Early Diagnosis of Autism Spectrum Disorders – Design of the Data Acquisition and Management System

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Abstract— **Autism spectrum disorders are not diagnosed until children reach 3-4 years of age. Early identification of pathological subjects is crucial as early intervention is much more effective. The current project is aimed at the development of a set of methods for improving the chances of early diagnosis. In this paper we focus on the design and development of the shared acquisition architecture. The requirements of a standardized acquisition protocol suggested the development of an integrated acquisition tool using a local storage. Each acquisition tool will allow a secure management of subject data, reducing the risk of mislabeled or lost data by using a guided procedure. A set of synchronization procedures allow a secure data communication with a central database. The requirements related to data management and privacy have been analyzed allowing the definition of the main access roles to the data repository.**

Keywords— **Autism spectrum disorders, multicentric acquisition, data protection.**

I. Introduction

Autism spectrum disorders (ASDs) are often not diagnosed until children reach 3-4 years of age. Yet 50% of parents of children with ASDs report that they suspected a problem before their child was 1 year of age [1] thus a more precocious diagnosis seems possible. So far, the study of the early symptoms of ASDs is mainly based on retrospective analysis of home videotapes, usually recorded during children's first birthday party. This method however presents some limits. First of all, existing data refer to the assessment of a restricted number of infants (e.g. 10-12). Second, only presence or absence of autistic symptom behaviors was considered. Overall, the method is not standardized because of methodological differences in quality of recording and observational setting. Recently, prospective studies of infant siblings of children with ASDs have been performed, using the Autism Observation Scale for Infants [2], which measures visual attention, response to name, social babbling, eye contact and sensory behaviors. Neither home video analysis nor high risk infants studies, detected consistent abnormalities earlier than 1 year of age. It is worth to notice that in other populations of infant at risk for neurodevelopmental disorders, the combination of neurophysiological and behavioral measures has allowed to evidence precociously atypical maturation of some neural circuits associated with auditory processing in infants at risk of later developmental problems [3]. Early identification of young children with ASDs, possibly through a set of behavioral and neurophysiological indexes, is crucial in light of findings indicating that early intervention is much more effective than interventions starting in later childhood [4].

This project intends to address this very important issue by an innovative multidisciplinary approach, involving both early neurobehavioral characterization of murine ASD models and clinical observation of normal and high risk infants during early neonatal period.

Animal models of ASD can provide translational tools to identify neurochemical markers and behavioral patterns that cannot be studied in the human infants since at present ASD cannot be diagnosed reliably before two years of age [5]. In this regard, mouse models bearing mutations identified in ASD candidate genes and that exhibit a clear autistic-like phenotype would be most promising. Moreover, ethical considerations do not allow exposing human infants to several blood samples or MRI scanning. A comparative approach like the present one might be successful in linking experimental findings obtained in animals to human infants, in order to identify as early as possible vulnerable behavioral patterns associated with alteration in selected biochemical markers.

In parallel with the experimental studies in animals, this project attempts to describe, for the first time during the first six months of life, normative ranges for both motor and acoustic parameters in a population of at least 200 newborn/infants (male and females), which up to now have been determined only for older infants. Since the diagnostic evaluation of ASD children is based on the assessment of unusual social interaction, imitation, play, insistence on sameness and preference for fixed routines, verbal and nonverbal communication [6], it is not surprising that a reliable diagnosis is not possible before two years of age. For this reason, we will focus our clinical analysis on age-specific

motor and vocal repertoires, which are known to be later impaired in children with ASD and that have been found altered in other different infant disorders. In fact, the general movements' analysis in infancy revealed disturbances that could be detected clearly at age of 4-6 months of age [7] whereas abnormal cry features occur in several neural disorders [8]. However, while the assessment of movement patterns, which are the infant's "first language", have already been performed in ASD children by home-videos, very few studies have investigated the specificity of cry in infants with ASDs [9,10]. and correlation between these two responses have never been reported before. And this is very peculiar considering the connection between crying and the functioning of the brainstem and limbic system, both areas compromised in children with ASD [11,12].

In conclusion, the association of general movements and cry analysis is desirable and of great relevance, since they both reflect the development and the integrity of the central nervous system and they can be exploited for early clinical diagnosis of several pathologies since they are easy to perform, cheap and completely non-invasive.

II. Methods

A. Acquisition protocol

Each subject will be involved in a set of measures, scheduled every six weeks, starting a few days after birth up to the 24th week of life (hence, each one will undergo five sessions). Each session will involve the following aspects:

- General movement analysis, performed using video recording of spontaneous movements of the subject. The video recording is performed while the subject is awake and not crying. The manual assessment of general movement patterns assumes the video recording lasts a few minutes (usually 3-5).
- Cry analysis, from an audio track. The analysis is performed on spontaneous cry episodes (excluding therefore pain-related stimulation). The acquisition procedure includes the recording of at least ten minutes of crying.
- Behavioural analysis, performed using a set of questionnaires (Italian Questionnaire of Temperament; Bayley Scales of Infant Development; the first child vocabulary, MacArthur - Bates Communicative Development Inventory and the Modified Checklist for Autism in Toddlers (*M-CHAT*))

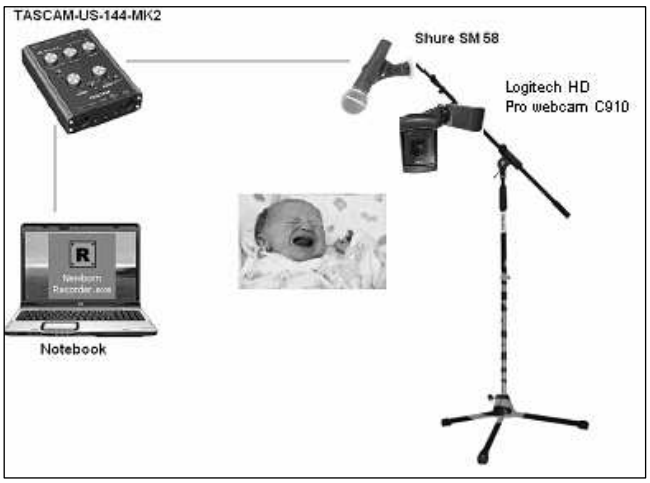

Fig. 1 Acquisition system

Informed consent will be obtained from all parents. The study protocol has been approved by the local ethical committee (Istituto Superiore di Sanità, Stella Maris, Bambino Gesù).

B. Study population

The project involves recruiting a set of normal subjects to be used as controls and a set of high risk subjects to be followed prospectively. By allowing accurate and detailed assessments of behavioral measures at fixed time points, prospective studies offer theoretical advantages to detect early modifications of ASD, while avoiding biases.

Presently, no diagnostic tool is capable to give an early assessment of autistic patients. Recent advances in early detection research have resulted from prospective studies carried out on populations at increased risk for ASD. We planned to recruit later-born infant siblings of children diagnosed with autism. These infant siblings are themselves at especially high risk for an autism or ASD diagnosis [13] and this population is arguably the most clearly defined high risk group available [14,15]

The planned acquisition procedure is totally not invasive, minimizing the ethical issues involved in the recruitment of control subjects and high risk infants.

Fig. 2 Sample acquisition window

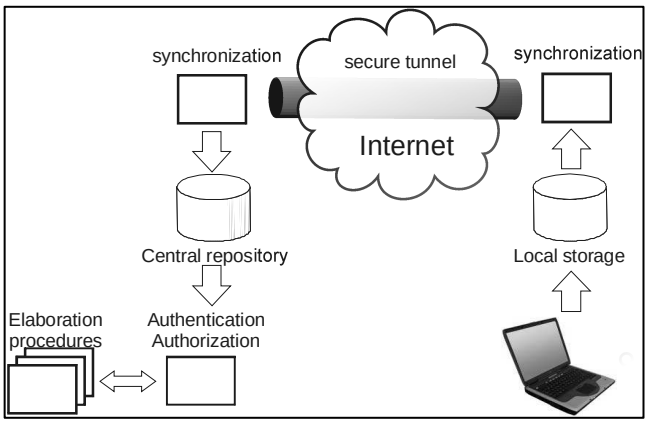

Fig. 3 Data management architecture

C. Acquisition system

The acquisition system needs to be used in the patient home, to minimize the discomfort for the involved subjects and to minimize the impact of the external environment on children habits. Hence, the basic requirement is the easiness for transporting the system and to assemble it without the need of a technician, allowing it to be used by the medical doctor. Accordingly to this requirement, the proposed system, shown in Fig. 1, includes a laptop which is connected to an high speed USB video camera (Logitech HD pro webcam C910), able to provide a 1280x1024 pixel video stream and an external audio acquisition device (Tascam US-144-MK2, as the quality of the embedded audio card is not adequate to the planned specifications) and a professional microphone (Shure SM58).

D. Newborn recorder

The proposed definition of a standardized acquisition protocol suggested the use of a custom recording procedure. The protocol, indeed, requires the recording of a set of anagraphic and anamnestic data, together with the acquisition of a video signal and an audio track. Moreover, as several recording sessions are planned for each subject, the software allows the generation of a database aimed to simplify the recording procedure avoiding data loss or mislabelling. The most critical issue which has been foreseen in the acquisition of the database concerns the different requirements on the subject state posed by general move ment analysis and cry analysis. The lack of collaboration of newborn subjects required the availability of an acquisition system which allows easy management of the possible transitions of the subject from calm state to crying state and vice versa.

Standard recording software would require to record, at the same time, audio and video signals with high quality, with manual annotation of the state of the patient on a separate device, and with a manual estimate of crying and calm periods, to ensure an adequate duration of the recording.

For these reasons, we designed and developed custom acquisition software, written in C++ language using the MFC architecture for the user interface, and the OpenCv [16] image processing library for video acquisition and recording. The user interface includes a main window for selecting the patient from the database, a dialog window for the editing of textual data, and an acquisition window.

The acquisition window (fig. 2) allows previewing of the video and audio quality before starting the recording, in order to ensure correctness of the acquisitions. It also allows marking the time frames corresponding to the different behavioural states of the newborn, showing separate running times for the crying state, to assess the duration of the audio signal available for the crying analysis, and the calm awake state, for the general movement analysis.

The markers will be stored together with the multimedia tracks, and are used to automatically extract the signals for the following steps.

E. Data management

The study involves a multicentric acquisition which poses several issues concerning data management and sharing. The data management architecture has been designed to use a set of private databases, one in each acquisition device, which are periodically synchronized with a central repository by automated procedures.

The acquisition procedure, indeed, will be performed at patient home, where it can not be assumed the availability of a high speed internet connection. The Newborn recorder uses, therefore, a local database for storing the anagraphic and anamnestic data. Efficiency issues suggested avoiding storing audio and video data directly in the database, and multimedia files have been stored in a dedicated folder, while the database contains only a reference to the file.

The constraints related to data security and privacy required using an encrypted file system for storing all sensitive data. Access to all data is granted only after a successful login to the encryption system. This approach avoids the implementation of a login procedure in the Newborn recorder, which would not, however, protect again direct access to the multimedia files.

The central database is located on a shared server, which can be accessed through internet connection (see fig. 3). The database acts as a backup repository to avoid any data loss in case of a fault in one of the acquisition systems, and allows selective access to data for the analysis. Data inside the central database will be anonymized, and only an identifier will be used to address subjects. We designed three

principal roles with specific access needs: the first role is the video processing, the second one is the audio analysis, and the third one is relates to statistical analysis of the data. The first two roles are very similar each other, apart for the set of data they need to access: these two roles require accessing the raw multimedia files (video and audio, respectively), and store the result of the elaboration of each file. No access to patient data is required, apart for the age of the subject when the file has been acquired. The third role needs to access the complete data set, excluding multimedia files, but including elaboration results. However, data does need to include any identification data.

Minor roles are required for implementing synchronization procedures and for performing administrative tasks.

Synchronization procedures have been designed to transfer a copy of all freshly recorded data from the acquisition system to the central database as soon as an internet connection can be established with the central server. The procedure involves the usage of a secure encrypted channel for transferring all data, as to guarantee privacy. As each site treats a separate patient group, there is no need, in normal operation, to transfer updated data from the central server to each acquisition system, so we perform a one-way data transfer. A manual procedure has been designed allowing for data recovery in case of a crash of the database in one of the acquisition systems.

III. Results and conclusions

The proposed architecture has been tested in a limited number of acquisitions in a controlled environment. Ate present, we verified the reliability of the acquisition software, and the amount of required resources.

As concerns the amount of resources, we benchmarked the encryption speed of the system, obtaining a maximum encryption seed, using the AES algorithm, of about 120MB/s, which is largely sufficient for the amount of data to be recorded. On the overall, the system is able to record a 640x480 video stream at a rate up to 15 frame/s, where the main limiting factor is the exposure time of the webcam.

The system has also proved to be very user friendly and non-technical operators manage to get full management of the system with about half an hour of training.

The major issue faced in the definition of the data collection and management strategy relates to the easiness of use of the system, combining the data protection requirements with the availability of a portable system which can be used in the subject home, without the need of technical support from specialized technical personnel.

The proposed approach solved the identified requirements by combining several independent modules.

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