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Short Communication

Can near Infrared Spectroscopy Links Pharmacological Effects And their Reversal upon Haemoglobin to Cerebral Metabolism? A Research Proposal

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Near infrared spectroscopy (NIRS) is a non invasive methodology [1,2], that has been shown able to to overcome the major limitation of invasive in vivo techniques to study brain activities in rodents as well as in man [3-5].

NIRS is indeed a non-ionizing technique that can be used to monitor oxygen saturation in the living tissue as well as changes in oxygenation of haemoglobin [1,6,7].

In particular, the absorption spectra of near-infrared light differ for the oxygenation–deoxygenation states of haemoglobin (oxygenated form HbO2 vs. deoxygenated form Hb, respectively) so that the two compounds can be directly monitored. Accordingly, the total haemoglobin concentration (HbO2 + Hb) can be considered as total blood volume (THC) [8].

All together, these measurements are indicative of the state of vascular activity and the state of the metabolism in the tissue analyzed. NIRS has been also recently indicated as valuable tool to monitor influence(s) of acute drug treatment(s) on metabolic activity of the brain [9].

In particular, the "pharmacological NIRS" (ph-NIRS) concept has been initially proposed as result of experiments where rodents were treated with drugs of abuse [6]. Then the phNIRS concept was sustained within specific treatments with cocaine when parallel NIRS and magnetic resonance imaging (MRI) experiments were performed [9]. The "ph-NIRS" concept has been successively supported in translational studies when this methodology was applied to compare the effect of alcohol as well as nicotine smoke upon brain metabolism in rodents versus man [3,5].

In order to further validate the "pharmacological NIRS" concept experiments could be performed to analyse the effect of various treatments involving different specific influences upon brain activities.

In particular, the specific analysis of pharmacological effect(s) upon NIRS parameters of selective neurotrasmitter receptor agonist(s) as well as the selective receptor antagonist(s), respectively can be proposed.

For istance, neurotrasmitter systems such as dopamine and serotonin systems would be tackled with receptor agonist and – or receptor antagonist., i.e.

a) Concerning the dopamine (DA) system: cocaine as DA receptor agonist and the selected D3 dopamine receptor antagonist SB-277011-A can be selected, while

b) Concerning the serotonin (5-HT) system: 8-OH-DPAT a 5-HT receptor agonist and 5-HT receptor antagonists (I.e. the 5-HT1A antagonist Way 100635) can be used. Specifically, these two neurotransmitter systems and therefore the chemicals proposed for the proposed study are selected based upon their well-known influence – effect upon the vascular system [10-13].

Briefly:

a) Concerning the dopamine (DA) system:

Experiments will be performed in anaesthetized rats treated i.e. with cocaine alone or preceded by treatment with the selective D3 receptor antagonist SB-277011-A as described earlier [14].

These experiments will be useful to reveal the possibility of using NIRS to detect i.e. the putative efficacy of the D3 receptor antagonist on modifying the effect of cocaine upon brain metabolism.

In addition, confirmation of specificity of NIRS evaluations could be performed comparing the efficacy of a selective versus non selective D3 receptor antagonists [15], on the effect of cocaine upon brain metabolism.

b) Concerning the 5-HT system:

The vasoconstriction effect of 5-HT receptor agonists such as 8-OH-DPAT [16,17], could be monitored using NIRS as above. In particular, the treatment with this 5-HT 1A agonist should result in a significant decrease of total volume (HbT) monitored in the brain of anaesthetized rats. Then, the complete or partial blockade of such effect(s) with selective antagonist [18], could be supportive of the phNIRS concept.

c) A further kind of experiment will be analysing the influence of inflammatory process upon NIRS parameters i.e. via experiments studying the effect(s) of interleukin-1 and the respective antagonist (IL-Ira):

Experimental evidence indicates that interleukin-1 (cytokine IL-1) is a pivotal mediator of inflammation playing a major role in neuroinflammation [19], and in neurodegeneration [20]. Furthermore, a major role of cytokines in the mechanism of action of HbO2 is proposed [21,22].

The respective endogenous specific receptor antagonist (IL-Ira) [23], is produced in numerous experimental animal models of disease as well as in human autoimmune and chronic inflammatory diseases [24], in which it has been shown to selectively inhibits the effects of IL1 [25], with possibly beneficial effect(s) upon human diseases [26].

The NIRS analysis of the effect(s) of interleukin-1 as well as of IL-Ira or that a further compound such as anakinra, a recombinant human IL1 receptor antagonist [26], will add knowledge on their putative influence upon brain HbO2.

Altogether these experiments will be of help on confirming the "pharmacological NIRS" concept as proposed in previous work. Therefore this will improve the quality of NIRS analysis as qualitative and possibly also quantitative in vivo non-invasive tool for studying brain metabolism in preclinical and possibly parallel translational clinical work.

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