***Original Article***

# Comparison of figure-of-8 and circular coils for threshold tracking transcranial magnetic stimulation measurements

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**Running title:** Figure-of-8 and circular coils for TMS measurements

**Abstract**

*Objectives:* The transcranial magnetic stimulation (TMS) technique of threshold-tracking short-interval intracortical inhibition (T-SICI) has been proposed as a diagnostic tool for amyotrophic lateral sclerosis (ALS). Most of these studies have used a circular coil, whereas a figure-of-8 coil is usually recommended for paired-pulse TMS measurements. The aim of this study was to compare figure-of-8 and circular coils for T-SICI in the upper limb, with special attention to reproducibility, and the pain or discomfort experienced by the subjects.

*Methods:* Twenty healthy subjects (aged: 45.5 ± 6.7, mean ± SD, 9 females, 11 males) underwent two examinations with each coil, in morning and afternoon sessions on the same day, with T-SICI measured at interstimulus intervals (ISIs) from 1-7ms. After each examination the subjects rated degree of pain/discomfort from 0-10 using a numerical rating scale (NRS).

*Results:* Mean T-SICI was higher for the figure-of-8 than for the circular coil at ISI of 2ms ($p<0.05$) but did not differ at other ISIs. Intra-subject variability did not differ between coils, but mean inhibition from 1-3.5ms was less variable between subjects with the figure-of-8 coil (SD 7.2% vs. 11.2% RMT, $p<0.05$), and no such recordings were without inhibition (vs. 6 with the circular coil). The subjects experienced less pain/discomfort with the figure-of-8 coil (mean NRS: 1.9 ± 1.28 vs 2.8 ± 1.60, $p<0.005$).

*Discussion:* The figure-of-8 coil may have better applicability in patients, due to the lower incidence of lack of inhibition in healthy subjects, and the lower experience of pain or discomfort.

**Keywords:** Circular coil; Figure-of-8 coil; Short interval intracortical inhibition; SICI; Threshold tracking; TMS; Transcranial magnetic stimulation

**Introduction**

Transcranial magnetic stimulation (TMS) is the practice of generating a magnetic field with which an intracortical current is induced [15]. Among other methods, TMS is used to examine cortical excitability [15]. This can be done by activating desired parts of the motor cortex while performing peripheral measurements of the resulting compound muscle action potentials, in this case called motor evoked potentials (MEPs) [7]. Utilizing paired pulses, the activation of the motor cortex can be facilitated or inhibited by a sub-threshold conditioning stimulus given before the test stimulus. The test response is typically inhibited when the interstimulus interval (ISI) is between 1 and 5 ms with the highest inhibition at 1 ms and 3 ms, whereas the response is facilitated for ISIs between 7 and 20 ms - these phenomena are called short-interval intracortical inhibition (SICI) and intracortical facilitation, respectively [4, 8, 12, 15].

Patients with amyotrophic lateral sclerosis (ALS) elicit decreased SICI as demonstrated by both conventional paired pulse TMS [19] and the more recent method of threshold-tracking TMS (TT-TMS) [16, 9, 17, 18]. Advantages have been claimed for TT-TMS, such as higher reproducibility, shorter examination time and smaller required sample size for interventional studies [13]. In TT-TMS, one first determines the resting motor threshold (RMT) as the intensity of a single pulse stimulus that delivers a fixed MEP amplitude [15, 18]. Then, paired-pulse stimuli are applied with a conditioning stimulus set to a fixed percentage of the RMT, while the test stimulus is varied in order to obtain the fixed MEP amplitude [1, 5, 15]. The required changes in test stimulus intensity with ISI are recorded as being inhibition or facilitation, expressed as percentages of RMT.

The figure-of-8 coil has the advantage of producing a more focal stimulus that requires a lower stimulus intensity [2, 17], but most studies proposing TT-TMS as a potential diagnostic and prognostic biomarker for ALS have used a circular coil [6, 10, 11]. Only one study has compared upper limb SICI and short-interval intracortical facilitation (SICF) between circular and figure-of-8 coils, and reported stronger SICI with circular, but stronger SICF with the figure-of-8 coil [14]. That study did not compare reproducibility or degree of pain and discomfort. Another study on lower limb SICI found little difference between circular and figure-of-8 coils, but lower RMTs and greater intracortical facilitation with a double cone coil [3]. The aim of the present study was to make a direct comparison between the circular and figure-of-8 coils in TT-TMS reproducibility and SICI-parameters from the abductor pollicis brevis (APB) muscle. Additionally, the study aimed to compare the degree of pain and discomfort experienced by the two coil types.

## Methods

### *Subjects*

The study included healthy subjects older than 18 years of age (mean age: 45.5±6.7, range: 32-55 years, 9 females and 11 males). The subjects were recruited from the staff at the Department of Clinical Neurophysiology, Aarhus University Hospital and from social media outreach. All participants gave a written informed consent in accordance with the Declaration of Helsinki II. The project was approved by The Central Denmark Region Committees on Health Research Ethics, and the Danish Data Protection Agency.

The following exclusion criteria were used: history of disease in the central nervous system or psychiatric disorders, use of medication known to affect the nervous system, implants containing metal, and pregnancy. Participants were asked to abstain from coffee (12 h), alcohol (24 h), and strenuous exercise (48 h) prior to the examinations.

*TT-TMS*

All examinations were performed by the same operator (SØ). Examinations were performed as two identical double sessions on the same day: in the morning, or around noon, and in the afternoon, respectively. Each double session consisted of an examination with a circular coil and then with a figure-of-8 coil, or vice versa. The coil order was randomized. A simple randomization procedure was used without any kind of software. When an order was applied in the morning session on a subject, the order was switched in the afternoon session.

The subjects were seated in an armchair wearing a swim cap. With both coils, stimulation started near the vertex to the left of the median plane. With the figure-of-8 coil, the starting angle was approximately 45 degrees to the parasagittal plane, whereas the circular coil was just placed tangentially to the curvature of the skull. With both coils, coil positioning was slightly changed while monitoring MEPs from the APB muscle in order to find the stimulation hotspot. Once the stimulation hotspot was localized, the outline of the coil was marked to enable a constant coil position. After this, the automated QtracS© (part of the QtracW package, Professor Hugh Bostock, Institute of Neurology, University College of London, UK) stimulation protocol was initiated using the QTMSG-09 QRP recording protocols.

Resting motor threshold

RMT for a 200 µV peak-to-peak response (RMT200) were measured by '4→2→1' tracking and logarithmic regression. Tracking started with a step size of 4% maximum stimulator output (MSO), which was reduced to 2% and 1% when a change of step direction was required, or the response was within the target error limits. Tracking then continued with steps of 1% (or 0% if within target limits) until 6 valid threshold estimates were obtained [13]. A valid threshold estimate was scored each time two responses bracketed the target, or the response was within the target error limits. After the first valid threshold estimate, the subsequent stimuli and responses were used to estimate the RMT by log regression. This method of threshold estimation was first described by Fisher et al. [5].

T-SICI protocol

The tracking method used was as previously described [15] [1]. After estimating RMT200, this was tracked continuously, and conditioning stimuli were set to 70% of this test-alone stimulus. Paired stimuli were started with an ISI of 1 ms and a stimulus of RMT200, but the test stimulus then tracked the 200 μV target continuously. ISI was increased when two valid threshold estimates were registered, where valid threshold estimates scored as for the RMT determination. The ISIs were increased gradually to 7 ms as 1, 1.5, 2, 2.5, 3, 3.5, 4, 5 and 7 ms.

The MEPs were measured from the APB muscle of the right hand using disposable pre-gelled surface electrodes placed in a belly-tendon fashion, with the active electrode placed on the APB muscle, the reference electrode on the 1st metacarpophalangeal joint and a ground electrode placed on the dorsum of the hand. The parts of the skin used for electrode placement were prepared using NuPrep® Skin Prep Gel. The MEP was amplified (x1000 gain) and filtered (3 Hz-3kHz) using a D440 2 Channel Isolated Amplifier (Digitimer Ltd.). A Humbug Noise Eliminator (Digitimer Ltd.) was used to remove 50/60 Hz noise, and the amplified signals were digitized at 10kHz with a 16- bit data acquisition system (NI USB-6251). The coils were a figure-of-8 Magstim® D70 Remote Coil and a circular Magstim® Remote Coil (Magstim Co.

Ltd.). The coil in use was connected to two Magstim® 2002 stimulators connected in a Bistim configuration.

*Rating of pain/discomfort*

At the end of each session, the degree of discomfort was evaluated using a numerical rating scale (NRS) from 0 to 10 (0 being no painful or discomforting sensation at all; 10 being the worst imaginable pain). NRS scores were interpreted as mild (NRS= 1-3), moderate (NRS=4-6), and severe (NRS=7-10).

*Data analysis*

Data for each person were extracted from QtracP (part of the QtracW® package, Professor Hugh Bostock, Institute of Neurology, University College of London, UK) and Bland-Altman plots were constructed in Excel. For each plot, a bias representing the average difference between the two sessions were calculated. The limits of agreement were then calculated as bias±1.96*SD(diff), where SD(diff) is the standard deviation of the calculated differences. They thus represent a prediction interval for a second measurement made on a subject whose first measurement was equal to the bias.

To compare the two coils, we can construct a null hypothesis that the limits of agreement do not differ, by saying that the SD of the differences do not differ between coils (a Pitman test). In mathematical terms:

$$H_0: SD(A1 - A2) = SD(B1 - B2)$$

Where A (Figure-of-8) and B (Circular) represent the two coils and 1 and 2 represent the first and second examination, respectively. This hypothesis can be tested by testing whether the correlation between the sum and the difference of the differences is 0. That is:

$$H_0: corr[(A1 - A2) + (B1 - B2), (A1 - A2) - (B1 - B2)] = 0$$

This was tested by setting up the new variables X=(A1-A2)+(B1-B2) and Y=(A1-A2)-(B1-B2) for each person, performing a linear regression analysis ($Y = \alpha + \beta * X$) and testing whether the slope is equal to zero using Excel ToolPak. The final hypothesis tested is thus:

$$H_0: \beta = 0$$

A linear regression analysis was also performed (using Excel ToolPak) for each of the Bland-Altman plots to evaluate any correlation between average SICI and difference in SICI. In this way, we checked for any possible correlation between SICI-values and the reproducibility of these values.

Mean SICI was compared between the two coils using paired t-tests, and the variation in thresholds was separated into within-subject and between-subject SDs, which were compared using the F-test. As an indication of the possible diagnostic utility of the method, the number of recordings without inhibition, defined as thresholds ≤ RMT, were compared for the two coil types.

## Results

### *Resting motor thresholds*

The average resting motor threshold for a 200 µV peak-to-peak response was significantly higher for the circular coil (mean: 64.2±10.90) than figure-of-8 coil (mean: 59.6±10.86) ($p < 0.05$).

*Reproducibility of figure-of-8 and circular coils*

Figure 1 shows Bland-Altman plots for the SICI-parameters of the two measurements with each coil type at ISI = 1, 2.5, 3, 1-3.5, and 1-7 ms. The limits of agreement did not differ between coils for any of the ISIs ($p > 0.1$); however, the intervals between the upper and lower bounds were quite wide ranging, from ± 11.5% (circular coil, ISI 1-7 ms) to ± 21.8% (figure-of-8 coil, ISI 3 ms), with an average width of ± 15.9%. There was also no significant correlation between the average SICI and difference in SICI for any of the ISIs ($p > 0.1$).

*Comparison of SICI parameters*

For both coils, the highest mean SICI was found at 3 ms, and mean SICI differed only at ISI = 2 ms between the coils (Table 1A, Figure 2a). As with the Bland-Altman measures of reproducibility, within-subject threshold variation did not differ significantly between coil types (Table 1B). On the other hand, threshold variation between subjects, as measured by SD, was less with the figure-of-8 coil than with the circular coil for nearly all ISIs, and significantly less in about half of the ISIs (Table 1C, Figure 2b). The number of recordings without inhibition, i.e., those with thresholds ≤ RMT, was lower with the figure-of-8 coil than with the circular coil at all ISIs from 1 to 3.5 ms, and only with the figure-of-8 coil were there less than 5% of the recordings without inhibition (Table 1D, Figure 3).

*Comparison of pain and discomfort during examinations*

Most subjects experienced mild pain/discomfort with both coils; however, the mean NRS scores were significantly lower for the figure-of-8 coil (1.90 ± 1.28) than for the circular coil (2.83 ± 1.60) ($p < 0.001$). Moderate discomfort (NRS = 4, 5 or 6) was reported six times in the 40 sessions (morning and afternoon) with the figure-of-8 coil and fourteen times with the circular coil. None of the subjects experienced severe pain/discomfort (NRS ≥ 7) with any of the coil types (Figure 4).

## Discussion

The most striking findings of this study are that the figure-of-8 and circular coils had similar reproducibility, but the figure-of-8 coil showed loss of inhibition in fewer healthy subjects than the circular coil, which is of clinical interest in the examination of patients. Moreover, examinations with the circular coil felt more unpleasant than with the figure-of-8 coil.

### *Comparison of reproducibility*

There were no statistically significant differences in the limits of agreement between the two coil types; however, both coils had quite wide limits of agreement. This displays a weakness in using SICI-parameters for diagnostic purposes. As such, repeat recordings are advisable to control for the natural variation in test results.

### *Comparison of SICI-parameters*

Like the previous studies [15] [1], we found that SICI peaks at an ISI of around 3 ms. This was seen with both the figure-of-8 and circular coils. A significant difference was found in the SICI time course at 2 ms ISI. The most probable explanation for this may be that, due to the different magnetic fields generated, the two coils are examining different structures [7, 13] [2,11]. Future studies could further investigate the reason behind this difference and any potential clinical implications.

Our findings do, however, conflict with the previous comparison between figure-of-8 and circular coils recording T-SICI from APB [14]. Van den Bos et al. found significantly less SICI at 3 ms and less SICI averaged over 1-7 ms with a figure-of-8 coil, whereas we found no significant difference in these values. From their standard error values, one can infer that they found a similar coefficient of variation (CV) for mean SICI from 1-7 ms with a circular coil (90.6%) as did we (89.8%), but with the figure-of-8 coil they found a similar CV (82.5%), whereas ours was smaller (60.5%), consistent with our finding of a reduced inter-subject variation. The reason for this different experience is unclear but may relate to the more critical positioning of the figure-of-8 coil.

A probably more interesting fact in the context of coil choice in a clinical setting is that there were no other significant differences in the average values of SICI-parameters between coil types. Some of the controls had large differences in SICI-parameters between coil types, but there did not seem to be systematic differences.

Since most laboratories use the figure-of-8 coil, it was of great clinical interest to compare these two coil types before other labs start testing the utility of T-SICI in ALS diagnosis. All of the previous studies suggesting TSICI as a possible biomarker for the diagnosis of ALS used circular coils [15-18], and therefore our study is of clinical relevance showing that the figure-of-8 coil is even more preferable in TSICI measurements. This study cannot provide information about which SICI parameter is most clinically relevant for diagnostic purpose; however SICI at 3ms ISI has been proposed to be decreased in ALS [15-18], and we did not find any difference in this parameter between the two coils. Interestingly, we found significantly lower between-subject

SDs of threshold measurements with the figure-of-8 coil than with the circular coil at most of the ISIs. This means that when it comes to comparing patients with controls, the figure-of-8 coil, which makes the different normal subjects appear more similar, is more likely to detect an abnormality in a patient. Accordingly, we found a lower incidence of lack of inhibition with figure-of-eight coil. Specifically, we found no figure-of-8 recordings without inhibition at ISIs of 3, 3.5 and 1-3.5ms, whereas the circular coil yielded a total of 13 recordings (10.8%) without inhibition at those ISIs. This may indicate a better applicability of the figure-of-8 coil in patients.

*Comparison of pain and discomfort during examinations*

We found significantly higher NRS-scores for the circular coil. However, most subjects experienced only mild pain/discomfort with either coil, and none had severe pain/discomfort. Considering that patients with ALS go through more unpleasant examinations during their investigations, the pain/discomfort threshold may be higher in patients. We do not think that one coil can be particularly recommended over the other because of pain/discomfort, before this is further tested in patients.

*Limitations*

This study has a number of limitations. First, the number of subjects was limited, and their age-range was relatively young compared to ALS patients. Second, similar tests could have also been performed in first dorsal interosseous muscle, which is commonly used in most labs. Additionally, comparing the two types of coils with conventional amplitude SICI measurements would be ideal.

*Conclusion*

In conclusion, we found similar reproducibility of figure-of-8 and circular coils, and mean SICI parameters did not differ between the two types of coils apart from ISI of 2 ms. The mechanisms underlying this difference remain unclear. The lower variability between subjects seen with the figure-of-8 coil makes the finding of lack of inhibition in a normal subject less likely with this coil, and it could therefore be more sensitive in distinguishing patients from controls. Finally, although the difference is modest and may have limited clinical relevance, this study provides evidence that the circular coil on average causes more pain and discomfort than the figure-of-8 coil.

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**Declaration/conflict of interest:**

Hugh Bostock and James Howells receive from UCL a share of the royalties for sales of the Qtrac software used in this study. No other authors have conflict of interest to declare or financial interest in this project.

## References


[1] Awiszus F, Feistner H, Urbach D, Bostock H. Characterisation of paired-pulse transcranial magnetic stimulation conditions yielding intracortical inhibition or I-wave facilitation using a threshold-hunting paradigm. Exp Brain Res 1999;129:317-24.

[2] Chen R, Cros D, Curra A, Di Lazzaro V, Lefaucheur JP, Magistris MR, et al. The clinical diagnostic utility of transcranial magnetic stimulation: report of an IFCN committee. Clin Neurophysiol 2008;119:504-32.

[3] Dharmadasa T, Matamala JM, Howells J, Simon NG, Vucic S, Kiernan MC. The effect of coil type and limb dominance in the assessment of lower-limb motor cortex excitability using TMS. Neurosci Lett 2019;699:84-90.

[4] Di Lazzaro V, Restuccia D, Oliviero A, Profice P, Ferrara L, Insola A, et al. Magnetic transcranial stimulation at intensities below active motor threshold activates intracortical inhibitory circuits. Exp Brain Res 1998;119:265-8.

[5] Fisher RJ, Nakamura Y, Bestmann S, Rothwell JC, Bostock H. Two phases of intracortical inhibition revealed by transcranial magnetic threshold tracking. Exp Brain Res 2002;143:240-8.

[6] Geevasinga N, Menon P, Yiannikas C, Kiernan MC, Vucic S. Diagnostic utility of cortical excitability studies in amyotrophic lateral sclerosis. Eur J Neurol 2014;21:1451-7.

[7] Hess CW, Ludin HP. [Transcranial cortex stimulation with magnetic field pulses: methodologic and physiologic principles]. EEG EMG Z Elektroenzephalogr Elektromyogr Verwandte Geb 1988;19:209-15.

[8] Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, et al. Corticocortical inhibition in human motor cortex. J Physiol 1993;471:501-19.

[9] Menon P, Geevasinga N, van den Bos M, Yiannikas C, Kiernan MC, Vucic S. Cortical hyperexcitability and disease spread in amyotrophic lateral sclerosis. Eur J Neurol 2017;24:816-24.

[10] Menon P, Geevasinga N, Yiannikas C, Howells J, Kiernan MC, Vucic S. Sensitivity and specificity of threshold tracking transcranial magnetic stimulation for diagnosis of amyotrophic lateral sclerosis: a prospective study. Lancet Neurol 2015;14:478-84.

[11] Menon P, Higashihara M, van den Bos M, Geevasinga N, Kiernan MC, Vucic S. Cortical hyperexcitability evolves with disease progression in ALS. Ann Clin Transl Neurol 2020;7:733-41.

[12] Nakamura H, Kitagawa H, Kawaguchi Y, Tsuji H. Intracortical facilitation and inhibition after transcranial magnetic stimulation in conscious humans. J Physiol 1997;498:817-23.

[13] Samusyte G, Bostock H, Rothwell J, Koltzenburg M. Short-interval intracortical inhibition: Comparison between conventional and threshold-tracking techniques. Brain Stimul 2018;11:806-17.

[14] Van den Bos MAJ, Menon P, Howells J, Geevasinga N, Kiernan MC, Vucic S. Physiological Processes Underlying Short Interval Intracortical Facilitation in the Human Motor Cortex. Front Neurosci 2018;12:240.

[15] Vucic S, Howells J, Trevillion L, Kiernan MC. Assessment of cortical excitability using threshold tracking techniques. Muscle Nerve 2006;33:477-86.

[16] Vucic S, Kiernan MC. Novel threshold tracking techniques suggest that cortical hyperexcitability is an early feature of motor neuron disease. Brain 2006;129:2436-46.

[17] Vucic S, Kiernan MC. Transcranial Magnetic Stimulation for the Assessment of Neurodegenerative Disease. Neurotherapeutics 2017;14:91-106.

[18] Vucic S, van den Bos M, Menon P, Howells J, Dharmadasa T, Kiernan MC. Utility of threshold tracking transcranial magnetic stimulation in ALS. Clin Neurophysiol Pract 2018;3:164-72.

[19] Ziemann U, Winter M, Reimers CD, Reimers K, Tergau F, Paulus W. Impaired motor cortex inhibition in patients with amyotrophic lateral sclerosis. Evidence from paired transcranial magnetic stimulation. Neurology 1997;49:1292-8.

**<u>Table 1</u>.** Comparisons between circular (Circ) and figure-of-8 (F8) coils

| | A. Mean threshold increase (% RMT) | | | B. SD threshold increase within subjects (% RMT) | | | C. SD threshold increase between subjects (% RMT) | | | D. Recordings without inhibition | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ISI (ms) | Circ | F8 | Circ – F8 | Circ | F8 | F ratio Circ/F8 | Circ | F8 | F ratio Circ/F8 | Circ | F8 |
| 1 | 6.42 | 4.54 | 1.88 | 5.88 | 4.95 | 1.41 | 9.75 | 5.12 | 3.63** | 9 | 7 |
| 1.5 | 5.15 | 7.02 | -1.87 | 4.94 | 4.43 | 1.55 | 9.20 | 6.55 | 1.97 | 10 | 3 |
| 2 | 3.69 | 9.46 | -5.77** | 4.94 | 6.03 | 0.67 | 9.15 | 9.92 | 0.85 | 11 | 1* |
| 2.5 | 9.43 | 13.05 | -3.62 | 6.03 | 7.08 | 0.72 | 15.52 | 10.70 | 2.10 | 9 | 1* |
| 3 | 14.18 | 14.62 | -0.44 | 6.62 | 7.73 | 0.73 | 15.83 | 9.27 | 2.92* | 4 | 0* |
| 3.5 | 13.79 | 13.15 | 0.64 | 6.50 | 6.82 | 0.91 | 13.44 | 9.77 | 1.89 | 3 | 0* |
| 4 | 12.38 | 10.90 | 1.48 | 6.55 | 5.80 | 1.27 | 11.95 | 9.08 | 1.73 | 2 | 4 |
| 5 | 10.52 | 8.23 | 2.30 | 5.42 | 5.88 | 0.85 | 12.24 | 8.02 | 2.33* | 6 | 5 |
| 7 | 2.90 | 2.99 | 0.59 | 5.52 | 6.71 | 0.68 | 13.32 | 6.85 | 3.78** | 10 | 11 |
| 1–7 | 8.74 | 9.23 | -0.59 | 4.06 | 4.40 | 0.85 | 10.45 | 6.55 | 2.55* | 5 | 1* |
| 1-3.5 | 8.77 | 10.3 | -1.54 | 4.80 | 4.64 | 1.07 | 11.15 | 7.19 | 2.40* | 6 | 0* |
| 2-3 | 9.10 | 12.38 | -3.28 | 5.12 | 6.26 | 0.67 | 13.02 | 9.37 | 1.93 | 9 | 1* |

A. Mean inhibition as percentage of resting motor thresholds (RMT), and difference between coils, ** = $P$<0.01 (paired t-test). B. Threshold variation expressed as within subject standard deviation (SD) and coils compared by F ratio (none significant). C. Threshold variation between subjects, * = $P$<0.05, ** = $P$<0.01 (F-test). D. Numbers of recordings (out of 40) without inhibition, i.e. with thresholds lower than RMT, * = <5%. The figure-of-8 coil has a clear tendency to produce less variable inhibition between subjects and fewer recordings without inhibition than the circular coil.

**Figure legends:**

**Figure 1.** Bland-Altman plots for evaluation of agreement between T-SICI obtained in morning and afternoon sessions for the figure-of-8 coil (left column) and the circular coil (right column) at different interstimulus intervals (ISI). Each point represents a control person, with the X-value indicating the mean value for the two sessions and the Y-value indicating the difference (Diff.) between the values of the two sessions. The bias (mean) is shown as a solid line, and the upper (ULA) and lower (LLA) limits of agreement are shown as dotted lines. The limits of agreement represent a constant multiplied by the SD of the differences between first and second sessions. The p-value for the comparison of limits of agreement for the two coils are stated on the left for each ISI.

**Figure 2.** Mean inhibition as a percentage of resting motor threshold (% inhibition) (part A), and threshold variation as standard deviations (SD) (part B) as a function of interstimulus interval. Data from both examinations with each coil are combined. Blue line: Figure-of-8 coil, Red line: Circular coil.

**Figure 3.** Coil comparison, showing the numbers of recordings with (above the line) and without (below the line) inhibition for A: average SICI from ISIs 1-3.5ms and B: at ISI of 2.5 ms.

**Figure 4.** Pain and discomfort rated by the subjects for the figure-of-8 (bottom) and circular coils (top) in the 40 sessions.

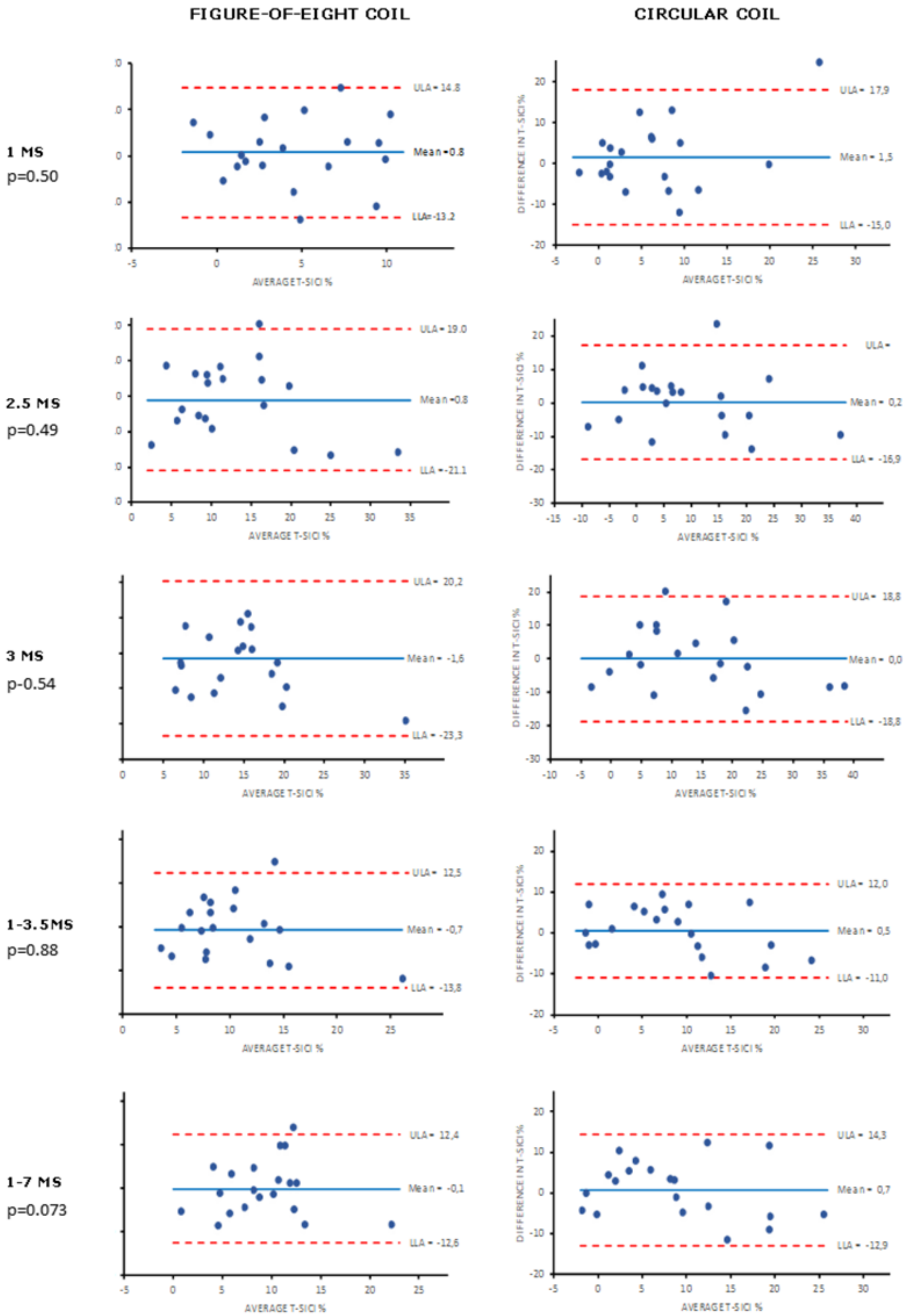


FIGURE-OF-EIGHT COIL
CIRCULAR COIL
1 MS
p=0.50
2.5 MS
p=0.49
3 MS
p-0.54
1-3.5MS
p=0.88
1-7 MS
p=0.073
ULA= 14.8
Mean=0.8
LLA=-13.2
ULA= 17,9
Mean= 1,5
LLA= -15,0
ULA= 19.0
Mean=0.8
LLA=-21.1
ULA=
Mean= 0,2
LLA= -16,9
ULA= 20,2
Mean= -1,6
LLA= -23,3
ULA= 18,8
Mean= 0,0
LLA= -18,8
ULA= 12,5
Mean= -0,7
LLA= -13,8
ULA= 12,0
Mean= 0,5
LLA= -11,0
ULA= 12,4
Mean= -0,1
LLA= -12,6
ULA= 14,3
Mean= 0,7
LLA= -12,9
AVERAGE T-SICI %
DIFFERENCE INT-SICI %

Figure 1

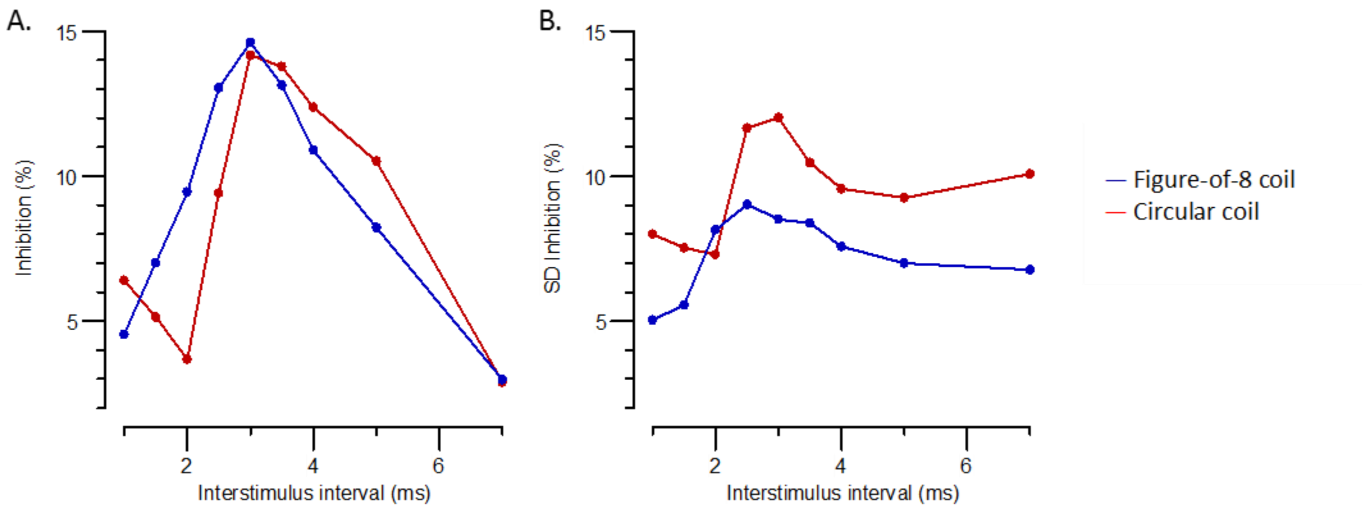



Figure 2

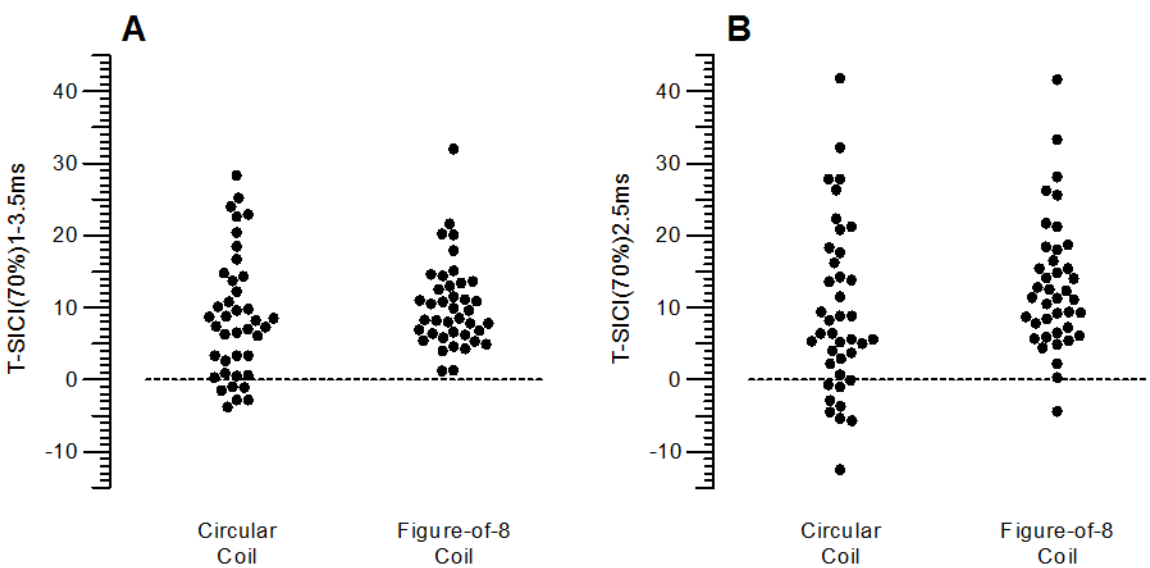
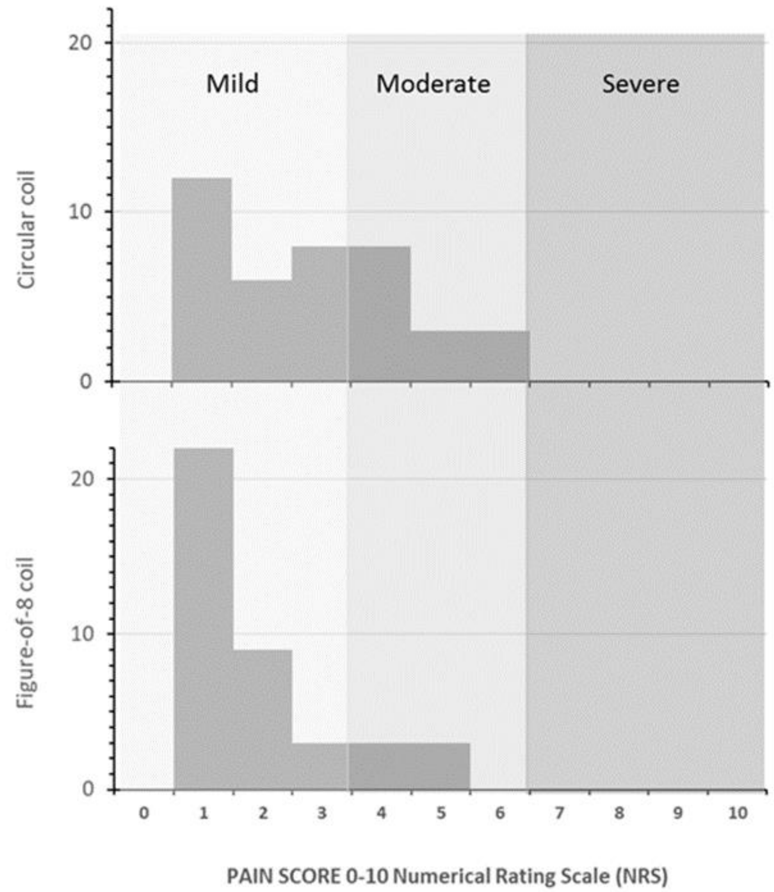



Figure 3



Mild
Moderate
Severe
Circular coil
Figure-of-8 coil
20
10
0
20
10
0
0
1
2
3
4
5
6
7
8
9
10
PAIN SCORE 0-10 Numerical Rating Scale (NRS)


Figure 4