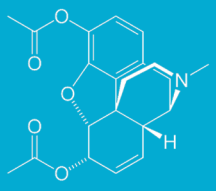
Acute mediofrontal and insular brain hypoperfusion after heroin administration in addicts



A within subject arterial spin labeling study

N. Denier, H. Gerber, M. Klarhöfer, M. Amann, M. Günther, A. Riecher, G. Wiesbeck, S. Borgwardt, M. Walter

PURPOSE

Heroin, chemically known as diacetylmorphine, is one of the most popular drugs used in non-medical settings and often leads to *very strong addiction*. The psychotropic effect of heroin per se could be distinguished in two phases, the *rush and the euphoric phase*. The rush is described as an only seconds lasting phase, which provides a fast release of inner tensions. The euphoric phase instead lasts for hours and is characterized by inner happiness, drowsiness and feeling distanced from all events around. However the *neurofunctional fundaments of subjectiv effects mediated by heroin are not well understood*. In the present study we examined *acute effects of heroin during the euphoria phase* To set the focus on self-referential processes, we examined cerebral blood flow patterns in a task free resting state condition by an arterial spin labelling (ASL) MRI technique. *We hypothesized perfusion changes in networks and areas processing emotions and self-relevant mental stimulations*.

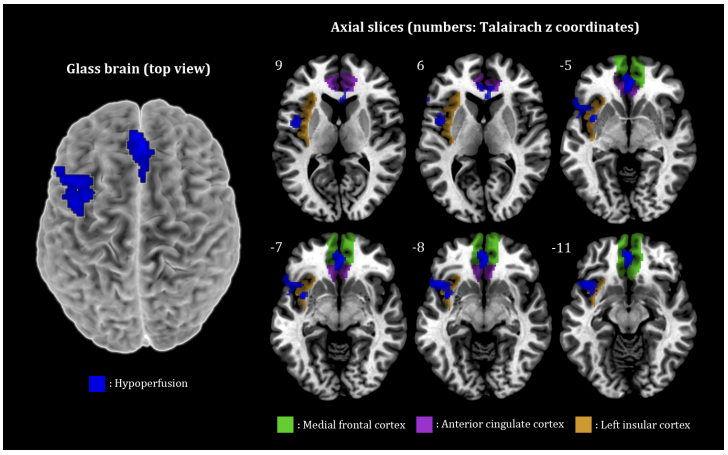
METHODS

Fifteen non-left-handed heroin-dependent subjects (9 male; mean age 41 ± 7 years) were included in the study. All subjects participated in the standardized heroin-assisted treatment program (JANUS Basel). Each participant was *scanned with heroin and a placebo* (injection of saline) with a one week interval between scans. A *pulsed ASL sequence* (single-shot 3D GRASE readout) based on a flow-sensitive alternating inversion recovery spin labeling scheme with 14 incremental inversion times was performed on a *3T-scanner*. For each inversion time two images were acquired; one after slice-selective inversion (control image) and one after non-selective inversion (labelled image). The control and labelled images were used to *calculate perfusion maps*. A *voxel-wise comparison analysis* of modulated and normalized perfusion map contrasts between heroin and placebo condition was done with a *basic general linear model in SPM 8*.

RESULTS

Compared to placebo condition, *heroin was associated with hypoperfusion in two main clusters*. One cluster within the area of the *medial prefrontal cortex (mPFC)*, the second in the *left temporal cortex* in the *area of the insula*.

Area	Hemisphere	Talairach coordinates of cluster maximum (x y z)	Cluster size (voxels)	Cluster p-value (uncorrected)	Cluster p-value (FWE corrected)
Contrast: Heroin < Placebo					
Anterior cingulate	R	2 42 -6	515	<.0001	0.003
Medial frontal gyrus	L	-2 48 -10			
Anterior cingulate	R	4 26 8			
Extra-Nuclear	L	-38 4 -6	580	<.0001	0.002
Superior temporal gyrus	L	-48 18 -8			
Precentral gyrus	L	-46 0 10			
Contrast: Heroin > Placebo					
None					



The axial slices and the glass brain are presented in standard neurological fashion, with the right hemisphere shown on the right of the figure. The glass brain contains an axial projection of the two significant clusters.

CONCLUSION

We found that *heroin administration in addicts* leads to *brain hypoperfusion* (during euphoria phase) *within the default mode network (DMN)*. The DMN is active when *self-relevant mental stimulations* are processed like non goal-oriented thinking, autobiographical memory retrieval, envisioning the future, and conceiving the thoughts and perspectives of others. The anatomy of the DMN could be divided into interacting subsystems including the medial temporal lobe which provides information from prior experiences in the form of memories and associations. The mPFC acts as integrative part and provides the flexible use of the temporal information during the construction of self-relevant mental stimulations. *Hypoperfusion in the mPFC could probably explain the deep sensation of calm and thought that the outer world no more exists described by heroin users*. The *insular cortex* instead plays a role in *regulation of emotions, self-awareness and pain perception*. Functions which could by down regulation shape the subjective effects of the heroin experience.

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