

Autonomic responsivity and semantic associative competences in disturb of consciousness

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ABSTRACT

Linguistic associative functions in Disorders of Consciousness patient (DOC) were studied in the present research by using autonomic measures (Skin Conductance Response, SCR; Heart Rate, HR). We intended to verify the preservation of semantic linguistic processes in Vegetative State (VS) and Minimal Consciousness State (MCS) by considering arousal modulation. Twenty-four patients and twenty controls were submitted to an auditory semantic task (congruous or incongruous word sequences). A similar increased SCR/HR was found for both DOC and control group in response to incongruous condition. This modulation was interpreted as a marker of the increased cognitive difficulty in processing and restoring incongruent information. However, MCS and VS groups quantitatively (but not qualitatively) differed in term of degree of increased arousal, since higher SCR and HR increasing was observed for MCS than VS. These results were interpreted as a marker that the semantic processing was partially preserved in both VS and MCS patients.

Keywords: Disturb of consciousness; SCR; HR; Arousal; MCS; VS

1. INTRODUCTION

Disorders of consciousness (DOC) were classified in terms of awareness and wakefulness (Gawryluk, D'Arcy, Connolly & Weaver, 2010). Awareness refers to a state in which people have complete experiences such as thoughts, memories and emotions. Wakefulness refers to the state in which people can open their eyes and presents motor responsiveness. Three different typologies of distinct disorders of consciousness can be defined based on these two states: Coma (C), where patients show absence of both awareness and wakefulness; persistent Vegetative State (VS), where there is wakefulness without awareness; Minimally Conscious State (MCS), where both awareness and wakefulness are partially preserved (Giacino et al., 2002; Harrison & Connolly, 2013). Clinical tests rely on a patient demonstrating awareness by means of overt behaviors, as does the Coma/Near-Coma Scale (CNC), the Glasgow Coma Scale (GCS) and the Disability Rating Scale (DRS) (Rappaport, 2005). Also recently Coma Recovery Scale-Revised (CRS-R) was developed to assess differences between levels of consciousness (Giacino, Kalmar & Whyte, 2004).

However, appropriate diagnostic tools that can ensure a more accurate assessment are needed to provide an exhaustive examination of the cognitive status of these patients. Available standardized tools specifically developed for the evaluation of patients with severe impairment are very limited and mostly relatively insensitive to minor changes in level of consciousness. Also they do not consider the obstacles that may affect the detection of responses to the presence of motor, sensory or cognitive deficits. Thus, to compensate the significant limitations of these behavioral measures, some approach considered as prominent the physiological criterion to evaluate DOC responsiveness to specific cognitive and emotive task (Balconi, Arangio & Guarnerio, 2013; Cavinato, Volpato, Silvoni, Sacchetto, Merico & Piccione, 2011).

One of the most common questions regarding patients with DOC is the preservation of their linguistic ability. The majority of ERP and fMRI studies in these patients seeks to answer just that question, not only in individual cases but also at the level of diagnostic category (Harrison & Connolly, 2013). Some previous research focalized on semantic processing by using classical linguistic task (Rämä, Relander-Syrjänen, Ohman, Laakso, Näätänen & Kujala, 2010; Vanhauzenhuysse, Laureys & Perrin, 2008; Harrison & Connolly, 2013). Preserved abilities were found in DOC in response to linguistic stimuli, that is in MCS and sometimes in single-case reports of VS (Schoenle & Witzke, 2004). On the contrary other studies did not find significant similarity between the two groups. However, due to the complexity of the stimulation conditions (whole sentences to be processed or visual

stimulation), it may be supposed that in some cases the absence of significant responses by some patients may be related to the experimental paradigm more than to the real absence of semantic abilities in DOC. Previous studies using some EEG markers (such as the N400 ERP effect) showed a significant homology between VS and MCS in processing semantic information induced by linguistic conditions (Balconi et al., 2013). This ERP value in terms of high-order cognitive processes may integrate the general spectrum of the cognitive functions that may be preserved in DOC, with specific attention to the semantic level.

The current contribution focuses on autonomic measures which are readily available across a range of clinical settings and thus provides an important tool for the consciousness. In previous studies on control subjects it was found that psychophysiological measures of autonomic nervous system activity in response to auditory tasks may provide a means of quantifying the effects of cognitive effort. A small number of studies has documented cardiac changes during auditory detection and discrimination tasks (Van der Molen, Somsen & Jennings, 1996). Moreover, linguistic expectancy violations were found to induce an increased Skin Conductance Response (SCR) in DOC patients (Scott, Minati, Dienes, Critchley & Seth, 2011). In general, arousal modulation induced by an increased task complexity or by more cognitive effort was found to determine a concomitant SCR and Heart Rate (HR) increasing.

However, no previous research used this measure to test the preserved linguistic skills in DOC by adopting a specific auditory linguistic paradigm. Within an experimental task, some DOC patients were required to implicitly process congruous vs. incongruous linguistic semantic associations related to word categorization abilities.

The present research aimed to support the DOC semantic abilities by monitoring their autonomic correlates (SCR; HR) to auditory linguistic task. Thus the main goal of the present research was to verify the consistence between traditional assessment measures (such as psychometric measures) and autonomic indexes. A significant autonomic activity was expected in response to incongruous patterns in comparison with congruous patterns for patients (both VS and MC) able to semantically process the linguistic anomaly. Thus similar profile was attended for both control and patient group.

2. METHOD

2.1. Participants

The sample included 24 patients (11 men and 13 women) aged between 25 and 62 (mean age = 53; SD = 8.98). The DOC patients followed a coma due to anoxia (9), traumatic brain injury (8), stroke (7). The time between coma onset and the experiment ranged between 6 and 60 months (mean = 44 months). The patients had no history of neurologic disorder prior to coma. The two scales (CNC and DRS) were submitted to the patients by three expert neuropsychologists following the standard guidelines (see details in Rappaport, Hall, Hopkins, Belleza & Cope, 1982; Rappaport, 2005). Based on these scorings patient group was sub-divided into two subgroups for the successive statistical analysis: VS and MCS patients. The first one included 11 patients who scored more than 2.00 on the CNC; more than 22 (range = 22-24) to the DRS; the second one 13 patients who scored between 0.00-2.00 on the CNC; less than 22 (range = 12-20) on the DRS. These two measures showed to be highly correlated and they are able to furnish a clear cut-off between high and low impaired DOC patients. Patients were staying in rehabilitation center supported by medical assistance and rehabilitation for all the hospitalization. 20 control subjects (10 men and 10 women) were included into the study. They were matched for age (range = 24-66, mean age + SD = 47 + 6.90), gender and education to patient group.

The study did not modify the usual medical practice and it complies with the *Declaration of Helsinki* relative to patients' rights. It was approved by the Ethic Committee of the University where the study was carried out.

2.2. Materials

Each auditory word sequence was composed of four words that were presented to the subjects, and it had a congruous (semantic related) or an incongruous (semantic unrelated) final word based on its semantic content. The semantically unrelated final words were chosen on the basis of belonging to distant semantic categories and a lack of association according to the association norms. For example subjects were presented the following incongruous words sequence: cherry, apple, melon, fork; or congruous words sequence: cherry, apple, melon, grapes. Specifically, the association norms were drawn from the DPSS psycholinguistics database (Peressotti, Pesciarelli & Job, 2002; De Mauro, Mancini, Vedovelli & Voghera, 1993).

2.3. Procedure

The task was performed in a quiet room (the hospital bedroom) in which patients were tested one at a time. They were familiarized with the task in a preliminary session, with the same associative implicit task (four examples, two for congruous and two for incongruous condition; these examples were not used also for the successive experimental session). The sequences (30 congruous and 30 incongruous sequences) were presented orally (four sub-sequences of 10 trials). Two loudspeakers were placed behind the participant, to the right and left at a distance of 30 cm. The volume was distinctly audible. They were introduced in a word-by-word presentation (duration range = 2-3 sec) with an ISI interval of 3 sec and an inter-trial interval of 15 sec. The order of the sequences was counterbalanced across participants.

2.4. Psychophysiological measures

Bio-feedback (Biofeedback 2000, version 7.01) connected to a PC was used to record the autonomic activity. One set of electrodes was connected to the Bio-feedback Amplifier. For SCR measure, before attaching the electrodes, the skin was cleaned with alcohol and slightly abraded. The electrodes (4 mm diameter Ag/AgCl electrodes), filled with Surgicon electrolyte paste, were positioned over the medial phalanges of the second and third finger of the non-dominant hand (Amrhein, Muhlberger, Pauli & Wiedermann, 2004). SCR, elicited by each stimulus, was registered continuously with a constant voltage. It was manually scored and defined as the largest increase in conductance during final word presentation, with a cut-off of at least 0.4 μ S in amplitude with respect to prestimulus mean values that were scored during 10 sec prior to stimulus onset. The electrocardiogram (HR) was recorded using electrodes on the left and right forearms. Inter-beat intervals of the electrocardiogram were converted to heart rate in number of beats per minute (scoring HR modulation during hearing the final word stimulus). Trials with artifacts were excluded from analysis, whereas trials with no detectable response were scored as zero.

3. RESULTS

Two sets of successive analysis were conducted: the first step was finalized to compare the general patient category with the control group. The second

step was aimed to compare VS with MCS sub-category each other. Two dependent measures were used, respectively the SCR and HR. Each dependent measure was entered into a two-way repeated measure ANOVA. Independent repeated factors were group (2) and congruence (2).

3.1. Patient vs. control comparison

With respect to SCR measure, a significant main effect was found for congruence ($F[1, 23] = 9.45, p = 0.001, \eta^2 = .40$). No other effect was significant (for all analyses $p > .10$). An increased SCR value was found in response to the incongruous condition, as compared to the congruous condition (Table 1). For HR measure, it was also found a significant congruence effect ($F[1, 23] = 9.06, p = 0.001, \eta^2 = .39$). An increased HR value was found in response to the incongruous than congruous condition (Table 1).

Table 1. Mean (SD) SCR (μS) and HR (beat/min) values as a function of group (Control vs. MSC vs. VS) and condition (congruous vs. incongruous)

	SCR		HR	
	M	(SD)	M	(SD)
CONTROL				
congruous	0.40	.07	2.97	.08
incongruous	0.68	.05	3.81	.09
MSC				
congruous	0.38	.06	3.03	.09
incongruous	0.62	.07	3.71	.05
VS				
congruous	0.36	.08	2.98	.08
incongruous	0.50	.06	3.30	.08

3.2. VS vs. MCS comparison

With respect to SCR, condition \times group interaction effect was significant ($F[1, 23] = 10.50, p < .01, \eta^2 = 0.42$). As shown by contrast comparisons, both groups showed increased SCR in response to incongruous than congruous condition (respectively for MCS $F[1, 23] = 6.09, p < .01, \eta^2 = 0.33$; for VS $F[1, 23] = 8.50, p < .01, \eta^2 = 0.37$). Moreover, MCS showed an

increased SCR than VS in response to incongruous condition ($F[1, 23] = 8.72, p < .01, \eta^2 = 0.37$). On the contrary, no difference was found for congruous condition across the two groups ($F[1, 23] = 1.09, p = .28, \eta^2 = 0.11$) (Figure 1, a-b).

About HR, significant interaction effect was found condition \times group ($F[1, 23] = 6.77, p < .01, \eta^2 = 0.34$). Contrast comparisons showed an increased HR for both groups in case of incongruous than congruous condition (respectively $F[1, 23] = 6.09, p < .01, \eta^2 = 0.34$; $F[1, 23] = 7.13, p < .01, \eta^2 = 0.36$). However, it was also found an increased HR for MCS than VS in response to incongruous condition ($F[1, 23] = 7.51, p < .01, \eta^2 = 0.37$).

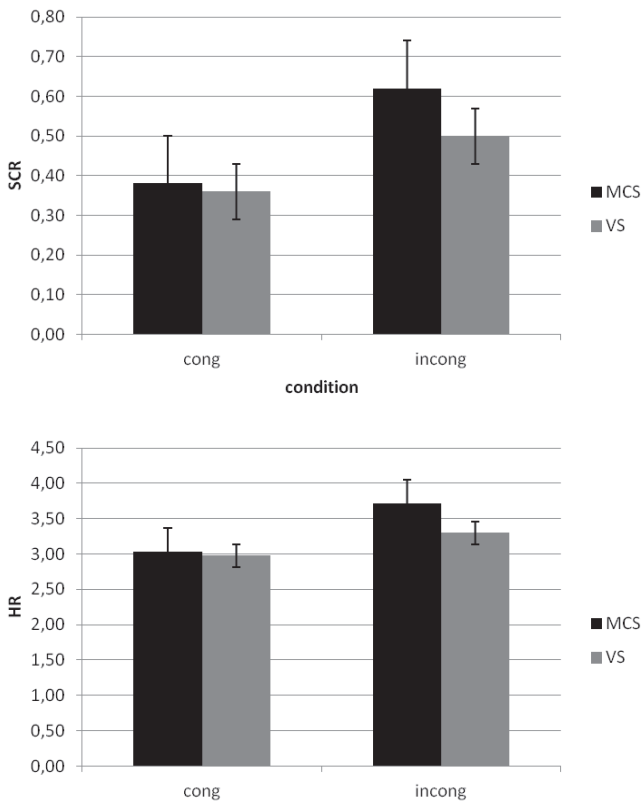


Figure 1. (a) SCR and (b) HR modulation as a function of MCS and VS groups in congruous and incongruous condition

4. DISCUSSION

Two main results were found in the present research: about the first, a significant autonomic responsiveness was found in response to incongruous condition for DOC patients. This effect was similar to the autonomic activation found in control subjects in response to semantic incongruence; about the second, although a significant increasing of SCR and HR was revealed for both VS and MCS patients in case of incongruence, the comparison between patient-groups showed a significant larger impact of the incongruous condition for MCS than VS.

Firstly, it was observed a significant modulation of arousal (in terms of SCR and HR increasing) in response to incongruence. The similarity of behavior revealed by patient and control subjects may underline that for DOC patients some relevant cognitive linguistic functions were preserved (Cavinato et al., 2011). Previous research found that some patients diagnosed as VS showed clear semantic capabilities (Rämä et al., 2010; Schoenle & Witzke, 2004). However, no consistent results were obtained comparing different research. The present contribution explicitly explored the semantic processing that includes the evaluation of conceptual relationship between words. We found that final words semantically unrelated to previous words elicited an increased arousal response than semantically related words in all DOC patients. Such a result shows that the autonomic effect goes in the direction of a significant modification induced by task complexity, since an increased difficulty in processing anomalous words may have determined the increasing of arousal. We may hypothesize that DOC patients showed autonomic amplitude variation depending on the difficulty of implicitly retrieving knowledge associated with unattended context. In fact, it was found that potentially unrelated information is processed with increased cognitive costs, as a function of how this information has to be mentally discarded as not relevant and the conceptual context has to be restored (Balconi & Pozzoli, 2008).

About the second result, VS appear generally less responsive to the incongruence, although they demonstrated a preserved ability to attribute relevance to the incongruence perception. Thus we may state that the difference between the patient groups may be considered more “quantitative” than “qualitative”. This fact goes against the concept of VS patients and the general supposition on their poor conceptual skills. Moreover, it shows as a critical point the supposition that DOC patients, and specifically patients diagnosed as VS, lack of significant conceptual and semantic competencies. The increase of autonomic response in case of specific condition may point out the role of autonomic measures in activating a more complex process-

ing related to the incongruence. Indeed, as shown in previous results, an increasing of arousal in case of similar linguistic task may be responsive of a higher difficulty in restoring the adequate semantic context when a semantic violation is recognized. This hypothesis was referred to as “memory retrieval account” and it was used to explain the variations due to the degree of relevance and general “coherence” of information within a context (Friederici et al., 2003).

5. CONCLUSION

About the functional significance of these results for study of DOC field, it was found to be particularly useful for indexing some preservation of awareness in response to semantic conditions, where an increased cognitive difficulty is present. Therefore, we may suppose that DOC patients partially maintain the ability to execute some high level linguistic functions and that these functions can be remarked by psychophysiological measures. Also patients previously classified as VS maintain a consistent ability to respond to the semantic meaning, by showing a significant preserved comprehension of incongruous associations. More generally, since DOC patients were able to process language, this is strong evidence for a partial preservation of some higher cognitive functions such as semantic association, and an argument against the assumption that these patients only respond at a basic perceptual level (Amantini, Carrai, Fossi, Pinto & Grippo, 2011). However, due to the sample size limitation and the number of patients included in the MCS and VS categories, future research should integrate the present data. Moreover, an exhaustive analysis about the relationship between different clinical profiles, psychometric measures and EEG (ERPs) could furnish a more complete overview.

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