J Neural Transm [P-D Sect] (1995) 9: 211–223

Journal of Neural Transmission

Does reserpine induce parkinsonian rigidity?

E. Lorenc-Koci, K. Ossowska, J. Wardas, and **S. Wolfarth**

Department of Neuropsychopharmacology, Institute of Parmacology, Polish Academy of Sciences, Kraków, Poland

Accepted April 21, 1995

Summary. The aim of the study was to find out whether the reserpine-induced rigidity is similar to that seen in parkinsonism. Simultaneous measurements of the muscle resistance of the hind foot to passive bending and stretching in the ankle joint, as well as of the electromyographic (EMG) activity of the gastrocnemius and tibialis anterior muscles of rats were carried out. Reserpine was injected in a dose of 10 mg/kg alone or with α-methyl-p-tyrosine (250 mg/kg) 1, 4 and 27.5 h before the measurements. Reserpine increased the muscle resistance of the rat's hind leg to passive movements. That effect was the strongest at 1–2 h after the injections, and diminished markedly afterwards. The rigidity was accompanied with an increase in the resting, as well as in the stretch-induced short- and long-latency EMG activity in the gastrocnemius muscle. However, the intensity of the latter symptom did not change for a long period of time, which seems to correlate with the striatal dopamine depletion. The results suggest that the reserpine-increased EMG activity is a good model of parkinsonian rigidity.

Keywords: Reserpine, rigidity, mechanomyogram, electromyogram, parkinsonism.

Introduction

Parkinson's disease is characterized by a triad of primary symptoms, namely akinesia, muscular rigidity and tremor. It has been generally accepted that the primary cause of this disease is a lesion of dopaminergic neurons in the pars compacta of the substantia nigra, which leads to a loss of dopamine in the striatum.

Reserpine is a model compound, commonly used to induce parkinsonian symptoms (akinesia, tremor and rigidity) in laboratory animals (Morrison and Webster, 1973; Goldstein et al., 1975; Jurna, 1976; Johnels et al., 1978; Johnels and Steg, 1982; Johnels, 1983; Colpaert, 1987; Klockgether and Turski, 1990; Wolfarth et al., 1992; Ossowska, 1994; Ossowska et al., 1994). It has been suggested that the reserpine-induced parkinsonian symptoms result from

depletion of striatal dopamine (Jurna, 1976; Johnels et al., 1978; Johnels and Steg, 1982; Johnels, 1983; Colpaert, 1987; Klockgether and Turski, 1990). This conclusion is supported by the fact that these symptoms are antagonized by dopaminomimetics and MAO inhibitors (Morrison and Webster, 1973; Jurna, 1976; Johnels et al., 1978; Johnels and Steg, 1982; Colpaert, 1987; Klockgether and Turski, 1990; Ossowska, 1994). Reserpine used in doses which induce extrapyramidal symptoms evokes a very long-lasting (more than 24 h) dopamine depletion in the striatum (Bean et al., 1989; Fornstedt and Carlsson ,1989; Elverfors and Nissbrandt, 1991). This biochemical finding correlates well with the reserpine-induced akinesia which is also a very long-lasting symptom (Colpaert, 1987; Starr and Starr, 1994). However, the experimental data on the time-course of the muscle rigidity induced by reserpine are controversial. The reserpine-induced rigidity measured as a muscle resistance to a passive displacement was reported to be a relatively short-lasting symptom, which reaches its maximum in approx. 1 h after the injection, and markedly diminishes afterwards (Johnels et al., 1978; Johnels, 1983; Colpaert, 1987; Ossowska et al., 1994). Contrariwise, Klockgether and Turski (1990) found that reserpine given in combination with α-methyl-p-tyrosine (αMT) induced a tonic EMG activity at rest, when measured 24 h after the injection. The latter authors suggested that the tonic EMG activity reflected the presence of muscle rigidity; however, they did not carry out any direct measurements of that symptom. Therefore a question arises whether the reserpine-induced rigidity is actually of a parkinsonian type.

Parkisonian rigidity is characterized by an increased resistance of limbs in response to passive displacement. It has been suggested that this symptom is due to potentiation of the stretch reflex response, especially of its long-latency EMG components, and to coactivation of antagonistic muscles in response to passive movements (Marsden et al., 1973; Lee and Tatton, 1975; Burke et al., 1977; Mortimer and Webster, 1979; Berardelli et al., 1983; Rothwell et al., 1983; Tatton et al., 1984; Lee, 1989; Meara and Cody, 1992). Furthermore, in parkinsonian patients a tonic EMG activity takes place at rest, which reflects a certain difficulty to relax the muscles (Lee, 1989).

In the present paper we examined the time-course of rigidity induced by reserpine and its EMG correlates in rats. To that end we used a previously described combined mechano- and electromyographic method which allows simultaneous measurements of the muscle resistance of the hind foot to passive bending and stretching in the ankle joint (MMG), as well as of the electromyographic activity of the antagonistic muscles of this joint – the gastrocnemius soleus and tibialis anterior (EMG). The present results seem to suggest that the reserpine-induced rigidity bears a number of similarities to the rigidity seen in Parkinson's disease.

Materials and methods

Mechanomyographic (MMG) and electromyographic measurements (EMG)

The experiment was carried out on male Wistar rats. A rat was placed in a special metaplex cage, well ventilated and adapted to its size. The rat's hind foot, which pro-

truded from a special opening at the bottom of the cage, was placed on an appropriately matched metaplex block and gently fixed to it using an adhesive tape (a modification of the previously described MMG method (Kolasiewicz et al., 1987)). Two pairs of flexible, stainless-steel wire electrodes (Cooner Wire Comp., Chatsworth, CA, U.S.A.,), which were teflon-insulated (ext. diameter 0.25 mm) except for a 4-mm uninsulated part (ext. diameter 0.1 mm), were inserted percutaneously into the gastrocnemius (extensor, plantar flexor) and tibialis anterior (flexor, dorsal flexor) muscles. The distance between the two electrodes of a pair in each muscle was ca. 5 mm. A grounding electrode was gently attached with a piece of wet tissue (0.9% NaCl solution) and a clip to fasten it to the rat tail. The experiment consisted of successive cycles of up-and-down movements of the block (30 s apart), which bent and stretched the rat foot in the ankle joint by 25° from the horizontal plane. Each movement lasted 250 ms. After a 30-min adaptation period, when only passive movements were executed but no measurements were performed, the proper experimental session started, and lasted for 60 min (60 cycles). The metaplex block was connected to a force sensor which recorded the resistance of the foot to passive movements (a mechanical moment, torque)(MMG). EMG signals from the electrodes were amplified and band-pass-filtered (80 Hz–10 kHz) (Polygraph Grass, Model 78B). The recording of the EMG and MMG signals started 500 ms earlier, and was continued for 250 ms throughout and 2,250 ms after the end of each passive movement. The EMG and MMG signals were sampled by AD Converters with a frequency of 10 kHz per channel, and fed into a PC.

Data analysis

Mechanomyogram

The maximum resistance (in comparison with the pre-movement value) of the hind leg muscles for each up (bending) or down (stretching) movement (MMGmax) was determined and accepted as a measure of the muscle tone (Fig. 1A,B). All the cycles disturbed by active movements of a rat were discarded.

Electromyogram

The EMG activity of the gastrocnemius and tibialis anterior muscles was averaged out with a time constant of 20 ms for each undisturbed up-and-down movement. In order to visualize the main tendency of the time-course of EMG activity during movements, all the individual EMG curves of the whole group of rats were superimposed and averaged out for either muscle (gastrocnemius or tibialis) and movement (up or down) (Fig. 2C). On the basis of the shape of the final averaged out EMG curve in control rats, the following parameters were chosen and estimated: (1) a mean of the pre-movement amplitude (EMG-baseline); (2) components computed as differences between the maximum amplitude in 3 periods of time after the start of a movement and the EMG-baseline: (a) EMG-A (0–20 ms), (b) EMG-B (40–60 ms), (c) EMG-C (80–160 ms) and (d) EMG-D (240–340 ms). All these components were measured automatically for each movement. All the cycles disturbed by voluntary movements were discarded.

Drugs

Reserpine (Polfa, Warszawa) was dissolved in a solution containing 0.25% citric acid, 2% benzyl alcohol and 10% Tween 80.

Two groups of rats were treated with reserpine (10 mg/kg ip). One group was injected with that drug at 1 hour (n = 10) , and the other – at 4 hours (n = 11) before the start of mechanomyographic and electromyographic measurements. A third group (n = 8) was treated with reserpine in a dose of 10 mg/kg ip and, additionally, with α-methyl-p-tyrosine (αMT, 250 mg/kg ip) at 24 h after reserpine. Mechanomyographic measurements after

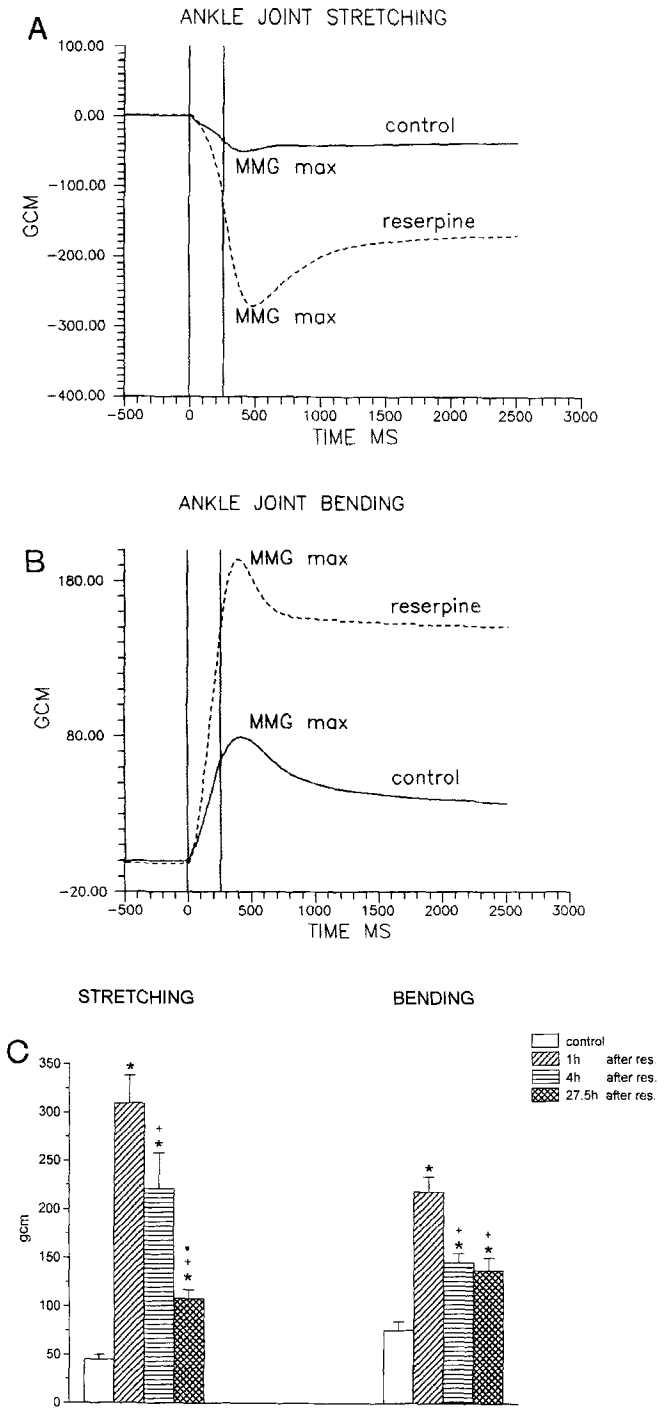

Fig. 1. Mechanographic recording (MMG) of the resistance developed during passive stretching (**A**) and bending (**B**) of the hind foot in the ankle joint of control (solid lines) and reserpine-treated (broken lines) rats. Reserpine was injected 1 h before the start of measurements. *Abscissa* – time in ms, *ordinate* – resistance of the hind foot in gcm. The values are shown to be negative during stretching, and positive during bending. Vertical lines denote the beginning and the end of a movement, respectively. MMGmax – the maximum resistance. **C** The maximum resistance (MMGmax) of the hind foot, developed during stretching and bending in the ankle joint in control and reserpine-treated (res) rats. The results are shown as mean + SEM. The mesurements were started 1h (n = 10), 4 h (n = 11) or 27.5 h after reserpine (n = 8). The last group was additionally treated with αMT (3.5 h before the start of the experiment). Contorl rats – n = 10. Statistically significant differences (the Kruskal-Wallis and Wilcoxon tests) at the level $p < 0.05$: *vs control animals, †vs 1h after res, • vs 4 h after res

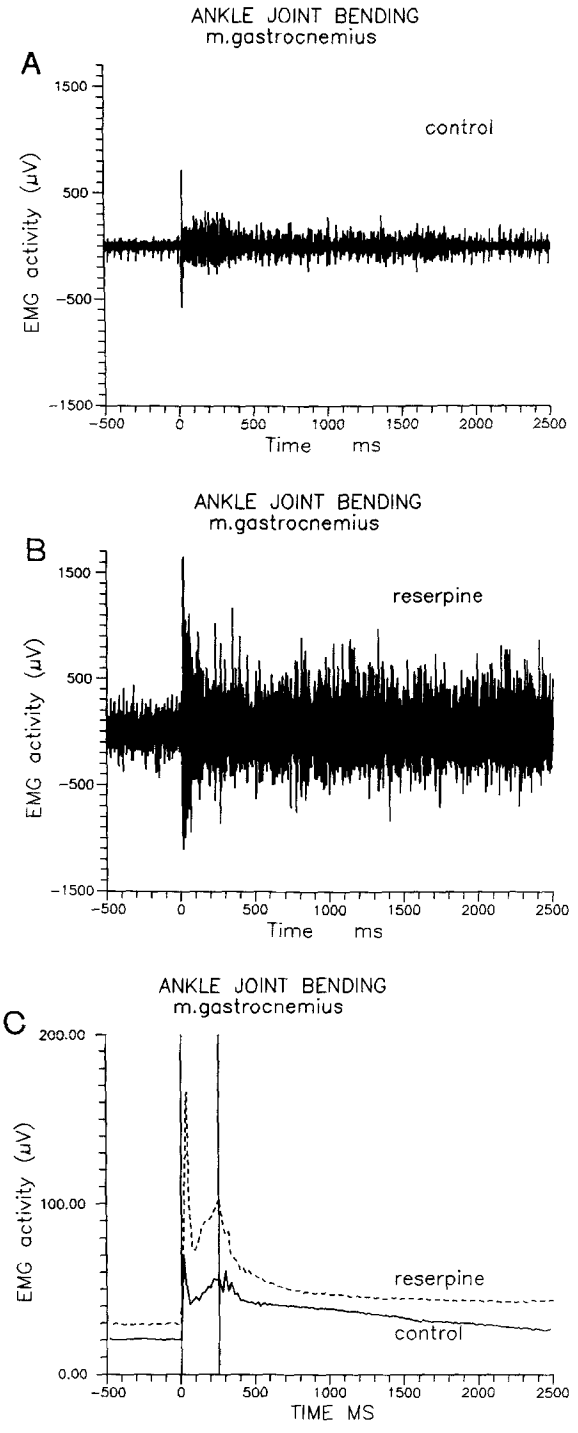

Fig. 2. Typical examples of the electromyographic EMG activity, recorded in the gastrocnemius muscle during bending of a rat's hind foot in the ankle joint in control (**A**), and in reserpine-treated animals (**B**); **C** The averaged out EMG curve, which was obtained by superimposition of EMG curves of undisturbed individual cycles, recorded for the group of control (solid line) and reserpine-treated (broken line) rats. Reserpine was injected 1 h before the start of the measurements. Vertical lines denote the start and the end of a movement, respectively. *Abscissa* – time in ms, *ordinate* – EMG activity in μV

joint treatment with reserpine and αMT were started 27.5 h after reserpine (3.5 h after αMT). Control rats (n = 10) were injected with the solvent.

Statistics

An analysis was carried out using the means calculated from all the correct cycles recorded for each rat. The statistical significance of differences was estimated using the Kruskal-Wallis and Wilcoxon tests.

Results

Mechanomyogram

During passive stretching or bending, the hind foot of control rats responded with an increasing resistance which reached its maximum (MMGmax) at about 150–200 ms after the end of movements (Fig. 1A,B). Afterwards, the hind foot muscles were relaxed, which was reflected in a lowered MMG curve (Fig. 1A,B). Reserpine injected in a dose of 10 mg/kg, alone or in combination with αMT (250 mg/kg), strongly increased the muslce tone (MMGmax) in rats (Fig. 1A,B,C). Reserpine also diminished the ability of the hind foot to relax. The level of the MMG curve at the end of the recording period (2,500 ms after the start of each movement) was markedly higher in reserpine-treated animals than in controls (Fig. 1A,B). The most pronounced rigidity was observed 1–2 h after the injection, during stretching and bending of the hind leg in the ankle joint (Fig. 1C). Afterwards, the rigidity was diminished in a statistically significant manner. The weakest effect was observed after joint treatment with reserpine and αMT (27.5–28.5 h after reserpine and 3.5–4.5 h after αMT) (Fig. 1C).

Electromyogram

The electromyographic (EMG) recording of the gastrocnemius (Fig. 2A) and tibialis anterior (data not shown) muscles in control rats showed large bursts of motor units in response to every passive movement. Those discharges started within the first 20 ms with a burst of high-amplitude potentials (Fig. 2A). Afterwards, the amplitudes of EMG discharges were diminshed. On the EMG curve, averaged out for the whole group of animals, the first peak was observed at 20 ms (the mean of a period of 0–20 ms), and then it was seen to decrease markedly. The second increase in the EMG activity started at 40 ms and reached its maximum shortly after the end of the movement. Afterwards, the EMG curve was slowly lowered (Fig. 2C). The estimated EMG-A component represented the first short-latency peak of the EMG activity. The EMG-B and EMG-C components reflected an increase in the second burst of the EMG activity, and the EMG-D component indicated its maximum (compare Figs. 3, 4 and 2C).

Reserpine given alone or jointly with αMT increased the EMG activity in the gastrocnemius muscle, recorded both before (EMG-baseline) and during the bending and stretching of the hind foot (EMG-A, EMG-B, EMG-C and EMG-D components (Figs. 2B,C, 3A, 4A). The effect seemed to be the

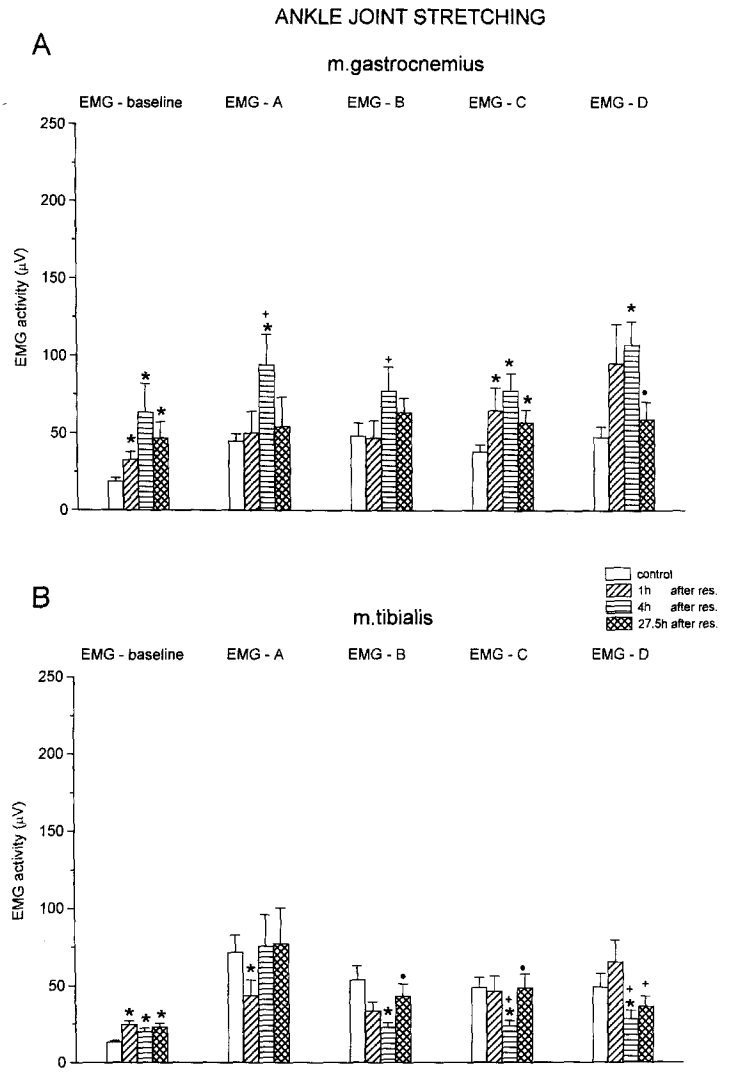

Fig. 3. The influence of reserpine administration on the electromyographic (EMG) activity in the gastrocnemius (**A**) and tibialis anterior (**B**) muscles during ankle joint stretching. Five components are shown: EMG-baseline (estimated before the movements), EMG-A, EMG-B, EMG-C and EMG-D (estimated at 0–20, 40–60, 80–160 and 240–340 ms after the start of movements). *Ordinate* – the EMG activity expressed in μV. For further explanations see Fig. 1C

strongest at 4–5 h after reserpine. However, only during stretching, the EMG-A and EMG-B components, measured 4–5 h after reserpine, were significantly increased in comparison with those measured earlier (1–2 h). The EMG-D component was significantly augmented during the movement in comparison with that measured later (27.5–28.5 h) (Fig. 3A).

The effect of reserpine on the EMG activity of the tibialis anterior muscle was inconsistent. Before ankle joint bending, that drug significantly increased the EMG-baseline and during that movement EMG-A, -C and -D components at 1–2 h after the injection (Fig. 4B). The EMG-A component remained to be significantly increased at 4–5 h after reserpine; however, no other signifi-

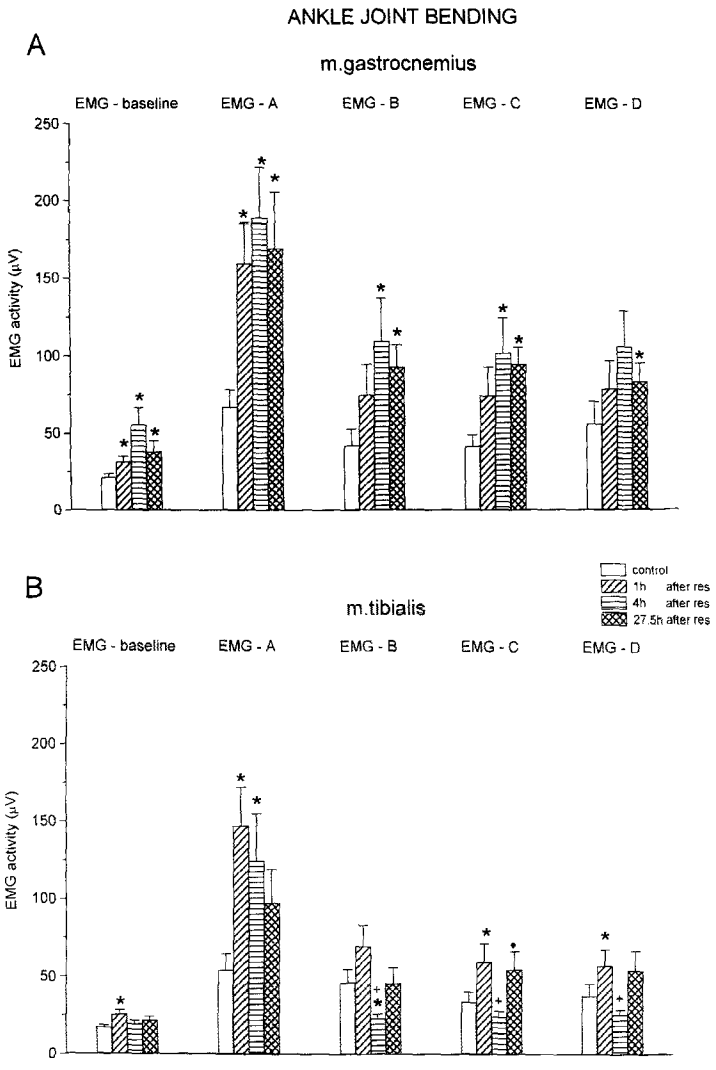

Fig. 4. The influence of reserpine administration on the electromyographic (EMG) activity in the gastrocnemius (**A**) and tibialis anterior (**B**) muscles during ankle joint bending. Five components are shown: EMG-baseline (estimated before the movements), EMG-A, EMG-B, EMG-C and EMG-D (estimated at 0–20, 40–60, 80–160 and 240–340 ms after the start of movements). *Ordinate* – the EMG activity in μV. For further explanations see Fig. 1C

cant increases were found in comparison with control animals (Fig. 4B). Contrariwise, the EMG-B component measured during that movement at 4–5 h after reserpine, was significantly decreased in comparison with controls and with animals examined 1–2 h after reserpine. The decreases in EMG-C and EMG-D components, observed after 4–5 h compared to those measured 1–2 h after reserpine were also statistically significant.

Before the ankle joint stretching, the EMG-baseline of the tibialis anterior muscle was elevated at all the examined time periods (Fig. 3B). No increases in the EMG activity during the ankle joint stretching were observed. Contrari-

wise, the EMG-A was decreased at 1–2 h and EMG-B, -C and -D components at 4–5 h after reserpine (Fig. 3B).

It is noteworthy that ca. 2 h after injection of reserpine (10 mg/kg) a serious diarrhea began which 24 h later resulted in a marked rat's body weight loss (12%, 334.5 g (before reserpine) vs 295.5 g (24 h after reserpine), $n = 8$, $p < 0.001$, a paired Student's test). Similar but weaker effects were observed 4 h after reserpine.

Discussion

The present results confirm many earlier data that reserpine induces muscle rigidity (Morrison and Webster, 1973; Goldstein et al., 1975; Jurna, 1976; Johnels et al., 1978; Johnels and Steg, 1982; Johnels, 1983; Colpaert, 1987; Klockgether and Turski, 1990; Wolfarth et al., 1992; Ossowska, 1994; Ossowska et al., 1994). In the present study that symptom was measured by an increased resistance developed by the rat's hind leg in response to passive movements. The reserpine-induced rigidity was accompanied with enhancement of the EMG activity in the gastrocnemius muscle, measured immediately before and during passive movements. In the tibialis anterior muscle, a rise in the EMG activity before movements and, occasionally (1–2 h after the injection), during ankle joint bending was also observed. The increase in the EMG activity before the movements reflects the appearance of the resting activity in both those muscles and seems to be connected with the animal's inability to relax completely during breaks between consecutive movements. The latter effect, observed at 27.5 h after joint treatment with reserpine and αMT, confirms a similar finding (a tonic EMG activity in the gastrocnemius muscle at rest) of Klockgether and Turski (1990) who used a similar injection procedure. The resting EMG activity was also observed in rigid parkinsonian patients (Lee, 1989).

Enhancement of the EMG activity, recorded during passive movements in the gastrocnemius muscle after reserpine, is in an agreement with similar finding in rats, reported by Johnels and Steg (1982). The development of the EMG activity during passive movements was also observed by a number of clinicist in humans, and was suggested to result from a reflex response of a particular muscle to stretching. Such a response was reported to have at least 2 components: of short- and long-latency. It was suggested that the short-latency peak, observed after ca. 17–45 ms (depending on the examined muscle), resulted from activation of the monosynaptic spinal loop, while components of longer latency (45–108 ms) were due to activation of long, polysynaptic, supraspinal (transcortical) loops (Lee and Tatton, 1975; Rothwell et al., 1983; Scholz et al., 1987; Lee, 1989; Davidoff, 1992; Matthews, 1991). In Parkinson's disease, a drammatic increase in long-latency components was observed (Lee and Tatton, 1975; Rothwell et al., 1983; Scholz et al., 1987; Lee, 1989; Bergui et al., 1992).

In the present study we observed the first burst of the EMG activity within the first 20 ms of the recording period. It was reflected in the first high-amplitude peak on the averaged out EMG curve at 20 ms (EMG-A compo-

nent). The onset of that component and time of its maximum were similar to the short-latency peak observed by Tracey et al. (1980) in cats. The latter authors suggested that the above-mentioned peak corresponded to the monosynaptic spinal response to stretching in humans. Therefore it may be assumed that also in our experiment with rats the EMG-A component is comparable with the early peak seen in humans, and is due – at least partly – to the spinal monosynaptic reflex.

The second burst of the EMG activity in our control experiment with rats started at 40 ms, gradually increased during the movement, and reached its maximum shortly after its end. The EMG-B and EMG-C components reflected the phase of the increase in that burst of the EMG activity, and the EMG-D component indicated its maximum. It may be supposed that the EMG-B and at least part of the EMG-C components correspond to the long-latency components found in humans. In contrast, the EMG-D component seems to have no equivalent in humans; nonetheless, passive movements in our experiment lasted relatively long (250 ms) in comparison with those in the above-cited experiments with humans (Berardelli et al., 1983; Rothwell et al., 1983; Scholz et al., 1987; Matthews, 1991; Bergui et al., 1992). Therefore it seems that for the whole duration of a movement short- and long-latency reflexes may be aroused and superimposed. Reserpine increased the entire second late burst of the EMG activity (EMG-B, C and D) in the gastrocnemius muscle in rats. This phenomenon seems to be similar to that observed in Parkinson's disease.

Our present results showing that reserpine increases the short-latency EMG component in rats may suggest that this drug increases not only the polysynaptic, long-latency reflexes but also the monosynaptic, short-latency spinal one. A similar conclusion was drawn by Grossman et al. (1973) who observed after reserpine an increase in the amplitude of monosynaptic reflexes, measured in ventral roots in response to stimulation of dorsal roots or the gastrocnemius-soleus nerve of rats. However, in Parkinson's disease the short-latency EMG components, as well as other monosynaptic spinal reflexes were reported to be unchanged or even inhibited (Delwaide et al., 1986; Scholz et al., 1987; Lee, 1989; Bergui et al., 1992). Therefore it seems that the increase in monosynaptic spinal reflexes after reserpine contrasts sharply with the unchanged or inhibited spinal reflexes observed in parkinsonian patients.

It is well known that reserpine depletes dopamine from nigrostriatal terminals (Bean et al., 1989; Fornstedt and Carlsson, 1989; Elverfors and Nissbrandt, 1991). After high doses of this drug, the depletion is almost complete as early as 1 h after the injection, and is maintaned for more than 24 h (Bean et al., 1989; Fornstedt and Carlsson, 1989; Elverfors and Nissbrandt, 1991). Hence the time-course of this biochemical change seems to parallel exactly the increase in the EMG activity in the gastrocnemius muscle observed in the present experiment.

A number of authors suggested that regulation of a normal or pathologically increased muscle tone is based on both the resting and the stretch-induced EMG activity (Davidoff, 1992). Therefore it may be expected that

changes in the muscle tone after reserpine should follow alterations in the EMG activity. Contrariwise, in the present study some discrepancy was observed between the mechanomyographically measured muscle rigidity and the EMG activity in the gastrocnemius muscle after reserpine administration. The highest level of rigidity was found at 1–2 h after reserpine injection. Afterwards, this symptom was markedly reduced, but it was still present many hours after the injection. The time-course of this symptom, observed in our experiment, was similar to that reported by Colpaert (1987). In contrast, the EMG activity seems to be not time-dependent either before or during passive movements. The reason for such a discrepancy is not clear. 1–2 h after reserpine injection, a significant increase in the short- and long-latency components was observed not only in the gastrocnemius, but also in the tibialis anterior muscle during bending. In contrast, after a longer period of time, amplitudes of the long-latency EMG components of the tibialis anterior muscle were no longer bigger than in controls. Therefore it seems that the simultaneously increased contraction of both the antagonistic muscles in response to bending at 1–2 h after reserpine injection could be responsible for the enhancement of the muscle tone at that time-period. A similar co-contraction of the antagonistic muscles in response to passive movements was also reported in parkinsonian patients and was suggested to be one of the causes of parkinsonian rigidity (Lee, 1989). However, such mechanism of reserpine action cannot account for an increase in the muscle resistance during streching because the stretch-induced EMG activity in the tibialis anterior muscle was not enhanced. Another cause of the rapid decrease in the mechanical muscle resistance (despite the unchanged EMG activity) could be dehydratation and changes in the mineral balance due to a serious diarrhoea. This disturbance started approximatively 2 h after reserpine and led to a marked body weight loss in rats (12%). Such changes in the mineral balance of muscles might easily alter contractile properties of muscle fibers and might contribute to the lack of time correlation between the EMG activity and muscle rigidity. Therefore it seems that the reserpine model of parkinsonism and, especially of a parkinsonian muscle rigidity should be used with caution.

Summing up, it seems that reserpine induces EMG and mechanical rigidity which, in many respects, resembles that seen in Parkinson's disease. However, some unknown mechanisms seem to contribute to the mechanical resistance developed in response to passive movements. Their relation with parkinsonism are still unclear and require further investigation.

Acknowledgements

This study was supported by the KBN Grant no. 4 4074 91 02.

References

Bean AJ, Adrian TE, Modlin IM, Roth RH (1989) Dopamine and neurotensin storage in colocalized and non-colocalized neuronal populations. J Parmacol Exp Ther 249: 681–687

Berardelli A, Sabra AF, Hallett M (1983) Physiological mechanisms of rigidity in Parkinson's disease. J Neurol Neurosurg Psychiatry 46: 45–53
Bergui M, Lopiano L, Paglia G, Quattrocolo G, Scarzella L, Bergamasco B (1992) Stretch reflex of quadriceps femoris and its relation to rigidity in Parkinson's disease. Acta Neurol Scand 86: 226–229
Burke D, Hagbarth KE, Wallin BG (1977) Reflex mechanisms in Parkinson's rigidity. Scand J Rehab Med 9: 15–23
Colpaert FC (1987) Pharmacological characteristics of tremor, rigidity and hypokinesia induced by reserpine in rat. Neuropharmacology 26: 1431–1440
Davidoff RA (1992) Skeletal muscle tone and the misunderstood stretch reflex. Neurology 42: 951–963
Delwaide PJ, Sabbatino M, Delwaide C (1986) Some pathophysiological aspects of the parkinsonian rigidity. J Neural Transm 22: 129–139
Elverfors A, Nissbrandt H (1991) Reserpine-insensitive dopamine release in the substantia nigra? Brain Res 557: 5–12
Fornstedt B, Carlsson A (1989) A marked rise in 5-S-cysteinyl-dopamine levels in guinea-pig striatum following reserpine treatment. J Neural Transm 76: 155–161
Goldstein JM, Barnett A, Malick JB (1975) The evaluation of anti-parkinson drugs on reserpine-induced rigidity in rats. Eur J Pharmacol 33: 183–188
Grossman W, Jurna I, Nell T, Theres C (1973) The dependence of the anti-nociceptive effect of morphine and other analgesic agents on spinal motor activity after central monoamine depletion. Eur J Pharmacol 24: 67–77
Johnels B (1983) Reserpine-induced rigidity in rats: drug effects on muscle tone from corpus striatum and nucleus accumbens. Pharmacol Biochem Behav 19: 463–470
Johnels B, Steg G (1982) A mechanographic method for measurement of muscle tone in the conscious rat. The calf muscle stretch response in reserpine-induced rigidity. J Neurosci Meth 6: 1–16
Johnels B, Steg G, Ungerstedt U (1978) A method for mechanographical recording of muscle tone in the rat: the effect of some antiparkinsonian drugs on rigidity induced by reserpine. Brain Res 140: 177–181
Jurna I (1976) Striatal monoamines and reserpine and chlorpromazine rigidity. Pharmacol Ther 2: 113–128
Klockgether T, Turski L (1990) NMDA antagonists potentiate antiparkinsonian actions of 1-DOPA in monoamine-depleted rats. Ann Neurol 28: 539–546
Kolasiewicz W, Baran J, Wolfarth S (1987) Mechanographic analysis of muscle rigidity after morphine and haloperidol: a new methodological approach. Naunyn Schmiedebergs Arch Pharmacol 335: 449–453
Lee RG (1989) Pathophysiology of rigidity and akinesia in Parkinson's disease. Eur Neurol 29 [Suppl 1]: 13–18
Lee RG, Tatton WG (1975) Motor responses to sudden limb displacements in primates with specific CNS lesions and in human patients with motor system disorders. Can J Neurol Sci 2: 285–293
Matthews PB (1991) The human stretch reflex and the motor cortex. Trends Neurosci 14: 87–91
Meara RJ, Cody FWJ (1992) Relationship between electromyographic activity and clinically assessed rigidity studied at the wrist joint in Parkinson's disease. Brain 115: 1167–1180
Morrison AB, Webster RA (1973) Reserpine rigidity and adrenergic neurones. Neuropharmacology 12: 725–733
Mortimer JA, Webster DD (1979) Evidence for a quantitative association between EMG stretch responses and parkinsonian rigidity. Brain Res 162: 169–173
Ossowska K (1994) The role of excitatory amino acids in experimental models of Parkinson's disease. J Neural Transm [P-D Sect] 8: 39–71
Ossowska K, Lorenc-Koci E, Wolfarth S (1994) Antiparkinsonian action of MK-801 on the reserpine-induced rigidity: a mechanomyographic analysis. J Neural Transm [P-D Sect] 7: 143–152

Rothwell JC, Obeso JA, Traub MM, Marsden CD (1983) The behaviour of the long-latency stretch reflex in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 46: 35–44

Scholz E, Diener HC, Noth J, Friedemann H, Dichgans J, Bacher M (1987) Medium and long latency EMG responses in leg muscles: Parkinson's disease. J Neurol Neurosurg Psychiatry 50: 66–70

Starr MS, Starr BS (1994) Potentiation of dopamine-dependent locomotion by clonidine in reserpine treated mice is restricted to D2 agonists. J Neural Transm [PD-Sect] 7: 133–142

Tatton WG, Bedingham W, Verrier MC, Blair RDG (1984) Characteristic alterations in responses to imposed wrist displacement in Parkinsonian rigidity and dystonia musculorum deformans. Can J Neurol Sci 11: 281–287

Tracey DJ, Walmsley B, Brinkman J (1980) Long-loop reflexes can be obtained in spinal monkeys. Neurosci Lett 18: 59–65

Wolfarth S, Kolasiewicz W, Ossowska K, Bober M (1992) Direct mechanomyographic measurement of myorelaxant action of baclofen and diazepam in normal and reserpinized rats. Naunyn Schmiedebergs Arch Pharmacol 345: 209–212

Authors' address: Dr. K. Ossowska, Department of Neuro-Psychopharmacology, Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna St., PL-31-343 Kraków, Poland.

Received January 23, 1995