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Tratamiento del tabaquismo en personas con trastorno por uso de sustancias

Smoking cessation treatment in individuals with substance use disorder

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RESUMEN DEL CONTENIDO DE TESIS DOCTORAL

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RESUMEN (en español)

La prevalencia de consumo de tabaco en personas con trastorno por uso de sustancias (TUS) es hasta cuatro veces mayor en comparación con la que se encuentra en población general. Además, los fumadores con TUS presentan mayores dificultades para alcanzar la abstinencia tabáquica y elevadas tasas de recaída. Hasta la fecha, se han realizado muy pocos estudios clínicos para examinar la efectividad a largo de plazo de los tratamientos para dejar de fumar en esta población. El objetivo de la presente Tesis Doctoral fue evaluar la efectividad a corto y largo plazo de dos protocolos de tratamiento psicológico para el abordaje del tabaquismo en personas en tratamiento ambulatorio por TUS. Se definieron los siguientes objetivos específicos: 1) realizar una revisión sistemática y metaanálisis de la efectividad del manejo de contingencias (MC) para dejar de fumar en personas con TUS; 2) estudiar la factibilidad y la aceptabilidad de implementar una terapia cognitivo-conductual (TCC) para dejar de fumar en combinación con el pensamiento episódico futuro (PEF); 3) analizar el efecto aditivo a corto plazo del MC comparado con la TCC + PEF sobre la abstinencia tabáquica y otras variables relevantes en el tratamiento, como es la retención, la asistencia a las sesiones y la adherencia a las pautas de reducción del consumo; 4) examinar el efecto específico del PEF sobre las variables constitutivas de la patología del refuerzo (i.e., toma de decisiones impulsiva y demanda hipotética de cigarrillos); y 5) analizar la eficacia aditiva, a corto y largo plazo, de añadir un componente de MC a una TCC + PEF, así como examinar la relación entre la abstinencia tabáquica y la abstinencia a otras sustancias. Los resultados mostraron que añadir un componente de MC para dejar de fumar mejora significativamente las tasas de abstinencia y reducción del consumo de tabaco a corto plazo, aunque su efecto disminuye a largo plazo. Además, la abstinencia tabáquica no impacta negativamente en la abstinencia de otras sustancias. Por último, el PEF ha mostrado ser factible, en términos de tasas de adherencia a la práctica del PEF, así como eficaz en la reducción del descuento por demora y la demanda de cigarrillos. En definitiva, el tratamiento que combina TCC con PEF y MC es un tratamiento factible, aceptable y eficaz a corto plazo para dejar de fumar en personas en tratamiento ambulatorio por TUS. Los resultados de esta Tesis Doctoral respaldan la necesidad de ofertar de forma sistemática programas de cesación tabáquica, así como la recomendación de dejar de fumar, a los fumadores en tratamiento ambulatorio por consumo de sustancias.

RESUMEN (en Inglés)

The prevalence of tobacco use in individuals with substance use disorder (SUD) is up to four times higher compared to that found in the general population. In addition, smokers with SUD present greater difficulties in achieving smoking abstinence, and elevated relapse rates. To date, very few clinical studies have been conducted to examine the long-term effectiveness of smoking cessation treatments in this population. The objective of this Doctoral Thesis was to evaluate the short- and long-term effectiveness of two psychological treatment protocols for smoking cessation in individuals undergoing outpatient treatment for SUD. The following specific objectives were defined: 1) to conduct a systematic review and meta-analysis of the effectiveness of contingency management (CM) for smoking cessation in individuals with SUD; 2) to study the feasibility and acceptability of implementing cognitive-behavioral therapy (CBT) for smoking cessation in combination with episodic future thinking (EFT); 3) to analyze the additive effect of CM compared to CBT + EFT on smoking abstinence at short-term, and other relevant intervention variables, such as retention, session attendance, and adherence to reduction guidelines; 4) to examine the specific effect of EFT on the constitutive variables of reinforcement pathology (i.e., impulsive decision making and hypothetical cigarette demand); and 5) to analyze the additive short- and long-term efficacy of adding a CM component to a CBT + EFT, as well as to examine the relationship between smoking abstinence and abstinence from other substances. The results showed that adding a CM component for smoking cessation significantly improves tobacco abstinence rates and smoking reduction at short-term, although its effect decreases at long-term. Additionally, smoking abstinence does not negatively impact abstinence from other substances. Finally, EFT has been shown to be feasible, in terms of adherence rates to the practice of the EFT, as well as effective in reducing delay discounting and cigarette demand. In conclusion, the treatment that combines CBT with EFT and CM is a feasible, acceptable, and effective treatment for smoking cessation in individuals undergoing outpatient treatment for SUD. The findings of this Doctoral Thesis support the need to systematically offer smoking cessation programs, as well as the recommendation to quit smoking, to smokers receiving outpatient treatment for substance use.

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1. Introducción

El consumo de tabaco es la principal causa aislada de mortalidad prevenible en el mundo, ya que es responsable de más de ocho millones de muertes anuales en el mundo (Organización Mundial de la Salud, 2021) y casi 60.000 en España (Ministerio de Sanidad, Servicios Sociales e Igualdad, 2016). Se estima que el 13% de las muertes en mayores de 35 años en nuestro país son atribuibles al tabaco (23% en hombres y 3% en mujeres) (Ministerio de Sanidad, Servicios Sociales e Igualdad, 2016).

El consumo de tabaco se considera un problema de salud pública, no solo por su alta toxicidad, sino también por su adicción, su elevada prevalencia y su evitabilidad. Se relaciona con una reducción en la esperanza de vida, así como con enfermedades cardiovasculares (e.g., enfermedad vascular periférica, accidente cerebrovascular) (Roy et al., 2017), respiratorias (e.g., enfermedad pulmonar obstructiva crónica) (Soriano et al., 2020), oncológicas (e.g., cáncer de pulmón, laringe, esófago) (Bade y Dela Cruz, 2020; Nocini et al., 2020) y problemas de salud mental (e.g., depresión) (Minichino et al., 2013). Todo ello conlleva un importante gasto sociosanitario, estimado en el 5% – 14% del gasto sanitario mundial, lo que supone más de 200.000 millones de dólares anuales, debido a la atención en salud y a la pérdida de productividad de los fumadores (Departamento de Salud y Servicios Humanos de los EE.UU., 2014; Goodchild et al., 2018; Xu et al., 2021).

1.1. Prevalencia del tabaquismo en Europa y España

Los datos epidemiológicos más recientes en Europa indican que el 18,4% de las personas mayores de 15 años consume cigarrillos de forma diaria (21,9% de los hombres y el 15,1% de las mujeres) (EUROSTAT, 2019). En el ámbito nacional, las encuestas estiman que la prevalencia de consumo diario de tabaco en población adulta se sitúa entre el 26% y el 32,3% (Ministerio de Sanidad, Consumo y Bienestar Social, 2017; Plan Nacional sobre Drogas, 2021). Aunque a nivel mundial se encuentra una disminución

significativa de las tasas de tabaquismo, en España la reducción de la prevalencia es muy pequeña (del 33,6% al 32,3% en los últimos 20 años) (Plan Nacional sobre Drogas, 2021), pero los datos de venta de cigarrillos muestran una reducción del 53,4% desde 2001 a 2021 (Ministerio de Hacienda y Función Pública, 2021).

Ante esta situación, distintos organismos y sociedades científicas han señalado de forma consistente la necesidad de dar prioridad al tabaquismo, en términos de endurecer las medidas de control, potenciar los tratamientos de cesación tabáquica y promover las estrategias preventivas (National Institute for Health and Care Excellence, 2021).

1.2. Consumo de tabaco entre las personas con trastorno por uso de sustancias

La prevalencia de consumo de tabaco es aún más elevada entre las poblaciones más vulnerables, como son las personas con trastornos psicológicos (e.g., esquizofrenia, depresión) y, en especial, las personas con trastorno por uso de sustancias (TUS) (Drope et al., 2018; Parker y Villanti, 2021).

De forma consistente, los estudios epidemiológicos indican que las personas con TUS presentan tasas de tabaquismo hasta cuatro veces mayores que las encontradas en población general, situándose entre el 49% y el 86% (Gass et al., 2018; Guydish, Passalacqua, et al., 2016; Guydish et al., 2020; Hayhurst et al., 2020; Ingram et al., 2017; J. Kelly et al., 2019; P. Kelly et al., 2012; Lien et al., 2021; Weinberger et al., 2018). Este porcentaje es más elevado en las personas consumidoras de opioides (85%) (Guydish et al., 2015; Mcclure et al., 2016), seguido de los consumidores de estimulantes (66% – 81%) (Mcclure et al., 2016) y los consumidores de alcohol (64% – 77%) (Fine et al., 2019; Guydish et al., 2015; Mcclure et al., 2016).

En personas con TUS, el consumo de tabaco se relaciona con una peor calidad de vida, un inicio más temprano en el consumo de tabaco, un mayor número de cigarrillos

al día, mayor dependencia a la nicotina, presencia de sintomatología de abstinencia más intensa, así como con mayores dificultades para abandonar el consumo de otras sustancias y mayor vulnerabilidad a la recaída de estas sustancias (Heffner et al., 2011; J. Kelly et al., 2019; Lien et al., 2021; McClure et al., 2014; Parker et al., 2018; Weinberger et al., 2017).

En relación a la calidad y esperanza de vida, las enfermedades relacionadas con el tabaco son un importante factor de morbilidad y mortalidad en esta población (Baca y Yahne, 2009; Hser et al., 1994). Se estima que entre el 36% y el 57% de todas las muertes son atribuibles a enfermedades relacionadas con el consumo de tabaco (Bandiera et al., 2015; Callaghan et al., 2018), siendo mayor la probabilidad de muerte debido al consumo de tabaco que por enfermedades relacionadas con el consumo de alcohol (R. D. Hurt et al., 1996).

1.3. Relación entre tabaquismo y trastorno por uso de sustancias

No se sabe con certeza si el consumo de tabaco es causa del consumo de otras sustancias, consecuencia o tiene un origen común con estas. En un intento de explicar la asociación entre el tabaquismo y los TUS, se han propuestos distintas hipótesis de tipo biológico, psicológico y económico-conductual.

1.3.1. Modelos biológicos

Las hipótesis biológicas tratan de explicar la coocurrencia entre el consumo de tabaco y el TUS a través de variables genéticas y neurobiológicas. Los estudios de consanguinidad (i.e., gemelos monocigóticos, estudios de adopción) estiman que alrededor del 50% de la vulnerabilidad individual al TUS es atribuible a factores genéticos (Juli y Juli, 2015). Los estudios genéticos destacan la importancia de los genes relacionados con el metabolismo de las drogas, los genes relacionados con la recaptación de neurotransmisores y los genes involucrados en la transmisión sináptica del sistema

colinérgico, glutaminérgico y dopaminérgico (Agrawal et al., 2015; Allegrini Msc et al., 2019; Cross et al., 2017; Otto et al., 2017; Prom-Wormley et al., 2017; Vink et al., 2014; Waaktaar et al., 2017). Desde el punto de vista neurobiológico, los estudios han señalado al sistema dopaminérgico mesolímbico (i.e., sistema de recompensa cerebral), donde toman relevancia áreas como el núcleo accumbens y el área tegmental ventral, entre otros (Doyon et al., 2013; Prom-Wormley et al., 2017).

Existen dos tipos de explicaciones neurobiológicas que tratan de dar cuenta del uso concomitante y de las interacciones entre el tabaco y otras sustancias. En primer lugar, el consumo de tabaco puede incrementar el efecto positivo subjetivo de la otra sustancia (i.e., reforzamiento cruzado), ya que ambas sustancias actúan sobre los mismos receptores colinérgicos (i.e., nAChRs), produciendo una liberación aditiva de dopamina en el núcleo accumbens (en comparación con la administración de una única sustancia). En segundo lugar, la tolerancia cruzada, es decir, la administración continuada de nicotina inhibe la función de los receptores, produciendo una disminución del efecto neurotoxicológico de la otra sustancia (e.g., efectos de intoxicación) (Adams, 2017; Verplaetse y Mckee, 2017; Yardley et al., 2015).

1.3.2. Modelos psicológicos

Las hipótesis psicológicas explican la alta concomitancia del consumo de tabaco y otras sustancias aludiendo a factores de aprendizaje individuales y a factores contextuales.

El condicionamiento clásico explica los procesos de adquisición de una conducta adictiva y otros procesos relacionados con la búsqueda de drogas y el *craving*. De acuerdo a este modelo, un estímulo inicialmente neutro (e.g., claves ambientales) adquiere la capacidad de provocar una respuesta condicionada al haber sido presentado junto al consumo de drogas. Concretamente, al presentarse simultáneamente el consumo de tabaco y de otras sustancias, ya sea por un consumo combinado (e.g., cannabis) o por

compartir claves contextuales (e.g., fiesta), fumar un cigarrillo desencadenará el deseo de consumir otras sustancias (Cross et al., 2017).

Desde el condicionamiento operante se entiende que la conducta se produce ante la presencia de un estímulo discriminativo y está mantenida por los reforzadores que le siguen, tanto positivos (e.g., refuerzo social, euforia) como negativos (e.g., eliminación de la sintomatología de abstinencia). El consumo de tabaco y otras sustancias comparten estímulos discriminativos (e.g., parafernalia, contexto lúdico, personas) y, además, el consumo de una sustancia puede actuar como reforzador del consumo de otra, como se observa en el caso del consumo de alcohol y tabaco (Adams, 2017; Fertig y Allen, 1995; Ginsburg et al., 2018).

Por último, la teoría de la responsabilidad común (*common liability theory*) (ver Vanyukov y Ridenour, 2012 para revisión) propone que la relación entre el consumo de tabaco y otras sustancias se atribuye a factores de riesgo compartidos, como por ejemplo características individuales (e.g., elevada impulsividad, dificultades en la regulación emocional, problemas de salud mental), variables microsociales relacionadas con el ámbito familiar (e.g., estilo educativo autoritario), relacional (e.g., consumo del grupo de pares) y académico (e.g., bajo rendimiento académico) y variables macrosociales (e.g., regulación legal) (Gallegos et al., 2021; Lemyre et al., 2019; Swendsen et al., 2010; Van Ryzin et al., 2012).

1.3.3. Modelos económico-conductuales

El modelo de la economía conductual, que integra los principios de la economía y de la psicología, es una forma novedosa de explicar las conductas relacionadas con la salud, incluyendo el consumo de sustancias, (Bhargava y Loewenstein, 2015; Matjasko et al., 2016). La teoría de la patología del refuerzo, sustentada en los modelos de la

economía conductual, conceptualiza la adicción como un trastorno de elección caracterizado por una devaluación de las recompensas futuras asociadas a la abstinencia en detrimento de la gratificación inmediata del consumo. Esta teoría permite explicar los procesos adictivos a pesar de las consecuencias negativas (sociales, económicas y de salud) ocasionadas por el consumo, aludiendo a dos procesos: una valoración excesiva del reforzador (i.e., demanda de la sustancia) y la toma de decisiones impulsiva o descuento por demora (DD) (ver Bickel et al., 2020; González-Roz, Secades-Villa, Martínez-Loredo, et al., 2020 para revisión).

La demanda evalúa la capacidad reforzante de una sustancia mediante la variación de su precio, por lo que se entiende que cuanto menor sea el coste, más probable será su consumo. Las personas con una elevada demanda consumen una cantidad mayor de droga, emplean más recursos para su obtención y son menos sensibles a los incrementos de su coste (Bickel et al., 2014). La demanda se evalúa a través de tareas hipotéticas que examinan la cantidad deseada de droga (e.g., número de cigarrillos) a distintos precios incrementales (González-Roz, Secades-Villa, Weidberg, et al., 2020; Martínez-Loredo et al., 2021). Este tipo de tareas ofrecen cinco indicadores: intensidad de la demanda (i.e., cantidad de sustancia demandada en ausencia de costes o restricción a su acceso), el punto de ruptura (i.e., precio por unidad al que el consumo cesa), O_{max} (i.e., gasto máximo), P_{max} (i.e., precio máximo asociado al gasto máximo) y elasticidad (i.e., sensibilidad de la demanda a un incremento del precio) (González-Roz, Secades-Villa, Martínez-Loredo, et al., 2020).

El DD es un proceso psicológico que denota la preferencia por los reforzadores inmediatos de menor valor objetivo (e.g., efectos positivos del consumo) en lugar de reforzadores demorados de mayor valor objetivo (e.g., buena salud). Se trataría de un indicador transdiagnóstico de diversos problemas de salud mental (Amlung et al., 2019;

Levitt et al., 2022) y, en especial, de las conductas adictivas. En lo relativo al consumo de sustancias, ha sido estudiado como un fuerte predictor del inicio, frecuencia y gravedad del consumo, así como de los resultados de tratamiento (i.e., abstinencia y recaída) (Amlung et al., 2017; Audrain-McGovern et al., 2009; Bickel et al., 2014, 2019; Coughlin et al., 2018; García-Pérez et al., 2021; Kräplin et al., 2020; MacKillop et al., 2011; C. McHugh y Balaratnasingam, 2018). La manera más habitual de evaluar el DD es a través de tareas informatizadas en las que se presentan distintas elecciones: elegir entre una cantidad de dinero inmediata (e.g., 500€), o una cantidad mayor (e.g., 1000€) en distintas demoras fijas (e.g., un día, una semana, un mes, un año). La cantidad inmediata va aumentando su valor para determinar el punto de indiferencia, esto es, el valor subjetivo que se le atribuye al reforzador demorado.

Numerosos estudios han encontrado tasas elevadas de patología del refuerzo (i.e., elevada demanda y DD) en las personas con TUS en comparación con la población general (Bickel et al., 2020). Por esta razón, en los últimos años ha crecido el interés en desarrollar y evaluar intervenciones conductuales que modifiquen la patología del refuerzo (Rung y Madden, 2018; Scholten et al., 2019).

2. Tratamiento del tabaquismo en fumadores con trastorno por uso de sustancias

Los centros de tratamiento de consumo de sustancias representan un entorno óptimo para las intervenciones para dejar de fumar, dado que la integración del tratamiento del tabaquismo en el tratamiento de otras adicciones ofrece un mensaje coherente. Sin embargo, la cesación tabáquica no suele ser considerada una prioridad en las personas con TUS (González-Roz et al., 2019; Kathuria et al., 2019; Parnell et al., 2020). Se estima que alrededor del 10% de los centros asistenciales de TUS proporcionan algún tipo de

tratamiento de cesación tabáquica (Currie et al., 2003). En España, entre el 20% y el 56% de los centros de tratamiento de sustancias ofrecen también intervenciones para dejar de fumar (Becoña et al., 2006; González-Roz et al., 2019; Nieva et al., 2022).

Las principales razones están relacionadas con la ausencia de conocimientos específicos sobre el abordaje del tabaquismo por parte de los terapeutas (Gentry et al., 2017; González-Roz et al., 2019; Nieva et al., 2022; Parnell et al., 2020), la falta de recursos (e.g., financiación y tiempo) (Gentry et al., 2017; González-Roz et al., 2019) y con aspectos estructurales del funcionamiento de los centros de tratamiento de adicciones (e.g., consumo de tabaco como parte de la rutina diaria, ausencia de un control del consumo) (Gentry et al., 2017). Si bien, una de las barreras más extendidas entre los terapeutas y los usuarios es la creencia de que la abstinencia del tabaco aumenta la probabilidad de recaer en el consumo de otras sustancias (Kathuria et al., 2019; R. K. McHugh et al., 2017). La evidencia a este aspecto es mixta: mientras que algunos estudios concluyen que dejar de fumar incrementa el riesgo de recaída (Fu et al., 2008; Weinberger et al., 2017), otros estudios muestran una relación nula (Alessi y Petry, 2014; Kahler et al., 2010; Rohsenow et al., 2015) y otros encuentran que dejar de fumar aumenta la probabilidad de mantenerse abstinente a largo plazo (Kalman et al., 2010; McKelvey et al., 2017; Myers et al., 2007; Prochaska et al., 2004; Thurgood et al., 2016; Tsoh et al., 2011).

Los hallazgos empíricos han mostrado que un elevado porcentaje de esta población desea dejar de fumar (~30%), incluso durante el tratamiento por consumo de sustancias (Fine et al., 2019; Guydish et al., 2020). Sin embargo, el porcentaje de personas que consiguen la abstinencia tabáquica sin un tratamiento es muy bajo, no superando el 1% (Haas et al., 2008), sobre todo si las intervenciones para dejar de fumar son de baja intensidad (e.g., consejo de las 5As, líneas telefónicas) (Vlad et al., 2020). Por otro lado,

tener diagnóstico o historia de TUS es un criterio de exclusión muy común en la mayoría de ensayos clínicos (Leeman et al., 2007), por lo que los resultados de eficacia hallados en población general no pueden ser extrapolados a esta subpoblación de fumadores. Todo ello nos indica la relevancia de animar a las personas con TUS a dejar de fumar, así como a llevar a cabo ensayos clínicos que examinen la eficacia de las intervenciones de cesación tabáquica específicamente en esta población.

En los últimos años ha crecido el interés por promover tratamientos basados en la evidencia para la cesación tabáquica en las personas con TUS. Los estudios han concluido que las intervenciones para dejar de fumar dirigidas a los fumadores con TUS aumentan la abstinencia tabáquica, aunque las tasas alcanzadas sean significativamente inferiores a las observadas en población general. El metaanálisis de Apollonio et al. (2016) indica que el 12,2% consigue la abstinencia a largo plazo, en comparación con el 7,3% en los grupos de comparación. Otros hallazgos señalan que entre el 6,6% y el 18,3% de las personas en tratamiento y el 8,8% – 19,6% de las que se encuentran en recuperación consiguen la abstinencia tabáquica a partir de los seis meses de seguimiento (Apollonio et al., 2016; Prochaska et al., 2004).

Aunque los fumadores con TUS parecen responder a los mismos tratamientos que han mostrado ser eficaces en población general (Schroeder y Morris, 2010), los estudios muestran que esta población parece beneficiarse de intervenciones más intensivas, esto es, tratamientos extendidos en el tiempo, sesiones más frecuentes y adaptadas a sus características (e.g., mayores niveles de dependencia a la nicotina, impulsividad y presencia de otros trastornos psicológicos) (Richter y Arnsten, 2006; Schroeder y Morris, 2010).

2.1. Tratamientos farmacológicos para dejar de fumar en personas con trastorno por uso de sustancias

Existen tres fármacos de primera línea para el tratamiento del tabaquismo, cuya eficacia y seguridad se encuentra respaldada tanto por la Administración de Medicamentos y Alimentos de los Estados Unidos (FDA) como por la Agencia Europea de Medicamentos (EMA): terapia sustitutiva de la nicotina (TSN), vareniclina y bupropión. Las revisiones sistemáticas han evidenciado que estos fármacos aumentan significativamente la probabilidad de estar abstinente un año después (odds ratio entre 1,5 y 3,1) alcanzando tasas de abstinencia entre el 18% y el 36% (Cahill et al., 2013; Howes et al., 2020; Hughes et al., 2016; Stead et al., 2012; U.S. Public Health Service, 2008).

Los estudios que examinan la eficacia de estos tres fármacos en personas con TUS presentan importantes limitaciones. Las tasas de abstinencia encontradas resultan difíciles de interpretar dada la heterogeneidad de las muestras utilizadas (e.g., consumidores de alcohol y cocaína), los diseños de investigación (e.g., ausencia de un grupo de control), los tamaños muestrales (e.g., menores a 20 personas por grupo) y la longitud de los seguimientos (i.e., menor a seis meses). Se presenta a continuación una síntesis de la eficacia de los fármacos mencionados en fumadores con TUS.

2.1.1. Terapia sustitutiva de la nicotina

La TSN consiste en la administración de nicotina por una vía de administración con una velocidad de absorción menor que la inhalada, propia del consumo de tabaco. Para ello, se han diseñado varios dispositivos que se administran por vía oral (comprimidos, chicles o spray bucal), vía transdérmica (parches) y vía nasal (inhalador).

La evidencia relativa a los fumadores con TUS indica que entre el 2,4% y el 8,3% de los fumadores en un programa de mantenimiento de metadona (Heydari et al., 2014;

Reid et al., 2008; M. B. Stein et al., 2013) y el 35,5% de los fumadores con trastorno por uso de alcohol (N. Cooney et al., 2009) consigue la abstinencia tabáquica a los seis meses. Si bien, estas tasas no difieren de las alcanzadas por el grupo control. Una de las alternativas propuestas es el aumento de la intensidad de la TSN, en términos de aumentar la dosis, aplicarla durante más tiempo, o combinarla (e.g., parches con chicles), lo que ha evidenciado mejorar las tasas de abstinencia a largo plazo en población general (Schlam et al., 2016; Schnoll et al., 2015). No obstante, el único estudio que ha analizado la eficacia de una mayor dosis de parches en fumadores con TUS, encontró que el grupo con parches de 42 mg alcanzó un 9,2% de abstinencia, comparado con el 16,9% de fumadores asignados al grupo de parches de 21 mg. Este estudio concluye que una mayor dosis de los parches de nicotina no aumenta significativamente las tasas de abstinencia tabáquica (Kalman et al., 2006).

2.1.2. Vareniclina

La vareniclina se trata del primer fármaco creado ad-hoc para dejar fumar tras su aprobación por la FDA y por la EMA en 2006. Es un agonista parcial de los receptores nicotínicos α4β2 de la acetilcolina, es decir, en ausencia de nicotina actúa como agonista, mientras que en presencia de nicotina actúa como antagonista. Es preciso señalar que todos los estudios realizados hasta el momento con vareniclina han utilizado Champix® o Chantix® (nombre con el que se comercializa este medicamento fabricado por Pfizer), cuyo fármaco fue retirado del mercado en julio de 2021 por su contenido en nitrosaminas.

Los resultados relativos a la eficacia de la vareniclina en fumadores con TUS son mixtos. En los fumadores con trastorno por uso de alcohol, entre un 9,4% y un 31,3% alcanza la abstinencia del tabaco a los tres meses (Bold et al., 2019; R. T. Hurt et al., 2018; O'Malley et al., 2018; Zawertailo et al., 2020) y un 6,3% – 22,5% está abstinente

a los 12 meses (Bold et al., 2019; Raich et al., 2018). En personas en un programa de mantenimiento de metadona, las tasas de abstinencia son del 8,3% – 15,4% a los tres meses (Poling et al., 2010; M. D. Stein et al., 2006), 3,6% – 4,7% a los seis meses (M. B. Stein et al., 2013; M. D. Stein et al., 2006) y 17,7% a los 12 meses (Raich et al., 2018). El metaanálisis de Guo et al. (2021) concluye que la vareniclina tiene un efecto aditivo a corto plazo (i.e., menor a 12 semanas) frente a los grupos de comparación, pero que dicho efecto desaparece a partir de las 12 semanas. La combinación de vareniclina con parches de nicotina ha mostrado ser eficaz para dejar de fumar a corto plazo en fumadores con un patrón de uso problemático de alcohol (44,3% vs. 27,9%) (King et al., 2022).

2.1.3. Bupropión

El bupropión, originalmente comercializado como antidepresivo, fue el primer fármaco no nicotínico que aprobó la FDA para el tratamiento del tabaquismo en 1997 en EEUU y la EMA en el 2000 en Europa. Se comporta funcionalmente como un antagonista no competitivo de los receptores nicotínicos y además inhibe la recaptación de dopamina y noradrenalina.

Con respecto a los fumadores con TUS, debido al riesgo de crisis convulsivas, el bupropión está contraindicado en personas en fase de desintoxicación por consumo de alcohol o benzodiacepinas. La evidencia relativa al bupropión en personas con trastorno por uso de alcohol indica que el 6% – 16,7% consigue la abstinencia a los seis meses, aunque las diferencias con el grupo control no son significativas (Grant et al., 2007; Kalman et al., 2011). Solo hay un estudio que analiza el efecto del bupropión en fumadores en un programa de mantenimiento de metadona, el cual concluye que el 15,8% consigue la abstinencia tabáquica a las 12 semanas, cuya tasa no difiere de la encontrada en el grupo control (10%) (Mooney et al., 2008).

2.2. Tratamientos psicológicos para dejar de fumar en personas con trastorno por uso de sustancias

Los tratamientos psicológicos para dejar de fumar surgen en la década de los 60 del pasado siglo con el surgimiento de las técnicas de modificación de conducta. Las primeras terapias que mostraron eficacia fueron las de tipo aversivo (e.g., fumar rápido, saciación) (Hajek y Stead, 2004), seguidas de las de reducción gradual de la ingesta de nicotina y alquitrán (Becoña, 2007) y la prevención de recaídas (Marlatt y Gordon, 1985), entre otras.

Los estudios de revisión y de metaanálisis que recogen información sobre la eficacia del tratamiento psicológico presentan varias limitaciones. En primer lugar, se considera tratamiento psicológico a cualquier intervención no farmacológica (e.g., consejo breve, autoayuda, línea telefónica), llevada a cabo por cualquier profesional, sin ser necesariamente un psicólogo (e.g., médicos o enfermeros). Todo ello resulta en una elevada heterogeneidad de resultados que dificulta el establecimiento de conclusiones firmes sobre el tratamiento psicológico para dejar de fumar (Fernández et al., 2014).

Respecto al formato del tratamiento, los estudios indican que tanto la terapia individual como la terapia en grupo son eficaces para dejar de fumar ($OR \geq 1{,}3$) (Hartmann-Boyce et al., 2014; U.S. Public Health Service, 2008). Los metaanálisis concluyen que la terapia individual es menos efectiva que la grupal ($OR = 0{,}78$; IC95% 0,64 – 0,95) (Hartmann-Boyce et al., 2022), o que no hay diferencias significativas entre ambas ($OR = 0{,}99$; IC95% 0,76 – 1,28) (Stead et al., 2017). Por lo que el tratamiento en grupo sería más eficiente, en términos de reducción de costes asociados a los recursos humanos (tiempo y coste de los terapeutas). En relación al número de sesiones, la evidencia sugiere la existencia de una relación dosis-respuesta entre el número de

sesiones y la efectividad del tratamiento, siendo más efectivo el tratamiento de ocho sesiones (*OR* = 2,3; IC95% 2,1 – 3,0) (U.S. Public Health Service, 2008).

A pesar de la evidencia acumulada sobre el tratamiento psicológico del tabaquismo, en la actualidad hay varias barreras que provocan una falta de ensayos clínicos que evalúen estas intervenciones y que además dificultan su implementación en contextos clínicos: 1) la falta de psicólogos clínicos dentro del sistema público de salud; 2) la ausencia de formación especializada de los psicólogos en el ámbito del tabaquismo; 3) la publicidad de las terapias farmacológicas, específicamente la TSN, en medios de comunicación; 4) la financiación del bupropión y la vareniclina –hasta julio de 2021– dentro del sistema público de salud; y 5) el deseo de los fumadores de dejar de fumar con el mínimo esfuerzo posible (Becoña et al., 2014).

En coherencia con la temática de la presente Tesis Doctoral, a continuación, se exponen las principales evidencias de la eficacia de la terapia cognitivo-conductual (TCC), el pensamiento episódico futuro (PEF) y el manejo de contingencias (MC) para dejar de fumar en personas con TUS.

2.2.1. Terapia cognitivo-conductual

Las terapias de corte cognitivo-conductuales se asientan en los principios derivados de la teoría del comportamiento, la teoría del aprendizaje social y la terapia cognitiva. Desde su emergencia en los años 80 del siglo XX, la TCC ha sido la intervención más empleada y evaluada a lo largo de la historia del tratamiento psicológico del tabaquismo. En líneas generales, la TCC consiste en el desarrollo de habilidades y estrategias dirigidas a lograr y mantener la abstinencia (Perkins et al., 2007; Sánchez-Hervás et al., 2004).

El tratamiento multimodal o multicomponente (ver e.g., Alonso-Pérez et al., 2014; Becoña, 2007; Ochoa-Prieto et al., 2010; Suárez-Varela Úbeda et al., 2019; Wen et al.,

2019) es un programa cognitivo-conductual que se caracteriza por el uso combinado de varias técnicas (i.e., técnicas motivacionales, técnicas específicas para el abandono del consumo y técnicas centradas en la prevención de recaídas) dirigidas a los factores que mantienen la conducta de fumar. Los componentes que se incluyen habitualmente en los programas multicomponentes son el feedback bioquímico, análisis funcional de la conducta de fumar, razones para dejar de fumar, entrenamiento en relajación, autoinstrucciones, control estimular, técnicas de solución de problemas y prevención de recaídas, entre otros. Los tratamientos multicomponentes constan habitualmente de tres fases: 1) fase de preparación, donde se incide en la motivación para el cambio, en el compromiso para dejar de fumar y en las razones para la cesación; 2) fase de abandono, donde se implementan las estrategias y técnicas que han demostrado ser efectivas para dejar de fumar; y 3) fase de mantenimiento, donde se trabajan las estrategias de afrontamiento del síndrome de abstinencia, el manejo de las caídas, e identificación y manejo de situaciones de alto riesgo.

En relación a su eficacia en población general, la TCC produce un efecto significativo a largo plazo en comparación con los grupos de control cuando se combina con TSN (31,22% vs. 23,26%) o con medicación (34,7% vs. 25,8%) (Denison et al., 2017). En concreto en los fumadores con TUS, muy pocos estudios han examinado la eficacia de la TCC para dejar de fumar. Las tasas de abstinencia oscilan entre el 0% y el 10,6% a los seis meses y entre el 5,6% y el 46,2% a los 12 meses después de finalizar el tratamiento (Hall et al., 2018; Mueller et al., 2012; Patten et al., 1998; Rüther et al., 2016).

2.2.2. Pensamiento episódico futuro

Una de las intervenciones más prometedoras sustentadas en la teoría de la patología del refuerzo es el PEF, esto es, la capacidad que tiene una persona de imaginar y simular

eventos que pueden ocurrir en el futuro (Atance y O'Neill, 2001). Surge como una manipulación experimental de la toma de decisiones impulsiva y en los últimos años se conforma como una intervención susceptible de ser aplicada en contextos clínicos.

La técnica consiste en describir y visualizar vívidamente un evento futuro, cuyo objetivo es la mejora en los procesos de toma de decisiones incrementando la valoración de los reforzadores demorados asociados a la abstinencia (Morris et al., 2020; Schacter et al., 2017). Desde el punto de vista procedimental, las personas generan eventos futuros asociados a situaciones de no consumo incluyendo detalles espaciales, temporales, secuenciales, sensoriales, cognitivos y emocionales y, por último, generan una frase corta que evoque dicho evento creado (e.g., "en un mes celebro mi cumpleaños"). Una vez generado el evento de forma escrita, se visualiza durante 2-5 minutos y se puntúan distintas características de dicha visualización (e.g., realismo, viveza, disfrute, importancia, relevancia personal) (Hollis-Hansen et al., 2019).

Hasta el momento, distintos estudios han examinado el efecto del PEF sobre la patología del refuerzo (i.e., DD y demanda) y el consumo de sustancias en contextos experimentales. En general, los hallazgos indican que el PEF reduce significativamente el DD en fumadores (Athamneh et al., 2021; Chiou y Wu, 2017; J. S. Stein et al., 2016, 2018), consumidores de alcohol (Athamneh et al., 2022; Bulley y Gullo, 2017; Mellis et al., 2019; Patel y Amlung, 2020; Snider et al., 2016), de cannabis (Sofis et al., 2020, 2021) y de cocaína (Forster et al., 2021). Respecto a los hallazgos del PEF sobre la demanda de consumo de sustancias, los estudios muestran que tiene un efecto sobre el punto de ruptura (Patel y Amlung, 2020), O_{max} (Voss et al., 2022), P_{max} (Patel y Amlung, 2020) y especialmente sobre la intensidad de la demanda (Athamneh et al., 2021; Bulley y Gullo, 2017; Patel y Amlung, 2020; Snider et al., 2016; J. S. Stein et al., 2018; Voss et al., 2022). Por último, también ha mostrado reducir el consumo de cigarrillos (Chiou y Wu, 2017; J.

S. Stein et al., 2016), alcohol (Athamneh et al., 2022; Voss et al., 2022), cannabis (Sofis et al., 2021) y cocaína (Forster et al., 2021). Recientemente, el PEF se ha comenzado a implementar en contextos clínicos dirigidos a personas consumidoras de sustancias (Forster et al., 2021; Patel y Amlung, 2020), pero aún existen pocos estudios y los resultados no son concluyentes.

2.2.3. Manejo de contingencias

A finales de los años 70 del pasado siglo, a la luz de las bajas tasas de abstinencia observadas en los tratamientos para las adicciones, se comienza a discutir qué componentes podrían mejorar los resultados y asegurar la abstinencia inicial, un fuerte predictor de la abstinencia a largo plazo (Stitzer, 1999). De esta manera, al conceptualizar el consumo de drogas como conducta, se comienzan a aplicar los principios del condicionamiento operante en el ámbito de las adicciones, surgiendo así el MC. En la actualidad, cuenta con más de una decena de metaanálisis y revisiones sistemáticas que avalan su efectividad para el tratamiento de sustancias (Ainscough et al., 2017; Benishek et al., 2014; Davis et al., 2016; Getty et al., 2019; Ginley et al., 2021; Griffith et al., 2000; Hartzler et al., 2012; Lussier et al., 2006; McPherson et al., 2018; Prendergast et al., 2006; Sayegh et al., 2017; Secades-Villa et al., 2015), incluyendo el tabaquismo (Cahill et al., 2015; Notley et al., 2019; Sigmon y Patrick, 2012).

El MC se fundamenta en el análisis del consumo de sustancias como una conducta operante que se mantiene o se modifica por las consecuencias que le siguen. De forma específica, el MC conlleva la aplicación sistemática de reforzamiento positivo contingente a la conducta objetivo, la cual puede estar relacionada con el consumo de sustancias (e.g., abstinencia o reducción del consumo), o con otros objetivos terapéuticos (e.g., asistencia a las sesiones, adherencia a las pautas, toma de medicación) que compiten

con el valor reforzante asociado al consumo de sustancias (Secades-Villa et al., 2021). Existen varios procedimientos de MC que han mostrado ser eficaces (Ginley et al., 2021), como es el *fishbowl* o programa de la pecera (i.e., reforzador de razón variable) (Benishek et al., 2014), o el MC basado en incentivos, siendo este el procedimiento que ha recibido una mayor atención. El MC basado en incentivos se sirve de la entrega de reforzadores tangibles, como por ejemplo incentivos, *vouchers*, privilegios clínicos, el acceso a empleo o alojamiento, o descuentos canjeables por bienes y servicios en la comunidad (Higgins et al., 2008).

Los principios generales de la aplicación del MC son los siguientes: 1) seleccionar y monitorizar frecuentemente la conducta objetivo mediante pruebas objetivas (e.g., bioquímicas); 2) aplicar el reforzador de forma contingente e inmediata a la emisión de la conducta objetivo; 3) incrementar el valor del incentivo para reforzar la abstinencia continuada (i.e., reforzamiento incremental de razón fija); y 4) reiniciar la magnitud del reforzador a niveles iniciales tras el incumplimiento de la conducta objetivo (Higgins et al., 2007; Lussier et al., 2006; Pfund et al., 2021; Rash y DePhilippis, 2019).

La investigación ha concluido que la eficacia del MC se relaciona con las siguientes características: 1) magnitud o intensidad del reforzador suficiente para competir con el valor reforzante del consumo, 2) inmediatez entre la conducta objetivo y el reforzador, 3) frecuencia de entrega de los reforzadores de un mínimo de dos veces a la semana (Rash y DePhilippis, 2019); e 4) incremento del reforzador y reinicio de la magnitud al no cumplir la conducta objetivo (Pfund et al., 2021; Rash y DePhilippis, 2019). En relación a la magnitud de los reforzadores, los estudios señalan que la cantidad del reforzador no es la variable más relevante y que incentivos de gran magnitud (i.e., mayores a 300$) no redundan necesariamente en tasas de abstinencia más elevadas (Breen et al., 2020; Petry et al., 2015).

En los últimos años, el número de estudios que han examinado la eficacia del MC para dejar de fumar se han incrementado considerablemente, en especial en aquellas poblaciones de riesgo o subgrupos de fumadores que presentan una mayor dificultad para alcanzar la cesación tabáquica, como son las mujeres embarazadas (Hand et al., 2017), adolescentes (Harvanko et al., 2019, 2020), personas con trastorno mental grave (Destoop et al., 2021; Tidey et al., 2011), personas sin hogar (Rash et al., 2018) o fumadores con TUS.

Con respecto al MC en fumadores con TUS, los estudios señalan tasas de abstinencia tabáquica que se sitúan entre el 25,5% y el 60,6% al final del tratamiento (J. L. Cooney et al., 2017; N. Cooney et al., 2015; Dunn et al., 2010; Hunt et al., 2010; Shoptaw et al., 2002; Sigmon et al., 2016; Tuten et al., 2012; Winhusen et al., 2014), 3% – 13,1% a los seis meses de seguimiento (J. L. Cooney et al., 2017; Drummond et al., 2014; Rohsenow et al., 2015, 2017; Winhusen et al., 2014) y 2,2% – 4,1% al año (Rohsenow et al., 2015, 2017; Shoptaw et al., 2002).

A pesar de su eficacia demostrada, el MC es un tratamiento para dejar de fumar con una baja implantación en el contexto clínico (Benishek et al., 2010). Varios factores dan cuenta de ello (ver Gagnon et al., 2020; Ledgerwood, 2008; Petry et al., 2017 para revisión). Uno de los motivos más extendidos es su alto coste percibido a pesar de que el MC ha mostrado ser costo-eficaz en distintas poblaciones (González-Roz, Weidberg, et al., 2021; López-Núñez et al., 2016; Olmstead et al., 2007; Olmstead y Petry, 2009; Van den Brand et al., 2019). No obstante, se han propuesto varias alternativas que solventan el coste relacionado con los incentivos, como es la búsqueda de financiación externa, considerar fuentes de reforzamiento naturales de tipo no monetario (e.g., privilegios clínicos), o utilizar otros procedimientos de MC, tal como el programa de la pecera (Alessi et al., 2008; Alessi y Petry, 2014) o el uso de depósitos de dinero (Jarvis y Dallery,

2017; Stedman-Falls y Dallery, 2020). Por otro lado, una de las condiciones requeridas por el MC es la monitorización frecuente del consumo, lo que supone la necesidad de verificar el consumo de tabaco varias veces por semana. En la actualidad, las nuevas tecnologías ofrecen alternativas a la verificación bioquímica del consumo de forma presencial (e.g., análisis del monóxido de carbono en aire espirado) mediante el uso de dispositivos electrónicos conectados al teléfono personal (Beckham et al., 2018; Getty et al., 2019; Kendzor et al., 2022). Por último, una de las cuestiones que más crítica ha suscitado es el mantenimiento de los efectos del MC a largo plazo una vez que los incentivos han sido retirados. La evidencia a este respecto es mixta: algunos estudios indican que los efectos disminuyen (Benishek et al., 2014; Prendergast et al., 2006; Sayegh et al., 2017), mientras que otros concluyen que el efecto aditivo se mantiene (Davis et al., 2016; Ginley et al., 2021). Esta disparidad de resultados se debe a las diferencias en la evaluación de la abstinencia (i.e., autoinformada o verificada bioquímicamente) y al tipo de tratamiento recibido, en términos de intensidad y modalidad (i.e., ambulatorio, residencial, programa de reducción de daños).

3. Limitaciones de la investigación previa

La investigación en el ámbito del tabaquismo en personas con TUS presenta algunas limitaciones que se exponen a continuación. Algunas de estas limitaciones han sentado las bases y los objetivos de los estudios que componen la presente Tesis Doctoral.

En primer lugar, existe una escasa investigación clínica centrada en la evaluación de la efectividad de los tratamientos para dejar de fumar en la población con TUS. Como se ha comentado con anterioridad, la mayoría de los estudios en población general presentan como criterio de exclusión presentar TUS, por lo que los hallazgos no pueden ser extrapolados a esta subpoblación.

Además, los estudios realizados con personas con TUS presentan notables limitaciones relacionadas con el bajo tamaño muestral (i.e., menos de 15 personas por grupo), con la heterogeneidad de la muestra (e.g., personas en tratamiento ambulatorio y residencial, personas consumidoras de cocaína y de alcohol), con el diseño de investigación (i.e., imposibilidad de dilucidar el efecto específico de un componente), con la disparidad del tratamiento, en términos de duración, componentes e intensidad, con la brevedad de los seguimientos (e.g., hasta los tres o seis meses) y por último, con la evaluación de la abstinencia tabáquica, dado que no todos los estudios proporcionan medidas de punto de prevalencia o de abstinencia continuada.

Por otro lado, la investigación en MC presenta limitaciones adicionales. En primer lugar, los estudios utilizan diversos procedimientos de MC, como es el programa de la pecera (Alessi et al., 2008; Alessi y Petry, 2014; Winhusen et al., 2014), o MC basado en incentivos (Beckham et al., 2018; Hunt et al., 2010; Tuten et al., 2012). El protocolo de MC es combinado mayoritariamente con tratamientos farmacológicos (ver e.g., J. Cooney et al., 2017; Sigmon y Patrick, 2012), siendo escasos los estudios que combinan el MC con tratamientos psicológicos protocolizados e intensivos, como la TCC. En cuanto a los incentivos, la cantidad que puede ganar una persona oscila entre 10$ (Guydish, Gruber, et al., 2016) y 910$ (Alessi et al., 2008). Por último, hasta la fecha, ningún estudio proporciona incentivos en los seguimientos, lo que ha mostrado ser efectivo en otras poblaciones de fumadores (Secades-Villa, González-Roz, et al., 2019). Estas limitaciones impiden establecer conclusiones firmes acerca de qué características del MC, en términos de duración, magnitud del incentivo y tipo de procedimiento, maximizan las tasas de abstinencia en los fumadores con TUS.

En relación al PEF, este componente presenta varias limitaciones debido sobre todo a su breve recorrido histórico. Cabe destacar que, hasta la fecha de realización de esta

Tesis Doctoral, solo hay cuatro estudios que implementen en PEF en una muestra de fumadores (Athamneh et al., 2021; Chiou y Wu, 2017; J. S. Stein et al., 2016, 2018). Considerando los estudios de PEF en personas consumidoras de sustancias, la mayoría de los experimentos se realizaron con una única sesión de PEF (ver e.g., J. S. Stein et al., 2016), mientras que la evidencia señala la importancia de la práctica repetida para observar un efecto significativo sobre la disminución del DD (Mellis et al., 2019). En esta línea, en un número elevado de estudios, las demoras (i.e., marcos temporales) propuestas en el trabajo en visualización del PEF coinciden con las demoras utilizadas en la tarea del DD y, además, la frase breve que resume el evento generado en el PEF se presenta durante la tarea del DD. Esta última característica ha suscitado un intenso debate, ya que se concluye que los efectos observados en el DD se deben a la presentación de la frase corta durante la ejecución de la tarea de DD (Rung y Madden, 2019). Además, el grupo de control es variado, mientras que algunos estudios implementan el pensamiento episódico reciente (J. S. Stein et al., 2016), otros consistían en recordar detalles de una historia narrada (Voss et al., 2022). Por último, las tareas hipotéticas de compra para evaluar la demanda de sustancias presentan una gran diversidad en el número y rango de precios empleados; al igual que ocurre con las tareas de elección impulsiva, donde varía el tipo de tarea (i.e., informatizada vs. autoinformada), el número de demoras (entre una demora y siete) y el indicador de elección impulsiva (ver González-Roz, Aonso-Diego, et al., 2021 para revisión).

Otra limitación importante es la notable escasez de evidencia en torno a la relación existente entre la abstinencia del tabaco y otras drogas. Los pocos estudios que analizan este fenómeno proporcionan medidas de resultado dispares (e.g., urgencia de consumir, punto de prevalencia, días de abstinencia continuada, porcentaje de analíticas negativas) (ver e.g., Campbell et al., 1995; Mooney et al., 2008; Orr et al., 2018), lo que dificulta la

comparación de resultados entre los estudios y el establecimiento de conclusiones firmes. Como se ha comentado, los hallazgos a este respecto son mixtos, habiendo resultados que indican que dejar de fumar reduce la probabilidad de mantenerse abstinente de otras drogas, que la abstinencia del tabaco aumenta la probabilidad de mantenerse abstinente, o que hay una relación nula entre ambas variables.

4. Objetivos

Teniendo en cuenta las limitaciones previamente expuestas, el objetivo general de esta Tesis Doctoral fue evaluar la efectividad a corto y largo plazo de dos protocolos de tratamiento psicológico para dejar de fumar en personas en tratamiento ambulatorio por TUS. Los objetivos específicos fueron los siguientes:

1) Realizar una revisión sistemática y metaanálisis de la efectividad del MC para dejar de fumar en personas en tratamiento y en recuperación por TUS.
2) Estudiar la factibilidad y la aceptabilidad de implementar un tratamiento estándar para dejar de fumar, la TCC, en combinación con el PEF.
3) Analizar el efecto aditivo del MC sobre la TCC + PEF sobre la abstinencia tabáquica a corto plazo y otras variables clínicamente relevantes en el tratamiento, como es la retención, la asistencia a las sesiones y la adherencia a las pautas de reducción.
4) Examinar el efecto del PEF, así como de la reducción del consumo de tabaco y el MC, sobre las variables constitutivas de la patología del refuerzo (i.e., DD y demanda).
5) Analizar, en términos de efectividad, el efecto de añadir un componente de MC a una TCC + PEF para dejar a fumar, así como examinar la relación entre la abstinencia tabáquica y la abstinencia a otras sustancias.

5. Publicaciones

La presente Tesis Doctoral se presenta mediante compendio de publicaciones. Se incluyen cinco estudios publicados en revistas internacionales con factor de impacto e indexadas en el *Journal Citation Reports (JCR)*.

5.1. Effectiveness of contingency management for smoking cessation in substance users: a systematic review and meta-analysis

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Factor de impacto: 5.348, Q1, Clinical Psychology (JCR 2020, SSCI)

Objective. We conducted a systematic review and meta-analysis (ID: CRD42019122315) to assess the evidence for the effectiveness of contingency management (CM) to promote smoking abstinence among individuals with substance use disorder or in recovery. **Method.** Databases were PubMed, PsycINFO, Cochrane, and EBSCO. The primary eligibility criteria for inclusion in our meta-analysis were as follows: any study examining the efficacy of CM for smoking cessation that reported smoking abstinence and/or cigarette reductions. The methodological quality of the included studies was assessed using the Effective Public Health Practice Project Quality assessment tool. Publication bias was examined using Egger's regression intercept, the Begg-Mazumdar test, and Tweedie's trim-and-fill approach. **Results.** A total of 22 articles were included, and 13 were included in three meta-analyses: abstinence at posttreatment (12 studies), abstinence at follow-up (8 studies), and reduction outcomes at posttreatment (6 studies). CM was superior to comparison arms in smoking abstinence (RR _ 2.555; 95% CI [1.730, 3.775]; p _ .001) and reduction (SMD = .601; 95% CI [0.372, 0.831]; p = .001) at end-of-treatment. At long-term follow-ups, CM did not show enhanced effects over abstinence beyond those shown in comparison arms (RR = 1.029; 95% CI [0.577, 1.836]; p _ .922). Smoking-cessation treatment (all treatments included CM) and smoking abstinence increased the likelihood of abstinence from alcohol and/or illicit drugs. All studies were rated as being of strong or moderate quality, and no marked presence of publication bias was found. **Conclusions.** CM for smoking cessation in individuals with substance use disorders performs significantly better than control conditions in reducing smoking at end-of-treatment.

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Effectiveness of Contingency Management for Smoking Cessation in Substance Users: A Systematic Review and Meta-Analysis

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Objective: We conducted a systematic review and meta-analysis (ID: CRD42019122315) to assess the evidence for the effectiveness of contingency management (CM) to promote smoking abstinence among individuals with substance use disorder or in recovery. ***Method:*** Databases were PubMed, PsycINFO, Cochrane, and EBSCO. The primary eligibility criteria for inclusion in our meta-analysis were as follows: any study examining the efficacy of CM for smoking cessation that reported smoking abstinence and/or cigarette reductions. The methodological quality of the included studies was assessed using the Effective Public Health Practice Project Quality assessment tool. Publication bias was examined using Egger's regression intercept, the Begg-Mazumdar test, and Tweedie's trim-and-fill approach. ***Results:*** A total of 22 articles were included, and 13 were included in three meta-analyses: abstinence at posttreatment (12 studies), abstinence at follow-up (8 studies), and reduction outcomes at posttreatment (6 studies). CM was superior to comparison arms in smoking abstinence (RR = 2.555; 95% CI [1.730, 3.775]; $p < .001$) and reduction ($SMD = .601$; 95% CI [0.372, 0.831]; $p < .001$) at end-of-treatment. At long-term follow-ups, CM did not show enhanced effects over abstinence beyond those shown in comparison arms (RR = 1.029; 95% CI [0.577, 1.836]; $p = .922$). Smoking-cessation treatment (all treatments included CM) and smoking abstinence increased the likelihood of abstinence from alcohol and/or illicit drugs. All studies were rated as being of strong or moderate quality, and no marked presence of publication bias was found. ***Conclusions:*** CM for smoking cessation in individuals with substance use disorders performs significantly better than control conditions in reducing smoking at end-of-treatment.

What is the public health significance of this article?
This study informs on the efficacy of contingency management for facilitating short-term smoking abstinence and cigarette reductions in substance users. Delivering contingency management solely or as an adjunctive smoking cessation intervention is advisable for a significant impact on public health.

Keywords: meta-analysis, contingency management, effectiveness, smoking cessation, substance use disorder

Supplemental materials: http://dx.doi.org/10.1037/ccp0000611.supp

Tobacco smoking is highly prevalent and is the leading behavioral risk factor causing a substantially large number of potentially preventable deaths worldwide (World Health Organization, 2012). Despite the significant decline in the prevalence of smoking in developed countries, rates of smoking among those with mental disorders remain elevated compared to the general population, with the highest rates among those with substance use disorders (SUD; Kelly, Greene, Bergman, & Hoeppner, 2019; Smith et al., 2020; Weinberger, Funk, & Goodwin, 2016; Winhusen, 2017). Individuals with SUD are more likely to smoke, smoke more heavily, and are three times more likely to be dependent on nicotine than those without SUD (Compton, Thomas, Stinson, & Grant, 2007; Minami et al., 2018; Weinberger et al., 2019). Moreover, this population experiences increased substance-related disease and premature mortality, and is more likely to die from tobacco-related causes than those using alcohol/illicit substances alone (Das & Prochaska, 2017; Hurt et al., 1996; Kelly et al., 2019; Rogers, Boardman, Pendergast, & Lawrence, 2015). Furthermore, smoking rates in recovering SUD populations are more than double those of the general population (Kelly et al., 2019). Previous research has also shown that quitting smoking increases long-term abstinence from other substances among individuals with SUD, but smokers with SUD have less success in quitting than the

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general population (Campbell, Le, Tajima, & Guydish, 2017; Weinberger et al., 2016).

Because of the increased health risks associated with smoking among people with SUD, there is a need to focus greater scientific and public health efforts on developing innovative approaches to support smoking cessation and reduce the harmful consequences of smoking for these individuals (Campbell, Yip, Le, Gubner, & Guydish, 2019; Das & Prochaska, 2017; Lembke & Humphreys, 2016; McHugh et al., 2017). Despite this, little is known about smoking treatment options for this population, and more research is needed to identify successful interventions.

Contingency management (CM) is a behavioral intervention in which patients receive reinforcement contingent upon biochemically verified abstinence. Two of the most widely implemented CM procedures are voucher-based reinforcement therapy (S. T. Higgins, Kurti, & Davis, 2019) and prize-based CM (Ledgerwood, Arfken, Petry, & Alessi, 2014). Whereas in voucher-based therapy, patients receive incentives exchangeable for retail items, environmental activities, or cash-equivalent checks, in the prize-based procedure, participants receive tickets that allow them to draw from a bowl for prizes of different magnitude.

The efficacy of CM has been demonstrated in a wide range of substance-using populations, including alcohol, cannabis, cocaine, and opiate patients (Ainscough, McNeill, Strang, Calder, & Brose, 2017; Benishek et al., 2014; Davis et al., 2016; Dutra et al., 2008; Getty, Morande, Lynskey, Weaver, & Metrebian, 2019; Lussier, Heil, Mongeon, Badger, & Higgins, 2006; McPherson et al., 2018; Prendergast, Podus, Finney, Greenwell, & Roll, 2006; Rash, Stitzer, & Weinstock, 2017; Schierenberg, van Amsterdam, van den Brink, & Goudriaan, 2012). There are also several reviews on cigarette smokers that have provided qualitative descriptions and analyses of the whole set of CM studies, showing that incentives are effective in reducing smoking (Cahill, Hartmann-Boyce, & Perera, 2015; Donatelle et al., 2004; Hand, Ellis, Carr, Abatemarco, & Ledgerwood, 2017; Ledgerwood, 2008; S. T. Higgins et al., 2019; Sigmon & Patrick, 2012).

Reviews and meta-analyses that specifically evaluate the effectiveness of smoking cessation interventions for patients with SUD are scarce. Some of these studies focus on special populations, such as pregnant women (Akerman et al., 2015) or individuals with methadone maintenance (Okoli et al., 2010). Most of these reviews do not examine the differential effects by treatment condition (Das & Prochaska, 2017; Prochaska, Delucchi, & Hall, 2004; Thurgood, McNeill, Clark-Carter, & Brose, 2016), exclude studies assessing CM interventions (Apollonio, Philipps, & Bero, 2016), or focus only on the effect of smoking cessation treatments on the use of other drugs, but not on tobacco smoking (McKelvey, Thrul, & Ramo, 2017). To our knowledge, only two meta-analyses have examined the effects of smoking interventions on smoking and substance use. The first meta-analysis included only one study evaluating a CM condition (Prochaska et al., 2004). More recently, in a subgroup analysis, Notley et al. (2019) addressed the issue of whether incentives facilitate long-term smoking abstinence for SUD populations. However, given that they focused on mixed populations (including smokers who do not use other substances), conclusions on CM efficacy cannot be drawn. Additionally, this review only included trials with at least six months of follow-up, although posttreatment outcomes were not included, and it reported abstinence rates but not smoking reductions or other substance misuse outcomes.

To fill this gap in knowledge, the primary aim of this review and meta-analysis is to evaluate the short- and long-term effectiveness of CM for smoking cessation among individuals with SUD. Moreover, with the aim of informing on CM parameters that affect treatment efficacy, we examine whether treatment setting, magnitude of incentives, or treatment length are associated with short- or long-term smoking outcomes. The secondary aim is to evaluate the impact of smoking cessation treatments on the use of substances other than tobacco. Finally, the presence of publication bias and the methodological quality of the included studies are also evaluated.

Method

A protocol was designed and registered in the International Prospective Register of Systematic Reviews, PROSPERO (ID: CRD42019122315). The systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews (PRISMA statement; Moher, Liberati, Tetzlaff, Altman, & the PRISMA Group, 2009). Both the Journal Article Reporting Standards and Meta-Analysis Reporting Standards were also conformed to, as detailed in Appelbaum et al. (2018).

Eligibility and Inclusion Criteria

The primary eligibility criteria were peer-reviewed published studies examining the effect of CM for smoking cessation that met the following conditions: 1) The study involved adult smokers (i.e., aged ≥18) with current drug use and/or enrolled in treatment/recovery for SUD; and 2) it provided a measure of smoking abstinence or reduction in cigarette use. Both the use of biochemical verification (e.g., carbon monoxide or cotinine) and reports on reduction of or abstinence from drugs other than nicotine were recorded but not required. Studies were excluded if the results were overlapping (i.e., multiple publications on the same data set, sample size, and outcomes).

Literature Search Procedure

Studies were identified through a comprehensive literature search with no restriction on the year of publication using the PubMed, PsycINFO, Cochrane, and EBSCO databases as of January 31, 2020 (see Figure 1). Search terms used pertained to CM (e.g., contingent reinforcement), smoking (e.g., cigarette), and substance use (e.g., marijuan*). The specific combinations of Boolean terms are provided in the online supplemental materials (see S1). Additionally, the authors conducted a manual search to identify systematic reviews and meta-analyses on the topic of the study.

Data Extraction

Two independent reviewers conducted the literature search and coded the studies independently. In cases where studies did not report the pertinent data, we requested the corresponding author to do so in order to permit inclusion in the analyses.

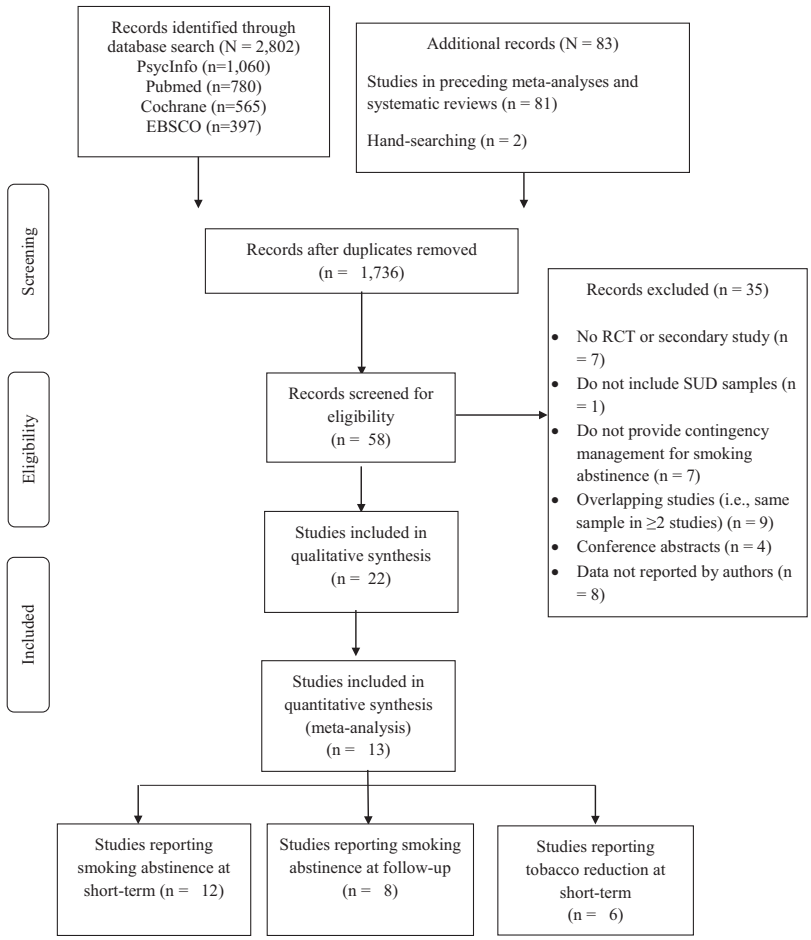


Figure 1. Flow diagram of the literature search procedure. SUD = substance use disorder; RCT = randomized controlled trial.

Narrative Synthesis

A narrative synthesis on the primary and/or secondary outcomes was given for study designs (i.e., studies including a single group or multiple groups with different treatment components) that prevented us from determining the main effect of CM on the outcomes.

Meta-Analytic Approach

Analysis was conducted using the Comprehensive Meta-Analysis software v3.3.070. Meta-analyses were based only on randomized controlled trials that allowed us to ascertain the unique effect of CM on smoking outcomes. The effectiveness of CM was assessed using two outcomes: smoking abstinence and smoking reduction. At end-of-treatment (EOT), the primary outcome measure chosen was biochemically verified point-prevalence, or else continuous abstinence or the percentage of negative samples for smoking abstinence. Regarding the measure of smoking reduction, the primary outcome was a decrease in number of cigarettes, or instead a reduction in cotinine or in CO. In the long-term follow-ups, point-prevalence was the only measure considered. The different types of smoking abstinence and reduction measures at EOT were combined in the meta-analysis given the high correlation between them (Hughes, Carpenter, & Naud, 2010). Due to the heterogeneity in the outcome variables, we computed effect sizes on the effects of the interventions on smoking abstinence and smoking reduction, separately.

In order to assess the effect sizes of smoking abstinence data, the risk ratio (RR) with a 95% confidence interval (CI) was calculated. In cells with zero events, we used the "adjusted Woolf" method to calculate the RR (Lawson, 2004). Effect sizes estimated from means and standard deviations of smoking reduction were calculated as follows (Kazis, Anderson, & Meenan, 1989): $d = (M_t - M_c)/SD_{pooled}$, where M_t refers to the mean of the treatment group, M_c to the comparison condition, and SD_{pooled} to the pooled standard deviation of the assessed arms. When abstinence or smoking reduction outcomes were not given, effect sizes were calculated from the reported values of t, F, or χ^2 statistics, as per prior recommendations (Cooper & Hedges, 2011). The meta-analysis was performed adopting a random effects approach. Cochran's Q test and I^2 were used to quantify heterogeneity of effect sizes. Cochran's Q tests the hypothesis that the studies are evaluating the same effect and indicates heterogeneity at a p value equal to .10. I^2 accounts for

the variation that is explained by heterogeneity; $I^2 \leq 25\%$ indicates low heterogeneity, ~50% suggests moderate heterogeneity, and ≥75% is indicative of high heterogeneity (J. P. T. Higgins, Thompson, Deeks, & Altman, 2003).

A mixed-effects analysis was conducted to examine whether smoking abstinence and reduction at EOT differed by type of CM combination (i.e., CM only, CM with psychological intervention, or with pharmacological intervention). As there were no studies reporting long-term outcomes using CM alone, mixed-effects analyses on long-term smoking abstinence and reduction were performed only with studies using psychological versus pharmacological CM combinations. The Q statistic associated with the between-groups difference in the mixed effects analyses was calculated for this purpose.

A set of metaregression analyses were carried out to examine whether treatment setting (i.e., outpatient vs. residential) and comparison arm (i.e., treatment as usual or no treatment vs. other active smoking cessation treatments), magnitude of incentives, and treatment length predicted CM short- (i.e., at EOT) and long-term (i.e., at the longest follow-up) smoking outcomes.

Methodological Quality Assessment

Two independent reviewers assessed the methodological quality of the studies included in the meta-analysis using the Effective Public Health Practice Project Quality assessment tool (EPHPP; Armijo-Olivo, Stiles, Hagen, Biondo, & Cummings, 2012). No discrepancies between reviewers were identified. This tool stands as appropriate for assessing the quality of a variety of study designs such as randomized controlled clinical studies and secondary ones. It comprises six domains: 1) selection bias, 2) study design, 3) confounders, 4) blinding, 5) data collection, and 6) withdrawals/dropouts. As per the EPHPP guidelines, each study domain is interpreted as weak, moderate, or strong and a global rating is calculated based on averaged scores: weak (1.00–1.50), moderate (1.51–2.50), or strong in quality (2.51–3.00).

Risk of Bias Assessment

The presence of publication bias was informed based on the interpretation of three different tests as a whole (Coburn & Vevea, 2015). Egger's regression intercept (Egger, Davey Smith, Schneider, & Minder, 1997) shows the asymmetry of the funnel plot indicating the absence of publication bias when the regression intercept is close to zero. The Begg and Mazumdar rank indicator (Begg & Mazumdar, 1994) correlates the standardized effect size and its variance, with deviations from zero suggesting the presence of publication bias. Duval and Tweedie's trim-and-fill approach (Duval & Tweedie, 2000) serves as an estimate of the unbiased effect size, as it corrects for the variance of the effects.

Results

A total of 1,736 articles were identified through the literature search and individually examined, after removing duplicates (see Figure 1). A full-text screening of 58 articles was performed. Of the reviewed articles, 22 studies published between 1995 and 2018 met the inclusion criteria and therefore were included in this review, and specifically 13 studies were included in the meta-analysis. Table 1 shows a summary of the characteristics of the reviewed studies.

Participant and Treatment Characteristics

The 22 studies involved 2,186 participants. The sample sizes ranged from 5 to 538 participants per study. The mean age of the total sample was 36.63 (SD = 8.45), and 58.01% were males. A total of 57.84% were Caucasian, 25.42% were African American, and the remaining races were Latino, Asian, and Hispanic, with minimal percentages (<20%). At baseline, the average number of cigarettes smoked per day was 17.78 (SD = 7.32). All studies were conducted in the United States.

Six studies (27.27%) were conducted in residential treatment (Alessi & Petry, 2014; Alessi, Petry, & Urso, 2008; Hunt, Rash, Burke, & Parker, 2010; Robles et al., 2005; Rohsenow, Martin, Tidey, Colby, & Monti, 2017; Rohsenow et al., 2015), nine (40.9%) in outpatient treatment (J. L. Cooney et al., 2017; Mooney et al., 2008; N. L. Cooney et al., 2015; Shoptaw, Jarvik, Ling, & Rawson, 1996; Shoptaw et al., 2002; Sigmon & Patrick, 2012; Tuten, Fitzsimons, Chisolm, Nuzzo, & Jones, 2012; Winhusen et al., 2014; Wiseman, Williams, & McMillan, 2005), one (4.54%) via the Internet (Beckham et al., 2018), four (18.18%) in a research clinic (Drummond et al., 2014; Dunn et al., 2010; Orr et al., 2018; Schmitz, Rhoades, & Grabowski, 1995), and two (9.09%) in a mixture of the above (Campbell, Wander, Stark, & Holbert, 1995; Guydish et al., 2016).

In the 22 studies included, five trials (22.72%) evaluated the effect of CM only on smoking (Alessi et al., 2008; Orr et al., 2018; Schmitz et al., 1995; Shoptaw et al., 2002; Tuten et al., 2012), and the remaining studies combined CM with other psychological (4/18.18%) or pharmacological interventions (13/59.09%). CM was added to a cognitive–behavioral treatment (CBT;Beckham et al., 2018; Campbell et al., 1995; Guydish et al., 2016; Hunt et al., 2010; J. L. Cooney et al., 2017, N. L. Cooney et al., 2015), counseling or brief advice (Alessi & Petry, 2014; Dunn et al., 2010; Mooney et al., 2008; Robles et al., 2005; Rohsenow et al., 2017; Rohsenow et al., 2015; Winhusen et al., 2014), relapse prevention (Mooney et al., 2008; Shoptaw et al., 2002), and motivational interviewing (Rohsenow et al., 2015). Finally, nine studies combined CM with nicotine replacement therapy (NRT; Campbell et al., 1995; Guydish et al., 2016; J. L. Cooney et al., 2017; N. L. Cooney et al., 2015; Rohsenow et al., 2017; 2015; Shoptaw et al., 2002; Winhusen et al., 2014; Wiseman et al., 2005), and four with other pharmacotherapy (Dunn et al., 2010; Mooney, Babb, Jensen, & Hatsukami, 2005; Sigmon et al., 2016; Winhusen et al., 2014).

Of the 22 CM studies, a total of 19 used CM based on voucher-based reinforcement therapy, eight of which provided monetary incentives (Beckham et al., 2018; Campbell et al., 1995; Drummond et al., 2014; Hunt et al., 2010; Mooney et al., 2008; Orr et al., 2018; Schmitz et al., 1995; Tuten et al., 2012). The remaining three studies (Alessi & Petry, 2014; Alessi et al., 2008; Winhusen et al., 2014) used a prize-based procedure through a fish bowl. Maximum earnings in vouchers within CM conditions ranged between US$10 and US$1,351, with an average of US$390.72.

All studies included biochemical validation (carbon monoxide or cotinine) as a measure of smoking abstinence. Moreover, the most common abstinence criterion was 7-day point-prevalence

Table 1
Study Characteristics

Author (year)	Sample size (% male)	Age $M \pm SD$	Cigarettes $M \pm SD$	Substance type (%)	Conditions	Maximum incentives value	Treatment length	Longest follow-up	Primary outcome measures included in meta-analysis
Alessi, Petry, and Urso (2008)	24 (100%)	36.6 ± 7.8	18.8 ± 7.0	ALC (96%), COC (58%), OPI (33%)	NC vs CM[b]	$910	12 weeks	6 months	EOT abstinence: % CO negatives Follow-up abstinence: NA EOT reduction: Number of cigarettes
Alessi et al. (2014)	45 (100%)	37.9 ± 9.9	18.7 ± 6.3	POLY (65%), OPI (18%), other drugs (18%)	Monitoring (brief behavioral support) vs Monitoring + CM[b]	$473	4 weeks	6 months	EOT abstinence: PP Follow-up abstinence: PP EOT reduction: Number of cigarettes
Beckham et al. (2018)	5 (20.0%)	43.6 ± 8.9	10.6 ± 11.2	THC (100%)	CBT + NRT + mobile CM for smoking and cannabis	$1351[a]	7 weeks	6 months	
Campbell et al. (1995)	90	—	23	OPI (50%), STI (28%), other drugs (21%)	CBT + NRT + CM vs Control (waiting-list)	$105	16 weeks	EOT	
N. L. Cooney et al. (2015)	151 (86.1%)	49.1 ± 9.0	16.2 ± 8.7	ALC (100%), COC (33%), THC (17%), other drugs (7%)	Intensive alcohol treatment (CBT + MI + 12 step) + CBT + NRT + CM for smoking vs Intensive alcohol treatment	$140	3 weeks	3 months	
J. L. Cooney et al. (2017)	83 (96.4%)	49.8 ± 9.9	20.3 ± 9.7	ALC (100%), COC (30%), other drugs (9%)	CBT + NRT vs CBT + NRT + CM	$140	3 weeks	6 months	EOT abstinence: PP Follow-up abstinence: PP EOT reduction: NA
Drummond et al. (2014)	100 (53.0%)	49.8 ± 9.9	>1 in the last month	ALC (51%), NON-IDU (32%), IDU (21%)	Usual Care vs Usual Care + CM	$225	1 day	6 months	EOT abstinence: NA Follow-up abstinence: PP EOT reduction: NA
Dunn et al. (2010)	40 (33.0%)	31.0 ± 1.8	18.5 ± 1.8	MTD (100%)	NC vs CM (both with counseling + bupropion under request)	$362.5	2 weeks	3 months	EOT abstinence: PP Follow-up abstinence: PP EOT reduction: Number of cigarettes
Guydish et al. (2016)	75 (0.0%)	39.7 ± 10.3	12.3 ± 5.6	STI (58%), ALC (25%), OPI (16%), other drugs (1%)	RG vs RG + CM	$10	3 weeks	1 months	
Hunt et al. (2010)	39 (100%)	—	14.5 ± 9.6	SUD	CBT vs CBT + CM	$90	4 weeks	3 months	EOT abstinence: PP Follow-up abstinence: PP EOT reduction: NA
Mooney et al. (2008)	40 (85.0%)	34.2 ± 11.2	23.8 ± 10.7	OPI, COC	Buprenorphine + bupropion vs Buprenorphine + placebo (both with counseling + RP + CM for cocaine, opiates and smoking)	$150[a]	10 weeks	EOT	
Orr et al. (2018)	34 (64.7%)	35.0 ± 10.5	17.6 ± 7.2	ALC (100%), THC (50%), other drugs (18%)	NC ALC and TOB vs CM ALC + NC TOB vs NC ALC + CM TOB vs CM ALC and TOB	$120	4 weeks	EOT	EOT abstinence: % CO negatives Follow-up abstinence: NA EOT reduction: NA

(*table continues*)

Table 1 (*continued*)

Author (year)	Sample size (% male)	Age $M \pm SD$	Cigarettes $M \pm SD$	Substance type (%)	Conditions	Maximum incentives value	Treatment length	Longest follow-up	Primary outcome measures included in meta-analysis
Robles et al. (2005)	16 (100%)	32.6 ± 1.3	15.3 ± 3.7	STI (63%), ALC (19%), OPI (13%), other drugs (6%)	CM + counseling + Bupropion	$823	4 weeks	2 weeks	
Rohsenow et al. (2015)	184 (44.6%)	34.5 ± 8.4	22.3 ± 9.4	COC (74%), ALC (71%), OPI (53%), THC (37%)	MI + CM vs MI + NC vs BA + CM vs BA + NC	$433	19 days	12 months	EOT abstinence: CA Follow-up abstinence: PP EOT reduction: NA
Rohsenow et al. (2017)	340 (67.0%)	37.6 ± 10.0	19.5 ± 7.4	ALC (76%), COC (60%), OPI (49%), THC (36%)	NC vs CM (both with BA + NRT)	$433	19 days	12 months	EOT abstinence: CA Follow-up abstinence: PP EOT reduction: Number of cigarettes
Schmitz et al. (1995)	5 (80.0%)	38.4 ± 5.5	—	MTD (100%)	CM	$40	10 weeks	EOT	
Shoptaw et al. (1996)	17 (76.5%)	43.8	30.0	MTD (100%), OPI (41%), COC (24%)	CM	$73	4 weeks	EOT	
Shoptaw et al. (2002)	175 (60.6%)	44.0 ± 7.8	22.1 ± 9.7	MTD (100%), ALC (17%), other drugs (43%)	NRT vs RP vs CM vs RP + CM (all with NRT)	$447.5	12 weeks	12 months	EOT abstinence: PP Follow-up abstinence: PP EOT reduction: NA
Sigmon et al. (2016)	63 (41.0%)	34.4 ± 10.3	18.2 ± 9.5	MTD (71%), BUP (29%)	NC vs CM (2 week after, all CM + bupropion under request)	$932.5	12 weeks	EOT	EOT abstinence: PP Follow-up abstinence: NA EOT reduction: Cotinine
Tuten et al. (2012)	102 (0.0%)	30.8 ± 6.0	18.0 ± 8.6	MTD (100%)	NC vs CM vs TAU	$857.5	12 weeks	6 weeks	EOT abstinence: PP Follow-up abstinence: NA EOT reduction: CO
Winhusen et al. (2014)	538 (52.0%)	36.4 ± 10.0	16.3 ± 7.9	STI (100%), ALC (27%), THC (14%), other drugs (5%)	SUD TAU vs SUD TAU + Bupropion + NRT + CM[b]	$380	10 weeks	6 months	
Wiseman, Williams, and McMillan (2005)	20 (100%)	40.1 ± 7.5	22.4 ± 6.3	COC (100%), ALC (30%), other drugs (5%)	NC + Placebo vs NC + NRT vs CM + Placebo vs CM + NRT	$100	2 weeks	EOT	EOT abstinence: CO negative Follow-up abstinence: NA EOT reduction: NA

Note. ALC = alcohol; COC = cocaine; OPI = opiates; NC = non-contingent; CM = contingency management; NA = not applicable; POLY = polydrugs; PP = point-prevalence; THC = cannabis; CBT = cognitive behavioral therapy; NRT = nicotine replacement therapy; STI = stimulants; MI = motivational interviewing; IDU = injection drug users; MTD = methadone; RG = smoking cessation readiness group; SUD = substance use disorder; RP = relapse prevention; EOT = end-of-treatment; TOB = tobacco; BA = brief advice; CA = continuous abstinence; BUP = buprenorphine; CO = carbon monoxide; TAU = treatment as usual.

[a] CM was used to reinforce abstinence from both smoking and other drugs. [b] CM was prize-based.

(13/59.09%), followed by continuous abstinence (6/27.27%), and percentage of negative CO samples (3/13.63%). The most utilized criterion for assessing smoking reduction was the number of cigarettes (14/63.63%) followed by a decrease in biochemical variables (carbon monoxide or cotinine; 3/13.63%).

Treatment length ranged from one single visit to 16 weeks, with an average of 6.66 weeks. With regard to the follow-ups, seven studies (31.81%) had no follow-up beyond EOT, six (27.27%) had the furthest follow-up between two weeks and three months, and another six (27.27%) had the longest follow-up at six months. The remaining three (13.63%) reported smoking outcomes at 12 months.

Two meta-analyses were carried out, with a total of 12 studies being obtained that offered abstinence results at short-term and eight studies that offered abstinence results at time frames beyond treatment termination. Additionally, one meta-analysis was carried out including six studies that reported smoking reduction at short-term. Given that only four trials reported smoking reduction outcomes beyond EOT, a meta-analysis was not carried out and the results were narratively presented instead. Regarding the substance use outcomes, due to the fact that only 12 studies reported this information and the outcome measures were heterogeneous, these results were presented narratively as well.

Meta-Analysis: Smoking Outcomes

Forest plots of smoking cessation results at short-term and long-term are shown in Figure 2. For short-term abstinence, random effects produced a pooled risk ratio of 2.555 (95% CI [1.730, 3.775]; $p \leq .001$), CM being significantly better than comparison arms. Heterogeneity was medium in magnitude ($I^2 = 30.987\%$; $Q = 15.939$; $p = .143$). In the longest follow-ups, CM interventions did not show enhanced effects on abstinence beyond those shown in comparison arms (RR = 1.029; 95% CI [0.577, 1.836]; $p = .922$). Heterogeneity was low in magnitude ($I^2 < 0.001\%$; $Q = 6.309$; $p = .504$).

A forest plot of smoking reduction results at short-term is shown in Figure 3. For short-term smoking reduction, random effects produced a pooled effect size estimate of .601 (95% CI [.372, .831]; $p < .001$), CM being significantly better than comparison groups. Heterogeneity was medium in magnitude ($I^2 = 34.12\%$; $Q = 7.589$; $p = .18$).

Moderation Analyses

Treatment setting did not moderate smoking abstinence outcomes either at posttreatment ($Q(1) = 0.22$, $p = .638$) or in long-term time frames ($Q(1) = 0.31$, $p = .576$), but it did work as an effective moderator for posttreatment smoking reduction outcomes ($Q(1) = 4.893$, $p = .027$). In particular, compared to residential settings (*SMD* = .448, 95% CI [.254, .643]), being in an outpatient treatment (*SMD* = .836, 95% CI [.553, 1.119]) significantly predicted higher effects.

An analysis of short-term smoking abstinence outcomes by CM combination did not yield statistical significance. Using CM only ($Q(2) = 4.41$, $p = .11$) did not differ relative to its combination with either psychological or pharmacotherapy (RR = 10.735 vs. 1.543 and 2.415, respectively). Similarly, there were no differences in smoking reduction at short-term ($Q(2) = 1.385$, $p = .50$), showing an effect size of .627, .265, and .658 for CM only and in

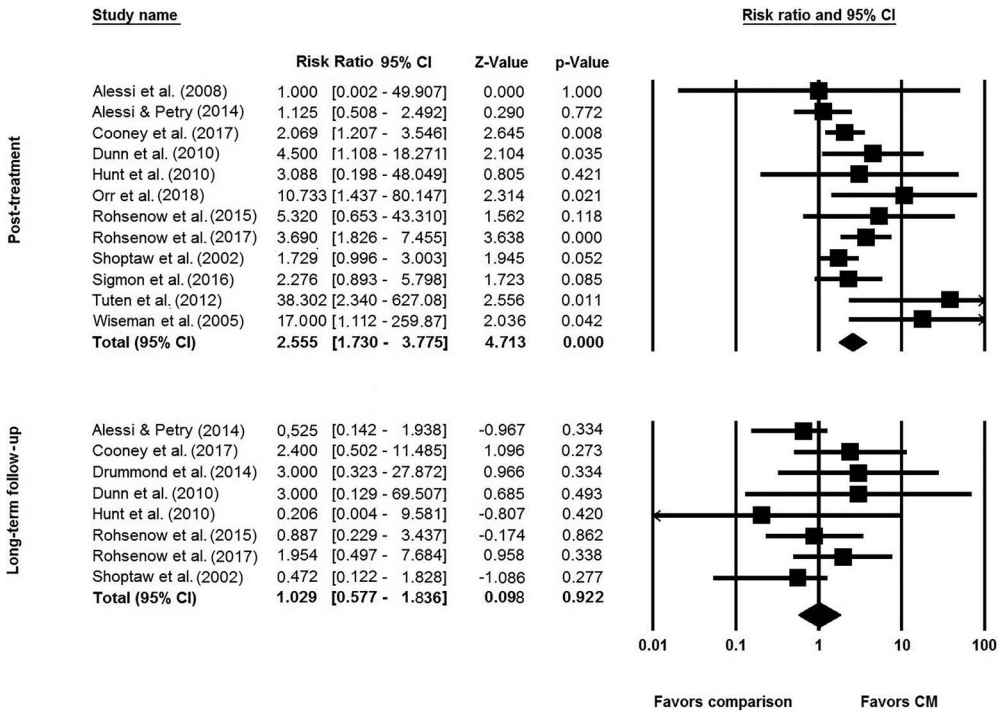
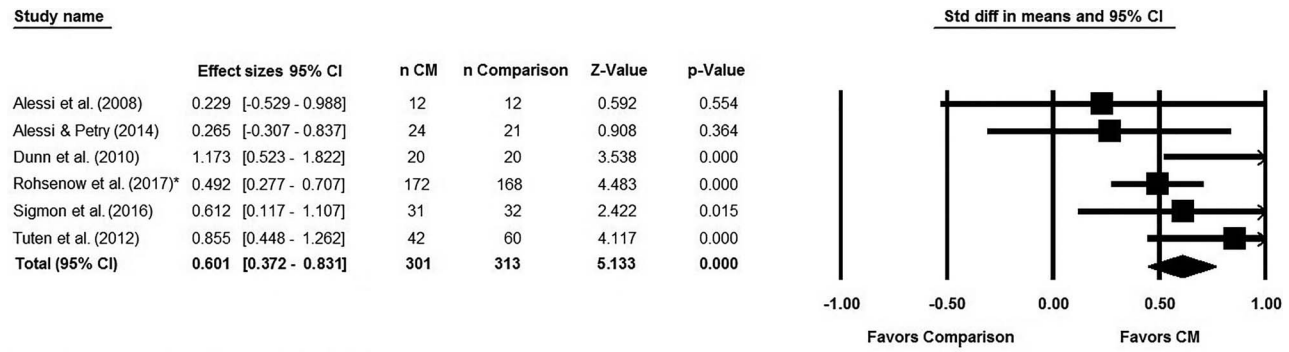


Figure 2. Forest plots of the meta-analytic findings of smoking abstinence results at end-of-treatment and follow-ups. CM = contingency management.



*Data for one months follow-up in included

Figure 3. Forest plot of smoking reduction results at end-of-treatment. CM = contingency management.

combination with psychological and pharmacological intervention, respectively. There were no significant differences in abstinence at long-term follow-up between the combination of CM with a psychological and a pharmacological intervention (Q(1) = .695, p = .404, RR = .791 vs. 1.317, respectively)

The comparison group arm used to assess CM efficacy (i.e., treatment as usual or nontreatment vs. other smoking cessation treatment) did not affect abstinence outcomes at short-term (Q(1) = 0.00, p = .99), or long-term (Q(1) = 0.02, p = .891). Similar results were observed for reduction at short-term (Q(1) = 0.32, p = .573).

Magnitude of incentives did not impact short- (p = .788) or long-term smoking abstinence (p = .199) or reduction outcomes (p = .945). Smoking abstinence rates at short-term (p = .602), long-term abstinence (p = .175), and reductions at posttreatment (p = .496), were not affected by treatment length.

Systematic Review: Smoking Outcomes

Most of the studies included abstinence rates (19/22, 86.36%), although not all studies offered abstinence rates by group or used 7-day point-prevalence. The use of substantially different smoking abstinence measures (percentage, number or average of negative CO tests, days of consecutive negative CO tests, number or average of negative cotinine samples, etc.) precluded the comparison of the results on smoking abstinence among the different measures.

Overall, considering all smoking cessation treatments regardless of whether they included CM, mean abstinence rates were 20.25% at EOT (Beckham et al., 2018; Campbell et al., 1995; Dunn et al., 2010; Guydish et al., 2016; Hunt et al., 2010; J. L. Cooney et al., 2017; Mooney et al., 2008; N. L. Cooney et al., 2015; Robles et al., 2005; Shoptaw et al., 1996, 2002; Sigmon et al., 2016; Tuten et al., 2012; Winhusen et al., 2014), 7.83% at three-month follow-up (Alessi et al., 2008; Dunn et al., 2010; Hunt et al., 2010; N. L. Cooney et al., 2015; Rohsenow et al., 2017, 2015; Winhusen et al., 2014), and 5.85% at six-month follow-up (Alessi & Petry, 2014; Alessi et al., 2008; Drummond et al., 2014; J. L. Cooney et al., 2017; Rohsenow et al., 2017, 2015; Shoptaw et al., 2002; Winhusen et al., 2014), respectively.

Taking into account only those studies that included CM in the experimental group compared to a control group, in which participants received the same treatment without the CM component, mean abstinence rates at EOT were 36.03% versus 7.84% (Dunn et al., 2010; J. L. Cooney et al., 2017; Hunt et al., 2010; N. L. Cooney et al., 2015; Shoptaw et al., 2002; Sigmon et al., 2016; Tuten et al., 2012; Winhusen et al., 2014), 12.86% versus 2.53% at 3-month follow-up (Dunn et al., 2010; N. L. Cooney et al., 2015; Rohsenow et al., 2017, 2015; Winhusen et al., 2014), and 7.80% versus 1.71% at six-month follow-up (Drummond et al., 2014; J. L. Cooney et al., 2017; Rohsenow et al., 2017, 2015; Shoptaw et al., 2002; Winhusen et al., 2014).

Of the nine studies that were excluded from the meta-analysis, either because they were not a RCT or because both groups included CM, six (66.67%) used pharmacological and psychological interventions in addition to CM. Beckham et al. (2018) and Campbell et al. (1995) used CBT + NRT + CM, and informed of abstinence rates of 40.0% and 11.0% at EOT, respectively. On the other hand, N. L. Cooney et al. (2015) and Winhusen et al. (2014) explored whether adding a smoking cessation treatment (CBT + NRT + CM, and bupropion + counseling + NRT + CM, respectively) to one that addressed other drugs helped to increase abstinence rates. Both found higher smoking cessation rates in treatments that included tobacco use cessation ($p < .05$). Specifically, abstinence rates at posttreatment were 50.5% versus 2.2% (N. L. Cooney et al., 2015) and 25.5% versus 2.2% (Winhusen et al., 2014). At three-month follow-up, statistical differences remained, with abstinence rates of 19.0% versus 0.0% (N. L. Cooney et al., 2015) and 19.0% versus 3.0% (Winhusen et al., 2014). The other two studies (Mooney et al., 2008; Robles et al., 2005), used both bupropion and CM for smoking cessation and found abstinences rates of 12.82% and 43.75% at EOT, respectively.

Only three studies (33.33%) not included in the meta-analysis did not incorporate any pharmacological strategy and delivered CM on their own. Guydish et al. (2016) showed a decrease in the number of cigarettes from the start to EOT ($p < .01$). In addition, four participants (5.33%) abstained from smoking at EOT. In a within-subjects study design (A-B-A-B), Schmitz et al. (1995) treated five smokers with methadone maintenance and found no effects of this intervention on smoking rates (p = .14). Finally, in the study of Shoptaw et al. (1996), none of the smokers achieved abstinence at EOT, however, 76.5% of smokers with methadone maintenance decreased their CO levels compared to the initial value.

Systematic Review: Substance Use Outcomes

Twelve studies out of 22 (54.54%) included some type of information about participants' drug use after treatment (Alessi & Petry, 2014; Beckham et al., 2018; Campbell et al., 1995; J. L. Cooney et al., 2017; Mooney et al., 2008; N. L. Cooney et al., 2015; Orr et al., 2018; Rohsenow et al., 2017, 2015; Shoptaw et al., 1996, 2002; Winhusen et al., 2014). Except for N. L. Cooney et al. (2015), all studies included a biochemical verification of substance use. A total of 9/22 (40.9%; J. L. Cooney et al., 2017; Mooney et al., 2008; N. L. Cooney et al., 2015; Orr et al., 2018; Rohsenow et al., 2017, 2015; Shoptaw et al., 1996, 2002; Winhusen et al., 2014) had an adequate design to explore the effect of the smoking treatment and/or smoking abstinence on non-nicotine substance use. Six of the 12 studies identified the unique effect of CM on substance use outcomes (Alessi & Petry, 2014; J. L. Cooney et al., 2017; Orr et al., 2018; Rohsenow et al., 2017, 2015; Shoptaw et al., 2002).

Regarding the impact of smoking treatments—which included CM combined with other smoking cessation treatments—on drug use, a total of 3/4 (75%) found significant reductions in drug use. Specifically, Winhusen et al. (2014) found that adding a smoking cessation treatment (which included bupropion, NRT, counseling, and CM) to treatment as usual for SUD, increased drug-free days at six-month follow-up. Similarly, both studies by Rohsenow et al. (2017, 2015) showed decreased drug use across time in all treatment conditions. On the other hand, N. L. Cooney et al. (2015) found no differences in rates of heavy drinking between intensive alcohol treatment plus smoking cessation intervention (CBT + NRT + CM) and intensive alcohol treatment only. However, both increased the frequency of alcohol-abstinent days from 40% of days at baseline to 95% of days at the three-month follow-up ($p < .001$).

Smoking abstinence had a positive impact on the use of other drugs. Shoptaw et al. (1996, 2002) reported that patients who attained longer periods of smoking abstinence were significantly less likely to use cocaine and more likely to provide negative opiate or cocaine urine tests ($p < .001$). Lastly, J. L. Cooney et al. (2017) found that tobacco abstinence mediated the relationship between alcohol and other drug abstinence at one-month follow-up.

Concerning the impact of CM on substances other than nicotine, only one study found a positive effect ($p < .05$) on alcohol abstinence compared with the control condition at EOT (Orr et al., 2018). The other five studies found no differences between CM and comparison groups. Alessi and Petry (2014) found no differences between CM and standard care in days of substance use at follow-ups ($p > .45$). Similarly, J. L. Cooney et al. (2017) found no differences in abstinence rates between CBT + NRT versus CBT + NRT + CM ($p > .05$). Moreover, both studies of Rohsenow et al. (2017, 2015) found no effect of CM on substances other than nicotine in any of the follow-ups. Lastly, Shoptaw, et al. (2002) found that relapse prevention led to lower rates of opiate use in comparison with CM and other interventions ($p < .001$).

Methodological Quality Ratings

Individual and global scores for each study included in the meta-analysis are in Table 2. Overall, seven trials (53.84%) were rated as strong, six (46.15%) were given a moderate quality score, and none of them were deemed to be weak. The main component that decreased the overall quality was the high drop-out rate of the interventions.

Publication Bias

There was no marked presence of publication bias, as evinced by nonsignificant results on the purported publication bias analyses. Egger's test was significant for the posttreatment smoking abstinence outcomes ($p = .019$). No publication bias was obtained for either the long-term abstinence ($p = .333$) or short-term reduction outcomes ($p = .338$). Kendall's test yielded no significant results (cigarette reduction: $\tau_{posttreatment} = .133$, $p = .71$; smoking abstinence: $\tau_{posttreatment} = .287$, $p = .19$; $\tau_{follow\text{-}ups} = .178$, $p = 54$), thus indicating absence of asymmetry. Although Tweedie's trim-and-fill analysis suggested the presence of four unpublished studies for the posttreatment results and one for those pertaining to subsequent follow-ups, the imputation of the data from these studies did not significantly alter the observed estimates ($RR_{posttreatment}$ before trimming: 2.307, 95% CI [1.746, 3.047]; $RR_{posttreatment}$ after trimming: 2.091, 95% CI [1.595, 2.741];

Table 2
Methodological Quality Assessment

Study	Selection bias	Study design	Confounders	Blinding	Data collection	Withdrawals	Global ratings
Alessi et al. (2008)	Weak	Strong	Strong	Moderate	Strong	Weak	Moderate
Alessi & Petry (2014)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
J. L. Cooney et al. (2017)	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Drummond et al. (2014)	Weak	Strong	Weak	Moderate	Strong	Weak	Moderate
Dunn et al. (2010)	Strong	Strong	Strong	Moderate	Strong	Moderate	Strong
Hunt et al. (2010)	Moderate	Strong	Strong	Moderate	Strong	Weak	Moderate
Orr et al. (2018)	Moderate	Strong	Strong	Moderate	Strong	Weak	Moderate
Rohsenow et al. (2015)	Strong	Strong	Strong	Moderate	Strong	Moderate	Strong
Rohsenow et al. (2017)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Shoptaw et al. (2002)	Strong	Strong	Strong	Moderate	Strong	Moderate	Strong
Sigmon et al. (2016)	Moderate	Strong	Strong	Moderate	Strong	Moderate	Moderate
Tuten et al. (2012)	Moderate	Strong	Strong	Moderate	Strong	Moderate	Moderate
Wiseman et al. (2005)	Strong	Strong	Weak	Strong	Strong	Strong	Strong

$RR_{follow\text{-}ups}$ before trimming: 1.029, 95% CI [0.577, 1.835]; $RR_{follow\text{-}ups}$ after trimming: 0.991, 95% CI [0.561, 1.751]).

Discussion

This systematic review and meta-analysis examined the effectiveness of CM on smoking cessation for patients with SUD. This study is relevant due to the high smoking-related burden and low smoking-abstinence rates observed in this population.

The meta-analysis revealed increased short-term smoking abstinence and reduction with CM relative to a set of pharmacological and behavioral treatments. In the studies included in the meta-analysis, patients treated with CM were more likely to successfully quit or reduce tobacco than the comparison groups at short-term. Of the studies that reported point-prevalence or continuous abstinence at short-term, patients in the groups that included CM were 4.59 times more likely to achieve smoking abstinence than comparison groups at that point. This aligns with the literature documenting the efficacy of CM in promoting smoking abstinence in the general population (Cahill et al., 2015; Sigmon & Patrick, 2012) and stresses the necessity to provide SUD smokers with CM, as it represents a clinically meaningful therapy option that facilitates initial smoking abstinence. Nevertheless, consistent with findings from a previous study (Notley et al., 2019), CM treatment effects were no longer significant at long-term follow-ups, showing similar abstinence rates between CM and comparison groups.

The deterioration of CM effects beyond treatment termination has been noted previously (Prendergast et al., 2006) and is consistent with other studies in SUD smokers where improved smoking abstinence within treatment did not result in meaningful smoking abstinence rates in the longer term (Notley et al., 2019; Thurgood et al., 2016). The maintenance of CM effects following the discontinuation of incentives is an important challenge in clinical research and thus a research priority. As per the CM literature (see, e.g., Secades-Villa et al., 2019; Vlad, Arnsten, & Nahvi, 2020), there is promising evidence that extended incentives during follow-ups promote sustained abstinence, both in tobacco and substance use. Combining CM with other interventions that provide skills for sustaining abstinence (e.g., CBT or relapse prevention treatment; Carroll et al., 2012) and the use of incentive programs in workplaces requiring the provision of negative tests for extended periods (Chudzynski, Roll, McPherson, Cameron, & Howell, 2015; Silverman, DeFulio, & Sigurdsson, 2012) have also been shown as effective vehicles to facilitate long-term abstinence. More recently, the use of technology platforms for CM delivery has gained interest as it represents a low-cost procedure that might facilitate continuing reinforcement over longer periods (Getty et al., 2019).

It is worth mentioning that CM combination (i.e., CM alone vs. added to pharmacotherapy or psychological treatment) did not impact abstinence outcomes. This suggests that providing CM alone for SUD smokers would be a more cost-efficient approach than using a combination protocol, particularly in view of the absence of additive effects of the latter. This, however, should be interpreted in the context of the limited number of studies, and warrants further investigation.

On another note, we found that treatment setting moderated CM effectiveness. Compared to SUD smokers undergoing outpatient treatment, those in residential settings attained lower smoking reductions. Quitting smoking is notoriously difficult in residential settings because tobacco use is a widespread coping strategy for dealing with anxious situations as well as being a form of socialization (Fallin-Bennett, Parker, Miller, Ashford, & Hahn, 2018). Given that cigarette smoking is commonly unrestricted in treatment facilities (e.g., it is permitted indoors or in outdoor spaces, such as the courtyard; González-Roz et al., 2019; Hahn, Warnick, & Plemmons, 1999), quitting attempts may be hampered by the lack of nonsmoking organizational cultures (Guydish, Wahleithner, Williams, & Yip, 2020; Ingram et al., 2017).

It is also worth mentioning that, contrary to prior research (Sigmon & Patrick, 2012), using higher magnitudes of reinforcement did not predict enhanced smoking reductions or abstinence. Nonetheless, given the low variability in the magnitude of incentives used in the reviewed studies, no definitive conclusions can be drawn on this issue, and further research is needed to determine the optimal magnitude of incentives that should be used in this population.

Results also showed that individuals in SUD treatment or recovery receiving smoking-cessation treatments that include a CM component might evidence not only improvements in smoking outcomes, but also in substance-use outcomes as well. This same patterning of results has also been more broadly reported (Baca & Yahne, 2009; Friend & Pagano, 2005; McKelvey et al., 2017; Piper, Kenford, Fiore, & Baker, 2012), and suggests that smoking cessation and even reductions in tobacco use may be associated with enhanced drug treatment outcomes. This is an important finding since integration of smoking cessation care in drug treatment settings is low (Skelton et al., 2019), and patients' and treatment providers' concerns about sobriety may still serve as substantial barriers to smoking cessation efforts during addiction treatment (Fine, Bearnot, Rigotti, & Baggett, 2019; González-Roz et al., 2019).

No superior effects of CM were obtained on substance use other than nicotine when compared to other effective smoking-cessation interventions. As evidenced by several studies (N. L. Cooney et al., 2015; Rohsenow et al., 2017, 2015; Winhusen et al., 2014), smoking cessation treatment appears to be related to higher substance use abstinence rates, whereas of the six CM studies, only one found statistically significant differences between groups in substance use abstinence. That is, although positive effects are shown when CM is delivered, its effect seems not to be enough to facilitate abstinence rates from substances other than nicotine beyond the effects of other efficacious approaches. Of note is that studies that assessed the sole effect of CM used excessively low magnitude reinforcers (i.e., US$10–US$73). Nevertheless, the evidence to date is insufficient, since only five studies analyzed the differential effects of CM over other effective treatments.

Results from this study are of major clinical importance; however, there are several limitations intrinsic to the reviewed studies that should be addressed. These limitations primarily pertain to the lack of consistency in CM procedures across studies (that is, different reinforcement magnitudes not based on gold standard guidelines; see Petry (2000)), and small study sample sizes, probably due to high attrition rates, especially after treatment termination. Also, the use of different measurements (i.e., smoking abstinence and reduction) precluded direct comparisons across studies and thus limited us in identifying effective interventions. Following the recommendations by the Society for Research on Nicotine

and Tobacco (Benowitz et al., 2020), smoking abstinence must be biochemically verified considering the same cut-off points according to the guidelines. This study is another example that shows that adopting one or more empirically validated and clinically relevant outcome measures is essential to advance research on smoking treatment. It is concerning that most of the studies that could not be meta-analyzed and were narratively reviewed merely placed attention on reporting statistically significant results instead of providing smoking or other substance use abstinence outcomes in terms of 7-day point-prevalence or continuous abstinence, the gold standard in tobacco research (Hughes et al., 2010). In the same vein, authors should be encouraged to provide abstinence rates using these aforementioned measures at least. Finally, close to 50% of the reviewed studies did not evaluate the effects of smoking cessation treatments on other substance use outcomes, thereby limiting the study's power to conclude any particular effect of either CM or smoking cessation on non-nicotine SUDs.

Strengths of this review include the fact that it concentrated mostly on randomized controlled trials, the large sample in terms of the number of studies and participants included ($n = 2{,}186$), and the comparability of trials in terms of participant characteristics. Also, all studies included in the meta-analysis were rated as strong or moderate in terms of methodological quality and no significant impact of publication bias was found.

Implications and Conclusion

In conclusion, CM for smoking cessation increases short-term abstinence in SUD patients undergoing treatment or in recovery, although long-term effects were not found. There have been concerns about the feasibility of providing CM and, more broadly, smoking cessation quitting aids to SUD patients in real-world contexts (i.e., substance abuse treatment facilities). This clearly demonstrates the feasibility of integrating smoking cessation interventions, and specifically CM, into existing SUD infrastructures. Individuals with SUD can successfully quit smoking and should be offered evidence-based smoking cessation treatments, including CM, especially given the positive effects of smoking abstinence on improvements in other substance outcomes.

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5.2. Episodic future thinking for smoking cessation in individuals with substance use disorder: treatment feasibility and acceptability

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Background. Smokers with substance use disorders (SUD) smoke approximately four times more than the general population. Current efforts are focused on improving smoking cessation treatments for this population. Episodic future thinking (EFT), a novel intervention aimed at decreasing impulsive choice, has shown promising results for reducing cigarette demand in experimental settings. This feasibility study sought to examine the feasibility and preliminary EFT effects on delay discounting (DD) and nicotine intake reductions throughout treatment. **Method**. Smokers in substance use treatment (N = 29; 75.9% males) received an 8-week cognitive-behavioral treatment (CBT) + EFT for smoking cessation. The study assessed feasibility through successful recruitment rates, retention, and adherence to treatment. Participants' satisfaction acted as our acceptability measure. We computed nonparametric range tests to analyze changes in continuous variables. **Results**. Among interested individuals, 42 (43.75%) met the inclusion criteria, and 29 entered the treatment program. Rate of treatment completion was 65.5% (19/29). Mean (SD) sessions attended were 7(1.11), and mean patient satisfaction rating with treatment was 8.83/10. The study observed low compliance with EFT, with 15.8% (3/19) of patients practicing at least 50% of the requested times. **Conclusions**. CBT + EFT is acceptable for the SUD population. However, future studies should implement some adjustments to improve the adherence and feasibility of EFT, such as reducing the number of practices and temporal intervals in EFT events. Given the small sample size, and the absence of a control group, future larger scale trials are needed to elucidate EFT effects on DD and smoking cessation.

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Episodic future thinking for smoking cessation in individuals with substance use disorder: Treatment feasibility and acceptability

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ABSTRACT

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1. Introduction

Nicotine dependence and substance use disorders co-occur at strikingly high rates. Individuals with a substance use disorder (SUD) smoke at much higher rates than those without SUDs (63.34% for SUD vs. 14% for non-SUD; Wang et al., 2018; Weinberger et al., 2018), they present more severe nicotine dependenec, and attain poorer treatment response as low abstinence rates evidence (8.7% for SUD vs. 34.5% for non-SUD) (Apollonio et al., 2016; Secades-Villa et al., 2019).

Cumulative research now recognizes the relevance of providing smoking cessation treatments to the SUD population (Derefinko et al., 2018; Knudsen, 2017), especially given that smoking abstinence is related to long-lasting sobriety from alcohol and illicit drugs (McKelvey et al., 2017; Thurgood et al., 2016). Several pharmacotherapies (e.g., varenicline and bupropion; Stein et al., 2013; Winhusen et al., 2014) and behavioral interventions (e.g., contingency management [CM] or cognitive-behavioral therapies [CBT]) have demonstrated efficacy in facilitating smoking abstinence (Rohsenow et al., 2015; Thurgood et al., 2016).

CBT is one of the most effective psychological treatments for smoking cessation in a range of populations (see e.g., Beckham et al., 2018; Çelik & Sevi, 2020; Cooney et al., 2017; Fiore et al., 2008; Vinci, 2020). However, abstinence rates remain moderate, ranging from 6% to 28% (Stead et al., 2017), so including components targeted at individual markers related to onset, maintenance, and relapse might enhance treatment outcomes (Kwako et al., 2018). One such variable is delay discounting (DD), a measure of impulsive choice that refers to the preference of smaller, sooner rewards (e.g., smoking) over larger delayed ones (e.g., positive abstinence effects) (Odum, 2012). Smokers with SUD excessively discount the value of rewards to a greater extent compared to non-SUD smokers (Amlung et al., 2017; Bickel et al., 2019; MacKillop et al., 2011), signifying a shortened time perspective (i.e.,

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temporal window) during decision-making (Petry & Bickel, 1998; Snider et al., 2016).

Of note is that DD is context dependent, meaning that it can be significantly malleable (García-Pérez et al., 2020; Koffarnus et al., 2013; Rung & Madden, 2018). Research has started to look at interventions that improve the valuation of future consequences for individuals with SUD (Athamneh et al., 2019; Mellis et al., 2019). A recent systematic review of behavioral DD trainings or manipulations showed that 78.8% (119/151) of studies report post-training DD decreases (Scholten et al., 2019). Among others, episodic future thinking (EFT), a technique that consists of vividly imagining and describing future scenes or situations (Atance & O'Neill, 2001; Schacter et al., 2017), seems to produce the largest effect magnitude (Scholten et al., 2019).

Previous studies have shown promising results of EFT in reducing DD in overweight patients (Daniel, Stanton, Epstein, 2013a, 2013b), and SUDs (Sofis et al., 2020). In the tobacco field, experimental research has shown that EFT is effective in reducing cigarette consumption (Chiou & Wu, 2017; Stein et al., 2016) and tobacco demand (Stein et al., 2018). So far, the study by Patel and Amlung (2020) represents the only attempt to examine the feasibility of EFT in an SUD population within a clinical context. In a sample of 28 patients, their findings supported the feasibility of one EFT session, as it significantly reduces alcohol demand and DD.

These promising results are tempered by important limitations. Most previous studies include only one session and measure DD directly after the manipulation in the session (see e.g., Shevorykin et al., 2019). Recent research has highlighted the importance of repeated practice to produce changes in DD (Mellis et al., 2019). Furthermore, because either time frames (Stein et al., 2016) or EFT cues are typically matched with those used during DD tasks (Rung & Madden, 2019), the observed effects cannot be directly attributed to EFT.

Against this background, before EFT can be regarded as effective for promoting smoking cessation, research needs to assess its feasibility and, particularly, to examine whether DD changes operate in a clinical context. To address this gap in the literature, this study sought to: 1) examine the feasibility and acceptability of EFT + CBT for smoking cessation in SUD smokers, and 2) preliminarily assess its effect on post-treatment DD and cotinine changes.

2. Method

2.1. Participants and procedure

The study sample comprised smokers with SUD from four substance use treatment facilities in the local area. The treatment facilities were outpatient-based and provided psychosocial interventions. None of them addressed tobacco use, and none had smoking restriction policies (i.e., banning smoking outdoors, controlling smoking hours, or regulating how many cigarettes patients could smoke each day).

The study conducted recruitment between January and May 2019 and included formal announcements through therapist referral and advertisements (i.e., posters, flyers, and mass media) posted around the community. All patients attended an initial motivational (1-h) session following the principles of motivational interviewing (MI) by Miller and Rollnick (2012). The session aimed to recruit potentially eligible patients interested in quitting smoking, and it covered the following topics: 1) pros and cons of smoking, 2) benefits of smoking cessation, 3) fears of quitting, 4) and feedback on carbon monoxide (CO) levels through expired air monitoring.

To determine eligibility, study staff asked interested individuals to contact the clinical unit by phone or e-mail to request an appointment. The eligibility criteria were: 1) being at least 18 years of age, 2) smoking at least 10 cigarettes per day in the last year, and 3) undergoing outpatient substance use treatment for opioids, stimulants, and/or alcohol use disorder. Exclusion criteria included: 1) not being able to attend the entire treatment, 2) having severe mental disorders (i.e., active psychotic disorder and/or suicidal ideation), 3) receiving pharmacological (i.e., bupropion, varenicline, NRT) or psychological smoking cessation treatment at the time of the intake assessment, and 4) self-reporting cannabis use only. Cannabis use was an exclusion criterion since both tobacco and cannabis share a route of administration, and their combined use is frequent (i.e., co-administration), so the cooximetry results could be contaminated (see e.g., Agrawal et al., 2012). The substance use treatment and the smoking cessation intervention were delivered independently, so relapse to substances other than nicotine was not used as an exclusion criterion from the tobacco study.

All participants provided written informed consent and the local Ethical Committee of Research of the Principality of Asturias (n°144/16) approved the study protocol, and we registered the study in the ClinicalTrials-gov database (ref. NCT03551704).

2.2. Measures

2.2.1. Demographics and substance use-related characteristics

During a single assessment session, participants completed an ad-hoc questionnaire, which collected sociodemographic data (i.e., sex, age, monthly income, educational level, and marital status) and substance use–related variables. Smoking-related characteristics were number of cigarettes smoked per day, nicotine intake (in milligrams), age of smoking onset, years of regular smoking, number of previous 24-h quit attempts, and current motivation to quit. The study also collected the following substance use characteristics for all participants: primary and secondary substance use, length of SUD treatment, and days of abstinence from their primary substance. Also, we assessed past year SUD diagnosis using the Structured Clinical Interview for the DSM-5 (Clinical Version) (SCID-5; First et al., 2016). All participants provided a urine sample for cotinine and drug testing (cocaine, opioids, amphetamine, methamphetamine, and cannabis) and a breath sample to assess CO and alcohol concentrations.

In addition, the study used the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991) to evaluate nicotine dependence. The FTND established five levels based on scores: very low (0–2), low (3–4), medium (5), high (6–7), and very high (8–10) (Fagerström & Kozlowski, 1990).

2.2.2. Feasibility and acceptability outcomes

The feasibility of EFT+CBT was based on: 1) recruitment success (percentage of individuals completing the baseline out of the total number of participants who met the inclusion criteria), 2) rates of treatment completion (percentage of patients that completed the treatment and attended all therapy sessions), 3) session attendance (average number of therapy and midweek sessions attended), and 4) adherence to the EFT component (number of EFT practices during the 8-week treatment, out of a maximum of 210 times).

To evaluate acceptability, the study considered post-treatment patient satisfaction using an ad-hoc questionnaire based on a dichotomous (yes/no) and a 10-point scale (from totally disagree to totally agree). Participants responded on: 1) smoking cessation treatment length defined as adequacy of number, duration, and frequency of therapy sessions; 2) utility of the smoking cessation treatment components (i.e., stimulus control, problem-solving, and diaphragmatic breathing), and specifically the EFT component; 3) practice difficulty in the above-mentioned components; 4) willingness to recommend this treatment to others; and 5) overall treatment satisfaction.

2.2.3. Preliminary effectiveness outcomes

The study assessed nicotine intake reductions throughout treatment by number of self-reported cigarettes per day and urinary cotinine concentrations. Samples were assessed at the time of the intake assessment and at each therapy session, using a BS-120 chemistry analyzer (Shenzhen Mindray Bio-medical Electronics CO. Ltd., Shenzhen, P. R. China). Values equal to or above 80 ng/ml indicated smoking abstinence

status.

The study assessed EFT effects over impulsive choice using changes in pre-post DD. Participants completed a computerized DD task and study staff instructed them to choose between several immediate amounts of money or US$1099 after a fixed delay (1 day, 1 week, 1 month, 6 months, 1 year, and 25 years). The immediate monetary value ranged from US$5.49 to US$1099, and we adjusted it through a titration procedure described previously (Holt et al., 2012).

2.3. Intervention

Masters- and doctoral-level psychologists with prior experience in smoking cessation treatments conducted the treatment. Before the project onset, the principal investigator (PI), and expertise in clinical psychology, trained and supervised each therapist on at least three cases. All session were audio-recorded, and the PI reviewed them each week to ensure that there were no deviations from the treatment protocol. The psychologists delivered the intervention across eight weekly therapy sessions lasting a maximum of 120 min each, in a group-based format (up to four patients). The study included seven additional midweek visits to collect CO and cotinine samples. Altogether, the study required patients to attend the clinic twice a week for a total of 15 visits.

The intervention included both CBT and EFT for smoking cessation and impulsivity management. The CBT was designed to provide coping skills training to patients to effectively manage their smoking withdrawal symptoms and to quit smoking. Treatment components included psychoeducation on the consequences of tobacco use; fears and myths on the smoking-substance use relationship; therapeutic commitment; self-monitoring of cigarette smoking; feedback on smoking reduction; and training in self-control strategies, stimulus control, management of craving with alternative activities, problem-solving skills, diaphragmatic breathing, and relapse prevention strategies. The study used a nicotine fading procedure, which consisted of a weekly reduction in nicotine intake of 20% (based on both tobacco brands and cigarettes) from the first to the sixth session.

Following prior recommendations for EFT implementation (see supplementary Table 1) (Hollis-Hansen et al., 2019; Snider et al., 2016), the study implemented the EFT component from the first session onward. The study required patients to develop a total of seven future nonsmoking situations occurring over different time periods (four situations in two weeks, two in a month, and one in six months), so they had to practice a total of 210 times. Psychologists delivered EFT following a three-step procedure: 1) the therapist asked patients to identify nonsmoking positive events (e.g., an outdoor family meal, a novel activity) that they were looking forward to within the purported time periods. 2) During each therapy session, the therapist asked patients to write down the situation on a sheet of paper (including their elected place, companion, feelings, activities, etc.), generate a short sentence that easily reminded them of the situation, and practice visualizing it for 2–3 min. 3) After that, patients rated the vividness on a 10-point scale. If they rated vividness below 6, therapists worked with patients in a collaborative way to identify difficulties in selecting or describing the requested situations and to help them to include more details that might facilitate the visualization. For homework during the week, therapists asked patients to practice the visualization twice daily and self-register the vividness of each practice from 0 to 10. The study based the EFT compliance on the number of times patients had both practiced the elected situations and rated their associated vividness.

2.4. Data analyses

We conducted descriptive statistics analyses to assess participants' baseline characteristics and provide data on feasibility and acceptability outcomes. The study used a set of nonparametric Wilcoxon Signed-Rank tests to analyze preliminary effectiveness outcomes. We calculated effect sizes as follows: $r = Z/\sqrt{n}$ (Rosenthal, 1994), with >0.10 being small, >0.30 medium, and > 0.50 large (Field, 2013).

We computed the AUC_{logd} as a measure of DD by calculating the log of each delay and dividing each logged delay by the longest one (25 years; see Borges et al., 2016). This index is a newly proposed indicator of discounting that corrects the unbalanced contribution of each indifference point (Myerson et al., 2001). It varies between 0 and 1, with lower values indicating higher levels of impulsive choice (i.e., steeper discounting). We analyzed data with the statistical package SPSS for Windows (version 24, SPSS, Inc., Chicago IL, USA).

3. Results

3.1. Feasibility outcomes

3.1.1. Recruitment success

Fig. 1 displays the participant flowchart. Among the 147 patients who attended the MI session, 51 did not meet the inclusion criteria, and 54 were not interested in participating after staff provided further study details. Therefore, our recruitment success was 43.75% (42/96). Of the 42 participants who completed the intake assessment, 13 were discarded due to time constraints or self-initiated quit attempts. This left 29 participants who we allocated to the CBT + EFT intervention (see Table 1 for participant characteristics).

3.1.2. Treatment completion and session attendance

A total of 65.5% (19/29) completed the treatment. The percentage of patients attending all therapy sessions was 42.1% (8/19). The participants underwent an average of 7 therapy (*SD* = 1.11) and 5.53 midweek sessions (*SD* = 1.5). Of the 29 patients who enrolled in

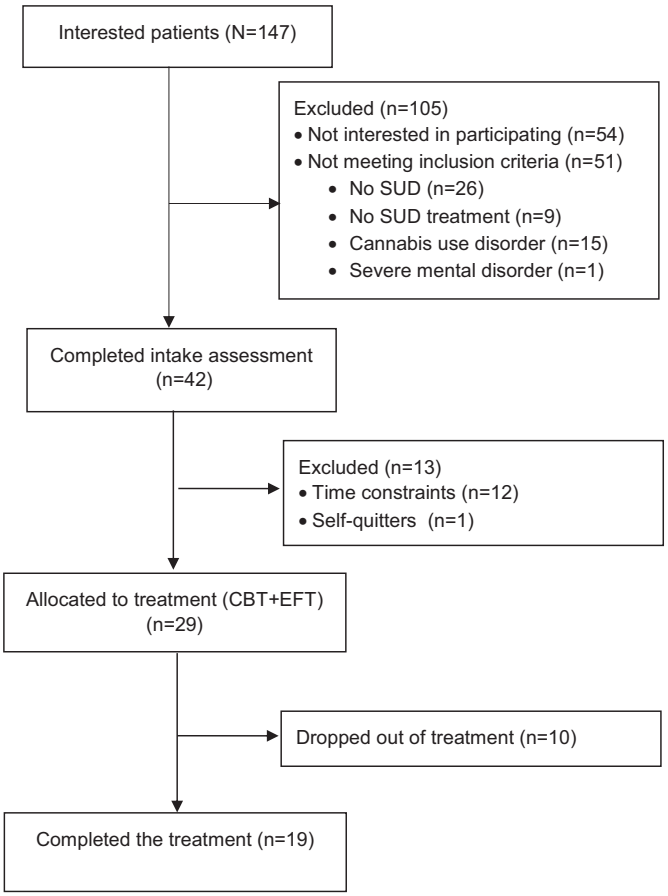

Fig. 1. CONSORT flow-chart of participants.
Note. SUD = substance use disorder, CBT = cognitive-behavioral treatment; EFT = episodic future thinking.

Table 1
Demographics, smoking, and drug-related characteristics.

	Overall $N = 29$	Completers $n = 19$	Withdrawals $n = 10$	p
Age(years)[a]	45.21 (10.23)	46.26 (10.04)	43.20 (10.83)	0.565
Sex (n/% males)	22 (75.9%)	15 (78.9%)	7 (70%)	0.593
Educational level (n/%)				0.705
<High school	23 (79.3%)	10 (52.63%)	6 (60%)	
≥High school	6 (20.7%)	9 (47.36%)	4 (40%)	
Monthly income (US $)[a]	1514.50 (1734.06)	1700.66 (2031.59)	1160.77 (942.37)	0.730
Marital status (n/% married)	7 (24.1%)	3 (15.8%)	4 (40%)	0.148
Primary drug use (n/%)				0.578
Cocaine	11 (37.9%)	6 (31.6%)	5 (50%)	
Alcohol	11 (37.9%)	7 (36.8%)	4 (40%)	
Opioids	6 (20.7%)	5 (26.3%)	1 (10%)	
Others	1 (3.4%)	1 (5.3%)	0 (0%)	
Secondary drug use (n/%)				0.527
Cocaine	2 (6.9%)	2 (10.5%)	0 (0%)	
Alcohol	5 (17.2%)	2 (10.5%)	3 (3%)	
Cannabis	4 (13.8%)	3 (15.8%)	1 (10%)	
Benzodiazepines	1 (3.4%)	1 (5.3%)	0 (0%)	
Dependence[a]				
CPD[a]	23.69 (9.67)	22.26 (7.45)	26.4 (12.94)	0.571
Years smoking	28.16 (10.21)	29.98 (10.13)	24.7 (9.94)	0.269
Days at drug treatment	496.14 (973.11)	590.79 (1154.26)	316. 3 (218.4)	0.630
Previous attempt to quit substance use	3.41 (5.89)	2.57 (2.98)	5.00 (9.27)	0.740
CO (ppm)[a]	21.9 (15.28)	23.16 (18.39)	19.5 (6.32)	0.800
Cotinine (ng/ml)[a]	1895.1 (653.42)	1828.04 (630.6)	2022.5 (719.5)	0.491
FTND[a]	7 (1.604)	7.11 (1.37)	6.8 (2.044)	0.742
Quit attempts	1.52 (2.18)	1.05 (1.268)	2.4 (3.2)	0.249
Stage of change (n/%)				0.755
Pre-contemplation	1 (3.4%)	1 (5.3%)	0 (0%)	
Contemplation	20 (69%)	13 (68.4%)	7 (70%)	
Preparation	8 (27.6%)	5 (26.3%)	3 (30%)	
Impulsive choice[a]				
DD (AUC_{logd})[a]	0.564 (0.172)	0.605 (0.162)	0.4869 (0.171)	0.169

[a] Mean (standard deviation); CPD = cigarettes per day; CO (ppm) = carbon monoxide in parts per million; ng/ml = nanograms/ml; FTND = Fagerström Test for Nicotine Dependence; DD = delay discounting; AUC_{logd} = base-10 logarithmic transformation of the area under the curve.

treatment, 10 patients dropped the treatment because they reported no motivation to quit smoking ($n = 7$) or they discontinued attendance to the SUD treatment facility ($n = 3$). Completers and withdrawals did not significantly differ in any baseline characteristics (all p values >.148, see Table 1).

3.1.3. Adherence to episodic future thinking (EFT)

Of the 210 required EFT practices, participants reported a mean of 51.11 ($SD = 61.16$). The average vividness in visualization was 8.44 ($SD = 1.04$). Three of 19 (15.8%) patients practiced at least 50% of the requested times, whereas 26% did not accomplish any visualizations at all.

3.2. Acceptability outcomes

Treatment satisfaction was high (8.83/10). Most patients were in total agreement that they would recommend the treatment to other SUD patients (9.17/10) and reported a mean of 8.61 ($SD = 1.69$) of perceived treatment utility for the SUD population.

In relation to treatment length, 66.7% of patients reported that 8 weeks of treatment was sufficient for quitting smoking. A total of 94.4% considered that the length of therapy sessions (i.e., 2 h/session) was appropriate, and 88.9% indicated that two sessions per week was adequate.

Perceived utility of treatment components was high. Patients rated stimulus control as the most helpful for smoking cessation (8.72/10), followed by problem-solving (7.78/10), diaphragmatic breathing (7.39/10), and EFT (6.11/10). Patients regarded EFT as the least demanding of the treatment components (3.56/10), followed by problem-solving (4.22/10), diaphragmatic breathing (3.72/10), and stimulus control (4.83/10).

3.3. Preliminary effectiveness outcomes

Number of self-reported cigarettes per day decreased significantly at the post-treatment [$Mdn_{\text{pre-treatment}} = 20$ (IQR, 20–30); $Mdn_{\text{post-treatment}} = 6$ (IQR, 0–6); $Z = -3.825$, $p < .001$, $r = 0.87$]. Congruently, there was a statistically significant reduction in cotinine levels (see Fig. 2): [$Mdn_{\text{pre-treatment}} = 1832$ (IQR, 1435.4–2252); $Mdn_{\text{post-treatment}} = 1299.5$ (IQR, 83.9–2251.7); $Z = -2.093$, $p = .036$, $r = 0.48$]. At treatment termination, 31.57% of participants (6/19) reached cotinine levels below 80 ng/ml.

A total of 42.11% (8/19) of participants increased their DD. The mean percentage of increase was 14.29% (ranging from 0.12% to 41.48%), and the mean percentage of decrease was 28.04% (from 6.84% to 54.93%) (see Fig. 3). Taken together, there were no significant pre-post changes in AUC_{logd} [$Mdn_{\text{pretreatment}} = 0.571$ (IQR, 0.477, 0.778); $Mdn_{\text{post-treatment}} = 0.565$ (IQR, 0.369, 0.792); $Z = -1.046$, $p = .295$, $r = 0.24$].

4. Discussion

This is the first clinical study to examine the feasibility and acceptability of EFT for smoking cessation in smokers with SUD. Three results are highlighted: 1) CBT + EFT for SUD smokers was acceptable and potentially feasible for individuals in SUD treatment if several adjustments are made, 2) CBT + EFT showed preliminary effectiveness for facilitating nicotine intake reductions, and 3) the study did not observe any significant pre-post treatment changes in DD.

The 43.75% (42/96) recruitment rate is substantially higher than the rates in other studies with smokers with SUD (0–26%) (Gass et al., 2018). However, the recruitment rate remains considerably low compared to non-SUD populations (Ebbert et al., 2015; Hickman et al., 2015; López-Núñez et al., 2016). The largest recruitment occurs when studies use online methods (Watson et al., 2018; Whitaker et al., 2017) or low-magnitude incentives (Brueton et al., 2013; Cheung et al., 2017). Thus, after motivational sessions, sending reminder emails or mobile

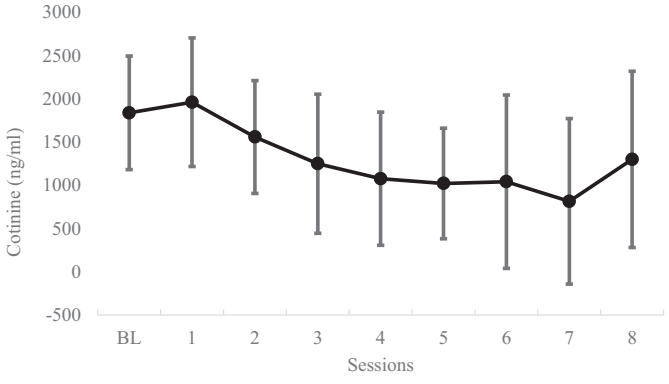

Fig. 2. Mean and standard deviation of urine cotinine reduction throughout treatment.
Note. ng/ml = nanograms per milliliter; BL = baseline session.

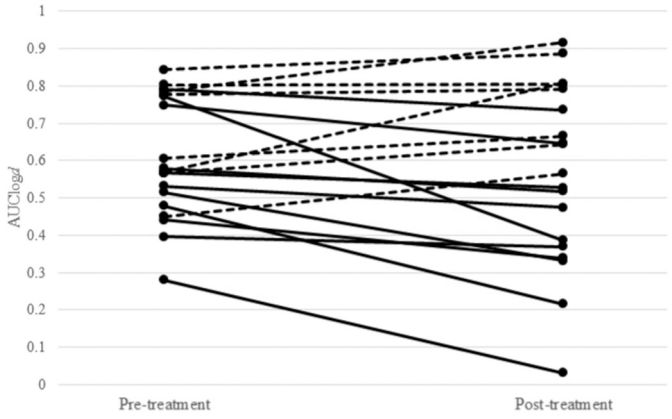

Fig. 3. Delay discounting rates at pre- and post-treatment for each participant. *Note*. Participants who decreased their delay discounting rate are shown with a solid line. Participants who increased their delay discounting rate are indicated by a dashed line. AUClog*d* = base-10 logarithmic transformation of the area under the curve.

messages in combination with vouchers, to be received once enrolled, might represent a feasible plan to enhance recruitment (Treweek et al., 2018).

Our findings also showed that treatment was feasible according to the completion rate (65.5%) and treatment attendance. This rate is within the average range shown in the field of substance use treatment (46.5%–74.9%; Lappan et al., 2020), and particularly for other smoking cessation treatments in this population (17%–100%; (Prochaska et al., 2004). Other studies with smokers with SUD using CM attain excellent retention rates, ranging from 80% to 98% (Cooney et al., 2017; Dunn et al., 2010; Winhusen et al., 2014). Delivering vouchers that reinforce retention or attendance could enhance treatment abstinence rates and produce fewer dropouts (López-Núñez et al., 2016; Notley et al., 2019).

Participants rated CBT + EFT as acceptable, with regard to treatment length, session duration, and frequency. Although the EFT component was rated as the least demanding, the adherence was considerably low, which is in line with recent studies (Patel & Amlung, 2020). The low compliance suggests that studies should make several adjustments to improve the practice's effectiveness and feasibility so that it can be implemented in clinical contexts. First, individuals with SUD present severe limitations in future thinking and self-projection (El Haj et al., 2019; Mercuri et al., 2018; Moustafa et al., 2018), so visualizing a distant personal future (i.e., 6 months) might be difficult. One way to solve this problem may be to reduce the number of required practices and to practice with shortened temporal windows (e.g., from one week to three months). On the other hand, although this study did not assess this, patients' low perceived utility of EFT might be explained by a low ability to understand the treatment rationale. Perceiving the task as worthwhile sets the framework for all sessions and is essential for patients' adherence to homework assignments (Hopko et al., 2011). In this sense, introducing EFT early in motivational sessions or baseline assessments might be critical to increase patients' understanding of EFT's rationale and prevent treatment failure. Finally, regarding practical issues related to EFT, it is worth noting the lack of commitment to providing self-reports. This lack of commitment could be solved by explaining the rationale for providing self-reports, using computerizing EFT self-reports (see e.g., Cebolla et al., 2010; Graham et al., 2017), or by using ecological momentary assessment (see e.g., Shiffman et al., 2008). These proposals should be considered in future clinical studies of EFT.

The significant nicotine intake reductions that this study observed throughout treatment further support the feasibility of CBT + EFT for facilitating smoking abstinence in this difficult-to-treat population. Despite that 5/19 patients successfully quit smoking, cessation rates remain considerably low, suggesting the usefulness of integrating CM to extend CBT + EFT effects. Providing incentives to reinforce abstinence may be a suitable aim, especially considering findings that indicate not only improved abstinence outcomes but also significantly better attendance and full retention in treatment (Cooney et al., 2017; Winhusen et al., 2014).

Taking into account all participants, our findings did not evidence a significant change in DD rates overall, although over half the participants (11/19; 57.89%) did reduce their DD rates. These outcomes are contrary to previous studies in individuals with alcohol use disorder (see e.g., Patel & Amlung, 2020; Snider et al., 2016). Several factors might explain this outcome. Unlike previous studies, the current study participants were not present with EFT cues when doing the DD task at treatment termination (Rung & Madden, 2019), and the study did not match the time frames in the EFT practices with those presented during the completion of the DD task (see e.g., O'Donnell et al., 2019; Patel & Amlung, 2020), to prevent participants from guessing the study hypotheses. In this sense, results suggest that the laboratory-based EFT effects might not generalize to a real-world context, such as SUD treatment facilities. However, not enough research has addressed these issues to date (see e.g., Rung & Madden, 2019); therefore, further control trials are needed to clarify it.

Second, findings may also be related to the low patient compliance with EFT, especially given that larger DD decreases are observed with repeated practice (Mellis et al., 2019). Finally, pre-treatment DD rates were very high (i.e., low impulsive choice), compared to non-SUD smokers (González-Roz et al., 2019; Weidberg et al., 2015), probably as a result of abstinence from non-nicotine substances and SUD treatment, which typically includes impulsivity-targeted components (e.g., problem solving). This ceiling effect may be a limitation for detecting significant reductions in the outcome. The screening processes might help us to determine which patients would be best suited to EFT training, in that shallow discounters may benefit more from less intensive impulsivity-targeted treatments, such as CBT treatments.

The findings here should be interpreted in the light of several limitations. First, the relatively small sample size may have led us to obtain insufficient statistical power to detect significant differences, so definite conclusions on EFT effectiveness for reducing DD cannot be yielded. Second, the study did not include a control or comparison arm; larger scale randomized controlled trials should examine EFT efficacy in real-world contexts. Third, the study cannot determine the causality of DD, since it was only assessed at baseline assessment and at the end of treatment, and using only two assessments does not enable us to establish potential changes in DD. Finally, the study discarded cannabis users, and our findings, therefore, may not generalize to the entire population of smokers with SUD. Notwithstanding these limitations, because this study was designed as a feasibility study, it allows us to identify barriers and difficulties to the effective implementation of EFT in clinical contexts.

5. Conclusion

In conclusion, this is the first study to assess EFT for smoking cessation in a real-world context (i.e., substance use treatment facilities). The study found that integrating EFT into a CBT program for smoking cessation was feasible and acceptable to smokers with SUD. Participants reported that EFT was useful for facilitating nicotine intake reductions and easy to practice; however, the study observed no changes in DD rates. The low compliance with EFT practices suggests the need to incorporate a number of adjustments, such as shortened time periods and a reduced number of practices. Future large-scale clinical trials should evaluate whether EFT facilitates smoking abstinence and decreases DD more than a comparison or control condition does.

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CRediT authorship contribution statement

Gema Aonso-Diego: Conceptualization, project administration, writing the original draft, formal analyses, data collection. **Alba González-Roz**: Conceptualization, project administration, writing the original draft, data collection. **Víctor Martínez-Loredo**: Software, formal analyses, data collection. **Andrea Krotter**: Formal analyses, data collection. **Roberto Secades-Villa**: Conceptualization, project administration, funding acquisition, supervision.

Declaration of competing interest

No conflict declared.

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5.3. Contingency management for smoking cessation among individuals with substance use disorders: in-treatment and post-treatment effects

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Introduction. Smokers with substance use disorders (SUDs) show elevated tobacco prevalence, and smoking abstinence rates are considerably low. This randomized controlled trial sought to compare the effect of a cognitive behavioral treatment (CBT) that includes an episodic future thinking (EFT) component with the same treatment protocol plus contingency management (CM). This study aims to examine the effect of CM on smoking outcomes and in-treatment behaviors (i.e., retention, session attendance and adherence to nicotine use reduction guidelines), and to analyze whether these in-treatment variables predicted days of continuous abstinence at end-of-treatment. **Method**. A total of 54 treatment-seeking participants (75.9% males, M = 46.19 years old) were allocated to CBT + EFT (n = 30) or CBT + EFT + CM (n = 24). Intervention consisted of eight weeks of group-based sessions. Tobacco abstinence was verified biochemically by testing levels of carbon monoxide (≤4ppm) and urine cotinine (≤80 ng/ml). **Results**. CM intervention increased 24-hour tobacco abstinence (50% vs. 20%, $\chi2(1) = 5.4$; $p = .021$) and days of continuous abstinence (M = 5.92 ± 7.67 vs. 5.53 ± 12.42; $t(52) = -0.132$; $p = 0.89$) at end-of-treatment in comparison with CBT + EFT intervention. Although not statistically significant, CBT + EFT + CM enhanced in-treatment behaviors, in terms of retention (83.3% vs. 70%; $\chi2(1) = 0.255$; $p = .208$), sessions attended (12.29 ± 3.22 vs. 10.93 ± 3.26; $t(52) = -1.527$; $p = .133$) and adherence to weekly nicotine use reduction targets (41.07% ± 31.96 vs. 35% ±2 6.28; $t(52) = -0.766$; $p = .447$). A higher percentage of samples meeting reduction guidelines ($\beta = 0.609$; $p < .001$) predicted days of continuous abstinence at end-of-treatment. **Conclusion**. Combining CM with CBT + EFT improves short-term quitting rates. Findings suggest the need to incorporate strategies for improving adherence to nicotine reduction guidelines.

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Contingency management for smoking cessation among individuals with substance use disorders: In-treatment and post-treatment effects

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ABSTRACT

Introduction: Smokers with substance use disorders (SUDs) show elevated tobacco prevalence, and smoking abstinence rates are considerably low. This randomized controlled trial sought to compare the effect of a cognitive behavioral treatment (CBT) that includes an episodic future thinking (EFT) component with the same treatment protocol plus contingency management (CM). This study aims to examine the effect of CM on smoking outcomes and in-treatment behaviors (i.e., retention, session attendance and adherence to nicotine use reduction guidelines), and to analyze whether these in-treatment variables predicted days of continuous abstinence at end-of-treatment.

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Conclusion: Combining CM with CBT + EFT improves short-term quitting rates. Findings suggest the need to incorporate strategies for improving adherence to nicotine reduction guidelines.

1. Introduction

Smokers with substance use disorders (SUDs) are considered hard-to-treat smokers due to high smoking rates (59% − 86%) (Gass et al., 2018; Guydish et al., 2016; Ingram et al., 2017; Weinberger et al., 2018), elevated nicotine dependence (Goodwin et al., 2014; Parker et al., 2018) and severe withdrawal symptomatology (Heffner et al., 2011).

Despite the existing effective smoking cessation treatments, abstinence rates remain considerably low among this population. At end-of-treatment, 21% of participants achieve tobacco abstinence, whereas rates decline to 12% in long-term follow-up (Apollonio et al., 2016; Prochaska et al., 2004). To enhance quitting rates, smoking cessation treatments need to be adapted to this population, in terms of intensity (i.e., number of sessions, duration and frequency) and type of intervention (i.e., behavioral, pharmacotherapy or combined) (Hughes, 2013; Murphy and McKay, 2004).

Cognitive-behavioral therapies (CBT) have shown positive effects on smoking cessation, although abstinence rates remain moderate, ranging from 6% to 20% (Stead et al., 2017). Previous research has suggested that including components targeted at participants' characteristics, such as high impulsive choice, might enhance treatment outcomes (Verdejo-García et al., 2008). In this line, episodic future thinking (EFT), an intervention that consists of visualizing future situations with the aim of valuing the future consequences (i.e., health), has demonstrated promising results in tobacco and impulsive choice reductions (see e.g., Bulley and Gullo, 2017; Chiou and Wu, 2017; Patel and Amlung, 2020; Rung and Madden, 2018).

Contingency management (CM) is a behavioral intervention based

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on providing incentives contingent upon abstinence or therapeutic achievements (Notley et al., 2019). It stands as one of the most effective substance use treatments (Ainscough et al., 2017; McPherson et al., 2018), and has shown additive effects on tobacco abstinence over standard smoking cessation treatments in difficult-to-treat populations (Hand et al., 2017; Secades-Villa et al., 2019a). A recent meta-analysis in smokers with SUD concluded that CM performs significantly better compared to control conditions, in terms of tobacco abstinence and reduction at end-of-treatment (Secades-Villa et al., 2020). Nevertheless, mean abstinence rates are considerably low (36%), so further research is needed to improve treatment effectiveness in this particular group.

Identifying factors associated with smoking cessation facilitates the improvement of treatments and thus, abstinence rates. In this regard, several in-treatment variables, such as a higher number of sessions attended (Dorner et al., 2011; Joo et al., 2020), greater treatment adherence (Marino et al., 2010) and early abstinence during the initial weeks of therapy (Ashare et al., 2013; Romanowich and Lamb, 2010) stand as consistent predictors of short- and long-term smoking abstinence among the general population. However, in-treatment behaviors in relation to smoking abstinence have been less studied in SUD populations. There are only two prior studies examining in-treatment behaviors among smokers with SUD. Rohsenow et al. (2017) showed that days of abstinence during treatment did not predict long-term smoking abstinence, although results at end-of-treatment were not analyzed. On the other hand, Okoli and Khara (2014) demonstrated that the number of sessions attended predicts smoking cessation at end-of-treatment, although the sample comprised both participants with SUD and with psychiatric disorders.

This randomized controlled trial was the first study to examine effects of adding CM to a CBT + EFT protocol in smokers with SUD. The study specifically sought to: 1) examine whether adding a CM component improves smoking outcomes and in-treatment behaviors (i.e., retention, session attendance and adherence to nicotine reduction); and 2) to analyze whether in-treatment behaviors predict days of continuous abstinence at end-of-treatment.

2. Method

2.1. Participants and procedure

This study was conducted at the Clinical Unit of Addictive Behaviors of the University of Oviedo (ClinicalTrials-gov, ref: NCT03551704). Patients were recruited through their referral SUD facilities and by local advertisements (radio, TV, mass media, posters and flyers).

Inclusion criteria were being at least 18 years old, smoking at least 10 cigarettes per day within last year and receiving outpatient SUD treatment. Having severe a mental disorder (e.g., active psychotic or suicidal ideation/temptation), engaging in current cannabis use and receiving

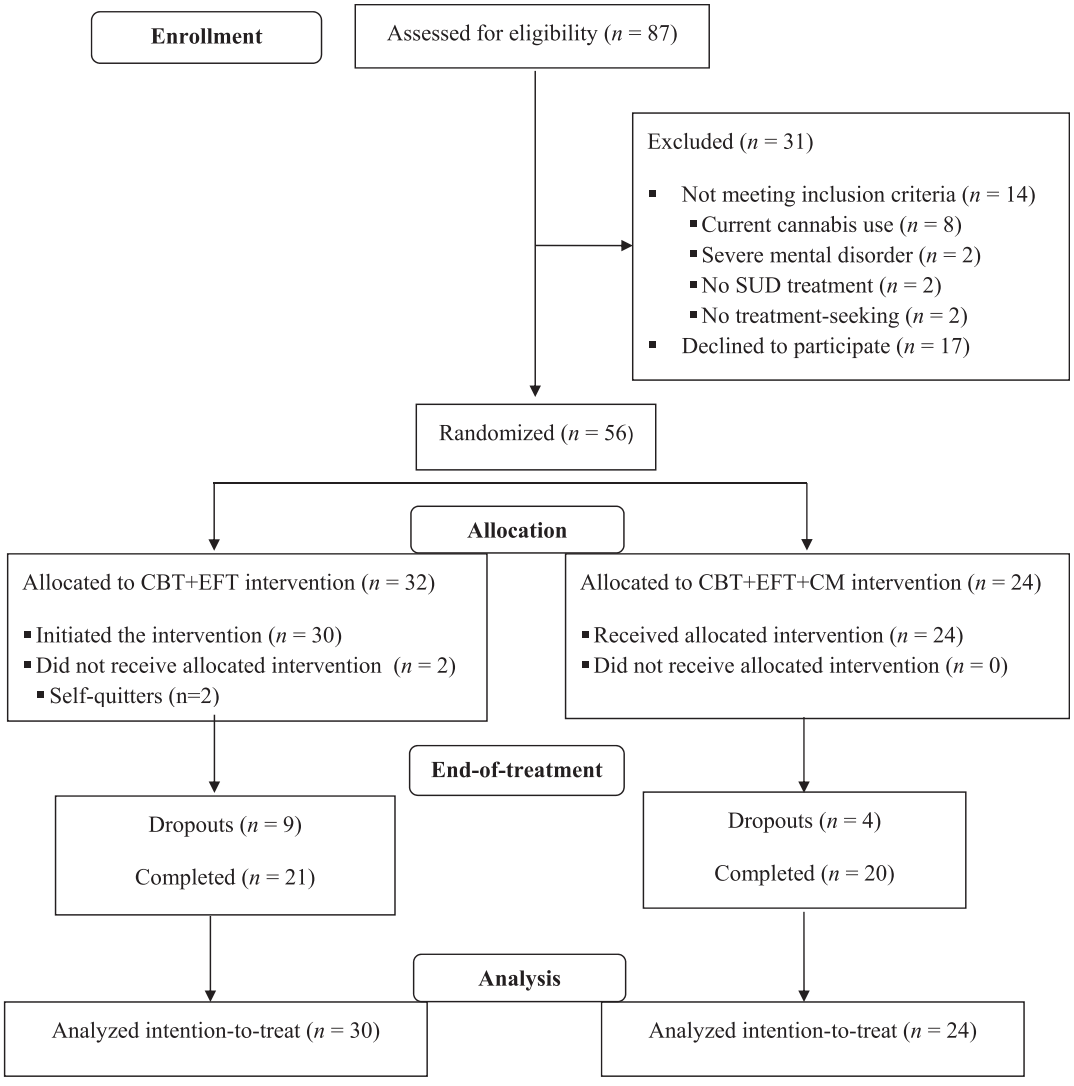

Fig. 1. CONSORT flow diagram of participants.

any other smoking cessation treatment were exclusion criteria.

Fig. 1 shows the flow of participants from enrollment to end-of-treatment. Out of the 87 participants initially assessed, 54 participated in the study and were assigned to the CBT + EFT group ($n = 30$) or the CBT + EFT + CM group ($n = 24$) (see Table 1). Treatment groups were randomized using a two-step random allocation approach: 1) generating a random assignment of participants implemented in excel, and 2) implementing the sequence in a way that conceals the treatments until patients have been formally assigned to their groups (Dettori, 2010). All participants provided informed consent and the study protocol was approved by the Research Ethics Committee of the Principality of Asturias (No. 114/16).

2.2. Measures

During the intake session, which lasted approximately an hour, participants were asked about sociodemographic data, substance use related characteristics, including tobacco use, and psychological variables. Sociodemographic characteristics included sex, age, marital status, educational level and monthly income. The following tobacco use variables were measured: cigarettes per day, years of regular use, previous 24-hour quit attempts and motivation to quit smoking. In addition, past year tobacco use disorder diagnosis was assessed using the Structured Clinical Interview for DSM-5 (SCID-5; First et al., 2016), and nicotine dependence was measured with the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991). Drug-related characteristics considered were primary and secondary substance used, days of abstinence from substances other than nicotine and days enrolled in SUD treatment. Both tobacco and drug use were also measured by biochemical analysis, using urine cotinine analysis, carbon monoxide (CO) and alcohol in expired air, as well as substance consumption through drug cassettes.

Table 1
Demographics, smoking and drug-related characteristics.

	CBT + EFT $n = 30$	CBT + EFT + CM $n = 24$	*p*-value
Age(years)[a]	44.97 (10.83)	47.71 (6.56)	0.257
Sex (males) n(%)	23 (76.6%)	18 (75%)	0.568
Educational level n(%)			0.261
< High school	15 (50%)	9 (37.5%)	
≥ High school	15 (50%)	15 (62–5%)	
Monthly income (US$)[a]	1,517.86 (1,664.57)	1,666.36 (1,437.26)	0.731
Marital status (married) n (%)	8 (26.6%)	6 (25%)	0.571
Primary drug use n(%)			0.887
Cocaine	12 (40%)	8 (33.33%)	
Alcohol	12 (40%)	12 (50%)	
Opioids	5 (16.66%)	3 (12.5%)	
Others	1 (3.33%)	1 (4.16%)	
Stage of change n(%)			0.547
Pre-contemplation	1 (3.33%)	0 (0%)	
Contemplation	19 (63.33)	17 (70.83%)	
Preparation	10 (33.33%)	6 (25%)	
Dependence[a]			
CPD[a]	22.63 (10.5)	20 (8.19)	0.319
Years smoking	27.25 (10.85)	29.08 (9.39)	0.522
Days at SUD treatment[a]	506.1 (929.43)	252.54 (276.05)	0.203
CO (ppm)	22.13 (15.87)	24.96 (17.89)	0.542
Cotinine (ng/ml)	1,738.1 (679.65)	2,563.96 (2037.31)	0.068
24-h quit attempts	1.33 (1.69)	1.88 (1.33)	0.205
FTND[a]	6.57 (2.19)	5.65 (1.89)	0.117
BDI-II[a]	14.1 (1.65)	13.38 (12.41)	0.818

Note. [a]Mean (standard deviation); CBT = cognitive-behavioral therapy; EFT = episodic future thinking; CM = contingency management; CPD = cigarettes per day; SUD = substance use disorder; CO (ppm) = carbon monoxide in parts per million; ng/ml = nanograms/milliliter; FTND = Fagerström Test for Nicotine Dependence; BDI-II = Beck Depression Inventory, second edition.

Psychological variables included were depressive symptomatology evaluated with the Beck Depression Inventory (BDI-II; Beck et al., 1996) and impulsive choice assessed through a DD task. The discounting task consisted of a computerized task in which participants had to choose between an amount of money now or €1,000 ($1,197) after a fixed delay (1 day, 1 week, 1 month, 6 months, 1 year, 5 years and 25 years). With this task, the immediate value, which ranges from €5 ($5.99) to €1,000 ($1,197), is adjusted by a titration procedure based on the participant's response (Holt et al., 2012) in order to estimate the indifference point for each of the delays. The indifference point refers to the subjective value where delayed and immediate reward are equivalent.

Smoking outcomes were analyzed according to three measures considering all participants: 24-hour and 7-day point-prevalence prior to end-of-treatment assessment and days of continuous abstinence at end-of-treatment. The following in-treatment variables were considered: a) retention (percentage of participants who completed the treatment), b) session attendance (mean total number of sessions attended) and c) treatment adherence (percentage of sessions in which patients met the cotinine criteria according to the weekly reduction of 20%).

2.3. Interventions

All therapists were master- and doctoral-level psychologists with previous training in specific protocols. All sessions were audio-recorded to ensure compliance with the study protocol.

2.3.1. Cognitive-behavioral treatment (CBT) + episodic future thinking (EFT)

The CBT protocol was based on Becoña (2007) but adapted to the SUD population (see Aonso-Diego et al., 2021). It consisted of eight weeks of group-based sessions with up to four patients. Participants had to attend the clinic twice a week: once for the therapy session ('session A') and once to provide CO and cotinine samples ('session B'). Therapy sessions took about 120 min, while mid-week sessions were of 30-minute duration. In total, patients had to visit the clinic 15 times.

Components included in CBT were psychoeducation about tobacco use, myths regarding the relationship between tobacco and drugs, monitoring of biochemical variables, stimulus control, problem-solving skills, relaxation for anxiety and relapse prevention strategies. The nicotine fading component consisted of reducing participants' nicotine intake by 20% each week (through weekly reductions in the number of daily cigarettes and changes in tobacco brands). Therefore, the quit day was set at 48-hours prior to the sixth session. The EFT component was added to promote the appraisal of the future reinforcers (i.e., personal future situations not related to tobacco use) against the current behavior (i.e., smoking). Participants had to visualize a total of five events related to future non-smoking situations (one in a week, two in two weeks, one in a month and one in three months) throughout the treatment. As homework, they had to self-report visualization practices twice a day and rate their realism on a 10-point scale.

2.3.2. Cognitive-behavioral treatment (CBT) + episodic future thinking (EFT) + contingency management (CM)

Patients allocated to this treatment condition received the same components as the ones describes above but with the addition of CM. Participants received points [one point was equivalent to one euro (US$ 1.13)] contingent upon biochemical confirmation of tobacco abstinence from the sixth session onwards. Smoking abstinence was defined as breath CO equal to or less than 4 particles per million (ppm) and urine cotinine equal to or less than 80 ng per milliliter (ng/ml), according to prior recommendations (Benowitz et al., 2020). Vouchers began at 20 points (US$ 22.60) and escalated by 5 points (US$ 5.65) for each consecutive negative sample. Additionally, patients could earn a bonus of 10 points (US$ 11.30) for achieving two consecutive negative smoking samples. A positive test or missed specimens reset the voucher value back to the initial 20 points (US$ 22.60), but when patients

provided two consecutive negative tests the vouchers value was re-established to the one given before the reset. The maximum amount that participants could earn at end-of-treatment was €170 (US$ 203.63), and the average earned in vouchers was €68.33(US$ 81.85).

2.4. Data analysis

Baseline descriptive statistics and treatment outcomes (smoking status at end-of-treatment and in-treatment variables) by intervention groups were examined using *t*-test for continuous variables and chi-square for categorical ones. Effect sizes were calculated using Cohen's *d* (Cohen, 1988), Cramer's *V* (Cramér, 1946) and phi coefficient (Fleiss, 1994), as appropriate.

A hierarchical linear regression was carried out to identify in-treatment predictors of days of continuous abstinence at end-of-treatment. The following variables were considered: mean total number of sessions attended (both therapy and control sessions) and percentage of samples meeting weekly nicotine reduction guidelines. Sex, AUC_{logd} as a measure of DD, number of cigarettes per day, nicotine dependence (FTND) and type of intervention (CBT + EFT vs. CBT + EFT + CM) were introduced as covariates.

An overall discounting rate was calculated using the $AUC_{logd.}$. This is a relatively novel indicator of discounting that addresses the limitations of the classic AUC calculation (Myerson et al., 2001). It is obtained by calculating the total AUC by dividing each logged delay by the longest logged delay (i.e., 25 years) (see Borges et al, 2016). The AUC_{logd} index varies between 0 and 1, with lower values indicating higher levels of impulsive choice (i.e., steeper discounting). The statistical package used was SPSS (version 24, Inc., Chicago, IL).

3. Results

3.1. Smoking outcomes

In the CBT + EFT + CM group, 58.33% (14/24) attained at least 24 h of tobacco abstinence during the treatment, and this figure was 40% (12/30) in the CBT + EFT condition ($\chi^2(1) = 1.136$; $p = .287$; $\varphi = 0.182$). At end-of-treatment, 24-hour abstinence was 50% (12/24) in CBT + EFT + CM group and 20% (6/30) in CBT + EFT ($\chi^2(1) = 5.4$; $p = 0.021$; $\varphi = 0.316$). Seven-day point-prevalence was 33.33% (8/24) in CBT + EFT + CM condition and 20% (6/30) in CBT + EFT ($\chi^2(1) = 1.234$; $p = 0.212$; $\varphi = 0.151$). Considering all participants, the number of days of continuous abstinence was higher, although not significantly, in CBT + EFT + CM versus CBT + EFT group ($M = 5.92 \pm 7.67$ vs 5.53 ± 12.42; $t(52) = -0.132$; $p = 0.895$; $d = 0.037$). Of the participants who had achieved tobacco abstinence on quit day (i.e., the sixth session), all of those in the CBT + EFT condition (6/6) and 54.54% (6/11) in CBT + EFT + CM were continuously abstinent at end-of-treatment.

In the CBT + EFT + CM group, a higher percentage of participants completed the treatment compared to CBT + EFT (70% vs 83.33%; $\chi^2(1) = 0.255$; $p = 0.208$; $d = 0.155$). Moreover, patients assigned to the CBT + EFT + CM group had a higher total number of sessions attended than CBT + EFT ($M = 12.29 \pm 3.22$ vs 10.93 ± 3.26; $t(52) = -1.527$; $p = 0.133$; $d = 0.419$). Adherence to weekly nicotine reductions, considered as the percentage of samples that met the recommended 20% reduction in nicotine use, was also higher in the CM group (CBT + EFT + CM: 41.07%; $SD = 26.28$; CBT + EFT: 35%; $SD = 31.96$; $t(52) = -0.766$; $p = 0.447$; $d = 0.344$). Adherence to nicotine reduction throughout treatment is displayed in Fig. 2.

3.2. Relationship between in-treatment behaviors and smoking abstinence

Table 2 presents the regression model that tested the relationship between in-treatment behaviors and days of continuous abstinence ($F(7,46) = 8.349$, $p < .001$). Adherence to nicotine fading and session attendance explained an additional 30.3%, so as a whole, this model accounted for 55.9% of the variance. Greater adherence to nicotine fading ($\beta = 0.512$; 95%CI 0.084, −0.288; $p = .001$) predicted higher days of continuous abstinence at end-of-treatment over and above covariates.

4. Discussion

This randomized controlled trial aimed to examine the effects of CM on smoking cessation and in-treatment behaviors in smokers enrolled in SUD intervention. Two results are highlighted: First, although both

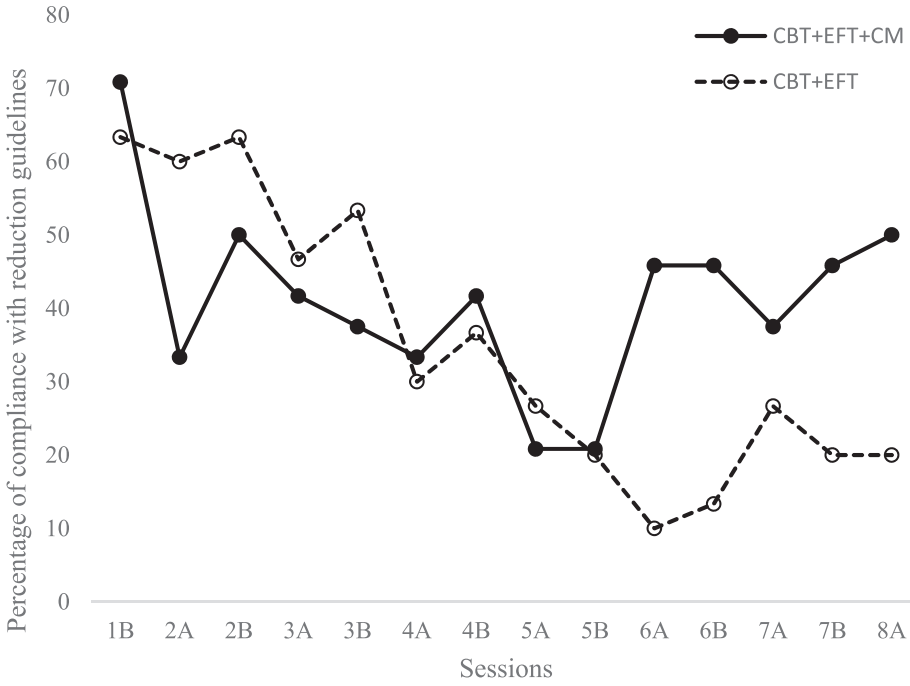

Fig. 2. Session-by-session progression of adherence to the nicotine reduction guidelines. Note. A = therapy session; B = mid-week session; CBT = cognitive-behavioral treatment; EFT = episodic future thinking; CM = contingency management.

Table 2
Predictors of continuous smoking abstinence.

	ΔR^2	F	B [95% CI]	β	p
Step 1	0.256	3.311			
Sex[a]			−0.746 [−7.109, 5.618]	−0.031	0.815
AUC_{logd}			12.044 [−4.044, 28.132]	0.195	0.139
CPD			−0.092 [−0.476, 0.291]	−0.084	0.631
FTND			−2.221 [−4.023, −0.418]	−0.445	0.017
Type of intervention[b]			−2.479 [−7.917, 2.959]	−0.119	0.364
Step 2	0.303	8.349			
Sex[a]			−0.998 [−6.014, 4.019]	−0.041	0.691
AUC_{logd}			3.882 [−9.118, 16.883]	0.063	0.551
CPD			−0.101 [−0.404, 0.201]	−0.092	0.503
FTND			−1.207 [−2.779, 0.364]	−0.242	0.129
Type of intervention[b]			−2.926 [−7.370, 1.517]	−0.140	0.192
Sessions attended			0.420 [−0.418, 1.259]	0.132	0.318
% of samples meeting weekly nicotine reduction targets			0.186 [0.084, 0.288]	0.512	0.001

Note. [a]Female sex was used as the reference category; [b]CBT was used as the reference category; ΔR^2 = increase in coefficient of determination; AUC_{logd} = base-10 logarithmic transformation of the area under the curve; FTND = Fagerström Test for Nicotine Dependence; CPD = cigarettes per day at baseline.

treatments produced similar smoking abstinence and in-treatment outcomes, the data indicate a tendency towards lower tobacco use and better in-treatment behaviors in the CBT + EFT + CM group compared to CBT + EFT. Secondly, adherence to nicotine reduction guidelines predicted more days of continuous abstinence at end-of-treatment.

Our results show that adding CM to a CBT + EFT treatment improves tobacco abstinence at end-of-treatment compared to the CBT + EFT group, which confirms and extends previous evidence showing that incentives can be successfully used for quitting tobacco use in smokers with SUD (Cooney et al., 2017, 2015; Hunt et al., 2010; Shoptaw et al., 2002; Sigmon et al., 2016; Tuten et al., 2012; Winhusen et al., 2014). Despite the fact that CM facilitates more individuals achieving 24 h of tobacco abstinence at end-of-treatment, the number of days of continuous abstinence was not significantly higher in this group. This result, which seems contradictory, indicates that implementing another reinforcement procedure, such as shaping (see e.g., Secades-Villa et al., 2019b), could yield more continuous abstinence results.

Abstinence rates at end-of-treatment (18/33.33%) were superior compared to other smoking cessation treatments in this population (20.52%; Prochaska et al., 2004). This finding can be explained due to three reasons. Firstly, participants were trained in effective CBT strategies to deal with high-risk situations and withdrawal symptoms. Secondly, the continuous biochemical monitoring of tobacco use throughout the entire treatment might have arguably led to enhanced smoking cessation rates, particularly through an increase in motivation (McPherson et al., 2014; Schuler et al., 2014). Thirdly, EFT has been proved to produce meaningful impacts on DD reductions (see e.g., Patel and Amlung, 2020; Snider et al., 2016; Stein et al., 2016), which is in turn a consistent predictor of smoking abstinence (see e.g., Coughlin et al., 2020; Miglin et al., 2017).

Concerning in-treatment behaviors (completion rates, number of sessions attended and percentage of adherence to nicotine reduction), incentive-based treatment yielded a clinically meaningful effect, although it was not significantly different from CBT + EFT. While the rates of session attendance were similar to those in other studies (see e.g., Cooney et al., 2017; Rohsenow et al., 2015; Shoptaw et al., 2002; Winhusen et al., 2014), the slightly superior average in the CBT + EFT + CM group over CBT + EFT may be related to increased motivation to attend sessions, as vouchers were only delivered upon participants' attendance.

A higher percentage of urine samples meeting nicotine use reduction targets was significantly related to days of continuous abstinence at end-of-treatment. This is in line with research in non-SUD populations (Ashare et al., 2013; Higgins et al., 2006; López-Núñez et al., 2016; Romanowich and Lamb, 2010). Gradual reduction of tobacco use could minimize withdrawal symptomatology and enhance motivation to quit, thus facilitating smoking cessation (Lindson et al., 2019). Moreover, in the addictions field, it has been shown that higher number of biochemical samples submitted is related to a greater likelihood of abstinence at end-of-treatment (Petry et al., 2006). The fact that participants provided biochemical samples (both CO and urine cotinine) twice a week may account for these results.

Several limitations should be considered. First, the relatively low sample size prevented us from obtaining sufficient representativeness, and it seems plausible that the failure to observe significant differences between treatment conditions was attributable to low statistical power. Secondly, this study only reported data at the end of treatment, thus, results cannot draw conclusions regarding long-term effectiveness. Further research should seek to examine long-term effects in larger and more diverse samples. Thirdly, the high percentage of dropouts (24.07%) may have important methodological and clinical implications for future research. Due to the small number of dropouts in the present study ($n = 13$), predictors of attrition could not be analyzed, however, future large-scale studies would benefit from identifying potential characteristics related to dropout in order to improve smoking cessation treatments for SUD populations. Finally, an isolated CBT group, without EFT, was not considered, so no conclusions can be drawn about the unique effects attributable to EFT.

In spite of these limitations, our findings suggested that adding CM into a CBT + EFT protocol facilitates tobacco abstinence and slightly superior completion rates, session attendance and treatment adherence. Moreover, participants who met the nicotine reduction criteria were more likely to achieve tobacco abstinence successfully. This underlines the importance of promoting adherence to weekly nicotine fading targets in this hard-to-treat population. The inclusion of biochemical feedback (Benowitz et al., 2020), offering a variety of incentives (cash, activities in the community), increasing their magnitude, or reinforcing behaviors other than abstinence (e.g., attendance or adherence to therapy activities for home practice) (Petry et al., 2018; Secades-Villa et al., 2019b) could be useful tools for this purpose.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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5.4. Effects of episodic future thinking on reinforcement pathology during smoking cessation treatment among individuals with substance use disorders

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Rationale. Reinforcer pathology (RP) is a theoretical model based on two processes: delay discounting (DD) and drug demand. Given that RP has been shown to have a predictive value on smoking behaviors, several studies have explored which interventions can reduce RP. Consistent with the RP framework, episodic future thinking (EFT) has shown effects on treatment outcomes and RP processes. The vast majority of studies that assess the effects of EFT on RP consist of experimental studies, and no previous research has tested these effects in a clinical sample of smokers. **Objectives**. The primary aim of this study was to assess the effects of EFT on RP throughout the course of a smoking cessation intervention in smokers with substance use disorders (SUDs). **Methods**. Participants were randomized to cognitive behavior therapy (CBT) + EFT (n = 39) or CBT + EFT + contingency management (n = 33). Cotinine, frequency of EFT practices, cigarette purchase task (CPT), and DD were evaluated in treatment sessions. Mixed-effects model repeated measures analysis was used to explore DD and CPT in-treatment changes as a function of EFT practices and cotinine levels. **Results**. Greater practice of the EFT component significantly reduced cigarette demand ($p < .020$) as well as DD ($p = .003$). Additionally, a greater reduction in cotinine levels coupled with greater EFT practice led to a greater decrease in cigarette demand ($p < .014$). **Conclusions**. EFT reduced the two facets of RP in treatment-seeking smokers with SUDs.

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ORIGINAL INVESTIGATION

Effects of episodic future thinking on reinforcement pathology during smoking cessation treatment among individuals with substance use disorders

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Abstract

Rationale Reinforcer pathology (RP) is a theoretical model based on two processes: delay discounting (DD) and drug demand. Given that RP has been shown to have a predictive value on smoking behaviors, several studies have explored which interventions can reduce RP. Consistent with the RP framework, episodic future thinking (EFT) has shown effects on treatment outcomes and RP processes. The vast majority of studies that assess the effects of EFT on RP consist of experimental studies, and no previous research has tested these effects in a clinical sample of smokers.

Objectives The primary aim of this study was to assess the effects of EFT on RP throughout the course of a smoking cessation intervention in smokers with substance use disorders (SUDs).

Methods Participants were randomized to cognitive behavior therapy (CBT) + EFT ($n = 39$) or CBT + EFT + contingency management ($n = 33$). Cotinine, frequency of EFT practices, cigarette purchase task (CPT), and DD were evaluated in treatment sessions. Mixed-effects model repeated measures analysis was used to explore DD and CPT in-treatment changes as a function of EFT practices and cotinine levels.

Results Greater practice of the EFT component significantly reduced cigarette demand ($p < .020$) as well as DD ($p = .003$). Additionally, a greater reduction in cotinine levels coupled with greater EFT practice led to a greater decrease in cigarette demand ($p < .014$).

Conclusions EFT reduced the two facets of RP in treatment-seeking smokers with SUDs.

Keywords Smoking · Delay discounting · Cigarette demand · Reinforcer pathology · Episodic future thinking · CPT

Introduction

Reinforcer pathology (RP) is a novel theoretical model in the field of addictions that allows us to understand substance use disorders (SUDs) based on two processes: (1) delay discounting (DD) and (2) drug demand (Bickel et al. 2014, 2019, 2020). DD refers to the observation that the value of a delayed reinforcer is discounted (reduced in value) compared to the value of an immediate reinforcer. In the context of RP, DD would involve the rapid devaluation of delayed and bigger consequences (e.g., health benefits of smoking cessation or losing weight) in preference of present and smaller rewards (e.g., smoking or overeating). On the other hand, drug demand consists of the evaluation of the motivation to procure and consume drugs. This is usually evaluated through the demand curve for a drug, whereby the consumption of a substance changes as its price increases. In the context of RP, drug demand would involve the overvaluation of a given substance compared to other reinforcers in a person's life (e.g., money).

Numerous studies have found that an elevated RP among smokers, that is, a high DD and/or a high cigarette demand, is related to greater cigarette consumption (González-Roz et al. 2019; Reynolds 2004) and nicotine dependence (Amlung and MacKillop 2014; Cassidy et al. 2020; González-Roz et al. 2019), as well as to lower abstinence rates after receiving smoking cessation treatment (Harvanko et al. 2019; Mackillop et al. 2016; Miglin et al. 2017; Murphy et al. 2017; Secades-Villa et al. 2016) and a higher risk of relapse (García-Pérez et al. 2021).

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Given that RP has been shown to have a predictive value on smoking behaviors, in recent years, several studies have sought to determine which interventions can reduce DD and cigarette demand (Scholten et al. 2019). Additionally, there are several interventions for smoking cessation (i.e., contingency management (CM), cognitive-behavioral therapy (CBT), varenicline, and low-nicotine cigarettes) that—despite not being primarily aimed at decreasing the two processes of RP—reduce DD (García-Pérez et al. 2020; Secades-Villa et al. 2014; Weidberg et al. 2015; Yi et al. 2008) and/or cigarette demand (Green and Ray 2018; Higgins et al. 2018; McClure et al. 2012; Murphy et al. 2017; Schlienz et al. 2014; Smith et al. 2017; Weidberg et al. 2018).

Consistent with the RP framework, episodic future thinking (EFT) is a novel treatment that consists of imagining future events in order to forego immediate pleasures in pursuit of longer-term aims (Hollis-Hansen et al. 2019; Rung and Epstein 2020; Schacter et al. 2017). EFT has shown effects on substance use, such as reduction of tobacco use (Chiou and Wu 2017; Stein et al. 2016), and reduction of alcohol use (Voss et al. 2021). Additionally, in substance users, EFT has been shown to reduce DD rates (Athamneh et al. 2021; Bulley and Gullo 2017; Chiou and Wu 2017; Forster et al. 2021; Mellis et al. 2019; Patel and Amlung 2020; Snider et al. 2016; Sofis et al. 2020; Stein et al. 2016, 2018) and drug demand indices (Athamneh et al. 2021; Bulley and Gullo 2017; Patel and Amlung 2020; Snider et al. 2016, 2018; Voss et al. 2021).

Despite this body of knowledge, important questions remain regarding the effectiveness of EFT. For example, previous research has yielded mixed results regarding the effect of EFT on RP in this specific population, mainly due to the limitations of these individuals in neuropsychological processes involving executive control, episodic memory, and decision-making (D'Argembeau et al. 2006; El Haj et al. 2019; Hallford et al. 2018; Mercuri et al. 2015, 2016, 2018; Moustafa et al. 2018). Also, the vast majority of studies that assess the effects of EFT on RP consist of experimental studies conducted in highly controlled laboratory settings (see, e.g., Chiou and Wu 2017; Stein et al. 2016, 2018), and no previous research has tested these effects longitudinally in a clinical sample of substance users, including smokers with SUDs.

The present study is derived from a randomized controlled trial (RCT) comparing the efficacy of CBT + EFT vs CBT + EFT + CM for smoking cessation in smokers with SUD, the results of which at end-of-treatment showed that the treatment group that included CM presented better smoking cessation outcomes (Aonso-Diego et al., 2021). According to the previous literature, both CBT and CM have been shown to be useful in reducing both DD and cigarette demand (García-Pérez et al. 2020; Secades-Villa et al. 2014; Weidberg et al. 2015, 2018; Yi et al. 2008). Therefore, with regard to the current study, combining these two components together with EFT could be remarkably beneficial for modifying RP.

The primary aim of this study was to assess the effects of EFT on the two dimensions of RP (i.e., DD and cigarette demand) throughout the course of a smoking cessation intervention in a sample of individuals with SUDs. The secondary objective was to examine the impact of tobacco use reduction and the two treatment conditions (CBT + EFT vs. CBT + EFT + CM) on RP.

Material and methods

Participants

This secondary analysis is derived from a randomized controlled trial (Clinical Trials-Gov Identifier: NCT03551704) aimed at the treatment of smoking in SUD individuals (Aonso-Diego et al. 2021), which was approved by the research ethics committee of the Principality of Asturias (n°144/16).

Participants were 72 treatment-seeking smokers with SUDs, and the inclusion criteria were (1) being at least 18 years old, (2) smoking at least 10 cigarettes per day for the last year, and (3) being in outpatient substance use treatment. Exclusion criteria were (1) not being able to attend the full treatment, (2) having severe mental disorders (i.e., active psychotic disorder and/or suicidal ideation), and (3) receiving another smoking cessation treatment (either psychological or pharmacological) at time of intake.

Interventions

Participants provided informed consent and were randomized to each of the following intervention conditions: CBT + EFT ($n = 38$) and CBT + EFT + CM ($n = 34$). Table 1 shows the sociodemographic and clinical characteristics of the sample.

All interventions were led by doctoral or master's level psychologists with experience in the treatment of smoking. The treatments were designed in a group format, with a maximum of four participants per group. The intervention lasted eight weeks, and participants attended one weekly therapy session (session A) and one-midweek session (session B) to collect information on biochemical data and other clinical variables. Figure 1 shows the retention of the participants throughout the treatment.

The CBT protocol for smoking cessation consisted of the following components: gradual fading of nicotine intake (20% per week), self-report of tobacco use, psychoeducation, stimulus control, coping skills training to help patients to effectively manage their smoking withdrawal symptoms,

Table 1 Baseline participant characteristics

	Total ($n=72$)
Age	44.46 ± 10.25
Sex (male)[a]	52 (72.22%)
Marital status (married)[a]	18 (25%)
Working status (employed)[a]	24 (33.33%)
Educational level (< high school)[a]	33 (45.83%)
Monthly income (€)	1314.73 ± 1329.94
Tobacco use-related variables	
CPD	19.96 ± 9.72
Years of regular use	26.24 ± 11.26
Previous quit attempts	1.36 ± 1.45
CO[a]	21.71 ± 15.55
Urine cotinine[a]	2181.35 ± 1464.01
Substance use-related variables	
Primary substance[a]	
Cocaine	27 (37.50%)
Alcohol	25 (34.72%)
Opioids	11 (15.27%)
Other[b]	9 (12.50%)
Secondary substance[a]	
None	46 (63.88%)
Cocaine	5 (6.94%)
Alcohol	10 (13.88%)
Cannabis	8 (11.11%)
Opioids	2 (2.77%)
Benzodiazepines	1 (1.38%)
Days of primary substance abstinence	274.60 ± 409.62
Days on substance use treatment	351.71 ± 633.89
BDI-II	14.34 ± 11.42
UPPS-P	
Lack of perseverance	7.58 ± 2.35
Lack of premeditation	8.01 ± 2.18
Positive urgency	10.96 ± 2.48
Negative urgency	11.54 ± 2.76
Sensation seeking	9.86 ± 2.94
DD (AUC)	0.671 ± 0.249
CPT index	
Intensity	21.24 ± 12.01
Breakpoint	11.80 ± 21.95
Omax	14.21 ± 16.27
Pmax	4.89 ± 10.43
Elasticity	0.023 ± 0.094

[a]frequency (percentage); [b]include cannabis, ketamine, GHB, and benzodiazepines. *CPD*, cigarettes per day; *CO*, carbon monoxide in parts per million; *BDI-II*, Beck depression inventory, second edition; *UPPS-P*, impulsive behavior scale; *DD*, delay discounting; *AUC*, area under curve; *CPT*, cigarette purchase task

problem-solving, and relapse prevention strategies. The quit date was set at 48 h before the start of the sixth session.

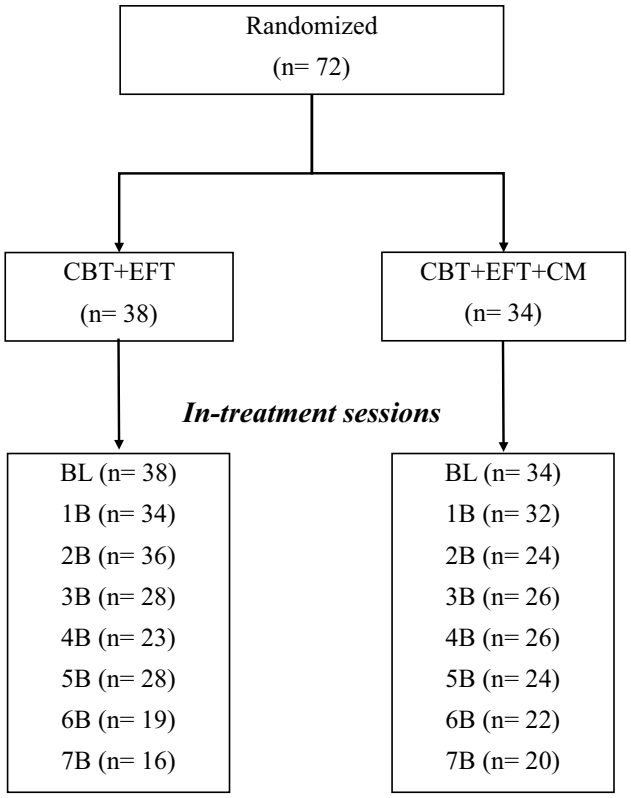

Fig. 1 Retention of participants for each group intervention. No differences were found in participant retention between the treatment groups ($\chi^2(7)=3.522$; $p=.833$). *BL*, baseline

Following prior recommendations (Hollis-Hansen et al. 2019; Snider et al. 2016), EFT was implemented from the first session. The aim of this component was to decrease patients' impulsive choice, and it required individuals to create a total of five future non-smoking situations at different time points (one situation in a week, two situations in 2 weeks, one in a month, and one in 3 months) throughout the 8 weeks of treatment. The participants were encouraged to practice EFT situations a total of 98 times. The procedure followed for its implementation was as follows: (1) in the therapy session, the therapist asked the participants to identify a positive non-smoking event (e.g., a walk in the fresh air) that they eagerly hoped would happen within the proposed time frame. (2) The therapist asked the individuals to write the situation on a sheet of paper (including the place they had chosen, the company, activities, feelings, etc.) and to practice visualizing it for 2–3 min. (3) Subsequently, the participants were asked to rate the vividness of the situation on a 10-point scale. If they rated it below 6, the therapists helped the patients to improve the description of the situation to facilitate the visualization practice. As homework, patients had to practice visualization twice a day, as well as record the vividness of each practice. Participants did not receive any reminder (i.e., via phone or message) to perform

the practice, but in the midweek sessions (or the B sessions) they were asked about the visualization practice, as well as whether they had doubts or questions related to the component. The total number of practices was the result of the number of times the person rated the vividness on the record sheet. Therefore, if the patient did not bring the sheet to the session, or the sheet was blank, even though they reported having performed the visualizations, the number of practices was considered to be zero.

CM is aimed at increasing substance abstinence rates by providing contingent reinforcers to the target behavior, usually substance abstinence. The efficacy of this therapeutic component is based on the increase in alternative reinforcers to drug use (Higgins, 1997). It is important to note that the effectiveness of this component is dependent on the magnitude and immediacy of the reinforcers given (Lussier et al., 2006). In this study, the CM component specifically consisted of providing incentives from the sixth session onwards in exchange for attaining tobacco abstinence, biochemically verified through CO ≤ 4 ppm and urine cotinine ≤ 80 ng/ml. In this sense, abstinent patients earned 20 points (equivalent to €20) in session 6, €25 in session 6B, €30 in session 7, €35 in 7B, and €40 in session 8 (i.e., post-treatment). In addition, for every two consecutive negative analyses, they would obtain a bonus of €10 extra in points. Therefore, a patient who had achieved tobacco abstinence could earn a maximum of €170. The article by Aonso-Diego et al. (2021) can be consulted for more information.

Measures

During the intake session, sociodemographic information (e.g., sex), substance use variables (e.g., primary substance use), and smoking variables (e.g., cigarettes per day) were collected through an ad hoc questionnaire. Additionally, nicotine dependence was assessed using the Fagerström test for nicotine dependence (FTND) (Heatherton et al. 1991).

All participants provided a urine sample for cotinine and drug testing (cocaine, opioids, amphetamine, methamphetamine, and cannabis). They also provided a breath sample in order to evaluate CO and alcohol consumption.

The outcome variables were DD and cigarette demand. The DD task was evaluated using a computer program. Participants had to choose between receiving an immediate amount of money available now (between €5 and €995) and a fixed amount of money available later (€1,000). The program finds the indifference point for each of the five delays presented through the trials (i.e., 1 day, 1 week, 1 month, 6 months, and 1 year). The indifference point refers to the subjective value in which the delayed reward has an equivalent value to the immediate reward. In order to find the indifference point, an adjusting amount procedure was used in this task based on the one proposed by Holt et al. (2012). All participants were informed that the amounts of money presented were hypothetical, but that they should try to answer as realistically as possible. The total duration of the task does not usually exceed 10 min. The EFT cues were not presented while participants completed the DD task.

The CPT instructions are based on the original recommendations from MacKillop et al. (2008). Participants had to answer the following question: "How many cigarettes would you smoke if they were ____ each?" The following 19 prices were inserted: zero (free), € 0.01, € 0.02, € 0.05, € 0.10, € 0.25, € 0.50, € 1, € 2, € 3, € 4, € 5, € 10, € 20, € 50, € 100, € 250, € 500, and € 1,000. The prices were presented in ascending order. To complete the task, the participants were told to assume the following: (1) your income and savings are what you normally have, (2) the cigarettes are your favorite brand, (3) there is no other way to get cigarettes or nicotine, (4) if you buy none, you don't smoke that day, (5) if you buy cigarettes, you must smoke them all on the same day, (6) cigarettes cannot be kept or given away, (7) your urge or desire to smoke is similar to how you feel today.

Both CPT and DD tasks as well as cotinine were evaluated eight times, once in the intake session and once a week in the midweek sessions. Furthermore, the total frequency of EFT practices during treatment was also recorded via self-report.

Data analysis

Both the CPT and DD values were standardized and compared with a critical value of $Z = \pm 4$ in order to detect outliers (Tabachnick et al. 2001). If an outlier was detected, these values were recorded as the highest non-outlying value (plus 0.01 for AUC and plus 1 for the CPT indices). In addition, CPT and DD values were analyzed in order to detect nonsystematic data following the original recommendations of Stein et al. (2015) and Johnson and Bickel (2008). Two responses to the DD task were eliminated due to being considered nonsystematic. There were no nonsystematic responses in the CPT because the task was computerized, and the program alerted the user of inappropriate responses.

The area under the curve (AUC) was calculated according to Myerson et al. (2001), in order to analyze the indifference points of each participant. AUC values close to 0 indicate maximum DD rates, while values close to 1 indicate minimum DD rates.

Five demand indices were generated from the CPT, as follows: (1) intensity (cigarette smoking at zero cost); (2) O_{max} (maximum amount of money spent on cigarettes); (3) P_{max} (price associated with the maximum expense); (4) breakpoint (first price at which consumption was interrupted); (5) elasticity (proportional change in consumption based on the proportional change in price). Intensity, Omax, Pmax, and breakpoint were generated using an observed values

approach. Elasticity was estimated using an exponentiated demand curve Eq. (1) (Koffarnus et al., 2015):

$$Q = Q_0 0 \times 10^{k(e-\alpha Q_0 C-1)} \quad (1)$$

In Eq. (1), Q is consumption at commodity price C, Q_0 is consumption at the minimum price, k is the range of consumption, and α is the elasticity of demand (i.e., the slope of the demand curve). Since 14% of the total CPT completed were classified as zero responders (60% in the last treatment session), it was decided to calculate the essential value (EV), which is inversely proportional to the α value, according to Eq. (2) proposed by Hursh and Roma (2016):

$$EssentialValue = \frac{1}{100 * \alpha * k^{1.5}} \quad (2)$$

Since the value of α is impossible to estimate in zero responders, according to previous studies (Heckman et al., 2019; Stein et al., 2017; Yoon et al., 2021), the EV was defined as 0 (i.e., the lowest potential value).

The validity of the RP tasks was analyzed in two ways. On the one hand, the Pearson correlation was used to compare clinically relevant variables with the CPT and DD indices. On the other hand, a nonlinear regression was used to generate an R^2 value to assess the goodness-of-fit of CPT.

Mixed-effects model repeated measures (MMRM) analysis with restricted maximum likelihood was used to explore whether the DD and CPT changes were due to treatment, number of EFT practices, or cotinine levels over time (in-treatment changes). An unstructured modeling of frequencies at each visit and within-subject error correlation structure was included in this analysis. Cotinine and the number of EFT practices were treated as time-varying covariates. The MMRM model allows us to analyze missing data from longitudinal studies (Vallejo et al. 2011). The statistical software used in this study was SPSS (v20, Chicago, IL).

Table 3 EFT practice in intra-treatment sessions

Session	Frequency of EFT practice[a]	Vividness of EFT practice[a]
2	6.57 ± 5.69	7.77 ± 1.40
3	5.84 ± 6.55	7.62 ± 1.82
4	6.50 ± 9.29	7.79 ± 1.30
5	6.08 ± 10.02	7.99 ± 1.57
6	7.28 ± 12.45	8.23 ± 1.34
7	5.90 ± 12.45	8.09 ± 1.53

a mean ± *SD*, *EFT,* episodic future thinking

Results

Correlations among the RP indices and smoking variables

As expected, cigarette demand and DD were related to some smoking variables, such as cigarettes per day. Furthermore, the CPT data of all participants presented a good fit in the exponentiated equation (median $R^2 = 0.97$) (see Table 2).

Effect of episodic future thinking on DD and cigarette demand

Overall, the participants performed the visualization tasks a mean of 33.227 ($SD = 44.602$) times with a mean vividness of 7.761 ($SD = 1.420$). Table 3 shows in detail the statistics of the EFT practice.

Table 2 Correlations among smoking-related measures, delay discounting, and cigarette demand indices

	1	2	3	4	5	6	7	8	9	10
1—Cigarettes per day	-	-	-	-	-	-	-	-	-	-
2—Years of regular smoking	.15	-	-	-	-	-	-	-	-	-
3—Urine cotinine	.42**	.12	-	-	-	-	-	-	-	-
4—FTND	.72**	.30*	.32**	-	-	-	-	-	-	-
5—AUC	.37*	− .26	.10	.25	-	-	-	-	-	-
6—Intensity	.79**	.16	.43**	.59**	.25	-	-	-	-	-
7—Breakpoint	.16	− .09	.16	.11	.12	.11	.-	-	-	-
8—Omax	.28*	.08	.49**	.27*	.14	.27*	.74**	-	-	-
9—Pmax	.13	− .06	.19	.10	.08	.09	.97**	.75**	-	-
10—EV[1]	.32**	.14	.42**	.37**	.11	.30*	.34**	.68**	.32**	-

[1]Elasticity was estimated using essential value equation, so high values imply less elasticity. *EV*, essential value; *FTND*, Fagerström test for nicotine dependence; *AUC*, area under the curve of delay discounting task

*$p \leq 05$; **$p \leq .01$

Tables 4, 5, 6, 7, 8, and 9 show the MMRM outcomes for each CPT index and AUC. The results show that the time effect was significant in all demand indices used (intensity, breakpoint, O_{max}, P_{max}, and EV), but not in the AUC. Figures 2 and 3 show the RP indices throughout the treatment sessions.

Greater practice of the EFT component significantly reduced both the breakpoint (model B: $\beta_2 = -0.560837$, $p = 0.001$) and the P_{max} (model B: $\beta_2 = -0.478805$, $p = 0.019$) as well as the DD (model B: $\beta_2 = 0.019587$, $p = 0.003$). Additionally, the EFT × COT interaction was significant both in intensity (model B: $\beta_2 = 0.0004879$, $p = 0.003$) and in O_{max} (model B: $\beta_2 = 0.000323$, $p = 0.013$), such that a greater reduction in cotinine levels coupled with greater EFT practice led to a greater decrease in both demand indices. On the other hand, EFT had no impact on EV (model A: $p = 0.985$).

Table 4 Results of fitting taxonomy of MMRM models to the intensity

Fixed effect	Model A				Model B[1]				Model C			
	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F
Time (β_1)	7	35	33.486	.000	7	43	44.280	.000	7	8	7.679	.005
EFT (β_2)	1	11	1.348	.271	1	1	.019	.907	1	12	.011	.919
EFT × time (β_3)									7	6	.066	.504
EFT × COT (β_4)					1	3	83.081	.003	1	5	4.318	.092
EFT × GRP (β_5)					1	2	51.826	.024	1	2	2.440	.250
GRP (β_6)	1	12	1.188	.297	1	20	9.920	.005	1	6	.489	.511
GRP × time (β_7)					1	46	1.909	.090	7	9	1.937	.174
GRP × COT (β_8)									1	7	.066	.805
COT (β_9)	1	18	135.545	.000	1	3	310.716	.000	1	9	41.459	.000
COT × time (β_{10})									7	4	5.457	.060
Goodness-of-fit (AIC/BIC/parameters)												
	2258.1/2397.9/47				2237.0/2375.9/56				2335.4/2472.7/71			

[1]Information criteria allow us to conclude that model B provides a better fit than models A and C. *EFT*, number of episodic future thinking exercises practiced; *COT*, urine cotinine; *GRP*, treatment group; df_N, numerator degrees of freedom; df_D, denominator degrees of freedom; *AIC*, Akaike information criterion; *BIC*, Bayesian information criterion

Table 5 Results of fitting taxonomy of MMRM models to the breakpoint

Fixed effect	Model A				Model B[1]				Model C			
	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F
Time (β_1)	7	35	5.016	.001	7	25	4.272	.003	7	38	1.636	.155
EFT (β_2)	1	24	12.246	.002	1	12	21.335	.001	1	58	.384	.538
EFT × time (β_3)									7	36	1.176	.341
EFT × COT (β_4)					1	29	3.249	.082	1	19	4.623	.045
EFT × GRP (β_5)					1	18	1.294	.270	1	15	1.483	.243
GRP (β_6)	1	24	3.650	.068	1	70	1.540	.270	1	75	.398	.530
GRP × time (β_7)					7	24	.485	.836	7	40	.442	.870
GRP × COT (β_8)									1	23	17.047	.000
COT (β_9)	1	30	2.726	.109	1	33	.095	.760	1	38	1.515	.226
COT × time (β_{10})									7	19	6.005	.001
Goodness-of-fit (AIC/BIC/parameters)												
	2981.6/3121.4/47				2960.2/3099.1/56				3025.4/3162.7/71			

[1]Information criteria allow us to conclude that model B provides a better fit than models A and C. *EFT*, number of episodic future thinking exercises practiced; *COT*, urine cotinine; *GRP*, treatment group; df_N, numerator degrees of freedom; df_D, denominator degrees of freedom; *AIC*, Akaike information criterion; *BIC*, Bayesian information criterion

Table 6 Results of fitting taxonomy of MMRM models to the Omax

Fixed effect	Model A				Model B[1]				Model C			
	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F
Time (β_1)	7	29	14.336	.000	7	23	14.454	.000	7	18	3.403	.016
EFT (β_2)	1	8	5.372	.049	1	7	4.010	.088	1	54	.072	.789
EFT × time (β_3)									7	19	.972	.479
EFT × COT (β_4)					1	19	7.529	.013	1	12	2.221	.161
EFT × GRP (β_5)					1	13	2.890	.113	1	20	.185	.672
GRP (β_6)	1	9	.014	.909	1	66	1.795	.185	1	79	.442	.508
GRP × time (β_7)					7	23	1.601	.184	7	21	1.019	.447
GRP × COT (β_8)									1	16	1.053	.320
COT (β_9)	1	9	72.019	.000	1	14	27.525	.000	1	15	26.674	.000
COT × time (β_{10})									7	8	15.933	.000
Goodness-of-fit (AIC/BIC/parameters)												
	2772.5/2912.3/47				2747.4/2886.3/56				2806.2/2943.5/52			

[1]Information criteria allow us to conclude that model B provides a better fit than models A and C. *EFT*, number of episodic future thinking exercises practiced; *COT*, urine cotinine; *GRP*, treatment group; df_N, numerator degrees of freedom; df_D, denominator degrees of freedom; *AIC*, Akaike information criterion; *BIC*, Bayesian information criterion

Table 7 Results of fitting taxonomy of MMRM models to the Pmax

Fixed effect	Model A				Model B[1]				Model C			
	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F
Time (β_1)	7	35	3.647	.005	7	32	3.195	.011	7	35	1.819	.115
EFT (β_2)	1	41	2.932	.094	1	35	6.099	.019	1	59	.627	.432
EFT × time (β_3)									7	31	.812	.584
EFT × COT (β_4)					1	86	.598	.441	1	74	1.119	.294
EFT × GRP (β_5)					1	34	2.558	.119	1	39	3.242	.080
GRP (β_6)	1	33	2.901	.098	1	78	1.751	.190	1	90	1.214	.274
GRP × time (β_7)					7	34	.530	.805	7	32	.544	.794
GRP × COT (β_8)									1	64	2.171	.146
COT (β_9)	1	73	.558	.458	1	78	.094	.760	1	105	2.398	.124
COT × time (β_{10})									7	36	4.243	.002
Goodness-of-fit (AIC/BIC/parameters)												
	2357.2/2497.0/47				2350.6/2489.5/56				2442.4/2579.7/71			

[1]Information criteria allow us to conclude that model B provides a better fit than models A and C. *EFT*, number of episodic future thinking exercises practiced; *COT*, urine cotinine; *GRP*, treatment group; df_N, numerator degrees of freedom; df_D, denominator degrees of freedom; *AIC*, Akaike information criterion; *BIC*, Bayesian information criterion

Effect of tobacco use reduction and treatment condition on DD and cigarette demand

The results showed that cotinine levels were significantly associated with some cigarette demand indices. Specifically, cotinine levels had a main effect on both intensity (model B: $\beta_2 = 0.004801$, $p < 0.001$) and O_{max} (model B: $\beta_2 = 0.003244$, $p < 0.001$). These results suggest that a greater reduction in cotinine, and therefore smoking consumption, was associated with a greater reduction in both demand indices.

On the other hand, the reduction of cotinine, especially in the first sessions of treatment (model C: $\beta_4 = 0.0001$, $p = 0.002$), was related to a decrease in DD. Nevertheless, of note is that the model that best predicted changes in DD did not include cotinine as the main or interactive effect (see Table 6, model B).

Finally, participants of CBT + EFT reduced intensity less in comparison with CBT + EFT + CM, even when the participants practiced the EFT component more. (model B: $\beta_2 = 1.102479$, $p = 0.024$).

Table 8 Results of fitting taxonomy of MMRM models to the EV (elasticity)

Fixed effect	Model A[1]				Model B				Model C[2]			
	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F
Time (β_1)	7	23	21.552	.000	7	21	22.323	.000	-	-	-	-
EFT (β_2)	1	14	.000	.985	1	17	.023	.882	-	-	-	-
EFT × time (β_3)									-	-	-	-
EFT × COT (β_4)					1	23	.005	.943	-	-	-	-
EFT × GRP (β_5)					1	9	.190	.673	-	-	-	-
GRP (β_6)	1	15	2.635	.125	1	60	.715	.401	-	-	-	-
GRP × time (β_7)					7	21	1.732	.156	-	-	-	-
GRP × COT (β_8)									-	-	-	-
COT (β_9)	1	17	.015	.904	1	27	.014	.908	-	-	-	-
COT × time (β_{10})									-	-	-	-
Goodness-of-fit (AIC/BIC/parameters)												
	− 3.9/135.1/47				43.1/181.2/56				2442.4/2579.7/71			

[1]Information criteria allow us to conclude that model A provides a better fit than models B and C. [2]It was not possible to estimate model C due to a problem in the convergence of the model. *EFT*, number of episodic future thinking exercises practiced; *COT*, urine cotinine; *GRP*, treatment group; df_N, numerator degrees of freedom; df_D, denominator degrees of freedom; *AIC*, Akaike information criterion; *BIC*, Bayesian information criterion

Table 9 Results of fitting taxonomy of MMRM models to the AUC

Fixed effect	Model A				Model B[1]				Model C			
	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F	df_N	df_D	*F*	Pr > F
Time (β_1)	7	10	2.741	.074	7	14	2.393	.078	1	13	1.008	.468
EFT (β_2)					1	8	17.551	.003				
COT (β_3)									1	9	19.632	.002
COT × time (β_4)									7	10	8.469	.002
Goodness-of-fit (AIC/BIC/parameters)												
	− 133.9/ − 23.0/44				− 134.0/ − 26.1/45				29.6/136.5/52			

[1]Information criteria allow us to conclude that model B provides a better fit than models A and C. It was not possible to create more complex models, as in CPT indices, due to a problem in the convergence of the models. *EFT*, number of episodic future thinking exercises practiced; *COT*, urine cotinine; *GRP*, treatment group; df_N, numerator degrees of freedom; df_D, denominator degrees of freedom; *AIC*, Akaike information criterion; *BIC*, Bayesian information criterion

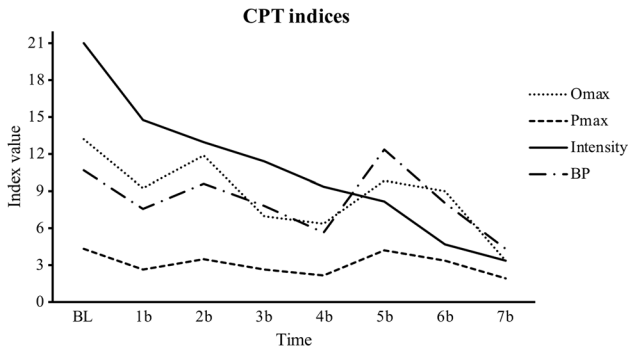

Fig. 2 Evolution of observable CPT indices throughout treatment

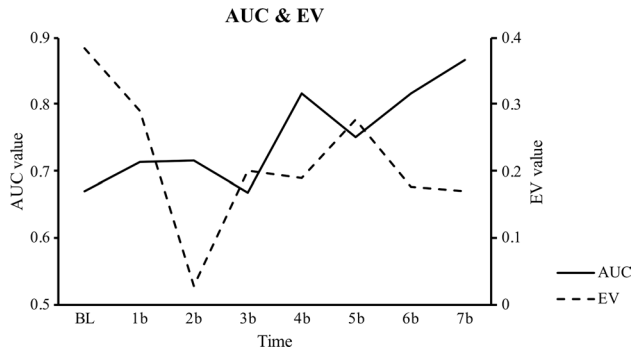

Fig. 3 Evolution of AUC and EV throughout treatment

Discussion

The current study is the first to examine the effect of EFT on RP (DD and cigarette demand) during smoking cessation treatment in individuals with SUDs. Three main results have emerged: (1) greater self-reported practice of EFT reduced the two facets of RP; (2) tobacco use reductions decreased intensity of demand and O_{max}; and (3) the addition of the CM component decreased the intensity of cigarette demand.

The number of EFT practices had an impact, either in isolation or interactively, on the two dimensions of RP (i.e., DD and cigarette demand). This outcome is explained by the effects of EFT which mainly consist of the expansion of the temporal window to subsequently produce an enhanced valuation of the future decisions (Snider et al., 2016). In this sense, EFT helps with the improvement of far-sighted decision-making, emotional regulation, prospective memory, and spatial navigation (Schacter et al., 2017). And ultimately, these functions of EFT can result in the initiation of healthy behaviors alternative to tobacco use, as well as in increasing the cost of smoking.

Regarding DD rates, these findings confirm and extend previous research in substance users (Bulley and Gullo 2017; Chiou and Wu 2017; Forster et al. 2021; Mellis et al. 2019; Patel and Amlung 2020; Snider et al. 2016; Sofis et al. 2020; Stein et al. 2016, 2018). Of note is that the short cues generated in EFT were not presented in the DD task. This is worth mentioning since a recent review has indicated that EFT decreases DD only when cues are present (Rung and Madden 2019). Furthermore, unlike several studies (see, e.g., Bulley and Gullo 2017; Chiou and Wu 2017; Mellis et al. 2019; Patel and Amlung 2020; Snider et al. 2016; Sofis et al. 2020; Stein et al. 2016), in the current one, the EFT delays (1 week, 2 weeks, 1 month, and 3 months), did not match the DD ones (1 day, 1 week, 1 month, 6 months, and 1 year). Despite previous research, this study indicates that these two conditions are not necessary to achieve a meaningful effect on DD.

An important and novel finding of the current study was that EFT also had a significant effect on the four observable indices of drug demand. Previous evidence has partially shown that EFT impacts on breakpoint (Patel and Amlung 2020), O_{max} (Voss et al. 2021), P_{max} (Patel and Amlung 2020), and especially on the intensity of demand (Athamneh et al. 2021; Bulley and Gullo 2017; Patel and Amlung 2020; Snider et al. 2016; Stein et al. 2018; Voss et al. 2021).

Several reasons may explain the effect of EFT on the two dimensions of RP. First, unlike other studies (see, e.g., Chiou and Wu 2017; Stein et al. 2016, 2018), this sample consists of treatment-seeking smokers, rather than current smokers without motivation to quit, a variable strongly related to RP (Sheffer et al. 2019; Veilleux and Skinner 2016). Second, the number of days of abstinence from substance use was higher (an average of 274.60), compared to previous EFT studies with SUD populations (see, e.g., Forster et al. 2021; Sofis et al. 2020; Voss et al. 2021). These differences in the participant profiles may have an impact on RP.

Taken together, these findings suggest that implementing an EFT component within a standard treatment for smoking cessation among smokers with SUDs could be useful for reducing RP, despite the difficulty of constructing specific future scenarios for the SUD population (see, e.g., D'Argembeau et al. 2006; El Haj et al. 2019; Mercuri et al. 2015, 2016, 2018; Moustafa et al. 2018). This may explain the number of EFT practices required (14 every week for 7 weeks) since this population needs intensive treatments in terms of the number of sessions and the time dedicated (Murphy and McKay 2004; Richter and Arnsten 2006; Schroeder and Morris 2010). Furthermore, several articles have recently pointed out the need to continue EFT practice to achieve a significant effect on RP (Mellis et al. 2019; Patel and Amlung 2020).

Consistent with the previous literature (see, e.g., Higgins et al. 2018; Nighbor et al. 2020; Smith et al. 2017; Streck et al. 2018; Weidberg et al. 2018), the reduction in tobacco use resulted in a decrease in cigarette demand, specifically in O_{max} and intensity of demand. Furthermore, this finding is congruent with others indicating that individuals with greater tobacco use show a higher cigarette demand (González-Roz et al. 2019). This result is aligned with the theory of relative reinforcing efficacy (Bickel et al. 2000), which highlights that an increase in cigarette cost, defined inclusively to encompass the monetary cost, effort, or time required to acquire cigarettes (Bickel et al. 2014), will produce a reduction in the reinforcing value of nicotine. Thus, nicotine fading along with other treatment components may reduce the motivation to smoke (Murphy et al. 2017) and, therefore, increase the cost of smoking behavior.

Finally, CM was associated with a greater reduction in the intensity of demand, as was found in Weidberg et al. (2018). It is likely that the increase in the availability of alternative reinforcers to tobacco use provided by CM (Higgins et al. 2008; Stonerock and Blumenthal 2017) yielded a decrease in the reinforcing value of nicotine, i.e., in cigarette demand. This result also points in the same direction as the meta-analysis by Acuff et al. (2020), where it is highlighted that introducing an opportunity cost could reduce the intensity of demand by altering the motivation to consume a substance.

At the clinical level, considering that changes in cigarette demand have been related to both short- and medium-term tobacco abstinence (Madden and Kalman 2010; Murphy et al. 2017), the current findings add support to the use of

behavioral strategies based on nicotine fading and the implementation of incentives that reinforce abstinence, as effective interventions for smoking cessation.

This study is not exempt from limitations, which are detailed below. First, the sample used was relatively small and this limited the statistical analyses performed and the complexity of interpreting the models tested. Despite this, the present work found several significant effects of relevance, and with regard to the target population (i.e., smokers with SUD), other published articles present a similar number of participants or fewer (Alessi et al. 2008; Alessi and Petry 2014; Cooney et al. 2017). Second, this work did not include a control group (i.e., CBT or EFT only), which would increase the strength of the results regarding the impact of EFT on RP. Furthermore, of note is that the number of EFT practices was self-reported, so it is not exempt from all the related biases.

In summary, the current study enhances the available knowledge about the effectiveness of EFT in reducing RP, both in terms of cigarette demand and DD. In addition, the results add support for the use of behavioral interventions (e.g., nicotine fading) in the treatment for smoking cessation among individuals with SUDs. Future studies should further explore the usefulness of EFT in the treatment of SUDs in clinical settings.

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Declarations

Informed consent All participants provided informed consent.

Conflict of interest The authors declare no competing interests.

Research involving human participants This study was approved by the research ethics committee of the Principality of Asturias (n°144/16).

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5.5. A randomized controlled trial of contingency management for smoking cessation in substance use treatment patients

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Background/Objective: Contingency management (CM) is one of the most effective interventions for smokers with substance use disorder (SUD), and no empirical assessment of its long-term efficacy has been conducted so far in a real-world context. The objectives were: (1) examine the additive effectiveness of CM on cognitive-behavioral treatment (CBT) for smoking cessation, and (2) examine the relationship between smoking cessation and substance use abstinence. **Method**: A total of 80 participants (75.8% males; M_{age} = 45.31; *SD* = 9.64) were assigned to two smoking cessation treatments: CBT or CBT + CM. A set of generalized estimating equations were conducted to examine the effect of treatment condition on smoking outcomes, as well as the effect of smoking status on substance abstinence. **Results**: Adding CM to CBT for smoking cessation improved tobacco abstinence rates at the end-of-treatment (p = .049). Tobacco abstinence rates declined over time (p = .012), but no significant effects of treatment condition were observed across follow-ups (p = .260). Smoking cessation was not significantly related to substance abstinence ($p \geq$ .488). **Conclusions**: CM facilitates early abstinence in smokers with SUD, although effects subside after treatment termination. The lack of association between smoking abstinence and substance use suggests no jeopardizing effects as a result of quitting smoking.

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ORIGINAL ARTICLE

A randomized controlled trial of contingency management for smoking cessation in substance use treatment patients

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Abstract
Background/Objective: Contingency management (CM) is one of the most effective interventions for smokers with substance use disorder (SUD), and no empirical assessment of its long-term efficacy has been conducted so far in a real-world context. The objectives were: (1) examine the additive effectiveness of CM on cognitive-behavioral treatment (CBT) for smoking cessation, and (2) examine the relationship between smoking cessation and substance use abstinence. *Method:* A total of 80 participants (75.8% males; M_{age} = 45.31; *SD* = 9.64) were assigned to two smoking cessation treatments: CBT or CBT+CM. A set of generalized estimating equations were conducted to examine the effect of treatment condition on smoking outcomes, as well as the effect of smoking status on substance abstinence. *Results:* Adding CM to CBT for smoking cessation improved tobacco abstinence rates at the end-of-treatment (p = .049). Tobacco abstinence rates declined over time (p = .012), but no significant effects of treatment condition were observed across follow-ups (p = .260). Smoking cessation was not significantly related to substance abstinence ($p \geq .488$). *Conclusions:* CM facilitates early abstinence in smokers with SUD, although effects subside after treatment termination. The lack of association between smoking abstinence and substance use suggests no jeopardizing effects as a result of quitting smoking.

Tobacco use rates have declined in recent years in general population (Wang et al., 2018), however, the smoking prevalence remains notably high among specific vulnerable populations (Drope et al., 2018). In particular, individuals with substance use disorders (SUD) are between two and four times more likely to report using tobacco compared with non-SUD populations (Fine et al., 2019; Guydish et al., 2020; Hayhurst et al., 2020). This behavior places this population at a highly vulnerable situation, where lower quality of life and impaired mental health are evinced (Lien et al., 2021). In comparison with non-smokers with SUD, smokers have a four-time higher premature mortality rate due to tobacco use (Hser et al., 1994), and are more likely to die from tobacco related diseases (Baca & Yahne, 2009; Hurt et al., 1996).

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Voucher-based contingency management (CM) is a well-established intervention for smoking cessation (e.g., Hand et al., 2017; Notley et al., 2019). It consists of providing incentives contingently upon biochemically verified substance use abstinence (Ginley et al., 2021), but also in relation to other therapeutic goals (i.e., adherence to therapy tasks or attendance) (Pfund et al., 2021). A recent meta-analysis among smokers with SUD (Secades-Villa et al., 2020) has shown that CM produces a 36% of tobacco abstinence (compared to 7.8% in comparison groups) at the end of treatment. Although no long-term additive effect was observed, abstinence rates declined at 7.8% (compared to 1.7% in control groups) at six-month follow-up. A common criticism of CM is that its effect may not endure after the discontinuation of rewards. Relatedly, research has informed of larger effects when the CM protocol includes bonus for consecutive good performance (Businelle et al., 2009) and when incentives are sustained after treatment termination (Secades-Villa et al., 2019), but there is no evidence available in this field, since few studies include incentives in the follow-ups (see Cooney et al., 2017; Rohsenow et al., 2017). On the other hand, very few studies have looked at long-term effects of CM in SUD population, and these present several methodological limitations related to low sample sizes (Beckham et al., 2018), or CM is combined with pharmacological treatments (Beckham et al., 2018; Rohsenow et al., 2017; Shoptaw et al., 2002).

Furthermore, there are few studies implemented in real world settings (see Higgins et al., 2019). One of the most widespread myths is the belief that quitting smoking jeopardizes abstinence from substances other than nicotine (Gentry et al., 2017; González-Roz et al., 2019a). While smoking appears to increase the risk of substance use relapse in some studies (Fu et al., 2008; Weinberger et al., 2017), others indicate protective effects of smoking abstinence over substance relapse (Berg et al., 2015; Magee & Winhusen, 2016). Regarding studies using CM only, some found a positive effect (Orr et al., 2018), whereas others reported a null effect (Cooney et al., 2017; Rohsenow et al., 2015, 2017). It is worthy of note that these studies included a low treatment duration (19 - 21 days), and tobacco abstinence rates were too low to establish a significant relationship between tobacco and substance abstinence (ranged from 3% to 12%).

This randomized controlled trial sought: (1) to examine the additive effectiveness of voucher-based CM to a CBT for smoking cessation among smokers with SUD at the end of treatment and follow-ups (i.e., 3, 6, and 12 months), and (2) to analyze the relationship between tobacco and substance use abstinence at long-term.

Method

Participants

Participants were recruited from SUD treatment facilities by means of therapists' referral. Inclusion criteria were self-reporting 10 cigarettes per day within the last year, receiving outpatient SUD treatment at the time of the study entry, and being able to attend the full smoking cessation treatment. Exclusion criteria were self-reported diagnosis of severe mental disorder (i.e., active psychotic disorder and/or suicidal ideation); current cannabis use; and current use of pharmacotherapy or behavioral treatment for smoking cessation.

A total of 97 participants were recruited for this randomized control trial, of which 17 were excluded due to cannabis use (n = 8), severe mental disorder (n = 2), not being in receipt of SUD treatment (n = 2), lack of motivation to quit tobacco (n = 2), self-quitting prior to treatment onset (n = 2), and electronic cigarette use (n = 1) (see Fig. 1). A total of 80 participants were randomly assigned to two treatment conditions: CBT (n = 46) or CBT+CM (n = 34). Fifteen participants in CBT and three in CBT+CM refused to participate after the baseline assessment, leaving a total of thirty-one participants in each treatment condition. There were not significant differences in baseline characteristics between treatment conditions (all p-values $\geq$ 0.115) (Table 1).

Instruments

All participants were interviewed in an individual single assessment which gathered data about sociodemographic characteristics (e.g., age, sex, monthly income, marital status), as well as tobacco- and substance-related variables. Variables related to tobacco were number of cigarettes per day, years of regular use, motivation to quit (i.e., pre-contemplation, contemplation, and preparation stages) and previous quit attempts. Nicotine dependence was evaluated through the Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012), which consist of 6 items. FTCD scores yield five levels of cigarette dependence: very low (0−2), low (3−4), medium (5), high (6−7), and very high (8−10) (Fagerström & Kozlowski, 1990).

The Structured Clinical Interview for the DSM-5 (SCID-5) was used to assess past year tobacco use disorder. The SCID-5 covers the 11 DSM criteria in a dichotomized scale (i.e., yes/no). SUD severity was interpreted based on the DSM-5 guidelines: absence (0−1), minimal (2−3), moderate (4−5), and severe (6−11). Substance-related variables were assessed as well, including primary and secondary substance of use, substance use abstinence (in days), and substance use treatment length (in days).

Both tobacco and substance use were biochemically verified. Carbon monoxide (CO) was used to assess tobacco use exposure at the baseline assessment and follow-ups, and urine cotinine was used to confirm smoking abstinence status from the sixth session, at the end of treatment, and each of the follow-up assessments. The cut-off for determining smoking abstinence were CO $\leq$ 4 ppm and urine cotinine $\leq$ 80 ng/ml. At the baseline assessment and each of the study visits, substance use (cannabis, cocaine, opioids, amphetamines, and methamphetamines) was assessed through test cassettes, and alcohol use was monitored through air expired. Worthy of note is that due to the COVID-19 lockdown (between March and June 2020), abstinence, both from tobacco and other substances, was not verified biochemically.

Procedure

The treatment protocols and study procedures were approved by the Local Research Ethics Committee (No. 144/

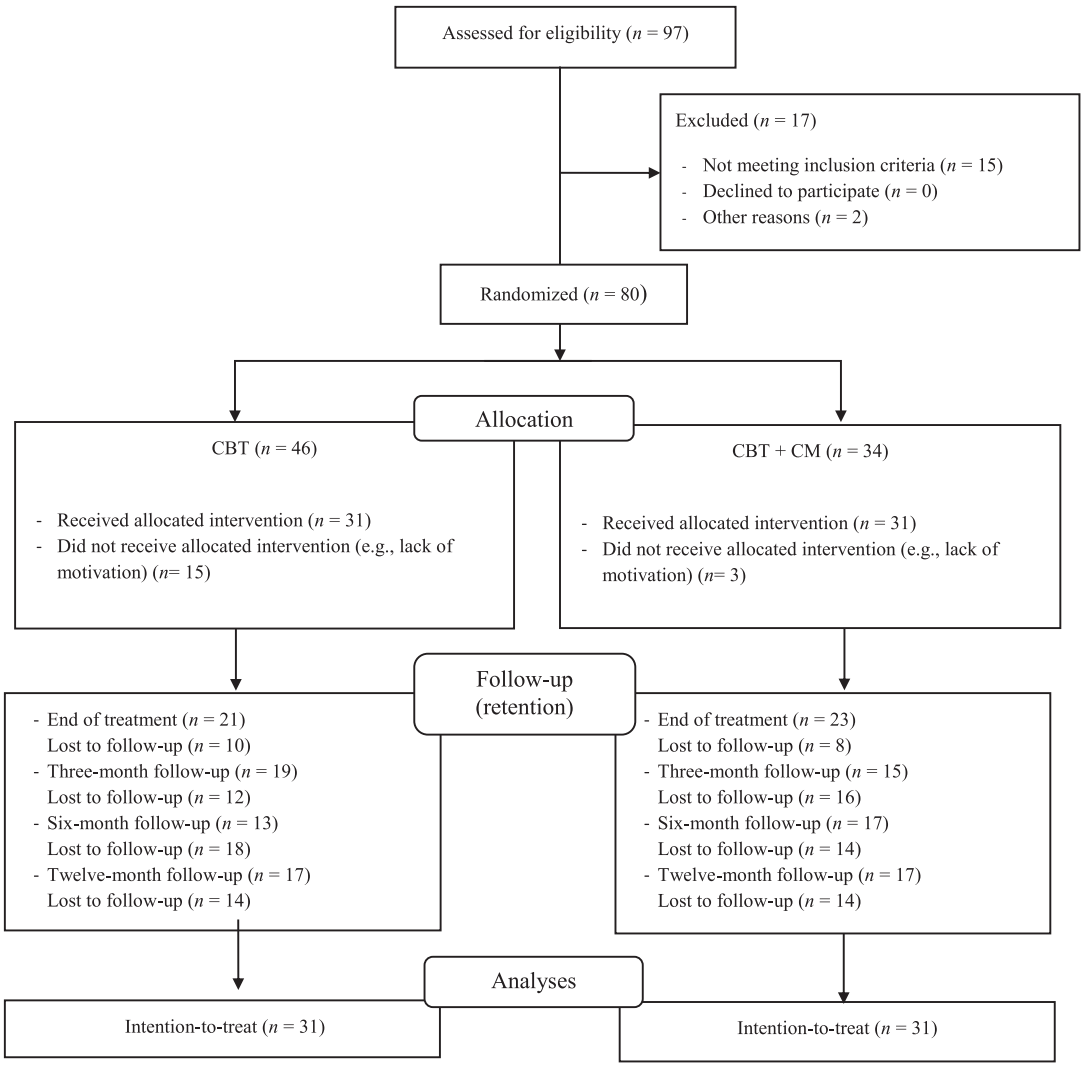

Figure 1 Consort flow diagram of study participants.

16) and registered in the ClinicalTrials-gov database (ref. NCT03551704). All participants provided a written informed consent prior to the baseline assessment.

Treatment interventions

Both treatment conditions (i.e., CBT and CBT+CM) included an eight-week smoking cessation treatment. Patients had to attend the clinic twice a week, one for the therapy session, with a duration of one hour and half, and the control session, whose objective is to collect biochemical samples.

Cognitive-Behavioral Therapy (CBT). The CBT protocol included several components previously described in standard cognitive-behavioral smoking cessation treatments (Secades-Villa et al., 2014) such as: psychoeducation, biochemical feedback, stimulus control, and training in strategies for reducing impulsivity, dealing with nicotine withdrawal symptoms, relapse prevention, and problem solving, among others. The CBT included a nicotine fading component that consisted of decreasing 20% of nicotine each week. Patients were asked to gradually reduce the number of cigarettes and switch their brand to lower-nicotine-content cigarettes each week. Patients were trained in EFT (the capability to pre-experience and project oneself into specific future events) (Morris et al., 2020). Further details on the EFT procedure may be consulted elsewhere (Aonso-Diego et al., 2021). In brief, participants were trained in the visualization of a total of five situations (one situation in one week, two in two weeks, one in a month, and one in three months), and practice visualizing them at each of the therapy sessions and at home.

Cognitive-Behavioral therapy (CBT) + Contingency Management (CM). This condition included the CBT, as described above, and voucher-based CM component for reinforcing tobacco abstinence. It consisted of providing contingent points (incentives) in exchange for biochemically verified tobacco abstinence (CO $\leq$ 4 ppm and urine cotinine $\leq$ 80 ng/ml). Incentives started at 20 points (€20) in the sixth session and increased by 5 points (€5) for each negative sample. Additionally, after each two consecutives negatives samples, patients received an additional 10 points. The reinforcement was continued through follow-ups: 45, 50, and 55 points were given to abstinent patients at one-, two-, and three-month follow-ups, respectively. The total maximum

Table 1 Baseline participants' characteristics.

	CBT (n = 31)	CBT + CM (n = 31)	p
Age	44.77 (10.70)	45.84 (8.59)	.667
Sex (male)[a]	24 (77.42%)	23 (74.19%)	.767
Marital status (married)[a]	8 (25.80%)	9 (29.03%)	.776
Working status (employed)[a]	10 (31.25%)	12 (38.71%)	.596
Educational level (< High School)[a]	15 (48.38%)	13 (41.94%)	.610
Monthly income (€)	1397.71 (1,527.73)	1450.45 (1,214.36)	.881
Tobacco use related variables			
CPD	22.55 (10.34)	20.58 (8.31)	.412
Years of regular use	27.05 (10.73)	27.50 (10.48)	.870
Previous 24 h quit attempts	1.35 (1.66)	1.55 (1.36)	.618
CO (ppm)	22.32 (15.64)	25.71 (15.96)	.402
FTCD	6.48 (2.2)	5.70 (1.82)	.136
SCID-5 — Tobacco use disorder	5.71 (1.93)	4.87 (2.19)	.115
Stages of change			.610
Pre-contemplation	1 (3.23%)	0 (0%)	
Contemplation	20 (64.51%)	20 (64.52%)	
Preparation	10 (32.25%)	10 (32.26%)	
Substance use related variables			
Days on substance use treatment	490.26 (918.06)	232.23 (250.60)	.136
Primary substance[a]			.836
Cocaine	13 (41.93%)	10 (32.26%)	
Alcohol	12 (38.71%)	13 (41.94%)	
Opioids	5 (16.13%)	6 (19.35%)	
Other[b]	1 (3.22%)	2 (6.45%)	
Secondary substance[a]			.612
Cocaine	2 (6.45%)	3 (9.68%)	
Alcohol	6 (19.35%)	3 (9.68%)	
Cannabis	4 (12.90%)	3 (9.68%)	
Opioids	0 (0%)	1 (3.23%)	
Benzodiazepines	1 (3.22%)	0 (0%)	
Abstinence (days) from primary substance of use	296.65 (541.85)	295.71 (427.87)	.993
Abstinence (days) from secondary substance of use	468.83 (810.33)	950.60 (1621.24)	.376

Note.
[a] frequency (percentage).
[b] includes cannabis, ketamine, GHB, and benzodiazepines.
CBT = cognitive-behavioral treatment; CM = contingency management; CPD = cigarettes per day; CO (ppm) = carbon monoxide in parts per million; FTCD = Fagerström test for cigarette dependence; SCID = Structured Clinical Interview for DSM-5 disorders.

amount of vouchers a patient could earn if abstinent throughout the entire treatment and follow-ups was 340 points.

Outcomes measures

The primary outcome variable was smoking abstinence, for which two measures were considered: (1) self-reported point-prevalence abstinence (24-hour tobacco abstinence at the end of treatment and 7 days in follow-ups), and (2) days of continuous abstinence (i.e., number of consecutive days without smoking, not even a puff). Substance use abstinence was a secondary study outcome and was operationalized as 7-day point-prevalence, as well as by biochemical analysis. Worthy of note is that some follow-up visits were not collected due to COVID, and abstinence was based on self-report assessments.

Following an intent-to-treat approach, participants with missed study follow-up visits were considered as smokers. It is worth noting that the intention-to-treat approach was not considered for substance use outcomes (other than cigarette smoking). This means that missing participants were not considered as actively using substances (other than nicotine) at their corresponding follow-ups but were removed from the analyses. As participants were receiving treatment at the time of the smoking cessation trial, interpretations of the 'true' effects of study treatments were less straightforward and considering an intent-to-treat approach would unequivocally lead to high rates of false positives.

Data analysis

Bivariate analyses and descriptive statistics were performed to examine differences in baseline characteristics and abstinence rates. Differences between the two treatment conditions in continuous variables were examined with t-tests, while chi-square analyses were run for categorical variables. Risk ratios (RR) were performed to determine the risk of

Table 2 Point-prevalence smoking abstinence and days of continuous abstinence at end of treatment and each follow-up.

	EOT			3-month FU			6-month FU			12-month FU		
	CBT	CM	*p*	CBT	CM	*p*	CBT	CM	*p*	CBT	CM	*p*
PP	6 (19.35%)	13 (41.94%)	.049	4 (12.90%)	5 (16.13%)	.718	2 (6.45%)	2 (6.45%)	1	2 (6.45%)	2 (6.45%)	1
CA[a]	5.65 (12.25)	5.52 (7.89)	.961	15.48 (41.10)	14.71 (36.48)	.938	14.06 (53.08)	12.77 (49.45)	.921	25.32 (98.96)	24.39 (94.40)	.970

Note.
[a] mean (standard deviation).
EOT = end of treatment; FU = follow-up; CBT = cognitive-behavioral treatment; CM = contingency management; PP = point-prevalence; CA = days of continuous abstinence.

being a smoker in the follow-ups compared to end of treatment. The RR was estimated by dividing the incidence in the exposed group (i.e., smokers) by the cumulative incidence.

To support methodological convergence, a set of three generalized estimating equations (GEEs) were conducted to examine the efficacy of the tested interventions across time. The first one was performed to assess the main effects of treatment condition (i.e., CBT+CM vs. CBT) and time (i.e., end-of-treatment, 3-, 6-, and 12-month follow-up), as well as its interactive effect, in predicting point-prevalence smoking abstinence. The second and third GEE were aimed at examining the predictive capability of point-prevalence smoking abstinence and treatment conditions on substance abstinence at medium-term (i.e., 3 and 6 months) and long-term (i.e., 12 months). Given that both dependent variables (i.e., smoking abstinence and substance use abstinence) were dichotomous, the model was adjusted using logit link function, assuming a binomial distribution for the random component and with an unstructured working correlation.

Descriptive analyses were conducted using SPSS (version 24, Inc., Chicago, IL, USA), whereas the GEE was implemented through the PROC GENMOD procedure using SAS software version 9.4 (SAS Institute, Cary, NC). The confidence level for all the analyses was set at a 95% level.

Results

Treatment effect on smoking abstinence

At the end of treatment, the 24-h point-prevalence was 30.65% (19/62). Nearly twice as many of the participants in CBT+CM vs. CBT attained at least 24-h tobacco abstinence (41.94% vs. 19.35%; $p = .049$; $\varphi = 0.245$). Smoking abstinence rates by treatment condition at follow-ups are displayed in Table 2. Seven-day point-prevalence tobacco abstinence rates were 14.52% at 3-month follow-up (CBT: 12.90%; CBT+CM: 16.13%; $p = .354$), and 6.45% at 6- and 12-month follow-up (CBT: 6.45%; CBT+CM: 6.45%; $p = 1$).

Although both smoking cessation treatments produced positive effects on smoking abstinence, the GEE revealed a non-significant effect of treatment condition over point-prevalence smoking abstinence across time (see Table 3), meaning no additive effects of CM over CBT beyond treatment termination. The main effect of time was statistically significant, meaning that the odds of abstinence progressively declined across follow-ups. Lastly, the interaction between treatment and time did not yield statistical significance ($\beta = -0.205$, $p = .260$). For the whole sample, the risk of being a smoker steadily increased at sixth months (*RR* = 3.30, 95%CI 1.33, 8.17), and remained stable at one year. An analysis by treatment condition revealed that such risk was statistically significantly higher at 6 and 12 months, only in CM condition (*RR* = 4.62; 95%CI 1.249, 17.146) (see Fig. 2).

Relationship between smoking status and substance use

At the end of treatment, 79.54% (35/44) of the participants remained abstinent from their primary and secondary substance (CBT: 76.19%; CBT+CM: 82.61%; $p = .668$). At three-

Table 3 Generalized Estimation Equations (GEE) predicting point-prevalence smoking abstinence.

	Estimate	95% CI	Z	*p*
Intercept (β_0)	−1.170	−1.950, −0.389	−2.94	.003
Treatment condition (CBT+CM vs. CBT)	.645	−0.373, 1.66	1.24	.214
Time	−0.266	−0.472, 0.059	−2.52	.012
Treatment condition x time	−0.205	−0.562, 0.152	−1.12	.260

Note. CM = contingency management; CBT = cognitive-behavioral treatment.

month follow-up, 88.24% (30/34) maintained substance abstinence (CBT: 84.21%; CBT+CM: 93.33%; p = .464), at six-month follow-up, 80% (24/30) (CBT: 76.92%; CBT+CM: 82.35%; p = .764), and at twelve-month follow-up 91.18% (31/34) (CBT: 94.12%; CBT+CM: 88.24%; p = .579).

A total of 63.16% (12/19) of those who quitted tobacco at end of treatment, remained abstinent from their primary and secondary substance in all follow-ups while 36.84% (7/19) of those who quitted were using substances at either follow-up. Among participants who did not successfully quit smoking, 55.17% (16/29) sustained substance abstinence across the entire study period (*RR* = 1.14, 95%CI 0.71, 1.84). An analysis by treatment condition suggested no significant increased risks in substance use as a result of quitting smoking [CBT: *RR* = 1.11, 95%CI 0.57, 2.17; CBT+CM: *RR* = 1.38, 95%CI 0.59, 3.23].

The GEE modeling the main effects of smoking abstinence, treatment condition, and its interaction with time (see Table 4) showed a non-significant effect of point-prevalence tobacco abstinence across time, neither medium-term (β = 0.489, p = .488) nor long-term (β = −0.456, p = .532). Similarly, the interaction between smoking abstinence and time was not significant ($p \geq .352$). Neither the main effects of treatment condition ($p \geq .740$) nor its interaction with time ($p \geq .548$) were statistically significant.

Discussion

The primary aim of this study was to examine the efficacy of CBT+CM compared to CBT only for smoking cessation in individuals receiving SUD treatment. It also sought to analyze the relationship between tobacco abstinence and substance use. Two results are underlined: (1) CM improved short-term tobacco abstinence rates, but treatment effects diminished across time; and (2) no evidence of negative impact of tobacco abstinence over substance use abstinence was observed.

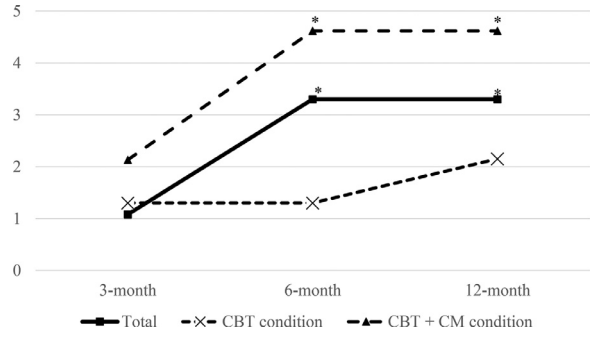

Figure 2 Risk estimates for cigarette smoking across follow-ups (3-, 6-, and 12-month) in the whole sample and by treatment arm. *Note*. Risk estimates (RR) are provided for each follow-up assessment in comparison to the end-of-treatment smoking status. * $p \leq 0.05$. CBT = cognitive-behavioral treatment; CM = contingency management.

Adding CM into a CBT protocol produced positive effects on smoking abstinence (41.94 % vs. 19.35%), suggesting CM facilitates end-of-treatment smoking abstinence, but its effect was diminished across follow-ups. Smoking abstinence outcomes were superior compared to other CM studies, which informed on 2.22% - 4.12% of tobacco abstinence rates at 12-month follow-up (Rohsenow et al., 2015, 2017; Shoptaw et al., 2002). CM effects are attributable to incentives that facilitate early abstinence in difficult to treat populations, such as those with mental health conditions (Secades-Villa et al., 2019). Incentives (e.g., cash, vouchers that are exchangeable for free time activities) act as competing reinforcers to nicotine use, thus making smoking less desirable (i.e., opportunity cost). Other explanatory mechanisms have been related to 'nudge' effects occurring with the provision of vouchers that facilitate increased involvement in non-substance use activities (González-Roz et al., 2019b). The fact that CM effects subsided beyond treatment termination are well described in the prior literature (Notley et al., 2019; Secades-Villa et al., 2020), and can be explained by the parameters considered in the CM treatment protocol. Both the immediacy (between targeted behavior and provision of the voucher) and frequency of incentives provision, are associated to improved abstinence (Pfund et al., 2021). In the present study, incentives were provided twice a week and a bonus for continuous smoking abstinence (i.e., two consecutive abstinence samples) during the smoking cessation treatment was considered. After treatment termination, frequency of incentives delivery was reduced, which could arguably explain the observed effects.

Long-term tobacco abstinence rates were similar to other studies conducted with SUD smokers, which reported 6% of tobacco quitters at 6- or 12-month follow-up (Apollonio et al., 2016; Prochaska et al., 2004). Worthy of note is that regardless of treatment condition, tobacco abstinence rates are notably low, even when CBT is considered one of the most effective interventions for smoking cessation. Findings suggest a meaningful decline in tobacco abstinence rates, which could be explained by the emotion regulation difficulties in this population (Garke et al., 2021; Johnson & McLeish, 2016), increased withdrawal symptoms (Johnson et al., 2020), as well as COVID impact on smoking behavior (Chen, 2020). In this sense, including emotion regulation strategies, recall sessions after end of treatment, and implementing mobile telephone-delivered CM (e.g.,

Table 4 Generalized Estimation Equations (GEE) predicting medium- and long-term substance abstinence.

		Estimate	95%CI	Z	*p*
Medium-term (i.e., 3- and 6- month follow-up)	Intercept (β_0)	−1.256	−2.361, −0.151	−2.23	.026
	Smoking abstinence	.489	−0.892, 1.871	.69	.488
	Time	.035	−0.350, 0.419	.18	.859
	Treatment condition (CBT+CM vs. CBT)	−0.237	−1.639, 1.165	−0.33	.740
	Smoking abstinence × time	−0.317	−0.985, 0.351	−0.93	.352
	Treatment condition × time	−0.109	−0.646, 0.428	−0.40	.690
Long-term (i.e., 12- month follow-up)	Intercept (β_0)	−1.306	−2.458, −0.153	−2.22	.026
	Smoking abstinence	.456	−0.974, 1.887	.63	.532
	Time	−0.323	−0.866, 0.220	−1.16	.244
	Treatment condition (CBT+CM vs. CBT)	−0.235	−1.668, 1.198	−0.32	.748
	Smoking abstinence × time	−0.214	−0.435, 0.863	.65	.519
	Treatment condition × time	−0.192	−0.434, 0.818	.60	.548

Note. CBT = cognitive-behavioral treatment; CM = contingency management.

DeFulio et al., 2021; Hammond et al., 2021; Zastepa, Sun, Clune, & Mathew, 2020), could be effective options for this purpose.

A second and important finding of the current study is that quitting smoking had no negative impact on substance use abstinence. This result is consistent with previous studies (McKelvey et al., 2017; Piercy et al., 2021) and may be explained by two rationales: (1) the skills learned during the smoking cessation treatment that can be extrapolated to other substances (e.g., problem solving, relapse prevention strategies, stimulus control), and (2) tobacco abstinence effects which relate to involvement in a healthy lifestyle incompatible with substance use (Sohlberg & Bergmark, 2020). This finding emphasizes the need of considering specific smoking cessation interventions as part of any comprehensive addiction treatment approach given the high prevalence of tobacco use among individuals with SUD.

This study should be interpreted under several limitations. The relatively small sample size might have impacted on the lack of significance of several results. Hence, future large-scale research should be conducted to elucidate the impact of CM on quitting rates. Second, the majority of sample was comprised of men, which precluded us from conducting analyses by sex. Third, the lockdown imposed by the Spanish government to prevent the spread of COVID-19 prevented us from carrying out face-to-face follow-ups, and therefore, collecting biochemical samples, which had a probable impact on tobacco use. Because some participants did not attend the follow-ups, we could not elucidate whether missing participants maintained abstinence from their primary and secondary substance, and were thus excluded from the proposed analyses, resulting in an overly conservative approach.

Conclusion

The study findings supported the effectiveness of CBT+CM for facilitating early abstinence in smokers with SUD. CM effects steadily diminish beyond the end of treatment and further research looking at effective procedures to sustaining abstinence is needed. The fact that smoking cessation did not impact on substance abstinence adds support to the convenience of providing simultaneous treatment for tobacco and other substances. Given the high rates of cigarette smoking in SUD populations and the negative impact it causes both physically and mentally, health professionals should provide smoking cessation treatments as a standard practice, as well as encouraging smoking cessation by increasing their motivation to change.

CRediT authorship contribution statement

Roberto Secades-Villa: conceptualization, resources, writing – review and editing, supervision, project administration, funding acquisition. **Gema Aonso-Diego:** conceptualization, methodology, software, formal analysis, data curation, writing – original draft. **Alba González-Roz:** conceptualization, data curation, writing – original draft, supervision.

Declaration of Interests

No potential conflict of interest was reported by the authors.

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6. Discusión y conclusiones

El objetivo general de la presente Tesis Doctoral fue evaluar la efectividad a corto y largo plazo de dos protocolos de tratamiento psicológico para el abordaje del tabaquismo en personas en tratamiento por TUS. Se desarrollaron cinco objetivos específicos, acorde a los cinco estudios que conforman la Tesis Doctoral. Concretamente, se revisó de forma sistemática la evidencia del MC para dejar de fumar en personas en tratamiento o recuperación por TUS. En segundo lugar, se examinó la factibilidad y aceptabilidad de incorporar la TCC + PEF en un contexto clínico, así como la relación entre el PEF y la patología del refuerzo (i.e., DD y demanda). Por último, se examinó el efecto a corto y largo plazo del MC para dejar de fumar en una muestra de fumadores en tratamiento por TUS, así como el impacto de la cesación tabáquica sobre la abstinencia de otras sustancias. A continuación, se resumen los principales hallazgos correspondientes a los objetivos específicos, atendiendo a los contenidos y no al orden de las publicaciones.

6.1. Efectividad del manejo de contingencias para dejar de fumar

La revisión sistemática y metaanálisis permitió concluir que añadir un componente de MC a un tratamiento estándar (farmacológico, psicológico o combinado) para dejar de fumar mejora significativamente las tasas de abstinencia y de reducción del consumo de tabaco a corto plazo. Concretamente, los participantes asignados al grupo de MC alcanzaron una tasa de abstinencia tabáquica en el postratamiento 4,6 veces mayor que sus grupos de comparación (36,03% vs. 7,84%). A largo plazo no se observó un efecto aditivo significativo en el grupo experimental (7,8% vs. 1,71%).

Los resultados obtenidos en la presente Tesis Doctoral son similares. Al término del tratamiento, los participantes asignados a la condición de MC presentaron mayores tasas de abstinencia tabáquica (41,94% vs. 19,35%), aunque a largo plazo (un año tras la

finalización de la terapia), no se observaron diferencias significativas entre ambas condiciones (6,45%). Además, las personas que recibieron MC evidenciaron una mayor retención en el tratamiento, asistencia a las sesiones y adherencia a las pautas de reducción, aunque las diferencias no fueron estadísticamente significativas. Estos resultados presentan una elevada relevancia desde un punto de vista clínico, sobre todo si se tiene en cuenta la dificultad para promover la abstinencia en esta población y las elevadas tasas de abandonos observadas en otros estudios (Lien et al., 2021; Lima et al., 2020).

Las tasas de abstinencia encontradas en la muestra de esta Tesis Doctoral son ligeramente superiores a las halladas en estudios previos (Apollonio et al., 2016; Prochaska et al., 2004). Varias razones pueden dar cuenta de estos resultados. En primer lugar, se ha combinado un protocolo de MC con la TCC y con técnicas que abordan la elección impulsiva (e.g., PEF). Por otro lado, para alcanzar la abstinencia tabáquica se implementó una reducción gradual de la ingesta de nicotina y alquitrán, técnica que facilita la abstinencia al reducir la gravedad de la sintomatología de abstinencia. En relación al componente de MC, el protocolo de incentivos incluía *bonus* por mantener la abstinencia continuada, lo que maximiza la abstinencia al poder acceder a un reforzador de mayor magnitud (Businelle et al., 2009). Por último, el tratamiento de cesación tabáquica presentaba una mayor intensidad que los estudios previos, en términos de la longitud del programa, y la duración y el número de sesiones.

La reducción de la efectividad del MC con el paso del tiempo se ha evidenciado en otros estudios previos que sugieren que proporcionar refuerzos extrínsecos (i.e., incentivos) es efectivo a corto plazo, pero su efecto se reduce en los seguimientos (Benishek et al., 2014; Prendergast et al., 2006; Sayegh et al., 2017). Aunque ningún estudio ha examinado qué características mejoran las tasas de abstinencia tabáquica a

largo plazo en las personas con TUS, los estudios que han evaluado el efecto del MC en la abstinencia de otras sustancias sugieren que la duración del MC es un moderador significativo de las tasas de abstinencia al año de seguimiento (Ginley et al., 2021), lo que sugiere ampliar la duración del MC. Por otro lado, reforzar otras conductas objetivo, como la asistencia y las disminuciones progresivas en el consumo de tabaco ha mostrado tener un impacto sobre la abstinencia tabáquica a largo plazo (Lussier et al., 2006; Petry et al., 2018; Secades-Villa, López-Núñez, et al., 2019). Este último aspecto es relevante porque es posible que muchos fumadores con TUS, con una menor motivación para dejar de fumar o una mayor dependencia a la nicotina, no consigan la abstinencia tabáquica y, por ende, incentivos.

Se requieren más estudios que analicen las características de los tratamientos de MC que maximizan las tasas de abstinencia tabáquica, como por ejemplo la magnitud del reforzador o el tipo de incentivo (e.g., *vouchers* vs. privilegios clínicos). Por último, una línea futura que aún no se ha examinado es la relacionada con el uso de las intervenciones digitales, conocidas como intervenciones *e-health* y *m-health*. Aunque todavía son pocos los estudios que han implementado esta modalidad (ver e.g., Beckham et al., 2018; Kendzor et al., 2022), algunos ensayos clínicos en fumadores han mostrado distintas ventajas frente a protocolos de MC presenciales protocolizados, como es la posibilidad de adaptar la intervención a las características de la persona, entregar los incentivos de forma inmediata y reducir costes asociados a la intervención presencial, entre otros (Coughlin et al., 2022).

En definitiva, estos hallazgos nos indican la importancia de implementar técnicas de MC para promover la abstinencia tabáquica a corto plazo. No obstante, los futuros estudios deberían de examinar cómo garantizar que la efectividad del MC se pueda mantener a largo plazo y evitar las recaídas.

6.2. Factibilidad y eficacia del pensamiento episódico futuro

En relación con el PEF, los resultados indican que su implementación en un contexto clínico, como es un centro de tratamiento de sustancias, resulta aceptable y factible. La TCC para dejar de fumar en combinación con el PEF resultó ser aceptable, ya que los participantes informaron de una alta satisfacción con el tratamiento (i.e., duración y frecuencia de las sesiones, duración y número de sesiones del tratamiento). En cuanto a la factibilidad, los participantes presentaron tasas adecuadas de retención en el tratamiento y asistencia a las sesiones. No obstante, la tasa de adherencia a las prácticas de visualización futura (componente del PEF) fue relativamente baja (el 74% realizó al menos una práctica), por lo que se sugieren varias modificaciones, como es la disminución de los eventos generados (i.e., de siete a cinco), de las prácticas requeridas (i.e., de 210 a 98), así como una reducción del marco temporal (i.e., de un año a tres meses vista).

Con respecto al cuarto artículo incluido en esta Tesis Doctoral, donde se analizó la relación entre el PEF y su efecto sobre la patología del refuerzo (i.e., DD y demanda), los hallazgos mostraron que una mayor práctica del PEF se asociaba a una reducción de los índices de DD y de demanda de cigarrillos durante el tratamiento. Estos resultados van en línea con la evidencia previa que señala cómo la práctica repetida del PEF produce una mayor reducción de la patología del refuerzo (Mellis et al., 2019); y que una reducción del consumo de tabaco se relaciona con una reducción de su valor reforzante.

A diferencia de estudios previos, en la presente Tesis Doctoral las demoras (i.e., marcos temporales) propuestas en el PEF no coinciden con las demoras utilizadas en la tarea del DD (O'Donnell et al., 2019) y, además, las frases breves que resumen el evento generado en el PEF no se presentaron durante la tarea del DD (Rung y Madden, 2019). Este hallazgo sugiere que estas dos características no son imprescindibles para observar

un impacto significativo en la patología del refuerzo, lo que indicaría que las disminuciones en el DD y la demanda de tabaco no se deben, como indican estudios previos (Rung y Madden, 2019), a la anticipación de la hipótesis del estudio por parte de los participantes.

La reducción de la ingesta de nicotina y recibir un tratamiento de MC disminuyeron la demanda de cigarrillos. Este hallazgo indica que reducir el consumo de tabaco y recibir incentivos a cambio de alcanzar la abstinencia tabáquica provoca una disminución en el valor reforzante de la nicotina (García-Pérez et al., 2020; Weidberg et al., 2015). El mecanismo explicativo subyacente está relacionado con el incremento del coste de respuesta al proporcionar incentivos contingentes a la abstinencia, así como con el aumento la disponibilidad de reforzadores alternativos al consumo que compite con el valor reforzante de la droga (e.g., entradas para el gimnasio, actividades de tiempo libre).

En conjunto, estos hallazgos tienen especial relevancia dado que la reducción en el reforzamiento del tabaco y la toma de decisiones impulsiva se vincula a buenos resultados, en términos de abstinencia tabáquica y otras variables (e.g., reducción de impulsividad) (Bickel et al., 2020). No obstante, se requiere un mayor número de estudios sobre el PEF, en especial en contextos clínicos, para establecer conclusiones firmes sobre su impacto sobre la patología del refuerzo y la abstinencia de sustancias. Además, los futuros estudios deberían de examinar las características del PEF que maximicen la adherencia al tratamiento (e.g., envío de recordatorios al dispositivo móvil) y su efectividad (e.g., número de prácticas requeridas, marco temporal). En este sentido, sería de interés el empleo de la evaluación ambulatoria mediante dispositivos electrónicos en entornos naturales con el fin de obtener información en tiempo real las veces que se precise (ver Fonseca-Pedrero et al., 2022 para revisión). En particular, la evaluación ambulatoria permitiría recoger información relacionada con la práctica de visualización

(e.g., realismo, viveza), así como el efecto de la práctica del PEF en situaciones naturales de consumo (e.g., craving). Por último, una de las líneas futuras de investigación es la integración del PEF en programas de realidad virtual, lo que permitiría crear un ambiente idóneo para simular los eventos futuros por el aumento de la viveza y de los detalles temporoespaciales, con el consiguiente impacto sobre las medidas de resultado (Wang et al., 2019).

6.3. Relación entre cesación tabáquica y abstinencia de otras sustancias

Respecto a la relación entre la abstinencia tabáquica y la abstinencia a otras sustancias, los estudios incluidos en la revisión sistemática presentan resultados mixtos: algunos de ellos indican que recibir un tratamiento para dejar de fumar y/o la abstinencia tabáquica tiene un impacto positivo en el consumo de otras sustancias; mientras que otros estudios encuentran un efecto nulo, es decir, que no hay relación entre recibir un tratamiento de cesación tabáquica –o la propia cesación tabáquica– y la abstinencia a otras sustancias.

Los resultados del quinto artículo de esta Tesis Doctoral evidenciaron que la abstinencia tabáquica no tiene un impacto significativo sobre la abstinencia de la sustancia principal y secundaria por la que demandan tratamiento. No obstante, hay una tendencia que resulta relevante desde un punto de vista clínico, dado que el 63,2% de las personas que dejaron de fumar se mantenían abstinentes de su sustancia principal y secundaria de referencia, en comparación con el 55,2% de los que no consiguieron la abstinencia tabáquica.

Estos resultados van en la línea de las investigaciones previas (McKelvey et al., 2017) donde se indica que la abstinencia tabáquica se relaciona con mejores resultados relativos a otras sustancias. Varios factores pueden explicar el efecto del abandono del

tabaco sobre el consumo de otras sustancias. En primer lugar, la persona con TUS que abandona el consumo de tabaco está expuesta a menos estímulos discriminativos, dado que la nicotina actúa como antecedente del consumo de otras sustancias, esto es, aumentando la probabilidad de craving de otras drogas (Ginsburg et al., 2018; Mello y Newman, 2011). Por otra parte, la abstinencia tabáquica reduce factores de riesgo comunes a otras sustancias (e.g., impulsividad), tanto legales como ilegales (García-Pérez et al., 2020; Secades-Villa et al., 2014). En esta misma línea, determinadas habilidades y estrategias que actúan como factores de protección del consumo de tabaco (e.g., habilidades de afrontamiento, regulación emocional) funcionan también como factores de protección de otras sustancias (Capella y Adan, 2017; Estévez et al., 2017; Fathiandastgerdi et al., 2015). Esto es, la persona que reciben un tratamiento para dejar de fumar y consigue la abstinencia tabáquica ha adquirido dichas habilidades, las cuales pueden ser aplicadas al resto de sustancias y así afrontar eficazmente las situaciones de alto riesgo.

A continuación, se plantean algunas líneas futuras de investigación relativas a la relación entre abstinencia tabáquica y abstinencia a otras sustancias. En primer lugar, los estudios que aborden la cesación tabáquica en esta población deberían de proporcionar también resultados sobre el impacto en la abstinencia de otras sustancias, así como facilitar medidas de resultados consistentes con la investigación previa (e.g., días de abstinencia continuada, definición de recaída) para facilitar la comparación de los hallazgos y disminuir la heterogeneidad en futuros estudios metaanalíticos. Por otro lado, sería de interés profundizar en la investigación acerca de los factores que explican la relación entre la cesación tabáquica y la abstinencia de otras drogas. Dichos factores podrían ser de tipo psicológico (e.g., reducción de la impulsividad o de la sintomatología depresiva), relacionados con la sustancia por la que se demanda tratamiento (e.g., tipo de

sustancia, días de abstinencia) o contextuales (e.g., cambio en el estilo de vida, activación conductual).

En conclusión, los resultados de esta Tesis Doctoral señalan que la cesación tabáquica no perjudica la abstinencia de otras sustancias y, potencialmente, puede aumentar la probabilidad de mantenerse abstinente a largo plazo. Dejar de fumar no solo va en coherencia con los objetivos distales del tratamiento de consumo de sustancias, sino que también tiene un impacto positivo en la salud de los pacientes y en su recuperación. Este hallazgo refuerza la necesidad de incorporar programas de deshabituación tabáquica en los programas de tratamiento de consumo de sustancias, así como de alentar a esta población a intentar dejar de fumar desde los servicios de salud mental, las unidades de tratamiento de toxicomanías o las ONGs que trabajen con consumidores de drogas.

6.4. Conclusiones

A continuación, se presentan las conclusiones que se derivan de esta Tesis Doctoral:

1) Los resultados del metaanálisis y revisión sistemática indican que el MC para dejar de fumar es efectivo para conseguir la abstinencia tabáquica y reducir el consumo a corto plazo (i.e., postratamiento), pero su efecto se reduce en los seguimientos.
2) Recibir un tratamiento para dejar de fumar y la cesación tabáquica no impacta negativamente en la abstinencia de otras sustancias.
3) La implementación de la TCC + PEF resulta factible en contextos clínicos o de tratamiento y aceptable por parte de las personas fumadoras con TUS.
4) La TCC + PEF + MC mejora significativamente los resultados de abstinencia del tabaco al término del tratamiento en comparación a los observados con la TCC + PEF, aunque su efecto disminuye a largo plazo.
5) El PEF resulta efectivo para reducir la impulsividad y la motivación al consumo (i.e., demanda de cigarrillos). Además, una reducción en el consumo de tabaco y recibir incentivos por alcanzar la abstinencia tabáquica reduce la demanda de cigarrillos.
6) La efectividad de la terapia psicológica sobre la abstinencia del tabaco y, en concreto, los excelentes resultados a corto plazo del MC respaldan la necesidad de ofrecer de forma sistemática este tipo de tratamientos en los servicios de cesación tabáquica, especialmente a las personas que se encuentran en tratamiento ambulatorio por consumo de sustancias.

6.5. Conclusions (bis)

The conclusions derived from this Doctoral Thesis are the following:

1) The results of the meta-analysis and systematic review indicate that CM for smoking cessation is effective in achieving smoking abstinence and reducing tobacco use in the short-term (i.e., posttreatment), but its effect is reduced in the follow-ups.
2) Receiving treatment for smoking cessation and tobacco abstinence does not negatively impact on abstinence from other substances.
3) The implementation of CBT + EFT is feasible in clinical or treatment contexts and acceptable by smokers with SUD.
4) CBT + EFT + CM significantly improves tobacco abstinence outcomes at the end of treatment compared to those observed with CBT + EFT, although its effect decreases in the long term.
5) EFT is effective in reducing impulsive choice and consumption motivation, (i.e., cigarette demand). Furthermore, a reduction in tobacco use and receiving incentives to achieve tobacco abstinence reduces cigarette demand.
6) The effectiveness of psychological intervention on tobacco abstinence and, specifically, the excellent short-term results of CM support the need to systematically offer this type of treatment in smoking cessation services, especially to individuals who are receiving outpatient treatment for substance use.

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