Trial Description

Title

Cross-modal validation of picture stimuli in addictive disorders and healthy individuals using eye-tracking.

Trial Acronym

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URL of the trial

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Brief Summary in Lay Language

The study will examine healthy volunteers, patients with BMI over 30, and patients with nicotine dependence. In this case, the examination is carried out on an outpatient basis. In addition, patients with alcohol dependence after detoxification are examined at our addiction center as well as in our addiction day clinic. The examination then takes place during the inpatient stay. The examination duration is about 2.5 hours for all participants. A measurement of the eye movement is carried out with the aid of a camera system (so-called eye tracking system) during the processing of two tasks during which images are viewed and, in some cases, also reaction time tasks are performed. There is a break between the two tasks.
All study participants will first be asked to answer different questionnaires. After filling in the questionnaire, we will take blood to determine blood levels (for example, stress hormones, appetite-regulating hormones, blood sugar) that may influence the perception of the image. This is followed by a 10-minute measurement of eye movement and the subjective assessment of different visual stimuli. This is followed by a second 10-minute measurement after a short break, during which the reaction time and the eye movements of all participants are examined for different image stimuli.
Since certain drugs (such as marijuana) may affect alcohol cravings and hormone levels, we also want to run a urine test on these substances.

Brief Summary in Scientific Language

Objective:

The study aims to validate visual material developed for use with eye-tracking in two experimental paradigms for the study of "cue-reactivity" and "attentional bias" using eye tracking in patient populations and a sample of healthy reference subjects.

Background:

Numerous findings indicate that learning mechanisms play a central role in the development and the course of addiction as well as disturbed eating habits. Of particular importance in this context are associative learning processes in which previously neutral stimuli and environmental context variables are linked to the

rewarding effects of substance use or eating behavior. According to the established "incentive-sensitization" theory by Robinson and Berridge (1993) [1], the repeated intake of dependency-producing substances via sensitization of the striatal dopaminergic activity leads to an association of dependency-related and previously neutral stimuli with the rewarding effects The consequence of this is that dependency-associated stimuli appear attractive and can strongly attract the attention of the individual ("attentional bias"). Studies have confirmed this theoretical assumption. Thus, it could be shown that the presentation of dependency-associated stimuli leads to shorter response times to a subsequent target stimulus than the presentation of neutral stimuli, which can be interpreted as an indication of a stronger attention steering on the dependency-associated stimuli. This finding has been demonstrated in smokers, alcoholic patients, and obese individuals [2-5] studies that used other measures to guide attention towards dependency-associated stimuli, e. Stroop paradigm, or directly examined the subjects' eye movements, could confirm the results [3, 6, 7]. Thus, a correlation could be established between the eye movements measured by eye tracking and the duration of fixation during a dot-probe paradigm with alcohol-associated stimuli and the craving for alcohol [8, 9]. In addition, similar findings were found in smokers with tobacco-associated stimuli [10, 11]. In the course of a disease of dependence, the responses to these stimuli, which can be detected on a subjective (eg, desire) and physiological level (eg, skin conductance, affect-modulated startle reflex, brain activity, eye movements) play an important role in maintaining dependence , For example, an association between the presentation of dependency-associated stimuli and craving for the respective substance could be demonstrated, which was also associated with an increased risk of relapse in some studies [12].Furthermore, a connection between the attention steering on dependence-associated stimuli and the risk of relapse could be demonstrated [13]. It was conspicuous that not every stimulus was equally suitable for provoking a subjective or objective reaction and that contextual factors of the stimuli (for example, the presentation of a drink in isolation or in the context of a bar) play an important role [14]. In addition, there were divergences in the objective and subjective responses to dependency-associated stimuli. Currently, there is little evidence of which stimulus properties are concretely responsible, that individuals experience a subjective change (e.g., increased desire), or a physiological response (e.g., pupillary response as a measure of noradrenergic activity in the locus coeruleus) and how both measures are temporally associated.
Eye-tracking offers a high-temporal resolution capability for investigating arbitrary and involuntary responses to the presentation of stimuli and associating the fixation of certain stimulus properties with a change in subjective and objective measures [15]. The non-invasive measurement of eye movements (fixations, saccades, pupil diameter and other parameters) is done by recording the corneal reflexes and the cornea size with the help of a special camera with high temporal resolution (1000 Hz) via a semi-transparent Mirror and with the help of an infrared light source detects the eye movements, while the subjects look at a screen. The test person sits at a defined distance in front of an LCD screen on which image stimuli are presented to him. The head lies on a chin rest to minimize head movements. However, there are high demands on the stimulus material with regard to the complexity, brightness and image contrast for the adequate detection of the eye movement and pupil reaction as well as the agreement on subjective perceptual dimensions [15, 16]. In the past, efforts have been made to create standardized image sets with dependency-associated stimuli [16-18]. However, none of the previously available image sets has been optimized for use with eye tracking. This is relevant since the detection of certain parameters critically depends on certain objective image properties (e.g., brightness - pupil response) [15]. In addition, some parameters recorded by eye-tracking show a latency dependent on the stimulus material (eg velocity of the

pupil reaction) and there are no validated paradigms for detecting this physiological response. Due to the aforementioned advantages of this methodology, its non-invasive character and its wide range of applications, the methodology seems to be suitable for investigating pathophysiological processes of dependency diseases with high temporal resolution. In various studies, a dependence of the response on addiction-related stimuli was demonstrated by humoral parameters. Thus, an association between ghrelin and leptin and the extent of alcohol-stimulus-induced craving could be demonstrated [19, 20]. Similar findings were also shown for the response to food stimuli [21, 22] and tobacco stimuli [23]. Further studies suggested the role of the hypothalamic-pituitary-adrenocortical axis (HPA axis) and its peptides cortisol and ACTH in the modulation of stimulus-induced responses and addictive desire [24, 25]. This is relevant to the current planned study because multiple studies indicated a change in brain activation dependent on the plasma levels of leptin, ghrelin (total, acetylated), ACTH and cortisol, among others. in areas that control eye movement [22, 25]. A dependence of the ocular responsiveness of these peptides seems to be plausible and should be taken into account in a validation work.

The planned investigations are intended to validate imagery optimized for eye-tracking examinations as well as for the detection of physiological ocular response of designed paradigms. Since previous studies pointed to a possible generalization of the stimulus response and the attendant bias [26], the validation studies should include image stimuli from different categories with the aim of achieving the highest possible validity while at the same time optimizing specificity and reliability for the respective stimuli to reach.

Amendement:
The amendment aims to validate visual material developed for use with eye-tracking in two experimental paradigms for the study of "cue-reactivity" and "attentional bias" using eye tracking in patient populations (amendment: in addition to the initial study design (2018-541N-MA (Dr. med. B.Sc. Patrick Bach)), we plan to investigate also obese patients before and after bariatric surgery) and a sample of healthy reference subjects.
Obese patients that already decided to receive bariatric surgery will be recruited for this study. Sociodemographic data, information on internal and neurological disorders, as well as information on eating habits was collected. In addition, participants were screened for any psychiatric comorbidities using the Structured Clinical Interviews for DSM-IV, SKID-I, (Wittchen et al., 1997). Additionally, a urine drug screening, and in females a pregnancy test will be conducted. These procedures replicate those of an already finished and publicated study (2011-268N-MA).
We hope that our research may contribute substantially to the understanding of how bariatric surgery works and is linked to alterations of food- related reward and cognitive processes in obesity. Derived from that, the future findings may aid in the understanding of existing and with the development of new anti-obesity drugs.

smokers, former smokers, and non-smokers using a dot-probe task. Drug Alcohol Depend, 2002. 67(2): p. 185-91.

alcoholics. Eur Addict Res, 2000. 6(2): p. 64-70.

Do you plan to share individual participant data with other researchers?

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Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00015187**
- Date of Registration in DRKS: **2018/07/30**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2018-541N-MA , Medizinische Ethik-Kommission II Medizinische Fakultät Mannheim der Universität Heidelberg**

Secondary IDs

Health condition or Problem studied

- ICD10: **F17.2 - Mental and behavioural disorders due to use of tobacco; Dependence syndrome**
- ICD10: **F10.2 - Mental and behavioural disorders due to use of alcohol; Dependence syndrome**
- ICD10: **E66 - Obesity**
- Free text: **Healthy individuals**

Interventions/Observational Groups

- Arm 1: **Comparison of four study groups (1: alcohol-dependent patients; 2: nicotine-dependent subjects; 3: Obese patients (AMENDEMENT: before and after bariatric surgery); 4: Healthy control subjects) by eye-tracking with examination of eye movements and measurement of the attentional bias on image stimuli of various categories (alcohol, neutral, food, tobacco), questionnaires, blood sampling**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Non-randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Active control (effective treament of control group)**
- Purpose: **Basic research/physiological study**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

The aim of the study is to detect the difference in the temporal duration of the visual fixation of individual image stimuli of different Stimuluskategorien (alcohol, neutral, tobacco, food) in milliseconds after the measurement has been completed and compared with to other test groups

Secondary Outcome

Saccades using eye-tracking;
Rating of Images using Computer based self-assessment manikin scales for valence, arousal and craving

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- Medical Center **Zentralinstitut für Seelische Gesundheit, Mannheim**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2018/12/30**
- Target Sample Size: **100**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **65 Years**

Additional Inclusion Criteria

•Men and Women between 18 and 65 years
•Group 1: Patients with alcohol use disorder(DSM 5)
•Group 2: Individuals with nicotine dependence (DSM 5)
•Group 3: Patients with Adipositas (WHO); BMI >30kg/m2, AMENDMENT: before and after bariatric surgery
•Group 4: Healthy individuals
•Capacity to provide informed consent
•Written Informed Consent
•Normal vision

Exclusion criteria

•Withdrawal of the declaration of consent
• severe withdrawal symptoms (CIWA-R> 4)
• Alcohol intoxication (breath alcohol concentration> 0.3 ‰)
• withdrawal complications or severe withdrawal symptoms in the past
• Axis I disorder according to ICD-10 and DSM 5 (except for alcohol dependence / nicotine dependence or nicotine abuse and specific phobia within the last 12 months)
• Pharmacotherapy with psychoactive substances within the last 14 days
• Current substance abuse (THC, amphetamine, opiates, benzodiazepines, barbiturates or cocaine)
• wearing glasses (without the possibility to wear contact lenses)

Addresses

- **Primary Sponsor**

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- **Contact for Scientific Queries**

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Sources of Monetary or Material Support

- **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Approval of ethics comm. (mandatory for transfer to Studybox) **Ethikvotum**
- trial protocol (mandatory for transfer to Studybox) **Prüfplan**
- Approval of ethics comm. (mandatory for transfer to Studybox) **Ethikvotum Amendment**

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*