

## CIGARETTE SMOKING HAS NO PRO-COGNITIVE EFFECT IN SUBJECTS WITH OBSESSIVE-COMPULSIVE DISORDER: A PRELIMINARY STUDY

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### SUMMARY

**Background:** The prevalence of cigarette smoking in patients with different psychiatric disorders is higher than that in the general population, which is partly explained by the pro-cognitive effect of smoking on cognitive functions. In subjects with obsessive-compulsive disorder (OCD), the prevalence of smokers is lower than that in other psychiatric disorders. We hypothesized that cigarette smoking does not provide benefits and even worsen cognitive performance in OCD.

**Subjects and methods:** We compared different executive function subdomains in 20 smoking and 20 non-smoking inpatients with OCD. At the beginning of hospitalization, we assessed visuo-spatial working memory, planning and set-shifting abilities (Cambridge Neuropsychological Test Automated Battery), smoking habits (standardized personal interviews), and the severity of obsessive-compulsive symptoms (Dimensional Yale-Brown Obsessive-Compulsive Scale).

**Results:** The performance of smokers and non-smokers did not differ significantly in any cognitive subdomain. The smoking duration was significantly associated with poorer visuo-spatial working memory performance ( $P=0.001$ ).

**Conclusions:** Our results showed that cigarette smoking did not provide cognitive enhancement across various executive function subdomains in subjects with OCD. The lack of beneficial cognitive effects of smoking may make these subjects less prone to smoking and may partially explain the lower rate of smokers in OCD compared with other psychiatric conditions.

**Key words:** obsessive-compulsive disorder – OCD – smoking – cognition - executive function

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### INTRODUCTION

The prevalence of cigarette smoking is higher among subjects with psychiatric disorders (35–80%) than the general population (19–24%) (Abramovitch et al. 2014). According to the “self-medication hypothesis,” this higher prevalence may be partly justified by the assumption that smoking ameliorates clinical symptoms and/or cognitive performance across many psychiatric conditions (Caldirola et al. 2013, Wing et al. 2011). In contrast, obsessive-compulsive disorder (OCD) is associated with lower smoking prevalence (approximately 13%), compared with other psychiatric conditions or with healthy individuals without mental health conditions (24%) in the US (Abramovitch et al. 2014). Bejerot & Humble (1999) hypothesized the following explanations for this: specific OC symptoms, including the fear of cleanliness/contamination or bodily harm/ diseases and parsimoniousness, may deter from smoking in individuals with OCD; reduced impulsivity and risk-taking behaviors in individuals with OCD, which are associated with smoking; genetic factors that may influence liability to both OCD and lack of nicotine-induced positive reinforcement; and

nicotine may exacerbate OC symptoms by increasing the frontostriatal circuit hyperactivity in these individuals. Abramovitch et al. (2014) recently found that smoking prevalence is also reduced in unaffected parents of individuals with OCD and suggested that this is related to the frontostriatal circuit dysfunction familiarity. Finally, the reduced smoking prevalence in subjects with OCD may be specifically linked to repeated engagement in negative reinforcement (Abramovitch et al. 2014). An additional explanation, which has not been investigated, may be associated with the impaired cognitive functioning of subjects with OCD, particularly in executive function (Abramovitch et al. 2013, Shin et al. 2014, Snyder et al. 2015). Abnormalities in a network of brain areas, including the frontostriatal circuit and parietal cortex, may underlie these deficits (Menzies et al. 2008). Neuroimaging studies have shown baseline hyperactivity in these areas (Menzies et al. 2008), possibly arising from imbalanced monoaminergic neurotransmission (Millet et al. 2013, Nikolaus et al. 2010). As nicotine enhances the cortical activity by promoting the release of several neurotransmitters (Wallace & Bertrand 2013), the nicotine-induced activation of an already hyperactive

system of subjects with OCD may not ameliorate cognitive performance and may even worsen it. This may explain, in part, why these subjects are less prone to smoking compared with other psychiatric populations, in which smoking enhances particularly executive functions (Caldirola et al. 2013, Morisano et al. 2013, Wing et al. 2011). To test this hypothesis, we compared the executive function performance of smokers and non-smokers with OCD.

## SUBJECTS AND METHODS

### Subjects

A total of 20 smokers and 20 non-smokers with OCD (DSM-IV-TR criteria) (American Psychiatric Association 2000) were consecutively recruited from a group of inpatients attending a 4-week psychiatric rehabilitation program at “Villa San Benedetto Menni” Hospital, Albese con Cassano, Como, Italy. The inclusion criteria were as follows: 18–65 years of age; smokers (actively and continuously smoking cigarettes daily for at least 4 weeks, with no periods of non-smoking for over 3 months in the previous 2 years), or non-smokers (having never used cigarettes or other tobacco products). The exclusion criteria were as follows: individuals suffering from other current Axis I disorders (DSM-IV-TR criteria); drug or alcohol abuse/dependence in the last 6 months; suspected or diagnosed mental retardation (IQ<70); and lifetime neurologic diseases/trauma, hypothyroidism/hyperthyroidism, relevant modifications of pharmacologic treatment in the 4 weeks preceding hospitalization (addition or discontinuation of drugs), and use of drugs not recommended for OCD. No smoking restriction was imposed during hospitalization. The study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Local Health Authority of the Province of Como, Italy. All participants provided voluntary informed consent

prior to participation. The data were collected between October 2012 and October 2013.

### Procedures and measures

Within the first 3 days of the hospitalization, prior to any pharmacological modification or starting the rehabilitation program, trained psychologists assessed a) executive function, using the Cambridge Automated Neuropsychological Test Battery (CANTAB), a tool suitable for cross-cultural comparisons providing normative population data, and largely used for neuropsychological evaluation in OCD (Abramovitch et al. 2013, Robbins et al. 1998). The tests selected included only those assessing executive function subdomains, which have been found to be impaired in previous neuropsychological studies in OCD populations (Abramovitch et al. 2013, Shin et al. 2014, Snyder et al. 2015) (Table 1). Administration took approximately 1 h and was performed late in the morning; b) smoking habits, including the age of onset, smoking duration, lifetime smoking habit, and the number of cigarettes smoked in the 24 h preceding the day of neuropsychological assessment and in the day of assessment, were assessed by a standardized personal interview; c) severity of OC symptoms using the total score (0–30) of the semi-structured Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) (Goodman et al. 1989). The psychologists were blind to the smoking habits of the subjects and/or to the results of the neuropsychological assessment.

### Statistical analyses

Continuous data, nominal data, and the association between variables were analyzed using a t-test for independent samples,  $\chi^2$  analysis, and Pearson’s correlation, respectively. Given the multiple comparisons, the significance level of  $\alpha=0.01$  was set. The data were analyzed using the Statistical Package for Windows (Statistica 10.0; Statsoft, Inc., Tulsa, OK, USA).

**Table 1.** Assessment of executive function subdomains. Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition Ltd)

Subdomain	Test	Outcome measure	Description
Planning, strategic processing	Stockings Of Cambridge (SOC)	Problems solved in minimum moves	Number of occasions upon which the subject has successfully completed a test problem in the minimum possible number of moves
Visuo-spatial working memory	Spatial SPan (SSP)	Span length	The longest sequence of boxes successfully recalled by the subject
	Spatial Working Memory (SWM)	Between errors Strategy	Number of times the subject revisits a box in which a token has previously been found Ability to follow a predetermined sequence by beginning with a specific box and then, once a token has been found, to return to that box to start the new searching sequence
Set shifting	Intra-Extra Dimensional Set Shifting (IED)	Extra-Dimensional Errors (ED)	Errors committed at the stage where the subjects in required to make an extra-dimensional shift

**Table 2.** Demographic and clinical characteristic of the sample. Comparisons between smokers and non-smokers

	OCD sample (n=40)	Smokers (n=20)	Non-smokers (n=20)	Statistic	P*
Female:male, n:n	22:18	8:12	14:6	$\chi^2=3.6$	0.06
Age, mean (SD), y	42.62 (11.96)	44.40 (11.80)	40.85 (12.14)	$t=-0.937$	0.35
Education, mean (SD), y	12.37 (3.72)	12.10 (3.52)	12.65 (3.98)	$t=0.463$	0.65
DY-BOCS total score, mean (SD)	21.70 (5.09)	21.17 (6.04)	22.21 (4.10)	$t=0.618$	0.54
Age at onset, mean (SD), y	17.85 (5.80)	17.8 (6.81)	17.9 (4.77)	$t=0.054$	0.96
Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition Ltd)					
IED ED errors (-)	12.80 (11.00)	14.20 (11.37)	11.40 (10.73)	$t=-0.801$	0.43
SOC problems solved in minimum moves (+)	7.47 (1.60)	7.15 (1.5)	7.8 (1.67)	$t=1.295$	0.20
SSP span length (+)	5.17 (1.71)	5.1 (1.77)	5.25 (1.68)	$t=0.274$	0.78
SWM between errors (-)	34.27 (20.27)	33.85 (18.76)	34.7 (22.15)	$t=0.131$	0.90
SWM strategy (-)	-0.51 (1.05)	-0.54 (1.23)	-0.48 (.86)	$t=0.177$	0.86
Medication, n (%)					
Serotonin Reuptake Inhibitors	36 (90)	18 (90)	18 (90)	$\chi^2=0.0$	1
Tricyclic antidepressants	8 (20)	4 (20)	4 (20)	$\chi^2=0.0$	1
Atypical antipsychotics	21 (52.5)	13 (65)	8 (40)	$\chi^2=0.8$	0.38
Benzodiazepines	19 (47.5)	11 (55)	8 (40)	$\chi^2=0.3$	0.60

\* Statistical significance:  $P < 0.01$ ; DY-BOCS = Dimensional Yale-Brown Obsessive Compulsive Scale; IED = Intra-Extra Dimensional Set Shifting; SOC = Stockings of Cambridge, SWM = Spatial Working Memory, SSP = Spatial Span (+) the higher the score, the better the performance; (-) the higher the score, the worse the performance

## RESULTS

The demographic and clinical characteristics of the sample groups are presented in Table 2.

The mean age at smoking onset was 19.65 years (SD 5.59), mean smoking duration was 25.29 years (SD 14.43), mean number of cigarettes smoked in the 24 h preceding the day of neuropsychological assessment was 12.5 (SD 9.74), and mean number of cigarettes smoked on the assessment day was 3.47 (SD 2.37). Compared with the normative data (Robbins et al. 1998), the whole sample showed significantly poorer performance in the subdomains we assessed: Stockings Of Cambridge (SOC) problems solved in minimum moves ( $t=-5.31$ ,  $P < 0.01$ ), Spatial Span (SSP) span length ( $t=-3.61$ ,  $P < 0.01$ ), Spatial Working Memory (SWM) strategy ( $t=-3.07$ ,  $P < 0.01$ ), SWM number of between errors ( $t=-2.99$ ,  $P < 0.01$ ) and Intra-Extra Dimensional (IED) Extra-Dimensional (ED) errors ( $t=-3.11$ ,  $P < 0.01$ ).

No significant differences were observed between smokers and non-smokers in any cognitive test (Table 2). No statistically significant differences were observed with regard to age, gender, years of education, psychotropic medication distribution, age at onset, or severity of OC symptoms (Table 2). Smoking duration was significantly correlated with an increased number of SWM between errors ( $r=0.64$ ,  $P < 0.01$ ). No other significant correlations were found.

## DISCUSSION

In a sample of inpatients with OCD, we compared the performance of smokers and non-smokers across

different executive function subdomains. Our results should be considered preliminary because this is the first study, to the best of our knowledge, to investigate this issue and the sample size was small. In line with previous studies (Abramovitch et al. 2013, Shin et al. 2014, Snyder et al. 2015), our sample showed impaired cognitive performance in the subdomains investigated. No significant differences were observed between the smokers and non-smokers in any of the investigated subdomains, whereas smoking duration was significantly associated with poorer performance in visuo-spatial working memory. The two groups did not differ in demographic or clinical characteristics; thus, it is unlikely that these variables influenced the results. Our results are in contrast with those showing that nicotine improves executive function in other psychiatric populations. In subjects with schizophrenia, smokers performed better in verbal/spatial working memory and response inhibition tasks than non-smokers (Morisano et al. 2013, Sacco et al. 2005, Wing et al. 2011, Zabala et al. 2009). These beneficial effects have been partly explained by the fact that nicotine increases dopamine levels in the prefrontal cortex, which are generally lower in schizophrenia (George et al. 2002). Similarly, preliminary results have shown that smokers with major depressive/bipolar disorder had better verbal working memory performance than non-smokers (Caldirola et al. 2013) and that pathological gamblers who smoked performed better in a response inhibition task than non-smokers (Mooney et al. 2011). In contrast, our findings suggest that cigarette smoking does not enhance the visuo-spatial working memory, planning, or set-shifting abilities in subjects with OCD. This may be explained

by certain specific neurobiological features of these subjects. In OCD, executive function deficits have been associated with abnormalities in several brain areas, including the frontostriatal circuit and parietal cortex (Menziés et al. 2008). Neuroimaging studies have found baseline hyperactivity in these areas (Menziés et al. 2008), possibly related to a central serotonergic-dopaminergic imbalance with dopaminergic hyperactivity (Nikolaus et al. 2010). Nicotine stimulates brain activity by acting directly on cholinergic signaling and promoting the release of several neurotransmitters, such as dopamine, serotonin, norepinephrine, and glutamate (Wallace & Bertrand 2013). Thus, smoking may increase the activity in brain areas, which are already hyperactive in subjects with OCD, resulting in a lack of beneficial effects on the executive function in this population. The lack of nicotine-induced cognitive enhancement may render these subjects less prone to smoking compared with other psychiatric populations. This hypothesis is speculative, and further studies are required for confirmation. The neural mechanisms responsible for the effects of nicotine on the executive function are complex and involve the balanced regulation of multiple neurotransmitters (Nikolaus et al. 2010). We cannot exclude the fact that smoking may have pro-cognitive effects on cognitive domains, which were not investigated in our sample. As OCD is a heterogeneous disorder (Cavedini et al. 2006), smoking may also exert different cognitive effects in OCD subpopulations with specific clinical and neuropsychological profiles. For example, a recent study observed a significantly different distribution of smoking behavior among patients with different OCD symptoms, with a higher prevalence in a symmetry-counting-repeating-ordering group (Tan & Tas 2015).

Our findings do not support the hypothesis that poorer cognitive performance is observed in smokers with OCD compared with non-smokers. However, the small sample size may have masked potential differences between the two groups (type II error), and smoking may exert detrimental effects on cognitive subdomains that were not investigated or in specific OCD subpopulations. All these variables should be investigated in future studies with a larger sample size and a broader number of cognitive tasks.

Our study has additional limitations. First, although previous studies showed the beneficial effects of smoking on executive function in other psychiatric populations, direct comparisons between subjects with OCD and subjects with other psychiatric disorders are required to provide more reliable conclusions. In addition, the blood/saliva levels of nicotine or its metabolites were not measured prior to the cognitive assessment. Thirdly, all the patients were hospitalized to attend a rehabilitation program; thus, our results may not be extended to other patients with OCD in different settings. The present study included only subjects who were either active regular smokers or who had never

smoked; thus, further studies involving subjects with other smoking habits are required. Finally, despite finding no differences in psychotropic medication distribution between the smokers and non-smokers, the potential interaction of medications with nicotine and/or the effects of psychotropic medications on cognitive performance cannot be excluded.

## CONCLUSIONS

Our preliminary results showed that in subjects with OCD, cigarette smoking did not enhance the executive function subdomains assessed. The lack of beneficial cognitive effects of smoking may make these subjects less prone to smoking and contribute towards explaining the lower rate of smokers in the OCD population than in other psychiatric conditions.

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**Conflict of interest:** None to declare.

## References

1. Abramovitch A, Abramowitz JS, Mittelman A: *The neuropsychology of adult obsessive-compulsive disorder: A meta-analysis. Clin Psychol Rev* 2013; 33:1163-71.
2. Abramovitch A, Pizzagalli DA, Geller DA, Reuman L, Wilhelm S: *Cigarette smoking in obsessive-compulsive disorder and unaffected parents of ocd patients. Eur Psychiatry* 2015; 137-44.
3. American Psychiatric Association: *Diagnostic and statistical manual of mental disorders, 4th edition, text revision (DSM-IV-TR)*. Washington, DC, American Psychiatric Publishing, 2000.
4. Bejerot S, Humble M: *Low prevalence of smoking among patients with obsessive-compulsive disorder. Compr Psychiatry* 1999; 40:268-72.
5. Caldirola D, Dacco S, Grassi M, Citterio A, Menotti R, Cavedini P, et al.: *Effects of cigarette smoking on neuropsychological performance in mood disorders: A comparison between smoking and nonsmoking inpatients. J Clin Psychiatry* 2013; 74:e130-6.
6. Cavedini P, Gorini A, Bellodi L: *Understanding obsessive-compulsive disorder: Focus on decision making. Neuropsychol Rev* 2006; 16:3-15.
7. George TP, Vessicchio JC, Termine A, Sahady DM, Head CA, Pepper WT, et al.: *Effects of smoking abstinence on visuospatial working memory function in schizophrenia. Neuropsychopharmacology* 2002; 26:75-85.
8. Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, et al.: *The yale-brown obsessive compulsive scale. Ii. Validity. Arch Gen Psychiatry* 1989; 46:1012-6.
9. Menziés L, Chamberlain SR, Laird AR, Thelen SM, Sahakian BJ, Bullmore ET: *Integrating evidence from neuroimaging and neuropsychological studies of*

- obsessive-compulsive disorder: The orbitofronto-striatal model revisited. *Neurosci Biobehav Rev* 2008; 32:525-49.
10. Millet B, Dondaine T, Reymann JM, Bourguignon A, Naudet F, Jaafari N, et al.: Obsessive compulsive disorder networks: Positron emission tomography and neuropsychology provide new insights. *PLoS One* 2013; 8:e53241.
  11. Mooney ME, Odlaug BL, Kim SW, Grant JE: Cigarette smoking status in pathological gamblers: Association with impulsivity and cognitive flexibility. *Drug Alcohol Depend* 2011; 117:74-7.
  12. Morisano D, Wing VC, Sacco KA, Arenovich T, George TP: Effects of tobacco smoking on neuropsychological function in schizophrenia in comparison to other psychiatric disorders and non-psychiatric controls. *Am J Addict* 2013; 22:46-53.
  13. Nikolaus S, Antke C, Beu M, Muller HW: Cortical gaba, striatal dopamine and midbrain serotonin as the key players in compulsive and anxiety disorders--results from in vivo imaging studies. *Rev Neurosci* 2010; 21:119-39.
  14. Robbins TW, James M, Owen AM, Sahakian BJ, Lawrence AD, McInnes L, et al.: A study of performance on tests from the cantab battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: Implications for theories of executive functioning and cognitive aging. *Cambridge neuropsychological test automated battery. J Int Neuropsychol Soc* 1998; 4:474-90.
  15. Sacco KA, Termine A, Seyal A, Dudas MM, Vessicchio JC, Krishnan-Sarin S, et al.: Effects of cigarette smoking on spatial working memory and attentional deficits in schizophrenia: Involvement of nicotinic receptor mechanisms. *Arch Gen Psychiatry* 2005; 62:649-59.
  16. Shin NY, Lee TY, Kim E, Kwon JS: Cognitive functioning in obsessive-compulsive disorder: A meta-analysis. *Psychol Med* 2014; 44:1121-30.
  17. Snyder HR, Kaiser RH, Warren SL, Heller W: Obsessive-compulsive disorder is associated with broad impairments in executive function: A meta-analysis. *Clin Psychol Sci* 2015; 3:301-30.
  18. Tan O, Tas C: Symptom dimensions, smoking and impulsiveness in obsessive-compulsive disorder. *Psychiatr Danub* 2015; 27:397-405.
  19. Wallace TL, Bertrand D: Importance of the nicotinic acetylcholine receptor system in the prefrontal cortex. *Biochem Pharmacol* 2013; 85:1713-20.
  20. Wing VC, Bacher I, Sacco KA, George TP: Neuropsychological performance in patients with schizophrenia and controls as a function of cigarette smoking status. *Psychiatry Res* 2011; 188:320-6.
  21. Zabala A, Eguiluz JI, Segarra R, Enjuto S, Ezcurra J, Gonzalez Pinto A, et al.: Cognitive performance and cigarette smoking in first-episode psychosis. *Eur Arch Psychiatry Clin Neurosci* 2009; 259:65-71.

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