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Maintaining reality: Relational agents for antipsychotic medication adherence

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ABSTRACT

We describe an animated, conversational computer agent designed to promote antipsychotic medication adherence among patients with schizophrenia. In addition to medication adherence, the agent also promotes physical activity and system usage, and includes verbal and nonverbal behavior designed to foster a therapeutic alliance with patients. We discuss special considerations in designing interventions for this patient population, and challenges in developing and evaluating conversational agents in the mental health domain. Results from a pilot evaluation study of the agent indicate that it is accepted and effective.

1. Introduction

Schizophrenia is a relatively common mental illness, resulting in an inability to recognize reality, and impairments in emotional responses, thinking processes and ability to communicate (Birchwood and Jackson, 2001). While the majority of individuals with schizophrenia can be treated with modern antipsychotic medications, the rate of long-term adherence to the medication regimens required to keep these individuals asymptomatic is very poor. Over the course of a year, half of all schizophrenia patients on antipsychotics will stop taking their medications, for a wide variety of reasons, typically resulting in relapse and the return of their symptoms (Weiden and Zygmunt, 1997).

A caring, trusting interpersonal relationship with a health provider (known as a "therapeutic alliance") has been shown to be one of the factors associated with improved medication adherence and positive outcomes for individuals with schizophrenia (Chue, 2006). Family and community social support has also been shown to be an important factor (Randolph, 1998). Unfortunately, many issues associated with the disease make it difficult for patients to seek out and receive the social support they need. Disordered thinking and impairments in emotions and communication make empathizing with these individuals very difficult, and the stigma associated with mental illness can make them socially withdrawn and reluctant to seek help from others.

Relational agents—animated conversational agents designed to establish therapeutic alliance with users over time—represent a potentially powerful technology for delivering health care services to patients with mental illness. Fig. 1 shows the relational agent interface used in our work. The social behavior of these agents may provide many of the benefits of therapeutic alliance and social support these patients need, but without the anxiety, stigma, or demands of face-to-face conversation with other people. The agents present a simplified form of conversation in which patients must be explicit about what they are communicating (including communication of feelings), making them potentially easier and less confusing to use by individuals with schizophrenia compared with human conversation. These interfaces use the easy-to-understand format of face-to-face conversation, making them less intimidating and more accessible to patients with a wide range of computer, reading and health literacy skills. Finally, automated systems in general have the potential to provide information and assistance to patients anytime and anywhere they need it, not just during a brief weekly visit with a clinician. For example, a home-based relational agent has the opportunity to discuss the importance of medication adherence at every dosing time in which a patient expresses reluctance or concerns about staying on their medication.

Of course, there are significant concerns with having individuals with a tenuous grasp on reality conversing with virtual human characters on a regular basis, especially about important topics concerning their health care. These patients may either reject the agent—developing paranoia about the agent itself, its developers, or people the agent may be transmitting its information to—or they may develop a parasocial relationship with the agent, confusing it with a real person in ways that individuals without thinking disorders would be unlikely to do.

In this paper, we describe a home-based relational agent system designed to promote antipsychotic medication adherence for patients with schizophrenia. The system is designed to interact with patients once a day to promote adherence to their prescribed

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Fig. 1. Relational agent interface.

antipsychotic medication regimen, in addition to promoting several forms of social support both by the agent and by others in the user's human social network. We also present the design methodology used and special considerations in designing conversational systems for individuals with schizophrenia, as well as addressing the concerns outlined above.

1.1. Schizophrenia and antipsychotic medication adherence

Schizophrenia, a chronic disease, affects 1% of the population, results in high health care costs, less work productivity, and requires long-term management of symptoms. Symptoms of social isolation, and auditory and visual hallucinations impair the individuals' concentration and subsequently influence their ability to function in society. New antipsychotic drugs can control the symptoms of the disease, permitting the individual to enjoy a fuller, more productive life. However, medication adherence—the degree to which an individual's medication taking behavior is consistent with that prescribed by their psychiatrist (Haynes et al., 1979)—is essential. Many individuals do not follow their prescribed drug regimen due to side effects and other factors. The incidence of medication nonadherence in schizophrenia approaches 50% the first year and 75% the second year (Weiden and Zygmunt, 1997), with ensuing relapse estimated at an annual rate of 42–50% (Csernansky and Schuchart, 2002). Research has shown that psycho-education plus the interpersonal relationship of a health care provider can affect outcomes in a positive way by improving adherence, decreasing hospital re-admissions, and improving symptoms (Kemppainen et al., 2003; Zygmunt et al., 2002).

Nonadherence has adverse effects on symptom management, functioning, and relapse prevention. Several factors have been associated with nonadherence to antipsychotic medications, including sociodemographic factors (male gender and low socioeconomic status) and illness factors (number of prior hospitalizations, illness duration, and history of substance abuse), in addition to factors that are common across all types of medications including patient factors, such as forgetting, provider factors, such as complex medication regimens, and health care system factors, such as medication costs (Dunbar-Jacob et al., 2009). In addition, acceptance and denial coping have been significantly associated with self-reported adherence to mood-stabilizing medications.

1.2. Relational agents for mental health applications

In recent years, interactive computer-based interventions, functioning as an adjunct to treatment, for educating patients, improving medication adherence, motivating health behavior and self-care, and disease monitoring in the home have been developed, with many of these programs demonstrated to be effective (Bickmore and Giorgino, 2006; Coyle et al., 2007; Owen et al., 2002). Narrowly scoped interventions in mental health, including those for screening and medication adherence, may represent promising areas of application for automated systems in general and relational agents in particular.

A basic premise in our work is that human clinicians represent the "gold standard" for interventions in behavioral medicine, even for computer-based interventions. Accordingly, to maximize patient acceptance and intervention effectiveness, it is important for these systems to display many of the same interpersonal and social characteristics as human health professionals. Empathy, caring, and trust demonstrated by health professionals and the ensuing establishment of a "therapeutic alliance" significantly improve outcomes for a wide range of medical interventions. Used as an adjunct with psycho-education and therapy, an animated health advisor that carries out interactive conversations can be developed and successfully evaluated in a medication adherence intervention for persons with schizophrenia (Bickmore et al., 2005b).

In addition, these agents can provide most kinds of social support that people provide each other, and social support is an important factor in positive outcomes in schizophrenia (Randolph, 1998). Relational agents can provide emotional support (e.g., esteem, reassurance of worth, affection, attachment, intimacy), appraisal support (e.g., advice and guidance, information, feedback), autonomy support, social network support (e.g., providing introductions to other people), and some kinds of instrumental support (e.g., making an appointment) (Berscheid and Reis, 1998).

1.3. Overview

In the rest of this article we first briefly review related work before describing the relational agent software platform that we used to implement the system and the design methodology we used. We then present a detailed description of the medication adherence intervention we developed followed by a discussion of a pilot evaluation study we conducted with 20 individuals with schizophrenia.

2. Related work

2.1. Technology in mental health

Coyle et al., provide an excellent review of technology in mental health interventions. The state-of-the-art in fielded interventions includes now common electronic modalities to support therapist-patient communication, such as email, text messaging and video conferencing, in addition to websites containing educational information, and online discussion groups and forums. A significant body of research also exists in automating validated self-report psychological assessment questionnaires, typically resulting in increased accuracy and efficiency of administration. A few systems have been developed to directly provide mental health treatment, either in conjunction with a therapist or stand-alone, using a variety of media and technologies from virtual reality to computer games to biofeedback (Coyle et al., 2007).

2.2. Conversational agents in mental health

Some of the earliest dialogue systems developed in healthcare were designed for psychotherapy applications. The ELIZA system was developed in 1966 to simulate the behavior of a Rogerian psychotherapist, in which the patient and the computer exchanged typed text messages (Weizenbaum, 1966). Although ELIZA was

not intended to be used for actual therapy, similar systems have been proven effective for therapy in which the system is essentially prompting a patient to think aloud and work through his or her own problems (Slack, 2000). In these applications, significant errors in understanding user input or in producing incoherent system output can often be tolerated, as the primary function of the system is just to keep the user engaged in the interaction.

Colby developed an ELIZA-like system that was designed to use Cognitive Behavioral Therapy to treat individuals with depression. In addition to providing typed text counseling with patients, the system provided text-based educational materials about depression (Colby, 1995). While Colby reported that the program was well-accepted by patients, evaluations by other researchers indicate the typed text medium confused some patients and the only comparative evaluation in the literature indicates that the system did not work as well as clinician-administered therapy (Wright, 2004).

Other researchers have identified the promise of using animated conversational agents in mental health interventions, given their ability to display emotion and other nonverbal behavior in the context of a simulated face-to-face conversation (e.g., (Lissetti and Wagner, 2008)).

2.3. Technologies to promote medication adherence

Several studies have examined technology-based reminders to take medications, showing them to have significantly improved medication adherence. Technologies include automated telephone-based systems (Interactive Voice Response) for monitoring and counseling patients (Friedman et al., 1996), video telephone calls (Fulmer et al., 1999), and an automatic pill dispenser integrated with voice activated messages (Winland-Brown and Vallante, 2000).

Beebe et al., evaluated a manual telephone-based intervention to promote medication adherence among 29 outpatients with schizophrenia. The intervention consisted of 3 months of weekly calls from a nurse to help patients solve medication problems such as forgetfulness or lack of knowledge about a medication. Patients receiving the intervention had significantly greater medication adherence compared to a control group (Beebe et al., 2008).

The Medication Advisor is a spoken dialogue system that uses an animated pill to communicate with older adults about their medications. It is designed to provide advice on prescription medications, particularly in situations of complex polypharmacy. The system has yet to be evaluated in a clinical trial (Ferguson et al., 2002).

A number of automated systems to provide generic reminders (including medication taking) have been developed for older adults with mild to moderate cognitive impairment. Perhaps the most sophisticated system developed in this area is Autominder, which incorporates sensing, planning and scheduling capabilities to adapt to the activities of the older adult user (Pollack et al., 2003). Autominder also communicates to its users in natural language, and uses a custom text generation algorithm to generate reminders that are as effective and non-repetitive as possible. However, it does not engage users in an interactive dialogue or have any social aspects to its planned communication.

3. Relational agents

Relational agents are computational artifacts designed to build long-term socio-emotional relationships with users, including trust, rapport and therapeutic alliance, for the purpose of enhancing adherence to treatment. These are typically deployed as computer-animated humanoid agents that can simulate face-to-face conversation with patients so that real-time dialogue, speech, gesture, gaze and other verbal and nonverbal channels can be used both to communicate therapeutic information and to establish and maintain a therapeutic alliance relationship.

Based on our previous work, the typical interface consists of an agent that talks to users with synthetic speech and synchronized nonverbal behavior animation, and users 'talking' by selecting an utterance from a dynamically-updated multiple-choice menu (Fig. 1). We have found that this multiple-choice input modality, compared to unconstrained speech or text input, and allows the system to be readily accepted and usable by individuals with a wide range of computer literacy levels and voice qualities. This input modality also avoids the potentially dangerous effects of misunderstanding ambiguous utterances about medical topics in unconstrained text or speech input by allowing all semantic interpretation to be performed at system design time. The use of multiple-choice input also clearly conveys to users the range of inputs the system can act upon at any point in the conversation. Although this modality does restrict user expressivity, we have found that the benefits of increased accuracy in input understanding outweigh the potential benefits of allowing users to say what they want, in at least some conversational contexts (Bickmore and Schulman, 2007). In designing the input menus, whenever possible we rely on empirical descriptive studies that enumerate the range of variables of interest, such as barriers to changing a particular behavior (e.g., (Hudson et al., 2004)). When we do not have such empirical data available, we use a process of iterative development in which dialogue authors (with input from behavioral scientists) develop an initial range of responses, then modify the list as needed in response to pilot testing.

These agents have been tested in two randomized trials for physical activity promotion, one with young adults (Bickmore et al., 2005a,b) and one with geriatrics patients (Bickmore et al., 2005a), both of which demonstrated effectiveness over standard-of-care control conditions. These trials were conducted on home desktop computers for one-to-two month interventions in which the agent talked with patients daily about their physical activity, negotiated short- and long-term behavioral goal-setting, provided positive reinforcement when goals were met and problem-solving to overcome obstacles when they were not met.

3.1. System architecture

The antipsychotic medication adherence system was built using an existing software framework for developing relational agents. In this architecture, interaction dialogues are specified using a custom scripting language that uses hierarchical transition networks to model dialogue structure, template-based text generation for agent utterances, and a persistent data store (Bickmore, 2003), with most agent nonverbal behavior automatically generated using BEAT (Cassell et al., 2001). The animated agent is capable of a range of nonverbal conversational behavior, including hand gestures, head nods, eye gaze movements, eye brow raises, posture shifts, proxemics, and facial displays of emotion. Although this architecture supports separation of the animation client and the dialogue server for distributed applications, we could not rely on our study participants having an internet connection, so the client and server were run stand-alone on each patient's computer.

As in our earlier work, the model of relationship was primarily stage-based, and was indexed by the number of contacts the agent had with each patient. Relationship building behavior included empathic exchanges, social dialogue, humor, and reciprocal self-disclosure (Bickmore and Picard, 2005).

4. Development methodology and design considerations

Our overall design methodology paralleled that described by Coyle and Doherty in the development of their technology-based mental health intervention (Coyle and Doherty, 2009; Coyle et al.,

2007). We also took an interdisciplinary approach to developing our intervention, as a collaboration between HCI specialists and research-oriented mental health practitioners. Our team comprised computer scientists, experts in psychiatric nursing and medication adherence, a psychiatrist and a biostatistician (Schlenk et al., 2006).

Coyle and Doherty also reported not having direct contact with their user population, complicating their design process. We had the same experience. To conduct user-centered design we leveraged the experience and judgment of the mental health practitioners on our design team to understand how users were likely to react to different design options, with the ultimate direct user feedback only available following the clinical trial. In contrast with Coyle and Doherty's work, however, our system was intended to be used by patients at home, without assistance or interpretation from a clinician, requiring a somewhat higher standard of usability. To meet this challenge, we ensured that the entire use experience was as seamless and straightforward as possible (see Section 5).

Finally, we used many of the same design decision making criteria that Coyle and Doherty used, including designing for engagement (Section 5.4), input from mental health professionals, previous research and mental healthcare theory (Section 4.1), and ethical requirements (Section 4.2) (Coyle and Doherty, 2009). In addition, because we were emulating the behavior of a mental health professional in a limited scope intervention, we made use of a role-playing methodology. We videotaped several sessions in which a psychiatric nurse interventionist conducted a mock daily check in with a patient (played by a member of the research staff) about their medications. The videotapes were transcribed, analyzed and discussed during design meetings, and used as the basis for the relational agent dialogue scripts.

4.1. Special design considerations for patients with schizophrenia

From the literature on psychiatric nursing care for patients with schizophrenia we identified several special considerations that were addressed in our system. Our user population consists of adults at outpatient clinics who meet the DSM IVR criteria for schizophrenia, are taking any antipsychotic medication, and who may or may not be computer literate. Our users are expected to be mostly stable on their medications and asymptomatic, but symptoms (e.g., hallucinations) may occur, for example, if a user stops taking his or her medications for some reason.

4.1.1. Intervention orientation and termination

In psychiatric nursing, special emphasis is made on the orientation (introductory) and termination phases of the nurse-patient relationship (Fortinash and Holoday-Worret, 1999). The orientation phase consists of developing rapport, demonstrating caring and interest in the patient, and establishing a contract for the interactions (roles, times of meetings, etc.). We implemented these behaviors by focusing the first several days of the intervention on rapport building and ensuring that the patient logs in every day, deferring any discussion of schizophrenia or medications until later in the first week (Fig. 2). The agent also spends some time in the first interaction defining her role ("My job is to help you set goals and overcome obstacles... You need to keep in mind that I am just a computer character with limited capability..."). The termination phase involves getting the patient ready for the dissolution of the relationship, and includes strategies such as reducing the duration of the interactions, discussing the patient's and agent's feelings about the termination, and expressing confidence in patients' ability to care for themselves. These strategies were implemented by having the agent begin to remind the patient about the termination several days prior to the termination (Fig. 2), and to periodically talk about feelings regarding the termination and confidence in the patient (e.g., "I will miss you, but I know you will do super on your own.").

4.1.2. Language

The literature on psychiatric nursing also provides a number of general guidelines for communicating with patients with schizophrenia, including: calling the client by name to reinforce reality, using clear and concrete language (avoiding abstraction and metaphor), and focusing on real events or activities to reinforce reality (Fortinash and Holoday-Worret, 1999). To implement these guidelines, we reviewed and modified the language used in our dialogue scripts so that the agent used simple, concrete directions as much as possible, and referred to the user by name whenever feasible and natural.

4.1.3. Agent nonverbal behavior

Psychiatric nursing guidelines also recommend using clear, direct verbal communication; never relying on nonverbal behavior alone to convey meaning (Fortinash and Holoday-Worret, 1999), which we implemented by removing complementary (non-redundant) gestures from the agent's nonverbal repertoire. We also removed the "gaze away" behavior of the agent, in which it briefly glances away from the user, typically at the start of speaking turns. This behavior is used to signal turn-taking in conversation, and our model implements the frequency and timing of gaze shifts at and away from an interlocutor seen in human conversation (Cassell et al., 2001). However, the mental health experts on the team indi-

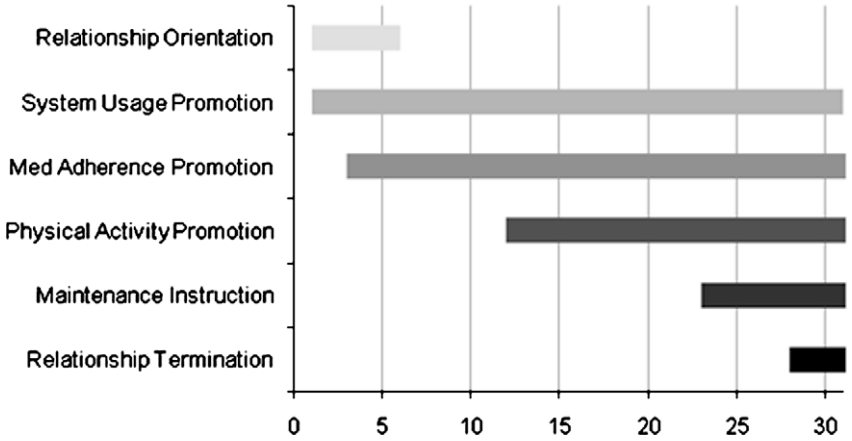

Fig. 2. 31-day intervention schedule.

cated that users may interpret this behavior as a cue for untrustworthiness, and may make them feel uncomfortable.

4.2. Ethical issues concerning relational agents in mental health

There are many ethical issues related to the development of technologies and interventions for individuals with mental health problems. In addition to those outlined by Coyle and Doherty (Coyle et al., 2007), we address two additional ones related to our intervention: the use of anthropomorphic interfaces by mental health patients and the use of automated systems to change user behavior.

4.2.1. Ethical issues with anthropomorphic interfaces in mental health

A concern specifically relevant to users with schizophrenia is that they may become paranoid, feeling that a computer system or its human handlers are surreptitiously monitoring them or intend them harm, and that an anthropomorphic interface may trigger or intensify this reaction. While this is ultimately an empirical question yet to be evaluated, we feel that the use of empathic displays and other behavior by an interface agent designed to establish a therapeutic alliance should serve to reduce the occurrence of this reaction, at least once the user has had a few interactions with the system. Of course, convincing them to get through these first few conversations may take work on the part of their therapist.

A common criticism of anthropomorphic interfaces in general is that users may be deceived into thinking they are interacting with a person, and this deceit is unnecessary since the same positive outcomes could be achieved with a non-anthropomorphic interface. This concern may be particularly important for users who are as impressionable as many mental health patients. Let us address the two parts of this criticism separately. First, in our study, users did not believe they were talking to a person when interacting with the agent. The experimenters never suggested this—the relational agent was introduced as a "cartoon character"—and the agent also periodically reminded subjects that she was "just a computer character with limited capabilities." The contention that the same effects could be achieved with a conventional (non-relational) interface has a significant amount of evidence against it, at least for helping applications such as the one presented here, given the many studies that have shown the importance of working alliance, empathy, and patient-centered communication for maximizing outcomes in long-term helping situations (Bickmore et al., 2005a,b). These behaviors require some elements of an anthropomorphic interface to implement, including at least language and at most some form of body for nonverbal behavior.

Another criticism that has been leveled at anthropomorphic interfaces in general, is that they undermine predictability and consistency, leading to increased user anxiety (Schneiderman, 1995, 1997). We believe that these interfaces can actually *enhance* users' perceptions of predictability and consistency by providing a single interface modality across a wide range of functions, and which leverages pre-existing knowledge and skills that everyone has (i.e., of how to conduct face-to-face conversation) as much as possible. This has been demonstrated in the evaluation of a relational agent interface designed to promote walking among older adults (Bickmore et al., 2005a,b). In this system, urban, mostly minority, older adults with very low levels of computer literacy were able to begin using the system with minimal training, rating the system highly on satisfaction and ease of use at the end of 2 months, and walking significantly more compared to a control group.

We would also argue that helping and psychotherapeutic applications such as the one presented here require the use of natural language in order to understand as much as possible about users' cognitions, feelings and behavior and to deliver appropriately tailored interventions, and that as soon as an interface uses natural language in any form (including text) it is, in effect, an anthropomorphic interface subject to all of the criticisms described above. One cannot present an utterance to a user (even brief text messages) without them making judgments about the personality, interpersonal attitude, relational stance and emotional state of the agent delivering the message (see Reeves & Nass for several examples (Reeves and Nass, 1996)). Thus it is impossible to build a non-trivial system for this kind of application that is *not* anthropomorphic.

4.2.2. The ethics of changing health behavior

The ethics of deploying technology to change user behavior ('programming the user') is another area of concern, especially given that our study population is often considered to be in need of special protection. We argue that the issues here are no different than those faced by a human helper who is interested in changing a client's health behavior (O'Connell and Price, 1983). The system can be said to be respecting the user's autonomy as long as: (1) the user is free to decide whether to use the system or not; (2) the user is free to decide whether to follow the system's recommendations or not; (3) the role of the system is primarily to provide information to enable the user to make informed choices; and (4) appropriate amounts of persuasion are used by the system only in cases in which the user is clearly making an unhealthy decision. Regarding this last point, while it is true that human helpers may be more understanding and adaptive than an agent (for now at least), the agent follows rules that are open to inspection and validation, and follows them in a consistent and unbiased manner, something that cannot always be said of human helpers. From a utilitarian ethical framework at least, we feel that the use of relational agents in this kind of intervention is well justified, given the health benefits of keeping individuals with schizophrenia on their antipsychotic medications.

5. System design

The medication adherence system runs on a dedicated-use laptop computer as a stand-alone application, and is designed for a 1-month intervention in which users conduct a daily 10-min interaction with the agent, named "Laura".

In addition to medication adherence, the agent promotes brisk walking as physical activity. Several studies have indicated a positive association between exercise and decreased mental health symptoms, including decreases in positive and negative symptoms and increases in quality of life for individuals with schizophrenia (Acil et al., 2008; Callaghan, 2004).

The system is designed to be configured by the study nurse for each user at the time she delivers the computer. Configuration parameters are entered via a form, and consist of: the user's given name; sex; name of the primary antipsychotic medication to track (and instructions for how the speech synthesizer is to pronounce it); prescribed dose (number of pills per day); the time of day the user is likely to use the system (scheduled to coincide with a time they should be taking their antipsychotic); whether patient is able to engage in brisk walking as a form of physical activity; and the name and social relation of a friend or family member who can provide instrumental support to the user if needed.

The relational agent system is designed to present a seamless experience to the user. Each day the user has to power on their

computer, but the agent software starts automatically, so they did not need to deal with the operating system and did not need to interact with the computer again except to select dialogue utterances from the multiple-choice menu. At the end of the interaction the computer automatically shuts itself off.

5.1. Daily interaction

Fig. 3 shows the transcript for a typical daily interaction. A typical conversation lasts 7.5 min and includes: (1) the agent walking on screen and greeting the patient; (2) conducting social and empathic chat; (3) assessing the patient's behavior since the last conversation; (4) providing feedback on this behavior (positive reinforcement or simple problem solving); (5) providing tips or relevant educational material (e.g., managing side effects, coping, etc.); (6) setting new behavioral goals for the patient to work towards before the next conversation; and (7) a farewell exchange, after which the agent walks off the screen. After this, a tip for the day is displayed as a text message, and a few self-report survey questions assessing the patient's attitude towards the agent may be automatically administered.

5.2. Medication adherence promotion

The agent tracks each user's medication taking behavior for a single antipsychotic taken by mouth in pill or capsule form based on self-report, but she also reminds patients to take all of their other medications as prescribed. Each day, the agent first asks for a self report of medication taking behavior, provides feedback on this behavior and reminds users of their goal behavior (prescription). Feedback on medication taking is provided with the aid of self-monitoring charts that show patients their behavior over time (Fig. 4). While we have not tested the ability of our target population to use these charts, past studies have shown them to be one of

Greeting & Social Chat

1. A: Hi, John. Great to see you.
2. U: Hi Laura.
3. A: How is it going?
4. U: Great! How are you?
5. A: Fine, thanks. Great job talking to me every day. I really appreciate it.
6. U: Thanks!

Prescription Change Check

7. A: John, has your prescription for Risperdal changed since yesterday?
8. U: No, my prescription has not changed.

Self-report Medication Assessment

9. A: OK. So, let us talk about how you have been doing with your Risperdal. Did you take your dose of Risperdal yet today?
10. U: Yes, I took it.
11. A: Way to go. That is terrific. Please enter the number of pills you took today.
12. U: I took ONE pill.
13. A: Wow. Great job on the Risperdal. We make a great team.

Self-report Exercise Assessment

14. A: So, let us talk about how you did on your walking. The last time we talked, you said you would walk for at least 20 minutes. How many minutes did you walk yesterday?
15. U: I took at 25 minute walk.
16. A: Looks like you met your exercise goals, that's great. So, can you go for a 25 minute walk before we talk again?
17. U: Sure.
18. A: That is awesome. We're doing some great work together.

Review Self-Monitoring Charts

19. So, let us review how you are doing.
20. U: OK
    Displays charts such as Figure 4.
21. A: Here is that picture of your progress. As you can see on the top chart, you are doing a terrific job talking to me every day. The middle chart shows an awesome job on the Risperdal. And finally, as you can see on the bottom chart, a perfect job on the exercise.
22. U: OK, I'm finished looking at this.

Social Chat & Self-Reward Talk

23. A: So, have you seen any good movies recently?
24. U: Nope.
25. A: That is too bad. You should treat yourself when you reach your exercise goals.
26. U: OK.

Session-Specific Questions

27. A: So, I would like to talk to you about a sensitive topic. You don't need to talk about it if you don't want to.
28. U: OK.
29. A: You know, drinking alcohol or taking illegal drugs can cause serious health problems, especially with the medications you are on.
30. U: Yes, I know.
31. A: Do you drink alcoholic beverages?
32. U: No, I don't drink at all.
33. A: Do you use illegal drugs?
34. U: No, I don't.
35. A: Thanks for sharing that with me. I know this can be difficult to talk about.

Closing

36. A: So, John, when can we chat again?
37. U: Tomorrow.
38. A: Wonderful. I am looking forward to it. So, let us summarize what you said you would do before we chat again.
39. U: OK.
40. A: You said you would go for a walk that was at least 25 minutes long. You also said that you would take your 1 daily dose of Risperdal as prescribed, and finally you said that you would talk to me again tomorrow.
41. U: Yes, that is correct.
42. A: Great. Take care John, I will talk to you tomorrow. Have a great day. Goodbye.
43. U: Bye Laura.

Fig. 3. Sample transcript of daily conversation.

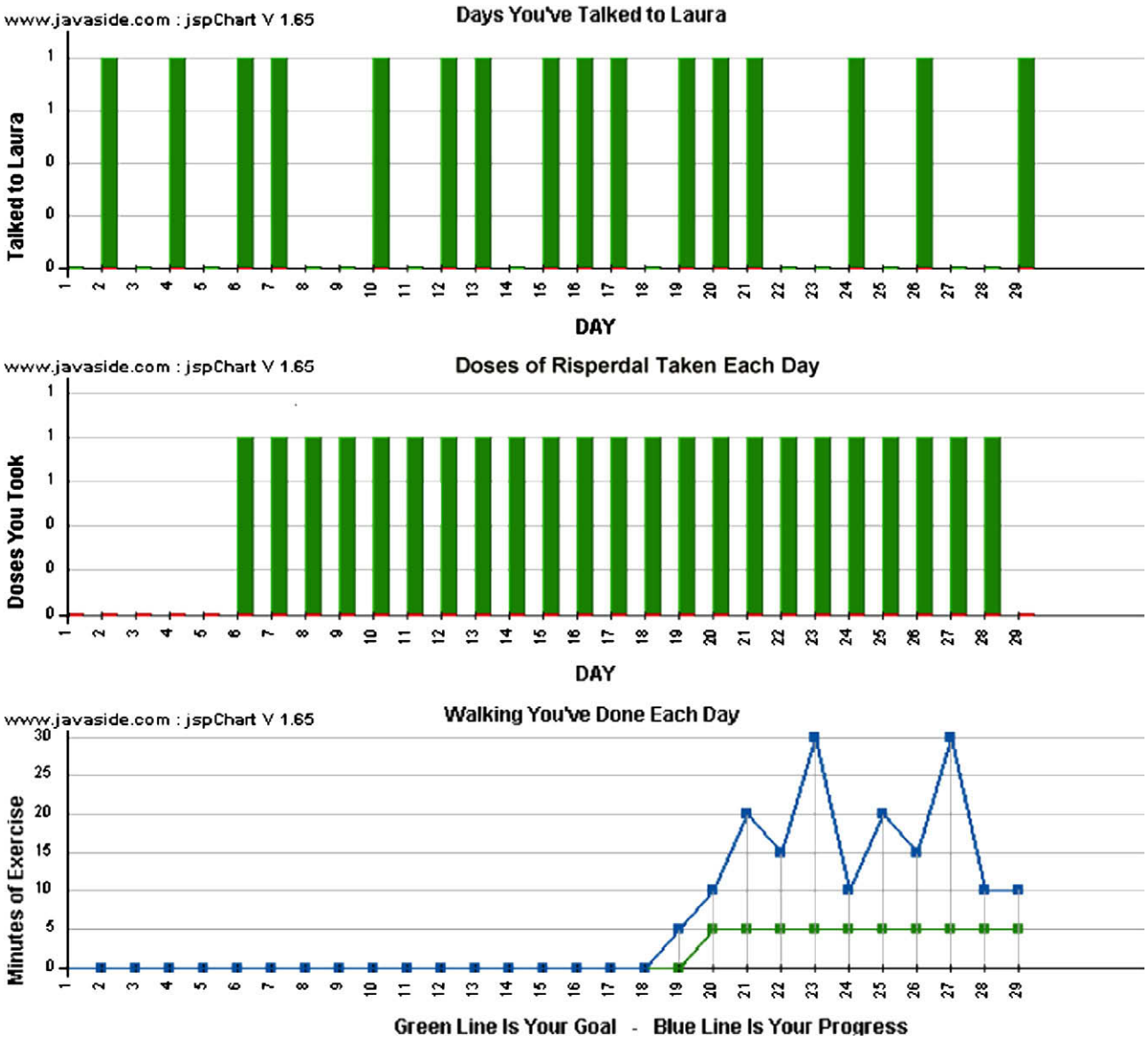

Fig. 4. Self-Monitoring charts used in the intervention top chart shows system use, middle chart shows medication adherence, bottom chart shows walking adherence.

the most useful and motivating components of a relational-agent-based health behavior change intervention (Bickmore, 2003).

There are several other unique aspects of the medication adherence dialogue used by the agent. Since the system is not networked to a central server, it asks the patient whether or not their prescription has changed at the start of each conversation, so that the agent does not promote an incorrect regimen. The system also keeps track of refill schedules and reminds patients to get refills before they run out of their tracked medication (including simple problem solving, such as recommending that a friend drive them to the pharmacy if they do not have transportation). Finally, the system uses a form of "direct observation" – a technique used in human medication adherence interventions in which a health provider watches while the patient takes their medication. To accomplish this, the patient is asked to conduct their chats with the agent at one of their prescribed medication taking times. When the agent asks the patient about their medication taking behavior it asks whether they have taken their dose for the current time of day yet (e.g., "Have you taken you evening Risperdal yet today?"). If the patient has not, the agent asks them to go ahead and take it while it waits.

Towards the end of the month, the agent begins instructing patients in techniques for self-maintenance. It starts by asking patients to obtain a multi-compartment pill box and calendar for self monitoring, then asking patients about this during every conversation until they do so. Once the patient has obtained these, the agent reviews techniques for self monitoring at periodic intervals until the end of the 31-day intervention period.

5.3. Physical activity promotion

Our walking intervention follows the same format as earlier walking interventions we have implemented with college students and older adults (Bickmore et al., 2005a,b; Bickmore and Picard, 2005). Beginning on day 11 of the intervention, the topic of physical activity is introduced, and the user is asked to try to go for a daily walk of any duration. Following this, the user's behavior is gradually "shaped" to walk 30 min a day by the end of the study, with behavior and goal tracking based on self-reported minutes of brisk walking. Common barriers to physical activity can be endorsed by a user, leading the agent to provide tips on how to overcome those barriers.

5.4. Maintaining user engagement: system use promotion

Although a dose–response relationship has yet to be established for automated behavior change interventions, it is our belief that the more contact users have with the relational agent system (up to once per day) the better their medication adherence and outcomes. Working from this assumption, we have designed several features into the system to motivate users to continue using the system over the course of the 31-day intervention.

First, the relational behavior the agent uses to build therapeutic alliance with users is explicitly targeted at maintaining both longitudinal engagement to the intervention and adherence to the agent's recommendations. In our system, relational behaviors included empathy (expressing verbal and nonverbal concern for a negative state of the user), social dialogue, appropriate humor, reciprocal self-disclosure, use of inclusive language ("we"), using close forms of address (calling the user by name), and nonverbal immediacy behavior (close proximity, more gazing at the user, more facial and gestural animation) (Bickmore and Picard, 2005).

Second, variability in dialogue content is provided at various levels of abstraction, from the interaction agenda (different educational and social topics each day) down to specific utterances (e.g., greeting variants selected at random each day). In a prior study, Bickmore demonstrated that variability alone was enough to boost adherence to a behavior change regimen (Bickmore and Schulman, 2009).

Finally, we treat system use as a first-class behavior change variable, promoted in the same way as medication adherence and exercise. From the very first interaction, the agent reminds the user of the importance of continuing use of the system every day, provides feedback on system use adherence (via dialogue and self-monitoring charts), helps the user problem solve barriers to system use (e.g., forgetting or not having the time), and obtains a behavioral commitment from the user at the end of every conversation to talk to the agent again at a specific time in the future.

5.5. Changing multiple behaviors concurrently

Simultaneous intervention on multiple health behaviors has been shown to be effective for many combinations of behaviors (Noar et al., 2008; Prochaska, 2008), yet few automated interventions have been designed to address this issue. Our approach to intervening on system use, medication adherence and exercise involves:

- Treating each target behavior in a similar manner, from theoretical orientation (behavioral reinforcement with social-cognitive "problem solving" to overcome barriers and build self-efficacy) to software implementation (dialogue modules for each behavior partitioned into introduction, behavior assessment, behavior feedback, and behavior commitment).
- Providing the user with an integrated visual self-monitoring chart for all behaviors (Fig. 4).
- Providing integrated behavior feedback and commitment summary statements in dialogue (utterances 21 and 40 in Fig. 3).
- Staggering the introduction of each behavior to give users a chance to get started on one behavior before the next one is introduced (Fig. 2).

5.6. Seven domains of patient education

We designed seven dialogue-based education modules for the intervention using a theoretical basis of learning principles to promote adherence. These modules are: understanding schizophrenia, managing side effects of medication, managing symptoms, using cues to schedule medication taking, overcoming setbacks, selecting appropriate coping, and finding social support. Each of these modules was presented to users twice during the 31-day intervention.

Some educational information is provided contingent upon potentially confidential and sensitive information, such as whether the patient drinks alcohol or not (such as turns 27–35 in Fig. 3). This information is not reported to the patient's clinicians or study staff, but used only to help tailor the intervention.

5.7. Provision of social support

As described in the introduction, social support is an important factor associated with positive health outcomes in general and with improved medication adherence in particular for individuals with schizophrenia. We sought to promote social support by having the agent suggest that a particular individual in the user's social network provide them with instrumental support. At enrollment time, the study nurse asks the patient for the given name of and relationship to someone who can help them with their medications. The agent then recommends that the user enlist the aid of this helper when certain conditions arise. Examples include asking the helper to remind the user to take their medications at a particular time, or to fill their prescription if they keep forgetting ("Do you think your sister Sally could remind you?"), or asking the user if the helper can drive them to the pharmacy if they indicate they are having trouble getting their prescription filled because of transportation problems.

5.8. Managing communication with a stand-alone system

We could not assume that our user population had Internet connectivity, and it was not practical to provide connectivity just for the purpose of a limited-duration intervention. However, there were several situations in which we wanted to alert the study staff that an important condition has occurred during a conversation between the agent and the user (Table 1). To address this, we added a mode in which the agent would ask the user if they could make a phone call immediately and, if the user said they could, the appropriate phone number and a brief text message (e.g., "Tell the study nurse that your prescription has changed.") were displayed on the screen until the user indicated that they had completed the call. If the user indicates that they cannot make a phone call, the agent asks them to write the information down and call at their earliest convenience.

6. Evaluation

We conducted a 31-day quasi-experimental pilot study to evaluate the medication adherence system using patients from a mental health outpatient clinic. Eligibility requirements for study participants included: meeting the DSM IVR criteria for Schizophrenia, being 18–60 years old, being on any antipsychotic medication, and having two or more episodes of nonadherence in the 72 h prior to recruitment.

Table 1
Conditions in which the system prompts user to call study nurse.

User prescription has changed
User is feeling down and thinking of hurting themselves or someone else
User has stopped taking their antipsychotic for three consecutive days
User plans to be away from their computer for more than 2 days
User has a barrier to medication adherence that the agent cannot assist with
End of intervention
Internal technical error in the system

The study was approved by the University of Pittsburgh Institutional Review Board. Several special procedures were used given the patient population, including referral of a patient to their clinical therapist if their symptoms worsened or they became significantly over- or under-adherent to their antipsychotic medication regimen. A psychiatric nurse maintained regular contact with participants during the study so that adverse events could be reported and/or dealt with.

6.1. Participants

The 20 participants enrolled in the study were 19–58 years old ($M = 43$, SD = 13), 67% female, all single (83% never married), 78% African American, with an average of 13 years of formal education (83% graduated from high school, 6% graduated from a 4-year college), and 89% unemployed.

6.2. Measures

Measures were gathered automatically and downloaded from each participant's computer at the end of the intervention. Measures included.

6.2.1. System use

Measured as the number of days the participant started a dialogue with the agent.

6.2.2. Medication adherence

Towards the start of each conversation, users were asked how many pills they had taken on every day since their last conversation with the agent. They were provided with an option to select if they did not remember their dosing on a given day.

6.2.3. Physical activity

Once the physical activity intervention was underway, users were asked how many minutes of physical activity they had performed on every day since their last conversation with the agent.

6.2.4. Satisfaction

Participants were presented with a text-based, scale self-report item on most days following their conversation with the agent, assessing different dimensions of their satisfaction with the system and attitude towards the agent (Table 2).

All user actions in the system were also logged to provide information about how often different features were used (e.g., direct observation).

6.3. Procedure

Study participants were provided with a dedicated-use laptop computer for the 31 days of the intervention. Following enrollment, the study nurse visited each participant's home. After setting up the laptop and configuring the software, she explained how to start the computer and use the mouse, then assisted the participant in completing an initial training interaction with the agent. After this, the computer was left in the participant's home for the 31 days of the intervention, at which time the nurse returned, debriefed the participant and collected the computer.

6.4. Results

Sixteen participants (80%) completed the study: four withdrew prior to the start of the intervention, and one participant's data file was corrupt, for a total of 15 participant log files analyzed.

Of the 16 who began the intervention, one participant expressed concern that the program was relaying their personal information to others, but the study nurse was able to re-orient them to continue the intervention. Another participant developed paranoia and stopped using the agent after a few days and could not be convinced to continue.

6.4.1. System use

System logs indicated that participants talked to the agent an average of 65.8% of the available days, with nine of the participants talking to the agent at least 25 times during the 31 day intervention (Fig. 5). The average session lasted 7.5 min.

6.4.2. Medication adherence

The agent asked participants to self-report their medication doses every day, beginning on day four. Prior to obtaining medication adherence, the agent would first ask if the participant has talked to or visited with their psychiatrist and if their medication prescription has changed. If a prescription changed, the agent would cease conversation on medication adherence and instruct the patient to contact study staff, in order to reset and verify medication dose values within the system, prior to continuing the intervention. This situation did not occur during the 31-day intervention period for any participant in the study.

Dose adherence is defined as the number of medication doses taken during the monitoring period, divided by the number of prescribed doses during the monitoring period. Over-adherence is penalized, and a wrap-around percentage is reported, for example 110% adherence is reported as 90% adherence. Two participants interacted with the system less than four days, and thus did not

Table 2
Satisfaction measures. Means are normalized (means of per-participant means).

Question	Anchor 1	Anchor 5	Number of participants reporting	Max (average) number of times assessed	Mean (SD)
How much do you feel that Laura **cares** about you?	Not at all	Very much	13	5 (3.31)	4.24 (1.08)
How much would you like to **continue** working with Laura?	Not at all	Very much	8	1 (1)	4.38 (1.06)
How **easy** is talking with Laura?	Very difficult	Very easy	14	5 (3.5)	4.28 (0.56)
How much do you **like** Laura?	Not at all	Very much	13	8 (5.92)	4.30 (1.16)
How would you characterize your **relationship** with Laura?	Complete stranger	Close friend	14	5 (3.57)	3.23 (1.22)
How **satisfied** are you with Laura?	Not at all	Very much	12	5 (4.00)	4.49 (0.65)
How much do you **trust** Laura?	Not at all	Very much	13	5 (3.54)	4.44 (0.66)

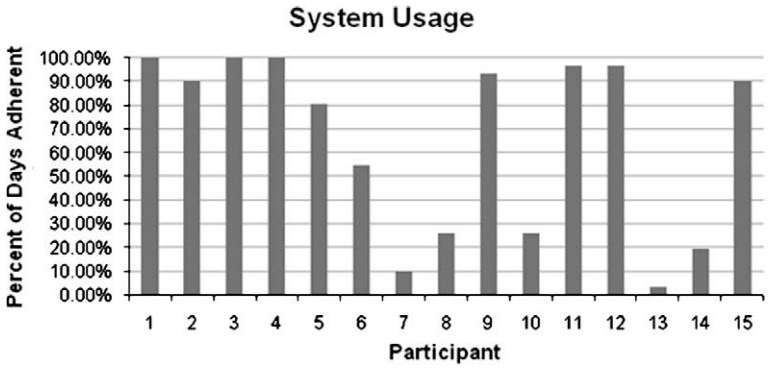

Fig. 5. System use per study participant.

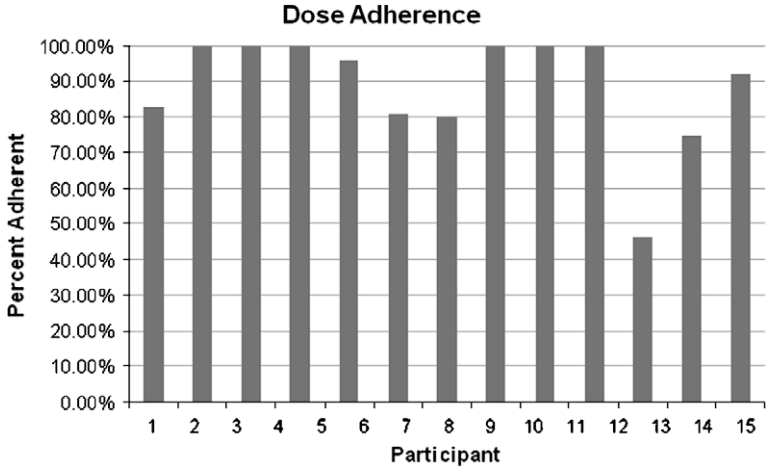

Fig. 6. Self-report medication adherence by dose, per participant.

receive the medication intervention. The remaining 13 participants are shown in Fig. 6. Self-reported participant dose adherence ranged from 46% to 100%, $M = 89\%$ (SD = 16%).

Day adherence, defined as the number of days that the correct number of medication doses were taken, divided by the number of days monitored, is shown in Fig. 7. The percentage of days with overdosing, underdosing and holidays (no dose) are also reported. Self-reported day adherence ranged from 8% to 100%, $M = 85\%$ (SD = 26%).

When participants reported taking an incorrect dose, the agent would prompt for reasons why the medication was taken incorrectly. Participants reported that they forgot to take the medication (once), they did not need the medication (twice), they do not like taking their medication (twice), they forgot or did not have time to get a refill (seven times), or that there was some other reason not in our list of specific responses (29 times). Ten participants reported side-effects from their medications, including drowsiness (five participants), dry mouth (three participants), and weight gain (two participants). Eight participants reported experiencing continued symptoms of schizophrenia, including trouble sleeping (three participants, seven occasions), hearing voices (four participants, nine occasions), hallucinating (two participants, two occasions) and feeling asocial (one participant, one occasion).

Direct observation was used by the agent a total of four times, for three participants. On one occasion, the system prompted a participant to call the research staff, after reporting an unknown obstacle to taking his medication.

6.4.3. Physical activity adherence

Physical activity promotion was discussed during the last 20 days of the intervention. Ten participants interacted with the system during these days, and they met their walking goals on average 84% of the time (Fig. 8). To measure physical activity satisfaction, the agent asking the question, "*Have you been enjoying your walking*?" (1 = not at all to 5 = very much), up to three times during the intervention. Participants were assessed on average 2.2 times and reported high levels of enjoyment related to their walking behavior ($M = 4.5$, SD = 0.31).

6.4.4. Satisfaction

Satisfaction measures were automatically assessed several times throughout the study, with participants receiving a text questionnaire at the end of each interaction assessing at least one measure, and a questionnaire at the end of the study assessing all measures. As shown in Table 2, participants reported high levels of liking, trust, and satisfaction with the agent. Variance among repeated ratings was low, with the exception of measures relating to system ease of use, and the relationship between the agent and participant. The question "How easy is talking with Laura?" produced a high amount of variation in early measurements, with universally high ratings at the end. Ease of use ratings were not correlated with system use $r = -.057$; participants who gave initial low ratings were as likely to use the system compared to those who gave initial high ratings. Relationship with the agent, assessed by "How would you characterized your relationship with Laura?" produced a high amount of variance among repeated

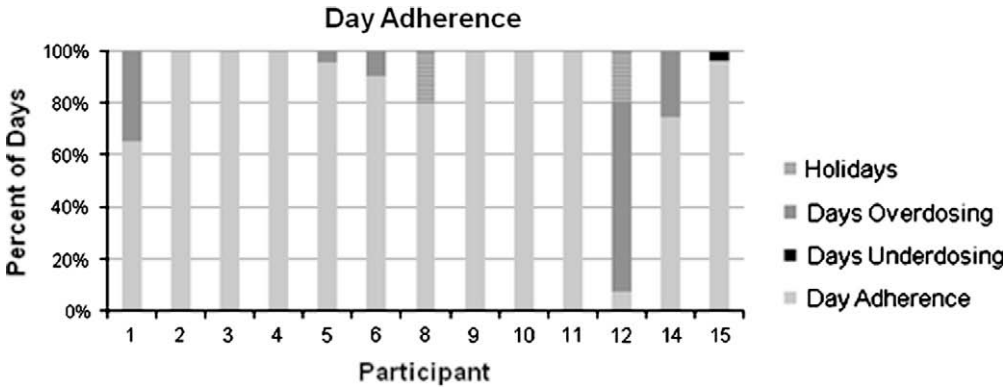

Fig. 7. Self-report medication adherence by day, per participant.

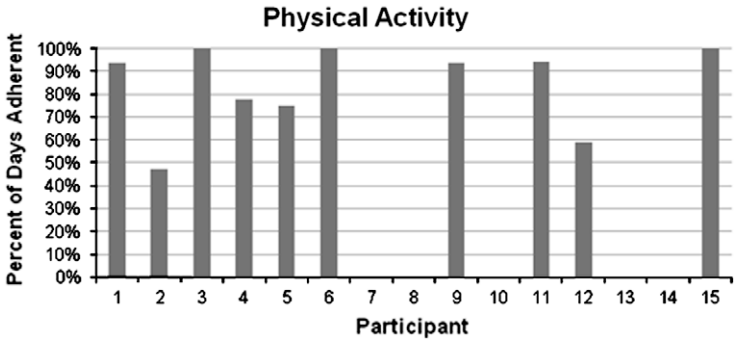

Fig. 8. Self-report physical activity adherence, per study participant.

measures, and was significantly correlated with system use, $r = .642$, $p < .05$. Participants that interacted with the agent for the entire duration of the study gave higher ratings than those that did not.

6.5. Discussion

The overall acceptance and use of the system was relatively high, with only one participant refusing to use the system, one who had to be re-oriented to it, and 15 who completed the intervention. Of those who completed, about two-thirds conducted at least half of the possible conversations with the agent. Ratings of satisfaction (4.5 out of 5.0), ease of use (4.3 out of 5.0) and desire to continue using the system (4.4 out of 5.0) were all very high as well. Together, these results indicate that relational agents represent a viable and promising medium for communicating with and counseling patients with schizophrenia.

Self-reported attitudes towards the agent were positive, with trust (4.4 out of 5.0) and liking (4.3 out of 5.0) of the agent fairly high. Characterization of the relationship with the agent ranged from "friend" or "close friend" at the end of the month for eight of the 15 users, "acquaintance" for three users, "someone I don't know very well" for two users, and "complete stranger" for one user (one user did not log in enough to receive the survey). The strong correlation between this measure and system use provides some validation of the importance of therapeutic alliance in maintaining engagement with an automated intervention for this population.

Self-reported medication and physical activity adherence were also very high (84–89%, across all measures). Of course, there are known problems with measuring medication adherence through self-report. However, having the agent ask patients daily about their dosing is most similar to the diary-based methods of measuring adherence, which has been found to be the most reliable of the non-electronic methods available (Garber et al., 2004).

Limitations of this study include the lack of a comparison group, the very small sample and short duration, and lack of an objective measure of medication adherence (electronic pill bottle caps or urine tests (Zygmunt et al., 2002)).

7. Conclusion and future work

To our knowledge, this is the first embodied conversational agent used to promote medication adherence, and the first such system used with patients with schizophrenia. On its face, having individuals with schizophrenia interact with computer-animated characters may not seem like a good idea. However, only one study participant reacted negatively to the agent and, according to self report measures, most participants liked the agent and the experience.

Relative to other user populations, individuals with schizophrenia do require closer monitoring and the availability of a mental health specialist to orient new users to the system and assist and re-orient them should negative reactions or other problems arise. More research needs to be done on the best way to introduce this technology to minimize early negative reactions, perhaps by providing a series of brief demonstrations to users over a period of time before the system is installed in their home. Exploring viable methods of electronic connectivity of the system to a central server (e.g., via phone link) would enable the system to more rapidly and reliably communicate emergent conditions to the user's care providers and enable the providers to remotely re-configure the system (e.g., if the user's prescription changes).

The multiple-choice input modality combined with template-based text generation provides a simplified form of conversation

that may not provide the degree of tailoring required for the needs of any particular patient. This is due partly to the constrained input modality, but mostly due to lack of dialogue content that can take all tailoring parameters of interest into account. There are several thousand utterances the agent can make, most of which are tailorable on one or more variables, but this is still a very long way from the generative power and specificity of human language generation. However, it is significantly more tailoring than patients would find in a health education pamphlet or book, and more than most "tailored print" systems which typically merge large blocks of prepared text-based on a few patient characteristics (Noar et al., 2007).

The strong correlation between perceived relationship with the agent and system use indicates the importance of establishing a therapeutic alliance in automated mental health interventions. Overall, these results indicate that relational agents may be an important technology to use for certain kinds of mental health interventions such as medication adherence.

7.1. Future work

This project represents an initial foray into a very large, complex, and important research space that is even more deeply concerned with the psychology of human–computer interaction than more conventional interfaces and user populations, and it raises many challenging questions and issues that need to be addressed.

Some of the open questions include:

- Are human clinicians really the "gold standard" for computerized interventions? Can computers do things in a fundamentally different way that would be better?
- Although many studies have shown that computers reduce social desirability effects when communicating about potentially stigmatizing conditions and behaviors, do anthropomorphic interfaces eliminate this advantage?
- What can be done to reduce the risk of anxiety and paranoia by individuals with schizophrenia to relational agents and automated interventions in general? Would specific types of characters or alternative interfaces (video, speech only, or text only) improve acceptance by this population?
- Does the simplified form of conversation make the agent interface more approachable and usable by individuals with schizophrenia, compared to conventional user interfaces or unconstrained text or speech dialogue systems, as we have found with individuals with low health, reading and computer literacy (Bickmore et al., 2005a,b, 2009)?
- Are there additional ethical issues that need to be considered for this population, such as special considerations regarding the automated messaging of helpers or clinicians?
- Are there longer term issues of mental health patients using relational agents, such as deleterious effects of developing parasocial relationships with agents, in which they actual confuse the agents with real people?

Much work remains, and there are many fruitful areas for further research.

Although we made many design decisions based on our understanding of the needs of individuals with schizophrenia—such as the elimination of gaze-away behavior by the agent—the evaluation study did not provide information on which of these decisions were correct ones. There are also many interface elements in addition to the agent—such as the self-monitoring charts—that may not be usable by this population. Several follow up studies manipulating each of these interface elements independently are required to determine which ones are effective and which require further refinement.

Obviously, the complexity of the dialogue scripts could be greatly increased so that the intervention is even more tailored to individual patients, and a more methodical exploration of the patient input menu options could be performed to increase patients' ability to say what they want in conversations with the agent.

Given that impairments in emotions is a symptom of schizophrenia, self-report in dialogue may not be best method for identifying the emotional state of patients. Much research on affect sensing has been performed in the last decade using vision, speech, skin conductance, and other modalities that could be used to improve the ability of the agent to determine negative emotional states in patients so that, for example, empathic feedback could be more accurate.

In the area of medication adherence promotion, the agent could be even more effective if it were objectively aware of patient medication taking behavior by incorporating sensor inputs that alerted it when a pill bottle or box was opened. Deploying the agent on a mobile platform (as we have done with exercise promotion (Bickmore and Mauer, 2009)) would enable it to alert patients and provide counseling and advice wherever and whenever it was needed. The ultimate form factor may be a mobile robot that is able to find the patient at medication time, dispense the medication, and motivate the patient to take it, using the increased social "presence" of the physical robot to maximize adherence (Kidd and Breazeal, 2004).

Finally, rigorous, randomized clinical trials are required to demonstrate the efficacy of these agents for medication adherence and patient well-being.

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