

Go up in smoke!

A proof of concept study on tobacco craving in a virtual reality environment

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Abstract

Background: Smoking is the most preventable cause of death worldwide. People with a psychiatric illness (including other dependency issues) and intellectual disabilities are disproportionately highly affected with smoking prevalence and therefore, form the vulnerable subgroup of tobacco dependent patients. Craving plays an important role in addiction, it makes quitting smoking more difficult and the risk of relapse increases. Looking at the absence of interventions and prevention programs designed for the vulnerable subgroup of tobacco dependent patients, there is a crucial public health issue. A potentially effective tool for a new treatment, which focuses on complex cue environments, is Virtual Reality (VR).

Goal: This present study is a first step towards further development of a suitable treatment for the vulnerable subgroup of tobacco dependent patients. The aim of this study is to investigate whether craving can be generated with the use of a VR environment where smoking cues are present.

Method: A proof of concept study with 23 participants at three Dutch Hospitals, focused on increasing craving using a VR environment with smoke-related cues. Participants had to explore and walk in the VR environment with smoke-related cues. To measure craving the QSU-Brief and VAS were used at baseline, during and after the VR usage.

Results: Results showed significant increased levels of craving after the cue-reactivity environment. Furthermore, there was a significant interaction effect of age and craving over time. There was no significant interaction effect on the level of nicotine dependency and gender on the increase of craving over time.

Discussion: Present study worked on a unique research investigating the possibilities of VR in a group that could potentially benefit greatly on theoretical grounds, but which has not been involved in research so far. Validated instruments and a combination of qualitative and quantitative methods have been used to maximize the learning from this small pilot. The main limitations of the study was that a confounder effect cannot be excluded, there is a possibility that another variable had influenced the increase of craving over time. Furthermore, a control group was missing which does not allow the study to assume with certainty that the increased levels of craving are a result of the VR environment with smoke-related cues. Also, the sample size was too small, potential social desirability bias and self-selection bias.

Conclusion: This study shows that using a VR environment can elicit craving in tobacco, in moderate to severe tobacco dependent patients with a psychiatric illness (including other dependency issues) and/or intellectual disability. Further studies need to explore whether the VR environment is also helpful to train patients in these groups to cope with or to reduce craving, and thus whether it can be used in treatment of tobacco use disorders.

1. Introduction

In the Netherlands a smoking ban applies at workplaces, in public buildings and areas (Rijksoverheid, 2019). This means that it is forbidden to smoke in for example hospitals, concert halls and airports. Furthermore, since 2014 a smoking ban also applies for hotels, restaurants and bars. In this way, the Dutch government is working towards a smoking free environment. Though smoking rates have declined over the last few decades (Ng, et al., 2014), approximately 19.2% of female and 25.7% of male adults in the Netherlands still smoke (Rijksinstituut voor Volksgezondheid en Milieu, 2018). Also, 3.3% of the population are considered as a heavy smoker: they smoke 20 or more cigarettes per day. 32.6% of the people between the age of 20-24 smoke. Most people who are addicted are in the age category of 20-30 years old (Rijksinstituut voor Volksgezondheid en Milieu, 2018). Highly educated people smoke less often than middle and lower educated people (Trimbos, 2018). In addition, the smoking rates are even higher in specific groups such as individuals with psychiatric illnesses (including other dependency issues) (Prochaska, Das & Young-Wolff, 2017) and intellectual disabilities (VanDerNagel, et al., 2017).

Studies from Prochaska, Das and Young-Wolff (2017) and R  ther, et al. (2014) show that people with a mental illness are disproportionately high affected with smoking prevalence. Prochaska and colleagues (2017) showed that people with a mental illness account for more than 200.000 of the 520.000 tobacco-attributable deaths in the United States. Furthermore, people with a mental illness, who also smoke, die 25 years prematurely on average. The study from Lasser, Boyd, Woolhandler, Himmelstein, McCormick and Bor (2000) supports these results. Lasser and colleagues (2000), conclude that persons with a mental illness are about twice as likely to smoke as other persons.

People with an intellectual disability form a risk group for addiction (VanDerNagel, et al., 2017). This can be explained due to specific characteristics (inadequate coping skills, poor executive functioning, including working memory) and social factors (vulnerable to peer pressure) (Slayter, 2008). VanDerNagel and colleagues (2017) did a research on substance use in individuals with a mild to borderline intellectual disability in the Netherlands. Their research showed that currently 61.6% of the respondents were using tobacco. These prevalence numbers are much higher than the prevalence numbers of people without mild to borderline intellectual disabilities.

Smoking is the most preventable cause of death worldwide (Vleeming, Rambali & Opperhuizen, 2002). In addition, it is one of the major lifestyle factors influencing the health

of human beings (Yanbaeva, Dentener, Creutzberg, Wesseling & Wouters, 2007). In the Netherlands, smoking is still the main cause of disease and death. Of the total burden of disease, 9.4% comes from smoking (Rijksinstituut voor Volksgezondheid en Milieu, 2018). Smoking causes diseases such as cancer, cardiovascular diseases, respiratory diseases, diabetes, inflammation, Alzheimer's, cataracts and blindness (US Department of Health and Human Services, 2014).

However, due to the addictive effect, it is difficult for smokers to quit. This usually results from the fact that the majority of stoppers return to their old pattern. The average success rate in stopping smoking is less than 4% (Hughes, Keely & Naud, 2004). Though treatment programs to help people stop smoking, such as counselling and nicotine replacement therapy are available, they are only successful (defined as quitting smoking for at least 6 months) within 10-16% of the patients (Lancaster & Stead, 2017). In addition, these programs may not reach or benefit vulnerable subgroups of tobacco dependent patients, including psychiatric patients (including other dependency issues), and individuals with intellectual disabilities (Kerr, Lawrence, Middleton, Fitzsimmons & Darbyshire, 2017; Dani & Harris, 2005). Thus, smoking prevalence within these populations remains relatively high (VanDerNagel, et al., 2017).

Researchers Strack and Deutsch (2004) proposed a dual process theory focused in the field of social psychology. They state that people behave according to two separate systems: the reflective system and the impulsive system. In the reflective system, decisions are made using knowledge and the information that is coming in from the situation being processed. In the impulsive system, on the other hand, decisions are made using schemes and there is little, or no thought required. This behaviour is a function of schemata, which can be understood as habits. Talking about addiction, people tend to "learn" and make use of the impulsive system instead of the reflective system (Evans & Coventry, 2006). Addiction can be seen as an unbalance between reflexive and reflective systems (Bechara, 2005). Reflective processes, on the one hand, encompass cognitive inhibitory control and delayed discounting of available reward, an ability to resist craving and make adapted decisions. In particular, people with an intellectual disability and addiction have much more issues in using the reflective system, which results in a greater impulsive reaction (VanderNagel, Kiewik & Didden, 2014).

Looking deeper at psychiatric patients and patients with other dependencies, it is harder for them to quit smoking because the tobacco provides desired positive mood influences (Dani & Harris, 2005). In addition to this, psychiatric patients often smoke to reduce the negative symptoms from their psychiatric illness (Snyder, McDevitt & Painter,

2008). The positive effects of smoking appear to outweigh any of the long-term health effects or concerns about medication adjustments that may be needed to manage their mental illness. Furthermore, psychiatric patients also often experience severe withdrawal symptoms, which also makes it more difficult for them to quit smoking (Dani & Harris, 2005).

Looking at the absence of interventions and prevention programs designed for people with dependency issues and mental disabilities, there is a crucial public health issue. The knowledge of professionals about addiction regarding this population is limited, and as a result healthcare experts have insufficient empirical evidence to support their clinical practice (Triantafyllou, 2019). In addition, people with intellectual disabilities find it more difficult to quit smoking because they are having difficulty in accessing mainstream health services (Kerr, Lawrence, Middleton, Fitzsimmons & Darbyshire, 2017). The general treatments for tobacco dependency have not taken into account the experienced difficulties of people who have cognitive impairments. This means that it cannot be assumed that generic approaches are appropriate for people with intellectual disabilities (Kerr, Lawrence, Middleton, Fitzsimmons & Darbyshire, 2017).

With regard to public health, there is a great demand for the development of new treatment methods (STIVORO, 2012). Research from Lawrence, Kerr, Darbyshire, Middleton and Fitzsimmons (2009) highlighted that tobacco-related health promotion interventions for people with an intellectual disability are rare. Their review demonstrated that worldwide, only five tobacco-related interventions for people with learning disabilities are developed. Looking at other comparable research a well-fitting and evidence-based prevention program for adolescents with mild to borderline intellectual disability and tobacco dependency is lacking (Schijven, Engels, Kleinjan & Poelen, 2015; Kiewik, VanDerNagel, Kemna, Engels & DeJong, 2016). However, designing a new treatment method would not only be in the interests of smokers and their environment, but the findings of a successful treatment for smoking addiction could also serve as a tool for the treatment of other addictions with a high relapse (Wiers, 2004). Because of the high prevalence numbers among psychiatric patients (including other dependency issues) and people with intellectual disabilities, the development of a new treatment for this vulnerable subgroup is necessary.

Craving plays an important role in addiction. Craving can be seen as the accompanied emotional state that is produced by conditioned stimuli that are associated with the reward effects of substances or behaviour (Franken, 2003). Research from Franken (2003) concluded that craving in particular makes quitting smoking more difficult and that the risk of relapse increases. It turned out that craving will never decrease completely after an attempt to quit. In

addition, 52% of the smokers who have quit smoking for five years still experience craving. Craving increases when there are some related stimuli present and will decrease immediately after smoking (Carter et al., 2008).

According to the research of Droungas, Ehrman, Childress and O'Brien (1995) drug-related cues with smoking content, trigger craving as well as physiological arousal in smokers. They state that craving and physiological arousal are most strongly triggered by cues specifically associated with the user's substance of choice. These are the results of Pavlovian conditioning. Droungas, Ehrman, Childress and O'Brien (1995) also state that craving is modulated by its perceived availability and accessibility. Their respondents felt less craving for cigarettes when they were in locations where smoking was not allowed. In addition, research from Prokhorov, Hudmon, Cinciripini & Marani (2005) shows that respondents, who were considered as heavier smokers, experience a higher level of craving than lighter smokers.

Looking at currently available treatment programs, Cognitive Behavioural Therapy (CBT) is a form of treatment where, among others, problem-solving skills of smokers are taught to resist the temptation to smoke in high-risk situations (Bordnick, Traylor, Carter & Graap, 2012). The disadvantage of this treatment-component is that smokers must imagine risky scenarios and role-play in a clinical setting. This setting often lacks the proper smoking related environmental context, and therefore, weakens the transfer of learning to real-world situations. A potentially more effective tool for a new treatment, which focuses on complex cue environments, is Virtual Reality (VR) (Bordnick, Traylor, Carter & Graap, 2012). The VR system uses a head-mounted display which responds to the participants movements. This means that the scene is continually changing as if the participant is actually looking around in the real environment. With the use of stereo audio, graphics and cues the participant experiences the feeling as if he or she is located in the real-time world. VR provides the opportunity to develop and practice coping skills while being confronted with smoking related cues in a VR environment (Bordnick, Traylor, Carter & Graap, 2012).

Bordnick, Graap, Copp, Brooks and Ferrer (2005) immersed smokers in a VR environment containing cue related smoking stimuli. The VR environment presented burning cigarettes, cigarette packs and people offering cigarettes. The participants who walked in the smoking cue related VR environment reported a significantly increase in craving compared to people who walked in a VR environment without smoking cues. Baumann and Sayette (2006) performed a similar research with a cue-exposure experiment where participants were presented with cue related stimuli on a computer monitor or a head-mounted display. The

participants showed a significant increase in the urge to smoke where the cue related stimuli were presented on the head-mounted display.

As mentioned before, CBT often does not transfer well to daily life because of the treatment taking place in a setting that lacks the cues and triggers from daily life, such as smoking cues. Therefore, in an ideal situation, the treatment would contain exposure, using CBT in a setting as real as possible (with the help of VR), for example a bar, a party, a home setting or a courtyard (Bordnick, Traylor, Carter & Graap, 2012). The tobacco dependent person can learn and practice coping skills in the complex cue environments. The opportunity to practice skills in realistic, risky environments should arouse emotional responses which can be used as teachable moments for specific skills (Pericot-Valverde, Secades-Villa & Gutiérrez-Maldonado, 2019). In other words, engaging coping skills training in VR may provide tobacco dependent patients with the additional support they need to resist cue-induced cravings. Therefore, the chances to remain abstinent of tobacco will increase (Bordnick, Traylor, Carter & Graap, 2012).

Unfortunately, there is no research known where the vulnerable subgroups of tobacco dependent patients, psychiatric patients (including other dependency issues) and people with intellectual disabilities, are treated with the use of VR. For these patients an approach in which behavioural change is elicited by embodied experiences and persuasive technology with a focus on 'doing' was proven to be more suitable rather than talking and contemplating (Klaassen, van Delden, VanDerNagel, Kamp, Thio & Heylen, 2019). In the treatment using VR, the tobacco dependent clients find themselves in a risky situation with high chances of substance abuse. Then self-control techniques will be learned. This technique is introduced in a treatment program from VanDerNagel (2016) called 'Minder Drank of Drugs'. This treatment program is specifically designed for people with an intellectual disability suffering from a substance use disorder. The self-control technique is called the six D's (or 6 A's in Dutch): Deals, Distance, Distraction, Declaring, Different thinking different acting and Doing great (VanDerNagel, 2016). The self-control techniques are implemented in the VR environment where the participant could interact with the environment and apply the learned self-control techniques.

Based on a small pilot in alcohol- and drug dependent patients, including an intellectual disability (Van Aggelen, 2017), it could be expected that using VR may provide a future opportunity to treat dependency issues in a safe and personalized environment (Klaassen, et al., 2019). This treatment provides more practical learning opportunities whereby it could serve as an extension of current treatments. In addition, participants can

repeat the exercises in their own pace and time, which could improve the treatment satisfaction and adherence of patients. Therefore, a treatment using VR would fit the needs of this vulnerable subgroup of tobacco dependent patients, such as psychiatric patients (including other dependency issues) and people with intellectual disabilities.

The aim of the present exploratory study as a first step towards further development of a suitable treatment for this vulnerable subgroup of tobacco dependent patients, is to investigate whether craving can be generated with the use of a VR environment where smoking cues are present. Therefore, the research question is formulated as follows:

- Can a virtual reality environment with smoke-related cues increase craving in tobacco dependent individuals with a psychiatric illness (including other dependency issues) or an intellectual disability?

Furthermore, it will be explored whether covariates such as age, gender and level of nicotine dependency are related to outcomes. Based on the literature review, the hypothesis for the research question is as follows:

- Due to the virtual reality environment with smoke-related cues, the craving of tobacco dependent individuals will increase.

2. Method

2.1 Design

This project incorporated a pilot study to induce and measure craving for smoking within a VR environment. The pilot was divided in three iterations, to allow further adjustments of both the VR environment and the measurements (figure 1).

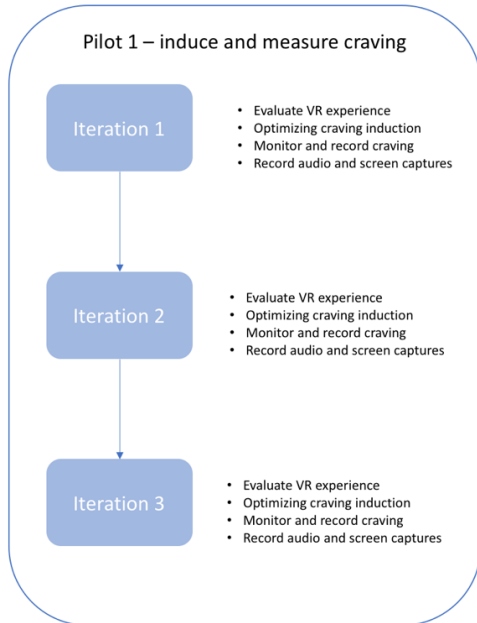


Figure 1. Study parts

Information yielded within each iteration was used to adjust and further develop the VR environment and/or to tune the measurements. Within iteration 1 synchronization of all sensors and recordings (audio and screen captures), participant's VR experience (density of smoking related cues, essential cues, essential cues that are missing) as well as development of craving during the intervention were evaluated. Within iteration 2, respondents were given cigarettes/shag and lighters in their hands. They could feel and smell these objects (they did not see the smoke objects because of the VR headset) in order to see whether the craving would increase (mixed-reality). Within iteration 3, respondents had to sit down and had to look through the VR headset at cigarettes/shag, a lighter and ashtray to see whether the craving would increase. This cue-reactivity assessment was to examine the potential to create a hierarchy of cues for each participant (Pericot-Valverde, Carcia-Rodriguez, Gutierrez-Maldonado, Ferrer-Garcia & Secades-Villa, 2011). This research did not go further in to the differences between the three iterations.

2.2 Participants

The inclusion and exclusion criteria in this research were that the participants had to be moderate to severe tobacco dependent patients from three participating clinics: Medisch Spectrum Twente (MST), Ziekenhuis Groep Twente (ZGT) and Tactus. Ten participants from each location, were included. Participants had to be able to wear a head-mounted display (VR headset), as well as skin conductance sensors and a heart rate sensor on their fingertips and or wrist. In addition, participants had to be sufficiently proficient in Dutch to understand instructions and verbalize their remarks and comments. Furthermore, the participants had to be moderate to severe tobacco dependent (operationalized as a score of 5 or higher on the Fagerström test for tobacco dependency). No light smokers were included because the aim of this study was initially to see where craving could be induced at moderate to severe tobacco dependent people. The expectation was that moderate to severe tobacco dependent people would show higher increases on craving. Candidates were excluded if they used nicotine replacement therapy or anti-tobacco craving medication, or when they were currently within the process of cessation of smoking (e.g. following a smoking cessation program). There were no inclusion criteria in terms of age, gender or residence. To include participants with an intellectual disability, only clients from the ward for patients with intellectual disability of Tactus were approached. To include participants with a psychiatric illness, only clients from the psychiatric department of ZGT were approached. The participants coming from the MST, were patients of the lung department with a medical condition.

2.3 The intervention: virtual reality environment

The intervention consisted of a VR environment which was presented to participants through a VR headset that is worn on the head, covering the eyes and ears. Participants could move within the VR environment, either by walking around for about three meters, or by ‘teleporting’ themselves using the controllers. The VR environment contained a basic tutorial (figure 2) and an enriched scene (figure 3). The tutorial scene was minimalistic and offered the participants the opportunity to learn to handle the controls by providing interaction possibilities in a basic way (such as handling cubes, or teleporting) or in a more complex way (bowling).

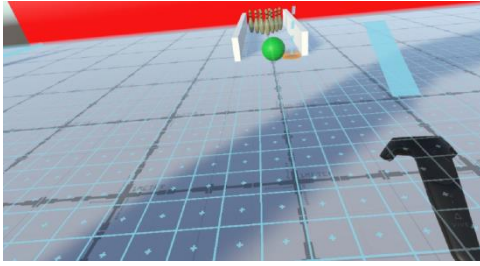


Figure 2. Tutorial scene – bowling



Figure 3. Enriched scene with smoking cues

The enriched environment consisted of smoking relevant scenes, such as a small restaurant, with an outside area (garden and smoking area) and a house with a living room, kitchen and garden. Cues were included to induce smoking related craving. There were smoking situations (e.g. smoking place outside buildings), smoking related props (lighter, ashtray, cigarettes etc.), and social cues (virtual agents who smoke or offer a cigarette, both verbally and non-verbally).

2.4 Measurements and other variables

2.4.1 Demographic information

The gender, age and previous experiences with VR were recorded before the VR exploration (see appendix 1). In addition, the participant was asked to provide information about his or her smoking, alcohol, illicit drug and medication use during the last month.

2.4.2 Recordings of patient’s behaviour

During the cue-reactivity environment, the research assistant kept a written log on the participant’s physical responses on their VR experience (e.g. their gestures, facial expressions, general movements, handling of controls). Participant’s comments, while exploring the VR, were encouraged (think aloud method) and were audiotaped. In addition, the participants could register moments in which they experienced craving, by pressing the ‘event marker’ button on the Empatica wristband. The implication of this part goes beyond the scope of this study, but this data was collected for further research in the future.

2.4.3 Questionnaires

The Fagerström’s test of nicotine dependence (FTNX, see appendix 2), the Dutch version of the FTNX (Vink, Willemsen, Beem & Boomsma, 2005) assessed the level of nicotine dependence at the baseline (T0). The questionnaire consists of ten questions (either multiple

choice or yes-no questions) and has a total score range from 0 to 10. Scores of >4 are indicative of moderate to severe dependency. The internal consistency from the questionnaire is acceptable with a Cronbach's alpha between 0.66-0.71.

The Brief Questionnaire on Smoking Urges (QSU-Brief, see appendix 3) (Littel, Franken, & Muris, 2011) is used to assess craving for smoking between the different parts of the exploration of the VR environment (T0, T1, T2 and T3). It consists of ten 7-point Likert scale items, representing the desire to smoke with either anticipation of pleasure from smoking or with relief from negative (withdrawal) effects. According to the research from Littel, Franken and Muris (2011) the Cronbach's alpha was 0.83 for the total score of the QSU-Brief. In this current research, a Cronbach's alpha of 0.96 was established.

The Visual Analog Scale (VAS) (see appendix 4) is used to measure variations in craving during the VR exploration. The participants have to score their craving, using a 10-point Likert scale. In this research, the scores of the VAS were used at baseline (T0) and afterwards (T3).

2.4.4 Additional measurements

Additional data was collected for further research, but the results of that data goes beyond the scope of this study and is therefore left out. A semi structured evaluation was conducted as well as the Unified Theory of Acceptance and Use of Technology (UTAUT) to evaluate the VR experience. Furthermore, the craving has also been measured using physiological data. The HTC VIVE PRO performed eye tracking, the Empatica E4 wristband and Shimmer wearable sensors, measured skin conductance and heart rate. This data did not require any extra activities from the participants, which could have influenced the increase of craving and has therefore no effect on the outcome of the current study.

2.5 Procedure

This study was carried out by two researchers from the University of Twente who worked as a team in each session. Research activities took place in a quiet room, with ample space for the participants to move when they used the VR. Participants were welcomed by the research assistants, who completed the informed consent procedure. The research assistant assessed whether participants had seen and understood the video and/or written information on the website, and, if needed provided additional information. The informed consent form had been read aloud by the research assistant, and - if agreed upon - was signed by the participant.

After informed consent, T0 questionnaires were completed (see table 1). The VR environment was then introduced in a step by step approach. First, the participant was asked to sit down, in order to apply the wristband and sensors. With the help of one of the research assistants, the participant was then introduced to the tutorial scene, wearing the VR headset and using the controls. When the participant was able to use the teleport options and control handling, the level of craving was measured using the QSU-brief (T1) and the enriched environment was introduced.

Participants were now invited to explore the VR themselves, while commenting on what they saw and experienced (think aloud method). During this phase, the research assistant asked every two minutes for a rating of craving using the visual analogue scale, that was projected within the VR environment. In addition, physiological measurements (skin conductance, heart rate, eye movement) were recorded. After this spontaneous exploration, craving was measured (T2, QSU-brief) and then the participant was guided towards cues in the VR environment that they had missed during the spontaneous exploration, with similar craving measurement during and after (T3) this episode.

The duration of both the spontaneous and the guided exploration had remained well under 20 minutes. Research activities ended here, providing data on physiological responses and self-reported craving during VR exploration. After the VR exploration the UTAUT was answered as well as the brief semi-structured evaluation. After the cue-reactivity environment, participants were offered a small gift as a token of appreciation. This present included a VR holder to put a Smartphone in, chocolate and a bag of nuts. Participants were also asked to submit their travel and parking expenses for compensation (if applicable). If they were interested, the researchers offered the participants information about smoking cessation programs that are locally available. Though participants were exposed to craving inducing cues within the VR environment, this phenomenon was not fundamentally different from their day-to-day experience with craving inducing stimuli. Because tobacco smoking is a highly frequent behaviour, with rapid recurring craving after initial relief during smoking, it was not attempted to decrease the craving within this study. The whole procedure took approximately 60 to 75 minutes. See table 1 for an overview of the research activities.

Table 1

Research activities

Activities	Preparation	T0	Exploration of Tutorial Environments Without SR stimuli	T1	Patient driven exploration With SR stimuli	T2	Researcher driven VR exploration	T3
Duration	10 min	10 min	Max 5 min	1-3 min	Max 5 min	1-3 min	Max 10 min	1-3 min
Measurements	Introduction Informed consent	Fagerström Demographics QSU brief VAS	Think aloud Skin conductance Hart rate Eye tracking VAS	QSU brief	Think aloud Skin conductance Hart rate Eye tracking VAS	QSU brief	Think aloud Skin conductance Hart rate Eye tracking VAS	QSU brief Evaluation UTAUT

2.6 Data analysis

The statistical analysis was performed by the Statistical Package for Social Sciences (SPSS V. 22). At first, the descriptive statistics were used to calculate the mean, standard deviation and frequencies. Secondly, the reliability of the QSU-Brief questionnaire was checked using the Cronbach's Alpha.

To answer the research question, to test the effects of the cue-reactivity environment, the differences between pre-test and post-test were analysed for the VAS. Therefore, paired-sample t-test was executed. To confirm a statistical significance, the results had to be $p < 0.05$. To see whether craving was increased, all four measurement moments of the QSU-Brief were used. A repeated measurement ANOVA was executed to test whether the VR environment with smoke related cues had an effect on the craving and to investigate whether the level of nicotine dependency, age and/or gender were related. To confirm a statistical significance, the results had to be $p < 0.05$

3. Results

The results of this section are based on the 23 respondents (N = 23) who participated in the study. The participants had a mean age of 44 years (SD = 13.44) and with a ratio of 13 male and 10 females. In addition, the majority (N = 20) had high to very high nicotine dependency. Further demographics are described in the table below (table 2).

Table 2

Demographics: Age, Gender, Location and Fagerström score

	Participants (N = 23)	(%)	M	±SD
Age (min-max)	(23-60)	-	44.69	13.44
Gender				
Male	13	56.5%	-	-
Female	10	43.5%	-	-
Location				
MST	9	39.1%	-	-
Tactus	9	39.1%	-	-
ZGT	5	21.7%	-	-
Fagerström score			7.04	1.22
Medium nicotine dependency	3	13%	-	-
High nicotine dependency	10	43.4%	-	-
Very high nicotine dependency	10	43.4%	-	-

N= number of participants; M= mean; SD= Standard Deviation; min=minimum age; max= maximum age

3.1 Effectiveness on the craving

In this current research, an attempt was made to investigate whether craving can be increased over time using VR with tobacco dependent individuals with a psychiatric illness (included other dependency issues) or an intellectual disability. A repeated measures ANOVA was calculated to investigate the increase of craving, using data from the QSU-Brief at T0, T1, T2 and T3. Mauchly's test indicated that the assumption of sphericity had been violated, $X^2(5) = 12.99$, $p = 0.024$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .68$). The results show that there is a borderline significant effect of craving over time $F(3, 38.747) = 3.246$, $p = 0.049$. The increase of the craving according to the scores on the QSU-Brief is displayed using a line graph (figure 4).

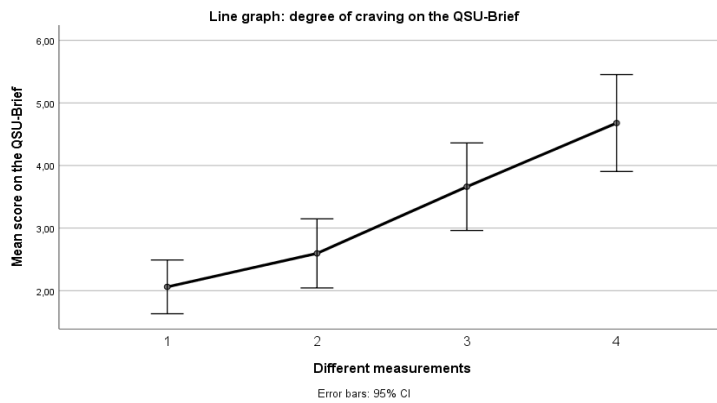


Figure 4. Degree of craving on the QSU-Brief at T0, T1, T2 and T3

To test change effect over time for the VAS, a paired-sample t-test was executed from T0 to T3. Looking at the degree of craving according to the VAS at the start of the cue-reactivity environment ($M = 3.39$; $SD = 2.44$) and at the end of the cue-reactivity environment ($M = 7.09$; $SD = 3.18$) the craving increases significantly ($t = -7.439$; $df = 22$; $p < 0.001$). The increase of the craving according to the scores on the VAS is displayed below using a line graph (figure 5).

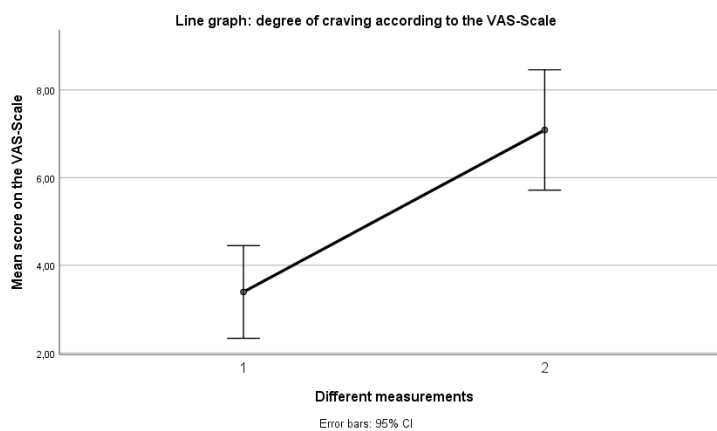


Figure 5. Degree of craving on the VAS-scale at T0 and T3

A repeated measures ANOVA was also calculated to investigate the increase of craving (using data from the QSU-Brief T0, T1, T2 and T3) based on respondents' level of nicotine dependency, age and gender. There is a significant interaction effect of age and craving over time $F(3, 38.747) = 5.896$, $p = 0.006$. There is no significant interaction effect on the level of nicotine dependency $F(3, 38.747) = 0.763$, $p = 0.475$ and gender $F(3, 38.747) = 0.137$, $p = 0.786$ on the increase of craving over time. An overview of the results can be found in table 3.

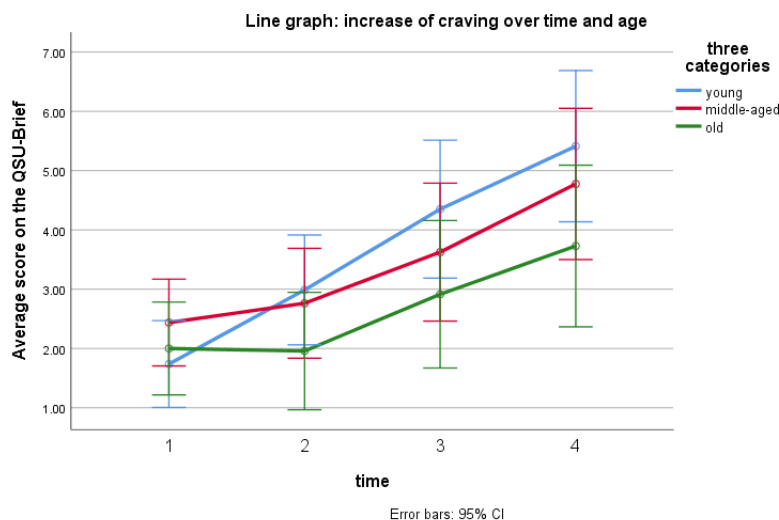
Table 3

ANOVA results

Predictor	Sum of squares	df	Mean square	F	p
Time	6.620	3	3.257	3.246	0.049
Time * age	12.024	3	5.916	5.896	0.006
Time * level of nicotine dependency	1.5560	3	0.765	0.763	0.475
Time * gender	0.279	3	0.137	0.137	0.876
Error	38.747	57	1.003		

Looking deeper into these results, the repeated measures ANOVA was once again executed, but without the covariates level of nicotine dependency and gender. These results show that there is a significant effect of craving over time $F(3, 40.595) = 17.227, p < 0.001$. Once again, there is a significant interaction effect of craving over time and age $F(3, 40.595) = 5.975, p = 0.006$. The hypothesis, that the craving of tobacco dependent individuals will increase, due to the virtual reality environment with smoke-related cues, can therefore be accepted. To display (see figure 6) the differential effects of increase in craving over time, a dummy variable has been created. This variable divided the participants in three equal groups of age: age between 22-35 years (young), age between 41-54 years (middle-aged) and age between 56-60 years (old). The figure shows that there is a large increase of craving from the youngest age group at T0 to T1, whereas the middle-aged and old age group show (almost) no increase of craving.

Figure 6. Differential effects of increase of craving for three age groups



4. Conclusion and discussion

The purpose of this pilot study was to examine the impact of a VR environment with smoke-related cues on the craving of tobacco. Participants, involved in the study, scored higher on levels of craving after the intervention with the VR. This occurrence was in line with the expectations. Comparing these results to earlier research (Bordnick, Graap, Copp, Brooks & Ferrer, 2005; Baumann & Sayette, 2006; Pericot-Valverde, Germeroth, & Tiffany, 2016), which investigated the effect of VR with smoke-related cues on craving, comparable results were shown for the vulnerable groups. Results have shown that participants in the VR cue-reactivity environment reported significantly more experienced craving afterwards. However, a confounder effect cannot be excluded, meaning there is a possibility that another variable could have influenced the increase of craving over time. For instance, the increased craving can be caused by a time bias. The study lasted about 60 to 75 minutes, during which the participants (who were all moderately to severe tobacco dependent) were not allowed to smoke. Because of the lack of a control group, it is not possible to differentiate between time effects and intervention effects.

Looking deeper at the results, an interaction correlation effect has been found on age and the increase of craving over time. García-Rodríguez, Ferrer-Carcía, Pericot-Valverde, Maldonado, Secades-Villa and Carballo (2011) also performed a research into increasing craving using smoke related cues with the use of VR. Their research showed that younger people (under the age of 27 years) reported significantly more increase of craving than the older group (age above 27 years). However, in this research, only 23 respondents participated in this explorative pilot study. This means that the sample size was too small to execute a statistical analyse to investigate the interaction correlation effect on age, divided in different groups of age (young, middle-aged and old). When looking at the line graph (displayed in the results section, figure 6) made of a dummy variable, it looks as if there is a large increase of craving from the youngest age group at T0 to T1, whereas the middle-aged and old age group show (almost) no increase of craving. Comparing results of this research and research from García-Rodríguez and colleagues (2011), it could mean that younger people are more sensitive for cue exposure and therefore show a larger increase in craving. However, this conclusion in this research is remarkable, because in the time between T0 to T1, the respondents had to practice in a tutorial VR scene, so that they would understand the controllers to teleport themselves and to pick up attributes in the VR environment. At this stage, no smoke-related cues were presented in the VR environment. This means that,

possibly, only the 'middle-aged' and 'old' respondents show an increase of craving because of the smoke-related cues that were presented in the VR environment. A possible explanation of this outcome can be given that most people who are addicted are in the age category of 20-30 years old and are seen as severe tobacco dependent (Rijksinstituut voor Volksgezondheid en Milieu, 2018). It is therefore possible that for the 'youngest' age group, only talking about their tobacco dependency (when filling in the questionnaires) was a trigger to increase craving. It could also be that because of tensions, potential small time bias, setting of the research and the fact that most of the 'younger' group had an intellectual disability, the 'youngest' age group already showed an increasing of craving when no smoke-related cues were presented. In addition, this also does not have to mean that their increase of craving from T1 to eventually T3 was caused by talking about tobacco dependency, tensions, small time bias, setting of the research and/or an intellectual disability. This increase (T1-T3) in craving could possibly be caused by the smoke-related cues, comparable to the conclusions from the research from García-Rodríguez and colleagues (2011). Because of the lack of a control group and a small sample size, it is therefore not possible to make a validated conclusion.

Another outcome of this explorative pilot study is that there was no significant interaction correlation effect on the level of tobacco dependency and the increase of craving over time. Looking at a research from Prokhorov, Hudmon, Cinciripini and Marani (2005) they found a correlation effect on the experienced craving between the different levels of tobacco dependency. Their results showed that heavy smokers score significantly higher on craving than lighter and moderate smokers. This also applies for the research from García-Rodríguez, Ferrer-Carcía, Pericot-Valverde, Maldonado, Secades-Villa and Carballo (2011), who concluded that heavy smokers show larger increases in craving than lighter smokers. These conclusions do not correspond to this research, because in this research no significant interaction correlation effect was found on the level of tobacco dependency and the increase of craving over time. An explanation can be given by looking at the target group who was included in this research, namely only moderate to severe tobacco dependent people and no light tobacco dependent people. Research from Prokhorov, Hudmon, Cinciripini and Marani (2005) and from García-Rodríguez, Ferrer-Carcía, Pericot-Valverde, Maldonado, Secades-Villa and Carballo (2011) included heavy, moderate but also lighter tobacco dependent respondents. Whereas in this research, only moderate to severe tobacco dependent respondents were included. This means that there is only a small difference between the level of tobacco dependency of the respondents. This might explain why no interaction correlation between the level of tobacco dependency and the increase of craving over time was found. It

is therefore not possible to look deeper at the correlation between the level of tobacco dependency and increase of craving over time when no lighter tobacco dependent respondents are included.

4.1 Strengths, limitations and recommendations

The present study combines several strengths which should be mentioned. The present study worked on a unique research investigating the possibilities of VR in a group that could potentially benefit greatly on theoretical grounds, but which have not been involved in research so far. The target group from this research is normally not easily investigated and has been investigated now in several ways. In this way, an important gap in knowledge is closed, namely the first step in developing a possible new intervention for the vulnerable subgroup of tobacco dependent patients. Further strengths of this research are that a quantitative method has been used to answer the research question. With the use of quantitative research, the data was collected objectively and systematically. The strict application of standardised procedures reduced systematic bias and eliminated erroneous conclusions. Therefore, quantitative research maximises internal validity and increases the probability of generalising the findings beyond the study sample. Another strength of this research is the use of the QSU-Brief which has a Cronbach's alpha of 0.96. This can be seen as an excellent internal consistency. This internal consistency results in a higher accuracy of measurements and higher variability of the test scores. In other words, the internal validity and the internal consistency of this research can be seen as excellent. Another strength of this research is that it worked out to include the vulnerable subgroup of tobacco dependent patients. All participants who showed up, understood and completed the full intervention. This means that the intervention is suitable and accessible for psychiatric patients (including other dependencies) and people with an intellectual disability.

On the other hand, the present study contains some limitations as well. At first, a confounder affect cannot be excluded because of the design of the study and the methodological issues. Furthermore, a control group was missing which does not allow the study to assume with certainty that the increased levels of craving are a result of the VR environment with smoke-related cues. Because of this it is advised that, in a future study, a control group, who will not be exposed to smoke-related cues, has to be included. In this way, the results can be compared in different conditions.

Second, the presence of two researchers in front of one respondent is seen as a confounding variable and therefore a limitation. The research was executed with two

researchers in the same room as was the respondent, therefore respondents may have answered in a socially desirable way. Respondents also had to answer the questions verbally, instead of writing the answers down. This may also have increased the chance of socially desirable answers. For future research it is therefore advised that the respondents need to have the option to fill in the questionnaire by themselves. This was already done while answering the VAS, but it also needs to be implemented when answering the QSU-Brief.

Another limitation of this study is the sample size of 23 participants, because it is a pilot study and therefore a limited number of statements can be given. As a result of the small sample size an a priori power analysis was conducted using G*Power3 (Faul, Erdfelder, Lang & Buchner, 2007) to test the difference from one sample case mean using a one-tailed test, a medium effect size ($d = .50$), and an alpha of 0.05. Result showed that a total sample of 45 ($n = 45$) was required to achieve a power of .95. This current research did, therefore, not reach the required sample size. In addition, the study was carried out in only three organizations (MST, Tactus and ZGT). Because of this, the results of the study are not generalizable. However, this is a explorative pilot study to assess whether using VR can be helpful for a possible future intervention. Current research has shown that the VR environment with smoke-related cues results in an increase of the craving. For this reason, it is recommended to perform similar studies in more different organizations that also work with the more vulnerable subgroups of nicotine dependency. In this way, the sample size will be larger and more varied, and therefore causing more generalizable conclusions.

Finally, it cannot be ruled out that a form of self-selection bias emerged. In the three organizations, respondents were approached by the researchers themselves and asked if they wanted to join the research. In this way, it is not certain that the sample size is a good representation of the vulnerable group of tobacco dependency. For further research it is therefore important that researchers make no exceptions within all respondents that are seen as the vulnerable group.

4.2 Practical implications

The need for a suitable treatment for the vulnerable subgroup of tobacco dependent patients, psychiatric patients (including other dependency issues) and people with intellectual disabilities is high. A first step towards a suitable treatment was to investigate whether craving can be generated with the use of a VR environment where smoking cues were present. The current study shows that craving can be increased using a VR environment with smoke-related cues. In practise, this VR environment can be integrated in a suitable treatment for the

vulnerable subgroup of tobacco dependent patients. This VR environment with smoke-related cues can be used to eventually reduce craving by using self-control techniques. The patients will be exposed to a VR environment with smoke-related cues where they need to adapt the self-control techniques to reduce their craving. Where they would previously smoke a cigarette, they now learn how not to smoke and reduce their craving. Changing their smoking habit will take several appointments and patients also need to practice at home. Eventually patients can cope in daily life, including the smoke-related cues and hopefully stop smoking. It would be interesting to do research on the effect of the learned self-control techniques in combination with the VR environment in a follow-up study. Furthermore, this intervention could be applied to sample with other dependency disorders which are characterized by craving. This study can be used to generate knowledge about craving in other dependency disorders and make VR broadly applicable across various types of disorders.

4.3 Conclusion

An overall conclusion for the current study is that the experienced craving in tobacco increases with most of the participants after being in a VR environment with smoke-related cues. Therefore, it can be assumed that the use of this VR environment has potential for a future treatment for the subgroups of tobacco dependent patients: psychiatric patients (including other dependency issues) and people with intellectual disabilities. However, future investigations are needed to overcome the limitations of the present study and to investigate whether this VR environment is also suitable when craving will be reduced. In practice, it is advised to promote this research among the vulnerable group of tobacco dependent patients, to increase the amount of people benefiting from a new suitable treatment, as it is hereby proven that the VR environment has the potential to become a useful tool in this domain and subgroup.

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Appendix 1. General information (T0)

Onderzoekscodes: _____ (study location, pilot # and inclusion order, e.g. MST_01_01)

Onderzoeker: _____

Datum: _____

Leeftijd: _____

Geslacht: _____

Gebruik in laatste maand van:

#Tabak ja / nee*

Indien ja: _____ (aantal) sigaretten/sigaren/pijpen/gram* per _____

Leeftijd eerste sigaret (in jaren) _____

Datum en tijdstip laatste sigaret _____

Aantal pogingen te stoppen _____

#Gebruik e-sigaret ja / nee*

Indien ja: _____ (aantal) sigaretten/sigaren/pijpen/gram* per _____

#Alcohol ja / nee*

Indien ja: _____ (aantal) standaard glazen per _____

#Drugs ja / nee*

Indien ja: _____ (aantal) _____ (omschrijf eenheid)** per _____

#Ooit behandeld in de verslavingszorg? ja / nee*

Indien ja: hoe lang? _____ maanden/jaren*

Eventuele aanvulling/toelichting op middelengebruik:

* Doorhalen wat niet van toepassing is

** Beschrijf soort gebruik (bijvoorbeeld: joint/lijtje/bolletje)

Actueel medicatie gebruik

Gebruik van nicotine pleister of kauwgom ja / nee

Eerdere ervaringen met VR:

Appendix 2. De Fagerström test (T0)

Onderzoekscode: _____ (study location, pilot # and inclusion order, e.g. MST_01_01)

Onderzoeker: _____

Datum: _____

Vraag 1: Hoe lang na het wakker worden rookt u uw eerste sigaret?

Binnen 5 minuten 3 punten

Binnen 6 – 30 minuten 2 punten

Binnen 31 – 60 minuten 1 punt

Na meer dan 60 minuten 0 punten

Vraag 2: Is het makkelijk voor u om niet te roken op plaatsen waar roken verboden is?

Ja 0 punten

Nee 1 punt

Vraag 3: Welke sigaret kunt u het moeilijkste missen?

De eerste 1 punt

Maakt niet uit welke 0 punten

Vraag 4: Hoeveel sigaretten rookt u per dag?

31 of meer 3 punten

21-30 2 punten

11-20 1 punt

10 of minder 0 punten

Vraag 5: Rookt u meer het eerste uur na het ontwaken dan de rest van de dag?

Ja 1 punt

Nee 0 punten

Vraag 6: Rookt u als u zo ziek ben dat u overdag in bed moet blijven?

Ja 1 punt

Nee 0 punten

Score Fagerström: _____

Appendix 3. The QSU-Brief (T0, T1, T2, T3)

Onderzoekscodes: _____ (study location, pilot # and inclusion order, e.g. MST_01_01)

Onderzoeker: _____

Datum: _____

Noteer in welke mate de proefpersoon het eens of oneens is met elk van de volgende stellingen (score tussen de 1 en 7, waarbij 1 voor 'helemaal oneens' staat, en 7 voor 'helemaal eens')

HELEMAAL MEE ONEENS |___|___|___|___|___|___|___| HELEMAAL MEE EENS

Vraag	T0	T1	T2	T3
1. Ik zou alles beter onder controle hebben als ik nu mocht roken				
2. Ik zou er bijna alles voor over hebben om nu te mogen roken				
3. Als ik nu mocht roken zou ik me minder depressief voelen				
4. Ik verlang op dit moment naar een sigaret				
5. Niets zou beter zijn dan nu een sigaret te roken				
6. Als het mogelijk was, zou ik waarschijnlijk nu een sigaret opsteken				
7. Het enige wat ik nu wil is een sigaret				
8. Een sigaret zou me nu wel smaken				
9. Ik ervaar een sterke drang om een sigaret te roken				
10. Zodra dit mogelijk is, ga ik roken				

Appendix 4. VAS trek meting

Onderzoekscade: _____ (study location, pilot # and inclusion order, e.g. MST_01_01)

Onderzoeker: _____

Datum: _____

VAS trek meting

Hoeveel trek heeft u nu? *

|-----|

0

10

* Deze vraag wordt tijdens de exploratie van de VR om de twee minuten gesteld. Participant kan deze score zelf invullen met behulp van de controllers.