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EDITORIAL

Impact of *FAAH* gene, hyperactivation in emotion processing brain regions and *Lavender* oil preparation Silexan in anxiety

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Growing evidence suggests that the endogenous cannabinoid system plays a role in normal emotional processing, specifically in the anxiety and stress response, and in affective disorders such as anxiety disorder and depression [1]. There are several lines of evidence suggesting either therapeutic potential or harmful effects associated with cannabis use in psychiatric disorders [2]. The integral enzyme fatty acid amide hydrolase (FAAH) is a catabolic enzyme and primary regulator anandamide signaling in the brain. The single nucleotide polymorphism in the human *FAAH* gene results in a missense mutation (385C to A) that converts a conserved proline residue to threonine (Pro129 to Thr), producing a FAAH variant that displays normal catalytic properties but an enhanced sensitivity to proteolytic degradation [3], resulting in the decreased expression of FAAH protein and enzymatic activity as well as increased anandamide levels in the brain. Thus, it is likely that genetic mutations in *FAAH* gene may support a potential link between functional abnormalities in the endogenous cannabinoid system and cannabis abuse. In this issue, the A-allele carriers in the *FAAH* gene in healthy young adults ($n=48$) show stronger fronto-amygdala connectivity during rest [4]. In addition, exploratory whole-brain analyses show differential functional activity of A- allele carriers during emotion reactivity and emotion regulation. This preliminary study suggests a link between *FAAH* C385A and fronto-amygdala connectivity during rest, and provides a finding for differential functional activity during emotion reactivity and emotion regulation depending on FAAH genotypes. Further study using a large sample size of patients with anxiety disorder is needed to confirm the role of *FAAH* C385A gene in emotion processing or anxiety disorders.

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Pathological health anxiety (PHA), formally termed hypochondriasis, is characterized by the conviction of suffering from a severe illness. PHA patients tend to automatically interpret bodily sensations as sign of a severe illness. It is hypothesized that differences in cognitive processes related to attention, memory, and evaluation of health threat may play a role in the pathogenesis of PHA [5]. Subjects with PHA showed a stronger attentional bias to health-threat-related information, more negative explicit (but not implicit) evaluations of health threat, and biased response behavior in light of health threat [5]. In this issue, Yan et al. [6] applied a functional magnetic resonance imaging adaption of a body-symptom implicit association test with symptom words in PHA patients in comparison with healthy subjects. On the behavioral level, PHA patients did not significantly differ from the control group. However, PHA patients showed hyperactivation independent of condition in bilateral amygdala, right parietal lobe, and left nucleus accumbens. Moreover, PHA patients showed hyperactivation in bilateral posterior parietal cortex and left dorsolateral prefrontal cortex during incongruent (i.e., harmless) versus congruent (i.e., dangerous) categorizations of body symptoms. These results suggest increased neural responding in key structures for the processing of both emotional and cognitive aspects of body-symptom information in PHA.

Subthreshold anxiety disorder (SSAD) is a common, recurrent mental health disorder that causes distress and impairs psychosocial and work functioning as often as several chronic somatic diseases [7]. Epidemiological data suggest that the prevalence of SSAD may exceed that of generalized anxiety disorder (GAD) in Europe and North America [7]. In contrast to GAD, SSAD is associated with a significant decrease in perceived social support, indicating the need for adequate treatment of SSAD.

Silexan is a special active substance with an essential oil produced from *Lavandula angustifolia* flowers by steam distillation. In Germany, the drug is registered as a medicinal product for the treatment of restlessness accompanying

anxious mood [8]. Kasper et al. [9] investigated the efficacy of Silexan in patients with SSAD in comparison with placebo. Patients treated with Silexan showed a Hamilton Anxiety Rating Scale (HAM-A) total score decrease of 16.0 points compared with 9.5 points in the placebo group after 10 weeks treatment [9]. In patients with SSAD or GAD, an anxiolytic effect of Silexan was evident after 2 weeks. HAM-A total score reductions between baseline and end of treatment were significantly superior to placebo in patients with SSAD and comparable with those achieved under lorazepam or paroxetine in patients with GAD. In addition, Silexan had beneficial effects on typical concomitant symptoms of anxiety disorders, such as impaired sleep, somatic complaints, co-morbid depression or decreased quality of life. Except for mild gastrointestinal symptoms, Silexan did not induce any adverse effects and did not cause drug interactions, sedation or withdrawal symptoms [8].

In this issue, Möller et al. [10] reported meta-analysis of Silexan in patients with SSAD. Three randomized, placebo-controlled trials in SSAD were analyzed. Silexan was superior to placebo in reducing the HAM-A total score during 10 weeks treatment. Silexan was well tolerated, with adverse event rates similar to those observed for placebo. Silexan had a beneficial effect on disturbed sleep secondary to anxiety and was associated with improvements in health-related quality of life. Importantly, the results could not be generalized to other lavender oil products [10]. Collectively, Silexan would be a useful compound to reduce the anxiety-associated symptoms in patients suffering SSAD, although further study using a larger sample size is needed.

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Compliance with ethical standards

Conflict of interest The author declares that there is no competing interest.

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