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#### Review

# The use of repetitive transcranial magnetic stimulation for modulating craving and addictive behaviours: A critical literature review of efficacy, technical and methodological considerations



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#### ABSTRACT

Objectives: Repetitive transcranial magnetic stimulation (rTMS) is a potential therapeutic intervention for the treatment of addiction. This critical review aims to summarise the recent developments with respect to the efficacy of rTMS for all types of addiction and related disorders (including eating disorders), and concentrates on the associated methodological and technical issues.

Methods: The bibliographic search consisted of a computerised screening of the Medline and ScienceDirect databases up to December 2013. Criteria for inclusion were the target problem was an addiction, a related disorder, or craving; the intervention was performed using rTMS; and the study was a clinical trial. Results: Of the potential 638 articles, 18 met the criteria for inclusion. Most of these (11 of the 18) supported the efficacy of rTMS, especially in the short term. In most cases, the main assessment criterion was the measurement of craving using a Visual Analogue Scale.

Discussion: The results are discussed with respect to the study limitations and, in particular, the many methodological and technical discrepancies that were identified. Key recommendations are provided.

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#### 1. Introduction

Addictions are complex illnesses, and are the subject of many research studies. A recent review paper suggested that over half the adult population of the United States reported symptoms reminiscent of current addictive disorders (Sussman et al., 2011). Addictions can be defined as "a condition in which a behaviour that can function both to produce pleasure and to reduce painful affects is employed in a pattern that is characterised by two key features: (1) recurrent failure to control the behaviour, and (2) continuation of the behaviour despite significant harmful consequences" (Goodman, 1990, 2008). Despite this minimalist but generally agreed upon behavioural definition, different addictions display many similarities in terms of risk factors, the frequency of comorbidities and the trajectory, which is marked by periods of relative control or abstinence alternating with periods of relapse (Goodman, 2008). Finally, different types of addiction share a number of clinical symptoms such as drug-seeking behaviour. feelings or thoughts directed towards pathological behaviour pervading the mind and impulsive action followed by periods of struggle with anxiety of varying length (Le Moal and Koob, 2007; Dickson et al., 2011). Compulsivity and impulsivity are the two main factors involved in a composite addiction cycle, which can be characterised by three successive stages: binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation, also known as the "craving stage" (Koob and Volkow, 2010).

Addictions are not only limited to substance use disorders (SUD). Indeed, it is now widely agreed that they also relate to non-drug behaviours (e.g. gambling or shopping) and substances that have not traditionally been viewed as addictive (e.g. food) (Gearhardt et al., 2011). Whether they are linked to SUD or behavioural addictions, also known as "related disorders" (RD), they actually have a great deal in common despite their apparent clinical heterogeneity and mainstream thinking increasingly views SUD and RD as a coherent whole. This is highlighted in the latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), where a new category entitled "Addiction and RD" combines SUD and gambling disorders and drops the former categories of abuse and dependence (O'Brien, 2011). Although not included in the DSM-5, several other disorders were considered relating to the Internet, sex, exercise and shopping (Potenza, 2014a). It is expected that this list is non-exhaustive. Addiction relating to food was not considered by the research workgroup, due to existing debates on the topic (Potenza, 2014a), and grouping eating disorders under the label "addictions" remains controversial. Despite this, more and

more authors support this idea (Speranza et al., 2012; Potenza, 2014b). The umbrella term of eating disorders encompasses a broad spectrum, with anorexia nervosa (AN) at one end and binge eating disorder (BED) at the other, and also includes bulimia nervosa (BN) and other specified feeding and eating disorder (OSFED). BN, BED and, to a lesser extent, OSFED share behavioural and clinical characteristics with other types of addictive disorders (Volkow and O'Brien, 2007; Kinzl and Biebl, 2010; Gearhardt et al., 2011; Speranza et al., 2012; Davis, 2013; Curtis and Davis, 2014). In particular, they meet the diagnostic criteria proposed by Goodman (Goodman, 2008; Speranza et al., 2012). They also share neurobiological processes with other addictive disorders (Cota et al., 2006; Cowin et al., 2011; Gearhardt et al., 2011; Avena and Bocarsly, 2012; Umberg et al., 2012; Kaye et al., 2013; Volkow et al., 2013). Conceptualising AN as a behavioural addiction is perhaps somewhat more complicated. Indeed, people with AN are not addicted to food but quite the opposite, they are addicted to food deprivation, and they show real determination instead of losing control. Because of these opposing behavioural features, AN and BN could be regarded as two sides of the same coin. In particular, they are characterised by a persistent preoccupation with food and dysfunctional cognition related to body weight and body image (Avena and Bocarsly, 2012), and by the same brain alterations, for example, increased grey matter volume of the medial orbitofrontal cortex and reduced white matter in the right temporal and parietal areas relative to healthy individuals (Frank et al., 2013). The neural molecular events driving self-restriction are detected in the nucleus accumbens, strengthening the idea of the addictive facet of restrictive diet underpinned by a rewarding effect associated with energy expenditure (Jean et al., 2012). For all of these reasons, AN could also be considered as a behavioural addiction or a RD, especially of the binge-eating/purging type.

Craving is one of the most striking symptoms of addiction and RD, as emphasised by the composite addiction cycle previously mentioned (Koob and Volkow, 2010). It has been the subject of growing attention, to the extent that it is listed as one of the diagnostic criteria in the category "Addiction and RD" (O'Brien, 2011). Craving is defined as a pressing, urgent and irrepressible desire to give in to an addictive behaviour, and results in the loss of control in most cases (Skinner and Aubin, 2010). In addition to the extensive literature in the field of drug craving, there is also a wide range of information about food craving (Bou Khalil and El Hachem, 2013; Jansen et al., 2013). Beyond the mere desire to take a drug or food or to gamble, for example, craving also includes the expectation of positive effects and the relief of negative effects as a result

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