

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The current model of myotonic dystrophy 2 (DM2) pathogenesis comprises interaction of CCUGexp pre-mRNAs of ZNF9 gene with CUG-binding proteins, which leads to their sequestration at ribonuclear foci and, in turn, to deregulation of transcription and alternative splicing of target RNAs. To characterize the role of ZNF9 loss and the CCUG repeat expansion, it is necessary to establish the identity of tissues and cell types in which the DMPK/ZNF9 protein and the ZNF9 mRNA are expressed. For this purpose, we have prepared an antibody against the ZNF9 protein and followed its immunohistochemical reactivity in human skeletal muscle, soft tissues and lymphocytes from the peripheral blood. Obtained reactivity was compared to the presence and localization of CCUGexp pre-mRNA foci and CUG/CUG-binding protein MBNL1. In the skeletal muscle of both DM patients and non-DM controls, the ZNF9 protein displayed fine granular deposits in the sarcoplasm. The protein was also found in the cytoplasm of the soft tissues and as a thin chain of perinuclear granules in the lymphocytes. The lymphocytes from DM2 patients also contained 1–2 intranuclear CCUGexp foci. MBNL1 protein in lymphocytes was detected as groups of intranuclear granules. Double label tests demonstrated that only a proportion of the MBNL1 intranuclear deposits revealed by the MB1a antibody were sequestered in the foci, while the rest of the protein was localized as intranuclear extrafocal granular deposits. Because of a low rate of sequestration of the protein in the cells, the alteration of MBNL1 protein function in lymphocytes of patients with DM2 is very questionable. Supported by the NS/9877-3 (Ministry of Health of CR) and IAA50040802 (GAAV CR) grants. Monoclonal antibody MB1a supplied by Prof Glenn Morris, MDA Monoclonal antibody resource, Wolfson CIND, RJAH Orthopaedic Hospital, Oswestry, UK.

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P5.6 Insulin receptor splicing in human adipose tissue of patients with DM2

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Insulin receptor splicing in human adipose tissue of patients with DM2

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The progression of muscle damage was studied in the patients with myotonic dystrophy type1 (DM1) using CT. We calculated % muscle volume index (%MVI) by using the histogram-based procedure. We applied this method to 115 CT scans of skeletal muscles retrospectively selected from 31 patients with DM1. %MVI was well correlated with the disability stage (p < 0.001). Patients were classified into following four groups according to sex and the length of CTG expansion; Ms. (male, (CTG) n < 1000, n = 11), MI (male, (CTG) n > 1000, n = 11), Fs (female, (CTG) n < 1000, n = 5), FL (female, (CTG) n > 1000, n = 3). We observed significant linear relationships between age at examination and %MVI in female patients (Fs, FI), but not in male patients (Ms, ML). The rate of progression in FL was significantly faster than that in FS. Under the middle of fifties, male patients are slightly severer than female patients. On the other hand, over the middle of fifties, male patients are significantly milder than female. These findings suggest sex differences in the progression of muscle damage in DM1. %MVI might serve as outcome measure for clinical trials in DM1.

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