S15.05
VIRTUAL REALITY BASED ASSESSMENT AND THERAPY FOR NEUROPSYCHOLOGICAL DEFICITS

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Information Technologies (IT) have a still growing and highly significant impact on society, human behavior and self representation concepts. Within the IT field, especially immersive projection technologies (IPT) as a special form of Virtual Reality techniques (VR) is expected to accelerate, leading to new possibilities for human experience, interaction and communication, not limited by physical reality. The integration of IPT with standard mental health methodologies will allow for the development of new assessment and treatment applications. Especially the potential of studying human neuropsychological processes with degrees of reliability and validity never seen before is one of the major advantages of these technologies, hopefully leading to a much better understanding of neuropsychological impairments as well as to new and promising training and treatment approaches.

S16. Is drug craving a still valid and evidence-based clinical construct in addiction?

Chairs: J. Ades (F), S. De Risio (I)

S16.01
NEUROBIOLOGICAL BASIS OF CRAVING AND PLEASURE EXPERIENCE: ONE OR MORE REWARD SYSTEMS?

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Craving is the uncontrollable desire for alcohol or any other drug of abuse. This multi-dimensional phenomenon is most readily measured via language-based descriptions following e.g., the presentation of cognitive stimuli, or by inducing certain mood states. It is difficult to measure craving in laboratory animals, and in each model only aspects of craving might be described. Most animal models measure the behavioural responses rather than internal states and are, therefore, better models for relapse rather than craving *per se*. However, some of the available animal models can serve as powerful tools for designing human craving studies.

In our model described in this presentation several months of alcohol availability are followed by a period of alcohol deprivation (i.e., a withdrawal phase). When alcohol is subsequently made available the animals increase their alcohol consumption and preference for alcohol. These animals clearly demonstrate a preference for alcohol over water and exhibit changes in their alcohol intake pattern. This alcohol deprivation effect leads to alcohol consumption of highly concentrated alcohol solutions, even at inappropriate times during the inactive light phase when drinking activity is usually low. These data show that there is a high motivation to drink alcohol following a period of deprivation. Animals will continue to work for alcohol significantly longer than they would before the alcohol deprivation.

Anti-craving substances have been registered for relapse prophylaxis in weaned alcoholics in various European countries (acamprosate) and the United States (naltrexone). Acamprosate and naltrexone most likely reduce ethanol abuse through different neuronal mechanisms. Acamprosate, the Ca-salt of N-acetyl-homotaurinate interacts with NMDA-receptor-mediated glutamatergic transmission in various brain regions. The opiate antagonist naltrexone most likely interfers primarily with the mesolimbic/mesotelencephalic dopaminergic brain-reinforcement systems. This structure *(extended amygdala)* involves the shell of the nucleus accumbens, the bed nucleus of the stria terminalis and the central nucleus of the amygdala.

All addictive drugs share the fact that they can act as a discriminative stimulus and induce positive reinforcement. The self-administration of drugs is prompted primarily by an increase in extracellular dopamine in the nucleus accumbens, a mechanism important for the initiation and the maintenance of drug-seeking. However, there is no doubt that more than a single receptor system is involved in these processes. Repeated and prolonged application of drugs of abuse changes the molecular mechanisms involved in signal transduction. Most principal components of the brain reward system receive glutamatergic input from heterogeneous structures, such as the medial prefrontal cortex, and are influenced by local GABAergic interneuronal activity. Functional imaging techniques in humans demonstrate that craving for alcohol, as well as other drugs of abuse, involves areas predicted from animal experiments. The various molecular targets responsible for the habit-forming action of drugs of abuse in humans and in experimental animals are presently detailed.

S16.02
CRAVING FOR OPIATES

M. Gossop

No abstract was available at the time of printing.

S16.03
CRAVING FOR ALCOHOL

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In the long-term process of alcohol dependence intoxication and withdrawal states are common events. Different vulnerability factors of alcohol dependent patients (biological as well as psychological ones) influence significantly the clinical picture. The time of intervention (early versus late) influences the symptoms to be diagnosed as well as the therapeutic strategy. In early stages socio-psychological factors and different basic disturbances influence drinking behaviour and craving. In late stages alcohol related disabilities and withdrawal states influence different mechanism of craving.

The classification of alcohol dependence according to ICD-10 and DSM-IV is not useful to develop different relapse prevention strategies. Different mechanism are leading to different types of craving. Emotional states and key-conditions are of increasing interest.

In an 18 year prospective follow up study we could show that only 9% of alcohol dependent patients are truly sober. One of the main causes of relapse has been alcohol seeking behaviour (craving). This therapeutic outcome shows clearly that we have to improve our therapeutic strategies. During recent years different pharmaceutical agents have been investigated, and some of these improved the therapeutic outcome. In the light of our results, we propose to distinguish between 5 different forms of craving leading to relapse. This drug seeking behaviour reflects mainly 4 different transmitter systems (dopamine, serotonine, endorphine

https://doi.org/10.1016/S0924-9338(00)94032-X Published online by Cambridge University Press

and GABA). Possible connections between craving types and transmitter systems will be discussed, stressing that different compounds should be used according to the different biological causes of craving and relapse.

Following these subgroups of alcohol dependent patients (Lesch typology) we could show that different pharmaceutical compounds influence craving and relapse rates. To assess craving the craving risk relapse questionnaire (Veltrup 1994) is recommended. Neurophysiological assessment could be done by the dynamic pupillometry.

The difference in typology rates between women and men explains different craving mechanism in male and female alcohol dependent patients.

S16.04
CRAVING FOR STIMULANTS

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The phenomenology of craving in stimulant abuse appears to be quite different from that of other addiction-producing drugs. For instance the relationship between craving and physical withdrawal is lacking in stimulant abusers, in spite of the high intensity and frequency of the wish, which may occur even after months following the last dose of cocaine or amphetamine, in the so-called "extinction" phase. Also the analysis of the temporal patterns of use accounts for a direct correlation between craving and loss of control in the stimulant bingeing, as well as sensitization to rewarding effects of stimulants has been observed and described in preclinical studies. Similarly, Halikas and Kuhn (1990) suggested that cocaine craving in humans was a behavioral manifestation of "kindling", the neuronal supersensitivity induced by the drug in animal studies, and that also other symptoms seen in chronic cocaine users could be the result of the same phenomenon.

Measurement of stimulant craving imply the assessment of intensity, frequency and duration as separate characteristics.

Our clinical evidence on cocaine craving in both withdrawal and post-withdrawal (by conditioned cues) phases points towards a relative independence of craving and withdrawal, as the former seems to be more related to the individual abuse history than to the actual and current substance use.

A variety of medications has been tried in order to reduce cocaine craving and cocaine relapse. Most recent trials include new anticonvulsants as mood stabilizers and atypical neuroleptics. Patterns of dependence, periods of administration and comorbid psychopathology appear to be first-rank variables able to influence the study outcome.

The most promising psychotherapeutical approach to treatment of stimulant abuse is one that recognizes the high risk of relapse and applies a range of cognitive and behavioral strategies.

S16.05
METHODOLOGICAL AND CLINICAL ISSUES IN CRAVING MEASUREMENT

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In ICD-10 the term craving is entirely subjective: 'a strong desire or sense of compulsion to take the substance'. Some authors include the experience 'recurrent and persistent thinking about the substance', akin to obsessional thinking. Others restrict the term to its use in ordinary language: a strong desire or urge. This excludes compulsive and obsessional experience, which have to do with *resisting the urge* – if the user perceives no disadvantage to using, he does not try to resist and thus experiences no conflict. Restricting the concept to subjective experience excludes behaviors (i.e. using the substance, or losing control over use), and physiological correlates of subjective experience. There are other mental processes, separate from craving: Intention (formulating a plan) and Motivation (the balance of pay-offs in the user's mind, at a given point in time, of abstaining or using).

Measurement: (1) Questionnaires sometimes mix items from conceptually separate domains and summary scores are hard to interpret. 2-dimensional analogue scales (e.g. 'Rate on a scale of zero to 10 how strongly you desire an alcoholic drink') by definition measure a single domain. (2) A fruitful distinction is between reward-craving (desire to use for elation, energy etc) and relief-craving (desire to use to relieve anxiety/physical discomfort): algorithms can be constructed for allocation to specific treatments. E.g. treatments which reduce the positive effects of use might lead to extinction of reward-craving in patients with high 'anticipation of positive outcome of use' as might treatments which offer other sources of reward. (3) It is tautological to measure *Use* to test the validity of a craving measure which itself measures use.

SES04. AEP Section "Psychopathology": Hallucinatory states: origin, conceptualisation, localisation and outcome

Chairs: S. Opjordsmoen (N), G. Stanghellini (I)

SES04.01
THE CONCEPT OF HALLUCINATIONS

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The conceptualization of hallucinations was initiated by Esquirol. He defined hallucinations as perceptions without an external object and conceived them as cerebral or psychological phenomena occuring independently from the senses. In this perspective he separated hallucinations from illusions and attributed the former to a complex central process involving memory, imagination and personal habits. Subsequently many modifications of Esquirol's concept have been suggested: several autors tried to improve the definition of hallucinations and he distinguish them not only from illusions but also from other closely related phenomena such as "eidetic images", "pareidolia" and "pseudohallucinations". The fact that the manifestation of hallucinations is not obligatorily restricted to morbid conditions led to the distinction between pathological and normal hallucinations; In contradiction to Esquirol assumption it has been proved that organic hallucinations are not limited to brain dysfunctions but may also occur in disorders of peripheral sense organs. This observation has, however not devaluated the hypothesis that imagination, rememberences and habits are an integral part of the emergeance of hallucinations. From this angle hallucinations are supposed to occur when emotionally invested mental representations are set in action and cannot be desactivated.

SES04.02
HALLUCINATIONS AS DISORDERS OF INTERSUBJECTIVITY

G. Stanghellini

No abstract was available at the time of printing.

https://doi.org/10.1016/S0924-9338(00)94032-X Published online by Cambridge University Press