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Does Assessment of Personal Exposure Matter During Experimental Neurocognitive Testing in MRI-Related Magnetic Fields?

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Purpose: To determine whether the use of quantitative personal exposure measurements in experimental research would result in better estimates of the associations between static and time-varying magnetic field exposure and neurocognitive test performance than when exposure categories were based solely on distance to the magnetic field source.

Methods: In our original analysis, based on distance to the magnet of a 7 T MRI scanner, an effect of exposure to static magnetic fields was observed. We performed a sensitivity analysis of test performance on a reaction task and line bisection task with different exposure measures that were derived from personal real-time measurements.

Results: The exposure measures were highly comparable, and almost all models resulted in significant associations between exposure to time-varying magnetic fields within a static magnetic field and performance on a reaction and line bisection task.

Conclusion: In a controlled experimental setup, distance to the bore is a good proxy for personal exposure when placing subjects at fixed positions with standardized head movements in the magnetic stray fields of a 7 T MRI. Use of a magnetic field dosimeter is, however, important for estimating quantitative exposure response associations. **Magn Reson Med 73:765–772, 2015. © 2014 Wiley Periodicals, Inc.**

Key words: magnetic resonance imaging; static magnetic fields; time-varying magnetic fields; personal exposure; dosimeter; neurocognitive tasks

INTRODUCTION

With the increased use of MRI scanners up to 9.4 T (1), possible biological effects of exposure to the strong magnetic fields became a major topic. With respect to neurocognitive functions, experimental studies performed in the stray fields around the bore have reported statistically significant negative effects of exposure to a combination of static magnetic fields (SMF) and time-varying magnetic fields (TVMF) on visuo-spatial orientation and attention/concentration (2–4). However, experimental studies performed within the bore without scanning, reported no significant cognitive effects of exposure to SMF or the combination of SMF and TVMF (5–8). As a consequence, consensus on the cause of these effects has not been reached, although occupational exposure levels associated with these strong SMF from MRI are regarded as safe (9).

One of the major challenges within these experimental studies is the exact characterization of exposure to SMF and TVMF. Inside the homogeneous SMF of the MRI scanner exposure can be reliably assessed. However, toward the edges of the bore and around the magnet the fields are very inhomogeneous due to the steep gradients that are present; exposure can therefore vary considerably over short distances. Even in a controlled experimental setting, it is difficult to estimate personal exposure within such inhomogeneous stray fields without the use of a measurement device, since exact spatial position and speed of movement are very important factors affecting exposure. Consequently, previously observed negative effects of exposure on cognitive functions may be a result of poor exposure estimates.

Accurate and precise measurement devices to assess personal exposure to magnetic field strength were unavailable until recently. In previous human experiments, exposure measures for SMF and TVMF have been based on field line maps as provided by the manufacturers of the system that show the spatial distribution of the magnetic flux densities (8,10,11), manually built devices (3,12), Hall sensors (7), a Gauss meter (4), or a prototype dosimeter (13). In addition, computer models are often used to estimate personal exposure to TVMF (14,15). Recently, a personal measurement device capable of measuring strong static magnetic fields and time-varying magnetic fields has been developed (Magnetic Field Dosimeter, University of Queensland, Australia) (16).

In a recent experimental study (4), we employed this device to investigate whether quantitative measurements of personal exposure to magnetic fields in experimental research would result in a better estimate of the associations between SMF and TVMF exposure and neurocognitive test performances. To this end, we performed a sensitivity analysis on selected cognitive tasks that previously showed a significant association with assigned exposure—that is, when exposure measures were based on predefined distances to the scanner bore by stationary measurement (4). We modeled

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different measures of personal exposure from the measurement data obtained during the experiment. In addition, we evaluated the standardized head movement protocol that was used to repeatedly induce similar levels of TVMF within the static magnetic stray field.

METHODS

Experimental Design

A group of 31 healthy volunteers who were unfamiliar with MRI were tested in a double-blind randomized crossover design. The group consisted of 10 male and 21 female subjects with an average age of 23.8 years (standard deviation, 6.4 years). To double-blind the experiment, the subject and experimenter were blindly guided into a tent. Each subject was tested on three occasions with 1 week in between. The low and high exposure conditions were located in the static magnetic stray fields of a passively shielded 7.0 T Philips Achieva MRI system located at the Utrecht Medical Center. The sham condition (<42 mT) was located outside the scanner room. The sequence of exposure was balanced and the order was randomly assigned to each subject before the start of the experiment.

The neurocognitive test battery consisted of 12 neurocognitive tasks and took on average 60 min to complete. In addition to the SMF already present, TVMF exposure was elicited by having volunteers made standardized head movements before every single task: 10 head movements were made in the horizontal direction, and 10 head movements were made in a vertical direction (covering an angle of 180° in 0.8 s). The start of each movement was indicated by an auditory cue.

In the current study, we report only on cognitive tasks that showed a statistically significant effect of exposure in the original study. These were observed for visuo-spatial orientation by use of a line bisection task [see Schenkenberg et al. in Lezak (17)] in which 20 horizontal lines with different line lengths had to be bisected in the middle. The (percentage of) deviation from the middle of the line was increased, meaning that subjects bisect lines more to the right side when exposed. In addition, attention/concentration was significantly affected as measured by a simple, complex, and inhibition reaction task (18,19). Subjects had to respond to one light (simple task) out of nine lights (complex task) that started burning and press the target button (left of the burning light in the inhibition task) as quickly as possible. Motion time (time between start of light burning and contact with the target button) and disengagement time (time between release of the target button and return to the "home" button) were significantly increased when exposed. The line bisection task was performed on average after 18 min of exposure and the three different versions of the reaction task after 44, 46, and 49 min of exposure, respectively. A description of the other 10 neurocognitive tasks that showed no effect of exposure can be found elsewhere (4). The study was approved by the local medical ethics committee of the University Medical Center in Utrecht.

Exposure Assessment Methods

In the original analysis (4), exposure was classified as low and high (estimated to be 500 mT and 1000 mT, respectively) based on the distance of the subject from the MRI magnet. A three-axis Hall Magnetometer (Metrolab THM 1176) was used to identify the locations within the magnetic stray fields of the MRI system that had magnetic field densities of 500 mT and 1000 mT. Measurements were taken at the presumed dosimeter location at head height in sitting position of 150 cm. During the experiment, the subject sat on a chair that was fixed to the prescribed locations, with his or her back toward the bore of the MRI system.

For the sensitivity analysis, personal exposure to magnetic fields was registered in real-time during each session of the experiment with a dosimeter (Magnetic Field Dosimeter, University of Queensland, Australia) that was attached to the inside top of a plastic helmet worn by the subject. The dosimeter registered exposure to static magnetic fields (with a sampling rate of 20 Hz) and time-varying magnetic fields (with a sampling rate of 10 kHz) in three directions, where the total static magnetic field is

$$|B| = \sqrt{B_x^2 + B_y^2 + B_z^2}. \quad [1]$$

and the total time-varying magnetic field is

$$|\mathrm{d}B/\mathrm{d}t| = \sqrt{(dB_x/dt)^2 + (dB_y/dt)^2 + (dB_z/dt)^2}. \quad [2]$$

Data Analysis

Dosimeter measurement data were first checked for out-of-range values and inconsistencies. Two experimental sessions were removed since out-of-range peaks in SMF and TVMF were recorded. The data for these two adjacent sessions were collected with the same dosimeter, suggesting that there may have been a problem with that particular dosimeter on that specific day.

Start and end times of each set of head movements and periods of task performance were identified by visual analysis of the personal exposure profiles (an example is given in Fig. 1). Time-weighted average exposure during head movements and task performance were estimated based on the dosimeter readings over these identified time slots as well as over an entire session. Cumulative exposure was calculated using the area under the curve up to the specific task.

From the dosimeter readings, four different measures were derived for SMF and TVMF separately:

1. Average exposure over one entire session of cognitive testing (~60 min) expressed as the time-weighted average exposure.
2. Exposure during head movements prior to the specific neurocognitive task expressed as the time-weighted average exposure. These time slots were presumably the periods of highest exposure to both SMF and TVMF.
3. Exposure during performance of a specific neurocognitive task. Presumably, SMF were the only type of magnetic fields present, as subjects sat still during task performance.

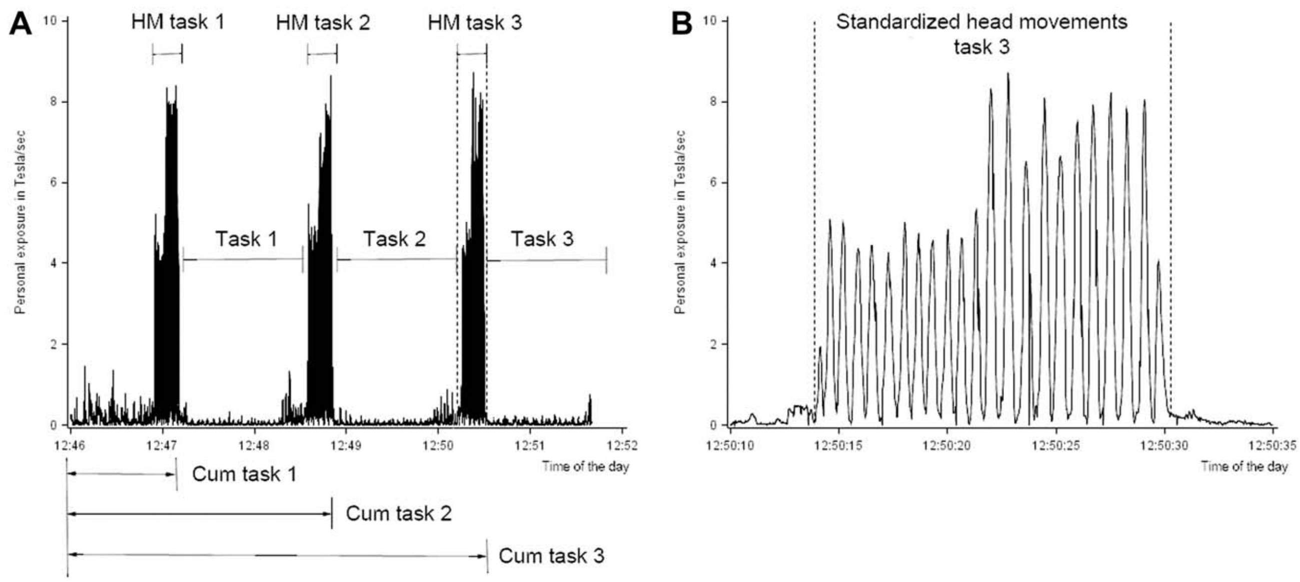

FIG. 1. Recording from a personal dosimeter of a subject in a 1000 mT condition during the experiment. **A:** Sum of personal exposure in x-, y-, and z-direction is depicted for TVMF expressed as T/s taken over the entire head rotation. Head movements (HM) consisted of 10 movements in horizontal direction (forth and back) followed by 10 movements in vertical direction (enlarged in panel **B**). They were defined by start of the sinus waves until the end of the sinus wave. Task performance was defined as the period between two head movement periods. Cumulative exposure (Cum) was defined as the area under the curve up until the specific task.

4. Cumulative exposure over the session up to but not including the specific neurocognitive task.

Statistical analysis was performed to calculate the correlation coefficients between the different exposure measures. Analysis of variance was performed to define the standardization of head movement protocol. To analyze the effect of different exposure measures on test performance, a linear mixed model was used to estimate the intercept and regression coefficient of the model. Within this sensitivity analysis, each of the exposure measures were separately entered as a continuous exposure variable in a linear mixed effects model assuming linear exposure-effect associations. In line with the original analysis, all sensitivity analyses were adjusted for session number, gender, and report of "ever experienced mild symptoms of motion sickness" (yes versus no). The line bisection task was adjusted additionally for handedness. The volunteers were modeled as random effects using heterogeneous compound symmetry, which assumes similar correlation between observations of the same subject but no correlation between different subjects. Statistical significance level was defined as $P \leq 0.05$. For comparison between models values of the Akaike Information Criterion (AIC) were estimated.

The limit of detection (LOD) of the dosimeter was set to 42 mT for SMF and 37 mT/s for TVMF. This was based on the maximum value obtained among 500 measurements of situations with no exposure (data not presented). Consequently, it was not possible to identify time intervals of head movements, task performance, and cumulative exposure up to the task in the sham condition. Therefore, in the main analyses, sham exposure values were set to the value of the LOD/$\sqrt{2}$. Applying alternative measures in the sham condition such as the original mean personal measured values or LOD/2 did not meaningfully change the results (data not shown).

Descriptive statistics, exposure measures, correlations, and analyses of variance were calculated using SAS (version 9.2; SAS Institute Inc., Cary, North Carolina, USA). Statistical analyses of inter- and intra-individual differences in test performance in association with exposure measures were performed with mixed-effects models using SPSS (version 20.0; IBM SPSS Statistics).

RESULTS

Thirty subjects completed all three test sessions resulting in 90 observations. The line bisection task had 86 observations (3 missing exposure and 1 missing outcome data) and the reaction task had 85 observations (2 missing exposure and 3 missing outcome data).

Measured time-weighted average exposure to SMF in the low exposure category over the entire session, during head movements or during task performance, varied between 79% and 115% of the distance-defined exposure value of 500 mT (Table 1). In the high exposure category, the exposure varied between 61% and 101% of the estimated 1000 mT value.

The average exposures to TVMF during the head movements were 1400 and 2400 mT/s for the low and high exposure condition, respectively (Table 1). During task performance, the average exposure to TVMF was almost negligible at around 55 and 80 mT/s in the low and high exposure condition, respectively. However, these levels are still significantly different from each other due to relatively small standard deviations of the distributions in the low and high exposure condition. When TVMF exposure was averaged over the entire session, encompassing both low (tasks performance) and

Table 1
Time-Weighted Average Personal SMF Exposure and TVMF Exposure in the Low and High Exposure Conditions per Task (n = 30)

	SMF Exposure (mT)						TVMF Exposure (mT)					
	Low			High			Low			High		
	Mean	GM	GSD	Mean	GM	GSD	Mean	GM	GSD	Mean	GM	GSD
Entire session	464	460	1.15	774	768	1.13	208	205	1.20	365	360	1.18
During head movements												
Simple RT	573	568	1.15	1000	989	1.16	1408	1385	1.21	2439	2415	1.16
Complex RT	575	570	1.14	993	984	1.16	1413	1392	1.20	2434	2410	1.15
Inhibition RT	559	551	1.19	997	986	1.17	1347	1309	1.30	2435	2407	1.17
Line bisection	577	574	1.12	1007	996	1.16	1401	1380	1.19	2469	2437	1.18
During task												
Simple RT	409	405	1.17	666	660	1.15	51.8	49.3	1.37	70.8	68.3	1.30
Complex RT	411	407	1.16	671	665	1.15	53.3	51.3	1.32	80.0	77.3	1.29
Inhibition RT	394	389	1.16	611	605	1.15	57.4	55.4	1.34	99.9	97.0	1.29
Line bisection	430	426	1.15	702	697	1.13	64.2	61.5	1.33	98.1	65.6	1.26
Cumulative*												
Simple RT	1251	1237	1.17	2015	1987	1.19	561	555	1.16	942	932	1.17
Complex RT	1326	1313	1.16	2100	2072	1.18	595	588	1.17	990	980	1.16
Inhibition RT	1382	1369	1.16	2188	2159	1.18	625	618	1.17	1040	1029	1.16
Line bisection	542	528	1.27	863	849	1.20	236	232	1.21	400	396	1.16

Abbreviations: GM, geometric mean; GSD, geometric standard deviation; RT, reaction task.
Sham exposure was below the level of detection. Eighty-five observations were used for the reaction tasks and 86 observations were used for the line bisection task.
*Cumulative exposure up to the respective task is given in T.s for SMF and T.s^2 for TVMF.

high (head movements) exposure periods that occurred during each exposure condition, the resulting TVMF exposures were 208 and 365 mT/s for the low and high exposure condition, respectively. Cumulative exposure to SMF and TVMF, as calculated from the start of a session until the start of a particular task, was much higher for the line bisection task compared with the reaction tasks. The reason for this was that the line bisection task took place well before the reaction tasks at 18 and 44 min, respectively. The correlations between different exposure measures (entire session, during head movements, during task performance, and cumulative exposure) for SMF and TVMF were moderate to very high (range, 0.63–0.99) for the simple reaction task and high to very high for the complex reaction task (range, 0.71–0.99), inhibition reaction task (range, 0.71–0.99), and line bisection task (range, 0.77–0.99) (data not shown).

Figure 2 shows the range of average personal exposure in the sham and the low and high exposure condition for the SMF and TVMF exposure measures in the inhibition reaction task. The time-weighted average exposure to SMF during the entire session (Fig. 2A), during head movement (Fig. 2C), and during task performance (Fig. 2E), differed only very slightly from each other. The average exposure during head movements (Fig. 2C) was only marginally higher than the average over the entire session (Fig. 2A) and the latter was, in turn, slightly higher than the exposure during task performance (Fig. 2E). As expected, the time-weighted average exposure to TVMF over the entire session (Fig. 2B) and during task performance (Fig. 2F) was negligible. Only during head movements was the exposure to TVMF significantly higher (Fig. 2D).

Individual average exposures to SMF and TVMF during each of the head movements are shown in Figure 3. Analysis of variance showed that the within subject variance appeared to be even smaller than the between subject variance in the low and high exposure condition for both SMF and TVMF exposure (Table 2).

Results of the mixed model analysis of the inhibition reaction task on disengagement time using distance-defined assigned categories and personal exposure measures are shown in Table 3. With the exception of the TVMF exposure during a task, the AIC, intercept, and regression coefficients are highly comparable to the original exposure category based on assigned distance to the bore only. When comparing the exposure measures, it should be taken into account that estimates, regression coefficients, and corresponding confidence intervals are not comparable between all models, since the interval ranges of the exposure proxies differed in level and range. However, regression coefficients and corresponding confidence intervals can be compared within each category of SMF, TVMF, and cumulative exposure. AIC and *P* values, however, could be compared directly across all models. Results of the line bisection, simple reaction task, and complex reaction task showed similar effect associations and can be found in the Supporting Information.

DISCUSSION

In this study, we compared the results obtained with distance-defined positions and personal exposure during a series of experiments investigating the effect of MRI-related SMF and TVMF exposure on neurocognitive test performances. Similar associations between exposure and neurocognitive test performance were found when using quantitative personal exposure measurements collected with a dosimeter compared with those based on distance to the bore of the MRI system as identified by a magnetometer.

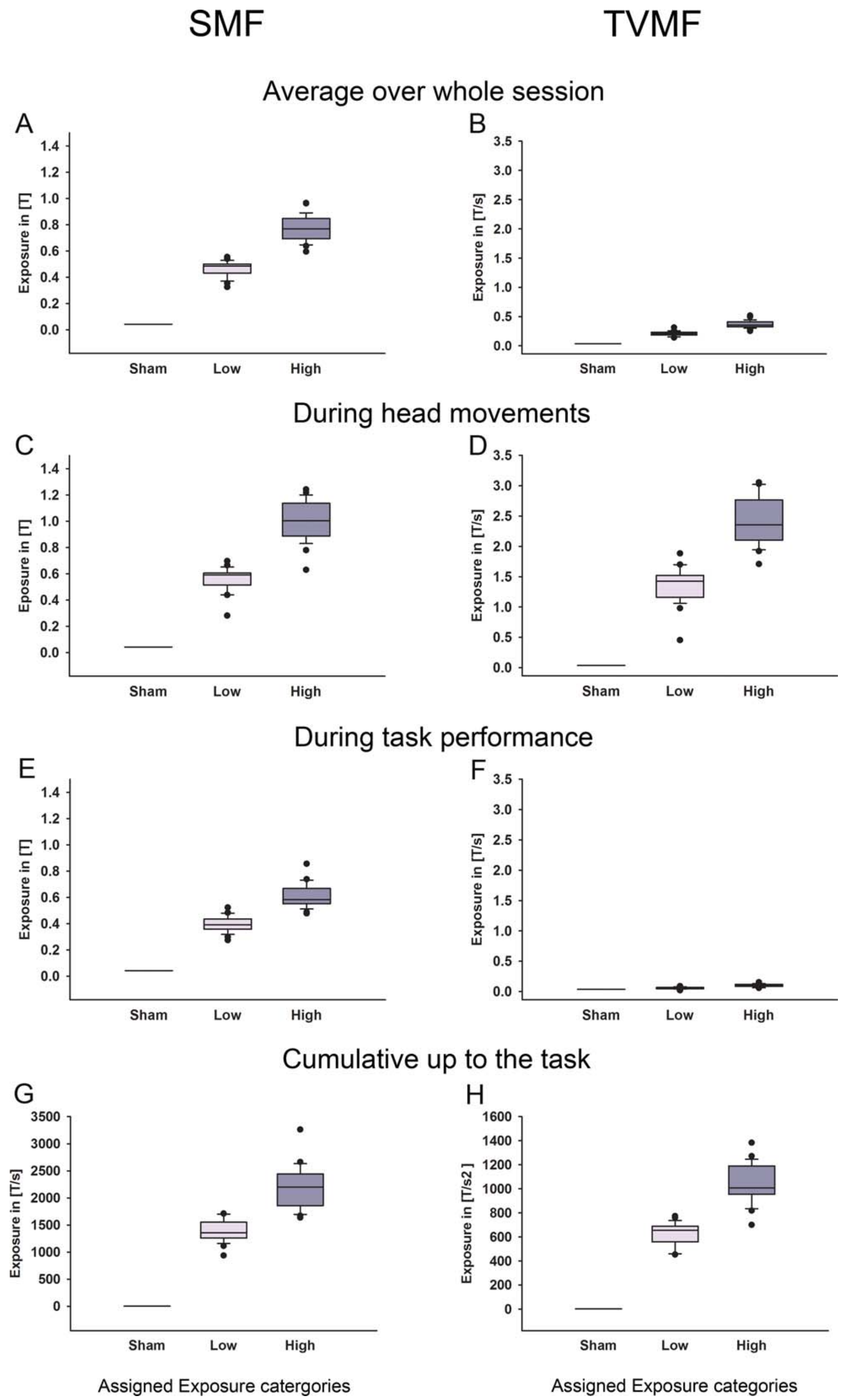

FIG. 2. **A–H**: Box and whisker plots of average personal exposure in the sham, low exposure, and high exposure condition. The median value is given by the horizontal line in the box. The lower and upper whiskers reflect the 5th and 95th percentiles, respectively. The graphs of exposure during head movements, during task performance, and cumulative up to the task are specific for the inhibition reaction task (**C–H**). Seventy-five single subject exposure measurements are used per graph (28 in sham, 28 in low, 29 in high condition).

The average measured exposures were generally close to what was expected for these categories as can be seen for the exposure estimates during head movements and task performance (Table 1). The discrepancies between measured personal SMF exposure values and distance-defined assigned SMF exposure were larger during task performance than during head movements and were more marked during task performance in the high exposure versus the low exposure condition (Table 1). Both can be explained by certain practical details of the experiment. First, during the head movements, subjects sat upright (with the dosimeter attached to their helmet)

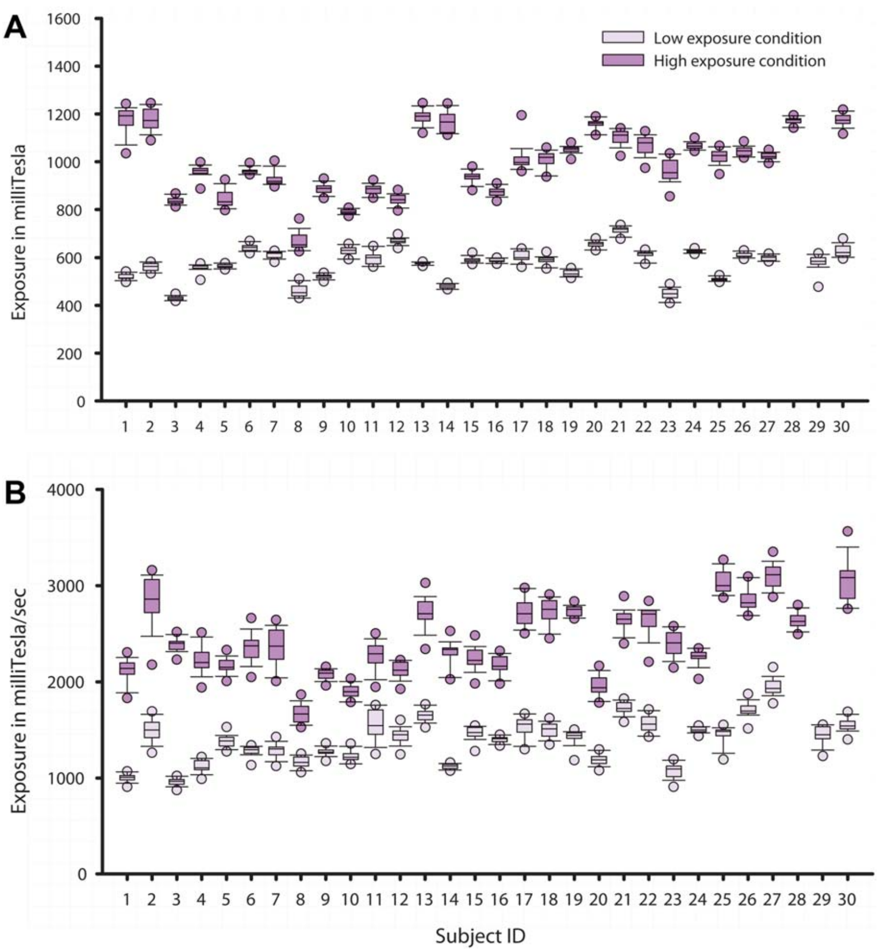

FIG. 3. **A, B**: Box and whisker plots of each single subject (n = 30) when exposed to SMF (**A**) and TVMF (**B**) during each series of head movements (n = 19). The median value for each subject is given by the horizontal line in the box. The lower and upper whiskers reflect the 5th and 95th percentiles, respectively. (Note: the low exposure condition of subject 28 and the high exposure condition of subject 29 are missing.).

with their heads closer to the bore and the marker at a height of 150 cm, where the magnetometer readings were taken. This resulted in very good agreement between the predicted predefined SMF exposure of 500 and 1000 mT and the measured personal exposure values during head movements. However, while performing a task, subjects leaned forward, away from the bore and the marker toward the table, resulting in lower SMF exposure levels in both exposure conditions. Second, in the high exposure condition, subjects were at the edge of the scanner bore where the gradient fields are considerably steeper than in the low exposure condition: a smaller change in distance as the subjects moved forward in the high condition therefore had a relatively larger impact on exposure level than a similar movement in the low condition.

The small within-subject variance in exposure indicates that subjects had similar exposure during each series of head movements (covering an angle of 180° in 0.8 s) within a session, and underscores the effectiveness of the standard protocol for standardizing head movements that was used to ensure that similar levels of TVMF were repeatedly induced. Although one subject (Fig. 3, subject 8) had in the high exposure condition a magnetic field exposure in the range of the low exposure condition, the exposure in the low exposure condition was also considerably lower for this subject compared

Table 2
Results of Analyses of Variance of Average Exposure During Each Head Movement for the Low and High Exposure Condition for SMF and TVMF (n = 30)

Condition	Field	Subjects	Variance	%	Ratio95*
Low	SMF	Within	0.0027	14.8	1.22
		Between	0.0153	85.2	1.62
	TVMF	Within	0.0038	12.1	1.27
		Between	0.0276	87.9	1.92
High	SMF	Within	0.0009	4.2	1.12
		Between	0.0203	95.8	1.75
	TVMF	Within	0.0027	10.4	1.23
		Between	0.0232	89.5	1.82

*Ratio of the 2.5% and 97.5% of the within and between individual exposure distribution.

Table 3
Results of the Linear Mixed Model Analyses of the Inhibition Reaction Task on Disengagement Time (in Milliseconds) Using Distance-Defined Assigned Exposure Categories and Personal Exposure in a Continuous Exposure Model (K = 30; N = 85)

Exposure	AIC	Intercept	RC	CI lower	CI higher	*P*
Assigned*	729.9	126.36	1.16	0.36	1.96	0.006
Session SMF†	729.9	125.58	1.49	0.40	2.58	0.008
HM SMF	729.8	125.59	1.20	0.37	2.03	0.006
Task SMF	729.4	125.34	1.90	0.51	3.29	0.008
Session TVMF†	726.4	124.14	3.71	1.34	6.08	0.003
HM TVMF	731.0	125.84	0.58	0.17	0.82	0.004
Task TVMF	728.1	124.21	12.12	0.40	23.83	0.043
Cumulative SMF	746.4	126.34	4.77 E-4	1.17 E-4	8.37 E-4	0.010
Cumulative TVMF	742.8	125.36	1.16 E-3	4.14 E-4	1.91 E-3	0.003

Abbreviations: CI, confidence interval; RC, regression coefficient per 100 mT; HM, during head movements before specific task; Task, during task performance; Session, average exposure over entire session.
For the sham, low exposure, and high exposure conditions, 28, 28, and 29 observations were available, respectively.
*Distance-defined assigned categories.
†Average exposure over entire session.

with that of the other. As a result, exposure categories were still distinctive from each other.

Furthermore, since small changes in a strong heterogeneous magnetic stray field can lead to considerable changes in exposure, we analyzed the effect of personal height on measured exposure. No effect was detected, most likely due to the fact that differences in personal height were relatively small (range, 154–200 cm; interquartile range, 9.25) and differences in position of the head would actually have been smaller, since tasks were performed seated.

Comparing the results of the different exposure assessment models shows that the AICs of models with exposure based on distance to the magnet were comparable to those where personal exposure was modeled (Table 3). Only the model of TVMF exposure during task performance resulted in a poor fit expressed by a large confidence interval and a high *P* value. This is mainly caused by very low exposure, since there was hardly any movement of the head during task performance. However, cumulative exposure to SMF and to TVMF from the start up to the specific task yielded the weakest fit of all models, as reflected by the high AIC values, since exposure during task and head movements up to that specific task were averaged.

Based on our analyses, it would appear that these two different types of exposure assessments and their resulting measures of exposure do not influence the outcome of the experiments. This suggests that the differences in outcomes between earlier performed research studies, inside and outside the scanner bore, cannot be explained by the exposure method used (assuming that the data were collected reliably, positioning was done properly, and movements were standardized). An explanation for the difference in effects should rather be sought in the divergence of the magnetic field lines and experimental setup used (eg, subject population, field strengths, duration of exposure, direction of the magnetic fields, and choice of cognitive tasks). Nonetheless, in some research areas (eg, those requiring estimates of real-life exposure), the use of a personal dosimeter has important additional value. Accurate estimates of in situ exposure to SMF and TVMF are very difficult to obtain without employing personal dosimeters, because differences in walking speed or a difference in position of a few centimeters from the exposure source can lead to considerable differences in exposure levels. This is especially true as one gets closer to the edge of the bore of MRI scanners with high magnetic field strengths, as was seen in this experiment. Radiographers, technicians, surgeons, and cleaning staff working in the MRI room have different activities, movement patterns, locations, and durations of activities in the MRI room that will determine their exposures to SMF and TVMF. These exposures by definition will vary in intensity over a working day and between working days. There will be also a host of workplace factors that influence personal exposure, including magnetic field strength, design of the scanner, shielding of the magnet, steepness of the gradient field (density of field lines), and direction of field lines. All of these factors can lead to considerable variation in exposure levels within and between workers and occupational groups. Capturing this type of variation can be important for epidemiological and occupational risk assessment studies, and it is easier to assess this variation using personal dosimeters. Therefore, application of personal dosimeters will enable a more accurate description of quantitative exposure-response associations in epidemiological occupational studies and result in more accurate occupational exposure standards for technicians and others working around MRI systems. This is not as easy to achieve using semiquantitative exposure assessment methods, such as those based on distance from and time spent around an MRI scanner.

However, for studies with a controlled experimental setup where exposure conditions and movements are strictly standardized and distinct exposure categories can be established (eg, based on distance to the bore), semiquantitative estimation of exposure is more straightforward than collecting personal exposure measurement using dosimeters.

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