Sacral Neuromodulation for Lower Urinary Tract and Bowel Dysfunction in Animal Models: A Systematic Review With Focus on Stimulation Parameter Selection

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ABSTRACT

Objective: Conventional sacral neuromodulation (SNM) has shown to be an effective treatment for lower urinary tract and bowel dysfunction, but improvements of clinical outcome are still feasible. Currently, in preclinical research, new stimulation parameters are being investigated to achieve better and longer effects. This systematic review summarizes the status of SNM stimulation parameters and its effect on urinary tract and bowel dysfunction in preclinical research.

Materials and Methods: The literature search was conducted using three databases: Ovid (Medline, Embase) and PubMed. Articles were included if they reported on stimulation parameters in animal studies for lower urinary tract or bowel dysfunction as a primary outcome. Methodological quality assessment was performed using the SYRCLE Risk of Bias (RoB) tool for animal studies.

Results: Twenty-two articles were eligible for this systematic review and various aspects of stimulation parameters were included: frequency, intensity, pulse width, stimulation signal, timing of stimulation, and unilateral vs. bilateral stimulation. In general, all experimental studies reported an acute effect of SNM on urinary tract or bowel dysfunction, whereas at the same time, various stimulation settings were used.

Conclusions: The results of this systematic review indicate that SNM has a positive therapeutic effect on lower urinary tract and bowel dysfunction. Using low-frequency-SNM, high-frequency-SNM, bilateral SNM, and higher pulse widths showed beneficial effects on storage and evacuation dysfunction in animal studies. An increased variability of stimulation parameters may serve as a basis for future improvement of the effect of SNM in patients suffering from urinary tract or bowel dysfunction.

Keywords: Fecal, incontinence, sacral nerve stimulation, stimulation paradigms, voiding dysfunction

Conflict of Interest: Gommert A. van Koeveringe declares to have a conflict of interest for Medtronic and Axonics. All other authors declare that they have no conflict of interest.

INTRODUCTION

Since the introduction in the 1980’s sacral neuromodulation (SNM) has been used in patients with lower urinary tract dysfunction (1, 2). Patients with urinary tract dysfunction reported not only a positive effect of SNM on their lower urinary tract symptoms but also on defecatory complaints. The latter resulted in the first electrical stimulation of sacral nerves for the treatment of fecal incontinence (3).

Nowadays, SNM is an established surgical intervention for urinary tract and bowel dysfunction, more specifically storage and evacuation disorders, intended to treat patients unresponsive to conservative treatment. In urinary tract dysfunction, conservative treatment includes physiotherapy or medication, and in bowel dysfunction, diet and fluid advice, medication, biofeedback therapy, and colonic irrigation. Storage disorders refer to an overactive bladder, a hypospensive rectum, an undervactive urethral or...
anal sphincter causing incontinence. Evacuation disorders refer to an underactive bladder, slow transit colon, and an overactive urethral or anal sphincter causing retention or constipation.

SNM is a minimally invasive therapy involving chronic electrical stimulation of the third sacral nerve root (S3). Successful SNM for both urinary tract and bowel dysfunction is often defined as an improvement in symptomatology of 50% or more compared to baseline. In an accompanying paper, we systematically reviewed the effect on stimulation parameters for sacral neuromodulation on lower urinary tract and bowel dysfunction related to clinical outcome (4). These results showed that the efficacy of SNM on both lower urinary tract and bowel dysfunction might be improved by changing stimulation parameters.

From the point of human ethical concerns, in addition to further understanding of the mechanisms of action, the effects and fine-tuning of SNM in the treatment of urinary tract and bowel dysfunctions is studied in animals. The reason to use preclinical animal studies on SNM is threefold: 1) finding the optimal balance between a positive effect of SNM and potential harmful side effects; 2) fully standardized research in patients with regard to the effect of SNM stimulation paradigms is limited due to ethical concerns and large clinical variability; and 3) implantable pulse generators (IPGs) currently used in clinics are restricted to only a limited range of SNM stimulation settings. In contrast, preclinical studies allow the use of SNM settings beyond conventionally used clinical stimulation paradigms and have previously provided valuable insights into the efficacy and working mechanisms of SNM. To date, no comprehensive overview of the effects of individual SNM parameters for treatment of urinary tract or bowel dysfunction in animal models is available. This systematic review of preclinical literature on SNM and its effect on urinary tract and bowel dysfunction with focus on stimulation parameters fills this gap in the literature. The combination of this systematic review on animal studies and a systematic review of the clinical studies of SNM in urinary tract and bowel dysfunction (4) serves as a basis for future improvement toward the effects of SNM in patients suffering from urinary tract or bowel dysfunction.

**MATERIALS AND METHODS**

**Search Strategy**

A systematic literature search was conducted using three databases: Medline (PubMed), Ovid (Embase) and PubMed. Search terms used for all databases are included in the Appendix. Results were uploaded to EndNote to assess for relevance. Reviewers were not blinded to author names, institution, or study title. One reviewer (PD) collected the following characteristics of the included studies: the first author, year of publication, species, sex and number of species, model of disorder, control condition, anesthesia used, stimulation settings, and results of the studies.

**Study Selection and Inclusion Criteria**

Two reviewers (P.D., R.A.) performed extensive searches of available literature up until January 14, 2020. This search was a shared search for the present preclinical review and a clinical review (see accompanying paper (4)) and results were allocated to each systematic review after the final study inclusion. Studies were eligible
| Study ID          | Species | Sex | Amount | Model                                                                 | Anesthesia                        | Procedure                      |
|------------------|---------|-----|--------|----------------------------------------------------------------------|-----------------------------------|--------------------------------|
| Boger et al. (14)| Cat     | m   | 6      | Detrusor sphincter dyssynergia; induced by S1/S2 stimulation         | α-chloralose and isoflurane       | Extradural cuff electrode      |
| Braun et al. (21)and Seif et al. (22) Minipig | n/a    | 12  |        | Detrusor hyperactivity induced by 0.25% formalin solution            | Anesthetized, without specification | Transforaminally                |
| Brouillard et al. (17) Rat | f      | 13  |        | Healthy                                    | Urethane and conscious            | Transforaminally                |
| Cong et al. (20)  Pig | both  | 7   |        | Urethral bladder acetic acid (control saline) | α-chloralose                      | Transforaminally                |
| Evers et al. (25) Rat | f      | 72  |        | Healthy                                    | Urethane                          | Transforaminally                |
| Evers et al. (26) Rat | f      | 32  |        | Intra-pelvic balloon inflation                                    | Urethane                          | Transforaminally                |
| Huang et al. (27) Rat | m      | 39  |        | Constipation induced by 2 mg/kg ip kopenamide (control saline)      | Urethane                          | Transforaminally, extradural    |
| Kaufman et al. (23) Minipig | n/a    | 8   |        | Detrusor hyperactivity induced by 0.25% formalin solution            | α-chloralose                      | Laminctomy of segments, intradural |
| Li et al. (6) Pig | both  | 13  |        | Bladder overactivity induced by 5% acetic acid (control saline)     | α-chloralose                      | Laminctomy of segments, intradural |
| Li et al. (7) Cat | both  | 7   |        | Pudendal nerve stimulation to mimic bladder underactivity          | α-chloralose                      | Laminctomy of segments, intradural |
| Potts et al. (24) Rat | f      | 24  |        | Healthy                                    | Urethane                          | Laminctomy of segments, transforaminally |
| Shaker et al. (15) Dog | m      | 11  |        | Detrusor sphincter dyssynergia; induced by spinal cord section at T10 level | Isoflurane                        | Laminctomy of segments, extradural cuff electrode |
| Sievert et al. (16) Dog | m      | 20  |        | Healthy                                    | Atropine and pentobarbital         | Laminctomy of segments, intradural and extradural |
| Snellings and Grill (8) Cat | m      | 14  |        | Healthy                                    | α-chloralose                      | Extradural cuff electrode       |
| Su et al. (9) Rat | f      | 164 |        | Healthy                                    | Urethane                          | Removed S1 processes            |
| Su et al. (10) Rat | f      | 159 |        | Healthy                                    | Urethane                          | Not specified                   |
| Su et al. (11) Rat | f      | 31  |        | Bladder overactivity induced by 0.3% acetic acid (control saline)   | Urethane                          | Removed S1 processes            |
| Su et al. (12) Rat | f      | 46  |        | Healthy                                    | Urethane                          | Removed S1 processes            |
| Su et al. (13) Rat | f      | 126 |        | Healthy                                    | Urethane                          | Removed S1 processes            |
| Zhang et al. (18) Cat | both | 19  |        | Healthy                                    | α-chloralose                      | Dorsal laminectomy, intradural  |
| Zhang et al. (19) Cat | both | 6   |        | Bladder overactivity induced by 0.5% acetic acid (control saline)   | α-chloralose                      | Dorsal laminectomy, intradural  |

f, female; ip, intraperitoneal; m, male; n/a, not available.
| Study ID | Location | Duration | Frequency (Hz) | Pulse width (μs) | Intensity | Extra information | Outcome |
|---------|----------|----------|----------------|-----------------|-----------|-------------------|---------|
| Boger et al. (14) | S1 | 60 or 90 sec | 20 | 100 | 7 ± 3 Vpp | Intermittent bilateral | HF-SNM (12.5 kHz) can prevent EUS activation and allow complete bladder voiding |
| Braun et al. (21) and Seif et al. (22) | S3 | 10 min interval | 15 | 100 | 20 V | Continuous | Quasi-trapezoidal SNM inhibited unstable detrusor contractions more than rectangular SNM |
| Bouillid et al. (17) | S1 left | 60 sec, started at the onset of the steep rise in bladder pressure signaling an imminent void | | 1000 | 1 mA | Sinusoidal waveform | HF-SNM can suppress imminent voiding for 35–262 sec |
| Cong et al. (20) | S3 left | During bladder filling | 14 | 64 | 5.64 ± 0.76 V (Tmot) | All pulse widths inhibited bladder overactivity compared to acetic acid levels. Motor threshold for pulse width of 64 μsec was significantly higher than the other two thresholds |
| Kaufman et al. (23) | S1 | Every 5 min | 15 | 210 | Unilateral left | Bilateral SNM reduced overactive detrusor contractions better compared to unilateral SNM |
| Li et al. (6) | S3 | 5 | | 200 | 1x, 1.5x, 2x Tmot | SNM at 15, 30 and 30 Hz increased bladder capacity. Frequencies higher than 15 Hz did not lead to better outcomes |
| Li et al. (7) | S1/S2 | DRT | During bladder filling | 15 | 200 | 1x, 1.5x, 2x Tmot | Bilateral S3 stimulation increased bladder pressure sign better than unilateral SNM |
| Potts et al. (24) | L6/S1 | During bladder filling | 10 | 100 | 1x, 1.5x, 2x Tmot | Bilateral, biphasic |
| Shaker et al. (15) | S2 and S1 left and right | 20 sec | 600 | 180 | 18 mA | All pulse widths inhibited bladder overactivity compared to acetic acid levels. Motor threshold for pulse width of 64 μsec was significantly higher than the other two thresholds |
| Shaker et al. (13) | L6 | 15 min | 100 | 100 | 0.08–10 V | Bilateral S3 stimulation increased bladder pressure sign better than unilateral SNM |
| Snellings and Grill (8) | S1 | For 30 sec after absolute bladder pressure | 2, 5, 7.5, 10, 15, 20, 30 | 100 | 0.8, 1, 2x Tmot | Bilateral, biphasic |
| Su et al. (9) | L6 | 10 min | | 100 | 2, 3, 4, 6x Tmot | Bilateral |
| Su et al. (10) | L6 left | 10 min | | 100 | 0.6 mA (supra T) | Bilateral, pulse match/mismatch |
| Su et al. (11) | L6 | On every void | 1 | 100 | 0.8x, 1x Tmot | High-intensity SNM is most effective for alleviating bladder activities |
| Su et al. (12) | L6 | 10 min | | 100 | 0.1, 0.2, 0.3 mA (Tmot) | All pulse widths showed inhibition of bladder activity, and no significant differences were found between pulse widths tested. Optimal pulse width was 40 μs |
| Su et al. (13) | L6 | 15 min | | 100 | 1 x Tmot | SNM in burst patterns reduced the number of bladder contractions with an optimum of a four-pulse burst interburst of 1 Hz and interburst of 40 Hz, but this burst pattern did exceed a continuous stimulation of 10 Hz |
| Zhang et al. (18) | S1,S2/3,DRT or VRT | 5, 15, 30 | 0.25, 0.5, 1, 2x Tmot | 1x Tmot | Bilateral, pulse match/mismatch |
| Zhang et al. (19) | S1,S2/3,DRT or VRT | 5, 15, 30 | 0.25, 0.5, 1x Tmot | 1x Tmot | Bilateral, pulse match/mismatch |

DRT, dorsal root; EUS, external urethral sphincter; HF-SNM, high frequency sacral neuromodulation; SNM, sacral neuromodulation; Tmot, motor threshold; VRT, ventral root.
for inclusion when in line with the following inclusion criteria: 1) preclinical or clinical study; 2) intervention of temporary or permanent SNM; and 3) comparison of various SNM stimulation parameters. In addition, no language limitations were used and both reviews and meta-analyses were excluded.

Quality of the literature included was assessed by two reviewers (P.D., R.A.) using the SYRCLE Risk of Bias (RoB) tool for animal studies (5). The items in the RoB tool relate to performance bias, selection bias, attrition bias, detection bias, reporting bias, and other biases. Papers were marked as low risk, high risk, or unclear risk. RoB was rated “high” if there were expectations of bias; “unclear” if information was missing, incomplete, or not clear; and “low” if all items were explained clearly and no bias was found.

RESULTS

Based on the online search, 5659 papers were identified and one additional paper was included through hand searching (Fig. 1 for flowchart). Of which 1534 were excluded because of duplications. Due to irrelevance by title and abstract screening, 4042 papers were excluded and 45 more papers were excluded after full text screening. Finally, 39 studies were relevant for inclusion, of which 22 were preclinical studies.

Characteristics of Included Studies

Papers included and relevant characteristics are shown in Table 1. Within these, a large variability was noted with respect to both approach and use of specific stimulation parameters and outcome parameters as well as the animal species. To analyze the outcome, papers were sub-grouped based on type of SNM stimulation parameters: frequency, intensity, pulse width, stimulation signal, timing of stimulation, and unilateral vs. bilateral stimulation. Intensity was often expressed as a percentage of the motor threshold ($T_{mot}$). $T_{mot}$ is defined as the lowest intensity to evoke pelvic floor muscle contractions, hind toe twitches, or tail twitches. Thereafter, a distinction was made based on outcome parameters: for urinary tract dysfunction: bladder activity, bladder capacity, external urethral sphincter (EUS) activity, and for bowel dysfunction: anal canal cortical evoked potentials (EPs) and rectal volume. Study design and primary outcome of the literature selected are shown in Table 2 (urinary tract dysfunction) and Table 3 (bowel dysfunction).

Risk of Bias Assessment/Methodological Quality

A methodological quality assessment was performed on all papers included (Table 4). In general, randomization (item 1, 4, 6), concealment (item 3), blinding (item 5, 7), and missing data (item 8) were poorly reported. Conversely, papers were free of selective reporting (item 9) and mentioned baseline characteristics (item 2). Other potential bias that could have led to high risk (item 10) regarded anesthesia used during the experiment and missing data about materials and stimulation parameters.

SNM and Urinary Tract Dysfunction

Effect of Frequency

Significant improvement of urinary tract dysfunction in animals has been found in several studies investigating SNM frequencies below 100 Hz (Table 5). Although not all studies on the effects of SNM frequency were performed with similar stimulation intensity or pulse width, stimulation seems to be optimal within a frequency range of 7.5–15 Hz (6–12). The use of SNM at various frequencies can improve bladder activity, bladder capacity, and EUS activity.

SNM and Bowel Dysfunction

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Table 3 Study Design and Outcome for Bowel Dysfunction.

| Study ID | Location | Duration | Freq (Hz) | Pulse width (μs) | Intensity | Extra information | Outcome |
|----------|----------|----------|-----------|------------------|-----------|--------------------|---------|
| Evers et al. (25) | S1 left | 30 min, 3 min, 18 s, 18 s 3 min | 0.1, 1, 10, 100 0.1, 1, 10, 25, 100 2 | 1000 | 15 V | No of pulses is 180 | Optimal frequency for anal canal cortical EPs is 2 Hz. SNM at 0.5x, 0.75x and 1x $T_{mot}$ increased anal EPs compared to 0x and 0.25x times $T_{mot}$ in rats. |
| Evers et al. (26) | S1 left | 10 min | 2 14 | 1000 | 1x $T_{mot}$ | Optimal frequency for anal canal cortical EPs is 2 Hz. |
| Huang et al. (27) | S3 right | 5 | 100, 210, 300, 500, 1000 | 210 | 90% of $T_{mot}$ | SNM inhibited constipation best using 5 Hz, 100 μsec and 90% of $T_{mot}$ |
frequencies (0.01–100 Hz) was shown to significantly reduce the number of bladder contractions per minute (9, 10, 13) or bladder pressure (8) using frequencies from 0.05 to 50 Hz, with the best results applying 4, 7.5, and 10 Hz stimulation. SNM in burst patterns (4–6 pulse burst; interburst 0.01–1 Hz, intraburst 0.1–1000 Hz) reduced the number of bladder contractions per minute with an optimum of a four-pulse burst 1 Hz interburst and 40 Hz intraburst (13), although this burst pattern did not exceed a continuous stimulation of 10 Hz.

Contradictory effects were reported (14–16) as low-frequency (LF)-SNM (10–30 Hz) was shown to affect voiding in dyssynergic reflexive EUS activity and showed elevated bladder and EUS pressure. The best SNM frequencies that inhibit EUS for voiding were 20 and 100 Hz, which resulted in the most optimal bladder response and the lowest EUS pressure and the fastest EUS fatigue, respectively (16). Stimulation at 30 Hz was applied to evoke maximal bladder pressure. Nonetheless, this stimulation also evoked EUS pressure, since the intensity threshold for EUS pressure is lower than the intensity threshold for bladder pressure (15). With focus on uncoordinated contractions of bladder and EUS, detrusor sphincter dyssynergia was induced by providing intermittent bilateral S2 SNM at 20 Hz to evoke bladder pressure and continuous S1 SNM at 20 Hz to evoke EUS pressure (14). The use of high-frequency (HF)-SNM (12.5 kHz, 600 Hz or 200 Hz) allowed voiding, caused by a possible EUS blockade (14, 15) or stimulation related EUS fatigue, which seemed closest to normal voiding (16). The optimal blocking parameters (600 Hz; 60 μsec; 1.3 mA) caused a maximum blocking of EUS pressure and a minimal blocking of bladder pressure (15). HF-SNM at 1 or 3 kHz was reported to suppress imminent voids for 35–262 sec when SNM was applied for 60 sec after the onset of an imminent void. Bladder pressure continued to rise steeply after the SNM onset and reduced rapidly to a lower level for the remaining 60 sec SNM until a void occurred (17).
The effect of different frequencies on bladder capacity in healthy and acetic acid (a.a.) induced overactive bladder (OAB) animals was investigated (6, 7, 11, 18, 19). SNM at 5 Hz increased bladder capacity (defined as inhibition of isovolumetric bladder contractions) in healthy and a.a. induced OAB in cats, whereas SNM at 15 and 30 Hz did not change bladder capacity (18, 19). Contrarily, SNM at 15, 30, and 50 Hz was shown to increase bladder capacity (defined as infused volume) in a.a. induced OAB pigs equally effective while SNM at 5 Hz did not change bladder capacity (6, 7). Conversely, the use of SNM at 10 Hz increased bladder function significantly as compared to sham, while at the same time, 1 Hz and 50 Hz SNM were ineffective (11).

**Effect of Intensity**

Stimulation intensities ranging from 0x to 6x T_{mot} (Table 6) were studied in animals with an overall optimal intensity of at least 1x T_{mot}. Higher intensity (2x T_{mot}) SNM caused significantly greater reductions in bladder activity than 0.8x or 1x T_{mot} (8). Stimulation at T_{mot} caused a delayed inhibition of the number of bladder reflex contractions per minute and stimulation at high intensity (2x to 6x T_{mot}) resulted in a prolonged inhibition in rats (9). Furthermore, the intensity required to cause significant inhibition of bladder activity was higher for unilateral SNM (2x T_{mot}) compared to bilateral SNM (0.8x T_{mot}), suggesting that bilateral SNM at the same intensity results in more/prolonged inhibition (10).

SNM increased bladder capacity at 1x and 2x T_{mot} as compared to 0x, 0.25x, and 0.5x T_{mot} (18, 19). Similar results were reported and showed that bladder capacity during 1x T_{mot} was significantly larger than sham, while bladder capacity during 2x T_{mot} was significantly larger than sham, 0.5x, and 1x T_{mot} (11). SNM at S1 (1–1.5x T_{mot}) applied together with pudendal nerve stimulation (PNS), used as a model to partly mimic bladder underactivity, blocked PNS inhibition and decreased bladder capacity to control levels, whereas SNM alone did not increase bladder capacity. SNM applied at 1.5–2x T_{mot} increased bladder capacity compared to control, and together with PNS, SNM blocked PNS inhibition. These results were not seen for SNM at S2, which only showed a significant increase when SNM alone at 1.5–2x T_{mot} was applied (7).

**Effect of Pulse Width**

SNM pulse widths significantly affected bladder capacity and inhibited bladder activity in animals. In order to detect the

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**Table 5 Frequency and Outcome in Urinary Tract Dysfunction.**

| Frequency (Hz) | Bladder activity | Bladder capacity | EUS activity | Reference |
|---------------|------------------|------------------|-------------|-----------|
| 0.01 - 5      | 0                | ?                | ?           | 6, 8, 11, 13, 18, 19 |
| 7.5 - 15      | -                | +                | +           | 6, 11, 13, 18, 19 |
| 20 - 40       | ?                | ?                | +           | 6, 11, 13-16, 18, 19 |
| 50            | -                | ?                |             | 6, 9, 11 |
| 100 - 200     | 0                |                 | ?           | 5, 13, 16 |
| 600 - 12500   | -                |                 |             | 14, 15, 17 |

● = inhibition or decrease; ○ = no changes; ◎ = excitation or increase; □ = ambiguous outcome

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**Table 6 Intensity and Outcome in Urinary Tract Dysfunction.**

| Intensity (x T_{mot}) | Bladder activity | Bladder capacity | Reference |
|-----------------------|------------------|------------------|-----------|
| 0.25 - 0.4            | 0                | 0                | 18, 19    |
| 0.5 – 0.9             | 0                | 0                | 8, 10, 11, 18, 19 |
| 1 – 1.9               | ?                | +                | 7-11, 18 |
| 2 - 6                 | -                | +                | 8-11, 18 |

● = inhibition or decrease; ○ = no changes; ◎ = excitation or increase; □ = ambiguous outcome
optimal pulse widths that achieve the best clinical effects, pulse widths of 64, 204, and 624 μsec (F = 14 Hz) were analyzed and shown to significantly increase bladder capacity as compared to the a.a. control level (20). Pulse widths between 30 μsec and 210 μsec (F = 10 Hz) were shown to significantly inhibited bladder activity (12). In neither of the studies, significant differences were noted between the pulse widths tested. The latter may be related to the various stimulation intensities used, which were provided at T_mot. An inverse exponential correlation was found between pulse width and corresponding T_mot (intensity) and the optimal pulse width determined by T_mot was 40 μsec in one study (12). The other study concluded that for a clinical approach, a pulse width of 204 μsec might be more appropriate for SNM in patients to optimize battery life and maintain patient comfort during stimulation (20).

Effect of Stimulation Signal
Several stimulation signals can be delivered to modulate the effect of SNM in animals. Sinusoidal SNM almost doubled the EUS pressure when compared to rectangular SNM using similar amplitudes (16). Using rectangular SNM, evoked bladder pressure decreased with an increased amplitude (higher than 6 V) which did not occur using sinusoidal SNM. It was concluded that rectangular SNM has many harmonics that stimulate other nerve fibers and that “cleaner” sinusoidal SNM may result in a more organ-specific stimulation (16, 21, 22). Further analysis of the effect of stimulation signal revealed that quasi-trapezoidal SNM inhibited induced detrusor overactivity significantly more than the conventional rectangular SNM (21, 22).

Effect of Unilateral Versus Bilateral SNM
Bilateral SNM in animals was shown to significantly increase bladder pressure (16) and decreased the number of hyperactive detrusor contractions more than unilateral SNM (10, 23). Interestingly, the intensity threshold for bilateral SNM was 0.8x T_mot and for unilateral SNM 2x T_mot. No significant differences were found in bilateral stimulation using balanced (time-matched pulses) and unbalanced (time-mismatched pulses) current intensities (10).

Effect of Timing
One study focused on the timing of SNM in relation to a specific phase of the bladder filling cycle. SNM delivered between 50–100% and 75–100% of the bladder filling cycle increased bladder capacity with 32% and 43%, respectively, over control fills. SNM delivered in the first 50% of the bladder filling cycle had no effect on bladder capacity (24).

SNM and Bowel Dysfunction
Effect of Frequency
A few studies focused on analysis of SNM parameters for bowel dysfunction (25–27). It was noted that frequency of SNM on amplitude of anal canal EPs is highly significant in healthy rats (25). Various frequencies (0.1–100 Hz) were tested and showed that 1 and 10 Hz stimulation significantly increased the amplitude of EPs compared to other frequencies (Table 7). Using a graph of nonlinear curve fitting for each time point, a frequency-potentiation relationship parabolic in form with a clear optimum at 2 Hz in these healthy rats was reported (25). These findings were further substantiated in a rodent model of fecal incontinence where SNM restored the decreased EPs after pudendal nerve injury and 2 Hz SNM also enhanced the decreased EPs more than 14 Hz (26). In the treatment of constipation, SNM significantly increased rectal volume. All frequencies tested increased rectal volume in rodents, with a reported optimal frequency of 5 Hz and an optimal pulse width of 100 μsec (27).

Effect of Intensity
Using the reported optimal frequency of 2 Hz, various stimulation intensities (0.25x, 0.5x, 0.75x, 1x T_mot, and sham) were investigated in healthy rats (25). SNM stimulation at 0.5x, 0.75x, and 1x T_mot significantly increased the amplitude of EPs compared to sham stimulation (Table 8).

### Table 7 Frequency and Outcome in Bowel Dysfunction.

| Frequency (Hz) | Anal canal EPs | Rectal volume | Reference |
|----------------|----------------|---------------|-----------|
| 0.1 – 5        | +              | +             | 25, 27    |
| 10 – 15        | +              | +             | 25, 27    |
| 25 – 30        | +              | +             | 25, 27    |
| 100            | 0              | 0             | 25        |

= no changes; + = excitation or increase; ? = ambiguous outcome

### Table 8 Intensity and Outcome in Bowel Dysfunction.

| Intensity (x T_mot) | Anal canal EPs | Reference |
|---------------------|----------------|-----------|
| 0.25                | 0              | 25        |
| 0.5                 | +              | 25        |
| 0.75                | +              | 25        |
| 1                   | +              | 25        |

= no changes; + = excitation or increase
DISCUSSION

This systematic review aimed to investigate the effects of various stimulation parameters of SNM for urinary tract and bowel dysfunction in animals. In general, all studies reported an acute effect of SNM on urinary tract or bowel dysfunction while various stimulation settings were used.

LF-SNM of 7.5–15 Hz appeared to be optimal in inhibiting bladder contractile activity and increasing bladder capacity, which is useful for patients with urinary incontinence, whereas HF-SNM inhibited EUS activity and caused voiding. It is important to note that some SNM frequencies within this range have only been studied to a limited extent, which might over- or underestimate the effect. Ambiguous results were reported using LF-SNM. Three studies reported that LF-SNM increased bladder activity (14–16) and three studies reported that SNM inhibited bladder activity (8–10). No clear explanation for these contradictory results was given causing the underlying mechanisms to warrant further research. Interestingly, studies that reported an increase in bladder activity applied SNM at L6 in female Sprague Dawley rats (9, 10) and S1 in male cats (8), whereas studies that reported a decrease in bladder activity applied SNM at S2 in male cats (14) and S1-S3 in male dogs (15, 16). These results may be caused by the various animal species used. But these results may also suggest that location of SNM is important as SNM at L6-S1 may increase the EUS activity and concomitantly inhibit bladder activity, whereas SNM at S1-S3 may shift the balance in the opposite direction.

HF-SNM was reported to block or fatigue EUS pressure and allow voiding (14–16). At the same time, HF-SNM was reported to suppress acute imminent voids (17). All studies reported low bladder pressure when HF-SNM was applied. It is highly probable that HF-SNM first increases EUS pressure and therefore suppresses voiding and after a short period decreases EUS pressure due to fatigue and thereafter allows voiding.

SNM at low frequencies that seem to be optimal in inhibiting bladder activity and increasing bladder capacity are similar to the conventional frequencies used in the clinic. Similarly, high frequencies that seem to cause voiding are not used. These high frequencies may have clinical utility for patients with voiding dysfunction. Moreover, in clinically related areas like anesthesiology and pain management, the use of spinal cord stimulation in treatment of chronic neuropathic (low back) pain has been shown to benefit from HF (10 Khz) (28). As the spinal network underlying bladder control and defecation has similarities with the nociceptive spinal network it is not unreasonable to speculate that similar HF paradigms may also achieve significant effects for lower urinary tract and bowel dysfunction (29).

For bowel dysfunction, the preferred SNM frequencies to increase anal canal EPs and rectal volume are lower than the conventional frequencies used in clinical settings. In addition, the preferred pulse width to increase rectal volume is lower, whereas the stimulus intensity seems equal to clinical settings.

For urinary tract dysfunction, values above 1x T_mot were optimal in achieving a positive acute effect. Only two papers showed an effect of sub-T_mot SNM (10, 24), and it is noteworthy that inhibition of bladder activity was reported in animals that received bilateral SNM (10, 24) but not in animals that received unilateral SNM (8, 10). In additional papers, it was concluded that bilateral stimulation increased bladder pressure and decreased the number of hyperactive detrusor contractions more than unilateral SNM with similar stimulation settings (16, 23). This may suggest that bilateral SNM is more effective at lower intensities than unilateral SNM. However in clinical studies, bilateral SNM was not reported to be more effective than unilateral SNM (30) and chronic SNM in clinical setting is always applied at (sub)sensory threshold, which is significantly lower than the motor threshold (31).

Preferred SNM frequencies for bowel dysfunction (2–5 Hz) are lower compared to urinary tract dysfunction (10 Hz) in animal models, whereas bowel dysfunction (31 Hz) in clinical settings is treated with higher SNM frequencies compared to urinary tract dysfunction (16 Hz). In contrast, experimental studies on bowel dysfunction apply lower intensities to achieve a positive effect compared to urinary tract dysfunction. In this respect, it should be noted that most experimental studies were performed under anesthesia which has been shown to affect outcome measurements. Under conscious conditions, stimulation at T_mot may cause an unpleasant perception or paresthesia.

The majority of the SNM pulse widths applied in the experimental studies on urinary and bowel dysfunction are similar to conventional settings used in clinical settings. The inverse exponential correlation and the optimal pulse width based on T_mot (40 μsec) was later reported to be the identical in anesthetized and awake sheep (32). This inverse exponential correlation suggests that the SNM total charge per second is relevant for a positive effect (20). However, when the total number of pulses for each frequency-duration combination was fixed at 180, not all combinations presented the same outcome in anal canal EPs. This suggests that SNM total charge is not important for the outcome. Only 0.1 and 1 Hz showed a significant effect, whereas 10 and 100 Hz did not. It is worth noting that the settings with a significant effect had the longest SNM duration; 30 min and 3 min, respectively. Other settings had a SNM duration of 18 and 1.8 sec (25). This may suggest that a minimal SNM duration is required to detect a significant outcome and that SNM total charge is still important for clinical outcomes.

Furthermore, SNM during the last 50% of bladder filling appeared to be the most optimal (24). In addition, a sinusoidal and quasi-trapezoidal signal seemed to be more organ-specific and inhibited induced detrusor overactivity more, respectively (21, 22). Both results were only reported in one study making it hard to draw definite conclusions from this data.

Previous research in the field of urology improved the understanding of the mechanisms of action behind SNM. It was once thought that an efficent EUS motor response causing detrusor relaxation was involved in the mechanisms of action underlying SNM. This theory solely is unlikely as SNM has shown to work when no EUS contractions are observed (33). Another theory supports activation of sensory nerves; research into the latency of the motor response (i.e., anal sphincter contraction) measured in women implied that the response is reflex mediated (34). In this context, it is also important to note that, although with use of intravaginal electrical stimulation in cat, the involvement of reflex pathways when recording effrent nerves to the bladder was noted (35). Research into cortical changes showed increased cortical activity after acute SNM and reduced cortical activity after chronic SNM. These observations were seen in both urinary and fecal incontinence (36). In addition, areas involved in micturition, awareness, and alertness showed changes in regional cerebral blood flow (rCBF) in the brain following SNM. This results display an increased awareness of bladder filling and pelvic floor contraction after SNM suggesting SNM restores normal urinary continence (37).
In line with this hypothesis, in cats dorsal root SNM (afferent pathways) at intensity threshold inhibited bladder activity more than ventral root SNM (efferent pathways) (18). Moreover, low-intensity SNM in rodents showed increased bladder capacity which was reported to be afferent mediated, whereas high-intensity SNM additionally attenuated the bladder contraction amplitude and was reported to be efferent mediated (9). These results suggest that low-intensity SNM only activates large myelinated fibers while high-intensity SNM additionally activates unmyelinated C-fibers (9, 10, 38).

Limitations within the reviewed studies for both urinary tract and bowel dysfunction were, mainly, the methodological quality assessment (5). Due to poor reporting most RoB items were scored with “unclear” risk for all studies. Only a few studies reported randomization or blinding while most studies did not report such details. Likewise, data required for replication of the experiment was missing, such as stimulation settings, device specification, and animal characteristics. More precise reporting is required to achieve higher quality animal studies during future investigations.

Furthermore, the diversity in outcome parameters and SNM settings made it difficult to compare studies. Primary outcome parameters (bladder activity, bladder capacity, EUS activity, and anal canal EPs) were not one on one comparable making it challenging to determine an optimal effect. Moreover, stimulation settings often differed. For example, stimulations with similar frequencies noted various results, which could be due to the large variability in other stimulation settings, such as intensity, duration, and location. Furthermore, use of heterogeneous animals across studies may result in differential effects of stimulation using similar stimulation settings. Looking forward, a more standardized methodological approach is needed for further research.

In summary, in animal studies, we found that LF-SNM of 7.5–15 Hz appeared to be optimal for storage dysfunction. HF-SNM is shown to diminish aberrant perceptions. For bowel dysfunction, it was difficult to determine optimal settings in clinical practice. A more standardized methodological approach is needed for further research.

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Authorship Statements
Perla Douven, Gommert A. van Koeveringe, Elbert A. Joosten, Stephanie O. Breukink, Jarno Melenhorst, and Roman Assmann designed and conceptualized the study. Perla Douven wrote the manuscript. Perla Douven, Roman Assmann, and Jos Kleijnen determined the systematic literature search strategy and performed the search. Perla Douven and Roman Assmann critically filtered and quality assessed the manuscripts. All authors have approved the final version of the manuscript.

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REFERENCES
1. Schmidt RA. Advances in genitourinary neurostimulation. Neurosurgery 1986;19: 1041–1044.
2. Tanagho EA, Schmidt RA. Bladder pacemaker: scientific basis and clinical future. Urology 1982;20:614–619.
3. Matzel KE, Stedelmaier U, Hohenfellner M, Gall FP. Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. Lancet 1995;346:1124–1127.
4. Assmann R, Douven P, Kleijn J et al. Will altering stimulation parameters for sacral neuromodulation in lower urinary tract and bowel dysfunction improve clinical outcome? A systematic review. Neuromodulation 2020.
5. Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW, SYRCLE’s risk of bias tool for animal studies. BMC Med Res Methodol 2014:14:43.
6. Li X, Liao L, Chen G, Wang Z, Deng H. Effects of acute sacral neuromodulation at different frequencies on bladder overactivity in pigs. Int Neurourol J 2017;21: 102–108.
7. Li X, Uy J, Yu M et al. Sacral neuromodulation blocks pudenial inhibition of bladder activity in cats, thus bringing hope on sacral neuromodulation in the management of overactive bladder in human beings. J Urol 2012:188:1383–1389.
8. Snellings AE, Grill WM. Effects of stimulation site and stimulation parameters on bladder inhibition by electrical nerve stimulation. BJU Int 2012:109:136–143.
9. Su X, Nickles A, Nelson DE. Neuromodulation in a rat model of bladder mic- turition reflex. Am J Physiol Renal Physiol 2013:302:F477–F486.
10. Su X, Nickles A, Nelson DE. Quantification of effectiveness of bilateral and unilateral neuromodulation in the rat bladder rhythmic contraction model. BMC Urol 2013:13:34.
11. Su X, Nickles A, Nelson DE. Optimization of Neurouromodulation for bladder control in a rat cystitis model. Neuromodulation 2016:19:101–107.
12. Su X, Simenson HA, Dinsmoor DA, Orser HD. Evaluation of pulse-width of spinal nerve stimulation in a rat model of bladder micturnition reflex. Neuromodulation 2017:20:793–798.
13. Su X, Simenson HA, Paralikar K, Orser HD. Comparison of bladder inhibitory effects of patterned spinal nerve stimulation with conventional neuromodulation in the rat. Neuromodulation 2017:20:787–792.
14. Boger AS, Bhadra N, Gustafson KJ. High frequency sacral root nerve block allows bladder voiding. Neurolouroudyn 2012:31:677–682.
15. Shaker HS, Tu LM, Robin S et al. Reduction of bladder outlet resistance by selective sacral root stimulation using high-frequency blockade in dogs: an acute study. J Urol 1998;160:901–907.
16. Sievert KD, Gleason CA, Junemann KP, Alken P, Tanagho EA. Physiologic bladder evacuation with selective sacral root stimulation: Sinusoidal signal and organ-specific frequency. Neurolouroudyn 2002:21:80–91.
17. Brouillard CB, Crook JK, Lovick TA. Suppression of urinary voiding “on demand” by high-frequency stimulation of the S1 sacral nerve root in anesthetized rats. Neuromodulation 2019:22:703–706.
18. Zhang F, Zhao S, Shen B et al. Neural pathways involved in sacral neuromodulation of reflex bladder activity in cats. Am J Physiol Renal Physiol 2013:304:F710–F717.
19. Zhang Z, Bandari J, Bansal U et al. Sacral neuromodulation of nociceptive bladder overactivity in cats. Neurouroloudyn 2017:36:1270–1277.
20. Cong H, Liao L, Wang Y et al. Effects of acute sacral neuromodulation at different pulse widths on bladder overactivity in pigs. Int Neurourol J 2019;23:109–115.
21. Braun PM, Seif C, Brosi S, Martínez Portillo FJ, Alken P, Junemann KP. Improved sacral neuromodulation in the treatment of the hyperactive detrusor: signal modification in an animal model. BJU Int 2003:91:711–715.
22. Kaufmann S, Naumann CM, Hamann MF et al. Unilateral vs bilateral sacral neuromodulation in pigs with formalin-induced detrusor hyperactivity. BJU Int 2002:89:206–213.
23. Potts BA, Degoski DJ, Brooks JM et al. Timing of sacral neuromodulation is important for increasing bladder capacity in the anesthetized rat. Am J Physiol Renal Physiol 2019;317:F1183–F1188.
25. Evers J, Devane L, Carrington EV et al. Effects of stimulation frequency and intensity in sacral neuromodulation on anorectal inputs to the somatosensory cortex in an experimental model. Br J Surg 2014;101:1317–1328.

26. Evers J, Devane L, Carrington EV et al. Reversal of sensory deficit through sacral neuromodulation in an animal model of fecal incontinence. Neurogastroenterol Motil 2016;28:665–673.

27. Huang Z, Li S, Foreman RD, Yin J, Dai N, Chen JDZ. Sacral nerve stimulation with appropriate parameters improves constipation in rats by enhancing colon motility mediated via the autonomic-cholinergic mechanisms. Am J Physiol Gastrointest Liver Physiol 2019;317:G609–G617.

28. Kapural L, Yu C, Doust MW et al. Novel 10-kHz high-frequency therapy (HF10 therapy) is superior to traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain: the SENZA-RCT randomized controlled trial. Anesthesiology 2015;123:851–860.

29. Burks FN, Bui DT, Peters KM. Neuromodulation and the neurogenic bladder. Urol Clin North Am 2010;37:559–565.

30. Scheepens WA, de Bie RA, Weil EH, van Kerrebroeck PE. Unilateral versus bilateral sacral neuromodulation in patients with chronic voiding dysfunction. J Urol 2002;168:2046–2050.

31. Koch SM, van Gemert WG, Baeten CG. Determination of therapeutic threshold in sacral nerve modulation for faecal incontinence. Br J Surg 2005;92:83–87.

32. Su X, Cutinella M, Koppes S, Agran JE, Dinsmoor DA. Electromyographic responses across different pulse-widths of sacral Neuromodulation in sheep. Neuromodulation 2019;22:684–689.

33. Groen J, Bosch JL. Neuromodulation techniques in the treatment of the overactive bladder. BJU Int 2001;87:723–731.

34. Fowler CJ, Swinn MJ, Goodwin RJ, Oliver S, Craggs M. Studies of the latency of pelvic floor contraction during peripheral nerve evaluation show that the muscle response is reflexly mediated. J Urol 2000;163:881–883.

35. Lindstrom S, Fall M, Carlson CA, Erlandsson BE. The neurophysiological basis of bladder inhibition in response to intravaginal electrical stimulation. J Urol 1983;139:405–410.

36. Janssen PTJ, Komen N, Melenhorst J et al. Sacral Neuromodulation for fecal incontinence: a review of the central mechanisms of action. J Clin Gastroenterol 2017;51:669–676.

37. Blok BF, Groen J, Bosch JL, Veltman DJ, Lammersma AA. Different brain effects during chronic and acute sacral neuromodulation in urge incontinent patients with implanted neurostimulators. BJU Int 2006;98:1238–1243.

38. Li CL, Bak A. Excitability characteristics of the A- and C-fibers in a peripheral nerve. Exp Neurol 1976;50:67–79.

39. Riemnsma R, Hagen S, Kirschner-Hermanns R et al. Can incontinence be cured? A systematic review of cure rates. BMC Med 2017;15:63.

APPENDIX: SEARCH TERMS

All search strategies are based on work published in Riemnsma et al.39

Embase (ovid): 1974–2020/01/13

Search 14.1.2020

1. incontinence/

2. continence/

3. (incontinen$ or continen$ or obstipat$).ti,ab,ot.

4. (urine$ or urinary or urinat$ or micturat$ or bladder$).ti,ab,ot.

5. (urine$ or urinary or urinat$ or micturat$ or bladder$).ti,ab,ot.

6. (SUI or OAB or BPS).ti,ab,ot.

7. (bladder$ or sacral$) adj2 (Autoaugment$ or Auto-augment$)).ti,ab,ot.

8. (urine$ or urinary or urinat$ or micturat$ or bladder$).ti,ab,ot.

9. (detrusor adj2 (overactiv$ or over-activ$)).ti,ab,ot.

10. (incontinentia urinae or enuresis ureterica or ureter enuresis or enuresis diurnal).ti,ab,ot.

11. (Unable or inabilit$ or abilit$ or able) adj3 control$.ti,ab,ot.

12. neurogenic bladder/.

13. ((neurogenic$ or neurologic$ or spinal or spastic$) adj4 bladder$).ti,ab,ot.

14. neurogenic vesical dysfunction$.ti,ab,ot.

15. ((Bladder sphincter dys$nergia or detrusor sphincter dys$nergia or neurogenic detrusor overactiv$)).ti,ab,ot.

16. feces incontinence/.

17. (Encopresis or incontinentia alvit).ti,ab,ot.

18. ((bowels or rectum or rectal$) adj4 (leak or leakage or leaks or leaking or seep or seepage or seeps or seeping or accident$ or esca$p or uncontrolled or trickl$ or “lack of control” or “no control” or “out of control” or “not voluntary” or involuntary or control$)).ti,ab,ot.

19. (Unable or inabilit$ or abilit$ or able) adj3 control$.ti,ab,ot.

20. ((faeces or faecal$ or faeces or faecal$ or stool$ or rectum or rectal$) or bowel$.ti,ab,ot.

21. ((diarrh$ or Pseudodiarrh$ or Pseudo-diarrh$) adj4 (leak or leakage or leaks or leaking or seep or seepage or seeps or seeping or accident$ or esca$p or uncontrolled or trickl$ or “not voluntary” or involuntary or control$)).ti,ab,ot.

22. (Unable or inabilit$ or abilit$ or able) adj3 control$.ti,ab,ot.

23. ((diarrh$ or Pseudodiarrh$ or Pseudo-diarrh$) adj4 (diarrh$ or Pseudodiarrh$ or Pseudo-diarrh$)).ti,ab,ot.

24. ((faeces or faecal$ or faeces or faecal$ or stool or stools or stool$ or rectum or rectal$) or defecat$ or soiling) adj4 (leak or leakage or leaks or leaking or seep or seepage or seeps or seeping or accident$ or esca$p or uncontrolled or trickl$ or “not voluntary” or involuntary or control$)).ti,ab,ot.

25. (urinary tract adj3 (dysfunc$t or disorder$ of syndrome$)).ti,ab,ot.

26. (LUTD or LUTS).ti,ab,ot.

27. (pelvic floor adj3 (dysfunc$t or disorder$ of syndrome$)).ti,ab,ot.

28. ((faeces or faecal$ or faeces or faecal$ or stool or stools or stool$ or rectum or rectal$) adj2 (store or stored or storag$) adj2 (disorder$ or dysfunc$t or malfunc$ or syndrome$)).ti,ab,ot.

29. ((disorder$ or difficulty$ or syndrome$) adj4 (urine$ or urinar$ or urinary or micturat$ or bladder$)).ti,ab,ot.

30. (overactive bladder/.

31. (detrusor adj2 (overactiv$ or over-activ$)).ti,ab,ot.

32. cystitis/ or interstitial cystitis/.

33. ((pain$ or discomfort$ or inflammation$ or infect$) adj4 (urine$ or urinar$ or urinary or micturat$ or bladder$ or pelvis or pelvic)).ti,ab,ot.

34. (megacystitis or cystitis or pericystitis).ti,ab,ot.

35. (detrusor adj2 (overactiv$ or over-activ$)).ti,ab,ot.

36. (bladder$ or hanner or hanneri or submucos$ or submucos$) adj2 (ulcus or ulcer$)).ti,ab,ot.

37. or/1-36

38. sacral nerve stimulation/

39. InterStim.ti,ab,ot.

40. (SNS or SNM).ti,ab,ot.

41. (sacral adj3 (neuromodulat$ or neuro-modulat$ or deafferent$ or de-afferent$ or neurostimulat$ or neuro-stimulat$)).ti,ab,ot.

42. medical electrical stimulation therap$.ti,ab,ot.

43. ((bladder$ or sacral$) adj2 (Autoaugment$ or Auto-augment$)).ti,ab,ot.

www.neuromodulationjournal.com © 2020 The Authors. Neuromodulation: Technology at the Neural Interface Neuromodulation 2020; 23: 1094–1107 published by Wiley Periodicals LLC. on behalf of International Neuromodulation Society.
This literature review on the effect of stimulation parameters of sacral neuromodulation on lower urinary tract and bowel dysfunction gives a clear overview of the preclinical animal data. It provides valuable information for researchers as well as for clinicians to get more insight in sacral neuromodulation.

Stefan de Wachter, MD, PhD
Antwerpen, Belgium

Comments

This is a systematic review that addresses various aspects of sacral neuromodulation stimulation parameters in animal studies. The findings of this review should be interpreted with caution since it only relates to animal studies and the methodologies within the studies analyzed were assessed with 'unclear' risk of bias and too diverse to present comprehensive and precise conclusions toward optimal settings in clinical practice.

Jerzy Gajewski, MD
Halifax, Nova Scotia, Canada

Sacral neuromodulation is a well-established therapy for bowel and urinary disorders management since the 1990’s. The usual criticism of this therapy is how it works and which are the best parameters for chronic stimulation. Animal models are imperfect and lacking. Companies usually promote their own parameters to make it more simple based on past publications not cited here. The authors tried to compile published data even if correlation with routine and human use cannot always correlate to it. As a researcher, this publication may help to plan new experiments. As a clinician, it may help to understand how to modify parameters in everyday life of implanted patients, even if sometimes changes are not related to efficiency but to side effects (pain, neurological target,…).