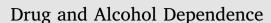
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Development and validation of a virtual agent to screen tobacco and alcohol use disorders



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A R T I C L E I N F O	A B S T R A C T
<i>Keywords:</i> Embodied conversational agents Virtual reality Addiction Systematic screening Alcohol Tobacco	<i>Background:</i> Substance use disorders are under-detected and not systematically diagnosed or screened for by primary care. In this study, we present the acceptability and validity of an Embodied Conversational Agent (ECA) designed to screen tobacco and alcohol use disorder, in individuals who did not seek medical help for these disorders. <i>Methods:</i> Individuals were included from June 2016 to May 2017 in the Outpatient Sleep Clinic of the University Hospital of Bordeaux. DSM-5 diagnoses of tobacco and alcohol use disorders were assessed by human interviewers. The ECA interview integrated items from the Cigarette Dependence Scale-5 (CDS-5) for tobacco use disorder screening, and the "Cut Down, Annoyed, Guilty, Eye-opener" (CAGE) questionnaire for alcohol use disorder screening. Paper version of CDS-5 and CAGE questionnaires and acceptability questionnaire was also self-administered. <i>Results:</i> Of the 139 participants in the study (mean age 43.0 [SD = 13.7] years), 71 were women, and 68 were men. The ECA was well accepted by the patients. Paper self-administered CDS-5 and CAGE scores had a strong agreement with the ECA ($p < 0.0001$). The Receiver Operating Characteristic (ROC) analysis of the ECA interview showed AUC of 0.97 (95% CI, 0.93–1.0) and 0.84 (95% CI, 0.69–0.98) for CDS-5 and CAGE respectively with p-value < 0.0001. <i>Conclusions:</i> This ECA was acceptable and valid to screen tobacco or alcohol use disorder among patients not requesting treatment for addiction. The ECA could be used in hospitals and potentially in primary care settings to help clinicians to better screen their patients for alcohol and tobacco use disorders.

1. Introduction

Tobacco use disorder estimate is 22% in worldwide general population (World Health Organization, 2016), and that of alcohol use disorder is 4.1% (World Health Organization, 2014). However, the proportion of individuals who have currently been engaged in alcohol or tobacco use disorder treatment is low, probably under 10% (Hasin and Grant, 2015; World Health Organization, 2017). Better screening of individuals for tobacco or alcohol use disorder to provide the appropriate care is of major interest. Substance use disorders are under-detected and not systematically diagnosed or screened in primary care (Tai et al., 2012). As many countries, French health authorities have recommended that health professionals must be involved in tobacco cessation promotion and that primary care physicians should systematically screen for tobacco, alcohol and other substance addictions (Haute Autorité de Santé, 2016). However, physicians reported lack of time as a major barrier to performing such a screening (Harris et al., 2016).

Self-administered questionnaires have been developed for the screening of tobacco and alcohol use disorders. The most used questionnaire is the 6-item Fagerström Test for Nicotine Dependence (FTND) and its simplified 2-item version, the Heaviness of smoking

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index (HIS) (Etter et al., 1999; Heatherton et al., 1991, 1989). Both have a good validity but a low internal consistency (Underner et al., 2012). The Cigarette Dependence Scale (CDS) was developed as a new self-administered measure of cigarette addiction and has been validated (Etter et al., 2003). Two versions of 12 and 5 items are proposed, and the two have acceptable internal consistency, better than the FTND (Etter, 2008).

For alcohol use disorder screening the most used questionnaires were the "Cut Down, Annoyed, Guilty, Eye-opener" (CAGE) questionnaire (Ewing, 1984) and the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993). The 10-item AUDIT presents moderate stability in clinical settings (Sahker et al., 2017). Both tests are effective, but the CAGE is shorter than the AUDIT (Bradley et al., 1998) which targets preferentially heavy drinkers (Seppa et al., 1998).

Although these self-administered questionnaires allow a quick screening for tobacco and alcohol addiction, their implementation is not that easy. They are not very attractive to patients that do not use them when made available in a waiting room (Audran, 2016). The physician will need to take time to encourage patients to fill them or to administer the questionnaire with the patient. Even when used in autonomy by the patient, the physician will need to score each questionnaire to determine what to do, which also takes time.

Recently, computerization of standardized procedures has been proposed to improve implementation of screening tests (Harris et al., 2016) and to allow efficient transmission of data to the individual's electronic health records. Some computerized-interviews for the screening of problematic substance use, such as the ACASI ASSIST have been developed and have been shown to be acceptable, valid and timeefficient (Harris et al., 2016; Kumar et al., 2016; McNeely et al., 2016). However, the dissemination of use of computerized tools remains an important issue in the field of mental and addictive disorders. Empathic interactions with human-machine interfaces are promising approaches to increase usage of computerized diagnostic tools in patients with mental and addictive disorders. Within the development of these technologies coupled with virtual reality, embodied conversational agents (ECA) (i.e., virtual agents) displayed on computer screen to create an interactive dialogue animation (Cassell et al., 1994) have received an increased interest in the health-related field (Insel, 2017; Nochomovitz and Sharma, 2018). ECAs come from affective computing and provide a strong means of human-system interaction. To date, use of ECA has not been applied to the addiction field. The added value of ECAs over computerized questionnaires is that ECAs have different gestures, facial and verbal expressions and have the potential for nonverbal expressions that is very appealing to human motivation (Philip et al., 2014). They also use specific interactive scenarios and non-verbal communication to appear empathic to the patient and to reinforce adherence to clinical evaluation. Indeed, they represent good candidates to improve and to standardize screening of substance use disorders. We initially designed ECAs to explore excessive daytime sleepiness (Philip et al., 2014) and to diagnose depression (Micoulaud-Franchi et al., 2016a, b; Philip et al., 2017). These ECAs have shown very promising results in term of sensitivity/specificity but also in term of acceptability by patients.

In line with these developments, we developed a new ECA (called Jeanne) able to perform a face-to-face interview to screen tobacco and alcohol use disorders. This paper aims to present the acceptability and the validity of this ECA Jeanne in patients who did not seek medical help for a substance use disorder. We hypothesized that ECA Jeanne would 1) be acceptable to screen for alcohol and tobacco use disorders, 2) present high concurrent validity compared to DSM-5 alcohol and tobacco use disorder diagnosis.

2. Material and methods

2.1. Participants

Participants were recruited from June 2016 to May 2017 among individuals who attended the outpatient sleep disorder clinic at the University Hospital of Bordeaux, France for evaluation of sleep complaints. All consecutive adults were asked to participate in the study after completion of their sleep-related evaluation unless they had insufficient capacity to understand and to answer the questionnaires or had visual/auditory deficits that could interfere with the use of the ECA. The local ethics committee for clinical research approved the study and participants gave their written informed consent. The present study is part of a larger ongoing research program on the validation of the virtual reality-based diagnosis of neuropsychiatric disorders (PHE-NOVIRT program (https://phenovirt.equipex.u-bordeaux.fr/en/), funded by a French Government Agency, Investissement d'Avenir Grant).

2.2. Description of the ECA "Jeanne" software

The ECA called "Jeanne" was developed with Unity 3D (Unity-Technologies, 2014) to screen for current alcohol and tobacco use disorders. This software-driven virtual human was adapted from previously developed software designed to self-conduct interactive face-toface clinical interviews (Philip et al., 2014). The morphology of "Jeanne" was generated by the software and gestures were captured by motion capture technology. Tobacco and alcohol use disorders were screened with an adaptation of the CDS-5 and the CAGE questionnaires in a virtual form. This self-conducted interview was optimized to obtain fluently expressed questions. The overall design and interactive mode of the software-driven virtual human were previously described (Philip et al., 2017). Specific items are integrated into the clinical interview to reinforce empathy of the virtual agent including questions on the comfort of the patient during the interview and its ability to answer the questions. The software is based on four modules: i) an interview manager that coordinates the whole interview and manages the other modules, ii) a 3D video module that displays the virtual human and plays animations, iii) a recorded real voice that creates the speech of the virtual human, and iv) a tablet interface to respond to the ECA. The software runs on a computer (Windows 8 - i7 3770@3.4 GHz-8 GB -NVidia 670 GTX) connected to a 40-inch vertical display.

2.3. Procedure

All participants completed a structured interview conducted by a specifically trained research assistant to collect socio-demographic variables and to explore the endorsement of DSM-5 tobacco and alcohol use disorder criteria. Then, participants were left alone in the room for the ECA Jeanne interview, with a research assistant available if needed. The ECA Jeanne introduced itself and asked questions about alcohol and tobacco use. When a participant reported smoking tobacco during the past 12 months, the ECA asked the CDS-5 questions during this period. When a participant reported drinking alcohol during the past 12 months, the ECA asked the questions of the CAGE questionnaire during this period. The duration of the ECA interview was recorded. After completion of the ECA, the participants were asked to complete the paper-based version of the CDS-5 and the CAGE. To control for possible priming effects, the order of DSM-5 criteria and ECA Jeanne interview assessment were randomized following simple fixed randomization process.

2.4. Clinical measures

DSM-5 criteria for substance use disorders were used as the gold standard for alcohol and tobacco use disorder in this study to validate ECA administered questionnaires as screening for use disorder (American Psychiatric Association, 2013; Hasin et al., 2013).

CDS-5 is a tobacco use disorder screening instrument validated in French (Etter et al., 2003) in general and patient population (Etter et al., 2009). The CDS-5 consists of five items that each score from 1 to 5. The final score ranges from 5 to 25.

The CAGE questionnaire is an alcohol problematic use screening tool (Mayfield et al., 1974). This tool is composed of four questions about alcohol use over the last 12 months: two positive responses suggest a high probability of alcohol use disorder.

The acceptability of the ECA Jeanne was evaluated with the Acceptability E-Scale (AES), a 6-item questionnaire that gathered individual's experience with the ECA evaluation (Micoulaud-Franchi et al., 2016a,b). Each item was ranked on a 5-point Likert scale, generating a total score of acceptability ranging from 6 (lowest acceptability) to 30 (highest acceptability).

2.5. Analyses

2.5.1. Acceptability

Descriptive analyses were performed to evaluate the acceptability of the ECA.

2.5.2. Internal structural validity

Item-internal consistency was assessed by correlating each item with its related factor using Pearson's coefficient for ECA CDS-5 interview (correlations of at least 0.4) and Cohen's Kappa coefficient for ECA CAGE interview (correlations of at least 0.6). Correlation thresholds were chosen for a moderate agreement for supporting item-internal consistency (Carey and Seibert, 1993).

Internal consistency reliability was assessed by Cronbach's alpha coefficient. It was recalculated after items were removed. To confirm consistency, we expected a coefficient of at least 0.7 (Carey and Seibert, 1993).

Floor and ceiling effects were reported to assess the response distribution. The rates of floor and ceiling effects were calculated as the proportion of individuals who obtained the lowest and the highest scores for any of the items.

2.5.3. External validity

Correlations analyses between the scores of the paper-based and ECA-based screening for CDS-5 and CAGE were performed using Pearson's coefficients.

2.5.4. Receiver operator characteristics (ROC)

ROC curves were performed to define the optimal threshold of the ECA-based CDS-5 and CAGE score to discriminate DSM-5 alcohol and tobacco use disorders versus no use disorder. Area under the curve, specificity, and sensitivity and predictive reports (positive and negative) and 95% confidence intervals were calculated. Comparison of the AUC between paper-based and ECA Jeanne questionnaires were performed.

For all correlation analyses, to minimize Type I error, only correlations significant at p < 0.001 level was considered as statistically significant. All the statistical analyses were performed using JMP[®] 13.0 (SAS Institute Inc., Cary, North Carolina).

3. Results

3.1. Sample selection

Fig. 1 describes the sample selection flowchart. During the time of the study, 646 patients attended the sleep clinic, and 508 were eligible. The majority declined participation due to lack of time. Finally, 139 individuals gave their consent to participate.

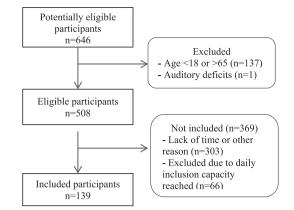


Fig. 1. Sample selection flowchart, with number of participants after each stage of the screening process.

Table 1

Demographic, psychiatric, tobacco use and alcohol use data in total participants.

	Total (n = 139)
Sociodemographic data	
Age - mean (SD)	43.0 (13.7)
Gender - Women n (%)	71 (51.1)
Education, years – mean (SD)	13.4 (2.9)
Psychiatric	
Current treatment for addiction – n (%)	2 (1.4)
Current treatment for other psychiatric disorder – n (%)	50 (36.0)
Tobacco use	
Reported tobacco use (in the last 12 months) - n (%)	62 (50.8)
CDS-5 score paper-pencil – mean (SD)	8.7 (5.9)
CDS-5 score ECA – mean (SD)	8.7 (5.7)
Current tobacco use disorder DSM-5 – n (%)	43 (30.9)
Alcohol use	
Reported heavy alcohol use (in the last 12 months) - n (%)	27 (19.4)
CAGE score paper-pencil – mean (SD)	0.4 (0.8)
CAGE score - ECA – mean (SD)	0.3 (0.7)
Current alcohol use disorder DSM-5 – n (%)	12 (8.6)
Interview time with ECA (minutes) - mean (SD)	4.4 (1.9)

3.2. Sample characteristic

Table 1 displays the characteristics of the 139 participants. Among them, 62 reported current tobacco use (in the last 12 months) and 27 current heavy alcohol use. The prevalence of current DSM-5 tobacco use disorder was 30.9% (n = 43), and 8.6% (n = 12) for current DSM-5 alcohol use disorder. The order of the DSM-5 interview and ECA Jeanne interview did not significantly modify the findings.

All 139 participants completed the requested interviews. Interview with the ECA was short, with a mean duration of 4.4 min (SD = 1.9).

3.3. Acceptability of the ECA interview

The ECA was highly accepted with high AES scores (24.8; SD = 4.2) that were not influenced by whether the ECA came before or after the face-to-face DSM-5 diagnostic interview (24.5; SD = 4.2 and 25.1; SD = 4.2 (p = 0.47)).

3.4. Internal structural validity

Item-internal consistency was satisfactory for all items for tobacco and alcohol questionnaires: each item achieved the predetermined standard threshold value.

Cronbach's alpha coefficients are presented in Table 2. Cronbach's alpha value for ECA CDS-5 interview and for CDS-5 paper version suggested that the items had very high internal consistency. Cronbach's

Table 2

ECA reliability: mean, standard deviation and Cronbach's total and after item was removed of the ECA interview and paper questionnaire for the evaluation of tobacco use (CDS-5 questionnaire) and alcohol use (CAGE questionnaire).

	ECA			Paper version			
	Mean	SD	Cronbach's α	Mean	SD	Cronbach's a	
CDS-5	8.7	5.7	0.94	8.7	5.9	0.96	
Tobacco-related items CDS-5							
#1: degree of dependence	1.76	1.36	0.92	1.76	1.38	0.94	
#2: daily number of cigarettes	1.56	1.03	0.92	1.59	1.07	0.95	
#3: time after waking for first cigarette	1.75	1.34	0.95	1.71	1.30	0.96	
#4: definitely stop use	1.76	1.20	0.91	1.74	1.16	0.94	
#5: irresistible need to smoke	1.91	1.46	0.91	1.87	1.42	0.94	
CAGE	0.3	0.7	0.63	0.4	0.8	0.71	
Alcohol-related items CAGE							
#1: need to decrease alcohol use	0.12	0.33	0.40	0.15	0.35	0.45	
#2: remarks of the entourage on your alcohol use	0.07	0.26	0.57	0.08	0.27	0.62	
#3: feel that you drink too much	0.14	0.34	0.36	0.13	0.34	0.53	
#4: need to use alcohol in the morning to be up	0.0	0.0	0.71	0.0	0.0	0.80	

alpha for ECA CAGE interview showed a poor internal consistency. Item 4 increased Cronbach's alpha if deleted for both ECA and paper version of the CAGE interview.

Floor effect ranged from 62.5% to 80.6 for ECA and from 65.5 to 81.3 for the paper version. Ceiling effect was present for both ECA interviews and paper version questionnaires (ranging from 0.0 to 0.7).

3.5. External validity

The correlation between the ECA CDS-5 and CAGE interviews and the paper version questionnaires scores were high (r(139) = .944, p < .0001 for CDS-5 and r(139) = .893, p < .0001 for CAGE).

3.6. Receiver operator characteristics

The receiver operator characteristics are presented in Table 3. For the ECA CDS-5, the AUC was 0.97 (CI 95%: 0.93–1.0; p < 0.0001) (Fig. 2a). For the ECA CAGE, the AUC was 0.84 (CI 95%: 0.69 – 0.98, p < 0.0001) (Fig. 2b). The order of interviews did not modify these results.

The ROC curves for the paper-based version of the CDS-5 and the CAGE questionnaires showed AUC of 0.95 for CDS-5 and 0.84 for CAGE. AUCs for paper-based CDS-5 and CAGE questionnaires and ECA-based CDS-5 and CAGE interviews were not significantly different (p = 0.33 for CDS-5; p = 0.26 for CAGE).

4. Discussion

This study aimed to describe the validity and acceptability of an ECA to screen for alcohol and tobacco use disorders in individuals attending a sleep disorder clinic for sleep complaints.

The prevalence of tobacco and alcohol use disorders in our sample (30.9% and 8.6% respectively) were comparable to the prevalence in French general population (Basstianic et al., 2013; Beck and Richard, 2014).

The ECA showed good acceptability for both alcohol and tobacco interviews. This is in line with results obtained from previous ECAs (Micoulaud-Franchi et al., 2016a,b) and consistent with most studies showing that patients accept computer interviews as well or better than human-driven interviews (Garb, 2007).

Items taken separately and total scores of ECA interviews were correlated with their equivalent paper questionnaires. Internal consistency of the ECA CDS-5 interview was very high, similar to the paper questionnaire and its validation study (Etter et al., 2003). On the other hand, internal consistency for ECA CAGE interview and CAGE paper questionnaire was not homogeneous enough, while it was a little better in the validation study of the paper version of the CAGE (from 0.60 to 0.89) (Mayfield et al., 1974). Once item #4 ("Have you ever had a drink in the morning to get rid of a hangover?") was deleted, internal consistency became acceptable. Because none of the participants endorsed this item, this could explain the observed ceiling effect. These results suggested that ECA CAGE interview could be shortened to the first three items only without modifying the interpretation. A previous study reported similar results (Malet et al., 2005). This item #4 is the only one that refers directly to a withdrawal symptom. A patient who needs alcohol when he wakes up could choose to not reply to this question because of its negative social representation. A ceiling effect was also observed for both paper and ECA CDS-5 interview, which could have limited the accuracy of the results.

The ECA interview obtained almost the same screening results than the paper self-administered questionnaires for both tobacco and alcohol screening. ROC analyses showed similar results suggesting that the ECA Jeanne screens as well as paper self-administered questionnaires. Similar results were reported in a study comparing computerized versus self-administered CAGE and other alcohol screening tests (Barry and Fleming, 1990).

Compared with the DSM-5 tobacco and alcohol use disorder criteria, the screening value of ECA Jeanne was very informative for tobacco and alcohol use disorders. ECA Jeanne was 91% and 67% sensitive, 96% and 95% specific for CDS-5 and CAGE respectively, with a

Table 3

Receiver operator characteristics: Area Under the Curve, sensitivity, specificity, positive and negative predictive value of ECA screening performance for total sample (DSM-5 diagnosis as standard reference).

-											
	AUC	P value	Sensitivity (%)	Specificity (%)	PPV	NPV	TP	TN	FN	FP	Threshold value
CDS-5 ECA	0.97	< 0.0001	91	96	0.91	0.96	39	92	4	4	> 9
CDS-5 Paper	0.95	< 0.0001	91	95	0.89	0.96	39	91	4	5	> 9
CAGE ECA	0.84	< 0.0001	67	95	0.53	0.97	8	120	4	7	> 1
CAGE Paper	0.84	< 0.0001	75	87	0.35	0.97	9	110	3	17	> 1

AUC = Area Under the Curve, NPV = Negative Predictive Value, PPV = Positive Predictive Value, TP = True Positives, TN = True Negatives, FN = False Negatives, FP = False Positives.

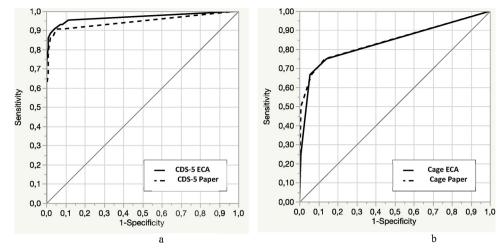


Fig. 2. Receiver operating characteristics curves of the CDS-5 ECA and the CDS-5 paper (fig. 2a) of the CAGE ECA and CAGE paper (Fig. 2b).

respective threshold of 9 for ECA CDS-5 and 1 for ECA CAGE interview. In our study, the optimal threshold value for ECA CDS-5 interview to screen tobacco use disorder was > 9, but the initial validation study found a threshold of 16 (Etter, 2008). This difference could be explained by the fact that the initial validation study compared CDS-5 with the DSM-IV criteria. When we applied our ROC curve with DSM-IV criteria, the optimal threshold increased to a score > 14. The optimal threshold value for ECA CAGE interview to screen alcohol use disorder was > 1; threshold corresponds to the paper CAGE questionnaire threshold (Mayfield et al., 1974).

Interview with the ECA was quick, with a mean duration of 4.4 min. This is important as the shorter, the better regarding acceptability (Beck et al., 2011). An advantage of ECA Jeanne interview compared to paper self-questionnaires is that the collected data can be directly sent to the patient's electronic record and is immediately available to the physician for clinical use as needed. This has considerable time-saving potential over the paper self-questionnaires that needs to be brought by the patient to the physician and will then take time on the physician for interpretation before any action can be programmed. Also, the ECA can make direct interactive contact with patients waiting and does not need the presence of a human aid. This is a potential major facilitator to expand the use of screening tools in primary care population that has been somewhat unsuccessful to date.

Some limitations must be acknowledged. In this study, the physicians asked patients if they would participate in the study before referring them to the research team. All those that declined participation and were not referred to the research team reported lack of time as the main reason. We cannot exclude that for some of those that declined for lack of time; this was due to the rejection of the ECA interview. However, none of those that accepted dropped out from the study and they showed a high level of acceptability for the ECA. Participants were included while attending an outpatient sleep clinic within a hospital. How our results can be generalized to patients in office-based primary care practice is to be determined. It must be considered that the ECA interview was introduced to the patient by a physician and that a research assistant was available during the test to assist the patient

In conclusion, this is the first time that an ECA is used in screening for addiction. This ECA Jeanne was able to conduct a face-to-face interview to screen patients for tobacco or alcohol use disorder. This virtual agent was very acceptable by participants. The ECA Jeanne could be used in waiting rooms to help clinicians to systematically screen their patients for alcohol and tobacco use disorders in order to facilitate access to best-individualized care. Future studies will need to test the ECA for other substance use disorders or behavioral addictions.

Contributors

Marc Auriacombe and Pierre Philip had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses.

Pierre Philip was the overall principal investigator of the study, obtained funding and access to participants. Marc Auriacombe was coinvestigator and obtained funding. Fuschia Serre and Jean-Arthur Micoulaud-Franchi developed the study design and methods. Sarah Moriceau, Stephanie Bioulac, Pierre Philip and Jean-Arthur Micoulaud-Franchi participated in patient recruitment and data collection. Sarah Moriceau, Fuschia Serre and Marc Auriacombe undertook analysis and interpretation of data and the drafting of the manuscript. Etienne de Sevin and Emilien Bonhomme created the Embodied Conversational Agent. Marc Auriacombe, Fuschia Serre, Jean-Arthur Micoulaud-Franchi, Cécile Denis, Mélina Fatseas and Pierre Philip undertook the critical revision of the manuscript for important intellectual content. All authors have reviewed and approved the current version of the manuscript.

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Conflict of interest

No conflict declared.

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