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Magnetic stimulation of the cavernous nerve for the treatment of erectile dysfunction in humans

A Shafik[1]*, O el-Sibai[2] and AA Shafik[1]

[1]*Department of Surgery and Experimental Research, Faculty of Medicine, Cairo University, Cairo, Egypt; and*
[2]*Department of Surgery, Faculty of Medicine, Menoufia University, Egypt*

A recent study in dogs has demonstrated that magnetic stimulation (MS) of the cavernous nerve produced an increase of the intracorporeal pressure and full penile erection. In view of these results, we tested the possible application of this procedure in humans with erectile dysfunction (ED). The study comprised 32 patients with ED (age 38.3 ± 9.6 y) and 20 healthy volunteers (age 36.8 ± 8.8 y). Routine erectile function tests suggested that impotence was neurogenic. A magnetic coil was placed over the dorsal aspect of the penis in the vicinity of the symphysis pubis. MS was performed using a stimulation of 40% intensity, 20 Hz frequency, 50 s on and 50 s off for 10 minutes duration. In the healthy volunteers, the coil was placed as aforementioned but was not activated. The intracorporeal pressure was recorded and penile tumescence and rigidity observed during MS in the patients and without stimulation in the controls. MS led to gradual increase in length and diameter of the penis until full erection was achieved; the penis became firm, rigid and pulsatile. The intracorporeal pressure increased significantly ($P < 0.0001$) at full erection. Mean latency to full erection was 19.3 ± 3.4 s. Upon off-stimulation, penile erection and intracorporeal pressure returned to baseline after a mean of 22.7 ± 3.2 s. Penile and pressure response to MS was resumed after an off-time of 50 s. The response was reproducible infinitely if the off-time was observed. The controls showed no penile tumescence or rigidity or increase of the intracorporeal pressure. In conclusion, MS of the cavernous nerve is effective in inducing penile rigidity. It is a simple, easy and non-invasive method which has no adverse effects. It might prove to be suitable for application in patients with ED. *International Journal of Impotence Research* (2000) **12,** 137–142.

Keywords: magnetic coil; magnetic stimulator; impotence; intracorporeal pressure; penile tumescence

Introduction

The causes of erectile dysfunction (ED) are variable and include hormonal, neurogenic, psychologic, arterial, and venous disorders.[1–5] Neurogenic disorders are caused by disease or dysfunction of the brain, spinal cord, cavernous and pudendal nerves and terminal nerve endings and receptors.[2] Diabetes mellitus is the commonest hormonal disorder.[3] Arteriogenic impotence is often a component of systemic arterial disease.[4] Venous flow abnormalities could result from a tunica albuginea defect, an excessive number or increased size of veins or fibrous replacement of cavernous smooth muscles.[5,6]

The treatment of ED depends on the etiology. Several now well-established procedures have been devised.[7–9] However, the results are still unsatisfactory in many cases.

The cavernous nerve (CN) is the autonomic efferent pathway which innervates the smooth muscles surrounding the helicine arterioles and lacunar spaces. Preceding studies in dogs[10] and in patients with ED[11] have demonstrated that extrapelvic CN stimulation effected full penile erection. In this procedure, the CN was exposed through a para-penile incision, and a bipolar platinum electrode was applied to the CN and connected to a subcutaneous receiver.

Magnetic stimulation (MS) has been used to activate the neuromuscular tissue[12–14] and magnetic stimulators are applied for neurophysiologic investigations.[12,13,15,16] Motor-evoked potentials

*Correspondence: A Shafik, 2 Talaat Harb Street, Cairo, Egypt.
E-mail: shafisci@link.com.eg
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were generated from the urinary bladder upon MS of the cauda equina.[15] Neuromodulation of detrusor hyperreflexia could also be achieved by MS of the sacral roots.[17] MS produces its effect by creating, according to Faraday's law, an electric field which can stimulate the neuromuscular tissue.[13]

Recently, a study on dogs[18] and another one on human healthy volunteers[19] have demonstrated that sacral MS of both the full and the empty rectum effected a significant increase in rectal and vesical pressures and a decrease in the anal pressure. Evacuation of the full rectum using intermittent MS was achieved.[18,19] MS was also used for the treatment of patients with constipation due to rectal inertia.[20]

A preceding study has shown that MS of the CN in dogs produced an increase of the intracavernosal pressure and full penile erection after a mean latency of 7.8 ± 2.5 .[21] Upon off-stimulation, erection and intracorporeal pressure returned to the baseline after a mean of 14.2 ± 3.2 s. After an off-time of 50 s the response returned and was reproducible infinitely, provided the off-time was observed.[21]

In view of the results obtained in the canine model, and considering the fact that the technique is non-invasive, simple, easy and with no complications, we were encouraged to perform the procedure in humans with ED. The current communication gives the results of the study. To our knowledge, the procedure has not been reported before.

Physioanatomic considerations

Efferent activity to the penis arises in the 2nd to 4th sacral spinal cord segments.[2,22,23] These sacral nerves, termed nervi erigentes, form three to six district trunks in humans.[2,24] They unite to form the pelvic nerve, which relays in the pelvic plexus. The CN, which is the autonomic nerve to the penis, arises from the pelvic plexus. It travels along the posterolateral aspect of the prostate to approach the membranous urethra at the 3 and 9 o'clock positions (Figure 1). The nerves on either side proceed forward with medial inclination. They pierce the urogenital diaphragm to enter the corpora cavernosa at the 1 and 11 o'clock positions beneath the symphysis pubis.

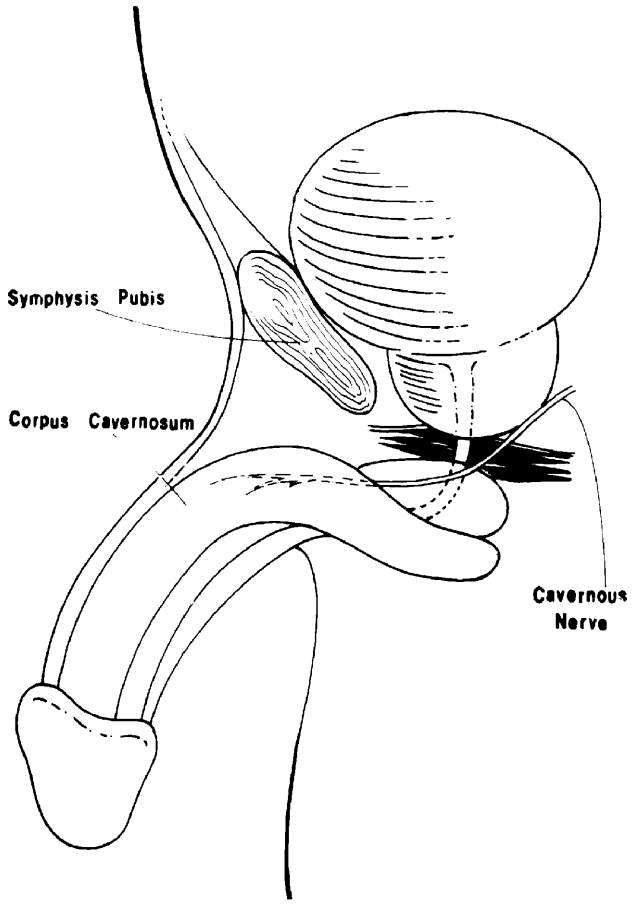

Figure 1 Diagram illustrating the course of the cavernous nerve as it passes below the symphysis pubis to reach the corpus cavernosum. From Shafik.[11]

Material and methods

Subjects

Thirty-two patients with ED (age 38.3 ± 9.6 y (mean $\pm$ s.d.), range 28–56) and 20 healthy volunteers (mean age 36.8 ± 8.8 y, range 30–53), who matched the patients in age, were enrolled in the study after giving informed consent. Our Faculty Review Board and Ethics Committee approved the study.

The patients had normal libido and were able to ejaculate when they masturbated. During masturbation, erection was partial. They had no history of diabetes, hypertension, penile trauma or smoking. All the patients used intracorporeal injection therapy for 6 months to 2 y (mean 13.2 ± 3.8), but the erection was partial, and all patients had discontinued the injection therapy 6–8 months prior to entering the study.

Physical examination, including neurologic assessment, was normal. Laboratory work and endocrine profile were unremarkable. Routine erectile function tests were performed. Nocturnal penile tumescence (NPT) was monitored in a sleep center. Circumference changes at the base and coronal sulcus of the penis were recorded. The sleep quality and quantity was also determined. NPT was absent in all patients. The penobrachial pressure index (PBPI) was normal; it recorded a mean of 0.83 (range 0.76–0.94) against a mean normal value in our

laboratory of 0.82. Doppler examination of the penile arteries showed normal results. Cavernosometry was performed after intravenous injection of 60 mg of papaverine. Saline infusion showed a mean initiation flow rate of 31.8 ± 4.8 ml/min (mean $\pm$ s.d.; range 29–37) and a maintenance rate of 6.6 ± 2.1 ml/mm (range 3–9) against the mean normal values in our laboratory of 33.8 ± 6.2 ml/min for the initiation rate and 6.2 ± 1.7 ml/min for the maintenance rate. These investigative findings suggested that impotence was neurogenic, because all the objective tests were normal except for the NPT that showed complete absence of tumescence. NPT is considered as the 'gold standard' tool in the differential diagnosis of ED.[25]

The healthy volunteers had normal libido and erection. They were married and had fathered children. They had no genitourinary complaint in the past or at the time of investigation.

Technique of MS of CN

The procedure was performed without anesthesia and with the subject lying supine. A commercially available magnetic stimulator (High-Speed MES-10, Cadwell, Kennewick, WA) with a 1 cm round magnetic coil was used in the study (Figure 2). The MES-10, when measured at the coil center, could generate a maximum field strength of 2.2 T. MS was performed using a stimulation of 40% intensity, 20 Hz frequency and 50 s on and 50 s off for 10 min duration, followed by 10 min of rest. We have chosen these parameters because they provide adequate penile stimulation without frequent overheating of the magnetic coil.

The magnetic coil was placed over the dorsal aspect of the base of the penis. The optimal magnetic coil location was determined by moving the center of the coil over the dorsum of the penis in the vicinity of the symphysis pubis while measuring the intracorporeal pressure, and observing the tumescence and penile rigidity. The optimal site of the coil was subsequently used to obtain maximal intracorporeal pressure and penile rigidity. Figure 2 shows the optimal position of the magnetic coil, which overlay the dorsal aspect of the penis in the vicinity of the symphysis pubis. The intracorporeal pressure was measured by means of a 21-gauge butterfly needle, which was inserted into each corpus cavernosum and connected to a strain gauge pressure transducer (Statham, 230b, Oxnard, CA, USA).

The test was carried out in healthy controls. The magnetic coil was placed and moved over the dorsum of the penis without activating it while the intracorporeal pressure was being measured and penile tumescence and rigidity observed.

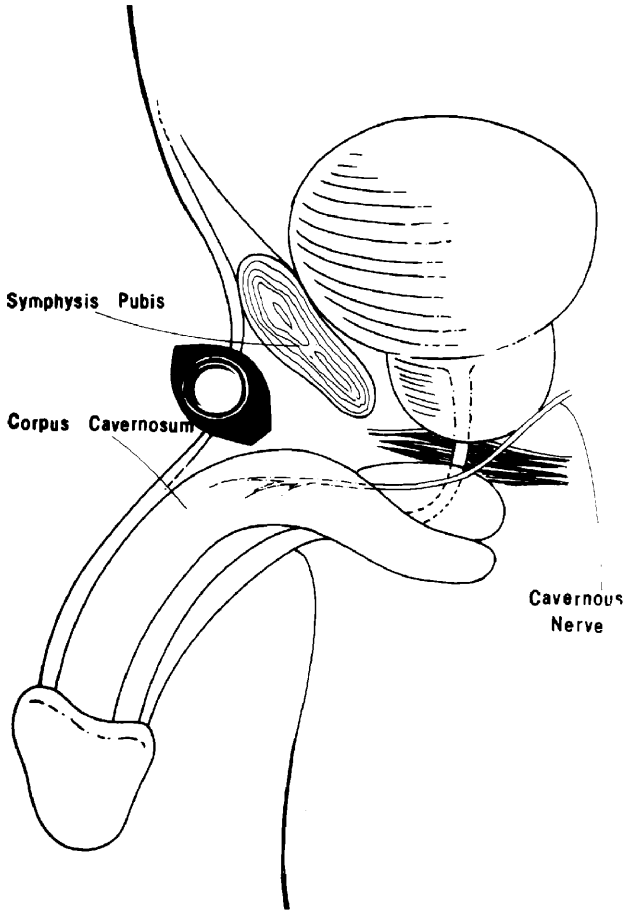

Figure 2 Diagram illustrating the position of the magnetic coil (placed on a grid) over the dorsum of the penis in the vicinity of the symphysis.

To assure reproducibility of the results, the aforementioned measurements were repeated at least twice in the individual subject, and the mean value was calculated. The results were analyzed statistically using the analyses of the variance (ANOVA). Differences assumed significance at $P < 0.05$, and values were given as the mean $\pm$ s.d.

Results

No adverse effects were encountered during the performance of the procedure and all the subjects were evaluated. The mean basal intracorporeal pressure in the patients was 5.1 ± 0.9 cm H_2O (range 4–6); the controls showed no significant difference ($P > 0.05$). MS with the aforementioned parameters in the patients led to gradual increase in the length and diameter of the penis until full erection was achieved. The glans penis became enlarged and congested. The deep dorsal vein was full and tortuous. On palpation, the penis was firm, rigid

and pulsatile. The intracorporeal pressure exhibited a significant increase to a mean of 112.4 ± 14.7 cm H_2O (range 92–128; $P < 0.0001$; Figure 3) at full erection.

The latency, which is the time from the onset of MS to the onset of penile and intracorporeal pressure response, ranged from 5–12 s (mean 8.3 ± 2.2). Maximum penile erection and pressure response were achieved after a mean latency of 19.3 ± 3.4 s (range 16–22). Penile erection was sustained as long as MS was maintained. Upon off-stimulation, the penile erection and intracorporeal pressure returned to the baseline after a mean 22.7 ± 3.2 s (range 19–26). Full penile and pressure response were achieved after 50 s off-time. Re-stimulation after a pause of less than that time produced a weak response. However, if the off-time was respected, the response was reproducible infinitely.

When the test was performed on the healthy controls without the coil being activated, there was neither an increase of the intracorporeal pressure nor appearance of penile tumescence nor rigidity.

The aforementioned results were reproducible with no significant difference when the tests were repeated in the individual subject.

Discussion

This study demonstrates the effectiveness of MS in producing increased intracorporeal pressure and penile tumescence and rigidity. It seems that MS has activated the cavernous nerve as it passes to the corpora cavernosa from underneath the symphysis pubis. The optimal site of the magnetic coil was found to lie over the dorsum of the penis in the vicinity of the symphysis pubis; it is presumed that the magnetic coil overlay the CN.

MS produces its effect by creating a magnetic field which, according to Faraday's law, generates an electric field that seems to activate the CN. Barker *et al*[12,13] reported that, when a time-varying magnetic field is applied close to neuromuscular tissue, the induced electric field creates a current that can stimulate the neuromuscular tissue. The magnetic fields can pass through structures of high resistance like skin, fat and bone.

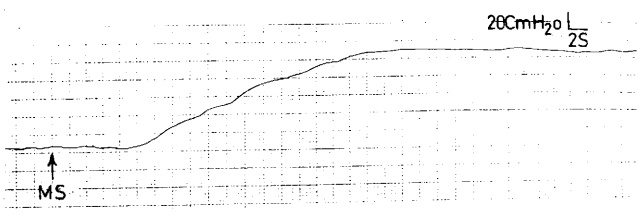

Figure 3 Pressure tracing showing the rise of the intracavernosal pressure upon magnetic stimulation of the cavernous nerve. MS = magnetic stimulation.

The magnetic coil, as it overlies the dorsum of the penis, might stimulate not only the CN but also the deep dorsal nerve of the penis. The latter, arising from the pudendal nerve, proceeds forward through the suspensory ligament to lie over the dorsum of penis where the magnetic coil was placed.[26] Branches of the CN travel on the dorsum of the penis in the vicinity of the dorsal nerve of the penis.[27] The dorsal nerve forms the afferent limb of the penile erectile reflex by transmitting sensory impulses from the penile skin, prepuce and glans.[28–30] It also contains efferent autonomic fibres in some species, such as the rats and cats,[31] and maybe in humans.[32] The physiological significance of these efferent pathways is uncertain. Investigators[30] postulated that such efferent contributions to the dorsal nerve of the penis control the blood vessels within the penile skin or modulate the sensitivity of afferent receptors. Although these investigators concluded that the nerve plays no direct role in penile erection, we believe that both its afferent and efferent pathways share in the penile erectile reflex.

CN activation by MS probably produces its effect, as aforementioned, by relaxing the smooth muscles surrounding the penile lacunar spaces and helicine arterioles. Full rigid erection was produced within a short latent period and was maintained as long as MS was sustained. The CN stimulation with penile erection could be repeated infinitely provided a 50 s off-time was observed.

The mean intracorporeal pressure upon MS recorded a value slightly lower than the systolic blood pressure. This is in accord with investigators who hold the view that electrostimulation of the cavernous nerve, which is autonomic, induces changes in blood flow, culminating in full erection with an intracorporeal pressure below the systolic blood pressure.[33] Stimulation of the pudendal nerve, which is somatic, causes contraction of the ischiocavernosus muscle which raises the intracorporeal pressure to above the systolic blood pressure.[33]

The question may arise of why did the patients respond with full erections to CN stimulation, but not to intracavernous pharmacotherapy. Actually, the patients had erections after intracorporeal injection therapy, but they were partial as already mentioned. The cause of erection being partial and not full is not known. It might be related to the type of the injected material, frequency of injections or to other factors.

In conclusion, MS of the CN is believed to be suitable for application in patients with ED. The method is effective in producing penile rigidity. It is simple, easy and non-invasive and has no adverse effects as compared with the invasive procedures used for the treatment of ED like the intracavernous

injections and penile vascular and prosthetic surgery.

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Editorial comment

The investigator, who has made many contributions to the development of neurourology is the first to show that magnetic stimulation at the infrapubic level is effective to induce penile erection in humans. This is an interesting finding that may be clinically applicable in the future.

To put Shafik's finding into perspective it is important to note that magnetic and electric stimulation have the same principal: **excitation of neurons**. In the former by an electric current that is produced by a changing magnetic field; in the latter by an electric current, that is directly applied to the neuron.

The concept of electrostimulation of penile erection is not new. In 1985, Lue *et al* were the first to show in animal experiments that electrical stimulation of the cavernous nerves elicits penile erection.[1] The first electrically stimulated erections