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Feasibility and relevance of an immersive virtual reality cancellation task assessing far space in unilateral spatial neglect

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Abstract

Unilateral spatial neglect (USN) is a highly prevalent neuropsychological syndrome. However, its assessment in clinical practice, mainly based on paper-and-pencil tests, encounters limits as only near space, called peripersonal, is assessed. However, USN is a multicomponent syndrome that can also affect far space, called extrapersonal. This space is not assessed in current clinical assessment although it can be more impacted than peripersonal space. Immersive virtual reality (VR) allows developing tasks in far space to assess this heterogeneity. This study aimed to test the feasibility and the relevance of an immersive VR task to assess far space. A cancellation task, the Bells test, was used in its original paper-and-pencil version and was also adapted into a far immersive VR version. Ten patients with left USN and sixteen age-matched healthy participants were included. A single-case method was performed to investigate the performance of each patient. Although five patients showed very similar results between both versions, the five others exhibited a dissociation with a more severe impairment in the VR version. Three of these five patients significantly differed from the healthy participants only on the VR version. As USN in far space is not brought to light by paper-and-pencil tests, immersive VR appears as a promising tool to detect USN affecting this space.

KEYWORDS

assessment, extrapersonal space, spatial neglect, virtual reality

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INTRODUCTION

Unilateral spatial neglect (USN) is a highly prevalent neuropsychological syndrome (Esposito et al., 2021). It is typically defined as a failure to respond to, orient towards, or report to stimuli presented on the contralesional side of space (Heilman & Valenstein, 1979). This syndrome can also correspond to a failure to initiate or complete movement in or towards the contralesional side of space or a failure to report and manipulate contralesional information stored mentally (Esposito et al., 2021). Thus, USN symptoms can be very heterogeneous, and several clinical subtypes have been identified according to spatial regions, processing stages, reference frames, and sensory modalities (Rode et al., 2017; Vuilleumier, 2013). However, while an accurate diagnosis of USN is crucial as it impacts overall functional recovery in stroke patients (Di Monaco et al., 2011), some subtypes, such as extrapersonal neglect, are rarely assessed in current clinical practice (Guilbert, 2023).

Growing evidence suggests that the brain processes space modularly, first distinguishing between one's body, personal space, and the external environment (Caggiano & Jehkonen, 2018). The external environment can also be divided into two subtypes: the peripersonal space, which corresponds to the space that a person can directly reach and act upon; and the extrapersonal space, which is the space a person can perceive beyond their reaching space (Halligan & Marshall, 1991). These two spaces are differently coded in the brain with dissociated neural systems (Berti & Rizzolatti, 2002). Peripersonal space employs dorsal visuomotor processing areas, whereas extrapersonal space is more based on ventral visuoperceptual processing areas (Weiss et al., 2000). USN can impact these spaces differently with dissociations between peripersonal and extrapersonal spaces (Aimola et al., 2012; Butler et al., 2004; Halligan & Marshall, 1991). Only one space can sometimes be impaired. Moreover, USN symptoms are sometimes reported as being more pronounced in extrapersonal than in peripersonal space (Butler et al., 2004; Cowey et al., 1991; Pitzalis et al., 2001). As daily life activities require peripersonal and extrapersonal spaces, there is a real need to assess both spaces to understand patients' difficulties.

USN is currently assessed with paper-and-pencil tests such as cancellation tasks, line bisection, or copying or drawing tasks (Checketts et al., 2021; Menon & Korner-Bitensky, 2004). Cancellation tasks, in which patients are required to cancel targets from a background of distractors, are considered more sensitive than other paper-and-pencil tests (Azouvi et al., 2002). In a study by Ferber and Karnath (2001), cancellation tasks detected 94% of 35 patients with well-defined USN. However, as paper-and-pencil tests only evaluate space on a sheet of paper, which corresponds to a limited portion of peripersonal space, they do not consider extrapersonal neglect (Appelros et al., 2003). A few tests have been developed to assess extrapersonal space such as far-line bisection with a laser (Facchin et al., 2016) or visual search tasks (Borsotti et al., 2020; Cunningham et al., 2017). However, the implementation of these tasks in clinical practice is difficult due to a lack of standardization but also as the tasks can be difficult to set up. Thus, standardized assessment of extrapersonal space is currently complex in clinical practice.

Based on the observation that conventional paper-and-pencil tests do not address real-life situations encountered by patients outside the clinical setting (such as in far space), several studies have proposed to complement them with computerized assessment to enhance the USN diagnosis (Ogourtsova et al., 2017). With the rapidly growing field of new technologies, computerized assessment went further in realism with virtual reality (VR) (Cavedoni et al., 2022; Pedroli et al., 2015). VR is a computerized interactive environment simulating a real environment, where the participant is actively engaged in activities. VR devices can be subdivided according to their degree of immersiveness from non-immersive to immersive. Nonimmersive VR systems have difficulties with reproducing and assessing far space as the environment is displayed on a screen. For instance, Buxbaum et al. (2012) have developed the virtual reality lateralized attention test (VRLAT), a computerized task in which patients are asked to name objects as they navigate along a virtual path. For 70 right-hemisphere stroke patients, the VRLAT detected more USN syndromes than classical paper-and-pencil tests. However, this task did not significantly correlate with extrapersonal neglect (assessed with laser line bisection task). Instead, it correlated with personal neglect and classical paper-and-pencil tests. It should be noted that the VRLAT was displayed on a computer screen placed in near space. Thus, patients may not have perceived the environment as extrapersonal space.

Conversely, using immersive VR with a head-tracked head-mounted display (HMD) can be a promising tool for extrapersonal neglect assessment as it can provide a controlled and standardized reproduction of the environment (Cavedoni et al., 2022). Yasuda et al. (2020) assessed far space in one patient with USN by using immersive VR. The patient was instructed to respond when he detected a red sphere. This red sphere could appear at different locations and distances (varying from .5 to 6m). The patient was significantly better at detecting left targets in near space than in far space. However, only one patient was included in this case study and clinical utility needs to be further explored (Cavedoni et al., 2022). Furthermore, the task was a simple detection task, which could be less sensitive than a more complex visual search (Azouvi et al., 2002). While a cancellation task was developed in immersive VR by Knobel et al. (2020), this task assessed the peripersonal space rather than the extrapersonal space as targets were displayed at a 55-cm reaching distance of the participants who had to touch them.

In the present study, a cancellation task, the Bells test (Gauthier et al., 1989), was adapted to immersive VR in far space. Both the original and the new VR versions of the Bells test were proposed to 10 patients with USN and 16 healthy participants. The objectives of the present study were to test the feasibility of the immersive VR task and its relevance in USN diagnosis. First, the equivalence between the two tasks in terms of difficulty level was verified in the control group. Patients' performance was also compared between the two tasks. Then, each patient's scores in each task were compared to the ones of the control group. Our main hypothesis was that the immersive VR cancellation task would be feasible for brain-damaged patients and able to reveal USN symptoms. Based on the literature, we hypothesized that performance could be worse in far space assessed with the immersive VR cancellation task than in near space assessed with the classical cancellation task for USN patients (Butler et al., 2004; Cowey et al., 1991; Pitzalis et al., 2001) and dissociations could emerge between the two tasks (Aimola et al., 2012; Butler et al., 2004; Halligan & Marshall, 1991).

METHODS

Participants

Ten right-handed patients were recruited from the neurological rehabilitation unit of Saint-Maurice Hospitals. All patients who had left USN signs reported in their medical files were eligible for participation (based on a neuropsychological assessment and occupational therapists' observations). Patients also needed to have a right cerebral lesion confirmed by magnetic resonance imaging (MRI) scans and no motor deficit with their right arm. All eligible patients within the recruitment period were included (see Table 1). Their previous neuropsychological assessment was also reported in Table 1. It should be noted that Patient 10 showed no sign of a left USN on this assessment, whereas signs of a left USN were reported by occupational therapists in her medical file. All patients were in the subacute phase of their stroke except Patient 3 and Patient 9 who reached the chronic phase. Seven of the patients also exhibited a left homonymous hemianopia.

The control group included 16 right-handed healthy participants (10 women and 6 men) with a mean age of 61.4 years (± 5.1). They had no prior history of neurological or psychiatric disease. The two groups did not significantly differ in terms of age (U=51.0, p=.13). Only Patient 2 and Patient 9 had an age significantly different from the control group (Patient 2: t=-4.83, p<.001; Patient 9: t=3.54, p=.003). The mean education of the control group was 12.8 years of schooling (± 2.0). The two groups significantly different in terms of schooling from the control group (Patient 4: t=3.49, p=.003; Patient 5 and Patient 8: t=-2.33, p=.034).

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9Male8011Right fronto-parietal haemorrhagic stroke8No 14.8^{a} 5.5^{a} $-$ 10Female6511Right fronto-parietal haemorrhagic stroke 2.5 No $.71$ 6 $-$	8	Male Female	60 65	10 8	Right fronto-parieto-temporal haemorrhagic stroke Right middle artery ischaemic stroke	4 ε	Left Left	41.3 ^a 16.4 ^a	2.5 ^a 3.5 ^a	3 ^a 1 ^a
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^aPathological scores; — task not administered.



FIGURE 1 Illustration of the cancellation-task interface and the laser pointer (here in light grey for printing purposes but displayed in blue in the VR environment) emerging from the hand-held controller inside the head-mounted display.

Material and procedure

Two cancellation tasks were proposed in the following order to participants: the Bells test (Gauthier et al., 1989) and a VR adaptation of this test. In each version, participants were seated and asked to find 35 targets (bells) among 280 distractors without any constraint of time. Targets were equally distributed in space: the space was divided into 7 columns (3 on the left side, 1 in the middle, and 3 on the right side) with 5 targets in each column. The disposition of targets and distractors was the same between the two tasks. In the original Bells test, bells and distractors were presented on a horizontal A4 sheet of paper on a table, and participants had to circle targets with a pencil. The VR version was developed by the team thanks to Unity with Steam VR. Participants wore a HTC-Vive Pro HMD and held a VR controller in their right hand. To adapt the original Bells test to immersive VR, targets and distractors were displayed on a virtual circular screen (width: 160°, height: 60°) at a 20-m viewing distance (extrapersonal space) so that all stimuli were at the same distance from the participant. To circle a target, participants pointed it with the hand-held controller and just had to validate their selection with the trigger of the controller. The controller was virtually reproduced in the environment to be visible. A blue beam that emerged from the controller played the role of a laser pointer and enabled participants to point at targets (see Figure 1). Before the VR task, participants were required to perform three familiarization trials in which they had to find some targets (one central target, three central targets, and six central targets mixed with 3 distractors) to ensure proper use of the VR system. In each version, the test stopped when the participant indicated that they believed all the targets had been circled.

Data analysis

Analyses were carried out on the total number of cancelled targets, the number of left omissions, the number of right omissions, and the left-right score, which is the difference between left- and right-sided omissions as calculated in the battery of tests "batterie d'évaluation de la négligence spatiale" (BEN; Azouvi et al., 2006). However, some patients only cancelled the extreme right targets and, thus, some of their omissions could be localized on the right side of the sheet. Therefore, we also chose to use the center of

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cancellation (CoC), which better reflects the USN severity than the difference between the left–right score (Rorden & Karnath, 2010). The CoC corresponds to the barycenter of all cancelled targets. This measure was standardized so that the CoC value ranges from -1 to 1, where zero indicates a symmetrical spatial distribution of cancelled targets. A positive CoC value indicates a bias towards the right side of space (due to left omissions), whereas a negative CoC value indicates a bias towards the left side of space (due to right omissions). Non-parametric Wilcoxon tests were used to compare the two tasks in each of the two groups with a threshold value for statistical significance set at .05 (one-tailed *p*-value). Moreover, the results of each patient were compared with the results of the control group using Crawford and Garthwaite's (2002) single-case tests. Scores were considered to be pathological when the *p*-value was under .05 (one-tailed *p*-value).

RESULTS

For the control group, the results between the two tasks did not significantly differ for all the five measures: total number of cancelled targets (W=33.0, p=.30), left omissions (W=19.5, p=.19), right omissions (W=17.5, p=.75), left-right score (W=43.5, p=.18), and CoC (W=37.5, p=.17). This suggests that the two tasks exhibited comparable levels of difficulty.

For the patient group, the total number of cancelled targets was significantly lower (W=1.50, p=.005), and the number of left omissions was significantly higher (W=26.5, p=.021) in the VR task than in the original task, suggesting lower performance in the VR task compared to the original task. CoC was also significantly higher in the VR task than in the original task (W=10.0, p=.042), underlying more rightward bias in the VR task. However, for the patient group, the number of right omissions and the left-right score did not significantly differ between the two tasks (right omissions: W=9.0, p=.22; left-right score: W=14.5, p=.10).

The scores on the two cancellation tasks are reported in Table 2 for each patient and the two groups. In addition, patients' pathological scores and associated *t*-values from Crawford and Garthwaite's tests (2002) are also reported in Table 2.

In the original Bells test, all patients significantly differed from the control group in terms of total omissions and left omissions, except for Patient 10 (see Table 2 for individual results). Patients 1 and 2 also differed regarding right omissions as they only cancelled a small number of extreme right-sided targets. Regarding the left–right score, all patients except Patient 9 and Patient 10, significantly differed from the control participants. However, as previously mentioned, this score did not markedly reflect USN severity as Patients 1 and 2, respectively, had a score of 5 and 6 due to right omissions. Only 7 out of 10 patients were pathological when considering their CoC value, underlying the presence of a USN. Patients 7, 9, and 10 showed no significant rightward biases on the CoC, and, thus, their USN was not detected by the original Bells test based on this measure.

In the extrapersonal VR cancellation task, all patients significantly differed from the control group in terms of total omissions and left omissions (see Table 2 for individual results). Four patients (1, 2, 6, and 7) also significantly differed from the control group regarding right omissions. All patients significantly differed from the control group regarding the left–right score, except Patient 10. Again, due to right-sided omissions, the scores of 6 for Patient 1 and of 3 for Patient 2 did not reflect the important severity of their USN. Regarding the CoC measure in the extrapersonal VR cancellation task, all patients had a pathological score underlying the presence of a USN.

Comparing the USN severity between the two tasks (see Figure 2), three patients (7, 9, and 10) did not have a pathological CoC score in the original version of the test. In contrast, they had a pathological score in the extrapersonal VR version. While Patient 4 and Patient 8 had pathological scores in both tasks, they had more severe scores in the extrapersonal VR cancellation task. For Patient 4, 8 out of 15 left targets were omitted in the original task, while 13 left targets were omitted in the VR task. For Patient 8, 5 out of 15 left targets were omitted in the original task, while all 15 left targets were omitted in the VR task. For the other five patients, the VR task did not reveal more pathological scores than the original task, suggesting equivalent results between the two tasks.

level for both the patients and control participants.	Extrapersonal VR Bells test	
ABLE 2 Scores on the original and the VR Bells tests for each patient and at the group	Original Bells test	

	Uriginal Bells test					Extrapersonal VK	bells test			
Patient	Cancelled targets (/35)	Left omissions (/15)	Right omissions (/15)	Left-right score	Center of Cancellation (CoC)	Cancelled targets (/35)	Left omissions (/15)	Right omissions (/15)	Left-right score	Center of cancellation (CoC)
1	5^{***} ($t = -22.3$)	$15^{***} (t = 17.2)$	$10^{***} \ (t=9.54)$	5^{**} ($t = 3.96$)	$.91^{***}$ ($t=29.5$)	$6^{***} (t = -19.0)$	$15^{***} (t = 11.1)$	9^{***} ($t = 16.28$)	6*** (<i>t</i> =4.25)	$.86^{***} (t = 41.5)$
5	6^{***} ($t = -21.5$)	$15^{***} (t=17.2)$	9*** (t=8.53)	6^{***} ($t = 4.74$)	$.87^{***}$ ($t=28.2$)	3^{***} ($t = -21.1$)	$15^{***} (t = 11.1)$	$12^{***} (t=22.0)$	3* (t=2.01)	$.91^{***} (t = 43.9)$
3	$17^{***} (t = -13.0)$	$14^{***} (t = 16.0)$	2 (<i>t</i> =1.46)	12^{***} ($t = 9.43$)	$.49^{***} (t = 15.9)$	$16^{***} (t = -12.1)$	$15^{***} (t = 11.1)$	1 $(t = 1.07)$	$14^{***} (t = 10.2)$	$.51^{***}$ ($t = 24.5$)
4	25^{***} ($t = -6.85$)	8^{***} ($t = 8.87$)	0 (t =57)	8^{***} ($t = 6.31$)	$.24^{***}$ ($t=7.86$)	$22^{***} (t = -9.87)$	13^{***} ($t=9.58$)	$0 \ (t =84)$	13^{***} ($t=9.47$)	$.39^{***} (t = 18.7)$
5	$26^{***} (t = -6.08)$	$9^{***} (t = 10.1)$	0 (t =57)	$9^{***} (t = 7.09)$	$.27^{***}$ (t = 8.83)	24^{***} ($t = -6.60$)	8^{***} ($t = 5.67$)	$1 \ (t = 1.07)$	7^{***} ($t = 4.99$)	$20^{***} (t=9.46)$
6	$27^{***} (t = -5.31)$	8*** (t=8.87)	0 (t =57)	8^{***} ($t = 6.31$)	$.21^{***}$ ($t=6.89$)	$23^{***} (t = -7.29)$	8^{***} ($t = 5.67$)	4^{**} ($t = 6.77$)	4^{**} ($t = 2.75$)	$.13^{***} (t=6.06)$
7	28^{***} ($t = -4.54$)	5^{***} ($t=5.32$)	2 (<i>t</i> =1.46)	$3^{**} (t=2.39)$	$.04 \ (t=1.39)$	23^{***} ($t = -7.29$)	9^{***} ($t = 6.46$)	2^{**} ($t = 2.97$)	7^{***} ($t = 4.99$)	$.23^{***} (t=10.9)$
80	$30^{**} (t = -3.00)$	5^{***} ($t=5.32$)	0 (t=57)	5^{**} ($t = 3.96$)	$.13^{***} (t = 4.30)$	17^{***} ($t = -11.4$)	15^{***} ($t = 11.1$)	$0 \ (t =84)$	15^{***} ($t=10.96$)	$.54^{***}$ ($t=26.0$)
6	$30^{**} (t = -3.00)$	2^{*} ($t = 1.78$)	2 (<i>t</i> =1.46)	0 (t=.047)	.02 (t = .74)	24^{***} ($t = -6.60$)	8^{***} ($t = 5.67$)	1 $(t=1.07)$	7^{***} ($t = 4.99$)	$(19^{***} (t=8.97))$
10	35 (t=.85)	0 (t =59)	0 (r=57)	0 (t=.047)	(760. = 100)	31^* ($t = -1.79$)	3^* ($t = 1.76$)	1 $(t=1.07)$	2 (<i>t</i> =1.26)	$.074^{***} (t=3.35)$
Patients	22.90 (±10.2)	$8.10 (\pm 5.30)$	2.50 (±3.81)	6.17 (±3.86)	.32 (±.33)	$18.9 (\pm 8.65)$	$10.9 (\pm 4.25)$	3.75 (±4.12)	7.88 (±4.63)	$.40(\pm .30)$
Controls	33.9 (土1.26)	.50 (±.82)	.56 (±.96)	06 (±1.24)	$003 (\pm .03)$	33.6 (土1.41)	.75 (±1.24)	.44 (±.51)	.31 (±1.30)	.005 (±.02)
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*p < .001). rp<.01, highlighted with asterisks (*p < .05, * control group are Note: Crawford and Garthwaite's Avalues are also reported for each patient's score, and pathological scores that significantly differ from the





DISCUSSION

The present study aimed to test the feasibility and the relevance of an immersive VR cancellation task to assess far space with ten patients with USN.

First, it should be noted that, in our study, none of the 10 USN patients included showed difficulties with the material or the task, such as in Knobel et al.'s (2020) cancellation task. Moreover, when interviewed at the end of the VR task, no healthy participant or patient reported symptoms of discomfort with the use of VR, thanks to the short duration of the task. Another significant point is that, when patients were asked about the task they preferred, all patients reported that the VR task was more attractive and motivating than the original Bells test. Although not assessed in the present study, patients with USN often lack awareness of their deficits (anosognosia), which can lead to difficulties adhering to conventional assessment (Jacquin-Courtois et al., 2009). As the acceptance of VR devices and engagement in VR tasks appear to be high in USN patients (Cavedoni et al., 2022; Pedroli et al., 2015), VR could be an alternative by offering more attractive tasks for these sometimes less adherent patients.

Concerning the results, our findings did not reveal any performance difference between the two tasks in the control group, suggesting that the difficulty was not different for healthy participants. In contrast, USN patients were significantly more severe in the VR task than in the original Bells tests. Individually, 5 out of 10 patients showed relatively similar results between the two cancellation tests, suggesting that their USN did not raise additional difficulties in the virtual far space and that this VR task did not appear more complex than the original version. Therefore, the VR task seemed as relevant as the original Bells test to assess these USN patients. However, the five other patients showed worse results in the immersive VR version than in the original version of the Bells test. This result could probably be linked to the fact that USN can be worse in extrapersonal space than in peripersonal space (Butler et al., 2004; Cowey et al., 1991; Pitzalis et al., 2001). Three of these patients (7, 9, and 10) did not have a pathological CoC score in the original Bells test, whereas their CoC scores were highly pathological in the extrapersonal VR cancellation task. Patient 10 had even no pathological scores in paper-and-pencil tests. This result favours a dissociation between the two tasks for these three patients, potentially due to a dissociation between near and far spaces as already found in the literature (Aimola et al., 2012). Moreover, Patient 8 presented a moderate USN in the original Bells test (5 left omissions and a CoC of .13) and in other paper-and-pencil tests while her USN in the extrapersonal VR cancellation task could be qualified as severe (15 left omissions and a CoC of .54). Although the potential influence of homonymous hemianopia (HH) on the VR task needs to be further explored, it has to be noted that the visual field is unlikely to explain the results in this task because two out of the three patients without HH (Patient 9 and Patient 10) showed a pathological CoC only in the VR task. In the same way, four out of the five patients with similar results in the two tasks presented a left HH, suggesting an equivalent influence of the HH in both tasks.

Hence, our immersive VR task appears feasible and able to reveal USN symptoms. Even more, for some patients, the symptoms were less severe (and even not detected) in the near-space original task compared to the far-space immersive VR task. The psychometric properties of the VR task need now to be assessed through a more comprehensive and extended study, which will also include patients with right brain damage (with and without HH) and without USN signs reported in daily life. Dealing with the same issue, daily life must also be assessed via questionnaires or more ecological tasks to assess the clinical relevance of our VR task (Azouvi, 2017; Azouvi et al., 2003). This information was not available for the patients included in this study.

Finally, the critical issue is to ensure that the immersive VR cancellation task correctly assesses extrapersonal space as a manual response is required with the controller. Several studies showed that using a tool to act in far space can extend peripersonal space (Berti & Frassinetti, 2000; Làdavas & Serino, 2010). However, the controller used in the present study cannot be considered since a tool as it was used as a laser pointer and prevented direct contact with the targets. Another argument is that no tactile-proprioceptive feedback was given (Neppi-Mòdona et al., 2007). Furthermore, evidence

from behavioural and neuroimaging studies showed that space dissociations were independent of the presence or absence of a motor response (Pitzalis et al., 2001; Weiss et al., 2003). Hence, future and further studies must include several tests for assessing extrapersonal space, not only in VR environments but also in real environments, to ensure the validity of the immersive VR cancellation task for extrapersonal space assessment. Moreover, there is no agreement in the literature on which test could be the more sensitive for extrapersonal neglect diagnosis. For instance, Keller et al. (2005) found that, at the group level, line bisection tasks can be more susceptible to be modulated by spatial distance than cancellation tasks, whereas Aimola et al. (2012) found the reverse. Adding other tasks in far space would also allow us to determine if batteries of tests could be more sensitive than isolated tests to diagnose extrapersonal neglect, as it is the case for peripersonal neglect (Azouvi et al., 2006).

AUTHOR CONTRIBUTIONS

A. Guilbert: Conceptualization; writing – original draft; formal analysis; supervision; writing – review and editing; methodology; funding acquisition. **T.-G. Bara:** Software; conceptualization; methodology. **T. Bouchara:** Writing – review and editing; conceptualization; funding acquisition; methodology; supervision. **M. Gaffard:** Investigation. **C. Bourlon:** Writing – review and editing; investigation; supervision.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data are available on the following link: https://osf.io/jtwk9.

ETHICS STATEMENT

Ethical approval was granted by the Paris Cité University Ethics Committee (NIRB: 00012021-33). All participants gave full informed consent.

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