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Detecting highly stabilized cumulative ~35-37kD isoforms of ⊗FosB in postmortem human brain tissue samples of the nucleus accumbens (NAc) of chronic opioid abusers

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The incitation of the ~33kD Mr (molecular mass) transcription factor ΔFosB, a member of the Fos family proteins, in the acute phase and then its displacement to ~35-37kD Mr isoforms due to chronic exposure to different inducements including stress, drugs of abuse and other psychoactive substances, but also psychotherapeutic agents leads to a consistent accumulation of highly stable ΔFosB isoforms in the nucleus accumbens (NAc), the reward center of the brain. These extraordinary stable ~35-37kD ΔFosB M_r derivatives insistently persist in this brain region for several weeks or even longer following cessation of the chronic stimulus - a major fact that seems to be responsible for the development of sustained neuronal plasticity. In case of long-term drug abuse, it ultimately leads to addictive behavior by representing a source of high relapse rates at the same time. With this in mind, we demonstrate for the first time the presence of accumulated ~35-37kD M_r ΔFosB isoforms in the NAc of chronic drug-sick deceased people with pronounced long-term opioid abuse anamnesis. The detection was possible even after a postmortem interval (PMI) of 8.47± 2.61 days, enabled by a distinct modification of protein purification methods. As expected, not any ~33kD M_r ΔFosB molecule, the rather unstable Fos family member, could be detected via immunoblotting. Our current results emphasize the remarkable high resistance of this phosphorylated transcription factor. The data confirm once more the strong impact of ΔFosB and its downstream transcriptional targets with regard to long-term biological consequences for and potentially fatal adaptations of the brain leading to addictive behavior and high relapse rates in response to chronic opioid abuse. Nevertheless, our exciting results regarding the detection of these highly stable 35-37kD M_r ΔFosB isoforms under such conditions (prolonged PMIs) provide a blessing and a curse in equal measure as the impact of this phosphorylated transcription factor achieves a much higher dimension. This in turn should be taken into consideration when thinking about establishment and interpretation of sensitive biomarkers on the one hand, and development of novel therapeutic strategies in terms of psychological disorders in general and especially in (drug) addiction on the other hand.

Biography

Monika Heidemarie Seltenhammer completed her VMD and PhD from VMU in Austria and Postdoctoral studies from Veterinary University of Vienna, Max Perutz Laboratories and Medical University of Vienna in Austria, where her core area of scientific work mainly consisted in cancer research (melanoma) and pathology, but also immunology, neurology and virology. She has received several honor and awards. She is a leading member of the scientific staff of Dr. Daniele Ugo Risser at the Department of Forensic Medicine of the Medical University Vienna, where she specializes in neurobiology and addiction behavior in close co-operation with Dr. Tibor Harkany, professor at the Department of Molecular Neurosciences of the Medical University of Vienna.

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