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#### ERS Symposia

#### **Emerging challenges in tobacco control – Heated tobacco products, Harm reduction and the Foundation for a Smoke-Free world** Sofia Ravara<sup>1,2</sup>

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In order to warrant tobacco industry's profits and overcome a declining cigarette market, tobacco companies have recently launched the novel heated tobacco products (HTPs), claiming a 90-95% reduction in harmfulness. While there is robust evidence that studies either performed or funded by the tobacco industry cannot be trusted, public health advocates have stressed that the short and long-term health effects resulting from continued consumption of these addictive products remain unclear. These new products mislead consumers about their safe use, and may potentially attract more users, recruit non-smokers and youths, and postpone quitting in regular smokers while promoting the social acceptability of tobacco use. However, while these products remain largely unregulated, the tobacco industry has been aggressively marketing them as safe products, and cessation and harm reduction tools.

This presentation will present the findings from independent research focusing on the potential of HTB to harm human health, while will discuss the need for strict regulation. Finally, it will highlight ERS leadership and engagement in tobacco control and present the ERS statement on the "Foundation for a Smoke-free world" and tobacco emergent products.

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#### H2020 SMOKEFREE BRAIN SYMPOSIA

## Running away from addiction: Exercise, smoking cessation and neuroscience

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#### **Background and purpose**

There is substantial evidence to suggest that exercise decreases nicotine withdrawal symptoms in humans; however, the mechanism mediating this effect is unclear. Here we investigate in a mouse model the effect of exercise intensity on nicotine withdrawal symptom severity and the binding of  $\alpha 4\beta 2^*$ ,  $\alpha 7$  nicotinic acetylcholine (nAChR),  $\mu$ -opioid (MOPr) and D2 dopamine receptors, and on brain-derived neurotrophic factor (BDNF) and plasma corticosterone levels.

#### **Experimental approach**

Male C57Bl/6J mice treated with nicotine (minipump, 24 mg/ kg/day) or saline for 14 days underwent one of three concurrent exercise regimes: 24, 2 or 0 hrs/day-1 voluntary wheel running. Mecamylamine-precipitated withdrawal symptoms were assessed on day 14. Quantitative autoradiography of  $\alpha 4\beta 2^*$ ,  $\alpha 7$  nAChRs, MOPr and D2 receptor binding was performed in brain sections of these mice. Corticosterone and BDNF levels were measured in plasma and brain regions, respectively.

#### **Key results**

Male C57Bl/6J mice treated with nicotine (minipump, 24 mg/kg/day) or saline for 14 days underwent one of three concurrent exercise regimes: 24, 2 or 0 hrs/day-1 voluntary wheel running. Mecamylamine-precipitated withdrawal symptoms were assessed on day 14. Quantitative autoradiography of  $\alpha 4\beta 2^*$ ,  $\alpha 7$  nAChRs, MOPr and D2 receptor binding was performed in brain sections of these mice. Corticosterone and BDNF levels were measured in plasma and brain regions, respectively.

#### **Conclusions and implications**

Exercise reduces nicotine withdrawal symptoms irrespective of intensity. This is concomitant with an upregulation of a7 nAChRs in the hippocampus. This novel mechanism may underline the beneficial effect of exercise on nicotine withdrawal.

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#### Smoking cessation, neurofeedback and sleep Andreas loannides<sup>1</sup>

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The concept of self has evolved over time to become one of the central pillars of the human mind. Work over the last two decades have began to relate the concept of self to large scale networks of the brain<sup>1</sup> and especially with the default mode network (DMN)<sup>2</sup>. Recent work from our team<sup>3</sup> has further suggested that the neural representation of self (NRS) is confined to two nodes at the very centre of the DMN. A node in the dorsal midline frontal cortex is likely the executive part of the NRS while a node on the mid-parietal cortex is likely the depository of the memory store of the NRS. The NRS may well be the pinacle of evolution in humans, but it also creates a conflict. For a number of fundamental evolutionary reasons<sup>3,4</sup> the NRS must retain its individuality intact while the world outside changes, often in dangerous ways, demanding that these changes are also reflected in the internal representation of the world. In this context safe learning emerged as a way of achieving experience-guided change of the internal representation of the world that makes only the minimal necessary changes to the NRS. It seems that evolution has resolved the conflict through seggregation of learning in time. Learning when practically no change in the NRS is incolved is allowed in real time, while learning that also demands changes of the NRS, is allowed in the form of safe learning only during special times, mainly during sleep. Detailed studies of the changes during light sleep have revealed how this safe learning (memory

consolidation) is prepared during spindles<sup>5</sup>: first the environment is checked and if judged as safe then the alerting system is actively inhibited so that influences from the environment are blocked; then and only then, memories that are temporarily stored in midtemporal brain areas are highlighted for spindle-mediated transfer to widespread brain areas. The changes of the NRS seem to be controlled by the rostral, executive, part of the NRS as the actual NRS-related memories are transferred to its caudal part 3. In the framework described above neurofeedback is seen as a safe yet incomplete process to reverse aberrant behaviour to physiological norms. The process is safe because it relies and exploits the natural ways of safe learning described above and for this reason it is incomplete: whatever is achieved during neurofeedback corresponds to directed experience related to the NRS that will be developed further during the day, but only consolidated during sleep, because only then the NRS is open for change. In the context of helping people stop smoking in the SmokeFreeBrain project, the influence of the object of addiction that overrides the normal controlling influence by the NRS is confronted by neurofeedback in two stages; in the first stage a small number of sessions are used to bring the NSR closer to normal physiological patterns. In the second stage the well-established alpha-theta protocol is used to address the addiction directly. Early results from the cases already completed show that both neurofeedback stages have a positive influence, with progress in the first stage beeing a prerequisit for successful outcome of the combined sessions.

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# How varenicline affects sleep quality and functional connectivity? A polysomnographic evaluation

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The SmokeFreeBrain (SFB), which is an EU, H2020-funded project aims to compare several antismoking approaches. Among them, the varenicline intervention seems to be extremely robust in terms of nicotine abstinence rate. However, there are some reports of side effects during sleep associated with insomnia and negatively aroused dreaming. However, these symptoms have never been objectively quantified. This study presents preliminary results from 17 participants who underwent entire polysomnographic (PSG) recordings before and 21 days after the intervention initiation. Our aim was to investigate how both smoking abstinence and varenicline treatment affect sleep quality. We employed both visual sleep scoring and functional connectivity analysis. The purpose of visual sleep scoring analysis, performed according to the guidelines of the American Association of Sleep Medicine (AASM) was to investigate sleep macro-architecture, defined as the sleep cycles during night. We calculated various sleep parameters like efficiency, onset, stage and latency duration, sleep fragmentation and the number of arousals during sleep. Additionally, we also estimated the co-operative degree among electroencephalographic time series as well as the interactions among brain and heart. The latter analysis aimed to quantify neuroplasticity changes associated both with smoking cessation and varenicline treatment. Early results demonstrated beneficial effects from nicotine abstinence (increased oxygen saturation level, facilitated sleep onset). However, there were neurophysiological patterns of increased arousal both on autonomic (heart rate variability features) and on cortical level (increased connectivity within beta band). These patterns observed even during deep sleep stages indicating poor sleep quality.

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# Information Wars: The era of massive digital misinformation. The footprint of tobacco industry in social media and mobile health Luis Fernandez Lugue<sup>1,2</sup>

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Internet and mobile technologies are nowadays used by most of the world population. These technologies are not just available for highly engaging and for many people an essential tool in their daily life. Not surprisingly, the use of mobile health and online health for smoking cessation is quite well studied and evidence shows they can be cost-effective. However, the tobacco industry is also leveraging the power of those channels for mass communication. Furthermore, we will explore how bogus smoking cessation "treatments", such as auto-hypnosis, are being promoted in apps stores or social media. Overall, we will study user cases on how social media and mobile technology has been used to promote harmful public health messages.

These case studies will be used to provide some guidelines on how to create strategies to use social technologies such as mobile apps and social networks to promote smoking cessation and increase awareness about tobacco risks. This presentation will also be based on our experience from the project SmokeFreeBrain where we combined online and mobile technologies for smoking cessation.

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