A questionnaire to collect unintended effects of Transcranial Magnetic Stimulation: A consensus based approach

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Abstract

In the last decades, transcranial magnetic stimulation (TMS) has been widely used in both clinical and research practice as a tool to modulate brain activity and behaviour. However, besides the intended modulatory effects, TMS might induce unintended sensations and undesired effects as well as serious adverse effects. Of note, serious adverse effects are extremely rare, while most participants report mild sensations that typically disappear a few minutes after the end of the stimulation. To date, no shared forms are available to report such unintended effects. The present study applied a web-based Delphi procedure to develop a questionnaire that would enable systematic reporting of TMS unintended effects and is based on consensus among TMS experts. A steering committee nominated a number of experts to be involved in the procedure, which resulted in a questionnaire that is applicable in clinical and research settings. Routine use of the questionnaire and standard reporting of the TMS effects will help to secure the safe use of TMS, particularly when applying new protocols that are not covered by the already published TMS safety guidelines. Use of the structured TMS questionnaire could in turn improve the quality of data collection as well as the interpretation of experimental findings.

Highlights

- A TMS questionnaire was developed to report secondary effects following TMS application;
- A Delphi procedure was used to reach a consensus on items among international TMS experts;
- The TMS questionnaire could improve the quality of data reporting in TMS studies;
- An online version of the questionnaire has been implemented.

Keywords: Transcranial magnetic stimulation, safety, TMS adverse events, TMS secondary effects, neuromodulation, non invasive brain stimulation

1. Introduction

Over the last 35 years, transcranial magnetic stimulation (TMS) has been widely used to modulate neural activity, directly or indirectly, in cortical or subcortical circuits through rapidly changing electromagnetic fields generated by a coil placed on the head (George and Post, 2011). TMS modulates brain activity and behaviour while remaining a safe and low-risk tool, justifying its growing application for research and clinical purposes (Rossi et al., 2009; 2021). Therefore, the number of laboratories and clinical institutions using TMS and the number of individuals undergoing TMS for research or therapeutic purposes has rapidly increased in recent years. Importantly, besides the intended

neuromodulatory effects, TMS might induce unintended sensations and undesired effects, ranging from very mild side effects (SE) to adverse events (AE) and serious adverse events (SAE) (Rossi et al., 2021; Sczesny-Kaiser et al., 2013). More specifically, SE refer to unintended and not harmful reactions, in addition to (or in extension of) the desired effects, that may generally include changes in hearing, local pain, muscle contractions, headache, and discomfort. On the other hand, AE and SAE refer to unintended, harmful, and undesirable reactions, that in case of SAE include syncope and seizures, to TMS application, although delivered at a correct "dose", within the boundaries suggested by international safety guidelines (Rossi et al., 2021). Of note, whereas AE and SAE are rare, most participants report SE that typically disappear within a few minutes after the end of the stimulation.

To date, no standardized agreed-upon procedures are available to report such events that may affect, to some extent, stimulation outcomes or participant's sensation towards the procedure. Therefore, unintended effects are not systematically and explicitly described in TMS papers. In addition, even when undesired effects are reported, there is a lack of details about potential risk factors related to participants, such as their medications or psychophysical state. This information, together with a more complete description of the stimulation parameters, should be systematically provided/shared to allow more reliable comparison among studies (Chipchase et al., 2012). By identifying further and more detailed potential risk factors of SE/AE/SAE, we will be better prepared to decide how to regulate stimulation parameters in light of the emergence of new stimulation protocols (e.g., patterned TMS; Sorkhabi et al., 2021). As pointed out during the International Federation of Clinical Neurophysiology (IFCN), Workshop which took place in Siena (Italy) in October 2018 on "Present, Future of TMS: safety, Ethical guidelines" there is the need for standardized SE/AE/SAE reporting modalities with forms that could be used by TMS practitioners and researchers. The absence of systematic reporting of TMS-related undesired effects leads to a consequent lack of information, also with respect to the benefit/risk ratio of this technique.

Systematically reporting TMS-related SE, even if very mild, is important for monitoring and accounting for factors that may potentially influence experimental outcomes, such as sensorial confounding factors. As previously suggested for electrical stimulation, SE might even invalidate the experimental and clinical results (Fertonani et al., 2015). Uncomfortable sensations might affect participants' performance (e.g., by distracting them) in experimental tasks or increase drop-out rates. For example, scalp discomfort caused by TMS has been shown to positively correlate with the number of errors made on cognitive tasks (Abler et al., 2005). A recent study (Meteyard and Holmes, 2018) assessed the relationship between discomfort and twitches induced by TMS delivered on several scalp locations and the performance in cognitive tasks: the authors found that the scalp sensations and sensory SE of TMS predicted slowing down of cognitive performance with increased reaction times. Such an influence of

TMS-induced sensory SE could also be analyzed on clinical, electrophysiological or neuroimaging outcomes.

Previous attempts to improve quantitative reporting of undesired effects associated with TMS have been made by some recent studies that explored these effects retrospectively (Lerner et al., 2019; Maizey et al., 2013). For instance, Lerner and colleagues (2019) conducted a survey to quantify seizure risk of TMS as well as the occurrence of other AE. The survey covered 318,560 TMS sessions conducted in several laboratories or clinics for a five-year period (2012-2016). In particular, researchers were asked to retrospectively report details about the TMS sessions and the occurrence of serious AE. Unfortunately, no information was collected about minor SE, which could have been neglected to be mentioned by the participants or the researchers, because not explicitly requested. In another study, Maizey and colleagues (Maizey, 2013) used a post-monitoring methodology to determine the incidence rate for a range of unintended TMS effects according to various factors, such as stimulation protocol and site as well as participants' subjective factors (e.g., medication). The authors found a moderate incidence rate of mild AE (39%) among participants. However, this data can be biased in a number of ways and there is always a need for more precise and causal inferences about these minor SE through a comprehensive, systematic and/or quantitative assessment.

To our knowledge, many clinicians and researchers working with TMS usually conduct an informal debriefing after each session. However, as there is not a standardized questionnaire to conduct such an interview, information collected across laboratories (or, even, from different experimenters within the same laboratory) lacks consistency and, as a consequence, the data might not be directly comparable.

To overcome this issue, the present work aimed at implementing an instrument (i.e., a questionnaire) for systematic reporting of TMS unintended effects through consensus among worldwide TMS experts. To this end, we adopted an observational approach using an online Delphi technique that is a reliable and broadly used method to reach consensus among experts of a specific topic (Vernon and Vernon, 2009). Additionally, after reaching consensus among the experts, the Delphi consented questionnaire was submitted for sharing in the IFCN website to gain further approval by the scientific community.

2. Methods

2.1 Delphi procedure

We conducted an online Delphi procedure approved by the Ethics Committee of the IRCCS San Camillo Hospital, Venice, Italy. The Delphi is a structured procedure that utilizes a series of questionnaires to collect information from experts. The Delphi methodology leads to a consensus among worldwide experts on a given area of interest. The consensus is reached through a series of rounds in which summaries of the data from each round are presented to the experts that are asked to provide their

opinion round by round until consensus is reached (Hasson et al., 2000). The Delphi procedure was chosen because it has several benefits: i) it is implemented on the web; ii) it allows the inclusion of a large number of experts across different countries; iii) it allows communication *via* email; iv) it allows to keep participants' anonymous; v) it makes it possible to collect feedback through consecutive rounds in which the questionnaire is progressively revised by many experts; vi) it allows analysis and summarization of the data; vii) it reduces the possibility that an expert or a group dominate the process. The Delphi procedure starts with the implementation of a steering committee that proposes the items on which opinion is requested, nominates the experts' panel that should evaluate them, and manages data collection and analysis. All the members of the steering committee had at least one publication in the field of non invasive brain stimulation.

In the present work, the steering committee, comprising all the authors, established the main characteristics of the questionnaire by creating a first draft of the survey to be submitted to the experts. Each member of the steering committee defined the essential criteria of the questionnaire, generated items and revised them in a shared online form. The questionnaire was developed based on the current evidence in the field. A first draft of the questionnaire was then shared among the members of the steering committee and piloted before starting the procedure to ensure that the instructions were clear. The pilot was conducted by administering the questionnaire to a group of 10 naive participants to a TMS study whose main aim was not the administration of the questionnaire. Afterwards, the questionnaire was implemented online in the Delphi decision Aid website and a uniform resource locator (URL) link to the website and to a related survey was created. Afterwards, each member of the steering committee provided a list of experts to be contacted. Nominated experts were searched across the major research databases (Scopus and PubMed) to verify they had at least 2 publications in the field of TMS. We invited 113 international participants from 85 hospitals or research institutions located in 29 different countries (Table 1). Experts were contacted through an invitation letter sent by email including the URL link to the questionnaire. When they accepted to participate, experts were given three weeks to provide their answers in each round. A reminder was sent to those experts who had not responded within one week. A total of three anonymous rounds were performed. During the first round, the survey was individually completed (online) by each expert and data were downloaded into a database by a member of the steering committee. As the Delphi decision Aid website was disabled without any notice by the site administrator after the end of the first round, all the subsequent rounds were implemented in a Google Drive module and experts were provided with a new link to the questionnaire by email. Two members of the steering (A.G., F.B.) collected data round by round and prepared a data summary to be shared with all other members of the steering committee.

In round 1, experts were first introduced to the aims of the Delphi procedure. Then, the questionnaire was presented, and they were asked to express their opinion about each item included in the

questionnaire. Specifically, each expert was invited to indicate which items they would have excluded from the questionnaire, to revise current language forms, to merge items, or to propose new items for each section. Additionally, each expert had the opportunity to provide extended comments and suggestions in a dedicated text box. The questionnaire was then revised in accordance with data obtained by this round.

In round 2, only the experts who completed the first round were contacted again by email and invited to fill out a new survey on a Google Drive module. In this round, experts were advised about items that had been removed after the results obtained during the first round, and about any other modifications. Additionally, a list of suggestions and comments that were proposed by the experts during the first round, for each section, was provided. Experts were asked to rank on a five-point Likert scale their opinion about the inclusion of each suggestion embedded in the list. A score of 5 indicated that the expert strongly agreed with the inclusion of an item in the questionnaire. Again, an open box was presented in each section of the survey so that experts could provide additional comments. Upon completion, data collected from round 2 were used by 2 members of the steering committee (A.G., F.B.) to further revise the survey.

Experts that completed round 2 were contacted to participate in round 3. In this round, they were presented with the final version of the questionnaire (comprising all revisions) as well as with a summary of experts' comments provided in round 2. Round 3 included the list of approved items from round 2. Again, a text box was available to report further comments and suggestions. At the end of the third round, each expert was invited to state if they approved or not the questionnaire in its final version, to reach final consensus.

2.2 Questionnaire design

The original version of the questionnaire (prepared by all the authors) comprises 5 sections and has been thought to be administered by the experimenter/clinician to participants taking part in TMS studies or therapeutic intervention immediately after the end of each stimulation session. In the questionnaire, section 1, named "*Participant general information*" requires reporting participants' demographic characteristics such as age and gender. Experimenters are also asked to specify whether participants took part in other TMS studies in the past and, in case of an affirmative response, information about participation in these previous studies is requested. In this section, a specific and dedicated subsection for patients is also included. This subsection aims at clarifying whether TMS is applied as a treatment for a specific disease and whether patients are affected by pathological conditions other than the one treated with TMS. Section 2, named "*Participant specific information*", includes a list of questions investigating participants' habits that are known to influence TMS outcomes (e.g., "how much sleep did you get last night?", "did you drink alcohol in the last 2 days?"). Section 3 is named "*Experimental*

protocol" and has been intended to be filled with details relative to the current TMS application (e.g., TMS device, coil size, stimulation site). Section 4, named "*Stimulation related sensations*", comprises a table listing possible sensations that arose during TMS administration. For each sensation, it is required to score the degree of possible discomfort with a 5-point Likert scale ranging from 0 (none) to 4 (strong), and to specify when the sensation began and how long it lasted, as well as the location of the sensation. In this section, participants also have to report their subjective feelings regarding the effects they believe the TMS-induced sensations had on their performance. Finally, section 5, named "*Adverse events*", comprised an open-ended question to report and score on a 5-point scale any adverse effect or serious adverse effect that might have occurred during the session. In this section, blood pressure and heart rate of the participants should be reported if measured in case of AE/SAE. The structure of the questionnaire did not much change throughout the Delphi procedure. In the last version, items mostly match items of the initial draft of the questionnaire. Overall, the following questions were added: "are you tired?", "which TMS device was used?" (monophasic/biphasic TMS). Moreover, additional information about TMS parameters (total number of pulses, inter-stimulus interval), the electric field direction and neuronavigation are now required.

2.3 Data analysis

All data was entered into Microsoft Excel. Medians were calculated where possible.

In the first round, the percentage of experts voting for exclusion was computed for each item of the questionnaire. Responses to the second round were reported in terms of the median of the 5-point Likert scale. Responses to the third round were reported in terms of percentage of experts approving the questionnaire as the final version. Rounds' results were shared and discussed among the members of the steering committee via email. In the first round, items were removed when more than 60% of the experts indicated that the item had to be excluded from the questionnaire (Chipchase et al., 2012). In the second round, items were included in the questionnaire if the median of the 5-point Likert scale was higher than 3. In the third round, experts were asked to report further comments and to approve or not the questionnaire as the final version. The consensus was reached when 60% of the experts approved the questionnaire as the final version.

3. Results

Overall, 21 of the 113 participants initially invited to participate contributed to the first round of the survey, 15 experts took part to the second round and 10 experts to the third one. Demographics about the participants are provided in Table 1. In the first round, only 2 items (IQ and ethnicity) reached the 60% threshold for exclusion (Figure 1). Additionally, each expert provided a list of new items to include in the questionnaire as well as a list of changes to apply to the current questionnaire's items.

Specifically, for section 1, experts' comments were related to the replacement of some words/sentences and to the inclusion of 6 new items in the questionnaire. For section 2, experts proposed to clarify some questions and to include a visual analogue scale (VAS) to gather more information in relation to some of the items. In section 3, experts proposed including new items related to the TMS stimulator brand and type and to stimulation characteristics. In section 4, experts proposed to add a VAS to report information also about the magnitude of perceived sensations. In section 5, experts proposed to add a question concerning information about the weight and height of the participants and to add a VAS to score the severity of the possible AE. Overall, a list of 29 items was derived from round 1 and presented to the experts in round 2. In this round, 18 out of 29 suggestions proposed by the experts reached the threshold to be included in the final version of the questionnaire (Figure 2).

In the third round, all the experts but one approved the survey as the final version. One expert did not approve the questionnaire as the last version since she/he suggested a few new changes on some questions. In particular, this expert proposed to remove the following item: "Are you playing video-games?" with the following motivation: "*it is very specific and if you go down that path you will need to include all other relevant hobbies/activities otherwise you are given undue weight to this one*". The suggestion was discussed among the members of the steering who decided to finally remove the item. The online version of the final questionnaire will be available at the Psytoolkit website after the publication of the manuscript.

4. Discussion

The aim of this study was to design a standardized questionnaire that helps reporting SE/AE related to TMS. The questionnaire was developed through a Delphi procedure, implemented online, with the aim of reaching a consensus among experts in the field. The questionnaire could be used in research as well as in clinical settings.

Reporting information about potentially undesired TMS effects in a standardized format will provide the unique opportunity to quantify the incidence of minor SE, such as discomfort and unpleasant sensations induced by the stimulation, in addition to major AE, which are generally reported and collected in the medical and research study record. The main objectives of a systematic recording of TMS-induced SE, even minor ones, should be to determine the participant features or stimulation parameters linked to the generation of these effects on the one hand, and to assess the potential impact of these effects on the outcomes of the stimulation on the other hand. Therefore, the use of this questionnaire might constitute an important starting point for future studies investigating the safety of new TMS protocols. Documenting specific (and more detailed) participants' characteristics and protocol parameters will further enrich the understanding of the processes resulting in TMS-related SE or AE, possibly leading to the development of measures to minimize their occurrence and reduce

complications, for instance in experimental blinding. Several studies have already investigated the influence of different stimulation parameters on the discomfort of TMS session and some have reported the possibility of modifying a variety of these parameters to improve tolerance and therefore reduce potentially deleterious influence of TMS-induced SE and unpleasantness on the clinical impact of the procedure (Borckardt et al., 2013, 2006; Peterchev et al., 2017; Tani et al., 2021).

It is known that methodological factors such as the type of TMS stimulator, pulse waveform, coil type, coil orientation, position over the scalp, and stimulation parameters strongly contribute to TMS effects and sensations and should be monitored and reported. For example, the mapping of TMS induced unpleasant sensations across the scalp sites would improve the implementation of control conditions that are still at a sub-optimal level (Arana et al., 2008; Rossi et al., 2007). Many TMS experiments use the stimulation of a different scalp location (with respect to the target one) as a control condition (Meteyard and Holmes, 2018). In this condition, the TMS coil is generally placed over a brain region that is sufficiently far from the target region on the scalp, and/or that is considered to be not crucial for the investigated task (e.g., vertex). However, in this case, an open issue is related to the fact that peripheral sensations induced by the stimulation of the control site may not be identical to the sensation of the target one, hence resulting in some differences reflected in the observed findings. Thus, improving the knowledge about the sensations associated with different stimulation sites will allow implementing optimized control conditions, matching the experimental ones more closely and thus better controlling for confounding factors. Depending on the study design, items from the questionnaire could also be used to determine whether the results of a study have been confounded by secondary effects of stimulation, in relation to participants' characteristics.

During the Delphi procedure, suggestions and comments made by the experts' panel were rather in line with currently available evidence. For instance, experts suggested quantifying the alcohol consumption in the days preceding the TMS session. Alcohol consumption has been shown to affect response to TMS in previous studies (Kähkönen and Wilenius, 2007). Similarly, other studies have found that consuming drugs or some medication might lower seizure threshold, concurring in determining secondary effects during TMS (Kähkönen and Wilenius, 2007; Ziemann et al., 2015). Therefore, these aspects should be addressed in each TMS session.

From the initial version of the questionnaire, a few items were removed round by round. For instance, experts suggested not to include items such as information about IQ and ethnicity. Compatibly, no studies have been reported linking IQ to TMS response. On the other hand, despite being suggested that ethnicity could be a biological factor influencing inter-individual variability in TMS experiments, investigations on this factor are currently limited to few studies. For instance, a previous study showed the effect of ethnicity on the BDNF genotype, and on the frequency of one of the polymorphisms of the BDNF gene, that is the Val[66]Met (Pivac et al., 2009), a polymorphism that has been shown to modulate

the response to TMS (Cheeran et al., 2008). Additionally, differences in motor cortex excitability have been found between Chinese and Caucasians as measured with TMS in a previous study (Yi et al., 2014). Further investigations are needed to clarify whether response to TMS changes depending on ethnicity. However, ethnicity should account mostly for inter-individual variability in response to TMS dose. Indeed, individual factors contribute to the variability observed in reported effects of TMS but probably not to TMS secondary effects. Similarly, anatomical factors have also been suggested to contribute to inter-individual variability of TMS responses, including skull or cerebrospinal fluid layer thickness (Li et al., 2015; Pellegrini et al., 2018). Mapping all possible factors contributing to inter-individual variability in TMS is beyond the aim of the present questionnaire. This could explain why experts decided to exclude ethnicity from the final questionnaire. However, we cannot exclude that this choice simply reflects the personal theoretical framework of the panel and these additional data, as well as other details that are not included in the proposed questionnaire, could be collected anyways by interested researchers.

Similarly, an item discussed among panelists and members of the steering committee was the one related to the use of video games. In the final version, this item was removed from the questionnaire, with the reason that asking such information would necessarily imply controlling many other activities, such as sports or other hobbies. As one of the main objectives of the steering committee was to keep the questionnaire as easy to handle and administer as possible, immediately after experimental procedures or therapeutic sessions, they decided not to include these items in the final version and not to increase the total time required to complete it (currently estimated to be just more than 10 minutes). Additionally, no evidence has still been reported showing that such activities could affect responses to TMS or might cause SE/AE.

In conclusion, through the Delphi methodology we were able to develop a consensus-based questionnaire, primarily aimed at systematically reporting information about the occurrence of TMS-related SE/AE with a specific focus on sensory SE. This will be useful to better define possible TMS "interference effects" during experimental protocols, that is an important matter to which still little attention is being paid in current practice. More specifically, following the findings of previous studies (Machii et al., 2006; Oberman and Pascual-Leone, 2009), we suggest that this questionnaire should be ideally used to report information relative to every TMS study. Information on experimental sessions, obtained from the questionnaire, could be reported in scientific articles to allow control for any individual, methodological, and risk factor that might affect TMS effects or safety. Of note, this information should be ideally reported also for patients, so that TMS effects might be classified in clinical applications. In other words, it is reasonable to expect that using this questionnaire and sharing the information provided by the questionnaire among scientists could result in new measures to improve TMS comfort and safety for both healthy participants and patients. Compatibly, this will allow us to

keep monitoring patients' responses to TMS and potential risk factors related to specific pathologies. The only risk of a systematically applied structured questionnaire is to induce answers linked to negligible or irrelevant effects, which would not be mentioned spontaneously by the participants during a free interview. This can induce an overestimation of the effects and potentially confuse the message concerning the safety of the technique at the level of its real clinical significance.

In the long term, the use of this questionnaire will contribute to: i) clarifying individual risk factors associated with the occurrence of TMS-related SE and AE/SAE; ii) clarifying risk factors associated with specific TMS protocols; iii) classifying all the SE and AE/SAE related to each TMS protocol; iv) monitoring the effects of emerging TMS protocols; v) developing new sham or control protocols based on a systematic knowledge of TMS effects, for instance, regarding scalp sensations; vi) sharing enriched and more homogeneous information among scientists; vii) establishing shared standardized procedures for collecting and reporting TMS-related SE and AE/SAE.

Conflict of Interest:

Hartwig R. Siebner has received honoraria as speaker from Sanofi Genzyme, Denmark and Novartis, Denmark, as consultant from Sanofi Genzyme, Denmark, Lophora, Denmark, and Lundbeck AS, Denmark, and as editor-in-chief (Neuroimage Clinical) and senior editor (NeuroImage) from Elsevier Publishers, Amsterdam, The Netherlands. He has received royalties as book editor from Springer Publishers, Stuttgart, Germany and from Gyldendal Publishers, Copenhagen, Denmark.

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Figures and tables

Table 1. Demographic data of the expert panel participating in the Delphi procedure

Characteristics	N
Female	14
Male	7
Country	
Australia	1
Canada	2
Italy	9
Japan	1
New Zealand	1
USA	4
Current role	
Clinical researcher	3
Post-doctoral	2
Professor	10
Researcher	4
Discipline	
Engineering	1
Psychiatry	2
Physiology	2
Psychology	7
Physical therapy	1
Neurology	6
Institution	
Hospital	4
University	15
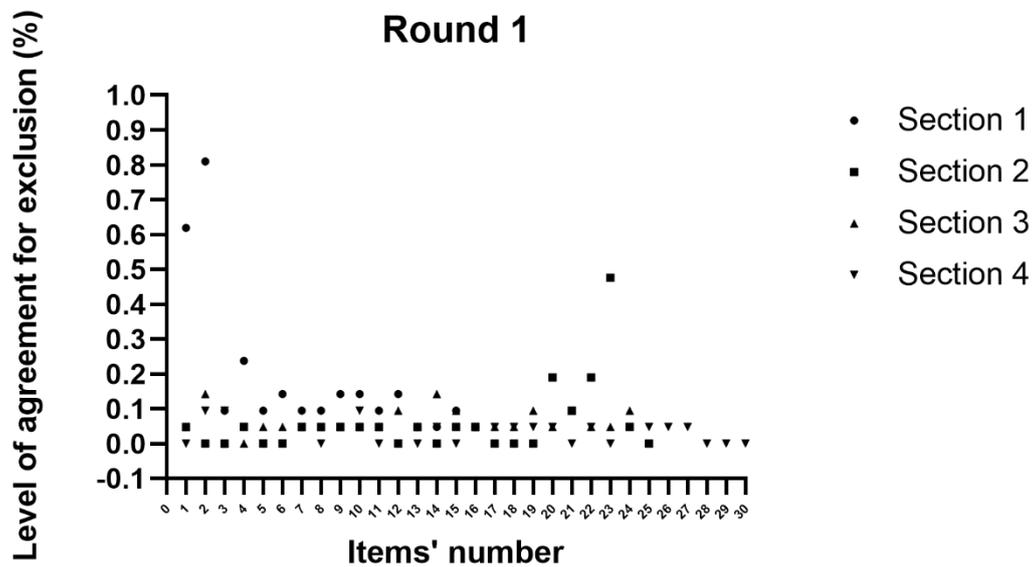
Figure 1. Percentage of experts voting for exclusion computed for each item in round 1. A percentage higher than 60% indicates that the item was selected to be excluded from the questionnaire. None of the items was proposed to be removed from section 5.
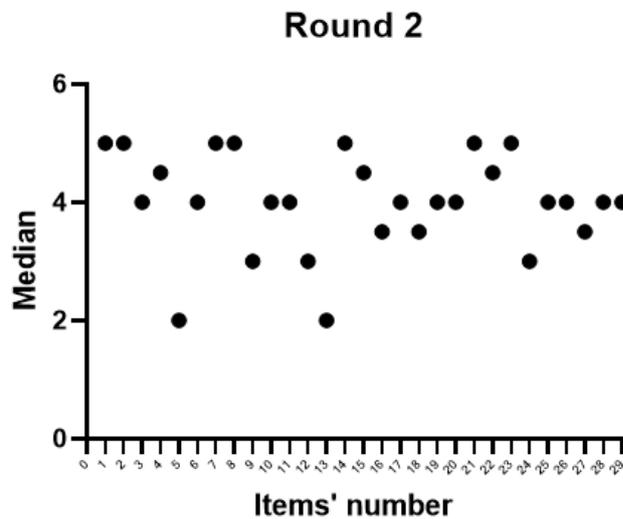
Figure 2. Median of the score in the 5-point Likert scale for each item of the Round 2. Five represents a response of 'strongly agree' with the inclusion of the proposed item in the questionnaire.

TMS ADVERSE EVENTS AND ASSOCIATED SENSATIONS QUESTIONNAIRE

The present questionnaire is intended to be administered by the experimenter at the end of each experimental session

Section I- Participant general information

To be filled for the first session only   **Date __ /__ /__**

Laboratory ID _____

Study ID *(please, specify an unique code for the study)* _____

Experimenter ID _____

Subject ID *(please, specify an unique code for the subject)* _____

Subject's group *(when applicable):* Patients ○   Healthy ○

Sex: F ○ M ○   *Handness_____*   **Age__**

Neurological/psychiatric/cardiovascular/ other diseases: past ○ current ○ *please,*

specify _____

- *Did you ever have any sort of brain stimulation in the past?* Yes ○ No ○
- *If yes, how many sessions?* _____ *How long the stimulation lasted approximately?* _____ *When did you take part in this session?* _____
- *Did you experience any adverse effect?*
- *Have you ever lost consciousness? If yes, how many times in the last year? Can you provide a brief description of the reason?* _____
- *How often do you drink alcohol?* _____
- *If so, how much do you drink per week?*
- *Are you a smoker?* _____
- *If so, how much do you smoke per week?*
- *Substance consumption Yes/Not*
- *If yes, which substances and when/how often?*

For patients only
For which disease is the TMS applied?_____

Does the patient have any other disease?_____

Did the patient experience a reduction/exacerbation of symptoms? If yes, what?
_____

Section II- Participant specific information

To be filled before each session

Experimental condition _____   Subject ID _____   Study ID_____
Date __ /__ /__

- *How much sleep did you get last night (hours)? _____, the quality of your sleep was good ○ inadequate ○ poor ○*
- *Do you feel rested? Yes □   not □*
- *Last menstruation (if applicable) _____   Do you assume any contraception or hormonal form? _____*
- *Did you drink alcohol in the last 2 days? _____, if yes, what?_____ how much (please specify unit)? _____, in the last day? _____*
- *How many cigarettes did you smoke in the last 24 h, approximately? _____*
- *How many coffees did you drink in the last 24 h? _____   how many coffees on average do you drink per day? _____*
- *Are you taking any medication? _____   if yes, what?_____ last consumption_____*
- *Any other substance use _____, if yes, what _____ how many times did you take this substance in the last 24 h? _____, how many times did you take it in the last year, approximately? _____*
- *Are you tired? (VAS)*
- *Did any Adverse Event occur since last visit? If yes fill out AE form (last section)*

Section III- Experimental protocol

If the experiment counts only one session or the same TMS parameters are used in each session (e.g., treatment) this part should be filled for the first session only. Please, fill this part whenever stimulation parameters differ from those used in the first session. If several protocols of stimulation are applied, please reprint this page, and fill it out for each applied protocol.

Subject ID _____ **Study ID**_____   **Date** __ / __ / __

Experiment: **Treatment** ○   **Single session** ○   **Multiple sessions** ○

For multiple sessions or treatment: Number of the current Session _____ Total number of Sessions _____   Hours/days passed between the current session and the previous session _____

Protocol
TMS device (name) _____   monophasic TMS ○   biphasic TMS ○

Online stimulation ○   Offline stimulation ○   Pulse width_____

Coil size/code_____: Figure 8 ○ double cone ○ circular ○ double cone coil ○ H coil ○

Parameters:
Single pulse ○ rTMS ○ patterned TMS ○   Paired- TMS ○
other ○ (please. specify)_____

Number of pulses _____ Frequency _____ (interpulse interval) Number of trains _____

Intertrains interval _____ Intensity _____ (% of maximum stimulator output)

Total duration _____

Input/output curve ○ intensities (%) _____; number of pulses for each

intensity _____;

Please. specify the type of threshold: MEP ○ contraction ○ active motor threshold in left

hand ○ right hand □ Resting motor threshold in dominant hand ○ Phosphenes ○ Other

(please, specify) ○ _____ Intensity _____ (% of the motor/phosphenes threshold)

E-field TMS intensity evaluation ○ please specify which software was used_____

Earplugs ○ white noise ○

Was the session completed ○ prematurely terminated ○ ? If prematurely terminated,

specify the reason

_____

Stimulation sites *(please specify)* _____

Please specify the exact coil position (and coordinate system) over the scalp
_____

How was the correct position found? Individual MRI □ Template MRI □ 10/20

system □ MEP □ Phosphenes □ Other □ (please specify): _____

Please specify whether TMS was preceded by □ followed by □ contemporary to □ other NIBS
(e.g., tDCS, tACS) _____

TMS was preceded by □ followed by □ contemporary to □ electroencephalography □ magnetic
resonance □ cognitive training/task □ other (please, specify) _____

Section IV- Stimulation related sensations

To be filled after each session

***Did you experience any of the following sensations? Please answer by inserting the number
that corresponds to the degree of the experienced discomfort, with 0 (None), 1 (Mild), 2
(Moderate), 3 (Considerable), 4 (Strong). Please, specify when the sensation started and how
long it lasted***

		When did the sensations begin				*How long did it last?*				*Location*
	Degree (from 0 to 4)	At the beginning of the stimulation	In the middle of the stimulation	Towards the end of the stimulation	After the end of the stimulation	It stopped quickly	It stopped in the middle of the stimulation	It stopped at the end of the stimulation	it stopped after the end of the stimulation (duration in min)	(e.g., head, arm, finger) Diffuse/localised/closed to stimulation

Scalp pain										
Toothache										
Tingling at scalp										
Tingling (peripheral nerves)										
Itching										
Burning or heat										
Headache										
Noise (e.g., tinnitus)										
Skin sensation										
Muscle contraction (excluding "targeted" MEPs)										
Fatigue										
Sleepiness										
Hearing changes										
Mood changes (depression)										
Mood changes (euphoria)										
Nausea										
Neck stiffness/ pain										
Coil pressure										
Anxiety/ Nervousness										
Difficulty in concentrating										
Other (specify)										

- *These sensations (when applicable): 1. enhanced the task performance ○; 2. hampered the performance ○; 3. did not affect performance ○*
- *If yes, how much?* Slightly ○   considerably ○   much ○   very much ○
- *Overall, your performance was enhanced □   hampered □   unchanged □ by the stimulation*
- *(For patients only) There has been any change in medication between sessions or in the last days?_____*

   Optional
- *Do you believe that in the current session you received a real or placebo/sham stimulation?* Real □   placebo □   I don't know □
- *Do you believe you received a placebo stimulation? _____, If yes, in which session? _____*

Section V- Serious adverse events

To be filled only in case of SAE/AE

Please report any adverse event (AE)/problem (e.g., dizziness, seizure, paresthesia, syncope, insomnia, anxiety or others, please specify) that occurred and classify the event on a scale from 1 (None) to 4 (Strong) and, when possible, specify the frequency.

_____
_____
_____
_____
If available, report blood pressure _____ and heart rate _____   values after the AE.
Notes:
_____
_____
_____
_____