View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

You have downloaded a document from
RE-BUŚ
repository of the University of Silesia in Katowice

Title: Ileal transposition in rats influenced glucose metabolism and HSP70 levels

Author: Dominika Stygar, Tomasz Sawczyn, Bronisława Skrzep-Poloczek, Iwona Karcz-Socha, Bogdan Doleżych, Agnieszka Zawisza-Raszka, Maria Augustyniak i in.

Citation style: Stygar Dominika, Sawczyn Tomasz, Skrzep-Poloczek Bronisława, Karcz- Socha Iwona, Doleżych Bogdan, Zawisza-Raszka Agnieszka, Augustyniak Maria i in. (2015). Ileal transposition in rats influenced glucose metabolism and HSP70 levels. "Open Life Sciences" (Vol. 10, iss. 1 (2015), s. 278-284), doi 10.1515/biol-2015-0029

Uznanie autorstwa - Użycie niekomercyjne - Bez utworów zależnych Polska - Licencja ta zezwala na rozpowszechnianie, przedstawianie i wykonywanie utworu jedynie w celach niekomercyjnych oraz pod warunkiem zachowania go w oryginalnej postaci (nie tworzenia utworów zależnych).

UNIWERSYTET ŚLĄSKI W KATOWICACH
Biblioteka Uniwersytetu Śląskiego
Ministerstwo Nauki i Szkolnictwa Wyższego

Communication **Open Access**

Dominika Stygar*, Tomasz Sawczyn, Bronisława Skrzep-Poloczek, Iwona Karcz-Socha, Bogdan Doleżych, Agnieszka Zawisza-Raszka, Maria Augustyniak, Krystyna Żwirska-Korczala, Wojciech Konrad Karcz

Ileal transposition in rats influenced glucose metabolism and HSP70 levels

Abstract: Objective: Ileal transposition procedure (IT), in combination with sleeve gastrectomy, is widely used to induce diabetes remission and to control related metabolic abnormalities. A transposition of a long segment of distal ileum in obese Zucker rats improved glucose tolerance 6 months after IT. The premise of our study was to to examine the long - term effects of ileum transposition on the liver glycolytic enzymes content in a euglycemic group of operated Zucker rats. Methods: Twenty male Zucker rats underwent either the transposition of 50% distal ileum or a sham surgery. Six months after surgery, liver tissue concentrations of glycogen synthase kinase alpha (GSK-3α), glucose 6-phosphatase (G6PC), glycogen phosphorylase (PYGM) and phosphofructokinase (PFK) and HSP70 were assessed by immunoenzymatic methods. Results: HSP70 values were significantly higher in the IT group compared to SHAM. G6PC liver concentrations in the IT group were almost 1.45-fold lower than in the SHAM operated rats. Statistical analyses (F-test) showed HSP70 levels were significantly related to caveolin-1and SHAM group. Conclusions: Lowered glycolytic enzyme concentrations assessed in the liver suggest positive effects on glucose metabolism in long-term observations.

Keywords: HSP70, ileal transposition, type 2 diabetes mellitus, obesity surgery, metabolic surgery

***Corresponding author: Dominika Stygar:** Department of Physiology, Medical University of Silesia, School of Medicine with Dentistry Division, Jordana Street 19, 41-808 Zabrze, Poland; E-mail: dstygar@sum.edu.pl

Sawczyn Tomasz, Skrzep-Poloczek Bronisława, Karcz-Socha Iwona, Żwirska-Korczala Krystyna: Department of Physiology, Medical University of Silesia, School of Medicine with Dentistry Division, Zabrze, Poland

Doleżych Bogdan, Zawisza-Raszka Agnieszka, Augustyniak Maria: Department of Animal Physiology and Ecotoxicology, University of Silesia, Katowice, Poland

Karcz Wojciech Konrad: Department of Surgery, Universitäts Klinikum Schleswig Holstein, Campus Lübeck, Germany

© 2015 Stygar Dominika et al. licensee De Gruyter Open.
This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 License.

Brought to you by | Uniwersytet Slaski - University of Silesia - Silesian University
Authenticated
Download Date | 8/22/17 11:24 AM

DOI 10.1515/biol-2015-0029
Received January 26, 2015; accepted March 29, 2015

1 Introduction

One of the effects of oxidative stress disorders in obesity and diabetes mellitus (type 2) is liver dysfunction manifested with deterioration in carbohydrate and lipid metabolism. These metabolic abnormalities promote steatosis, fibrosis, cirrhosis, hepatitis and biliary disease. The increased hepatic glucose production, hepatic glucose uptake and glycogen storage is one of the effects of insulin resistance and hyperglycemia observed in Zucker diabetic fatty (Crl:ZUC-Lepr^{fa}) rats, a widely used obese metabolic syndrome and pre-diabetes model [1]. Ileal transposition procedure (IT) is widely used to induce diabetes remission and to control related metabolic abnormalities. A transposition of a long segment of the distal ileum in obese Zucker rats improved glucose tolerance for 6 months after IT [2,3]. This was the premise to examine the long-term effects of ileum transposition on liver glycolytic enzymes and HSP 70 content in a euglycemic group of operated Zucker rats.

Heat shock proteins (Hsps) are up-regulated in response to cellular stresses such as inflammation and oxidative stress and are considered to be molecular chaperones that assist in the folding, assembly and degradation of other cell proteins [4,5]. In general, Hsps are known to regulate signal transduction, protein trafficking, cellular proliferation, and cell differentiation [6]. HSP70 is a big family of ATP-dependent chaperones, which takes part in protein folding and protect against cellular stress and toxicity [7]. In the conditions of insulin resistance, HSP levels are low in the insulin dependent tissues like liver, skeletal muscle and adipose tissue [8].

The improvement in glucose metabolism after bariatric surgery may be achieved through physiological and biochemical mechanisms contributing to weight loss, improved hepatic and peripheral insulin sensitivity

[9]. Enzymes assayed in this project were selected due to their central role in the regulation of carbohydrate and energy homeostasis. It has been recognized that glucose-6-phosphatase (G6PC) is one of the crucial regulatory enzymes of gluconeogenesis and is expressed in the liver, skeletal muscle and small intestine [10]. Glycogen phosphorylase (PYGM) is the major enzyme in glycogenolysis responsible for the glucose-1-phosphate release from glycogen [9]. Glycogen synthase kinase-3 (GSK-3 EC 2.7.11.26) is involved in glycogen synthase (GS) regulation, phosphorylation and its deactivation. GSK-3 shows enhanced activity in insulin-resistant states and has been proposed as a potential therapeutic target for the treatment of diabetes [11]. Phosphofructokinase (PFK) is a sensitive indicator of the glycolytic pathways in diabetic states and a key rate-limiting enzyme in glycolysis [12].

This paper is a continuation of a research project examining the long term effect of ileal transposition in term of physiologic background and long-term adaption in Crl:ZUC-Lepr^{fa} Zucker rats [3,13]. The principal goal of this study was to investigate the impact of transposition of 50% of distal ileum on separated, selected parameters of glucose administration and HSP70 concentration levels during *in vivo* experiments on the Crl:ZUC-Lepr^{fa} rat's liver six months after IT surgery.

2 Materials and Methods

This paper is the third part of a wider experiment which concerned ileal transposition treatment of obesity and insulin resistance, in the obese rat model: Crl:ZUC-Lepr^{fa} Zucker rat [3,13]. All surgical and experimental procedures were precisely described earlier by our research group [3,13], thus in this paper we briefly present only the main points. The animal experimental protocols were approved by the Ethics Committee of the University of Freiburg [3,9,13]. In short, 11 to 12-week-old, 200-220 g, obese male Zucker rats (Crl:ZUC-Lepr^{fa}) were purchased from Charles River Breeding Laboratories (Wilmington, Mass). The rats were housed individually and maintained on a 12/12-hour light/dark cycle with free access to water and rat chow diet (ProvimiKliba AG, Kaiseraugst, Switzerland). The chow contained 24% protein, 4.9% fat, 7% crude ashes, 4.7% crude fiber, lysine (13.6 g/kg), calcium (12 g/kg), methionine (4.5 g/kg), and phosphorus (8.3 g/kg).

2.1 Surgery

After a 7–8 day acclimation period, 10 rats underwent an ileal transposition surgery on 50% of distal ileum [3]. The animals were fasted for 12 hours before surgery. Anesthesia was induced and maintained using Isoflurane 2% (Abbott GmbH & Co. KG, Wiesbaden, Germany) and oxygen flow at 2 L/min under spontaneous breathing. After a midline incision of 4–5 cm to gain abdominal access, Bauhin's valve was identified. Previously, we had determined the total small bowel length of Zucker rats to be approximately 85 cm. Transections of 50% distal segment (25 cm) was conducted in relation to Bauhin's valve.

2.1.1 IT

For IT, the Treitz's ligament was identified and the jejunum divided 5 cm aborally. The ileal loop was then interpositioned in an isoperistaltic fashion forming two end-to-end anastomoses. Mesenterial openings were closed with Prolene 6/0 (Ethicon). Fascia and skin closure were performed as a continuous suture using Monocryl 4/0 and Vicryl 4/0. Postoperative analgesia was ensured via subcutaneous Carprofen (Rimadyl, Pfizer, Switzerland) injection (4 mg/kg) at the beginning of the operation. Animals were fasted on day 1 after the operation with free access to tap water, and oral food was continuously built up to free access until day 6 [3,13].

2.1.2 SHAM

Ten male Zucker rats were selected for SHAM surgery. A division of small intestine with subsequent anastomoses was performed at the 3 corresponding positions without IT. Pre and postoperative treatment was identical for the IT group [3,13].

2.2 Blood and tissue collection

Six months after surgery, anesthesia was induced and maintained using isoflurane 2% and oxygen flow at 2 L/min under spontaneous breathing. A cannula (26-gauge) was placed in the tail vein for blood collection. We drew 400 µL of whole blood *via* the cannula at 0 and 20 minutes after oral glucose (1.5 mg/kg) was given via tubes containing 10 mL EDTA (Sigma-Aldrich, St. Louis, Mo). After centrifugation at 4.000 rpm for 10 minutes at 4ºC, plasma samples were collected and snap frozen in liquid nitrogen and stored at -80ºC until analysis. After blood sampling, the animals were sacrificed and tissues were harvested. Liver tissue was explanted and snap frozen in liquid nitrogen and stored at -80ºC until further analysis.

Brought to you by | Uniwersytet Slaski - University of Silesia - Silesian University
Authenticated
Download Date | 8/22/17 11:24 AM

2.3 Tissue HSP70 assessment

HSP70 liver tissue concentrations were assessed in duplicates by immunoenzymatic method with the commercially available ELISA kits (USCN Life Science Inc., USA). To assess the validity and predict tissue concentration of chosen parameters in 100 mg of tissue, the optimal sample dilutions were preliminarily determined. Tissue samples were prepared by homogenization and sonification (15 s) on ice in tissue cell lysis buffer containing protease inhibitors (Gold Biotechonology, USA). After that, the homogenates were centrifuged at 5000 × *g* for 15 minutes at 4°C, then the supernatant was removed and diluted according to previously assessed protocols and used in the ELISA assay. The microtitre plate was pre-coated with a monoclonal antibody specific to rat HSP70. Standards and samples were added to microtitre plate coated with biotin-conjugated polyclonal antibody preparation specific for HSP70. Subsequently, a mixture of a biotin specific antibody and horseradish peroxidase (HRP) was added to each well and incubated. For detection, each well was incubated with a substrate solution and measured in a microplate reader at a wavelength of 450 nm ± 10nm. For those wells that contained HSP70, biotin-conjugated antibody and enzyme-conjugated Avidin exhibited a change in color. The concentration of HSP70 in the samples was determined by comparing the optical density O.D. of the samples to the standard curve. The data were expressed in ng/mL. The sensitivity of the kit was ≤ 0.045 ng/mL.

2.4 Tissue glycolytic enzymes assessment

Tissue concentration of glycogen synthase kinase alfa (GSK-3α), glucose 6-phosphatase (G6PC), glycogen phosphorylase (PYGM) and phosphofructokinase (PFK-1) in the liver was assessed in duplicate using immunoenzymatic methods with the commercially available ELISA kit (USCN Life Science Inc., USA) after optimization procedure. To assess the validity of our methods and to be able to predict the tissue concentration of chosen parameters in 100 mg of tissue, optimal sample dilutions for particular elements of the ELISA bioassay were preliminarily determined. Tissue samples were prepared by homogenization and sonification (15 s) on ice in a tissue cell lysis buffer containing protease inhibitors (Gold Biotechonology, USA). After that, the homogenates were centrifuged at 5000 × *g* for 15 minutes at 4°C, then the supernatant was removed and diluted according to the previously assessed dilution and used in the ELISA assay.

2.5 Statistics

Statistical analysis was conducted using the Statistica package (STATISTICA 10.0, StatSoft Inc., 2010). For HSP70 group comparison Mann-Whitney U post-hoc tests were used and $p < 0.05$ was considered significant. Spearman's rank correlation coefficient was calculated for $p < 0.05$. For estimation of the relationships among the analyzed variables F-test was applied, $p < 0.005$. For enzymes, we used ANOVA and Tukey's post-hoc tests and the values are presented as mean ± standard deviations (SD).

3 Results

This study is the third part a of previously presented experiment [3,13]. The general characteristics of IT operated rats and the SHAM group with regards to body mass, the oral glucose tolerance test (OGTT), incretin hormones and insulin serum levels were presented by Grüneberger [13].

3.1 Glycolytic enzymes tissue concentration (GSK-3α, PYGM, G6PC, PFK-1) and liver HSP70 concentrations

To assess the glycolytic enzyme concentrations, all values were calculated and presented as ng enzyme/mL/mg of wet tissue. Concentrations of PYGM, G6PC, PFK-1 were significantly different between the analyzed IT and SHAM groups. G6PC liver concentrations in the IT group were almost 1.45-fold lower than in the SHAM operated rats (64.868 ± 26.6 vs. 44.150 ± 7.2 ng/mL/mg w.t, $p < 0.006$; fig.1). The effects of IT on PYGM and PFK-1 liver concentrations were more discreet (respectively; 10.734 ± 1.1 vs. 9.623 ± 1.3, $p < 0.01$ and 108.029 ± 12.1 vs. 97.572 ± 10.9 ng/mL/mg w.t, $p < 0.01$; Fig.1,2.). No significant differences in liver concentration of GSK-3α were found between IT and SHAM groups (31.072 ± 3.5 vs. 30.678 ± 2.9 ng/mL/mg w.t, $p < 0.81$; Fig.2.). There were significant correlations between selected enzymes (Tab.1). For HSP70 tissue assessment all values, calculated and presented as ng/mL/mg of wet tissue, were significantly higher in IT group compared to SHAM (Fig. 3.).

3.1.1 F-test results

HSP70 levels were significantly related to SHAM group (ß = -0.239; +95% CI = -0.334; -95% CI = -0.144; p = 0.000001).

Brought to you by | Uniwersytet Slaski - University of Silesia - Silesian University
Authenticated
Download Date | 8/22/17 11:24 AM

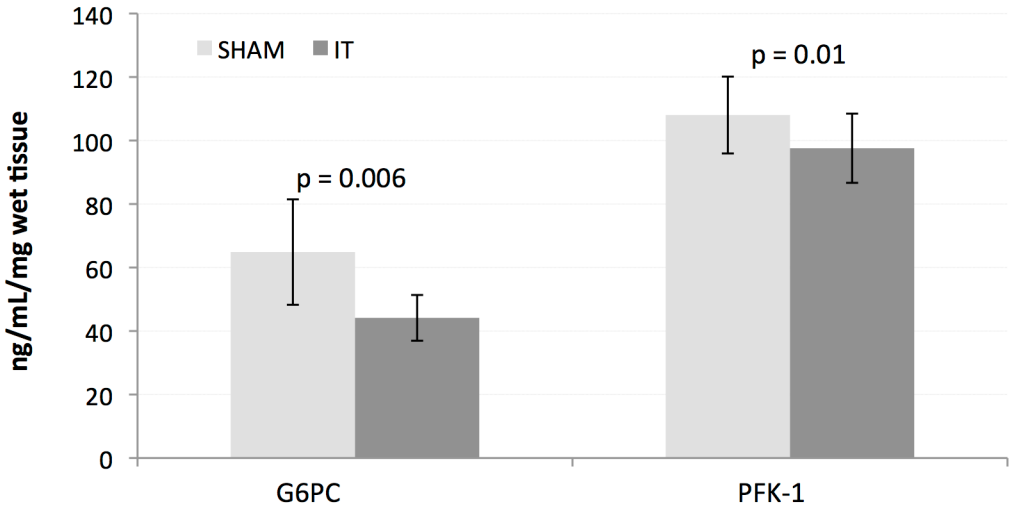

Fig.1: The tissue concentrations of glucose 6-phosphatase (G6PC) and phosphofructokinase (PFK) in the liver. Optimalized enzyme-linked immunosorbent assay assessment for tissue concentration [ng/mL/mg wet tissue], SHAM versus 50% distal IT, six months after surgery, Tukey test, $p < 0.05$.

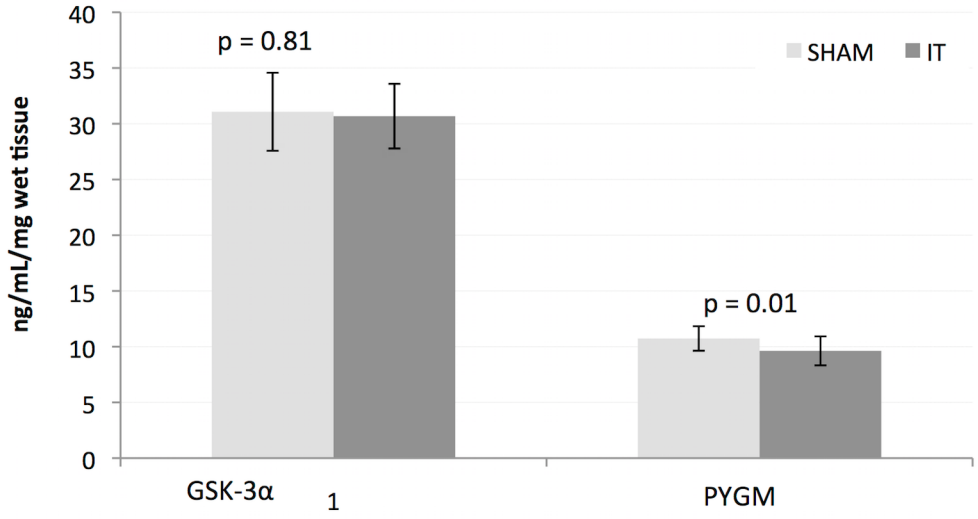

Fig.2: The tissue concentrations of glycogen synthase kinase alpha (GSK-3α), glycogen phosphorylase (PYGM) in the liver. Optimalized enzyme-linked immunosorbent assay assessment for tissue concentration [ng/mL/mg wet tissue], SHAM versus 50% distal IT, six months after surgery, Tukey test, $p < 0.05$.

4 Discussion

As anti-inflammatory agents HSP70 plays role in response to oxidative cell stress, which is characteristic for obesity and insulin resistance. The levels of HSP70 were found lowered in all insulin-dependent tissues in conditions of obesity, diabetes 2 mellitus and insulin resistance which were also associated with low heat shock factor-1 (HSF-1), low HSP expression, and low HSP levels in insulin-sensitive tissue [8,11]. Decreased HSF1 levels correlate to lowered HSP concentrations in liver and skeletal muscles tissues of diabetic animals in the streptozotocin-induced animal model. In this study, serum HSP70 levels were significantly higher in IT group compared to SHAM, which may be associated with improved insulin resistance. Garcíaa et al. (2012) a presented very interesting

Brought to you by | Uniwersytet Slaski - University of Silesia - Silesian University
Authenticated
Download Date | 8/22/17 11:24 AM

Table 1: Significant correlations between analyzed parameters in IT and SHAM groups, spearman correlations, p < 0.05.

ANALYSED PARAMETERS	R Spearman	t (N-2)	p
G6PC : GSK-3 α	0.720	3.448	0.005
G6PC : PYGM	0.722	3.468	0.005
PYGM : PFK-1	0.647	2.817	0.016
PFK-1 : GSK-3 α	0.604	2.516	0.028
PFK-1 : G6PC	0.773	4.041	0.001

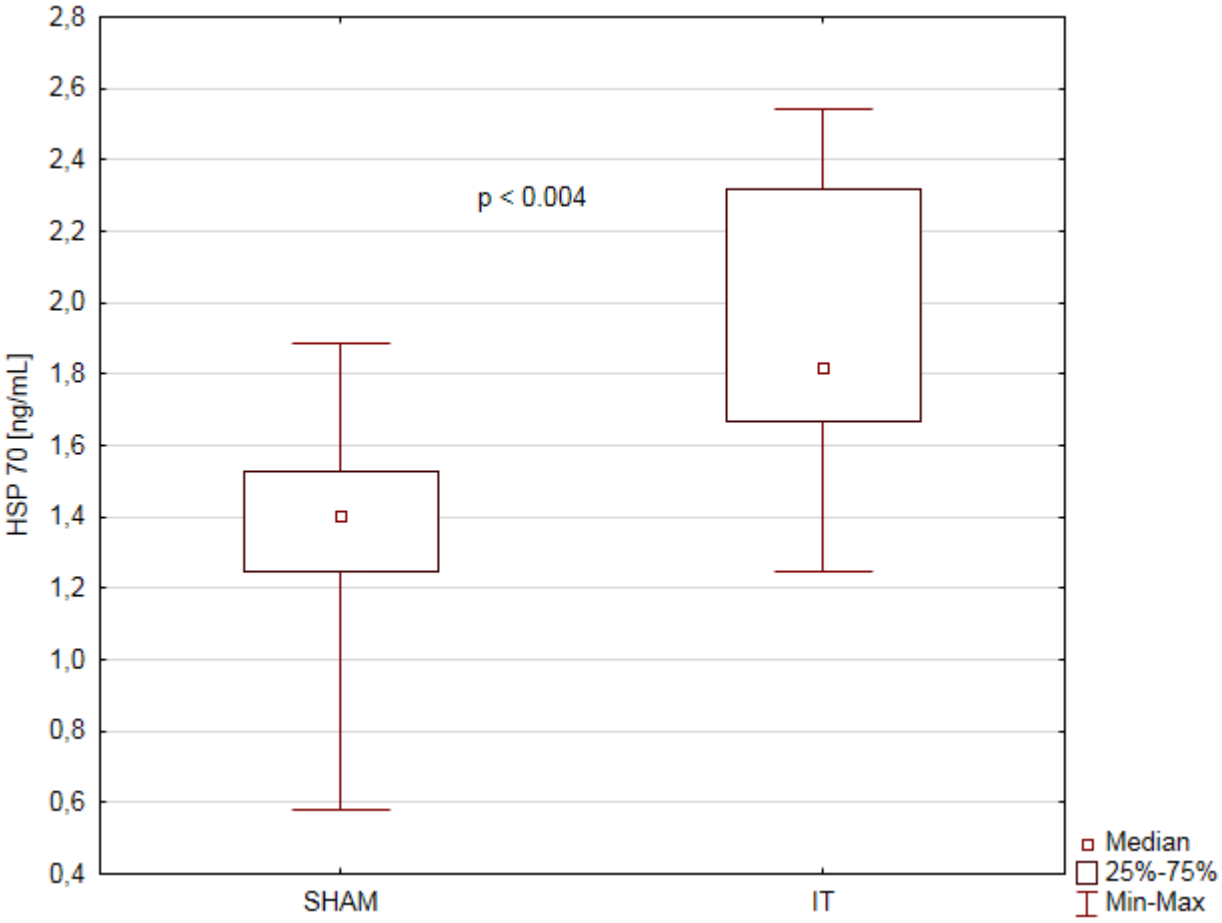

Fig.3: Comparison of HSP70 concentration [ng/mL] in SHAM and IT groups. Mann-Whitney U test, p < 0.05. Results are presented as median with first and third quartile.

study where downregulation of caveolin-1 related to upregulation of eNOS/HSP70 in tubulointerstitial fibrosis injury in neonatal early kidney obstruction treated with rosuvastatin [14]. HSP70 liver concentration can be higher in IT group due to increased expression, which was not assessed in this experiment [15]. Influencing the induction of heat shock proteins was widely proven as highly beneficial, particularly in patients suffering from diabetes or being insulin-resistant, protecting them from complications. HSP family reduces ischemia-reperfusion injury in the heart [16 powers] and provides favorable effects on neuropathy and nephropathy in diabetic rodents [10,17]. Induced expression of HSP70 can provide broader health advantages in patients after IT. To increase the picture of changes in glucose metabolism after ileal transposition, we assessed the content of key rate-limiting glycolytic enzymes. The concentrations of PYGM, G6PC, PFK-1 in liver tissue of rats after IT were significantly lowered compared to SHAM groups (Figs 1, 2). Glucose-6-phosphatase level was the most decreased in comparison with other analyzed enzymes. Glucose homeostasis in the liver consists of a number of mechanisms, but low release

Brought to you by | Uniwersytet Slaski - University of Silesia - Silesian University
Authenticated
Download Date | 8/22/17 11:24 AM

of glucose into the blood from the liver could be the dominant cause of lower glucose fasting concentrations after IT [3,13]. Glucose-6-phosphatase is widely expressed in skeletal muscle, the liver and the small intestine. Gluconeogenesis also occurs in the kidney, thus the future investigation of expression of G6PC can be assessed also in that tissue. Perhaps, glucose management can also be altered in the kidney. In this project, G6PC was chosen as one of the key enzymes involved in glucose metabolism to examine the reasons of benefits linked with an improvement in glucose tolerance after IT procedure. Both gluconeogenesis and glycogenolysis result in the formation of glucose 6-phosphate, which has to be hydrolyzed by glucose-6-phosphatase (G6PC) before entering the bloodstream as glucose. The inhibition of glucose-6-phosphatase results in hepatic entrapment of glucose and *de novo* lipogenesis, leading to massive steatosis within several hours. Also, acute inhibition of glucose-6-phosphate translocator activity leads to increased *de novo* lipogenesis and development of hepatic steatosis without affecting VLDL production in rats [18]. It is worth mentioning that 20 weeks after duodenal - jejunal bypass in Goto-Kakizaki rats, G6PC levels within the liver were lower than in the SHAM operated group [9]. DJB operation consists of elements other than IT, but the effect could be similar, meaning low levels of G6PC in the liver. The effects of IT and duodenal-jejunal bypass on G6PC levels could be comparedIt may suggest lower utilization of glucose and glycogen with a concomitant increase in the level of plasma triglycerides. In our study, glycogen phosphorylase (PYGM) and phosphofructokinase (PFK1) levels were also lowered 24 weeks after IT surgery. PYGM is responsible for the release of glucose-1-phosphate from glycogen. Glycogenolysis is catalyzed in liver, muscle and brain by tissue specific isoforms of glycogen phosphorylase and the regulation of the hepatic glucose output through glycogenolysis is an important target for type 2 diabetes therapy [19]. Low hepatic PYGM levels in IT animals may suggest that during periods of fasting, the liver releases less glucose than in SHAM animals. This is the probable reason for lower glucose fasting levels in IT animals, therefore this mechanism is not marked like in G6PC changes. Due to the central role of this enzyme in glycogen metabolism, PYGM has been exploited as a model for structure-assisted design of potent inhibitors, which may be relevant to the control of blood glucose concentrations in type 2 diabetes [20]. PFK-1 is the other key regulatory enzyme in glycolysis. In IT animals we observed lower PFK-1 levels in the liver, which could suggest that glucose is more likely to be stored in the liver than released into the bloodstream. A recent study reported PFK-1 upregulation changes after IT in Sprague-Dawley rats, in the adipose tissue and skeletal muscle [21]. According to literature data and to our study, the IT operations could reproduce the correct storage of glucose in the liver to allow? utilization in peripheral tissues, such as adipose tissue and skeletal muscle. GSK3-α shows a modulating effect on heat shock protein expressions through heat shock factor-1 (HSF-1) [11]. Hooper suggested that the condition of reduced level of HSP is an effect of failed inactivation of GSK-3, and results in phosphorylation and deactivation of HSF-1 [11]. In this study the liver tissue concentration of GSK3-α remained unchanged between IT and SHAM groups. All those findings suggest a suppressed hepatic glucose production, uptake and also reduced metabolism and storage of glycogen. The present study for the first time presents the long-term effect of ileal transposition on HSP70, and glycolytic enzyme concentrations in the liver. In our experiment, six months after transposition of 50% of the ileum, levels of glycolytic enzymes assessed in the liver were lowered.

Acknowledgements: Funding agencies: The study was supported by grant from Freiburg University, Germany. Author contributions: DS, TS conducted IT surgery; IK-S, BS-P analyzed the data; BD, AZ-R, MA carried out experiments; DS, KZ-K, WKK conceived the study; DS, B S-P were involved in writing communicate. All authors had final approval of the submitted and published version.

Conflict of interest: The authors have no conflicts of interest or financial ties to disclose.

Statement of Animal Rights: Procedures followed were in accordance with the ethical standards of the Ethics Committee of the University of Freiburg, Germany.

References

[1] Augstein P., Salzsieder E., Morphology of Pancreatic Islets: A Time Course of Pre-diabetes in Zucker Fatty Rats, Methods. Mol. Biol., 2009, 560, 159-89

[2] Koopmans H.S., Sclafani A., Fichtner C., Aravich P.F., The effects of ileal transposition on food intake and body weight loss in vmhobese rats, Am. J. Clin. Nutr., 1982, 35, 284-93

[3] Grüeneberger J.M., Fritz T., Zhou C., Meyer S., Karcz-Socha I., Sawczyn T., Stygar D., Goos M., Hopt U.T., Küsters S., Long segment ileal transposition leads to early amelioration of glucose control in the diabetic obese Zucker rat, Videosurgery, 2013, 8(2), 130-8

[4] Macario A.J.L., Conway de Macario E., Molecular chaperones: Multiple functions, pathologies, and potential applications. Front. Biosci., 2007, 12, 2588-2600

Brought to you by | Uniwersytet Slaski - University of Silesia - Silesian University
Authenticated
Download Date | 8/22/17 11:24 AM

[5] Liberek K., Lewandowska A., Ziętkiewicz Sz., Chaperones in control of protein disaggregation, EMBO J, 2008, 27, 328-335
[6] Helmbrecht K., Zeise E., Rensing L., Chaperones in cell cycle regulation and mitogenic signal transduction: a review, Cell. Prolif., 2000, 33(6), 341-365
[7] Macario A.J., Conway de Macario E., Molecular chaperones: multiple functions, pathologies, and potential applications, Front. Biosci., 2007, 12, 2588-2600
[8] Hooper Ph.L., Hooper P.L., Inflammation, heat shock proteins, and type 2 diabetes, Cell Stress Chaperones, 2009, 14, 113-115.
[9] Sun D., Wang K., Yan Z., Zhang G., Liu S., Liu F., et al., Duodenal-jejunal bypass surgery up-regulates the expression of the hepatic insulin signaling proteins and the key regulatory enzymes of intestinal gluconeogenesis in diabetic Goto-Kakizaki rats, Obes. Surg., 2013, 23(11), 1734-42
[10] Biro K., Palhalmi J., Toth A.J., Kukorelli T., Juhasz G., Bimoclomol improves early electrophysiological signs of retinopathy in diabetic rats, Neuroreport, 1998, 9, 2029-2033
[11] Hooper L.P., Insulin signaling, GSK-3, heat shock proteins and the natural history of type 2 diabetes mellitus: a hypothesis, Metab. Syndr. Relat. Disord., 2007, 5(3), 220-30
[12] Shimizu T., Parker J.C., Najafi H., Matschinsky F.M., Control of glucose metabolism in pancreatic β-cells by glucokinase, hexokinase, and phosphofructokinase, Model study with cell lines derived from β-cells, Diabetes, 1988, 37(11), 1524-1530
[13] Grüeneberger J.M., Karcz-Socha I., Sawczyn T., Kosmowski J., Stygar D., Goos M., et al., Systematic ileal transpositionin Zucker rats shows advantage for long segment distal transposition, Surgery, 2014, 155(1), 165-72
[14] Garcíaa I.M., Mazzeia L., Benardóna M.E., Oliverosc L., Cuello-Carriónd F.D., Gil Lorenzob A., Caveolin-1–eNOS/Hsp70 interactions mediate rosuvastatin antifibrotic effects in neonatal obstructive nephropathy, Nitric Oxide, 2012, 27(2), 95-105
[15] Bocanegra V., Manucha W., Peña M.R., Cacciamani V., Vallés P.G. Caveolin-1 and Hsp70 interaction in microdissected proximal tubules from spontaneously hypertensive rats as an effect of Losartan, J. Hypertens., 2010, 28(1), 143-55
[16] Powers S.K., Locke A.M., Demirel H.A., Exercise, heat shock proteins, and myocardial protection from I-R injury, Med. Sci. Sports. Exerc., 2001, 33, 386-392
[17] Nanasi P.P., Jednakovits A. Multilateral in vivo and in vitro protective effects of the novel heat shock protein coinducer, bimoclomol: results of preclinical studies, Cardiovasc. Drug. Rev., 2001, 19, 133-151
[18] Bandsma R.H., Wiegman C.H., Herling A.W., Burger H.J., Harmsel A., Meijer A.J., et al., Acute inhibition of glucose-6-phosphate translocator activity leads to increased de novo lipogenesis and development of hepatic steatosis without affecting VLDL production in rats, Diabetes, 2001, 50, 2591-2597
[19] Oikonomakos N.G., Glycogen Phosphorylase as a Molecular Target for Type 2 Diabetes Therapy, Curr. Protein. Pept. Sci., 2002, 3, 561-586
[20] Ramzy AR, Nausheen S, Chelikani PK., Ileal transposition surgery produces ileal length-dependent changes in food intake, body weight, gut hormones and glucose metabolism in rats, Int. J. Obesity, 2014, 38(3), 379-387
[21] De Paula A.L., Stival A.R., Halpern A., De Paula C.C., Mari A., Muscelli E., et al., Improvement in insulin sensitivity and beta-cell function following ileal interposition with sleeve gastrectomy in type 2 diabetic patients: potential mechanisms, J. Gastrointest. Surg., 2011, 15, 1344-53

Brought to you by | Uniwersytet Slaski - University of Silesia - Silesian University
Authenticated
Download Date | 8/22/17 11:24 AM