

An Integrated Ambient Intelligence System in the Monitoring and Rehabilitation of the Disorder of Consciousness.

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Abstract—Ambient Intelligence (AmI) collectively refers to a family of sensitive electronic systems responsive to humans and mediating in the human interaction with devices and environment. This novel paradigm of information technology complies with the international standards for the functional integration of biomedical domotics and informatics in hospital and homecare. We have designed and implemented an AmI system with sensor networks for the continuous automatic monitoring of subjects with severe brain damage and disorder of consciousness hospitalized in the S. Anna-RAN Institute for medical care and rehabilitation. The system was designed to allow real-time analyses of relevant environmental parameters and the subjects' vital signs. Main purposes are to identify: 1- partially preserved or recovered circadian/ultradian rhythms; 2) functional changes potentially associated to prognostic indicators; 3) momentary subject/environment interactions or functional changes possibly indicative of residual/recovered responsiveness; 4) predictive models of responsiveness. The system also supports the clinician in decision making. In this respect, AmI should be regarded as equivalent to a traditional laboratory for data collection and processing, with substantially reduced dedicated equipment and staff and limited costs. Moreover, the AmI should provide an accurate system of observation of the patient-ambient interaction, offering a better support to the clinical decision in the rehabilitation phase.

Keywords-Monitoring Systems; Decision Making; Disorders of Consciousness; Ambient Intelligence; Sensory Device .

I. INTRODUCTION

The label Ambient Intelligence (AmI) collectively indicates a family of electronic systems that are sensitive and responsive to humans and mediate in the human interaction with devices and environment. It provides pervasive but unobtrusive sensing and computing devices and ubiquitous networking for human/environment interaction [1]. This novel paradigm of information technology complies with the international Integrating Healthcare Enterprise board (IHE) [2] and eHealth HL7 technological standards [3][4] for the

functional integration of biomedical domotics and informatics in hospital and home care. The European Commission charted a path for research on AmI in 2001 [5]. The use of biomedical robotics and informatics in hospitals is also involved in the processes for medical decision making - a complex aspect of the patient's care whereby a high level of cognitive processing is required to manipulate large datasets of disparate kind, origin and significance [6]–[8].

Subjects with disorder of consciousness due to severe brain injury who are in the vegetative (VS/UWS) or minimally conscious (MCS) states [9]–[12] need constant monitoring; a continuous stream of clinical/neurobiological/ behavioral information is required for appropriate care by the medical and nursing staff and to optimize the rehabilitation therapy [13]. A dedicated AmI system has been designed and developed for this purposes, to provide an accurate system of observation of the patient-ambient interaction and to have a better support to the clinical decision in the rehabilitation phase. In section II of the paper is described the method of data acquisition; the section III is dedicated to the biometric and environmental nodes, while the section IV is dedicated to the data analysis; the section V contains a brief description of the Heart Rate Variability and the importance of its analysis in the rehabilitation therapy; finally the section VI reports the conclusions.

II. DATA ACQUISITION

Daily medical and nursing care and the rehabilitative protocols in hospital require multi- and cross-disciplinary activities. Data acquisition and analyses are core facilities in the rehabilitation process, with both scientific and applicative implications; computational environments capable of integrating heterogeneous representations from different fields are also mandatory in this context. Such environments should integrate heterogeneous formalisms in the same model and assist the modeller in designing and implementing

new models based on new knowledge acquired in the rehabilitation environment.

We have designed and implemented an AmI system with *ad hoc* sensor networks for the continuous monitoring of subjects in VS/UWS or MCS hospitalized in the S. Anna - RAN Institute for medical care and rehabilitation. The system can be implemented to allow exporting the facility to homecare with control in remote. The acquisition and integration procedures are implemented to record, store and process both biometric and environmental data from dedicated nodes. The monitoring system is designed to allow real time analyses of the subject's vital signs and of the environmental parameters in which he/she lives (Figures 1 and 2). Samples of recorded data are shown in figure 3.

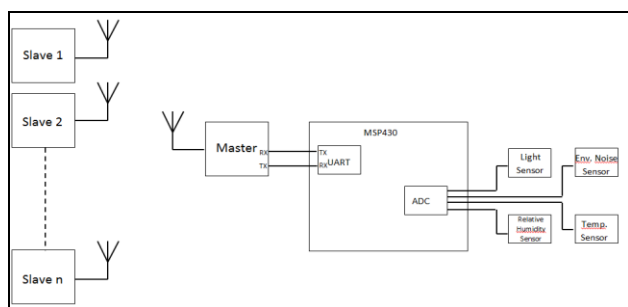


Figure 1: Block diagram of the monitoring system

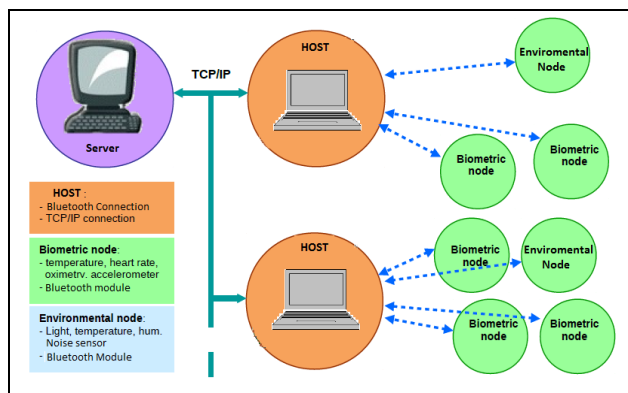


Figure 2: System overall architecture.

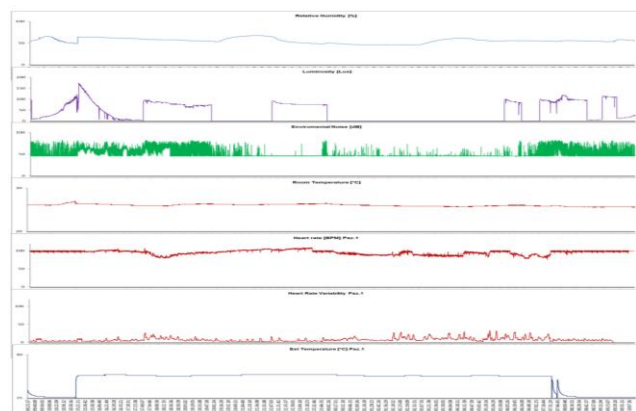


Figure 3: Sample plot of data from the patient and ambient parameters. From top to bottom: humidity, luminosity, noise, room temperature, HR, HRV and Patient temperature.

III. BIOMETRIC AND ENVIRONMENTAL NODES

Data transmission from the subject to the biometric node is realized via Bluetooth by mean of Zephyr Bioharness 3 devices [14]–[16] positioned on a chest strap. Electrodes are built to monitor heart rate, heart rate variability, respiration rate, temperature, movement and oxygen saturation. Specifically:

- Two electrodes for heart rate and heart rate variability;
- A sensor on the strap right side for respiration;
- A triaxial accelerometer incorporated in the device to detect the posture angle and activity indexes;
- An infrared temperature sensor to measure skin temperature.
- A photoplethysmographic sensor to measure PO2.

Four sensors detect environmental parameters:

- Temperature (Texas Instruments LM 35);
- Relative Humidity (Honeywell HIH 3605);
- Noise (Omnidirectional condenser electret microphone);
- Light intensity (Light Dependent Resistor).

The Texas Instrument LM35 is a high-precision integrated sensor for detecting ambient temperature. It has a linearly proportional output voltage-temperature characteristic, with scale factor: +10 mV/°C and a range of measurements from -55°C to 150 °C, with ± 0,5°C accuracy at 25 °C in addition to the low current draw. The system core is based on a microcontroller. The Honeywell HIH 3605 Environmental Relative Humidity sensor is an integrated sensor with linear voltage-relative output, low current draw, fast response in time and high accuracy. It works, with a 5 V voltage supply in the 0-100 % range; accuracy is ± 2%. The datasheet provides formulas to calculate the relative humidity and compensate for temperature in respect to the relative humidity. The device has three terminals. Light intensity is detected by mean of a light sensor using a light dependency resistor (LDR) that through its conditioning circuit returns a voltage signal that is converted into light intensity. It is a passive sensor relay for the variation in a semiconductor electric resistance due to the incidence of electromagnetic radiation with wavelength from 1mm to 10 nm. The LDR used in the prototype has a range of operating temperature between -30°C and 70°C. At dark, it offers a resistance of 2 MΩ and response time of 30 ms. The characteristic of the spectrum response is similar at human eye, with peak value at 560 nm. The Condenser Electret Microphone is an omnidirectional microphone to detect environmental noise. Its operative sensitivity of -38 dB ± 3 dB at f = 1 kHz, with operating 2-10V range offers a signal-to-noise ratio of 58 dB and a frequency spectrum similar to that of the human ear (20 ÷ 20000 Hz). The MSP430 family [17][18] is a series of mixed-signal processors for ultra-low power signals, with 16-bit Von Neumann architecture, RISC-based. In our project, the Texas Instruments MSP430F2274 was used to handle, compute and make a first filtering of the signals; low power microcontrollers will allow implement a battery-powered device. Each sensor requires a conditioning

circuit making the output signals from each sensor suitable for transmission, display or recording meeting the requirements of the device following in the line. A conditioning circuit comprises electronic circuits performing each of the following functions: amplification, level shifting, filtering, impedance matching, modulation, demodulation. The accuracy and reliability of environmental sensors and measures have been tested in the Nexus Laboratories of the Department of electronic engineering, University of Calabria, Italy.

Msp430 used in this prototype module starts through its UART (Universal Asynchronous Receiver Transmitter)[19] a serial communication at 9600 baud/sec in configuration 8N1 (8 data bit, no parity bit, 1 stop bit). The microcontroller pins for signal transmission and reception are linked to those of the Bluetooth module, which serves as the master interacting with the slave sensor node networks (environmental and biometric). The bit sent contains digital information of parameters monitored from sensors. An analogic/digital converter is integrated in microcontroller for data transmission; it is a SAR [17], 10 bit resolution, with internal reference, set at 1,5 V for greater signal accuracy.

A. Architecture of the system

The structure of the system (server) (Figures 2 and 3) has been designed to collect data from smaller structures (nodes and hosts) distributed in the hospital ambient suitable of, and requiring, monitoring. Specifically, each ambient will be equipped by a host (personal computer) collecting data to be sent to the server and a series of biometric sensors worn by the patients, that will send the biometric data to the host. Host collects data information from sensor nodes of network by Bluetooth communication. Servers will collect all data from the network by TCP/IP protocol communication.

B. Application Software

A Labview National Instruments environment [20] is installed in the host to communicate with biometric and environmental devices and to acquire physiological and environmental information useful for monitoring. The Labview application front panel (Figure 4) serves as a graphic user interface for the user to display (in graphs, waves or numbers) any measured physical quantity.

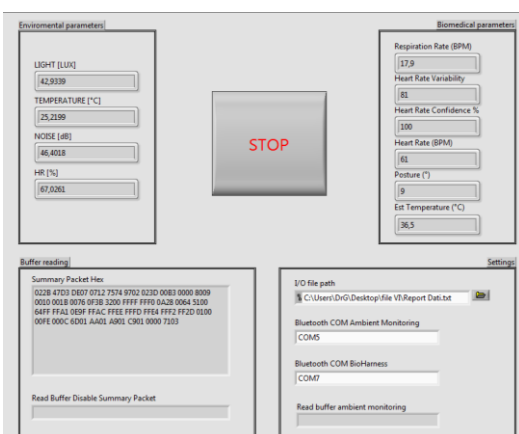


Figure 4: Front panel Labview application

The block Visual Instrument Software Architecture (VISA) [21], that allow the control of data stream of serial port necessary to control in a specific time, is used for handling serial communication by means of the G language of Labview. The application communicates with the two sensor nodes of networks by two similar Bluetooth protocols for the procedures of communication and data transfer to share the same core characteristics. The information collected by Labview is stored in real time in a .txt file. The weight of .txt files of the environmental parameters is 2160 bytes/min, while the biometric parameters .txt file weight is composed by a linear coefficient characterized by mean weight of one parameter (4 bytes) multiplied for the number of parameters chosen and the time of recording calculated in seconds. The reliability of acquired information (status info) and battery status are shown in Table I. In a chosen example of example 4 biometric parameters, the weight of the .txt file would be 11.84 Mb/day.

TABLE I: DAILY WEIGHT STORAGE

Info	Weight(byte)s	Weight(byte)m	Weight(byte)h	Weight(byte)day
Date	10	600	3600	0.864
Time	8	480	28800	0.691
Environment Parameters	9x4	2160	129600	3.11
Biometric Parameters	4xn	240xn	14400xn	0.346xn
Battery Info	4	40	1400	0.346
Formatt.Byte	13	780	46800	1.123

C. Information about the rehabilitation process

These data are obtained through clinical observations ranked according to established rating scales filled in by the attending physician and nursing staff. The scales in use are:

- The Coma Recovery Scale Revisited – CRS [22];
- The Wessex Head Injury Matrix – WHIM [23];
- The Levels of Cognitive Functions – LCF [24];
- The Nociception Coma Scale – NCF [25].

Dedicated web applications have been developed to enable medical and nursing staff to fill in each scale item with the appropriate values. Data are stored in the central database and integrated with the information for further processing and correlative studies.

IV. DATA ANALYSIS

The traditional biomedical model treats disease as a binary variable, whereby a subject is or is not ill. However, most chronic disorders are gradual processes and cannot be classified as binary, while the threshold determining severity can be ambiguously set (the evolution from VS/UWS to MCS is an example in this regard) [11][26]. Many biological variables, such as cholesterol, blood pressure, and blood glucose are normally distributed in the population and a convenient and reliable cutoff can be determined to separate disease from health. In the definition of the disease and its severity and prognosis, judgment needs to be based on knowledge and experience for a correct interpretation of clinical and laboratory information [27]. In our project, measurements and analyses of datasets with information

from environmental and biometric sensors follow a straightforward strategy, with major focus on variability, either spontaneous or in response to environmental changes [28]. Sources of variation are manifold and can reflect changes in the functional status or in responsiveness as well as the existence of residual endogenous mechanisms of self-regulation or circadian/ultradian cycles. Functional changes in VW/UWS or MCS subjects can also depend on interaction with the staff or relatives, result from the nursing or rehabilitation procedures, or reflect endogenous mechanisms [29].

The main lines of research are: 1) identification of correlations between sets of stimulus-conditions administered to subjects with disorder of consciousness and changes in the recorded variables [30]–[32], and 2) analysis of the two-way interaction between the cardiovascular system, the central nervous system and the central autonomic network model [33]–[36]. The goals in these lines of investigation are: 1) to verify whether circadian/ultradian rhythms are partially preserved or have recovered to a significant extent in individual VS/UWS or MCS subjects; 2) to identify functional processes potentially associated to prognostic indicators; 3) to detect momentary interactions between the subject and the environment or other functional changes possibly indicative of residual/recovered responsiveness; 4) to develop predictive models of responsiveness in patients with disorder of consciousness; 5) support the clinician in decision making.

The Decision Support System implemented to help the attending physician is based on *R*, an Open Source statistical package expanded with custom modules [37]; traditional and advanced techniques of statistical analysis are also used. Among these are: the regression analysis (to identify relationships among variables), the Neural network (a sophisticated pattern detection algorithm using machine learning techniques to generate predictions), the Clustering/Segmentation processes (to create groups for applications), the Association Rules techniques (to detect related items in a dataset), Bayesian statistics, Data mining, Neural network, etc.) [38][39].

V. HEART RATE VARIABILITY

Systematic investigation on the heart rate variability (HRV) (i.e. the heart rate fluctuations around the mean value over the time sample) is a major scientific and applicative approach to the functional understanding of VS/UWS and MCS at the Institute S. Anna - RAN [30][35][40][41]. HRV reflects in time the momentary function of the cardio-respiratory control system and is regarded as a reliable index of the sympathetic/parasympathetic functional interplay [34] and intrinsic influence on heart rate. HRV is also thought to provide independent information on the autonomic nervous system and its two-way functional integration with the central nervous system, to express physiological factors modulating the heart rhythm and homeostatic adaptation to the changing conditions. It is anatomically and functionally described by the central autonomic (nervous) network (CAN) model [42][43]. The autonomic system influences

heart rate adaptation through multiple connections (inputs from sensory and baroreceptors within the heart and great vessels, respiratory changes, vasomotor regulation, thermoregulatory system and changes in endocrine function and neuroendocrine interaction) [34][44]. HRV indirectly reflects the organization of affective, physiological, cognitive, and behavioural elements and is emerging as a possible descriptor of the brain functional organizations contributing to homeostasis and homeostatic responses [35][45][46]. Research on the possible patterns of correlation between HRV measures and the functional models available today is crucial in the diagnosis and prognosis of disorder of consciousness and in the online monitoring of patients with severe brain injury.

VI. CONCLUSIONS

The medical care, daily management and rehabilitation of subjects with severe brain damage and disorder of consciousness require inter- and cross-disciplinary activities. This is the basic approach in research on consciousness and rehabilitation. The extensive monitoring of all aspects of the subject's functional condition and reactivity in his/her daily activity is a prerequisite to understand the real efficacy of ambient conditions/changes potentially contributing to the recovery of the consciousness in the *rehabilitative milieu*. In this context, we need a reliable computational environment capable of integrating the heterogeneous representations from different rehabilitative and scientific approaches into heterogeneous formalisms in a useful model. To this end, our AmI system has been contrived to contribute in the efficient representation of the rehabilitative environment, by studying and correlating biometric parameters with environmental variables. The current development in electronic systems and pervasive intelligent devices and computing in the surrounding environment is the new trend and a new frontier of research in the rehabilitative science. New scenarios of application are supported by the ongoing miniaturization of electronic circuits and increasing computational power. New devices can be implemented at low cost to help researchers and clinicians.

A major advantage of our AmI system is the integration of artificial intelligence technology [6][28][47]–[49] with traditional or advanced data acquisition systems such as those in use in the monitoring of clinical or functional parameters of inpatients or of subjects under remote medical control. In this respect, our AmI platform complies with the standards of the international IHE board and the eHealth HL7 format as hedge technological approach in the eHealth functional integration of biomedical and traditional domestic equipments and informatics in hospital and home care. Our AmI system has been designed and implemented to monitor and help treat and rehabilitate subjects with disorder of consciousness. It is a multipurpose hw/sw tool suitable of extensive application in patients' monitoring as well as in medicine and neuroscience when large biomedical datasets are acquired and measures of spontaneous or condition-dependent variability are needed. In this respect, AmI should

be regarded as equivalent to a traditional laboratory for data collection and processing, with substantially reduced dedicated equipment and staff, and limited costs, providing an accurate system of observation of the patient-ambient interaction and a better support to the clinical decision in the rehabilitation phase.

REFERENCES

[1] E. Aarts, H. hawig, and S. Schuurmans, "Ambient Intelligence," in *The Invisible Future*, Denning J., McGraw Hill, 2001.

[2] K. Anyanwu, A. P. Sheth, J. Cardoso, J. A. Miller, and K. J. Kochut, "Healthcare enterprise process development and integration," 2003.

[3] R. Gajanayake, R. Iannella, and T. Sahama, "Sharing with Care: An Information Accountability Perspective," *IEEE Internet Comput.*, vol. 15, no. 4, pp. 31–38, Jul. 2011.

[4] D. M. López and B. Blobel, "Architectural Approaches for HL7-based Health Information Systems Implementation:," *Methods Inf. Med.*, vol. 49, no. 2, pp. 196–204, Mar. 2010.

[5] K. Ducatel, M. Bogdanowicz, F. Scapolo, J. Leijten, and J.-C. Burgelman, *Scenarios for ambient intelligence in 2010*. Office for official publications of the European Communities, 2001.

[6] B. W. Pickering, J. M. Litell, and O. Gajic, "Ambient Intelligence in the Intensive Care Unit: Designing the Electronic Medical Record of the Future," in *Annual Update in Intensive Care and Emergency Medicine 2011*, P. J.-L. Vincent, Ed. Springer Berlin Heidelberg, 2011, pp. 793–802.

[7] B. W. Pickering, O. Gajic, A. Ahmed, V. Herasevich, and M. T. Keegan, "Data Utilization for Medical Decision Making at the Time of Patient Admission to ICU*," *Crit. Care Med.*, vol. 41, no. 6, pp. 1502–1510, Jun. 2013.

[8] W. W. Stead, J. R. Searle, H. E. Fessler, J. W. Smith, and E. H. Shortliffe, "Biomedical Informatics: Changing What Physicians Need to Know and How They Learn:," *Acad. Med.*, vol. 86, no. 4, pp. 429–434, Apr. 2011.

[9] G. G. Celesia and W. G. Sannita, "Can patients in vegetative state experience pain and have conscious awareness?," *Neurology*, vol. 80, no. 4, pp. 328–329, Jan. 2013.

[10] G. Dolce, W. G. Sannita, and for the European Task Force on the, "The vegetative state: A syndrome seeking revision?," *Brain Inj.*, vol. 24, no. 13–14, pp. 1628–1629, Dec. 2010.

[11] S. Laureys, G. G. Celesia, F. Cohadon, J. Lavrijsen, J. León-Carrión, W. G. Sannita, L. Sazbon, E. Schmutzhard, K. R. von Wild, A. Zeman, G. Dolce, and \$author firstName \$author.lastName, "Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome," *BMC Med.*, vol. 8, no. 1, p. 68, Nov. 2010.

[12] The Multi-Society Task Force on PVS., "Medical aspects of the persistent vegetative state.," *N Engl J Med*, vol. 330, pp. 1499–508, 1572, 1994.

[13] L. Flotta, F. Riganello, and W. G. Sannita, "Intelligent Monitoring of Subjects with Severe Disorder of Consciousness," in *SENSORDEVICES 2013*, The Fourth International Conference on Sensor Device Technologies and Applications, 2013, pp. 135–138.

[14] J. A. Johnstone, P. A. Ford, G. Hughes, T. Watson, and A. T. Garrett, "Bioharness™ Multivariable Monitoring Device: Part I: Validity," *J. Sports Sci. Med.*, vol. 11, no. 3, pp. 400–408, Sep. 2012.

[15] J. A. Johnstone, P. A. Ford, G. Hughes, T. Watson, and A. T. Garrett, "Bioharness™ Multivariable Monitoring Device:

Part. II: Reliability," *J. Sports Sci. Med.*, vol. 11, no. 3, pp. 409–417, Sep. 2012.

[16] E. Jovanov, D. Raskovic, A. O. Lords, P. Cox, R. Adhami, and F. Andrasik, "Synchronized physiological monitoring using a distributed wireless intelligent sensor system," in *Proceedings of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2003, 2003, vol. 2, pp. 1368–1371 Vol.2.

[17] J. H. Davies, *MSP430 Microcontroller Basics*. Elsevier, 2008.

[18] J. Polastre, R. Szewczyk, and D. Culler, "Telos: enabling ultra-low power wireless research," in *Information Processing in Sensor Networks*, 2005. IPSN 2005. Fourth International Symposium on, 2005, pp. 364–369.

[19] Thakare, "A Review on Implementation of Serial Communication by Universal Asynchronous Receiver Transmitter," *Int. J. Res. Comput. Eng. Electron.*, vol. 2, no. 1, 2013.

[20] R. Bitter, T. Mohiuddin, and M. Nawrocki, *LabView: Advanced Programming Techniques*, Second Edition. CRC Press, 2006.

[21] H. Zhao and Z. Y. Dong, "Design and Implementation of USB-based Microwave Power Sensor," *Appl. Mech. Mater.*, vol. 347, pp. 1039–1042, 2013.

[22] J. T. Giacino, K. Kalmar, and J. Whyte, "The JFK Coma Recovery Scale-Revised: Measurement characteristics and diagnostic utility," *Arch. Phys. Med. Rehabil.*, vol. 85, no. 12, pp. 2020–2029, Dec. 2004.

[23] A. Shiel, S. A. Horn, B. A. Wilson, M. J. Watson, M. J. Campbell, and D. L. Mclellan, "The Wessex Head Injury Matrix (WHIM) main scale: a preliminary report on a scale to assess and monitor patient recovery after severe head injury," *Clin. Rehabil.*, vol. 14, no. 4, pp. 408–416, Jan. 2000.

[24] C. Hagen, D. Malkmus, and P. Durham, "Rancho Los Amigos levels of cognitive functioning scale," *Downey CA Prof. Staff Assoc.*, 1972.

[25] C. Schnakers, C. Chatelle, A. Vanhaudenhuyse, S. Majerus, D. Ledoux, M. Boly, M.-A. Bruno, P. Boveroux, A. Demertzi, G. Moonen, and S. Laureys, "The Nociception Coma Scale: a new tool to assess nociception in disorders of consciousness," *Pain*, vol. 148, no. 2, pp. 215–219, Feb. 2010.

[26] A. Bosco, G. E. Lancioni, M. O. Belardinelli, N. N. Singh, M. F. O'Reilly, and J. Sigafos, "Vegetative state: efforts to curb misdiagnosis," *Cogn. Process.*, vol. 11, no. 1, pp. 87–90, Feb. 2010.

[27] R. M. Kaplan and D. L. Frosch, "Decision Making in Medicine and Health Care," *Annu. Rev. Clin. Psychol.*, vol. 1, no. 1, pp. 525–556, Apr. 2005.

[28] L. Pignolo, F. Riganello, G. Dolce, and W. G. Sannita, "Ambient intelligence for monitoring and research in clinical neurophysiology and medicine: the MIMERICA* project and prototype," *Clin. EEG Neurosci.*, vol. 44, no. 2, pp. 144–149, Apr. 2013.

[29] F. Riganello, G. Dolce, M. D. Cortese, and W. G. Sannita, "Responsiveness and prognosis in the severe disorder of consciousness," *Brain Damage Causes Manag. Progn. Schäffer AJ Müller J Eds Pp*, pp. 117–135, 2010.

[30] A. Candelieri, M. D. Cortese, G. Dolce, F. Riganello, and W. G. Sannita, "Visual Pursuit: Within-Day Variability in the Severe Disorder of Consciousness," *J. Neurotrauma*, vol. 28, no. 10, pp. 2013–2017, 2011.

[31] F. Riganello, M. D. Cortese, G. Dolce, and W. G. Sannita, "Visual pursuit response in the severe disorder of consciousness: modulation by the central autonomic system and a predictive model," *BMC Neurol.*, vol. 13, no. 1, p. 164, 2013.

[32] P. Urbenjaphol, C. Jitpanya, and S. Khaoropthum, "Effects of the sensory stimulation program on recovery in

- unconscious patients with traumatic brain injury,” *J. Neurosci. Nurs.*, vol. 41, no. 3, pp. E10–E16, 2009.
- [33] V. Napadow, R. Dhond, G. Conti, N. Makris, E. N. Brown, and R. Barbieri, “Brain correlates of autonomic modulation: Combining heart rate variability with fMRI,” *NeuroImage*, vol. 42, no. 1, pp. 169–177, 2008.
- [34] F. Riganello, G. Dolce, and W. Sannita, “Heart rate variability and the central autonomic network in the severe disorder of consciousness,” *J. Rehabil. Med.*, vol. 44, no. 6, pp. 495–501, 2012.
- [35] F. Riganello, S. Garbarino, and W. G. Sannita, “Heart Rate Variability, Homeostasis, and Brain Function: A Tutorial and Review of Application,” *J. Psychophysiol.*, vol. 26, no. 4, pp. 178–203, 2012.
- [36] R. Lane, K. Mcrae, E. Reiman, K. Chen, G. Ahern, and J. Thayer, “Neural correlates of heart rate variability during emotion,” *NeuroImage*, vol. 44, no. 1, pp. 213–222, Jan. 2009.
- [37] J. Marques de Sá, “Directional Data,” *Appl. Stat. Using SPSS Stat. MATLAB R*, pp. 375–401, 2007.
- [38] A. Candelieri, G. Dolce, F. Riganello, and W. G., “Data Mining in Neurology,” in *Knowledge-Oriented Applications in Data Mining*, K. Funatsu, Ed. InTech, 2011.
- [39] I. H. Witten, E. Frank, and M. A. Hall, *Data Mining: Practical Machine Learning Tools and Techniques*, Third Edition, 3 edition. Burlington, MA: Morgan Kaufmann, 2011.
- [40] G. Dolce, F. Riganello, M. Quintieri, A. Candelieri, and D. Conforti, “Personal interaction in the vegetative state: A data-mining study,” *J. Psychophysiol.*, vol. 22, no. 3, pp. 150–156, 2008.
- [41] F. Riganello, A. Candelieri, M. Quintieri, D. Conforti, and G. Dolce, “Heart rate variability: An index of brain processing in vegetative state? An artificial intelligence, data mining study,” *Clin. Neurophysiol.*, vol. 121, no. 12, pp. 2024–2034, Dec. 2010.
- [42] E. E. Benarroch, “The central autonomic network: functional organization, dysfunction, and perspective,” *Mayo Clin. Proc.*, vol. 68, no. 10, pp. 988–1001, 1993.
- [43] E. Benarroch, W. Singer, and M. Mauermann, *Autonomic Neurology*. Oxford University Press, 2014.
- [44] E. E. Benarroch, “The Autonomic Nervous System: Basic Anatomy And Physiology” *Contin. Lifelong Learn. Neurol.*, vol. 13, pp. 13–32, 2007.
- [45] E. E. Benarroch, “Pain-autonomic interactions,” *Neurol. Sci.*, vol. 27, no. 2, pp. s130–s133, May 2006.
- [46] B. H. Friedman and J. F. Thayer, “Autonomic balance revisited: panic anxiety and heart rate variability,” *J. Psychosom. Res.*, vol. 44, no. 1, pp. 133–151, 1998.
- [47] C. Ramos, J. C. Augusto, and D. Shapiro, “Ambient intelligence—the next step for artificial intelligence,” *Intell. Syst. IEEE*, vol. 23, no. 2, pp. 15–18, 2008.
- [48] G. Riva, “Ambient intelligence in health care,” *Cyberpsychol. Behav.*, vol. 6, no. 3, pp. 295–300, 2003.
- [49] W. Weber, C. Braun, R. Glaser, Y. Gsottberger, M. Halik, S. Jung, H. Klauk, C. Lauterbach, G. Schmid, X. Shi, T. F. Sturm, G. Stromberg, and U. Zschieschang, “Ambient intelligence - key technologies in the information age,” in *Electron Devices Meeting, 2003. IEDM '03 Technical Digest. IEEE International*, 2003, pp. 1.1.1–1.1.8.