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Review

A questionnaire to collect unintended effects of transcranial magnetic stimulation: A consensus based approach

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HIGHLIGHTS

- A TMS questionnaire, TMSens_Q, 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.

ABSTRACT

Transcranial magnetic stimulation (TMS) has been widely used in both clinical and research practice. However, TMS might induce unintended sensations and undesired effects as well as serious adverse

Abbreviations: TMS, transcranial magnetic stimulation; SE, side effects; AE, adverse events; SAE, serious adverse events; URL, uniform resource locator; IFCN, International Federation of Clinical Neurophysiology.

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Delphi procedure

effects. To date, no shared forms are available to report such unintended effects. This study aimed at developing a questionnaire enabling reporting of TMS unintended effects. A Delphi procedure was applied which allowed consensus among TMS experts. A steering committee nominated a number of experts to be involved in the Delphi procedure. Three rounds were conducted before reaching a consensus. Afterwards, the questionnaire was publicized on the International Federation of Clinical Neurophysiology website to collect further suggestions by the wider scientific community. A last Delphi round was then conducted to obtain consensus on the suggestions collected during the publicization and integrate them in the questionnaire. The procedure resulted in a questionnaire, that is the TMSens_Q, applicable in clinical and research settings. Routine use of the structured TMS questionnaire and standard reporting of unintended TMS effects will help to monitor the safety of TMS, particularly when applying new protocols. It will also improve the quality of data collection as well as the interpretation of experimental findings.

Contents

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 behavior while remaining a safe and low-risk tool, justifying its growing application for research and clinical purposes (Rossi et al., 2009, 2021; Turriziani et al., 2019). 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, non-specific tingling, 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). Once identified potential risk factors of SE, AE, SAE, we will be better prepared to decide how to regulate stimulation parameters, also in light of the emergence of new stimulation protocols (e.g., patterned TMS; Rogić et al., 2014; 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 standardized forms that TMS practitioners and researchers could use. 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. Moreover, systematically reporting TMS-related SE, even if very mild, is important for monitoring and accounting for variables 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 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 et al. (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 it was not explicitly requested. In another study, Maizey et al. (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, these data can be incomplete and 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 achieve consensus among experts of a specific topic (Vernon and Vernon, 2009). Additionally, after reaching consensus among the experts, the Delphi consented questionnaire was shared with the scientific community on the IFCN website, to gain further comments and suggestions.

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. Delphi is a structured procedure that utilizes a series of questionnaires to collect feedback 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 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.

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

Characteristics	N
Gender	
Female	16
Male	19
Country	
Italy	11
USA	7
Germany	4
Australia	4
Canada	2
Japan	2
UK	2
France	1
Russia	1
Malaysia	1
Position	
Professor	23
Researcher	9
Clinical researcher	3
Background	
Medicine (physiology, neurology, psychiatry)	18
Psychology	15
Engineering	1
Physical therapist	1
Institution	
University	29
Research centres	6

Each member of the steering committee, including all the authors, collaborated in building the questionnaire, defining its structure and main characteristics, generating items and revising them. The questions were developed based on the current evidence in the field (e.g., Lerner et al., 2019). A first draft of the questionnaire was then shared among the members of the steering committee and piloted before starting the Delphi 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 was created. Then, 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. A total of 113 international experts on TMS, from 85 hospitals or research institutions located in 29 different countries, were invited (Table 1). The experts were contacted through an invitation letter sent by email including the URL link to the questionnaire. Once they accepted to participate, they 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 (A.G.). 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 the 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 indicate which items they would have excluded from the questionnaire. Additionally, they were asked to provide any feedback and 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 at 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 5-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 also 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 declare if she/he approved or not the questionnaire in its final version, to reach a consensus.

After having completed the third round, the questionnaire, named TMSens_Q, and an original draft of the manuscript were publicized for a 4 weeks period on the IFCN website to collect suggestions from the wider scientific community. Collected suggestions and comments were submitted to the experts through a fourth round of the Delphi procedure. For this round, the 113 experts invited for the first round as well as 19 new experts and vendors from many TMS companies were contacted to gain a final consensus on the questionnaire and on the manuscript. Experts were given two weeks to provide their comments. The feedback from this last round was used for a final revision of both the manuscript and the questionnaire.

To expand the content validity of the questionnaire, we asked 20 researchers currently conducting experiments with TMS, to complete a rating scale to evaluate the final TMSens_Q (Martz, 2010). The following criteria were included in the rating scale: applicability, clarity, comprehensiveness, concreteness, ease of use, intelligibility, fairness, conciseness, and pertinence to the content area. Researchers were asked to rate each of the criteria on a 9 points Likert scale (1 strongly agree- 9 strongly disagree). Additionally, the following questions were included:

- Would you use the questionnaire in your next experiments?
- Is the questionnaire user-friendly?

Finally, we obtained an Italian version of the questionnaire through a backward translation. Namely, two independent translators read the English version of the questionnaire. A bilingual translator who was aware of the rationale and characteristics of the questionnaire translated it into her mother tongue (i.e., Italian). Afterwards, a bilingual naïve translator who was unaware of the objective of the questionnaire, produced a second translation from the Italian version to an English one. There were no significant differences between the two English versions of the questionnaires. However, minor points and discrepancies between the translations were discussed and solved among the translators and the authors.

2.2. Questionnaire design

The original version of the TMSens_Q (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 (or evaluated) 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 might arise 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 4-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 also reported (if measured), in case of AE/SAE.

2.3. Data analysis

In the first round, the percentage of experts voting for exclusion was computed for each item. According to a previous work, an item was removed when more than 60% of the experts voted for exclusion (Chipchase et al., 2012). In the second round, new proposed items were included in the questionnaire if the median of the 5-point Likert scale was higher than 3. In the third round, the percentage of experts approving the whole questionnaire as the final version was computed. The consensus was considered reached when at least 60% of the experts approved the questionnaire. In the fourth round, items proposed in the IFCN website were included if 60% of the experts approved their inclusion in the questionnaire. For each round, results were shared and discussed among the members of the steering committee via e-mail. Finally, a modified content validity index (I-CVI) was computed for each item of the rating scale by dividing the number of experts giving a rating of '1', '2', '3' or '4' by the total number of experts (Bakhshandeh Bavarsad et al., 2022). A mean CVI (CVI-ave) was then calculated as the average across all the I-CVI. According to

previous studies, a threshold acceptance level for each criterion was defined as a I-CVI > 0.80 (Rubio et al., 2003). A I-CVI lower than 0.80 would lead to a revision of the questionnaire with respect to the specific criterion not reaching the threshold. Similarly, a CVI-ave lower than 0.80 would imply a global revision of the questionnaire according to participants' suggestions.

3. Results

Overall, 21 (of the 113 experts initially invited) participated in the first round of the Delphi procedure. Fifteen out of 21 experts took part in the second round, 10 experts in the third one, and 6 experts in the fourth round, which was held after the publicization on the IFCN website. Fourteen new experts entered at this stage the Delphi procedure. Thus, a total of twenty experts completed the fourth round. Demographics about participants are provided in Table 1.

In the first round, only 2 items (IQ and ethnicity) reached the 60% threshold for exclusion. 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 (e.g., tiredness). In section 3, experts proposed to include 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, also adding a VAS to score the severity of the possible AE. Overall, a list of 29 items to be added was derived from round 1, and presented to the experts in round 2. In this round, 18 out of 29 items proposed by the experts reached the threshold to be included in the final version of the questionnaire.

In the third round, all the experts but one approved the survey as the final version. In particular, this expert suggested removing the 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.

During the 4 weeks of publicization on the IFCN website, the following items were proposed to be included in the section 1 of the questionnaire: "*Did you ever have any brain or spinal cord surgery in the past? If yes, when?*"; "*What is your weight and height?*"; "*Did you had any experience with electroconvulsive therapy?*"; "*Do you have any vision impairment?*"; "*When did you have your last meal?*"; "*At what time was the stimulation performed?*". In section 2, the following question was proposed to be included: "*Can you provide some information about your menstrual history?*". In this section, the question "*How many coffees did you drink in the last 24 h?*" was proposed to be modified to consider also other caffeine-containing drinks (e.g., tea, energy drinks). For section 3, the following items were proposed to be added: "*Rate your stress level on a VAS*"; "*Was any robotic assistance used for TMS coil placement?*". No suggestions were provided for section 4, whereas, in section 5, experts suggested to add the report of specific information related to possible syncope or loss of consciousness, such as, for instance, muscle tone, presence of involuntary contractions, eyes condition (open vs. closed), presence of incontinence, tongue biting.

In the fourth round of the Delphi, 3 items reached the threshold to be included in the questionnaire: "*Did you ever have any brain or spinal cord surgery in the past? If yes, when?*"; "*At what time was the stimulation performed?*"; "*How many caffeine-containing drinks (e.g., coffee, energy drink, tea) did you drink in the last 24 h?*". In section 5, specific information about SAE, such as muscle tone, eyes condition, and tongue biting, were embedded in the questionnaire.

The I-CVI, computed on data derived from the rating scale, ranged from 0.85 to 1 (Table 2). The average CVI across all the criteria was 0.92. As every item had a CVI of 0.80 or greater, the questionnaire was not revised further.

Overall, the structure of the questionnaire did not change substantially throughout the Delphi procedure. In the last version, items mostly matched items of the initial draft of the questionnaire, even if some questions have been added and others changed, in accordance with suggestions of the panel of experts. However, the number and structure of the main sections did not change. The final form of the questionnaire is appended to the manuscript (see the supplementary Appendix). Also, an online version was implemented, available at the following URL https://www.psytoolkit.org/c/3.4.0/survey?s=AC9ZE, on the Psytoolkit website (Stoet, 2010; Stoet, 2017).

Table 2
Results of the rating scale for each criterion. Item content validity index (I-CVI) was calculated as the number of participants rating < 5 divided by the total number of participants.

Item	Participants giving rating score < 5	I-CVI
Applicability	17	0.85
Clarity	18	0.9
Comprehensiveness	20	1
Concreteness	19	0.95
Ease of use	17	0.85
Fairness	19	0.95
Conciseness	18	0.90
Pertinence to the content area	19	0.95
Intelligibility	19	0.95
Would you use the questionnaire in your experiments?	18	0.90
Is the questionnaire user friendly?	17	0.85

4. Discussion

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

Several approaches were applied to improve the validity of the questionnaire. Firstly, we performed a pilot study to assess the questions' wording, the clarity of the questionnaire's items and its ease of use. Furthermore, we used a systematic approach involving a panel of experts with different backgrounds to rate, and consequently validate, the questionnaire with respect to several aspects such as comprehensiveness, concreteness, and ease of use. Of note, the use of the Delphi panel as well as the publicization process and the final rating scale fulfill the content validity of the present questionnaire (Messick, 1995; Martz, 2010; Tsang et al., 2017). The questionnaire is not intended to measure a construct or a specific factor and a correlation between items or between the questionnaire and other surveys (i.e., construct validity), is not neither expected nor needed, the high I-CVI values confirm that it could properly account for its intended use.

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 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. 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 associated with TMS 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., 2006, 2013; 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 suboptimal 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 and caffeine 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). Further, since caffeine intake can modulate brain oxygen metabolism, consumption of caffeine might affect TMS outcomes (Merola et al., 2017). Therefore, these aspects should be addressed in the questionnaire after each TMS session.

From the initial version of the TMSens_Q, a few items were removed/added 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 work showed the effect of ethnicity on the brain derived neurotrophic factor (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.

During the publication of the questionnaire on the IFCN website, some experts suggested the importance of including a section for children as the interest towards the application of TMS in this population is growing (Zewdie et al., 2020). This suggestion was very valuable. As the topic would raise several important additional aspects to take into account, the steering committee decided that extending the questionnaire to the pediatric population will be an important next step that would deserve a dedicated survey in future works.

Importantly, a few participants among those completing the rating scales suggested that the questionnaire could take too much time to be administered during the experimental sessions and that some items could be removed to shorten the survey. However, we believe that removing items would result in a loss of important information. Moreover, in both the paper-and-pencil version and in the web-based versions of the questionnaire each item is optional and can be skipped by the experimenter if needed. Additionally, the questionnaire has a modular structure so that some sections (e.g., participant's general information) could be filled only in the first experimental session ensuring time saving for subsequent ones.

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 TMSens_Q 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 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 the TMSens_Q 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.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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