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T.Mokrusch

MAGNETIC RESONANCE IMAGING IN SKELETAL MUSCLE FOLLOWING DENERVATION AND ELECTRICAL STIMULATION

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Abstract. Following chronic denervation, MRI evaluation of fast rabbit muscles revealed a distinct increase of signal intensity and T_2 relaxation time. These changes were missing or less pronounced after treatment with a new type of electrical stimulation, which previously had proved effective in avoiding muscle atrophy. One month after denervation, there was a slight increase of signal intensity as well in the stimulated as in the untreated animals, after two months, however, the increase was statistically significant only in the non-stimulated muscles. T_2 relaxation time showed a slight increase after one month of therapy, while there was a significant increase after one and two months without therapy. After 3—6 months of electrical stimulation, there was no increase of T_2 at all. The results indicate 1), that MRI can be used when monitoring stimulation effects on denervated muscle, and 2), that, for this purpose, T_2 relaxation time is more useful than signal intensity.

Т.Мокруш

ВИЗУАЛИЗАЦИЯ СКЕЛЕТНЫХ МЫШЦ МЕТОДОМ ЯДЕРНО-МАГНИТНОГО РЕЗОНАНСА ПОСЛЕ ДЕНЕРВАЦИИ И ЭЛЕКТРИЧЕСКОЙ СТИМУЛЯЦИИ

Реферат. Визуализация методом ядерно-магнитного резонанса мышц кролика с хронической денервацией на фоне голодания позволила обнаружить явное увеличение интенсивности сигнала и времени релаксации T_2. Эти изменения не наблюдались или были менее выражены после лечения электростимуляцией, которая ранее оказалась эффективной в профилактике атрофии мышц. Через месяц после денервации наблюдалось небольшое возрастание интенсивности сигнала как у стимулированных, так и у нестимулированных животных. Однако через 2 мес его возрастание было статистически значительным только в стимулированных мышцах.

Т.Мокруш

ДЕНЕРВАЦИЯ ҺӘМ ЭЛЕКТР СТИМУЛЯТОРЫННАН СОҢ СКЕЛЕТ МУСКУЛЛАРЫН ТӨШ-МАГНИТ ТИРБӘНЕШЕ ЫСУЛЫ БЕЛӘН ВИЗУАЛИЗАЦИЯЛӘҮ (КҮЗӘТҮ, ТИКШЕРҮ)

Ачлык аркасында килеп чыккан хроник денервацияле йорт куяны мускулын төш магнит тирбәнеше ысулы белән күзәтү (визуализацияләү) сигнал көченең үсүен һәм T_2 релаксация вакыты артуын тапты. Элек мускул атрофиясен (зәгыйфьләнүен) дәвалаганда әйбәт нәтиҗәләргә китергән электр стимуляциясе белән дәвалаганнан соң, мондый үзгәрешләр сизелерлек кимеде яисә бөтенләй күзәтелмәде. Денервация башланып, бер ай узганнан соң, стимуляцияләнгән хайваннарда да, стимуляцияләнмәгән хайваннарда да сигнал көченең бераз үсүе күзәтелә, ләкин 2 айдан үсеш бары тик стимуляцияләнгән мускулларда гына сан ягыннан сизелерлек була.

Denervation atrophy and electrical stimulation

Following chronic denervation, a lot of well known changes occur in a skeletal muscle, particularly concerning contractile properties and morphological features [6]. While contraction force decreases, the muscle fibres become smaller and histologically an increase of fat and connective tissue is found.

Despite many investigations during the last decades, the discussion on the efficacy of electrotherapy in chronic denervation is still controversial. In most of the earlier investigations, electrotherapy was found to delay, but not to avoid atrophic changes [7,9,12,15,18,20,32]. In recent investigations, a new type of electrical stimulus, developed in our group, proved to be highly effective. In animal experiments, the contraction force of fast rabbit muscles was maintained at a level of 40—100% of normal, and in patients denervation induced changes showed to be reversible even several months after complete and chronic denervation [14,15, in preparation].

MRI of muscle

Muscle tissue normally is characterized by the classical methods of histology, enzyme histochemistry and electron microscopy. During the last few years, these morphological methods became supplemented by imaging techniques (ultrasonography, computer tomography, MRI), and in particular MRI promises to become an important tool in the clinical evaluation of muscle diseases [22].

The relaxation times T_1 and T_2 are more specific than signal intensity and show typical values in different tissues [5], and so they are considered to be clinically more useful. In denervation atrophy, muscles show a decrease of T_1 and an increase of T_2 [2,22], while the relaxation times are not influenced by a long time resting or immobilisation atrophy [10]. A reversible increase of T_2 has been described following an intensive muscle training [4]. As to our knowledge, the influence of electrotherapy on MRI of muscle has never been investigated before.

As our new method of electrical stimulation has proved effective in avoiding atrophy and loss of muscle strength in chronic denervation, it was of a certain interest, whether MRI can be used to monitor the influence of electrotherapy on the denervated muscle. Being a non invasive method, MRI can be repeated easily, and possibly some (invasive) histological examinations could be supplemented or even replaced by magnetic resonance imaging. Preliminary results, as presented earlier [17] had been encouraging.

Material and Methods

20 adult white New Zealand rabbits were examined. In 16 animals, the right hindlimb was denervated totally and chronically as reported previously [15]. Electrical stimulation was performed in 7 animals twice daily via surface electrodes with an effective stimulation time of 2×7,5 minutes. 9 animals remained untreated after denervation, and 4 animals served as normal controls. For stimulation, bidirectional rectangular inpulses with a frequency of 25 Hz and an intensity of 40 mA were used, as they had proved effective in maintaining contraction force and muscle bulk. Observation time was 1 month for short-term effects, 2 months and 3—6 months for long-term effects.

MRI examinations were performed in general anesthesia (ketamine and xylazine i.v.) on a SIEMENS Magnetom 1,5 T. In a "head coil", the legs were tied up in a parallel position, care was taken of a side by side position of the knee joints for having identical muscle regions of both legs on the same store.

For the measurement of signal intensity in T1 weighted images, a repetition time (TR) of 0,6 sec was chosen, and an echo time (TE) of 15 msec. T2 relaxation time was calculated from CPMG sequences: 8 echos from 22 to 176 msec, each with a TR of 0,6 and 1,8 sec. Usual slice thickness was 4 mm, except for multi echo-sequences (8 mm).

In each animal, two fast contracting muscles — the tibialis anterior muscle (TA), and the flexor digitorum sublimis muscle (FDS) were evaluated. Signal intensity and T_2 relaxation time were measured within one slice of the middle third of the crus. In each muscle, the average values were calculated from 5 measurements in regions of interest (ROI) with an area of 6 pixels, which is equivalent to a volume of about 0,1 cm^3. Care was taken to that the ROIs did not include any visible fascia or blood vessel. From both signal intensity and T_2 relaxation time, right/left ratios were evaluated.

Results

Signal intensities:

In both muscles of the four normal controls, as expected no difference was found between the two legs, indicating a good reliability of the measurements. Five animals were investigated one month after denervation. Here an increase of signal intensity was observed in both muscles as well in the stimulated as in the untreated animals. These changes did not reach significance, and there was also no difference between TA and FDS.

After long term denervation in six animals, there was a significant increase of signal intensities in both muscles without electrotherapy, whereas there was only a slight increase in the long-term stimulated muscles (Fig. 1).

T_2 relaxation times:

Like for signal intensities, no side differences were found for T_2 relaxation times in the normal muscles (normal values: $TA=32,0+2,0$ msec, $FDS=30,9+1,3$ msec), in the treated muscles, the changes of T_2 were more distinct than those of signal intensities. Already one month after denervation, an influence of electrical stimulation was found. Without stimulation, T_2 had clearly increased in both muscles (TA=157%, FDS=151%), whereas only a tendency (FDS) or a slight significance (TA) for changes were found in the stimulated muscles. In the long-term denervated animals, similar changes were found in the non stimulated muscles (increase of TA=150% and of FDS=157%), whereas there were no changes at all in the treated muscles (Fig. 2).

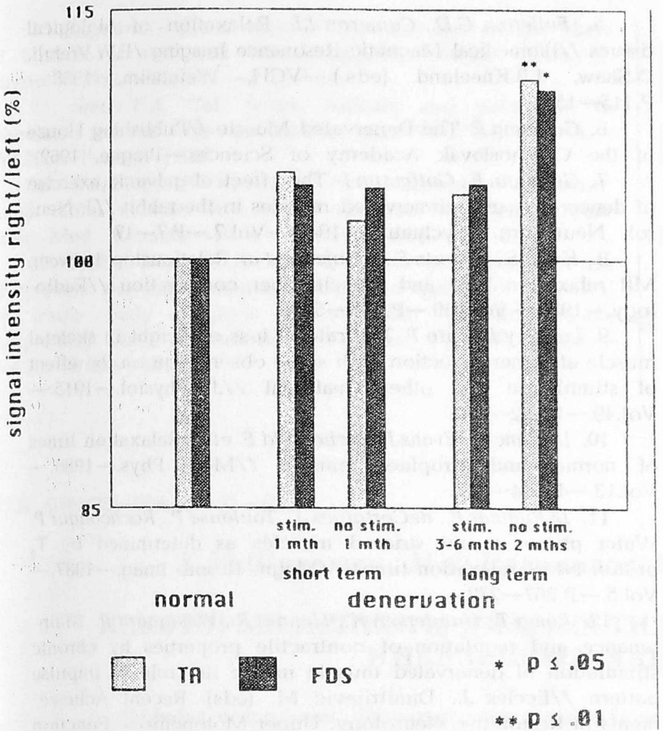

Fig. 1. Changes of signal intensity in fast skeletal muscles of rabbit following short and long term denervation. Influence of electrical stimulation. Ratio: right = denervated/left = normal, scale from 85—115%. TA = tibialis anterior muscle, FDS = flexor digitorum sublimis muscle

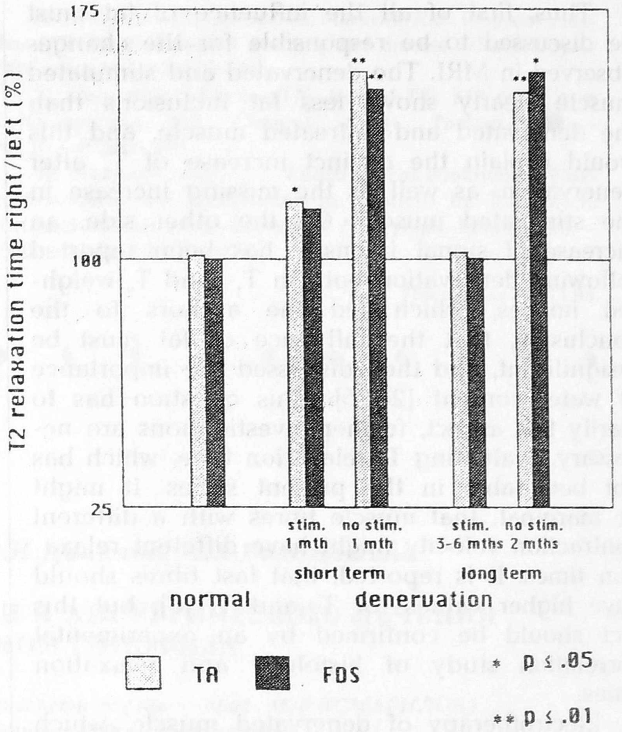

Fig 2. Changes of T_2 relaxation time following denervation and electrical stimulation (explanation see fig. 1) Note the larger scale in the diagram, reaching from 25—175%

Discussion

Since MRI has been introduced in clinical practice and investigation, a lot of observations have been presented, describing muscle pathology. By most of the authors, the findings concerning signal intensity and relaxation times are explained with changes of fat and water content [1,10,19,22,24,30,31]. The binding capacity of macromolecules, electrolytes, pH, temperature and some other factors may have an influence too [5].

In this investigation, it has been necessary to evaluate very small ROIs, because within the anyway small objects of FDS and TA muscles, areas of fascia and fat had to be excluded. However, this has been possible without problems because of the high resolution of MRI, which is said to be less than 1 mm [23]. The good reproducibility is shown by the low standard deviation of normal values, which already has been found in a previous investigation [17].

In denervation atrophy, the decrease of muscle volume always parallels with an increase of connective tissue and fat, while the water content remains constant [6]. In our study, the effect of denervation was clearly visible not only histologically (unpublished observations), but also in MRI. While the results of signal intensity were only poor, T_2 proved to be a valuable tool to differentiate a denervated muscle from a normal or a denervated-stimulated one. In both muscles, T_2 relaxation time clearly increased after one and two months of denervation alone, while it increased significantly less during electrotherapy. Similar observations, concerning a different behaviour of signal intensity and relaxation times, have been made in physiological short time reactions of muscle too, describing no changing of signal intensity but a distinct increase of T_2 during muscle exercise [4,19,29].

Effects of muscle exercise on MRI may occur due to a changing of water content and electrolyte concentration [4,26,27], and there is no difference, if muscle contractions are performed voluntarily or induced by electrical stimuli [11,27]. These changes, however, are only short term effects and cannot explain the findings of one or two months later. So, the long term effects cannot be explained by muscle contractions alone.

Long term immobility is known not to influence the relaxation times, although it might be accompanied by a marked atrophy [10]. Hence, the denervation induced increase of T2 must be explained by other factors than a simple decrease of muscle fibre diameter. In later stages of atrophy, the muscle degenerates, e.g. it becomes fibrotic, and muscle fibres are replaced by fat and connective tissue [6]. Fat is known to influence relaxation times, and its amount even can be calculated, when trying to separate this effect from the influence of water and proteins. Fat and water are thought to be the most important factors, even if they might be controlled and modulated by the pH level, the concentration of electrolytes or the temperature [5].

Thus, first of all the influence of fat must be discussed to be responsible for the changes observed in MRI. The denervated and stimulated muscle clearly shows less fat inclusions than the denervated and untreated muscle, and this would explain the distinct increase of T_2 after denervation, as well as the missing increase in the stimulated muscle. On the other side, an increase of signal intensity has been reported following denervation both in T_1- and T_2-weighted images, which led the authors to the conclusion, that the influence of fat must be insignificant, and they discussed the importance of water content [24,25]. This question has to clarify this aspect, further investigations are necessary, evaluating Tl relaxation time, which has not been able in the present series. It might be marginal, that muscle fibres with a different contraction velocity might have diffetent relaxation times. It is reported, that fast fibres should have higher values for T_1 and T_2 [8], but this fact should be confirmed by an experimental correlation study of histology and relaxation times.

Electrotherapy of denervated muscle, which for a long time had missed to prove effective, now is developing a clinically valuable method, using our type of stimulus. Using surface electrodes, the stimulation is able to lift the patient's leg when lying on the bed or sitting on a chair [16]. In other patients, a strong tetanic contraction of the biceps muscle is possible, and the flexion of the ellbow is a useful movement. So, if in future our new concept of electrotherapy should stand the test clinically, a tool is necessary to monitor the effect of the therapy on the denervated muscle. Histological examinations always need an (invasive) biopsy, while MRI is a non invasive method, which can easily be repeated, even if it is expensive. The first couple of measurements in patients showed, that an increase of T_2 can be reversible after the onset of electrotherapy even several months after denervation, indicating and parallelling an increase of muscle bulk and contraction force (in preparation). So we think, that MRI will be a useful tool for monitoring the success of electrotherapy in chronically denervated muscles.

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НЕКОТОРЫЕ АСПЕКТЫ ДИАГНОСТИКИ И ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ИНВАЗИВНЫХ АДЕНОМ ГИПОФИЗА

Кафедра неврологии, нейрохирургии и медицинской генетики (зав.— проф. М.Ф.ИСМАГИЛОВ)
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Республиканская клиническая больница (гл.врач — Р.Г.ФАТИХОВ) Минздрава РТ

Реферат. Анализируется клиническая картина заболевания у 85 больных с аденомами гипофиза. Вскрыты причины поздней диагностики заболевания. Приведены непосредственные результаты хирургического лечения больных.

Х.М.Шульман, М.Ф.Исмәгыйлев,
В.И.Данилов, А.Х.Соломатина

ГИПОФИЗДАГЫ ИНВАЗИВ АДЕНОМАЛАРНЫ ХИРУРГИЯ ЮЛЫ БЕЛӘН ДӘВАЛАУ ҺӘМ ДИАГНОЗ КУЮНЫҢ КАЙБЕР ЯКЛАРЫ (АСПЕКТЛАРЫ)

Гипофиз аденомалы 85 авыру чиренең клиник картинасы анализлана. Авыруга диагноз соң куелуның сәбәпләре ачыклана. Авыруларны хирургия юлы белән дәвалауда ирешелгән нәтиҗәләр китерелә.

Kh.M.Shulman, M.F.Ismagilov,
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SOME ASPECTS OF DIAGNOSTICS AND SURGICAL TREATMENT OF THE INVASIVE PITUITARY ADENOMAS

Clinical patterns of 85 patients with pituitary adenomas are analysed. Causes of late diagnostics of the disease are revealed. Immediate results of surgical treatment of patients are given.

К инвазивным аденомам гипофиза относятся опухоли, выходящие за пределы гипофизарного (дурально-арахноидального) ложа, или редко встречающиеся аденомы, первично растущие из туберального отдела аденогипофиза [2].

Гипофизарные аденомы — часто встречающаяся нейрохирургическая и эндокринологическая патология, она составляет 13,3% всех случаев нейроонкологических заболеваний. 75% больных этой категории составляют лица в возрасте от 30 до 50 лет [1]. По данным С.Н.Федорова [3], ежегодный прирост больных с этой патологией в нашей стране составляет примерно 3000 пациентов, а общее число требующих лечения или активного наблюдения достигает 80—100 тыс.

Результаты лечения больных с аденомами гипофиза в значительной степени зависят от ранней диагностики заболевания. Она приобретает особую актуальность в связи с развитием грубого и необратимого неврологического дефицита, характеризующего поздние стадии заболевания.

В диагностическом процессе аденом гипофиза в последние годы произошли существенные позитивные сдвиги благодаря внедрению в клиническую практику радиоиммунного метода определения гормонального спектра и использованию современных методов обследования, таких как магнитно-резонансная томография (МРТ), компьютерная томография (КТ), ангиография (АГ) и др. Это значительно расширило возможности раннего распознавания опухолей. Вместе с тем до настоящего времени обращает на себя внимание частое обращение больных за лечебной помощью на поздних стадиях заболевания. Среди причин запоздалой диагностики в первую очередь необходимо отметить низкий уровень общебиологической образованности населения и медицинских работников. Не менее существенной причиной является недостаточная онкологическая настороженность среди эндокринологов, гинекологов, сексопатологов, окулистов и представителей традиционной