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Rationale and protocol for using a smartphone application to study autism spectrum disorders : SMART AUTISM

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Rationale and protocol for using a smartphone application to study autism spectrum disorders : SMARTAUTISM

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Abstract

Introduction

Longitudinal studies on the evolution of autism spectrum disorders (ASD) symptoms are limited, and mainly use repeated measurements several months apart. However, changes in everyday life should be closer to the "real life" of the patient and its family. We propose to study both the child's symptoms and effect

on quality of life, psychological status and anxiety for families over a 6 months period using SMARTAUTISM, a smartphone application.

Method and Analysis

This is a prospective, longitudinal, exploratory, open study with a 6-month follow-up to collect natural, multi-weekly and longitudinal elements on quality of life and anxiety from parents of autistic children and the children's functional symptoms and assess the feasibility of using a smartphone application designed for parents of ASD patients.

Primary objective: Explore the evolution of a child's behavior over 6 months and the effects on the family (psychological and social).

Secondary objective: Assess feasibility by examining the filling rate and use of our application by parents for six months.

Inclusion of 100 families with with ASD diagnosed child. Other inclusion criteria are as follows: (i) having at least one smartphone and (ii) having signed a consent for participation. The main exclusion criterion is patients with more than two living areas. For the baseline, socio-demographic, psychiatric and medical data will be recorded. For general epidemiological data (main outcome in application), the correlations will be detected using a multivariate analysis. The application filling rate (calculated from an ideal filling rate) will be generated by the application itself and will assess the feasibility (2nd outcome).

Ethics and dissemination

The SMARTAUTISM study has approval for local ethic committee and encryption and secure medical server assure protection of data. Results will be presented in

peer-review article and the application will be proposed in autism resource center across France.

297 words

Keywords: Autism Spectrum Disorders, Ecological Momentary Assessment, Smartphone Application, Quality of Life

Strength of our study

- First Ecological Momentary Assessment smartphone application for behavioral symptoms of ASD and quality of life of parents
- Six months follow-up
- Application providing an easy access and readable feedback to enhance parents motivation in the filling process

Limitation

- Subjective evaluation provided by parents
- Items are simple and unexpected situation may not be recordable

Contributorship statement

- ✓ OB, DB, PD and AD were involved in conception and design of the study
- ✓ OB was drafting the article, DB, PD and AD were revising it critically for important intellectual content, Figures were made by AD and OB.
- ✓ OB, DB, AD, PD, MM and JG were involved in the conception of the smartphone application

- ✓ All authors gave final approval of the version to be published.

Competing interests

All authors declare no competing interest regarding this study

CONTEXT

Information communication technologies (ICT), including on-line or off-line smartphone applications, are now a rapidly progressing reality in medicine. Many devices and applications have been developed by private companies but are not evaluated for effectiveness or feasibility. However, there are approximately 100. 000 apps in the android or apple markets stores [1]. This impressive number should be nuanced as many "health" applications are only "entertainment applications" without scientific approval, including coaching, well-being advice or sports applications. Among the medical specialties, psychiatry is a part of this phenomenon; more than just a trend, this may be a revolution in doctor-patient relationships.

A simple way to use this device-based technology is to provide access to health care through smartphone applications in countries where equipment and medical personnel levels are low [2]. Further, this technology can also be conceptualized as mainstream news media to reduce stigmatization [2]. It may also be helpful in remote support via SMS, voice or visual phone consultations. In an other hand, medicine, and psychiatry in particular, requires data from patients or their families. These data might be obtained from questionnaires that can be completed under natural conditions; this technique is referred to as an ecological momentary assessment (EMA [3]) or a sampling method experience (ESM) [4]. The first EMA experiments used beepers to remind users to complete the questionnaires on a

computer; the compliance and answer quality results were disappointing, and the schedules were not respected [5]. The arrival of PDAs and smartphones has provided important perspectives that are rapidly developing. The medical fields of use are varied, but psychological state and behavior are a particularly appropriate topic, including behavioral addictions [6], eating behaviors [7] and anxiety [8] as well as severe psychiatric disorders, such as bipolar disorder [9] or schizophrenia [10]. A subject's social functioning, quality of life and psychological state are the most frequently studied elements and are more appropriate for this technique. The filling rate for such applications varies based on the type and duration of use (both for filling and period of use) but might be as high as 70% based on one of the few studies measuring this parameter [11]. As demonstrated in anxiety disorder research, smartphones are a more practical and effective media, and the data generated therefrom are better quality than data generated from other media [8]. The literature on this domain is limited and mostly includes preliminary data or study protocols with variable durations (days to weeks) or performed on a small number of subjects (10-100 subjects). A recent survey on a population of psychiatric disorder patients showed that 77% of the patients owned a smartphone in the U.S., and they would be willing to use it to inform their mental state [12]. Such a study is only indicative, but it at least demonstrates interest in this type of approach.

The core concept underlying EMAs is obtaining behavioral data provided by the subject (and potentially his family or caregivers). These natural data are a novelty and will affect our understanding of disorders as well as therapeutic relationships

(see examples from eating disorders [6 7 13] or addictions [14]. However, the assessment is based on a patient's desire to provide data that are useful collectively but not individually. Few research programs include a specific level of feedback by the application (see one rare example for schizophrenia [13] or bipolar disorders [9 15 16]).

One study of particular interest includes 52 subjects and proposes to compare behavioral interpersonal therapy to therapy available on demand using a smartphone or tablet (dematerialized adaptation) during a 5-month period [17]. The percentage of treatment responders was 54% for the "mobile" group compared with 8% for the conventional group, which is surprisingly low. Among other interests, a certain degree of feed-back seems to increase acceptance and filling rates; for example in a sample of patients with schizophrenia one recent work showed an acceptable level of use (50% spontaneous use and 38% use generated by the application) and excellent acceptance (90% satisfied) for an application based on psycho-educational support (information, resources, etc.) with a small portion of self-care and feed back [18].

In summary, combining an EMA and feed-back is a promising approach, and we developed such an application in the autism spectrum disorders (ASD) field.

The SMARTAUTISM project

This ongoing (starting May 1rst 2016) study received funding from the Regional Health Agency (ARS) and the Autism Resource Centre (CRA) of the Loire Valley on the west coast of France. It also received a grant from National Center for Autonomy (CNSA) / Research Institut of Epidemiology and Public Health (IRESP).

ASD symptoms are now better understood, but ASD studies are most often transversal or, when they are longitudinal, are mostly retrospective, such as based on a reference diagnosis scale, the autism diagnosis interview (ADI). Real longitudinal studies on symptom evolution remain limited, and researchers continue to use repeated measurements several months apart [19-21]. However, daily changes should be more accurate and, above all, closer to the "real life" of the patient and his family.

Autistic children and their parents often face difficult situations daily that are related to behavioral symptoms (agitation, feeding difficulties, sleep disturbances, obsessive behavior, refusal of authority, etc.). Further, the parents' quality of life is strongly affected by everyday life with their autistic children [22 23]. Data on these behavioral disorders are currently being collected in a transverse manner using surveys, questionnaires and parental recall. This mode of data collection entails an clear bias in all studies. An interesting study would include both a child's symptoms and the impact on a family's quality of life, psychological status and anxiety over a long time period (six months) using a daily information source that includes parental observations. Moreover, an EMA application that includes feedback could be useful for a parent's necessary adaptive educational behavior and a doctor (who will have access to the data during regular consultations).

Anxiety is a dimension that we will consider for parents in addition to quality of life. Parents of ASD children face greater anxiety levels than parents of children without a developmental specificity (for a recent meta-analysis on the subject, see [24] using 15 studies). The major autism symptoms, communication disorders or aggression, are the most important stressors (Davis and Carter 2008). These works are mostly cross-sectional studies, which evaluate parents using a single semi-structured interview or questionnaire.

An EMA has never been used to study the parents of autistic children both for quality of life and anxiety level. However, an EMA has not been used by a parent to longitudinally evaluate a child's behavior in natural situations.

The SMARTAUTISM application is an amalgamation of a classic EMA and feedback that may be used by parents to adapt their educational behavior and by doctors to better understand their patients and propose more accurate treatments. The parents must provide regular ratings (twice a week at least) for a long time period (6 months for our study). We propose that the parental rating time and application design includes two main points.

1. The rating time will range from 3 to 10 minutes depending on the answers provided. The questions will be simple and user oriented (see Figures 1 & 2). We will ask questions about sleep; behavior; ASD symptoms, such as stereotyping or withdrawal; and social life, such as lunch period or leisure activities. For the parents, the questions will be about anxiety and

psychological state of mind but also quality of life elements (ability to function in everyday domestic / professional / friendly tasks and social contact). To save time, we will use the visual analogic scale (VAS). The VAS is accurate and facilitates repetitive measurements in psychiatry (see, for example, the MATHYS experiment, [25]). Users will provide a rating from 0 to 10 by scrolling their finger on the touch screen (see Figure 3).

2. For the design, we have collaborated with a specialized private company with expertise on this topic. SMARTAUTISM is personalized with, for example, the potential for featuring a particular child's picture on the back screen (see Figure 4). Each screen provides information using soft color and typography.

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Insert Figure 1 about here

Figure 1. Snapshots of SMARTAUTISM smartphone application.

Insert Figure 2 about here

Figure 2. Questions for parents about them and social life in the SMARTAUTISM application.

Insert Figure 3 about here

Figure 3. Questions for parents regarding their children in SMARTAUTISM application.

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SMARTAUTISM provides a menu section with general information about ASD and local resources (health care facilities, emergency numbers, etc.). It also allows the user to change the parameters, particularly the rating reminder notification. The application also provides two summary screens for the data collected from the first use. These screens are user friendly and readable.

We propose (i) to evaluate the feasibility of applying EMA to investigate a child's symptoms as well as a parent's quality of life / psychological state and daily anxiety over 6 months, (ii) to collect epidemiological data. The SMARTAUTISM study will begin in March 2015. It has received the support from the ARC of Pays de la Loire and financing from ARS Loire Valley.

OBJECTIVES

Our goal is to use this application to regularly care for people with autism. Medical consultations can be widely spaced and cannot properly consider changes in symptoms from previous assessments or everyday life hazards and repercussions. This application is aimed at measuring these parameters for more effective consultations. This application can also be a useful epidemiological tool provided in a longitudinal and environmentally friendly manner to address both environmental effects (family) from and changes in a child's functional symptoms.

The primary main objective is an epidemiological study on the evolution of a child's behavior over 6 months and the effects on the family.

Our secondary main aim is to assess the feasibility of such an innovative approach and, as the primary endpoint, to study the filling rate and use of our application by the parents over six months.

METHODOLOGY

This is a prospective, longitudinal, exploratory, open study with a 6-month follow-up to collect natural, multi-weekly and longitudinal elements on quality of life and anxiety from parents of autistic children and the children's functional symptoms and assess the feasibility of using a smartphone application designed for parents of ASD patients.

These data will provide an epidemiological perspective for (i) studying the fluctuation of different variables over six months and (ii) assessing the links between a child's symptomatic status and a parent's quality of life / anxiety.

Population

We propose the study to patients diagnosed with ASD based on HAS (Health National Authority) recommendations (ADI-R diagnoses) from 3-16 years old in the Pays de la Loire region. We propose to include 100 families. The study is exploratory in nature; thus, randomizing patients is unnecessary. We will include the first 100 families that agree to participate in the study and meet the inclusion criteria.

Inclusion criteria:

- Having a child with an ASD diagnosis based on the ICD 10 criteria.
- Having at least a smartphone (iOS Apple or Android).
- Signing the consent for participation.

Exclusion criteria:

- Having several children with an ASD diagnosis.
- Children with more than two living areas.

Method

After an interview to explain the study, sign consent forms and present operation of the application, parents will receive a code to download the app from the "store" of their choice (depending on their smartphone).

During implementation of the initial setup, socio-demographic data (age, sex, socio-professional category, etc.) of the parent and child will be noted.

During the study, we will also note the following.

- Sibling rank and marital status.
- Lifestyle: rural or urban; single room or not; and housing surface.
- Educational and teaching load and conditions (special education, inclusive education and partial or full time, etc.).
- The therapeutic management (speech therapy, psychomotor therapy, etc.).
- The age of diagnosis.
- Potential drug treatments.
- Comorbidities (associated epilepsy, mental retardation and organic pathology).
- Medical and psychiatric family ATCD.
- Original scores on the ADI-R and ADOS at the time of diagnosis.
- Childhood Autism Rating Scale [26], CARS French version (http://www.autisme.qc.ca) performed for the baseline and at the end of the study.

A default schedule parameter to fill the application (see Figures 2 & 3 with the algorithm) with a notification reminder will then be proposed to the parents. The default settings can be modified by the parents if necessary but must include 3 fillings each week. Missing data will be included in the assessments. Each filling will require a short time period (less than ten minutes in the longest

configuration). The key questions are closed-ended (yes/no), and the visual analogue scale is primarily used to evaluate the symptoms and disorders.

The first question concerns the environmental context of the days around the filling (unusual, holiday, etc.). For the child, the questions will focus on sleep, food and behavior concerning himself and others (such as aggressiveness, agitation, stereotypes or cries, etc.). To avoid redundant or inappropriate questions, the questions will be presented as an algorithm (see Figures 1 and 2).

In certain instances, both parents will have a smartphone, everyone will have the application, and filling will be performed by anyone. The data will be aggregated per family. Two simultaneous assessments by both parents are unnecessary for this study.

During the 6-month inclusion period and 6-month follow-up, we will record anonymized data from the smartphone when the parents are connected to a Wi-Fi network using a secure medical server.

We have developed a qualitative questionnaire for the participants and patient's doctor as well as a semi-directed, face-to-face interview to assess the change in the doctor-patient relationship when using the application.

Statistic analysis

For this feasibility study, the primary endpoint (which corresponds to the primary objective) will be the application filling rate, which is calculated from an ideal

filling rate (all three days) and considers the number of fillings (at least half of the items requested).

The secondary endpoints will requires more precise analyses, such as analyzing the medium filling rate variation over time. We will collect a considerable quantity of data due to the multiplicity of variables such that we can perform exploratory epidemiology using descriptive and analytical statistics, which compose an essential and unique information source.

Generally, we distinguish two groups: groups with a single place of family life and those with two places of family life. The data encoded by the parents are subjective, but we do not distinguish the data on a child based on the parent. However, the quality of life data will be distinguished based on the rater parent. Thus, we have included 100 patients and over 100 data points on quality of life.

The analysis will be performed in two stages: (i) a longitudinal data analysis of each group (parents and children) and (ii) multivariate analyses on relationships between variables of the group "parents" and the group "children."

Conclusions

Ecological natural data on ASD patients are limited in the literature. The SMARTAUTISM application will be a unique source for such longitudinal ecological observations. Clearly, the design and ergonomic quality of the application is a key element for feasibility. The user must also receive useful feedback from their rating, which may be used for contextualization and

adaptation their educational behavior. Our study aims to confirm that such a application may be regularly used by parents of ASD children.

Furthermore, the patient and family relationships with their doctor may be profoundly changed. Because appointments with the patient's referring physician can be far apart, an important frustration is not being able to "tell all." Parties tend to speak only about the most recent events. Finally, for the doctors, this application can provide a perspective closer to reality and, above all, a context that can aid in care and therapy.

Our application is a first step, but it is consistent with an on-going revolution linked to using such technologies in psychiatry.

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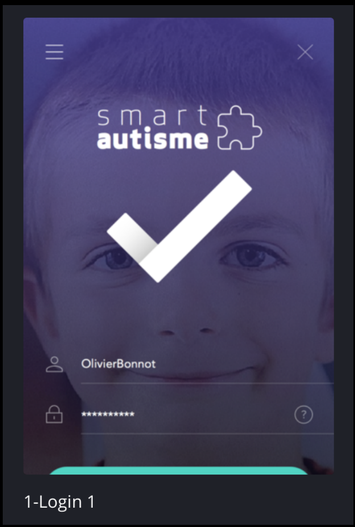

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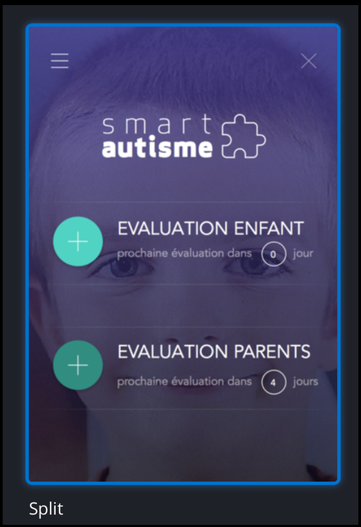

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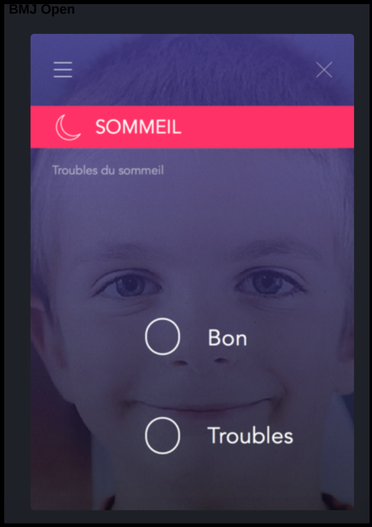
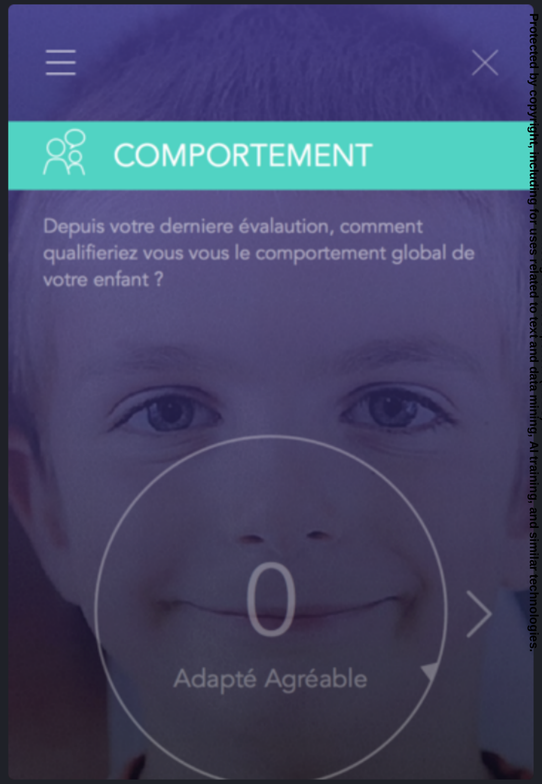


SMART AUTISM ®



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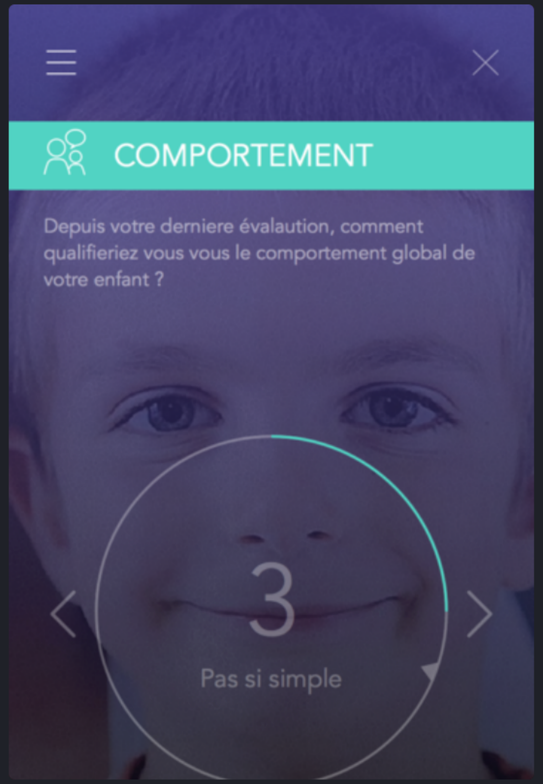

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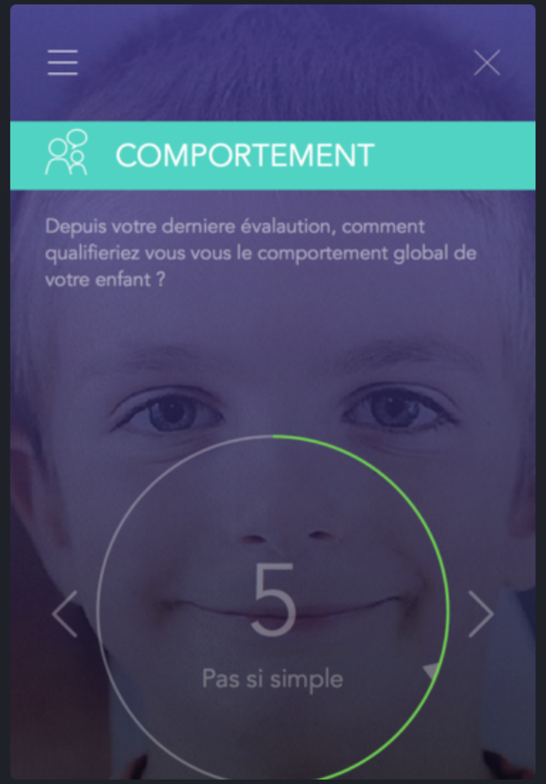

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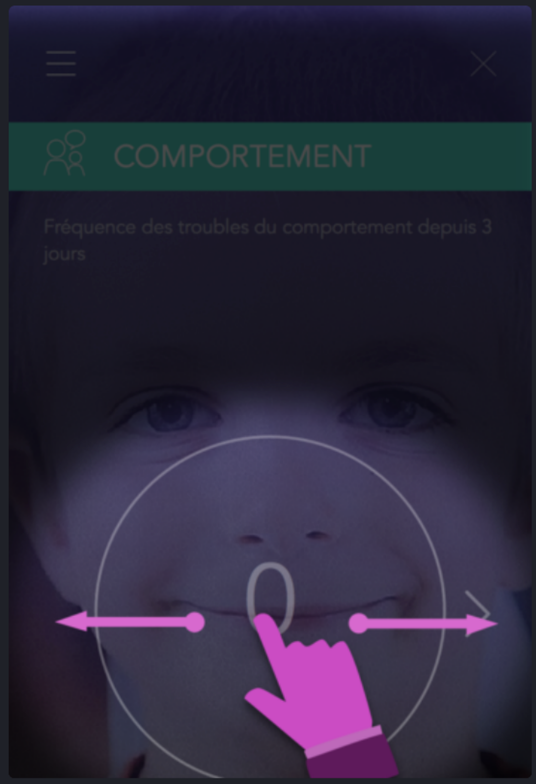

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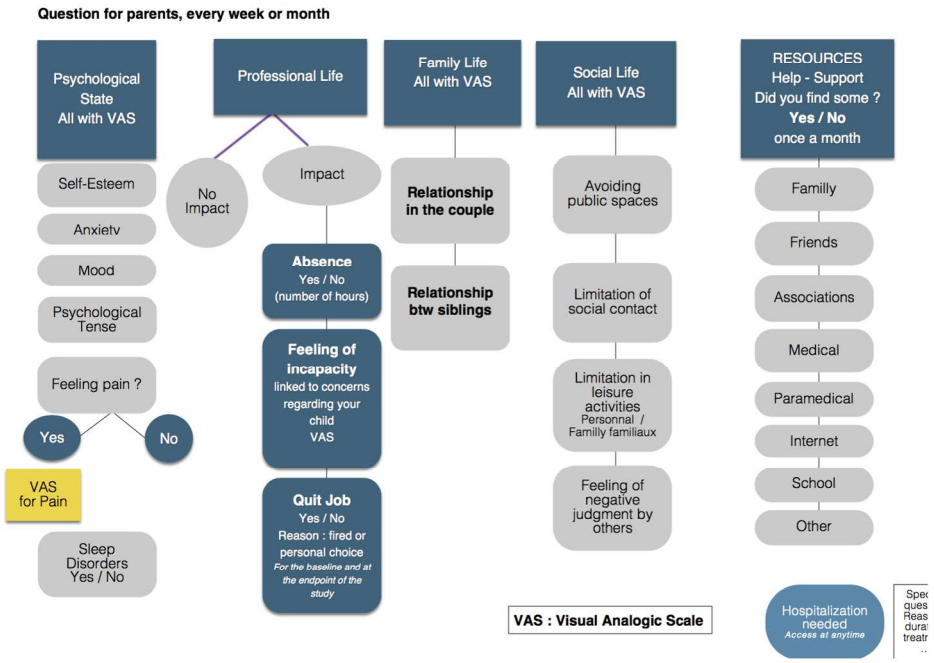

Figure 2. Questions for parents about them and social life in the SMARTAUTISM application.

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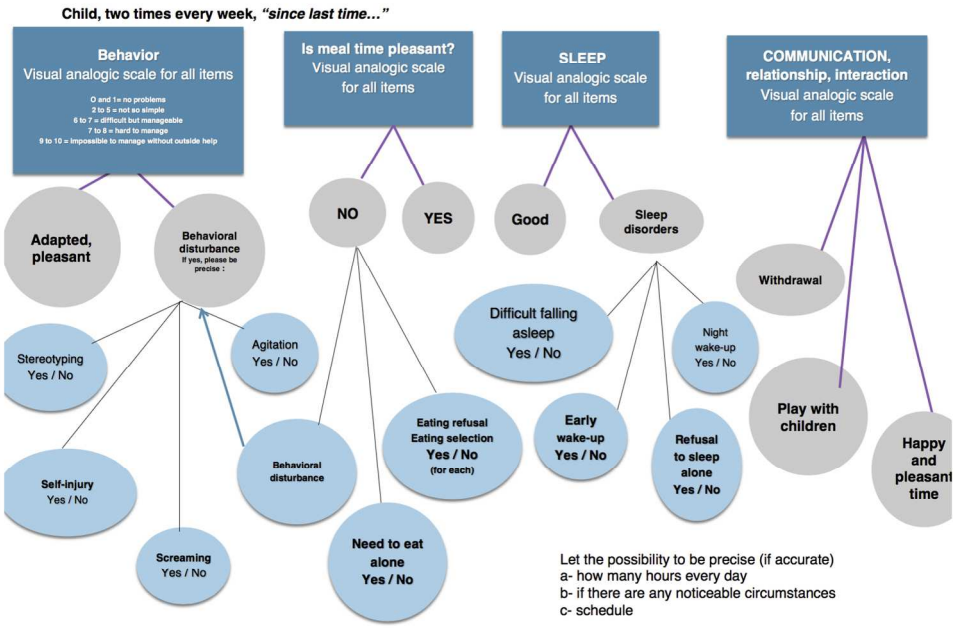

Figure 3. Questions for parents regarding their children in SMARTAUTISM application.

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Abstract

Introduction

Longitudinal studies on the evolution of autism spectrum disorder (ASD) symptoms are limited and have primarily used repeated measurements performed several months apart. However, measurements of changes in everyday life should more closely reflect the "real life" of the patient and his or her family. We

propose to study both the child's ASD symptoms and their effect on the quality of life, psychological status and anxiety of the child's parents over a 6-month period using SMARTAUTISM, a smartphone application.

Method and Analysis

This is a prospective, longitudinal, exploratory, open study with a 6-month follow-up period. Data will be recorded longitudinally over multiple weeks under natural conditions. The factors affecting the quality of life and anxiety of parents of children with ASD and the children's functional symptoms will be examined, and the feasibility of using a smartphone application designed for parents of ASD patients will be assessed.

Primary objective: Explore the evolution of a child's behavior over 6 months and the (psychological and social) effects of these changes on the family.

Secondary objective: Assess the feasibility of our application by examining the filling rate and application usage by parents for six months.

100 families containing one child diagnosed with ASD will be included. At baseline, socio-demographic, psychiatric and medical data will be recorded. The correlations of the general epidemiological variables (primary outcome measure) will be evaluated via multivariate analysis. The application filling rate (relative to the ideal filling rate) will be used to assess the feasibility of the application (secondary outcome measure).

Ethics and dissemination

The SMARTAUTISM study has the approval of the local ethics committee, and data security will be ensured via the use of encryption and a secure medical

server. The use of this application will be proposed at autism resource centers across France.

296 words

Keywords: Autism Spectrum Disorders, Ecological Momentary Assessment, Smartphone Application, Quality of Life

Strengths of our study

- First smartphone application enabling ecological momentary assessment of behavioral symptoms of children with ASD and quality of life of parents
- Six months of follow-up data
- Application providing easy access and readable feedback to enhance parents' motivation in the filling process

Limitations

- Subjective evaluation is provided by parents
- Items are simple, and unexpected situations may not be recordable

Contributorship statement

- ✓ OB, DB, PD and AD were involved in the conception and design of the study.
- ✓ OB drafted the article, DB, PD and AD revised it critically for important intellectual content. The figures were prepared by AD and OB.
- ✓ OB, DB, AD, PD, MM and JG were involved in the conception of the

smartphone application.

✓ All authors gave final approval of the version to be published.

Competing interests

All authors declare no competing interests related to this study.

CONTEXT

Information communication technologies (ICT), including on-line or off-line smartphone applications, are a currently rapidly progressing reality in medicine. There are approximately 100,000 apps in the Android or Apple market.[1] Many of these apps, including coaching, well-being advice or sports applications, have no medical purpose but are labeled as "health" applications. However, in the field of psychiatry, as for all medical specialties, apps are more than just a trend. In fact, apps may represent a revolution in research and doctor-patient relationships.

Apps may be used in different ways. The simplest way to use this device-based technology is to provide access to health care through smartphone applications in countries where the availability of equipment and medical personnel is limited.[2] Further, this technology can be conceptualized as mainstream news media to reduce stigmatization.[2] Apps may also be helpful in remote support via SMS, voice or visual phone consultations for medical purpose.

More importantly, medicine, as well as psychiatry, requires data from patients or their families. These data might be obtained from questionnaires that can be completed under natural conditions; this technique is referred to as ecological momentary assessment (EMA[3]) or the experience sampling method (ESM).[4] The first EMA experiments used beepers to remind users to complete the questionnaires on a computer; in general, the results for compliance and quality were disappointing, and the filling schedules were not respected.[5] Since the

release of PDAs and smartphones, individuals are carrying their device everywhere. This is a breakthrough for medical research in various fields, but psychological status and behavior, including behavioral addictions,[6] eating behaviors,[7] anxiety[8] and severe psychiatric disorders, such as bipolar disorder[9] or schizophrenia, appear to be particularly appropriate topics for application-based studies.[10] Apps are very useful for evaluating the social functioning, quality of life and psychological status of individuals. As demonstrated in anxiety disorder, EMA using smartphones is a practical and effective approach, and the data generated have higher quality than data generated via other methods.[8]

There are two major issues regarding the use of apps in psychiatry. The first issue is their feasibility (*Will subjects use the app?*), and the second is their efficiency.

The feasibility of an application-based method is important to assess. One of the few studies measuring this parameter suggested that the filling rate varies depending on the type and duration of app use (for both filling and educational purposes) but might be as high as 70%.[11] The literature in this domain is limited and largely consists of preliminary data or study protocols with varying durations (days to weeks) or performed on a small number of subjects (10-100 subjects). Interestingly, a recent survey showed that 77% of a US population of patients with a psychiatric disorder owned a smartphone and that these patients would be willing to use their smartphone to register their mental state.[12]

The core concept underlying EMA is the collection of behavioral data provided by the subject (and potentially the subject's family members or caregivers). These naturalistic data are a novelty and will affect our understanding of disorders as well as therapeutic relationships (see examples for eating disorders[6, 7, 13] or addictions[14]). However, the efficacy of EMA depends on the patient's desire to provide data that are useful collectively but not individually. Few research programs include a specific level of feedback by the application (see rare examples for schizophrenia[13] or bipolar disorder[9, 15, 16]).

App-generated feedback might be an incentive for filling the application, but it also represents a potentially important change in the doctor-patient relationship. One study of particular interest includes 52 subjects and proposes to compare behavioral interpersonal therapy with therapy available on demand using a smartphone or tablet (dematerialized adaptation) over a 5-month period.[17] The percentage of treatment responders was 54% for the "mobile" group compared with 8% for the conventional group, which is surprisingly low. Among other factors, a certain degree of feedback appears to increase acceptance and filling rates; for example, in a sample of patients with schizophrenia, one recent work showed an acceptable level of use (50% spontaneous use and 38% application-induced use) and excellent acceptance (90% satisfied) for an application based on psycho-educational support (information, resources, etc.) with a small portion of self-care and feedback.[18]

In summary, combining EMA with feedback is a promising approach for (i) increasing the feasibility of smartphone app-based research methods and (ii)

promoting a qualitative change in the doctor-patient relationship. We developed such an application in the autism spectrum disorder (ASD) field.

The SMARTAUTISM project

This ongoing (starting September 1st, 2016) study received funding from the Regional Health Agency (ARS) and the Autism Resource Centre (CRA) of the Loire Valley, as well as a grant from the National Center for Autonomy (CNSA)/Research Institute of Epidemiology and Public Health (IRESP).

ASD symptoms are now better understood, but ASD studies are most often transversal or mostly retrospective. Actual longitudinal studies on symptom evolution remain limited, and researchers continue to use repeated measurements recorded several months apart.[15, 19, 20] However, daily changes should be more accurate and, above all, should more closely reflect the "real life" of the patient and his or her family.

Children with ASD and their parents often face difficult situations daily that are related to behavioral symptoms (agitation, feeding difficulties, sleep disturbances, obsessive behavior, refusal of authority, etc.). Further, the parents' quality of life is strongly affected by everyday life with their children with ASD.[21, 22] Data on these behavioral disorders are currently being collected in a transverse manner using surveys, questionnaires and parental recall. This mode of data collection causes a clear, and classical, bias in all studies.

Our goal is to study both a child's ASD symptoms and their impact on a family's quality of life, psychological status and anxiety over a long time period (six months) using a daily information source that includes parental observations. Moreover, our EMA application that includes feedback could be useful for facilitating parents' necessary adaptive educational behavior and for informing the doctor (who will have access to the data during regular consultations).

In addition to quality of life, anxiety of the parents is a dimension that we will consider. Parents of children with ASD have greater anxiety levels than parents of children without a developmental disorders (for a recent meta-analysis on this subject, see,[23] which included 15 studies). The major autism symptoms, communication disorders and aggression, are the most important stressors (Davis and Carter 2008). Most of these reports describe cross-sectional studies that evaluated parents using a single semi-structured interview or questionnaire.

An EMA app has never been used to study the parents of children with ASD in terms of quality of life and anxiety level. Additionally, there are no epidemiological studies of this kind in the literature.

The SMARTAUTISM application represents a combination of a classic EMA with feedback that may be used by parents to adapt their educational behavior and used by doctors to better understand their patients and propose more accurate treatments. The parents must provide regular ratings (twice a week at least) for a

long period (6 months for our study). In our proposal, the parental rating time and application design are two main factors.

1. The rating time will range from 3 to 10 minutes, depending on the responses provided. The questions will be simple and user oriented (see Figures 1 & 2). We will ask questions about sleep; behavior; ASD symptoms, such as stereotyping or withdrawal; and social life, such as lunch period or leisure activities. With respect to the parents, the questions will be about anxiety and psychological state of mind in addition to quality of life elements (ability to function in everyday domestic / professional / friendly tasks and social contact). To save time, we will use a visual analog scale (VAS). The VAS is an accurate tool that facilitates repetitive measurements in psychiatry (for example, see the MATHYS experiment,[24]). Users will provide a rating from 0 to 10 by scrolling their finger on the touch screen (see Figure 3). To maintain a short filling time, all responses will be selected from a list of words yes/no buttons or from a VAS. Our choice is radical, and we anticipate that the relatively reduced quality of the data will be counterbalanced by the volume of data.
2. The design of the application was a continuous concern throughout the development process; we have research collaborations with a specialized private company with expertise on this topic. Each screen provides information using soft color and typography. SMARTAUTISM is also personalized. For example, users may use a particular child's picture as the wallpaper (see Figure 4).

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Insert Figure 1 about here

Figure 1. Snapshots of the SMARTAUTISM smartphone application.

Insert Figure 2 about here

Figure 2. Questions for parents about their daily and social life in the SMARTAUTISM application.

Insert Figure 3 about here

Figure 3. Questions for parents regarding their children in the SMARTAUTISM application.

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SMARTAUTISM provides a menu section with general information about ASD and local resources (health care facilities, emergency numbers, etc.). It also allows the user to change the settings, particularly the rating reminder notification. The application also provides two summary screens for the data collected from the first input (a feedback). These screens are user friendly and readable. Users will be able to have a graphic view (current and past) of their child's behavior after each assessment. This visual feedback will be presented to the user and can be shown to a third party (such as a doctor).

We propose a study (i) to evaluate the feasibility of using EMA to investigate a child's ASD symptoms as well as a parent's quality of life, psychological state and daily anxiety level over 6 months and (ii) to collect epidemiological data. The SMARTAUTISM study will begin in September 2016.

OBJECTIVES and ASSESSMENT CRITERIA

Primary objective

The primary main objective is to assess the feasibility of this innovative app-based approach.

Primary criteria

The primary criteria will be the filling rate (R) and the use of our application by the parents over six months.

$$\frac{\text{Number of fillings}}{60^{1}} = R$$

Secondary Objectives

Our secondary objective is an epidemiological study on the evolution of a child's behavior over 6 months and the simultaneous self-reported psychological status of the family.

Secondary criteria

Secondary criteria include data from the application, which is filled by the parents, predominantly using a VAS from 0 (no) to 10 (severe) to measure the following variables:

- For the child (see figure 3): (i) behavior with pairs and communication, (ii) sleep disorders, (iii) eating disorders and (iv) general behavior.

[1] Every 3 days over 6 months = 6X30/3 = 60 filling dates.

- For parents: (see figure 2): (i) psychological status (self-esteem, anxiety, sleep, mood, pain and psychological stress), (ii) professional life, (iii) personal life, (iv) social life and (v) support and resources.

We will also be able to access more descriptive data regarding the use of the application, such as (i) the duration of use, (ii) the time of use and (iii) the rate of complete filling.

METHODOLOGY

This is a prospective, longitudinal, exploratory, open study with a 6-month follow-up period to assess the feasibility of using a smartphone application designed for parents of patients with ASD and to longitudinally collect data on the quality of life and anxiety of parents of children with ASD and the children's functional symptoms over multiple weeks under natural conditions.

Population

We propose to study individuals diagnosed with ASD based on National Health Authority (HAS) recommendations (on ADI-R diagnoses) from 3-16 years of age in the Pays de la Loire region. We propose to include 100 families. The study is exploratory in nature; thus, randomizing patients is unnecessary. We will include the first 100 families agreeing to participate in the study and meeting the inclusion criteria. All participants will be recruited from the Department of Child

and Adolescent Psychiatry of CHU de Nantes and from the Regional Center for Autism (CRA des Pays de la Loire).

Inclusion criteria:

- Having a child with an ASD diagnosis based on the ICD 10 criteria.
- Having at least one smartphone (iOS Apple or Android).
- Signing the consent form for participation.

Exclusion criteria:

- Having several children with an ASD diagnosis.
- Having children living in more than two areas.

Method

At the inclusion visit, parents will receive a code to download the app from the "application store" of their choice (depending on their smartphone) and sign an informed consent form (see flow chart, figure 4).

All type 1 data from the inclusion visit will be stored in an electronic database and in the smartphone application (during the setup process).

This initial evaluation by the investigator will include the following type 1 data:

- Sibling rank and marital status,
- Lifestyle: rural or urban; single or multiple occupants of the chid's bedroomroom and housing type and surface,

- Educational and teaching load and conditions (special education, inclusive education, partial or full time, etc.), and
- The therapeutic management (speech therapy, psychomotor therapy, etc.).

Type 2 data will be stored in the electronic database only:

- Age at diagnosis,
- Current drug treatments (name, starting date and dose),
- Comorbidities (associated epilepsy, mental retardation and organic pathology),
- Medical and psychiatric family ATCD,
- Original scores on the ADI-R and ADOS at the time of diagnosis, and
- Scores on the French version of the Childhood Autism Rating Scale[25] (CARS) (http://www.autisme.qc.ca) at baseline and at the end of the study.

Insert flow diagram in Figure 4 here

A default schedule for filling out the routine application questions (as shown in Figures 2 & 3) with notification reminders will then be proposed to the parents. The default settings can be modified by the parents if necessary but must include at least 3 fillings each week. Missing data will be included in the assessments. Each filling will require a short time period (less than ten minutes in the longest configuration, if all answers are yes). The key questions are closed-ended (yes/no), and a VAS is primarily used to evaluate the degrees of statuses, symptoms and disorders.

The first question concerns the environmental context in the days surrounding the filling date (unusual, holiday, etc.). With respect to the children, the questions will focus on sleep, food and behavior concerning themselves and others (such as

aggressiveness, agitation, stereotypic behaviors or cries). To avoid redundant or inappropriate questions, the questions will be presented as an algorithm (see Figures 1 and 2).

In cases in which both parents have a smartphone, both will have the application, and filling may be performed by either parent. The data will be aggregated per family. Simultaneous assessments by both parents are unnecessary in this study.

During the 6-month inclusion period and the 6-month follow-up period, we will record encrypted data from the smartphone when the parents are connected to a Wi-Fi network using a secure medical server (16-digit encryption key + a personal temporary code for access to data).

We have developed a qualitative questionnaire for the participants and the patients' doctors as well as a semi-directed, face-to-face interview to assess the change in the doctor-patient relationship after using the application.

Statistical analysis

For this feasibility study, the primary endpoint (which corresponds to the primary objective) will be the application filling rate, which is calculated relative to the ideal filling rate (three days per week every week) and considers the number of fillings (of at least half of the items requested).

The secondary endpoints will require more precise analyses, such as examination of the variation in the rate of responding to at least half of the requested items

over time. We will collect a considerable amount of data due to the number of variables; as such we will be able to perform exploratory epidemiology on this essential and unique database using descriptive and analytical statistics.

Generally, we will compare two groups: the group with a single place of family life and the group with two places of family life. The data encoded by the parents are subjective, but we do not distinguish the data on a child according to the parent. However, the quality of life data will be distinguished based on the parent who provided the rating. Thus, we will include 100 patients and more than 100 parents reporting on quality of life.

The analysis will be performed in two stages: (i) a longitudinal data analysis of each group (parents and children) and (ii) multivariate analyses on the relationships between variables specific to the parents and variables specific to the children.

Safety issues

Protection of personal data is a very important issue with very restrictive regulations in France and Europe. Therefore, to obtain approval from the National Center for Informatics and Liberty (CNIL, www.cnil.fr), we have designed a secure pathway of data handling. Data will be stored in the application on the parents' smartphones and will be inaccessible by unauthorized people (an individual code will be required on application opening). In particular, there is no Internet connection needed to run the application. As part of the research, and after considering the opinion of the CNIL, families included in this study will transmit these data to the investigators using a strict, secure, 5-step process:

1. Encryption of data in the smartphone of the participant (in-app coding) with a 16-digit encryption key + a personal temporary code for access to data,
2. Transmission of the encrypted data to a secure server of a company based in France (Ivory Healthcare, Inc.),
3. Physical transfer from the server to Nantes University Hospital secure medical server (USB stick or disk) at the end of the study period,
4. Once the data are uploaded on the intranet of the University Hospital, decryption in situ using specific software after entry of a short, automatically generated validation code by the principal investigator, and
5. Organization of the obtained data in the form of a statistically exploitable Excel file.

Discussion

Ecological naturalistic data on ASD patients are limited in the literature. The SMARTAUTISM application will be a unique source of such longitudinal observations.

The association of EMA with feedback in a carefully designed smartphone application might be valuable for three main reasons:

- The feedback provided by the application may be encouraging to users. Therefore, the filling rate should be higher and the epidemiological naturalistic data more accurate.

- The feedback might also be used by parents for contextualization and adaptation of their educational behavior. This aspect is crucial and will be evaluated in an ancillary study. The "self-care" potential of SMARTAUTISM, through personalized educational tips, is a major developmental project for us. We plan to develop a second version of the application.
- The feedback may also be shown to a doctor by the parents during regular consultations. Medical consultations can be conducted at wide intervals and cannot properly consider changes in symptoms from previous assessments or in everyday life hazards and the associated repercussions. The relationships of the patient and the family with their doctor may be profoundly changed by the use of this app. Because appointments with the patient's referring physician can be far apart, a major frustration is not being able to "say everything". Parties tend to speak only about the most recent events. For the doctors, this application can provide a perspective that more closely reflects reality and, above all, can reveal context that can aid in care and therapy. Therefore, using this application could generate a major breakthrough in the patient-doctor relationship. This issue will also be examined in an ancillary qualitative study. We plan to contact, with their permission, doctors who have used SMARTAUTISM with parents during consultations and ask about their impressions.

Our application is clearly a first step, but it is consistent with an on-going shift toward the use of such technologies in psychiatry. Our goal is to use this

application to regularly care for people with autism. Therefore, our research protocol is focused on feasibility (as demonstrated by the filling rates) and the quality of the data obtained. If, as we expect, the results are encouraging, we will proceed further.

Conclusions

The SMARTAUTISM project and research protocol are situated in the major changes in medical care that have been driven by the digital revolution. These changes affect both our ability to obtain naturalistic epidemiological data reflecting real life and our capacity to provide medical care to patients and their families.

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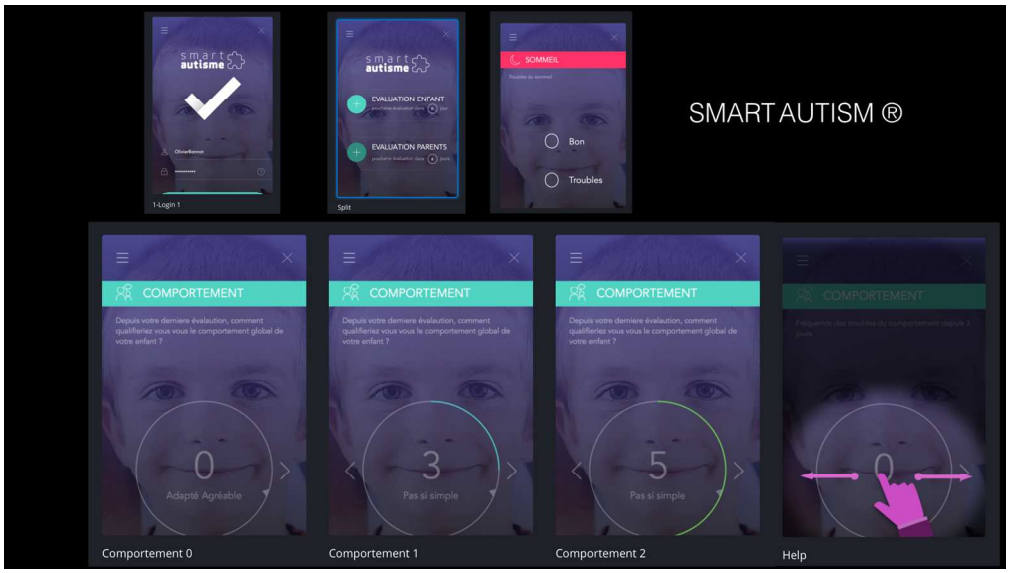

Figure 1: Snapshots from SMARTAUTISM Application

162x91mm (300 x 300 DPI)

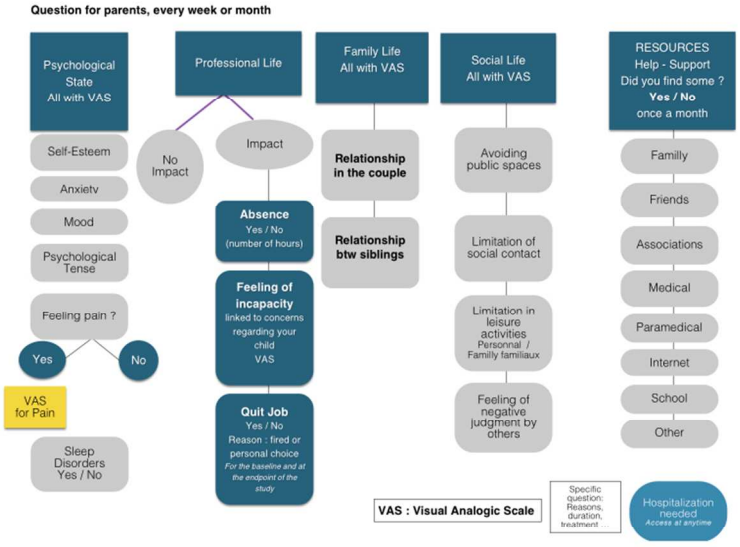

Figure 2. Questions regarding psychology and quality of life for parents

86x65mm (300 x 300 DPI)

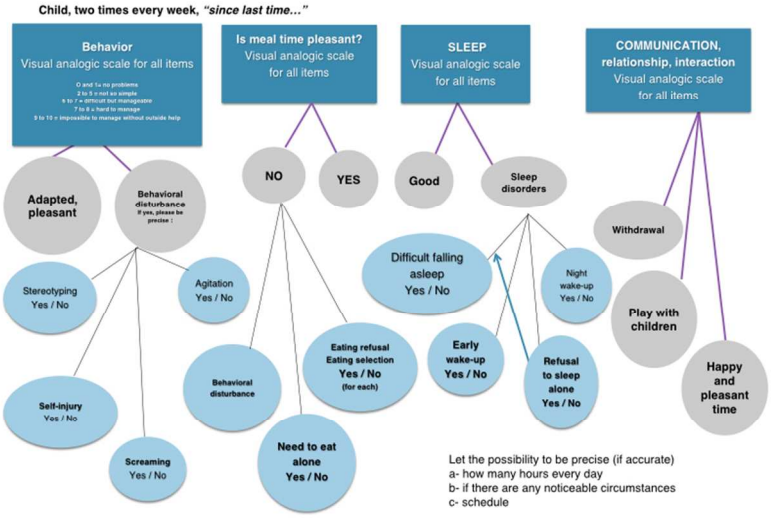

Figure 3. Questions regarding behavior of individuals with autism spectrum disorders.

86x65mm (300 x 300 DPI)

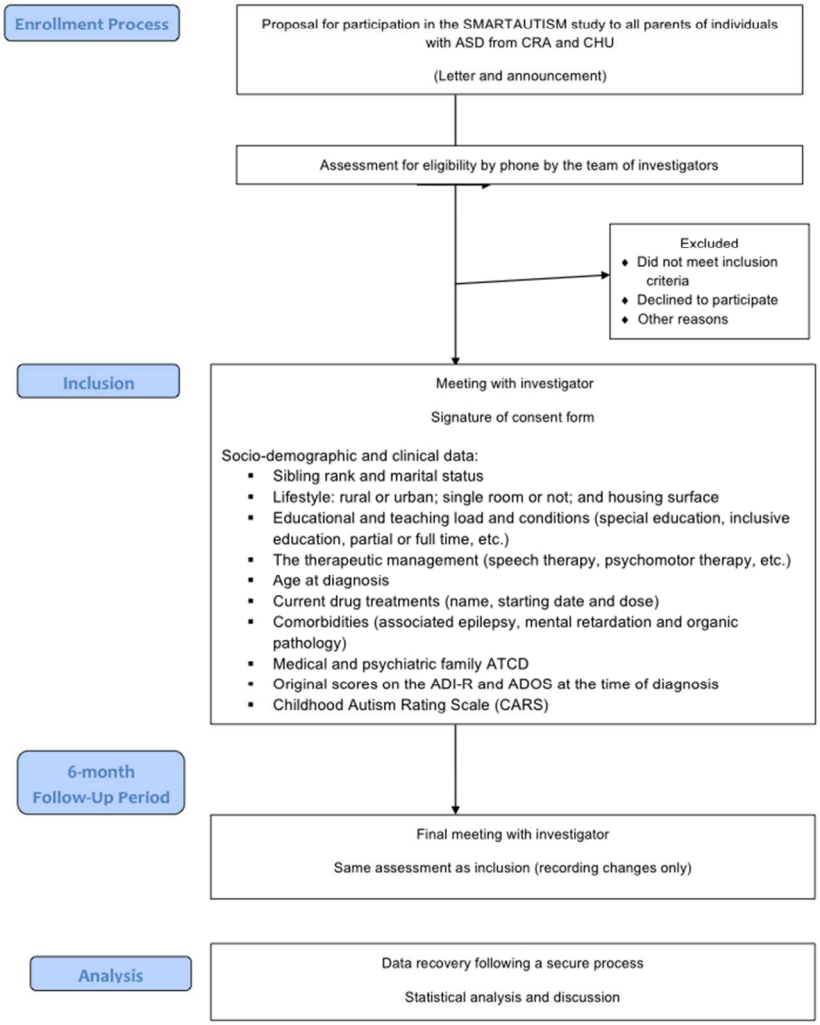

Figure 4. SMARTAUTISM Protocole Diagram Flow

65x86mm (300 x 300 DPI)