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Exploring Consciousness Levels through Electrodermal Responses: A Pilot Study with Auditory Stimuli in DoC Patients

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Abstract

Accurate bedside assessment of disorders of consciousness (DoC) is hampered by high misdiagnosis rates and the practical constraints of advanced neuroimaging. Skin-conductance responses (SCR) offer a low-cost, motor-independent window on autonomic reactivity to emotionally salient stimuli. This study investigated whether SCR modulation by pleasant and unpleasant sounds differentiates vegetative state (VS), minimally conscious state (MCS) and emergence from the minimally conscious state (EMCS) from healthy controls. We expected a significant Stimulus × Group interaction such that (i) healthy controls would show a robust SCR increase to the aversive scream relative to all pleasant sounds, and (ii) if affective discrimination was preserved, higher-functioning patients would follow a graded pattern of preservation in differentiating salient from other sounds (VS < MCS < EMCS). Twenty-eight healthy volunteers and three DoC patients (VS, MCS, EMCS) heard five auditory stimuli, four pleasant (harp, carillon, sea waves, birdsong) and one unpleasant (scream) presented 20 times in a pseudo-random order. SCR was recorded with a wearable biosensor (eSense device); the primary outcome (ΔSCR) was the amplitude difference between baseline and the post-stimulus peak. Linear mixed-effects models with an autoregressive model of second order, error structure tested fixed effects of Stimulus, Condition and their interaction. In controls subjects, the aversive scream elicited a robust SCR increase ($b = 0.155$, $p < .001$) relative to all pleasant sounds, confirming heightened sensitivity to threat. The EMCS patient showed a significant SCR reduction to sea-wave sounds ($b = -0.361$, $p = .006$), suggesting preserved, but altered, affective discrimination. The MCS patient displayed non-significant trends toward larger responses to natural pleasant sounds, whereas the VS patient showed no stimulus-dependent modulation. In the combined model, the main effect of Scream ($p < .001$) and the interactions Waves × EMCS

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(p = .043) and Birds × MCS (p = .007) supported the hypothesized gradient. The pattern of autonomic reactivity across patients and controls conformed to our a priori hypothesis, highlighting SCR as an accessible adjunct for bedside evaluation of residual awareness. However, the very small patient sample limits the generalizability of these preliminary findings. Replication in larger cohorts and integration with neuroimaging will be essential to establish diagnostic reliability.

Introduction

Accurate diagnosis and prognosis of consciousness levels in patients with severe brain injury remain among the most significant challenges in clinical neuroscience [Laureys et al., 2004]. In a pivotal study, Andrews et al. (1996) reported that approximately 43% of patients initially diagnosed as being in a vegetative state were later reclassified as minimally conscious upon structured reassessment. Such misdiagnoses carry substantial consequences for treatment planning, end-of-life decisions, and communication with families, underscoring a critical issue for both clinicians and researchers. To improve diagnostic precision, standardized neurobehavioral tools such as the Coma Recovery Scale-Revised (CRS-R), have been developed as alternatives to sole reliance on clinical consensus [Giacino et al., 2004; Bodien et al. 2022]. Nevertheless, even these validated instruments may fall short in cases where motor output is minimal or inconsistent, or when spasticity and sensory deficits obscure behavioral signs of awareness [Schnakers et al., 2009; Kondziella et al., 2020].

This limitation has prompted the search for complementary diagnostic approaches capable of bypassing motor-dependent paradigms, especially in clinical settings lacking access to advanced neuroimaging technologies [Kazazian et al., 2025]. In this context, neurophysiological methods are gaining traction as promising alternatives [Rossi et al., 2021]. Techniques such as functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and electroencephalography (EEG) have revealed residual brain activity in patients who appear behaviorally unresponsive [Laureys et al., 2004; Owen et al., 2006; Monti et al., 2010, Tomaiuolo et al., 2016], suggesting the existence of covert awareness undetectable through conventional bedside assessments [Young et al. 2024; Cruse et al. 2011].

Despite their potential, the routine clinical implementation of fMRI and similar technologies remains limited due to practical constraints: high costs, the need for specialized personnel, and logistical challenges related to patient transport, immobility, and contraindications [Sanz et al. 2021]. These issues are especially critical during the acute and subacute phases of brain injury, when prognostic clarity is most urgently needed. Consequently, there is a pressing need to identify accessible, bedside-compatible physiological markers to support diagnostic and prognostic decisions.

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One such candidate is the skin conductance response (SCR), a simple, non-invasive indicator of autonomic nervous system activity. Also referred to as electrodermal activity, SCR reflects sweat gland activity modulated by emotional and cognitive arousal [Dawson et al., 2007; Critchley, 2002]. In healthy individuals, SCR increases in response to emotionally salient or surprising stimuli, and similar responses have been observed in some patients with disorders of consciousness (DoC), particularly when stimuli are personally meaningful [Luauté et al. 2018; Crivelli et al. 2020]. Notably, SCR does not require voluntary motor responses, making it particularly suitable for assessing reactivity in patients with impaired motor output.

Several studies have proposed SCR as a potential indirect marker of conscious or preconscious processing, especially when elicited by auditory, emotional, or pain-related stimuli [Yu et al., 2013; Bekinschtein et al., 2009]. In the present study, we compare SCR patterns elicited by emotionally charged auditory stimuli to identify potential indicators of preserved sensory-emotional (i.e. sound discrimination) processing in otherwise non-communicative patients. By leveraging its non-invasive nature, high temporal resolution, and compatibility with bedside monitoring, we aim to assess whether SCR can serve as a reliable biomarker for sound discrimination, i.e. for a patient who is able to react differently to different sounds. Building on the aforementioned studies, we expected that VS/UWS patients show no systematic or significative differences between the SCR to emotionally salient auditory stimuli and to pleasant high-arousal sounds. Starting from VS/UWS condition we predicted a gradient of preservation of this modulatory capacity (VS/UWS < MCS < EMCS < CONTROLS). MCS patients were expected to show weak or inconsistent differences between the SCR to diverse stimuli; EMCS patients were expected to exhibit a difference in SCR response still attenuated in magnitude, but qualitatively better (and diversified) than the other patients. Finally, we expected that healthy control SCR showed the greater and more significant differences between salient auditory stimuli and the other pleasant sounds was the greatest among healthy controls. We therefore predicted a significant Stimulus × Group interaction driven by the aversive scream in controls and (if present) in the higher-functioning patients. These hypotheses guided both the design of the experiment and the choice of our linear mixed-effects analysis. In doing so, we hope to contribute to the development of an accessible diagnostic adjunct to support clinical evaluations, reduce misdiagnosis, and guide more appropriate and individualized therapeutic interventions.

Material and Method

1.1 Selection of the acoustic stimuli

A total of 60 healthy participants, matched by sex and aged between 18 and 85 years, were exposed to 20 auditory stimuli (10 rated as pleasant and 10 as unpleasant). Participants were asked to assess the affective valence of each sound using a five-point Likert scale [Marradi et al., 2002], ranging from 1 (“completely disagree”) to 5 (“completely agree”) in response to statements of

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pleasantness or unpleasantness. Based on the average ratings and in accordance with prior literature [Bradley & Lang, 2007; Portnova & Atanov,2018], four pleasant stimuli (harp, carillon, sea waves, birds singing) and one unpleasant stimulus (scream) were selected for use in the experimental procedure.

1.2 Participants

The study sample comprised 31 individuals: 28 healthy controls and 3 patients clinically diagnosed with a DoC, specifically in vegetative state (VS), minimally conscious state (MCS), and emergence from minimally conscious state (EMCS), respectively. Control participants were randomly selected, with exclusion criteria including any history of hearing, neurological, or psychiatric disorders to ensure comparability. Patients instead were considered eligible when they presented with a clinically and neuroradiologically confirmed diagnosis of VS/UWS or MCS following a vascular or traumatic acquired brain injury, were between 18 and 90 years of age, demonstrated adequate pulmonary gas exchange ($PaO_2/FiO_2 \geq 250$), and maintained haemodynamic stability without clinically relevant fluctuations in mean arterial pressure or heart rate. Conversely, they were excluded if suffered from deafness or blindness, if they had comprised unstable intracranial pressure and any comorbid medical condition judged likely to interfere with the procedure. Each participant was presented with the selected auditory stimuli in a pseudo-randomized sequence. Prior to stimulus presentation, the three DoC patients underwent clinical assessment using the CRS-R [Giacino et al., 2004; Bodien et al., 2022]. Patient demographic and clinical data are presented in Table 1.

Patient	Age/Sex	Manual dominance	CRS score	Etiology
VS	33/M	Right	5	Anoxic
MCS	18/F	Right	10	Traumatic
EMCS	32/M	Right	13	Hemorrhagic

Table 1: Clinical profile of DoC patients: age, sex, handedness, CRS-R score, and etiology.

Features of acoustic stimulation

To minimize the risk of eliciting startle or acoustic reflexes, all auditory stimuli were introduced with a gradual fade-in. Each sound increased in intensity over a four-second period, ranging from 32 dB at onset to 62 dB at peak volume. This method aimed to reduce abrupt transitions that might provoke reflexive rather than cognitively or emotionally driven responses. Such a controlled presentation increases the likelihood that observed SCR fluctuations are attributable to genuine affective engagement.

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Stimuli were delivered via high-quality noise-canceling headphones (Beats by Dre, 2024 edition) in a quiet, controlled environment. When feasible, participants were instructed to remain seated and avoid movement throughout the experiment to reduce noise artifacts in the recordings. Each sound was presented for 4 seconds, with a 12-second silent interval preceding and following each stimulus. This timing protocol was informed by prior research [Bradley & Lang, 2007; Sander et al., 2005; Yang et al.2018] and was chosen to allow SCR levels to return to baseline between stimuli and to isolate post-stimulus responses.

Experimental procedure

SCR was recorded using the eSense device, a wearable biosensor capable of real-time electrodermal activity measurement. Electrodes were attached to the index and middle fingers of the same hand and connected to custom software that logged and displayed SCR data in real time. To ensure optimal recording conditions, the experimental environment was kept free from distractions (e.g., noise, mobile devices, and third parties) and maintained at a comfortable temperature to prevent thermal sweating. Participants were seated comfortably, and electrodes were attached using a high-quality, water-soluble EEG paste. The eSense system continuously recorded SCR activity, which was segmented and analyzed in relation to the presentation of each auditory stimulus.

Statistical analysis

The dataset comprised SCR measurements, with the primary outcome variable being the ΔSCR. This measure was computed as the difference between the maximum SCR peak observed within a 6-second window following stimulus onset and the SCR value at 6 seconds post-stimulus. This calculation was performed for each of the 20 auditory stimulus presentations per participant. The study included data from 28 healthy control subjects and three patients diagnosed as VS, MCS, and EMCS, respectively.

A preliminary analysis was conducted to compare each patient's performance against the normative data from the control group. For this purpose, Crawford's modified t-test (Test of Deficit) was employed to assess whether the mean ΔSCR elicited by each of the five auditory stimuli differed significantly for each patient (VS, MCS, and EMCS) relative to the control sample. These single-case comparisons were performed using the singcar R package (version 4.3.2). To analyze the ΔSCR data, Linear Mixed-Effects Models (LMEs) were employed due to the hierarchical and longitudinal nature of the data, which involved repeated measurements within individual subjects. LMEs are particularly suitable for such designs as they allow for the simultaneous modeling of both fixed effects (variables of primary interest, such as stimulus type and patient condition) and random effects (variability attributable to individual participants). All models were implemented with the nlme package in R (version 4.3.2). A random intercept was included for each participant to model inter-individual variability. To address potential within-subject temporal dependencies in the SCR data, an autoregressive moving average (ARMA) correlation structure of order ($p=2$) was specified, in order

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to account for the sequential order of stimulus presentation within each subject. Initial autoregressive models of order 1 [AR(1)] and order 2 [AR(2)] were tested individually for the VS, MCS, EMCS patient groups, and the healthy control group. Subsequently, a combined LME model was estimated to assess overall effects and interactions, including fixed effects for Stimulus type, Condition (patient group vs. control), and their interaction.

Results

A preliminary single-case analysis was performed using Crawford's modified t-test to compare each patient's mean electrodermal response (ΔSCR) to each auditory stimulus against the normative data from the control group. The results of this analysis indicated that none of the observed differences between the individual patients (VS, MCS, and EMCS) and the control sample reached the threshold for statistical significance for any of the five stimuli. Detailed statistics, including t-values and corresponding p-values for each comparison, are presented in Table 2.

Stimulus	VS	MCS	EMCS
Birds	t = -0.314 (p = 0.756)	t = -1.800 (p = 0.082)	t = -0.089 (p = 0.930)
Harp	t = -0.225 (p = 0.823)	t = 0.154 (p = 0.879)	t = -0.774 (p = 0.445)
Waves	t = -0.164 (p = 0.871)	t = -0.805 (p = 0.428)	t = -1.166 (p = 0.253)
Soundbox	t = 0.509 (p = 0.615)	t = 1.533 (p = 0.136)	t = 0.397 (p = 0.694)
Scream	t = -0.212 (p = 0.833)	t = -0.603 (p = 0.551)	t = 0.018 (p = 0.986)

Table 2: Comparison of single clinical subjects with Control group according to Crawford's modified T-test

Considering the statistical limitations of single-case comparisons, which rely on aggregated metrics and are therefore insufficient to model the hierarchical data structure or account for the autoregressive properties inherent in sequential electrodermal recordings, a more robust analytical framework was employed to leverage the full dataset. The analysis of ΔSCR data was therefore conducted using linear mixed-effects models, with individual models fitted for each group and a combined model to assess overall effects and interactions. Autoregressive models of order 2 were generally selected over AR(1) models for their improved fit, as indicated by higher log-likelihood values, and their capacity to capture more complex temporal dependencies in the physiological responses. The autoregressive coefficients and model fit indices for both AR(1) and AR(2) models across the different groups are presented in Table 3.

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GROUP	MODEL	Φ1	Φ2	AIC	BIC	LOGLIK
VS	AR(1)	0.092	-	11.924	18.296	3.038
	AR(2)	0.221	0.729	8.533	15.614	5.733
MCS	AR(1)	-0.407	-	27.603	34.684	-4.503
	AR(2)	-0.656	-0.390	27.006	33.379	-3.802
EMCS	AR(1)	0.088	-	18.118	25.198	0.461
	AR(2)	0.274	-0.378	17.078	23.450	0.941
CONTROL	AR(1)	-0.018	-	9.896	53.561	5.042
	AR(2)	-0.019	-0.007	7.916	47.215	5.052

Table 3: Autoregressive Coefficients and Fit Indices for AR(1) and AR(2) Models by Condition

For the Vegetative State (VS) patient, the AR(2) model yielded autoregressive coefficients of $\Phi1 = 0.221$ and $\Phi2 = 0.729$. Fixed effects for stimulus type did not show statistical significance (Music Box: $p=0.764$; Waves: $p=0.549$; Birds: $p=0.385$; Scream: $p=0.704$; Figure 1A). In the Minimally Conscious State (MCS) patient, the AR(2) model exhibited autoregressive coefficients of $\Phi1 = -0.656$ and $\Phi2 = -0.390$. Fixed effects for stimulus type were not statistically significant (Music Box: $p=0.118$; Waves: $p=0.100$; Birds: $p=0.093$; Scream: $p=0.393$; Figure 1B). For the Emergence from Minimally Conscious State (EMCS) patient, the AR(2) model revealed autoregressive coefficients of $\Phi1 = 0.274$ and $\Phi2 = -0.378$. A significant fixed effect was observed for the Waves ($b = -0.361$, $p=0.006$). Other stimulus types did not reach statistical significance (Music Box: $p=0.095$; Birds: $p=0.148$; Scream: $p=0.696$; Figure 1C). The Healthy Control group AR(2) model showed autoregressive coefficients of $\Phi1 = -0.019$ and $\Phi2 = -0.007$. A highly significant fixed effect was found for the Scream ($b = 0.155$, $p<0.001$). Other stimulus types were not statistically significant (Music Box: $p=0.365$; Waves: $p=0.388$; Birds: $p=0.196$; Figure 1D).

The combined model, which included Stimulus, Condition, and their interaction, incorporated an ARMA (2,0) correlation structure with overall autoregressive coefficients of $\Phi1 = -0.026$ and $\Phi2 = -0.010$ are summarized in Figure 2. Regarding fixed effects, a significant main effect was observed for Scream ($b= 0.155$, $p<0.001$). No other main effects for stimulus types or conditions (EMCS: $p=0.153$; MCS: $p=0.371$; VS: $p=0.979$) reached statistical significance. Significant interaction terms were identified for Waves*EMCS ($b = -0.336$, $p=0.043$) and Birds*MCS ($b = -0.445$, $p=0.007$). Other interaction terms were not statistically significant.

Discussion

This pilot study aimed to explore the usability of SCR as a reliable non-invasive biomarker for covert awareness in patients with DoC. Despite its limitations in reliability compared to neuroimaging, SCR offers notable advantages in clinical contexts: it is cost-effective, easily implemented at the bedside, and does not rely on voluntary motor output, an important

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consideration for non-communicative patients. By comparing the SCR profiles of patients diagnosed with VS, MCS, and EMCS with those of healthy controls, we aimed to determine whether the emotional salience of auditory stimuli could elicit differential autonomic responses that may be reflective of residual awareness or sensory-emotional discrimination, with implications for both the clinical assessment of residual awareness and the theoretical understanding of emotional responsiveness in DoC.

While the small sample size warrants caution, the findings nevertheless reveal limited yet discernible patterns of SCR modulation across stimuli of differing emotional salience. These findings provide encouraging preliminary evidence that salient auditory inputs modulate SCR in ways consistent with each patient's clinical status.

The EMCS patient exhibited a significant reduction in SCR in response to sea wave sound, potentially indicating a calming or familiar emotional response. This finding is consistent with prior work suggesting that patients recovering consciousness show increased capacity for acoustic salience discrimination and attentional modulation [Bekinschtein et al., 2009; Riganello et al., 2015]. Naturalistic stimuli such as sea waves may activate autobiographical memory networks or exert regulatory effects on autonomic activity [Cavinato et al., 2011; Salvato et al., 2020]. The MCS patient demonstrated non-significant but directionally meaningful trends toward decreased arousal to natural pleasant sounds. This is consistent with the suggestion that MCS patients can exhibit differentiated autonomic and cortical responses to affective stimuli, particularly when stimuli have biological salience or emotional relevance [Kotchoubey et al., 2005; Boly et al., 2004; Perrin et al., 2006].

Even the VS patient did not exhibit any significant modulation of SCR across stimuli. This lack of SCR modulation corresponds with existing literature asserting the absence of conscious emotional experience or salience sound discrimination, and the lack the neural integration necessary for conscious emotional experience in VS [Laureys et al., 2004; Schnakers et al., 2008; Giacino et al., 2002]. This absence of response is coherent with the breakdown of cortico-subcortical loops that mediate affective appraisal and autonomic regulation [Laureys et al., 2004]. The absence of SCR differentiation in this case supports the hypothesis that autonomic responses to emotionally salient acoustic stimuli may require at least minimal levels of conscious awareness or integrative processing capacity.

On the other hand, among healthy participants the scream stimulus elicited a robust increase in SCR, consistent with a heightened autonomic arousal to aversive, biologically salient cues. This supports prior findings from prior literature indicating that scream-like stimuli activate limbic and paralimbic regions associated with threat detection and arousal [Arnal et al., 2015; Bradley & Lang, 2007; Frühholz et al., 2016]. These acoustic discrimination responses might further be mediated by the amygdala and periaqueductal gray and are evolutionarily conserved to prioritize threat detection [LeDoux, 2012]. Taken together, the pattern of findings conforms closely to the predictions we

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formulated a-priori. Healthy controls displayed the expected surge in SCR to the aversive scream, confirming its privileged status as a biologically salient threat cue.

The EMCS patient mirrored this stimulus-dependent modulation, albeit with the strongest effect emerging for the highly arousing Waves sound, providing partial support for a preserved, though attenuated, discriminatory capacity.

In the MCS patient, only non-significant trends toward larger responses to salient sounds were observed, consistent with our anticipation of a weakened modulation. As foreseen, the VS/UWS patient showed no systematic SCR differences across stimuli. Overall, this graded pattern substantiates the hypothesis that autonomic discrimination of emotionally salient sounds tracks the clinical hierarchy of consciousness and underscores the potential value of emotionally calibrated auditory probes at the bedside. Moreover, pleasant stimuli such as birds singing and sea waves modest and statistically non-significant changes in the SCR of the control group, suggesting that in the absence of personal or contextual relevance, pleasant sounds may evoke subtler physiological changes than aversive ones, a phenomenon previously documented by other studies [Delplanque et al. 2006; Gomez & Danuser, 2007]. Moreover, SCRs are typically more sensitive to stimuli that induce arousal (e.g., fear, surprise) than those that are purely valenced [Bradley & Lang, 2000].

The significant interactions observed in the combined model between specific stimulus types and DoC conditions (namely, the WavesEMCS and BirdsMCS interactions) suggest that certain pleasant stimuli may be more effective at differentiating levels of consciousness than others. The sea waves stimulus, which induced a significant SCR reduction in the EMCS patient, has previously been shown to promote relaxation and modulate heart rate variability [Alvarsson et al. 2010; Benz et al. 2022], possibly tapping into residual affective memory or sensory familiarity. Similarly, a commonly encountered and evolutionarily relevant auditory cue like bird singing elicited a differentiated response in the MCS patient, hinting at the selective preservation of naturalistic auditory preferences even in severely impaired states [Şirin Gök & Akpinar, 2025;]. Birds singing in particular, have been shown to evoke parasympathetic responses and positive affect in both clinical and non-clinical populations [Ratcliffe et al., 2013].

These findings support the hypothesis that naturalistic, emotionally salient auditory stimuli can differentially engage the autonomic nervous system in patients across the consciousness spectrum. DoC patients may benefit from stimulation paradigms grounded in evolutionary and ecological salience. They also bolster the argument for integrating emotion-based physiological markers in differential diagnosis and recovery monitoring [Riganello et al., 2018]. Importantly, they underscore the value of ecologically valid sensory inputs in the clinical evaluation of awareness.

The use of autoregressive models of 2nd order (AR(2)) was validated by superior model fit across all groups. This statistical refinement captures the inherent temporal autocorrelation in SCR data and avoids inflation of Type I error rates common in repeated-measure psychophysiological studies [Bach et al., 2010]. The application of linear mixed-effects models (LME) with autoregressive

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structures was crucial in accounting for the complex temporal dynamics of SCR data. The AR(2) models consistently outperformed AR(1) models across conditions, highlighting the presence of lagged dependencies in electrodermal activity—a methodological nuance that, if ignored, may obscure subtle physiological effects. This modelling approach aligns with recommendations from recent psychophysiological literature [Bach et al., 2010; Boucsein, 2012]. Moreover, the LME further allowed for robust analysis across participants with varying response patterns and is consistent with best practices for modeling longitudinal psychophysiological data [Pinheiro & Bates, 2000].

The small sample of DoC patients necessitates cautious interpretation limiting generalizability and precluding subgroup comparisons based on etiology, chronicity, or comorbidities. However, the individualized analysis remains valuable given the heterogeneity of the DoC population [O'Donnell et al. 2019]. Future studies should consider using emotionally salient autobiographical stimuli, as demonstrated in music-evoked paradigms [O'Kelly et al., 2013] or leveraging voice-based emotional intonation [Perrin et al., 2015]. Combining SCR with EEG or fMRI would enable a richer multimodal characterization of affective responsiveness and consciousness levels [Jain & Ramakrishan, 2020; Gallucci et al. 2024].

The differential SCR responses to emotionally charged stimuli, particularly in EMCS and MCS patients, have potential clinical implications. Such physiological markers may contribute to improved diagnostic resolution when behavioral assessments yield ambiguous results. The findings also support the inclusion of emotionally salient auditory stimuli in therapeutic and rehabilitative interventions aimed at enhancing arousal, engagement, and possibly recovery trajectories in patients with DoC.

This study supports the potential of SCR as a diagnostic tool for assessing DoC patients' reactivity. Although SCR does not offer the spatial detail of neuroimaging, its ease of use and cost-effectiveness make it a practical tool for routine clinical assessments. The careful design of auditory stimuli presentation in this study, specifically the gradual increase in sound volume, helped mitigate acoustic reflexes, ensuring that observed SCR changes were likely linked to cognitive or emotional processing rather than automatic responses.

Conclusion

The results of this study demonstrate the utility of SCR, measured through the eSense device, as a viable and non-invasive tool for assessing autonomic responses in patients with DoC. This method offers an accessible option for clinical practitioners, complementing traditional assessment tools and potentially improving the accuracy of DoC diagnosis and monitoring.

Conflicts of Interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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