

**Pathogenetic role of diabetic central and peripheral polyneuropathy in the development
of impaired gastrointestinal motility**

PhD Thesis

Dr. Várkonyi Tamás

1st Department of Medicine, University of Szeged

2003

1. Introduction, background and aims

From studies during the past few decades it has become evident that none of the late complications of diabetes mellitus (DM) affects so many organs and functions as polyneuropathy. It is also now clear that such neuropathy is not a separate clinical entity, but a component of several related complications in a high number of different organs. The latter observation led to the definition of neuropathy as an interdisciplinary subject, which is of interest in diabetology, gastroenterology, cardiology, urology and neurology. Both autonomic and peripheral sensory neuropathy have a number of characteristic manifestations, many of them lead to a poor prognosis for diabetic patients. The progressive damage to the fibres of the parasympathetic and sympathetic nervous systems is the root of the abnormalities in autonomic neuropathy (AN). The involvement of those fibers that innervate the cardiovascular system is one of the most important complications of AN. The increased mortality is the most important consequence of cardiovascular AN. A further important aspect of cardiovascular AN is that almost all of the manifestations (changes in the regulations of the heart rate and blood pressure, and impairment of the cardiac repolarization) can be described by numerical parameters providing quantitative methods for testing of the presence or severity of neuronal impairment. Besides the well-studied patterns of the cardiovascular complications of AN, various characteristics of the digestive manifestations are still poorly understood. It is now recognized that the digestive complications in DM are very frequent, but there is a lack of prevalence data in separate subgroups of DM patients selected via the different parameters of duration, type, treatment and glycaemic control. The high frequency of the various severe symptoms and signs, the worsened quality of life and the altered carbohydrate absorption due to the extreme blood glucose level excursions are all those undesirable consequences of gastrointestinal dyfunctions which necessitate further research efforts. Although all the digestive functions can be deficient in diabetic neuropathy, the motility seems to be primarily affected and the alterations in secretion and absorption are reported to be secondary complications. Regulation of the gastrointestinal motility is predominantly influenced by the nervous systems. Most of the unfavourable effects of AN on the digestive tract can be derived from the imbalance of the parasympathetic/sympathetic activity. This process results in an attenuation of one of the neuron systems and a relative dominance of the other. The final influence of the relative attenuation or augmentation of the parasympathetic/sympathetic system on the motility patterns can be different in separate organs. The complex nature of AN is presumably one of the causes of the contrast in the description of its manifestations in the organs of the gastrointestinal tract. The most harmful feature of the altered motility is the impaired postprandial emptying, which leads to an imbalance of the carbohydrate metabolism and/or induces a large number of symptoms. The question is still open as concerns what degree of emptying impairment is associated with the different stages of AN. The consequences of the separate or the common damage to the parasympathetic/sympathetic systems have not been explored. The fate of the emptying disorders during the progression of AN is not known. It would be important to evaluate the similarities or differences of the manifestations of AN in various digestive organs in the same patient groups. It has not yet been elucidated, whether the efferent or afferent functions or both are involved in the pathogenesis of AN. Besides AN, the other frequent form of diffuse neuropathies, the distal symmetric sensory polyneuropathy results in a sensory loss due to the altered afferent nerve function. Quantitative determination of the severity of the sensory neuronal dysfunction provides staging data on the degree of the overall neuropathic process, and on the other hand, supplies a description of the state of those fibres which are involved in the afferent function. The increasing evidence of the cerebral dysfunction in DM suggests that the neuronal structures of the central nervous system may be involved in polyneuropathy. The neurons of the central nervous system might not be preserved from the general harmful effects resulting in neuropathy. The impairment of the central afferent function might be a prominent part of the aetiology of neuropathy, because the intact afferent activity is similarly as important as the efferent function in the achievement of the physiological regulation in the autonomic system. The possible similarities or differences between the peripheral sensory neuropathy and the central afferent function may supply new data about the common sensitivity of afferent fibres to the pathogenetic process.

The present work had the aim of an evaluation of the characteristics of the postprandial emptying of the oesophagus, stomach and gallbladder in long-standing type-1 DM and their comparison with the values for age-matched healthy control subjects. The gastric emptying was also measured in type-1 DM following a long-term survival of transplanted islets. Further work was carried out to explore the gastric emptying in long- and short-standing type-2 DM. The patterns of cardiovascular autonomic and the sensory neuropathy were evaluated in all patient groups and controls. To explore the central afferent function, the auditory- and visual-evoked potentials were examined in long-standing type-1 DM. Finally, correlations were calculated between the severity of autonomic and sensory neuropathy, the central dysfunctions and the motility parameters.

2. Patients, methods

2.1. Patients

In accordance to the aims of our study, patients with type-1 and type-2 DM were selected. Altogether 64 patients were enrolled (duration of DM: 19.2 ± 1.7 yrs, age: 53 ± 1.4 yrs, BMI: 25.9 ± 0.7 ; mean $\pm$ SE). 32 patients had type-1, 13 patients had insulin-treated type-2 DM and 19 patients had type-2 DM with oral antidiabetic treatment.

2.2. Evaluation of AN by means of cardiovascular reflex tests

The cardiovascular reflex tests performed in our studies were in accordance with the description of Ewing et al.. The heart rate tests mainly (but not absolutely) reflect the parasympathetic function, while the blood pressure tests supply information concerning the sympathetic innervation. The results of each of the five tests were scored as 0 (normal), 1 (borderline) or 2 (abnormal), and a final autonomic score was calculated (range 0-10) to express the severity of the overall autonomic disorder.

2.3. Assessment of peripheral sensory neuropathy by application of Neurometer

The peripheral sensory function was studied with a Neurometer (Neurotron Incorporated, Baltimore, MD, USA), following the methodological instructions of Masson and Boulton. This device is suitable for the quantification of the function of different nerve fibres, and provides a simple, non-invasive and quantitative measure of peripheral sensory function. Low voltage, electric sine wave stimulation was applied transcutaneously and the current perception threshold (CPT) values were determined. In our studies the median and peroneal nerves were tested.

2.4. Radionuclide oesophageal emptying

The radionuclide studies of oesophageal emptying were performed in a supine position under a gamma camera linked to a micro processor. After an overnight fast, 20 MBq ^{99m}Tc EHIDA diluted in 15 ml of water was ingested with swallow. The oesophageal transit in our studies was defined as the percentage of the oesophageal emptying by the 15th s which elapsed from appearance of the activity at the cricoid cartilage. 90 % or higher emptying was determined as normal values.

2.5. Scintigraphic gastric emptying

At the start of the test the patients after an overnight fast ingested a breakfast containing a bread roll, 200 ml of water and 2 hard-boiled eggs labeled with 40 MBq ^{99m}Tc human serum albumin macroaggregates. The test was terminated after 120 minutes. Generation of time-activity curves over the whole stomach as a region of interest made it possible to analyze the quantitative characteristics of gastric emptying. Calculation of the scintigraphic gastric half-emptying time (HTE) provided a numeric parameter characterizing the postprandial stomach motility.

2.6. Quantitative hepatobiliary scintigraphy

Patients were tested in fasting state in the morning hours. The gamma camera was positioned over the right upper abdomen of the supine patient. At the start of the measurement, an isotope-labeled agent was injected intravenously which binds to serum proteins. 60 minutes after the injection, almost 70% of the secreted radioactivity enters the gallbladder during fasting. When the gallbladder was filled with radioactive bile, a cholecystokinin (CCK) analog was administered over 10 min. at a rate of 1 ng/kg/min. Following the generation of time-activity curves and after a background subtraction, the gallbladder ejection fraction (EF) was determined, expressed as a percentage of the pre-contraction volume. The half-time of ejection ($T_{1/2}$) was measured as the time at which the maximal activity was halved. The latent period (LP) was defined as the interval which elapsed between the administration of the CCK analog and the onset of the gallbladder contraction.

2.7. Evaluation of brainstem auditory-evoked potentials

Seven electrical waves are generated along the nerve tracts of the auditory system within the first 10 ms after the delivery of the audible click of short duration. The characteristics of five waves were measured in this study (waves I., II., III. and V). Two parameters of the waves were analyzed: 1. The peak latency was measured from time of the stimulus onset to the appearance of each wave 2. Inter-peak latency (IPL) was determined as the delay from wave I to waves III, and V (IPL I-III, I-V) and III-V (IPL III-V).

2.8. Detection of visual-evoked potentials

The visual-evoked potentials were recorded from an active electrode placed at the occipital region. The latency values of the major positive component of the visual evoked potentials (P100) were evaluated in this study. The latency, expressed in ms, was defined as the time interval between the onset of the stimulus and the generation of the peak of P100 wave.

3. Results

3.1. Assessment of gastrointestinal motility in long-standing type-1 DM

3.1.1. Oesophageal emptying

The emptying of 15 ml water labeled with radioactive agent from the oesophagus was insufficient in diabetic patients in comparison with the emptying of healthy subjects. 65.8 ± 7.7 % (mean $\pm$ SE) of the peak activity left the oesophagus at the 15 s interval from the appearance of the radioactivity at the cricoid cartilage.

3.1.2. Gastric emptying

Evaluation of the HTE for the stomach revealed an impairment of solid meal emptying in the group of patients with long-standing type-1 DM. The mean value of the HTE in the type-1 diabetic group with long disease duration was 98.3 ± 10.1 min., while 49.6 ± 5.5 min. was the HTE in healthy controls ($p < 0.01$).

3.1.3 Gallbladder emptying

The evaluation of hepatobiliary scintigraphy revealed a decrease in the gallbladder EF in response to the CCK analog in the type-1 diabetic group as compared with the control values of the subjects with a normal glucose metabolism (EF: 30.5 ± 3.46 vs 84.5 ± 4.5 %, long-standing type-1 DM vs controls, $p < 0.01$). None of the patients had an ejection fraction inside the normal range.

3.1.4. Gastric emptying of fetal pancreatic islet-transplanted and non-transplanted type-1 diabetic patients

No significant difference was found in the comparison of the gastric emptying in the transplanted (tx) diabetic group with that of the healthy subjects (69.7 ± 10.7 vs 49.6 ± 5.5 min, $p > 0.05$, tx DM vs healthy controls). Further analysis of the gastric emptying rates in the type-1 DM groups demonstrated a difference between the tx and the control non-tx patients (115 ± 15.1 vs 69.7 ± 10.7 min, $p < 0.05$, non-tx vs tx).

3.2. Determination of gastric emptying in patients with type-2 DM

3.2.1. Gastric emptying in patients with long-standing type-2 DM

The mean HTE of the stomach in this group of patients was delayed in comparison with the healthy controls (84.4 ± 8.8 vs 49.6 ± 5.5 min., type-2 DM vs controls, $p < 0.05$).

3.2.2. Gastric emptying in patients with short-standing type-2 DM

62.1 ± 7.3 min. was the mean HTE of the stomach in this patient group which did not differ significantly from the value of control subjects

3.3. Characterization the relations between impaired gastrointestinal motility and cardiovascular autonomic neuropathy

3.3.1. Analysis of the severity of cardiovascular AN in long-standing type-1 diabetic patients

3.3.1.1. Cardiovascular AN in type-1 diabetic patients with impaired oesophageal and gallbladder motility

The determination of the AN score revealed a severe overall autonomic dysfunction in this group of patients (AN score: 5.9 ± 0.8 vs 0.33 ± 0.2 , $p < 0.0001$, long-standing type-1 DM vs control). The results of the cardiovascular reflex tests reflected an impairment of both the parasympathetic and sympathetic functions with more pathologic parameters of the parasympathetic tests.

3.3.1.2 Cardiovascular AN in type-1 diabetic patients with impaired stomach motility

Severe overall AN was found (AN score: 4.4 ± 0.5 vs 0.33 ± 0.2 , $p < 0.0001$, long-standing type-1 DM vs control). Both parts of the autonomic regulation were involved with a dominance of more severely impaired parasympathetic function in accordance with the results of the previously described group of type-1 diabetic patients with long-standing disease.

3.3.1.3. Cardiovascular AN in pancreatic-islet transplanted and non-transplanted type-1 diabetic patients with long-standing disease duration

The results of the cardiovascular reflex tests of the two diabetic groups revealed an increased severity of the overall AN in the control non-tx type-1 diabetic group (AN score: 6 ± 0.7 vs 3.9 ± 0.7 , $p < 0.05$, non-tx vs tx). Differences were also observed between the diabetic groups during the detailed analysis of each cardiovascular test. The heart rate responses to deep breathing differed markedly, higher values being found in the tx group. Both the Valsalva and the 30/15 ratio parameters were lower in the non-tx patients without reaching the significance at comparison to the tx patients. The mean values of the systolic blood pressure response to standing were definitely abnormal in the non-tx patients and less severe parameters were found in the tx subjects. The diastolic blood pressure response to a sustained handgrip was non-significantly less higher in the non-tx group.

3.3.2. Analysis of the severity of cardiovascular AN in long- and short-standing type-2 diabetic patients

A high AN score was observed in insulin-treated type-2 diabetic patients with long-standing disease (AN score: 7.1 ± 0.5 vs 0.25 ± 0.1 , $p < 0.0001$; long-standing type-2 DM vs control). A moderate impairment of the parasympathetic and sympathetic innervations were established in short-term type-2 DM (AN score: 3.4 ± 0.4 vs 0.25 ± 0.1 , $p < 0.0001$). During the comparison of the two diabetic groups, two heart rate tests differed significantly (AN score: 3.4 ± 0.4 vs 7.1 ± 0.5 , $p < 0.0001$, heart rate response to deep breathing: 11.9 ± 1.3 vs 7.3 ± 1 beat/min, $p < 0.01$, Valsalva ratio: 1.5 ± 0.04 vs 1.16 ± 0.04 , $p < 0.001$).

3.3.3. Correlations between cardiovascular AN and oesophageal emptying in long-standing type-1 DM

The statistical analysis of the oesophageal emptying rates and the results of the cardiovascular reflex tests or the AN score did not reveal any significant association between the impairment of oesophageal function and the severe parasympathetic or sympathetic dysfunction.

3.3.4. Correlations between cardiovascular AN and gastric emptying in type-1 and type-2 DM

3.3.4.1. Correlations between cardiovascular AN and gastric emptying in long-standing type-1 DM

The analysis revealed associations between AN and the impairment of gastric emptying. There was a positive correlation between the AN score and HTE ($r = 0.60$, $p < 0.01$), while negative correlations were found between two heart rate tests and HTE (heart rate variation-HTE: $r = -0.62$, $p < 0.001$; Valsalva ratio-HTE: $r = -0.46$, $p < 0.05$). A positive association was found between the orthostatic hypotension and HTE ($r = 0.52$, $p < 0.01$).

3.3.4.2. Correlations between cardiovascular AN and gastric emptying in short- and long-standing type-2 DM

There was a non-significant relationship between the seriously altered heart rate or blood pressure responses during the analysis of cardiovascular reflex tests and the abnormal values of gastric emptying in short- or long-standing type-2 DM.

3.3.5. Correlations between cardiovascular autonomic neuropathy and gallbladder emptying in long-standing type-1 DM

A negative correlation was found between the AN score and the gallbladder EF in the diabetics. Both the heart rate response to deep breathing and the Valsalva ratio correlated positively with the gallbladder EF (heart rate response to breathing-EF: $r = 0.79$, $p < 0.01$; Valsalva ratio-EF: $r = 0.81$, $p < 0.01$). There was also a positive association between the 30/15 ratio and gallbladder emptying ($r = 0.69$, $p < 0.05$).

3.4 Characterization of peripheral sensory nerve function in patients with type-1 and type-2 DM

3.4.1. Peripheral sensory nerve function in long-standing type-1 DM

3.4.1.1. Peripheral sensory nerve function in type-1 diabetic patients with impaired oesophageal, gastric and gallbladder motility

The assessment of the CPT values in this groups of type-1 diabetic patients with long-standing disease revealed hypaesthetic peripheral sensory neuropathy on the upper and lower limbs. The mean CPT on the median nerve was frequently higher than the range of the healthy subjects at the tested frequencies, while more abnormal parameters were detected at the

peroneal nerve. All mean CPT values at all three tested frequencies were significantly higher than that for the healthy controls pointing to the seriously impaired function of three different sensory fibres of the peroneal nerve.

3.4.1.2. Peripheral sensory nerve function in fetal pancreatic islet transplanted and non-transplanted type-1 diabetic patients

There was a non-significant tendency to values lower of the mean CPT values on the median nerve of the tx patients than those in the control non-tx diabetic patient group at three tested frequencies. Increased CPT mean values were frequently detected at peroneal nerve in both diabetic groups, with less severe hypesthetic conditions in the tx group. The differences in CPT values between the two groups at 5 Hz were statistically significant.

3.4.2. Peripheral sensory nerve function in type-2 diabetic patients

3.4.2.1. Peripheral sensory nerve function in long-standing type-2 DM

The mean CPT values reflected hypesthetic conditions in this group of type-2 diabetic patients in comparison with healthy controls proven by the statistical differences at five from six frequencies of stimulation.

3.4.2.2. Peripheral sensory nerve function in short-standing type-2 DM

The mean CPT values were higher in diabetic patients than in controls, but these parameters were within the normal range and only at 5 Hz stimulation frequency differed significantly from healthy controls. These measurements reflect normal conditions of sensory nerve function in this patient group.

3.5. Analysis of the relations between the impairment of auditory-evoked potentials and the severity of cardiovascular autonomic and peripheral sensory neuropathy in long-standing type-1 DM

3.5.1. Characterization of auditory-evoked potentials in long-standing type-1 DM

The latencies of all of the tested waves of the auditory-evoked potentials were consequently longer in patients with long-standing type-1 DM than in controls.

3.5.2. Cardiovascular AN in type-1 diabetic patients with impaired auditory-evoked potentials

The evaluation of cardiovascular AN revealed the same conditions of impaired neuronal function in this group of patients with the previously described patient groups with long-standing type-1 DM.

3.5.3. Correlations between the impairment of auditory-evoked potentials and the severity of cardiovascular AN in long-standing type-1 DM

Positive correlations were observed between the AN score and the lengths of the latencies of the third and fifth waves (AN score-wave III latency: $r=0.61$, $p<0.01$, AN score-wave V latency: $r=0.49$, $p<0.05$). In accordance with this finding, there was a negative relationship between the results of three heart rate tests (heart rate response to deep breathing, 30/15 ratio, Valsalva ratio) and the prolongation of the latencies of waves III and V.

3.5.4. Peripheral sensory function in type-1 diabetic patients with impaired auditory-evoked potentials

The same degree of hypesthetic sensory neuropathy with a dominance on the lower limb was established in this group of type-1 diabetic patients with long-standing disease.

3.5.5. Correlations between the impairment of auditory-evoked potentials and the severity of peripheral sensory neuropathy

The analysis of the relations between CPT values at the median and peroneal nerves and the auditory-evoked potentials revealed strong positive correlations between higher CPT values obtained at 2000 Hz and 250 Hz at the peroneal nerve and the latencies of waves III and V. The CPT values on the median nerve did not correlate with the latencies of the further waves of the auditory-evoked potentials.

3.6. Analysis of the correlations between the impairment of visual-evoked potentials and the severity of cardiovascular autonomic and peripheral sensory neuropathy in long-standing type-1 DM

3.6.1. Characterization of visual-evoked potentials in long-standing type-1 DM

The latency values of the major positive component of the visual-evoked potentials (P 100) were higher in this group of patients than the highest value of the range of healthy controls (100 ms) at both eyes (right eyes: 108.8 ± 2.28 ; left eyes: 110.9 ± 2.71 ms).

3.6.2. Cardiovascular AN in type-1 diabetic patients with impaired visual-evoked potentials

In accordance with the previous findings we observed a severe cardiovascular AN in this group of patients with more abnormal parameters of the parasympathetic function.

3.6.3. Correlations between the impairment of visual-evoked potentials and the severity of cardiovascular AN in long-standing type-1 DM

Significant positive correlations were found between the AN score and the lengths of the latencies of P100 waves of the right and left eyes. Further analyses revealed a negative relationship between the results of three heart rate tests (heart rate response to deep breathing, 30/15 ratio and Valsalva ratio) and the prolongation of the P100 latencies at both eyes.

3.6.4. Peripheral sensory function in type-1 diabetic patients with impaired visual-evoked potentials

The severity and the form of manifestation of sensory neuropathy was similar with the above mentioned groups of the same long duration of type-1 DM: a hypesthetic sensory neuropathy was found with more abnormal parameters on the peroneal nerve.

3.6.5. Correlations between the impairment of visual-evoked potentials and the severity of peripheral sensory neuropathy

The impaired sensory nerve function manifested in high CPT values at 2000 Hz, 250 Hz and 5 Hz stimulation frequency reflecting hypesthesia at the peroneal nerve correlated positively with the P100 latencies of right and left eyes. The CPT values of the median nerve did not correlate with the abnormal central visual function.

3.7. Analysis of the correlations between the impairments of the auditory- and visual-evoked potentials in long-standing type-1 DM

The statistical analysis was performed with the data of those nine patients with long-standing type-1 DM, who were involved in both studies of the detection of auditory and brainstem potentials. During this statistical procedure all tested parameters of brainstem auditory-evoked potentials were analyzed with the latencies of the P100 waves of the visual-evoked potentials of both eyes. The latencies of wave V of auditory-evoked potentials showed statistical

correlations with the latencies of P100 of both eyes (wave V latency-P100 latency of right eyes: $r = 0.53$, $p < 0.05$; wave V latency-P100 latency of left eyes: $r = 0.61$, $p < 0.01$).

4. Discussion

To summarize the present work, we have proved new associations between the cardiovascular, the peripheral sensory and the central afferent manifestations of diabetic neuropathy and the postprandial hypomotility of the gastrointestinal tract. Several findings were demonstrated as concerns the nature of the progression of diabetic polyneuropathy and the digestive dysfunction and the influence of successful therapeutic intervention. In many previous studies, there were no quantitative parameters evaluated for the gastrointestinal and the neurological alterations. The explanation of our new findings is that we had an outstanding interdisciplinary possibility to apply reproducible, sensitive methods for all the tested functions, which ensured the quantitative characterization of the gastrointestinal motility, the AN, the peripheral sensory function and the central afferent activity. Besides the manner of the selection of methods, the creation of homogeneous patient groups allowed the detection of the new data. We hope that the determination of the frequent relationship of the affected autonomic, sensory and central neuronal functions and gastric and gallbladder hypomotility in humans will add to the knowledge of the digestive complications of DM with new pathogenetic and diagnostic aspects.

5. Conclusions and new findings

- An impaired oesophageal emptying is frequently found in long-standing type-1 diabetes in the presence of parasympathetic and sympathetic autonomic and peripheral hypaesthetic sensory neuropathy.
- The seriously delayed emptying of a solid meal from the stomach is a characteristic feature in both long-standing type-1 and type-2 diabetes, while this digestive dysfunction was not found in a decade-long type-2 diabetes. Accelerated gastric emptying was not detected in any of the patients. Parasympathetic and sympathetic autonomic neuropathy seem to be the primary factors in the aetiology of gastric hypomotility in type-1 diabetes, while besides the autonomic dysfunction, the pathogenesis is more complex in type-2 diabetes.
- In the presence of a continuously better glycaemic control in type-1 diabetic patients with functioning transplanted islets, less severe neuropathy and gastric hypomotility are found.
- A severely impaired gallbladder contractility is demonstrated in all patients with long-standing type-1 diabetes. The parasympathetic autonomic neuropathy is strongly associated with the degree of gallbladder dysfunction.
- From comparisons of patient groups with different types and duration of diabetes and glycaemic control, it was elucidated that in the early phase of diabetic neuropathy the parasympathetic autonomic and lower limb hypaesthetic sensory neuropathy are frequently detected.
- A peripheral hypaesthetic sensory neuropathy is consequently found with more abnormal parameters on the peroneal nerve in the presence of impaired oesophageal, gastric and gallbladder hypomotility.
- The central auditory and visual pathways are equally seriously altered with the degree of parasympathetic and distal peripheral hypaesthetic neuropathy in long-standing type-1 diabetes. The impairment of parasympathetic and lower limb sensory functions develops earlier in the course of diabetes. These data may suggest that the abnormalities of the auditory and visual pathways should be regarded as early central manifestations of diabetic neuropathy.

The thesis is based on the following publications to which are cited in the text:

1. Várkonyi T. T., Lengyel Cs., Madácsy L., Velősy B., Boda K., Kempler P., Fazekas T., Csernay L., Lonovics J.:
[Gallbladder hypomotility in diabetic polyneuropathy] Epehólyag-hypomotilitas diabéteszes polyneuropathiában
Orv. Hetil., 1997, 138, 1177-1182
2. T. T. Várkonyi, Cs. Lengyel, L. Madácsy, B. Velősy, P. Kempler, T. Fazekas, L. Pávics, L. Csernay and J. Lonovics:
Gallbladder hypomotility in diabetic polyneuropathy
Clin. Aut. Res., 2001, 11, 377-381 (IF: 1.041)
3. T. T. Várkonyi, F. Tóth, L. Rovó, Cs. Lengyel, J. G. Kiss, P. Kempler, J. Lonovics:
Impairment of the auditory brainstem function in diabetic polyneuropathy
Diabetes Care, 2002, 25, 631-632 (IF: 5.404)
4. T. T. Várkonyi, G. Farkas, Zs. Fülöp, P. Vörös, Cs. Lengyel, P. Kempler, J. Lonovics:
Beneficial effect of fetal islet grafting on development of late diabetic complications
Transplant. Proc., 1998, 30, 330-331 (IF: 0.568)
5. T. T. Várkonyi, T. Pető, R. Dégi, K. Keresztes, Cs. Lengyel, M. Janáky, P. Kempler, J. Lonovics:
Impairment of visual evoked potentials: early central manifestations of diabetic neuropathy?
Diabetes Care, 2002, 25, 1661-1662 (IF: 5.404)
6. T. T. Várkonyi, Cs. Lengyel, R. Takács, P. Légrády, L. Madácsy, M. Lázár, R. Róka, L. Rovó, F. Tóth, J. G. Kiss, Zs. Fülöp, T. Pető, R. Dégi, M. Janáky, T. Fazekas, L. Pávics, Gy. Farkas, P. Kempler, J. Lonovics:
Manifestations of diabetic polyneuropathy in the digestive tract and the central nervous system
Diabetol. Hung. 2002, 10 (suppl. 2), 44-50

List of publications related to the subject:

7. Gyöngyösi M., Németh J., Várkonyi T. T.:
Elevated levels of plasma vasoactive intestinal polypeptide in human acute myocardial infarction
Int. J. Cardiol., 1996, 56, 159-161 (IF: 1.164)
8. Lengyel Cs., Thury A., Várkonyi T. T., Ungi I., Boda K., Fazekas T., Csanády M.:
[Evaluation of heart rate variability and the spatial and temporal dispersion of QT interval in diabetic autonomic neuropathy] A szívfrekvencia-variabilitás, valamint a QT-intervallum térbeli és cirkadián diszperziójának vizsgálata diabéteszes autonom neuropathiában
Magy. Belorv. Arch., 1997, 50, 431-438
9. Avramov K., Mayer P., Várkonyi T. T., Lengyel Cs., Bódi I., Dibó Gy., Fazekas T., Vécsei L.:
[Upper limb diabetic amyotrophy] Felső végtagi amyotrophia diabetica
Magy. Belorv. Arch., 1997, 50, 464-468
10. Rosztóczy A., Várkonyi T. T., Fehér A., Lengyel Cs., Fazekas T., Kempler P., Wittmann T., Lonovics, J.:
[Motility disorders of the digestive tract in diabetic autonomic and sensory neuropathy] A tápcsatorna motilitászavarai autonom és szenzoros neuropathiával szövődő cukorbetegségben
Magy. Belorv. Arch., 1997, 50, 413-419
11. Cs. Lengyel, T. Török, T. T. Várkonyi, P. Kempler, L. Rudas:
Baroreflex sensitivity and heart-rate variability in insulin-dependent diabetics with polyneuropathy
Lancet, 1998, 351, 1436-1437 (IF: 13.251)

12. Várkonyi T. T., Farkas Gy., Fülöp Zs., Vörös P., Lengyel Cs., Kempler P., Lonovics J.:
[Decreased progression of late diabetic complications following fetal islet transplantation]
A cukorbetegség késői szövődményeinek lassult progressziója foetalis szigetsejtek
transzplantációját követően
Lege Artis Medicinae, 1999, 9, 491
13. Várkonyi T. T., Rosztóczy A., Wittmann T., Tornóczy J., Simon L., Lonovics J.:
[Diabetes mellitus and gastrointestinal motility] Diabetes mellitus és gastrointestinális
motilitás
Hippocrates 2000, 2, 217-221
14. Tóth F., Várkonyi T. T., Kiss JG., Rovó L., Lengyel Cs., Légrády P., Jóri J., Czigler J.:
Brainstem auditory-evoked potential examinations in diabetic patients.
Scand. Audiol. Suppl. 2001, 30 (suppl. 52), 156-159 (IF: 0.652)
15. F. Izbéki, I. Kiss, T. Wittmann, T. T. Várkonyi, P. Légrády, J. Lonovics
Impaired accommodation of proximal stomach in patients with alcoholic liver cirrhosis
Scand. J. Gastroenterol., 2002, 37, 1403-1410 (IF: 1.826)
16. L. Kovács, D. Paprika, R. Takács, M. Papós, A. Kardos, T. T. Várkonyi, Cs. Lengyel, Z.
Csenke, A. Kovács, R. Róka, L. Pajor, L. Pávics, L. Rudas, Gy. Pokorny:
Autonomic nervous system dysfunction in primary Sjögren's syndrome
Rheumatology 2004, 43, 95-99 (IF: 3.06)
17. L. Kovács, M. Papós, R. Takács, R. Róka, Z. Csenke, A. Kovács, T. T. Várkonyi, L.
Pajor, L. Pávics, Gy. Pokorny:
Autonomic nervous system dysfunction involving the gastrointestinal and the urinary
tracts in primary Sjögren's syndrome.
Clin Exp Rheumatology 2003, 21, 697-703 (IF: 1.614)

List of published abstracts related to the subject:

18. Zs. Lénárt, T.T Várkonyi, I. Jakab, J. Lonovics:
The effects of magnesium sulfate and nifedipine on cholecystokinin octapeptide (CCK-8)-
stimulated gallbladder and sphincter of Oddi motility
Z. Gastroenterol., 1991, 29, 192. (IF: 0.803)
19. J. Lonovics, Zs. Lénárt, T. T. Várkonyi, I. Jakab, B. Velösy, V. Varró:
Mechanism of magnesium sulfate- and nifedipine-induced gallbladder and sphincter of
Oddi relaxation in rabbits
Eur. J. Gastroenterol. and Hepatol. 1991, 3 Suppl. 1, 47 (IF: 1.58)
20. T. T. Várkonyi, Cs. Lengyel, L. Madácsy, B. Velösy, T. Fazekas, J. Lonovics, L. Csernay:
Impairment of cerulein-induced gall bladder emptying in insulin-treated diabetics
measured by quantitative hepatobiliary scintigraphy
Z. Gastroenterol. 1995, 33, 314 (IF: 0.803)
21. T. T. Várkonyi, Cs. Lengyel, K. Boda, T. Fazekas:
QT interval dispersion (QTd) in diabetes mellitus
Card. Hung. 1995, Suppl. 3, 43
22. Mayer P., Avramov K., Dibó Gy., Fazekas T., Várkonyi T.T., Lengyel Cs., Vécsei L.,
Lonovics J.:
[Diabetic amyotrophy or toxic polyneuropathy? – Case report] Amyotrophia diabetica
vagy polyneuropathia toxica? - Esetismertetés
Ideggyógyászati Szemle 1995, 48 (9-10), 338
23. A. Rosztóczy, A. Fehér, T. T. Várkonyi, Cs. Lengyel, T. Fazekas, I. Molnár, T. Wittmann:
Esophageal, gastric and ano-rectal motility disorders in diabetes mellitus
Z. Gastroenterol. 1996, 34, 329 (IF: 0.803)
24. Avramov K., Várkonyi T. T., Lengyel Cs., Mayer P., Dibó Gy., Fazekas T., Lonovics J.,
Vécsei L.:
[Upper limb diabetic amyotrophy] Felső végtagi amyotrophia diabetica
Diabetol. Hung., 1996, 4, Suppl 1, 3
25. Várkonyi T. T., Lengyel Cs., Madácsy L., Velösy B., Kempler P., Fazekas T., Boda K.,
Lonovics J., Csernay L.:

- [Assessment of gallbladder motility in diabetic autonomic and sensory neuropathy]
Epehólyag-motilitás vizsgálatok autonóm és szenzoros neuropathiával szövődő diabetes mellitusban
Diabetol. Hung., 1996, 4, Suppl. 1, 62
26. A. Rosztóczy, A. Fehér, T. T. Várkonyi, Cs. Lengyel, T. Fazekas, I. Molnár, T. Wittmann:
Esophageal, gastric and ano-rectal motility disorders in diabetes mellitus
Z. Gastroenterol., 1996, 34, 329 (IF: 0.803)
 27. T. Wittmann, A. Rosztóczy, A. Fehér, T. T. Várkonyi, Cs. Lengyel, I. Molnár, J. Lonovics:
Oesophageal, gastric and ano-rectal motility disorders in patients with diabetic neuropathy
Gut, 1996, 39 (suppl. 3) A198 (IF: 6.17)
 28. Lengyel Cs., Thury A., Várkonyi T. T., Ungi I., Boda K., Fazekas T., Csanády M.:
[Comparison of heart rate variability and cardiovascular reflex tests in autonomic neuropathy associated to insulin-dependent diabetes] A szívfrekvencia-variabilitás és a cardiovascularis reflex tesztek összehasonlító vizsgálata autonóm neuropathiával szövődő inzulindependens diabetes mellitusban
Magy. Belorv. Arch., 1996, 49, Suppl.2. 175.
 29. Várkonyi T. T., Lengyel Cs., Mayer P., Avramov K., Dibó Gy., Bódi I., Kempler P., Fazekas T., Lonovics J., Vécsei L.:
[Upper limb diabetic amyotrophy] Felső végtagon jelentkező amyotrophia diabetica
Magy. Belorv. Arch., 1996, 49, Suppl.2. 211
 30. Wittmann T., Rosztóczy A., Fehér A., Várkonyi T. T., Lengyel Cs., Fazekas T., Molnár I., Lonovics J.:
[Impairment of esophageal, gastric and anorectal motility in patients with diabetic neuropathy] Nyelőcső, gyomor és anorectalis motilitászavarok diabeteses neuropathiás betegekben
Magy. Belorv. Arch., 1996, 49, Suppl.2. 215
 31. Várkonyi T. T., Lengyel Cs., Madácsy L., Rosztóczy A., Fehér A., Hermányi Zs.:
[Impairment of gastrointestinal motility in long-standing diabetes mellitus] A gastrointestinalis motilitás zavarai hosszú ideje fennálló cukorbetegségben
Diabetol. Hung. 1997, 5, Suppl. 1., 27-28
 32. Lengyel Cs., Thury A., Várkonyi T. T., Ungi I., Boda K., Fazekas T., Csanády M.:
[Assessment of heart rate variability and the spatial and circadian fluctuations of ventricular repolarization in diabetic autonomic neuropathy] A szívfrekvencia-variabilitás, a kamrai repolarizációs idő térbeli inhomogenitásának és napszaki ingadozásának vizsgálata diabeteses autonóm neuropathiában
Diabetol. Hung., 1997, 5, Suppl. 1., 14-15
 33. Thury A., Lengyel Cs., Várkonyi T. T., Ungi I., Boda K., Fazekas T., Csanády M.:
[Disturbances of heart rate variability and spatial and temporal QT intervals in diabetic autonomic neuropathy] A szívfrekvencia-variabilitás változásának, a QT-szakasz térbeli diszperziójának és időbeli ingadozásának vizsgálata diabeteses autonóm neuropathiában
Card. Hung., 1997, 26, Suppl. 3., 59
 34. A. Fehér, A. Rosztóczy, T. T. Várkonyi, Cs. Lengyel, I. Molnár, T. Wittmann:
Comparative study of gastric manometry (GM) and electro-gastrography (EGG) in diabetic gastric motility disorders
Z. Gastroenterol., 1997, 35, 375 (IF: 0.803)
 35. Cs. Lengyel, A. Thury, T.T. Várkonyi, I. Ungi, T. Fazekas, M. Csanády:
Disturbances of heart rate variability and spatial and temporal QT intervals in diabetic neuropathy
PACE, 1997, 20, 1503 (IF: 1.197)
 36. Cs. Lengyel, A. Thury, T. T. Várkonyi, K. Boda, T. Fazekas, M. Csanády, J. Lonovics:
Decreased heart rate variability and circadian fluctuation of QTc interval with enhanced spatial QTc dispersion in diabetic autonomic neuropathy
J. Peripher. Nerv. Syst., 1997, 2, 281 (IF: 1.298)
 37. T. T. Várkonyi, Cs. Lengyel, K. Boda, P. Kempler, Gy. Farkas, J. Lonovics:
Long-term effect of pancreatic islet transplantation on development of autonomic and sensory neuropathy in IDDM patients

- J. Peripher. Nerv. Syst., 1997, 2, 312 (IF: 1.298)
38. Cs. Lengyel Cs., A. Thury, T. T. Várkonyi, I. Ungi, K. Boda, T. Fazekas, M. Csanády:
Disturbances of heart rate variability and spatial and circadian QTc intervals in diabetic patients with autonomic neuropathy
Diabetologia, 1997, 40, (suppl. 1), 574 (IF: 6.299)
 39. T. T. Várkonyi, Cs. Lengyel, A. Rosztóczy, A. Fehér, P. Kempler, T. Fazekas, T. Wittmann, J. Lonovics:
Multiple-site gastrointestinal motility disorders in patients with autonomic and sensory polyneuropathy
Diabetologia, 1997, 40 (suppl. 1), 570 (IF: 6.299)
 40. T. T. Várkonyi, Zs. Fülöp, P. Vörös, Cs. Lengyel, P. Kempler, J. Lonovics, Gy. Farkas:
Beneficial effect of fetal islet grafting on the development of late diabetic complications
Acta Diabetol., 1997, 40, 111 (IF: 0.817)
 41. Várkonyi T. T., Lengyel Cs., Kempler P., Farkas Gy., Lonovics J.:
[Evaluation of diabetic neuropathy in type-1 diabetes following fetal islet transplantation]
A diabeteses neuropathia vizsgálata foetalis Langerhans szigetek transzplantációját követően inzulin-dependens cukorbetegségben
Diabetol. Hung. 1998, 6, (suppl. 1) 73
 42. Lengyel Cs., Török T., Várkonyi T. T., Légrády P., Parika D., Kempler P., Rudas L., Lonovics J.:
[Baroreflex sensitivity in type-1 diabetes with polyneuropathy] Baroreflex-szenzitivitás vizsgálata polyneuropathiával szövődő inzulin-dependens cukorbetegségben
Diabetol. Hung. 1998, 6, 48
 43. Farkas Gy., Fülöp Zs., Vörös P., Várkonyi T. T.:
Effect of fetal islet grafting on the development of late diabetic complications]
Embriionális Langerhans-sziget transzplantáció hatása a diabeteses másodlagos szövődmények alakulására
Diabetol. Hung. 1998, 6, 13
 44. Lengyel Cs., Török T., Várkonyi T. T., Légrády P., Paprika D., Kempler P., Rudas L., Lonovics J.:
Baroreflex sensitivity in diabetic patients with polyneuropathy
Card. Hung. 1998, 27, (suppl. 1), 56
 45. T. T. Várkonyi, R. Róka, Cs. Lengyel, P. Légrády, L. Madácsy, B. Velösy, P. Kempler, L. Pávics, J. Lonovics:
Evaluation of gall bladder and stomach motor function in long-standing diabetes mellitus.
Z. Gastroenterol. 1998, 36, 451 (IF: 0.803)
 46. I. Kiss, A. Rosztóczy, T. T. Várkonyi, A. Fehér, Cs. Lengyel, R. Róka, L. Pávics, É. Varga, J. Náfrádi, L. Mádi-Szabó, T. Wittmann:
2D transabdominal ultrasound characteristics of gastric antum motility in diabetic gastroparesis
Z. Gastroenterol. 1998, 36, 429 (IF: 0.803)
 47. T. T. Várkonyi, Cs. Lengyel, Zs. Fülöp, P. Kempler P, Gy. Farkas, J. Lonovics:
Influence of long-term pancreatic islet graft function on development of late diabetic complications
Diabetologia, 1998, 41, (suppl. 1) 6 (IF: 6.299)
 48. Cs. Lengyel, T. Török, T. T. Várkonyi, P. Légrády, P. Kempler, L. Rudas, J. Lonovics:
Baroreflex sensitivity in diabetic patients with polyneuropathy
Diabetologia, 1998, 41, (suppl. 1) 303 (IF: 6.299)
 49. R. Róka, T. T. Várkonyi, Cs. Lengyel, P. Légrády, L. Madácsy, B. Velösy, P. Kempler, J. Lonovics, L. Pávics:
Evaluation of gall bladder and stomach motility in long-standing diabetes mellitus
Eur. J. Nucl. Med., 1998, 25, 981 (IF: 3.464)
 50. T. T. Várkonyi, R. Róka, Cs. Lengyel, P. Légrády, L. Madácsy, B. Velösy, P. Kempler, L. Pávics, J. Lonovics:
Evaluation of diabetic cardiovascular autonomic and peripheral sensory neuropathy in patients with impaired gallbladder and gastric emptying.
Neurogastroenterol. Mot., 1998, 10, 435 (IF: 2.5)

51. A. Rosztóczy, T. Wittmann, T. T. Várkonyi, A. Fehér, Cs. Lengyel, R. Róka, L. Pávics, É. Varga, J. Náfrádi, L. Mádi-Szabó L, I. Kiss:
Impaired receptive relaxation of the gastric antrum in diabetic gastroparesis
Neurogastroenterol. Mot., 1998, *10*, 452 (IF: 2.5)
52. Túri A., Lengyel Cs., Várkonyi T. T., Ungi I., Boda K., Fazekas T., Csanády M.:
Heart rate, spatial and temporal QT variability in diabetic patients with autonomic neuropathy
J. Am. Coll. Cardiol. 1998, *31*, (suppl. C), 184 (IF: 6.374)
53. Légrády P., Várkonyi T.T., Róka R., Lázár M., Lengyel Cs., Hermányi Zs., Madácsy L.:
[Evaluation of gallbladder and gastric emptying in long-standing diabetes] Az epehólyag- és gyomormotilitás vizsgálata hosszú ideje fennálló cukorbetegségben
Diabetol. Hung. 1999, *7*, (suppl. 1) 24
54. Lengyel Cs., Farkas Gy., Török T., Légrády P., Várkonyi T.T., Kardos A., Gingl Z., Kempler P., Rudas L., Lonovics J.:
[Baroreflex sensitivity in diabetic patients following pancreatic islet transplantation] Baroreflex szenzitivitás vizsgálata Langerhans-sziget transzplantáción átesett cukorbetegekben
Card. Hung. 1999, *28*, (suppl. 2) 59
55. T. T. Várkonyi, R. Róka, Cs. Lengyel, P. Légrády, L. Madácsy, B. Velösy, P. Kempler, L. Pávics, J. Lonovics:
Impairment of gallbladder and stomach emptying in patients with diabetic autonomic and peripheral sensory neuropathy
Gastroenterology 1999, *116* (4) 1097 (IF: 13.02)
56. T. T. Várkonyi, R. Róka, P. Légrády, M. Lázár, Cs. Lengyel, L. Madácsy, B. Velösy, P. Kempler, L. Pávics, J. Lonovics:
Characterization of gastrointestinal motor dysfunction in patients with long-standing diabetes mellitus
Z. Gastroenterol. 1999, *37*, 455 (IF: 0.803)
57. T. Wittmann, A. Rosztóczy, T. T. Várkonyi, Cs. Lengyel, I. Kiss, J. Lonovics:
Fasting upper gastrointestinal dysmotility patterns do not show close correlation with autonomic neuropathy in diabetes mellitus
Z. Gastroenterol. 1999, *37*, 456 (IF: 0.803)
58. Róka R., Várkonyi T. T., Lengyel Cs., Légrády P., Madácsy L., Kempler P., Lonovics J., Pávics L.:
Evaluation of gallbladder and gastric motility in long-standing diabetes] Az epehólyag és a gyomor motilitás vizsgálata hosszú ideje fennálló cukorbetegségben
Magyar Radiológia 1999, (suppl.) 17.
59. Lengyel Cs., Farkas Gy., Török T., Légrády P., Várkonyi T. T., Kardos A., Gingl Z., Kempler P., Rudas L., Lonovics J.:
[Baroreflex sensitivity in pancreatic-islet transplanted diabetic patients] Baroreflex szenzitivitás vizsgálat Langerhans-sziget transzplantáción átesett cukorbetegekben
Cardiol. Hung. 1999, *29* (suppl. 2), 59
60. T. Wittmann, T. T. Várkonyi, A. Rosztóczy, Cs. Lengyel, R. Róka, L. Pávics, J. Lonovics:
Severity of autonomic neuropathy correlates with postprandial but not fasting state upper gastrointestinal dysmotility patterns in diabetes mellitus
Neurogastroenterol. Mot., 1999, *11*, 301 (IF: 2.5)
61. Cs. Lengyel, Gy. Farkas, T. Török, P. Légrády, T. T. Várkonyi, A. Kardos, Z. Gingl, P. Kempler, L. Rudas, J. Lonovics:
Influence of pancreatic islet transplantation on baroreflex sensitivity in diabetic patients
Diabetologia, 1999, *42*, (suppl. 1), A297 (IF: 6.299)
62. T. T. Várkonyi, R. Róka, P. Légrády, M. Lázár, Cs. Lengyel, L. Madácsy, B. Velösy, P. Kempler, L. Pávics, J. Lonovics:
Evaluation of diabetic neuropathy in patients with multiple-site gastrointestinal hypomotility
Diabetologia, 1999, *42*, (suppl. 1), A301 (IF: 6.299)
63. Cs. Lengyel, Gy. Farkas, T. Török, P. Légrády, T. T. Várkonyi, A. Kardos, Z. Gingl, P. Kempler, L. Rudas, J. Lonovics:
Spontaneous baroreflex sensitivity in diabetic patients after pancreatic islet transplantation

- Eur. Heart. J., 1999, 20, (suppl.), P2209 (IF: 5.153)
64. R. Róka, T. T. Várkonyi, M. Lázár, Cs. Lengyel, P. Légrády, Gy. Farkas, P. Kempler, J. Lonovics, L. Pávics:
Beneficial effect of long-term pancreatic islet function on gastric emptying in patients with type-1 diabetes mellitus
Eur. J. Nucl. Med., 1999, 26, 1042 (IF: 3.464)
 65. T. T. Várkonyi, R. Róka, M. Lázár, P. Légrády, Cs. Lengyel, L. Pávics, P. Kempler, Gy. Farkas, J. Lonovics:
Characterization of gastric emptying and neuropathy in pancreatic islet-transplanted and non-transplanted diabetic patients
Z. Gastroenterol., 2000, 38, 429 (IF: 0.803)
 66. T. Wittmann, A. Rosztóczy, T. T. Várkonyi, Cs. Lengyel, R. Róka, L. Pávics, É. Varga, J. Náfrádi, I. Kiss:
Impairment of the antral receptive relaxation in diabetic gastroparesis
Gastroenterology, 2000, 118 (4), 384 (IF: 13.02)
 67. A. Rosztóczy, T. Wittmann, T. T. Várkonyi, Cs. Lengyel, R. Róka, L. Pávics, J. Lonovics:
Postprandial but not fasting upper gastrointestinal dysmotility correlates with the severity of autonomic neuropathy in diabetes mellitus
Gastroenterology, 2000, 118 (4), 383 (IF: 13.02)
 68. T. T. Várkonyi, R. Róka, M. Lázár, P. Légrády, Cs. Lengyel, L. Pávics, P. Kempler, Gy. Farkas, J. Lonovics:
Evaluation of gastric emptying in pancreatic islet-transplanted and non-transplanted diabetic patients
Gastroenterology, 2000, 118 (4), 383 (IF: 13.02)
 69. Várkonyi T. T., Róka R., Lázár M., Légrády P., Lengyel Cs., Madácsy L., Velösy B., Kempler P., Pávics L., Lonovics J.:
[Multiple-site assessment of the digestive motility in long-standing diabetes] Az emésztőszervek működésének komplex vizsgálata hosszú ideje fennálló cukorbetegségben
Diabetol. Hung. 2000, 8 (suppl. 1), 96-97
 70. Lengyel Cs., Farkas Gy., Várkonyi T. T., Török T., Légrády P., Kempler P., Rudas L., Lonovics J.:
[Evaluation of spontaneous baroreflex sensitivity in pancreatic islet transplanted type-1 diabetic patients] A spontán baroreflex szenzitivitásának vizsgálata Langerhans-sziget transzplantációján átesett 1-es típusú cukorbeteggekben
Diabetol. Hung. 2000, 8 (suppl. 1), 53-54
 71. Farkas Gy., Dégi R., Várkonyi T. T., Lengyel Cs, Vörös P.:
[Effect of pancreatic islet transplantation on the development of late diabetic complications] Pancreas szigetsejtek transplantációjának hatása a diabeteszes másodlagos szövődményekre
Diabetol. Hung. 2000, 8 (suppl. 1) 18
 72. Lengyel Cs., Légrády P., Török T., Várkonyi T. T., Gingl Z., Ábrahám Gy., Kempler P., Rudas L., Lonovics J.:
[Heart rate variability in type-1 diabetic patients with polyneuropathy] Vérnyomás variabilitás vizsgálata polyneuropathiával szövődő 1. típusú diabetes mellitusban
Cardiol. Hung. 2000, 29, (suppl. 3), 77
 73. T. T. Várkonyi, F. Tóth, Cs. Lengyel, P. Légrády, JG. Kiss, L. Rovó, P. Kempler, J. Lonovics:
Evaluation of auditory brainstem function in diabetic neuropathy
Diabetologia 2000, 43 (suppl. 1), A49 (IF:6.299)
 74. G. Farkas, R. Dégi, T. T. Várkonyi, P. Vörös, Cs. Lengyel:
Fetal islet grafting prevents secondary diabetic complications
Diabetologia 2000, 43 (suppl. 1), A29. (IF: 6.299)
 75. Wittmann T., Rosztóczy A., Várkonyi TT., Lengyel Cs., Róka R., Pávics L., Kiss I.:
Impaired filling of the antrum in diabetic gastroparesis] Az antrum telődésének károsodása diabeteses gastroparesisben
Magy. Belorv. Arch. 2000, 53 (suppl. 3) 164
 76. Várkonyi T. T., Lengyel Cs, Légrády P., Lázár M., Róka R., Kempler P., Farkas Gy., Pávics L., Lonovics J.:

- [Evaluation of diabetic neuropathy and gastric emptying in type-1 diabetes following pancreatic islet transplantation] A diabeteses neuropathia és a gyomorürülés vizsgálata Langerhans szigetek transzplantációját követően 1-es típusú cukorbetegségben
Magy. Belorv. Arch. 2000, 53 (suppl. 3) 157-158
77. Lengyel Cs., Farkas Gy., Légrády P., Török T., Várkonyi T. T., Kempler P., Rudas L., Lonovics J.:
[Baroreflex sensitivity in pancreatic islet transplanted diabetic patients] Baroreflex-szenzitivitás vizsgálata Langerhans-sziget-transzplantáción átesett cukorbetegekben
Magy. Belorv. Arch. 2000, 53 (suppl. 3), 112
78. Légrády P., Lengyel Cs., Török T., Várkonyi T. T., Ábrahám Gy., Kempler P., Rudas L., Lonovics J.:
[Spectral evaluation of heart rate variability in type-1 diabetes] A vérnyomás-variabilitás spektrális elemzése 1-es típusú cukorbetegségben
Magy. Belorv. Arch. 2000, 53 (suppl. 3), 111
79. C. Lengyel, P. Légrády, T. Török, T. T. Várkonyi, Z. Gingl, Gy. Ábrahám, P. Kempler, L. Rudas, J. Lonovics:
Spectral analysis of blood pressure variability in type 1 diabetic patients with polyneuropathy
Diabetes Research and Clinical Practice 2000, 50 (suppl. 1) S222 (IF: 1.639)
80. T.T. Várkonyi, R. Róka, P. Légrády, M. Lázár, Cs. Lengyel, L. Madácsy, B. Velósy, P. Kempler, L. Pávics, J. Lonovics:
Evaluation of esophageal, gastric and gallbladder motility in long-standing type-1 diabetes mellitus
Diabetes Research and Clinical Practice 2000, 50 (suppl. 1) S336 (IF: 1.639)
81. Légrády P., Lengyel Cs., Török T., Várkonyi T. T., Ábrahám Gy., Kempler P., Rudas L., Lonovics J.:
[Decreased low frequency parameters in type-1 diabetes with polyneuropathy] A vérnyomás-variabilitás alacsony frekvencia-tartományának csökkenése polyneuropathiával szövődött 1. típusú cukorbetegségben
Hypertonia és Nephrologia 2000, 4 (suppl. 3), 89
82. Róka R., Várkonyi T. T., Lázár M., Légrády P., Madácsy L., Lengyel Cs., Kempler P., Pávics L., Lonovics J.:
[Evaluation of gastric emptying and diabetic neuropathy in pancreatic islet transplanted type-1 diabetic patients] A gyomorürülés és a diabeteses neuropathia felmérése Langerhans sziget transzplantáció után 1-es típusú cukorbetegségben
Diabetol. Hung. 2001, 9 (suppl.1), 36-37
83. Takács R., Várkonyi T. T., Róka R., Lázár M., Légrády P., Madácsy L., Lengyel Cs., Kempler P., Pávics L., Lonovics J.:
[Evaluation of gastric emptying, diabetic neuropathy and digestive symptoms in long-standing type-1 diabetes] A gyomorürülés, a diabeteses neuropathia és az emésztőszervi tünetek vizsgálata hosszú ideje fennálló 1-es típusú cukorbetegségben
Diabetol. Hung. 2001, 9 (suppl.1), 44
84. T. T. Várkonyi, R. Róka, R. Takács, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel, P. Kempler, L. Pávics, J. Lonovics:
Gastric emptying, neuropathy status and digestive symptoms in type-1 diabetes mellitus. Is there a relationship?
Gastroenterology 2001, 120 (suppl. 1), A468 (IF: 13.02)
85. T. T. Várkonyi, R. Róka, R. Takács, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel, P. Kempler, L. Pávics, J. Lonovics:
Evaluation of the relationship between gastric emptying, neuropathy status and digestive symptoms in type-1 diabetes mellitus
Z. Gastroenterol 2001, 39, 429 (IF: 0.803)
86. T. Wittmann, F. Izbéki, I. Kiss, T. T. Várkonyi, P. Légrády, J. Lonovics:
Impairment of gastric emptying in alcoholic cirrhotic patients with autonomic neuropathy
Z. Gastroenterol 2001, 39, 430 (IF: 0.803)
87. T. T. Várkonyi, R. Róka, R. Takács, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel, L. Pávics, P. Kempler, J. Lonovics:

- Neuropathy status, gastric emptying and digestive symptoms in type-1 diabetes mellitus: Is there a relationship?
Diabetologia 2001, 44, (suppl. 1), A291 (IF: 6.299)
88. T.T. Várkonyi, R. Takács, R. Róka, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel, P. Kempler, L. Pávics, J. Lonovics:
Connections between gastric emptying, neuropathy status and digestive symptoms in type-1 and type-2 diabetes
Gastroenterology, 2002, 122 (4) A452 (IF: 13.02)
 89. Várkonyi TT., Takács R., Róka R., Lázár M., Légrády P., Madácsy L., Lengyel Cs., Kempler P., Pávics L., Lonovics J.:
[Relationships between gastric emptying, diabetic neuropathy and digestive symptoms in long-standing type-1 and type-2 diabetes] A gyomorürülés, a diabeteszes neuropathia és az emésztőszervi tünetek összevetése hosszú ideje fennálló 1-es és 2-es típusú cukorbetegségben
Diabetol. Hung. 2002, 10 (suppl. 1), 88
 90. Takács R., Várkonyi T.T., Lengyel Cs., Róka R., Lázár M., Ács P., Pávics L., Lonovics J.:
[Beneficial effect of large molecular weight polysaccharid (guar gum) in the dietary treatment of type-2 diabetes] Nagy molekulatömegű poliszacharid (guar gumi) hatékonyságának vizsgálata a 2-es típusú cukorbetegség diétás kezelésében
Diabetol. Hung. 2002, 10 (suppl. 1), 75
 91. T. T. Várkonyi, R. Takács, R. Róka, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel, P. Kempler, L. Pávics, J. Lonovics:
Determination of gastric emptying, autonomic neuropathy and digestive symptoms in type-1 and type-2 diabetes
Z. Gastroenterol. 2002, 40, 364 (IF: 0.803)
 92. I. Kiss, T. Wittmann, R. Róka, F. Izbéki, A. Rosztóczy, T. T. Várkonyi, J. Lonovics:
Imidazoline receptor agonist moxonidine improves gastric emptying in diabetic gastroparesis
Z. Gastroenterol. 2002, 40, 341 (IF: 0.803)
 93. T.T. Várkonyi, T. Pető, R. Dégi, Cs. Lengyel, M. Janáky, P. Kempler, J. Lonovics:
Impairment of visual evoked potentials: early central manifestation of diabetic neuropathy?
Diabetologia 2002, 45 (suppl. 2), 329 (IF: 6.299)
 94. T. Wittmann, I. Kiss, A. Rosztóczy, F. Izbéki, T. T. Várkonyi, R. Róka, J. Lonovics:
In diabetic gastroparesis moxonidine an imidazoline receptor agonist improves gastric emptying
Diabetologia 2002, 45 (suppl. 2), 335-336 (IF: 6.299)
 95. L. Kovács, R. Takács, M. Papós, D. Paprika, A. Kovács, TT. Várkonyi, Cs. Lengyel, L. Rudas, L. Pávics, Gy. Pokorny:
The assessment of autonomic neuropathy in primary Sjögren's syndrome patients
Ann. Rheum. Dis., 2002, 61 (suppl. 1), 225. (IF: 3.18)
 96. A. Nemes, Cs. Lengyel, T. Forster, TT. Várkonyi, R. Takács, J. Lonovics, M. Csanády:
Correlation between coronary flow reserve and standard cardiovascular reflex tests in patients without epicardial coronary artery stenosis
Eur. J. Echocardiography, 2002, 3 (suppl. 1) 10.
 97. Róka R., Várkonyi TT, Takács R., Lázár M., Légrády P., Lengyel Cs., Kempler P., Pávics L., Lonovics J.:
[Gastric emptying studies in long-standing diabetes associated with autonomic neuropathy] Gyomorürülés-vizsgálatok autonóm neuropathiával szövődő, hosszú ideje fennálló cukorbetegségben
Diabetol. Hung., 2003, 11. (suppl. 1) 42
 98. Takács R., Várkonyi TT., Róka R., Lázár M., Légrády P., Lengyel Cs., Nagy I., Kempler P., Pávics L., Lonovics J.:
[Assessment of diabetic neuropathy and gastric emptying in type-2 diabetic patients on oral antidiabetic treatment]. A diabeteszes neuropathia és a gyomorürülés felmérése orális antidiabetikummal kezelt 2-es típusú cukorbetegségben
Diabetol. Hung., 2003, 11. (suppl. 1) 46-47

99. A Szepes, L. Madácsy, V. Bertalan, B. Velösy, T.T. Várkonyi, L. Pávics, J. Lonovics:
Differentiation between functional and organic forms of gallbladder dysfunction by
quantitative hepatobiliary scintigraphy
Z. Gastroenterol., 2003, *41*, 460 (IF: 0.803)
100. T.T. Várkonyi, R. Takács, R. Róka, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel,
P. Kempler, L. Pávics, J. Lonovics:
Determinants of impaired gastric emptying and digestive symptoms in type-2 DM
patients.
Z. Gastroenterol., 2003, *41*, 464 (IF: 0.803)
101. T. Wittmann, I. Kiss, F. Izbéki, A. I. Rosztóczy, T. T. Várkonyi, R. Róka, J. Lonovics:
Improvement of gastric emptying in patients with diabetic gastroparesis by moxonidine
Gastroenterolgy, 2003, *124* (4), A222-A223 (IF: 13.02)
102. T.T. Várkonyi, R. Takács, R. Róka, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel,
P. Kempler, L. Pávics, J. Lonovics:
Comparative evaluation of the characteristics of neuropathy status, gastric emptying and
digestive symptoms in patients with long-standing type-1 and type-2 diabetes
Diabetes & Metabolism 2003, *29*, 4S278 (IF: 1.546)
103. Cs. Lengyel, A. Nemes, T. Forster, T. T. Várkonyi, R. Takács, I. Nagy, P. Kempler, J.
Lonovics, M. Csanády:
Coronary flow reserve, insulin resistance and autonomic function in patients with
normoglycemia: is there a relationship?
Diabetes & Metabolism 2003, *29*, 4S323 (IF: 1.546)
104. A. Nemes, Cs. Lengyel, T. Forster, T. T. Várkonyi, R. Takács, I. Nagy, J. Lonovics, M.
Csanády:
Correlations between coronary flow velocity reserve, autonomic dysfunction and insulin
resistance
Eur. Heart J. 2003, *24*, 490 (IF: 5.153)
105. T.T. Várkonyi, R. Takács, R. Róka, P. Légrády, M. Lázár, L. Madácsy, Cs. Lengyel,
P. Kempler, L. Pávics, J. Lonovics:
Comparative evaluation of neuropathy status, gastric emptying and digestive symptoms in
type-2 diabetic patients with different disease durations
J. Peripher. Nerv. Syst., 2003, *8*, 197-198 (IF: 1.298)

Acknowledgements

At first I wish to express my thanks to Professor János Lonovics, who as a tutor and Head of the Department has been promoting my scientific and clinical career continuously since the final year of my university studies. In my first few years in the Department I had the opportunity to join his hepatobiliary team, where I could learn from him the basics of the experimental and clinical research. In 1993, he gave me the chance to become a member of the newly-organized diabetes team. I deeply appreciate his constant mental, human and economic support whereby all of my scientific aims could be realized. His guidance, pragmatic advice and effective management are greatly acknowledged.

I thank Professor Vince Varró, the first Head of the Department of my scientific career for the admission to his staff after my graduation, and for the initiation of my professional activity.

I am deeply grateful to Professor Peter Kempler for the possibility of cooperation. In the course of this, he readily made available new unique examination methods, and constantly shared with me his great experience and extremely valuable theoretical and practical advice. Besides his professional help, I deeply appreciate his unselfish friendly support.

My thanks are due to Professor Tamás Fazekas, who played an indispensable part in the planning and attainment of the investigations at the beginning of my scientific activities, and from whom I obtained enormous help in the evaluation of the results and in the preparation of the first manuscripts.

I wish to express my thanks to Professor László Csernay and Professor László Pávics for furnishing all the necessary help for me to be able to study gastrointestinal motility in the Department of Nuclear Medicine.

I am grateful to Professor Gyula Farkas who provided me with the possibility to carry out examinations on his patients who had undergone islet cell transplantation with the unique methodology that he had developed.

I thank Dr. Márta Janáky, Dr. Zsuzsanna Fülöp, Dr. József Géza Kiss, Dr. László Rovó and Ferenc Tóth for making available the results of their high-level measurement techniques, with which I was able to study the functioning of the central nervous system.

My thanks are due to Dr. Borbála Velősy for her decisive support in the realization of the gallbladder motility studies.

I am very grateful to my friends, Dr. Csaba Lengyel and Dr. László Madácsy. Since the beginning of my scientific career, they have selflessly granted me their friendly support without thought for time or energy.

My younger colleagues, Dr. Róbert Takács, Dr. Péter Légrády, Dr. Richárd Róka and Dr. Máté Lázár have always given me their systematic and enthusiastic support.

My special thanks are due to my mother, my wife and my son, on whose support I could always count. I dedicate my work to the memory of my father, Dr. László Várkonyi, for his exemplary professional and human standards.