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Acceptability and effectiveness for withdrawal symptom relief of a novel oral nicotine delivery device: a randomised crossover trial

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ABSTRACT

Rationale: Existing nicotine replacement therapies (NRT) improve the chances of smoking cessation but are limited by either relatively slow nicotine absorption rates or unpleasant side-effects, leaving scope for the development of more effective and acceptable products.

Objectives: To test the acceptability and effectiveness for withdrawal symptom relief of a novel nicotine delivery device, the 'Nicotine Cannon' (NC), compared with three existing, equivalent products: the nicotine lozenge, mini-lozenge and nicotine inhalator.

Methods: A repeated-measures crossover trial, where participants were randomised to one of two conditions (one or ten hour abstinence) and in each condition to one of 24 possible sequence permutations to test each product for ten minutes. Standard socio-demographic and smoking characteristics were assessed as well as withdrawal and NRT use symptoms before, during and after NRT use and product satisfaction after use.

Results: The results were similar across both durations of abstinence. The NC was significantly more effective than the inhalator in reducing withdrawal symptoms ($F(3,196)=3.5$, $p=0.015$) and together with the mini-lozenge performed better than other NRT in alleviating urges to smoke ($F(3,563)=9.6$ $p<0.001$) and desire for cigarettes within ten minutes of use ($F(3,727)=26.1$, $p<0.001$). The NC induced fewer adverse side-effects than other NRT and was judged to be more enjoyable ($F(3,87)=13.56$, $p<0.001$) and satisfying to use ($F(3,92)=12.35$, $p<0.001$).

Conclusions: The 'Nicotine Cannon' is at least as effective as equivalent NRT in reducing withdrawal symptoms and more acceptable to users, suggesting that it would be a useful addition to existing NRT. The acceptability profile could make it particularly useful as a 'harm reduction' tool.

Keywords: nicotine replacement therapy, withdrawal symptoms, acceptability, smoking cessation, novel treatment

INTRODUCTION

Although the majority of smokers would like to stop, less than half achieve abstinence in their lifetime (WHO, 1998), reflecting the powerful addictive nature of tobacco (e.g. Anthony et al., 1994). This is primarily a result of the alkaloid nicotine contained in tobacco which by actions in the midbrain changes dopaminergic response in the reward centre in the brain (Watkins et al., 2000). Over time, these changes lead to operant learning where smoking is rewarded (positive reinforcement) and abstinence punished (negative reinforcement), resulting in nicotine addiction (West and Shiffman, 2007). Cigarettes are designed to be very effective nicotine delivery devices to exploit this process, allowing smokers 'fingertip control' over the dose of nicotine delivered, as they can adjust the intensity and frequency of puffing to suit their personal preferences (e.g. West, 2009).

Despite its addictive properties, pure nicotine in the doses that smokers receive is relatively safe; it is other components in tobacco smoke, primarily tar and noxious gases, that cause smoking-related health effects (Royal College of Physicians, 2000). Nicotine is therefore provided to smokers in the form of nicotine replacement therapy (NRT) to alleviate withdrawal symptoms, reduce motivation to smoke and also to provide a control or coping mechanism to deal with the behaviour change. In clinical trials, NRT has been found to increase long-term abstinence rates in those trying to stop by 60% (Stead et al., 2008). There is no good evidence that one form is significantly better than any other in promoting cessation (Hajek et al., 1999). This may be because improvements in potential efficacy of nicotine replacement from faster acting products are counterbalanced by increased aversiveness. Thus the fastest acting product, the nicotine nasal spray, while having a somewhat greater abuse liability (West et al., 2000) is also initially the most aversive to use (Sutherland et al., 1992).

For this reason a number of novel nicotine delivery devices have been introduced into the market or are under development. These include high-dose nicotine patches (Shiffman et al., 2006), rapid delivery nicotine gums (Shiffman et al., 2009), a nicotine pouch (Thornley et al., 2009), a nicotine mouth spray (Bolliger et al., 2007), e-cigarettes (Bullen et al., 2010) and pulmonary nicotine delivery devices (e.g. Rose et al., 2010). In general, these products appear to be at least as effective as existing products, are usually well tolerated and may provide even faster craving relief (e.g. McRobbie et al., 2010). However, the development and licensing of novel products is costly which is likely to be passed on to consumers. We were therefore interested to test a new design that makes use of existing technology to provide nicotine rapidly and with 'fingertip control' while not being aversive: the 'Nicotine Cannon'. Two of the authors (RW and AM) have shared of a patent for the device but at present plans to bring it to market have not been formulated.

The 'Nicotine Cannon' (NC) is a wide-bore nicotine inhalation device consisting of a tube that holds up to five removable nicotine cartridges (manufactured for the nicotine inhalator) through which air can be drawn so that nicotine vapour enters the mouth and upper airways (see Fig.1). The design features of the NC aim to provide a more rapid delivery and greater dose of nicotine to users while mimicking to some degree the 'fingertip control' of cigarettes: the dose of nicotine delivered is adjustable as smokers can use as many cartridges as needed and inhale through a wide bore hole. By adapting an existing NRT, this design also has the advantage of being potentially very cheap and easy to produce and license.

(Fig.1 about here)

The NC has been demonstrated in a recent pharmacokinetic study to yield relatively high blood nicotine concentrations quite rapidly. Results showed that compared with other NRT products, the NC delivered the highest blood nicotine concentration after use, while its speed of delivery was only surpassed by the nicotine nasal spray (McEwen et al., 2008). Following on from the promising results of the pharmacokinetic study of this novel device, this trial therefore sought to further evaluate the NC in terms of its impact on withdrawal symptoms and acceptability to users as a function of abstaining for either one or ten hours. In particular, this study addressed the following research questions:

1.) Is the 'Nicotine Cannon' as effective as, or more effective than, comparable existing NRT products in reducing withdrawal symptoms?
2.) Does the 'Nicotine Cannon' have a similar or better side-effect profile than comparable existing NRT products?
3.) Is the 'Nicotine Cannon' considered to be equally or more satisfactory to use than comparable existing NRT products?

METHODS

Products

The NC (see Fig.1) consists of a tube of approximately 3cm in diameter and 4cm in length capable of holding securely five removable nicotine cartridges that are covered by gauze saturated with Eucalyptus oil. It allows air to be drawn through those cartridges so that nicotine vapour enters the mouth and upper airways easily. The dimensions of the device are important insofar as it needs to be discreet and compact to be acceptable to consumers but wide enough to allow inhaled nicotine to pass as far as possible into the upper respiratory tract. Prior to using the device, smokers can adjust the concentration of

nicotine ingested by piercing the foil at either end of one, more or all of the five cartridges.

The NC was compared with three existing NRT products, the nicotine inhalator, the nicotine lozenge (4mg) and mini-lozenge (4mg). The inhalator was chosen as it is the most similar product to the NC currently available on the market. The lozenge was selected as previous research has shown that its pharmacokinetics match the NC most closely and among existing NRT products it is able to deliver the largest acute dose of nicotine (McEwen et al., 2008). Finally, the mini-lozenge was chosen at the time of designing the study it was the latest addition to the range of NRT products available to consumers, particularly developed for short-term abstinence and for convenient use (it is smaller than the ordinary nicotine lozenges and dissolves more easily). While the nicotine nasal spray is currently the fastest acting NRT product available, it was considered impractical for inclusion in a short-term withdrawal study of naïve NRT users given its aversive side-effects (burning sensation, sneezing and cough) resulting from the direct application of nicotine to the nasal mucosa, which takes users some time to get accustomed to.

Procedure

In order to maximize power and be able to evaluate the effectiveness of NRT products with regards to short-term abstinence, we opted for a mixed (within-subjects and between-groups) design. The between-groups factor was smoking abstinence prior to testing (one hour versus ten hours abstinence) and the within-subjects factor was NRT product use (four NRT products tested by all participants), thus each participant functioned as their own control. Consent and baseline measures were taken over the phone before the first study day and participants were computer-randomized to the two

abstinence conditions and within each condition randomized to different permutations of the order in which NRT products were tested to balance potential sequence effects (Fig.2). Laboratory sessions took place in the morning and early afternoon at University College London.

(Fig.2 about here)

On the first study day, written consent was obtained and abstinence verified by an expired air carbon-monoxide (CO) reading. Participants were then given written instructions for the correct use of the allocated NRT, were able to familiarise themselves with the product for five minutes and self-administered NRT for ten minutes. Participants were instructed to aim for at least four inhalations per minute for the 'Nicotine Cannon' and nicotine inhaler and to suck actively until there is a hot and peppery taste from the nicotine lozenge and mini-lozenge and to continue inhaling and sucking respectively throughout the ten minute period of use. Each participant was required to return to the laboratory to test each NRT product with a minimum of seven days between adjacent laboratory sessions. Participants were reimbursed for their time and effort at their last study visit. The study received approval from University College London Ethics Committee (Ref 0483/001) to confirm adherence to EU ethical research standards.

Participants

Smokers were recruited through advertisements in local newspapers, emails, or posters on public bulletin boards at or around University College London. Participants had to be adult (18+), regular smokers for at least a year (5 ≥ cigarettes/day); be in good health and not pregnant or current users of NRT products. Overall, 48 participants (24 per group) were recruited into the study to ensure that within each group all possible

permutations of NRT sequences were covered. Power analysis (Faul et al., 2007) indicated that this sample was sufficient to detect medium-to-large within and between subject differences (f=0.25) with a power of 80% at a standard Type I error rate (α=0.05), using a multiple repeated measures design. Table 1 provides an overview of participant characteristics.

Measures

The baseline questionnaire assessed smoking history, cigarette consumption and dependence measured by the Heaviness of Smoking Index (HSI; Heatherton et al., 1989), intention to stop smoking and prior NRT use as well as standard socio-demographic characteristics. In order to verify abstinence, participants provided a breath sample measured with a standard monitor (Smokerlyzer®, Bedfont Scientific Ltd, Kent, UK) to obtain expired air carbon monoxide levels at the beginning of each session, a valid and reliable measure of recent exposure to cigarette smoke (Jarvis et al., 1986).

Both before and after NRT use, participants completed the Moods and Physical Symptoms Scale (MPSS, West and Hajek, 2004), a validated and reliable measure of cigarette withdrawal symptoms (West et al., 2006). The MPSS consists of five single-item 5-point ratings of depressed mood, irritability, restlessness, hunger and poor concentration. It also assesses ‘time spent with urges to smoke’ and ‘strength of urges to smoke’ on a 6-point Likert scale. In addition, participants completed a questionnaire adapted from the Shiffman-Jarvik scale (Shiffman and Jarvik, 1976) that has previously been used in this form (McEwen et al., 2008) and which assesses the effects of pharmacological treatments on a 10-point rating scale ranging from 1 (none) to 10 (extreme). It measures NRT use symptoms covering craving (urge to smoke, desire for cigarette), negative (agitation) and positive (pleasant feeling) affect as well as somatic

symptoms (feeling unwell, nausea, throat irritation, dizziness). This questionnaire was administered immediately before NRT use (at 0 minutes), during NRT use (at 3, 6 and 10 minutes) and immediately after NRT use (at 13, 16 and 20 minutes). At the end of each session, satisfaction with the NRT product was assessed with an adapted version of the modified Cigarette Evaluation Scale (Cappelleri et al., 2007) which measures satisfaction ('Was the NRT use satisfying?'; 'Did the NRT taste good?'), enjoyment ('Did you enjoy the NRT use?') and psychological reward ('Did the NRT use calm you down?') from 1 (not at all) to 7 (extremely).

Analysis

Baseline group differences were assessed by independent t-test and X^2-test for continuous and categorical variables, respectively. Given the mixed design of this study, within subjects and between group differences were tested with general linear mixed models. These have the advantage over standard repeated-measures ANOVA that they are less sensitive to missing data and violations of the sphericity assumption since the covariance structure can be specified (e.g. Krueger and Tian, 2004). Akaike's Information Criterion was used to select the most appropriate repeated covariance structure to provide a best fit to data. Depending on the analysis, NRT or NRT by time was specified as the within-subject variable and abstinence condition as the between group variable in the linear-mixed models. Where appropriate, changes in ratings from before to after NRT use were tested with paired t-tests for given NRT products. Statistical significance was set at a standard level (α=0.05) and adjusted in post-hoc analysis for multiple comparison using the Bonferroni correction.

RESULTS

The study sample was relatively young with a mean age of 31 years, educated (over half had obtained a degree), of mixed ethnic background and included slightly more men than women. The majority had started smoking in their teens, smoked between 11-20 cigarettes per day and had made a previous quit attempt. Only a quarter of participants had used NRT before (Table 1).

(Table 1 about here)

One hour vs. ten hour abstinence

While group characteristics were largely similar, those who abstained for one hour were marginally more likely to have previously attempted to quit and, as expected, had significantly higher expired air carbon-monoxide readings compared with those abstaining for ten hours. However, no main effect of abstinence condition (1h vs. 10h) on baseline withdrawal symptoms, changes in withdrawal symptoms from before to after NRT use, symptoms of NRT use or product satisfaction were observed. Results were therefore pooled for all subsequent analyses.

1.) Withdrawal symptoms

On average, participants displayed moderate cigarette withdrawal symptoms on the MPSS (Fig.3). In the total sample, there were significant reductions across all products in feeling anxious ($F(1, 214)=20.8$, $p<0.001$); irritable ($F(1, 319)=8.0$, $p=0.005$), restless $F(1, 241)=26.2$, $p<0.001$); hungry $F(1, 318)=4.5$, $p=0.034$) as well as in having poor concentration ($F(1, 281)=6.3$, $p=0.013$), in time spent with urges ($F(1, 236)=27.5$, $p<0.001$) and strength of urges ($F(1, 213)=40.9$, $p<0.001$) from before to after NRT use. There was a main effect of NRT product on the change score of the MPSS scale ($F(3, 196)=3.5$, $p=0.015$). Post-hoc analysis showed that the overall reduction in withdrawal

symptoms was significantly greater for the NC compared with the inhalator (p=0.026). Further paired t-tests revealed a significant reduction in six out of eight withdrawal symptoms for the 'Nicotine Cannon', five for the nicotine lozenge, four for the nicotine mini-lozenge and only two for the nicotine inhalator (Fig.3).

(Fig.3 about here)

2.) NRT use symptoms

We next investigated the impact of products on symptoms of NRT use. To this end, changes in symptoms from baseline scores were computed for the twenty minute time period during and immediately after NRT use (Fig.4). There was a main effect of time on changes in all NRT use symptoms except for feeling pleasant, which remained stable. Over the period of using NRT, participants felt more unwell ($F(5, 367)=7.9$, $p<0.001$); nauseous ($F(5, 316)=8.6$, $p<0.001$); dizzy ($F(5, 260)=2.9$, $p=0.014$) and experienced more throat irritation ($F(5, 434)=49.1$, $p<0.001$). They also felt less agitated ($F(5, 319)=5.2$, $p<0.001$) and the desire for cigarettes ($F(5, 350)=8.2$, $p<0.001$) as well as urges to smoke decreased while using NRT ($F(5, 349)=7.8$, $p<0.001$). There were no interactions between NRT product and time, suggesting that the time course of changes in symptoms was not significantly altered by the type of NRT used. However, there was a significant main effect of NRT product for feeling unwell ($F(3, 356)=18.9$, $p<0.001$), nauseous ($F(3, 198)=12.2$, $p<0.001$) and dizzy ($F(3, 367)=8.4$, $p<0.001$) and for experiencing throat irritation ($F(3, 363)=15.6$, $p<0.001$), pleasant feelings ($F(3, 727)=26.1$, $p<0.001$), the desire for a cigarette ($F(3, 560)=10.5$, $p<0.001$) and the urge to smoke ($F(3, 563)=9.6$ $p<0.001$).

Post-hoc analysis revealed that across the whole time-span, the NC performed better than all other products in terms of feeling unwell, experiencing throat irritation and feeling pleasant. The NC and inhalator were better than other products with regards to feeling nauseous and the NC and the mini-lozenge were more effective than the inhaler and lozenge for reducing urges to smoke. The NC also performed better than the lozenge in lessening the desire to smoke but the lozenge was better than all other products in terms of dizziness. Importantly, the observed greater decrease in urges to smoke and desire for a cigarette while using the NC compared with other NRT was already significant during the first ten minutes of use. While the mini-lozenge was more effective than the lozenge and inhalator for reducing the desire for cigarettes, it also made participants feel more unwell and felt less pleasant than all other products.

(Fig.4 about here)

3.) Satisfaction

Lastly we evaluated what participants felt about the different NRT products. Overall, there were significant differences in terms of taste ($F(3, 82)=11.2$, $p<0.001$), satisfaction ($F(3, 92)=12.35$, $p<0.001$), calming effect ($F(3, 88)=6.0$, $p=0.001$) and enjoyment ($F(3, 87)=13.56$, $p<0.001$). Post-hoc analyses showed that the NC was judged to be more enjoyable to use and to taste better than all the other products (Fig.5). Participants also felt that it was more calming and satisfying than either the lozenge or mini-lozenge and the inhalator was thought to be more satisfying than the lozenge.

(Fig.5 about here)

DISCUSSION

This study provides evidence that a novel nicotine delivery device, the ‘Nicotine Cannon’, is at least as effective as comparable, existing NRT products in reducing withdrawal symptoms while being more acceptable to users. The NC significantly decreased withdrawal symptoms compared with the inhalator and performed best out of all the products in terms of individual withdrawal symptoms, significantly reducing six out of the eight symptoms measured. In addition, the NC together with the mini-lozenge was significantly more effective at reducing urges to smoke quickly than the other NRT tested. Importantly, this acute impact on withdrawal symptoms was not accompanied by an increase in aversive side-effects. On the contrary, the NC performed better than the other NRT in terms of feeling unwell, experiencing throat irritation and feeling pleasant. By comparison, the other most effective product for relieving withdrawal symptoms, the mini-lozenge, was judged to feel less pleasant, made people feel more nauseous and unwell than the NC. In agreement with these findings, users rated the NC to be more enjoyable to use and to taste better than other products and to be more calming and satisfying than the mini-lozenge.

As the NRT products included in this study have proven efficacy as aids to smoking cessation (Stead et al., 2008), these results suggest that the NC is likely to be effective for helping smokers quit. Given its favourable user profile, the NC may increase medication compliance and therefore may arguably improve abstinence rates compared with other NRT. Moreover, as increases in cravings have been linked with the occurrence of relapse within a short-time period of around ten minutes (Shiffman et al., 1996), the faster onset of action on urges and desire to smoke of the NC compared with the inhalator and lozenge may also help prevent relapse. These acute effects on withdrawal symptoms of the NC reflect its pharmacological profile which shows higher

levels of blood nicotine levels within eleven minutes of use compared with existing products including the inhalator, lozenge, gum and nasal spray (McEwen et al., 2008).

Besides its use as a traditional smoking cessation intervention, the NC may also have potential as an aid to harm reduction. Legislative changes have been implemented in some countries to allow smokers to use NRT to cut down the number of cigarettes smoked prior to attempting to stop smoking completely over a six month period, to use NRT for temporary abstinence (MHRA, 2010) and there are even calls for providing NRT long-term to smokers who can or will not stop smoking (Shahab and West, 2010). This is on the basis of evidence suggesting that the use of NRT for smoking reduction or temporary abstinence may motivate such smokers to make a quit attempt (Moore et al., 2009;Beard et al., 2010). This places obvious demands on the acceptability of NRT for these purposes and requires NRT products to be palatable and satisfying in order to maintain the concurrent use of NRT and cigarettes and an eventual switch to a sole use of NRT. However, the nicotine delivery profile of current NRT has been criticised for being too low and slow to be effective as an alternative to cigarettes (Royal College of Physicians, 2007). Given its high acceptability and fewer side-effects, especially compared with a product designed for temporary abstinence such as the mini-lozenge, together with its fast action in reducing withdrawal symptoms compared with existing NRT would make the NC therefore an ideal candidate for harm reduction purposes.

Unlike other novel products in development, the NC has the advantage of simply adapting an existing product to provide a more effective mode of nicotine delivery. Dependent on user preferences, the potentially increased use of nicotine cartridges may make the NC more expensive than the inhalator, but its development costs are very low and the device itself could be sold very cheaply. It appears also less likely to cause

aversive side-effects of fast-acting products as has been reported for the mouth spray and the nicotine nasal spray for instance (Sutherland et al., 1992; Bolliger et al., 2007).

To the extent that the Nicotine Cannon delivers somewhat fast nicotine than many other products while still being pleasant to use (McEwen, 2008), concerns may be raised about abuse liability (West et al., 2000). The concept of abuse needs to be defined in this context. A smoker switching long-term to a pure nicotine product instead of continuing to smoke would presumably not constitute abuse. If young people who would otherwise have smoked were to do the same thing there would similarly be a significant public health gain. Thus the important question is how far young people who would never have smoked would take up a product such as the Nicotine Cannon. There is no evidence to date of any nicotine products being attractive to non-smokers of any age. Regulators arguably should weigh up the public health costs and gains of any decision on products such as this. Currently there appears to be a different of approach between regulators on either side of the Atlantic with European regulators being more willing to consider net public health gain than the FDA in the US.

This study had a number of limitations. The study was not powered to detect subtle interaction effects. Moreover, the lack of a difference between abstinence conditions taken together with relatively low baseline urges to smoke would suggest that longer periods of abstinence may be required to induce the full gamut of withdrawal symptoms. This may also have limited the extent to which changes in withdrawal symptoms could have been observed. As this was a preliminary laboratory-based study, the current design does not provide a definitive comparison of the acceptability or clinical efficacy of these NRT products. A longer period of NRT use will be required to adequately evaluate chronic effects and the potential for long-term use. However, this study benefited from

studying a sample that was relatively naïve to NRT products, thus lessening the impact of prior views on the NRT products tested. The fact that participants were not intending to stop smoking also allowed us to better mimic the use of these NRT for harm reduction purposes. Further research using a longer abstinence period, administration of NRT products and larger sample size are now required to confirm findings from this initial trial.

In conclusion, a novel nicotine delivery device, the ‘Nicotine Cannon’, appears to have a superior profile of effectiveness, side-effects and acceptability to several other NRT products. It could make a useful addition to the range available and may be particularly effective for harm reduction given its effectiveness and acceptability profile.

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FIGURES AND TABLES

Figures

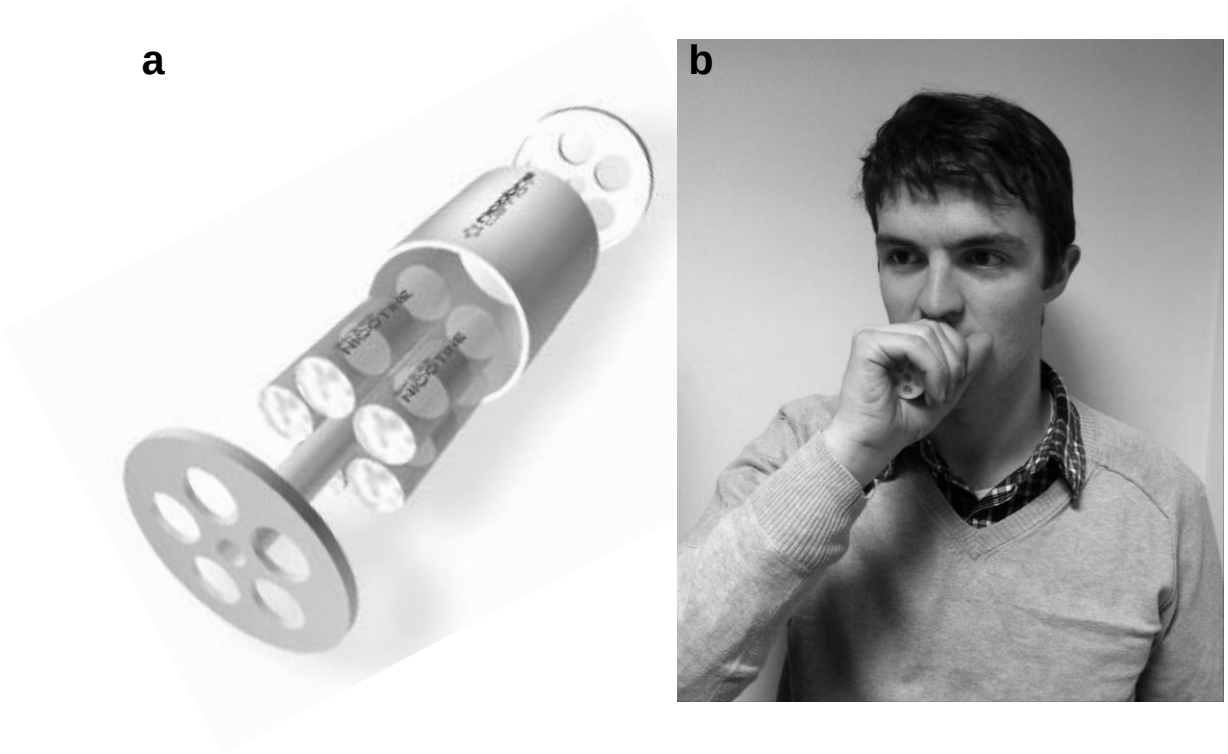

Fig.1 Nicotine Cannon; a: Device design, b: Example of use

Initial contact Baseline measures, verbal consent, randomisation[a]	**Day 1** Written consent, CO test, NRT product 1 evaluation	**Day 8** CO test, NRT product 2 evaluation	**Day 15** CO test, NRT product 3 evaluation	**Day 22** CO test, NRT product 4 evaluation, remuneration
On phone		10 h abstinence prior to NRT use (N=24) 1 h abstinence prior to NRT use (N=24)		

Fig.2 Participant flow-chart; [a]Randomisation to both abstinence condition and NRT sequence (24 possible permutations) was computerised

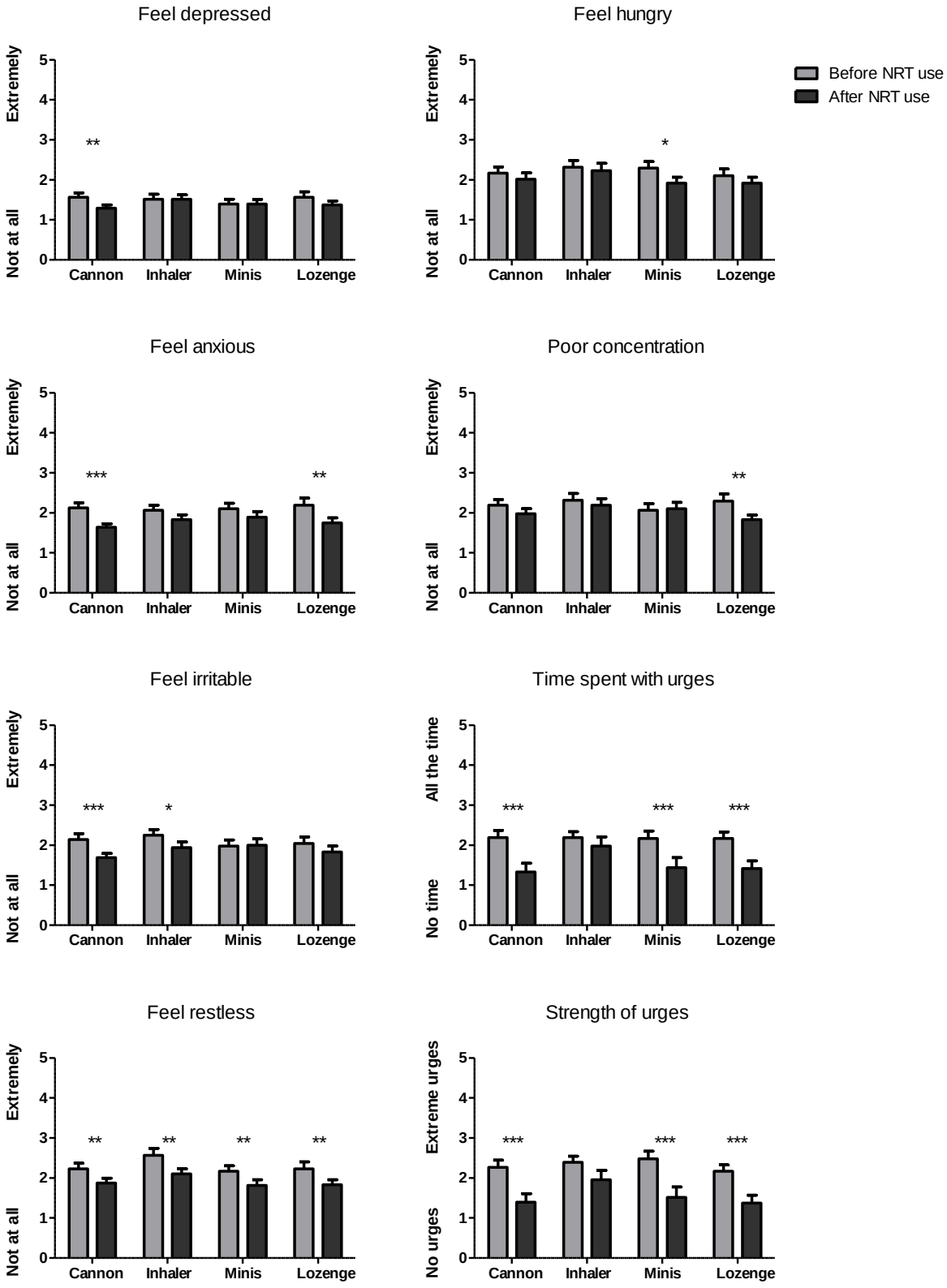

Fig.3 Moods and physical symptoms ratings of cigarette withdrawal before and after NRT use by product; *p<0.05, **p<0.01, ***p<0.001; data are presented as mean, error bars are standard error of the mean

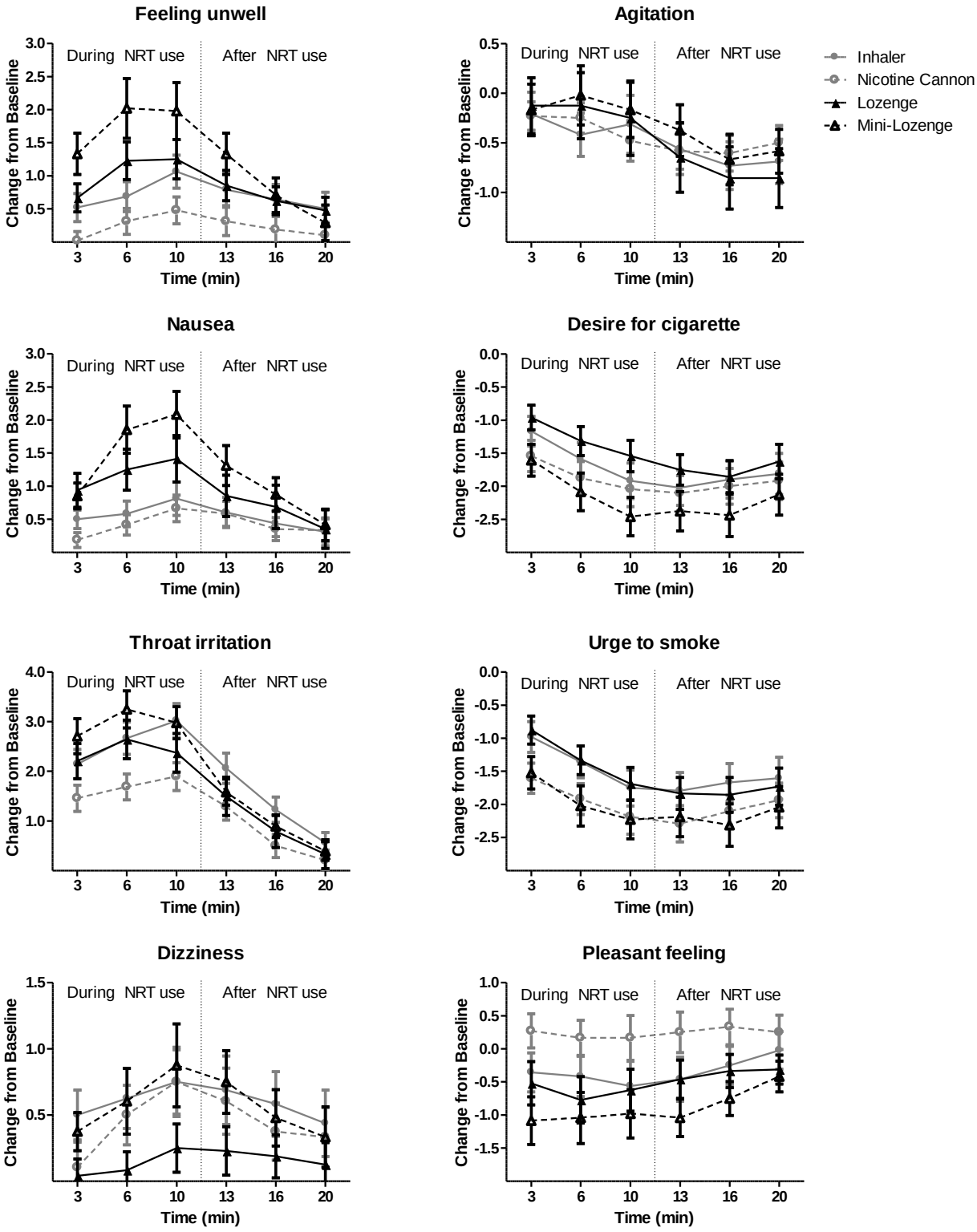

Fig.4 Change in symptoms of NRT use during and after NRT use by product; data are presented as mean, error bars are standard error of the mean

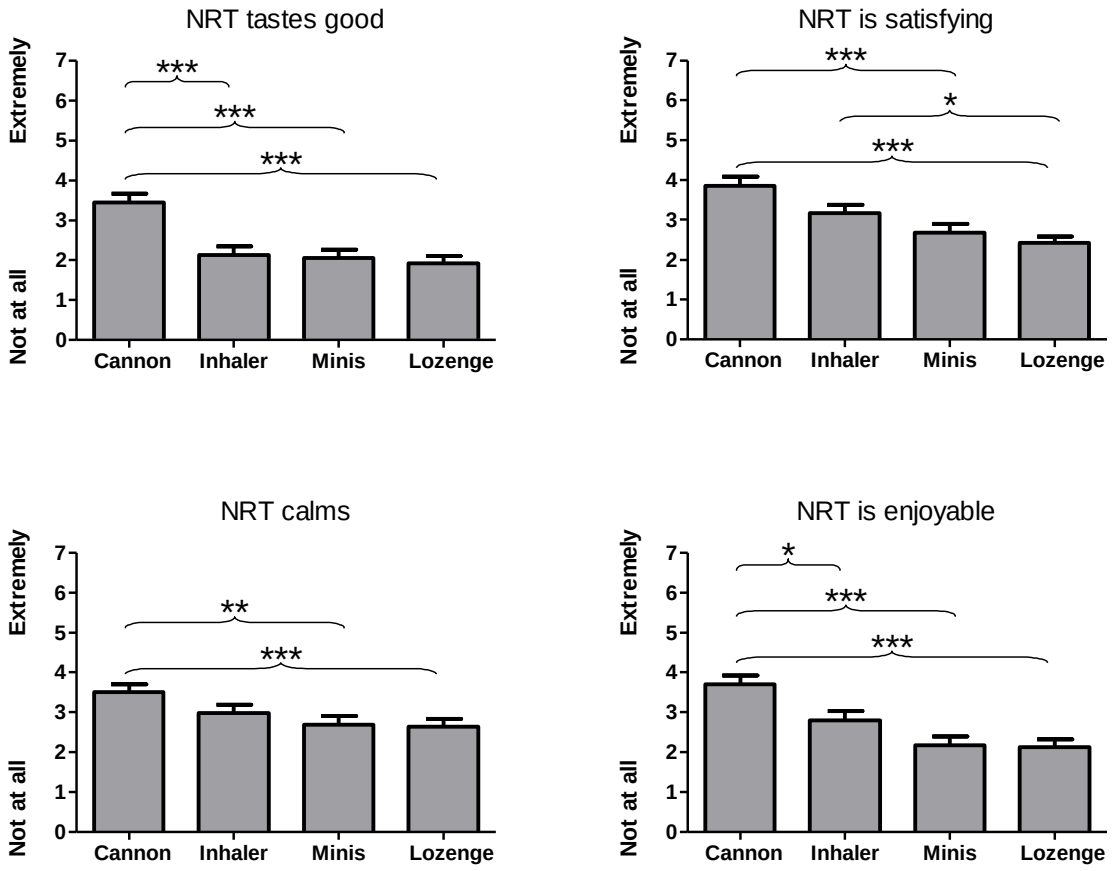

Fig.5 NRT satisfaction by product; *p<0.05, **p<0.01, ***p<0.001; data are presented as mean, error bars are standard error of the mean

Tables

	Total Sample (n=48)	1h Abstinence (N=24)	10h Abstinence (N=24)	P
Socio-demographic characteristics				
Mean (SD) Age, years	31.0 (11.3)	30.3 (9.3)	31.7 (13.1)	*0.667*
% (N) Male	54.2 (26)	66.7(16)	41.7 (10)	*0.073*
% (N) Single	81.3 (39)	87.5 (21)	75.0 (18)	*0.468*
% (N) Ethnicity				
White	62.5 (30)	58.3 (14)	66.7 (16)	
Black	8.3 (4)	16.7 (4)	0 (0)	
Asian	12.5 (6)	12.5 (3)	12.5 (3)	*0.263*
Mixed	8.3 (4)	4.2 (1)	12.5 (3)	
Other	8.3 (4)	8.3 (2)	8.3 (2)	
% (N) Education				
GSCE/Equivalent	8.3 (4)	8.3 (2)	8.3 (2)	
A-level/Equivalent	27.1 (13)	37.5 (9)	16.7 (4)	
Degree/Equivalent	56.3 (27)	50.0 (12)	62.5 (15)	
Other	8.3 (4)	4.2 (1)	12.5 (3)	
Smoking characteristics				
Mean (SD) Age started to smoke	17.7 (3.6)	17.9 (3.0)	17.4 (4.1)	*0.646*
Cigarettes smoked per day				
≤10	37.5 (18)	29.2 (7)	45.8 (11)	
11-20	56.3 (27)	62.5 (15)	50.0 (12)	*0.459*
21-30	6.3 (3)	8.3 (2)	4.2 (1)	
31+	0 (0)	0 (0)	0 (0)	
Mean (SD) HSI score[a]	2.3 (1.1)	2.6 (1.1)	2.0 (1.1)	*0.075*
Mean (SD) CO reading, ppm[b]	5.5 (4.4)	8.2 (4.7)	2.9 (1.5)	*<0.001*
% (N) Previous quit attempt	60.4 (29)	75.0 (18)	45.8 (11)	*0.038*
Mean (SD) Length of previous quit attempt (days)	21.2 (36.6)	14.0 (20.9)	28.4 (46.8)	*0.177*
Mean (SD) Intention to stop next month[c]	3.4 (1.7)	3.4 (1.6)	3.3 (1.8)	*0.932*
% (N) used NRT before	27.1 (13)	37.5 (9)	16.7 (4)	*0.104*

Table 1 Participant characteristics; [a]HSI: Heaviness of smoking index, scale from 0-6; [b]ppm – parts per million; [c]On scale from 1 (very unlikely) – 7 (very likely)