Does repeated coffee consumption during chronic sleep restriction affect A_1 adenosine receptor availability in humans?

Anna L. Pierling[a,b], Eva-Maria Elmenhorst[c,d], Denise Lange[c], Diego M. Baur[e], Simone Beer[a], Tina Kroll[a], Bernd Neumaier[f], Daniel Aeschbach[c,g,h], Andreas Bauer[a], Hans-Peter Landolt[e], David Elmenhorst[a,i,j]

[a] Forschungszentrum Jülich, Institute of Neuroscience and Medicine (INM-2), Wilhelm-Johnen-Strasse, 52428 Jülich, North Rhine-Westphalia, Germany.
[b] RWTH Aachen University, Department of Neurophysiology, Institute of Zoology (Bio-II), Worringerweg 3, 52074 Aachen, North Rhine-Westphalia, Germany.
[c] German Aerospace Center, Institute of Aerospace Medicine, Linder Höhe, 51147 Cologne, North Rhine-Westphalia, Germany.
[d] RWTH Aachen University Hospital, Institute for Occupational, Social and Environmental Medicine, Pauwelsstrasse 30, 52074 Aachen, North Rhine-Westphalia, Germany.
[e] University of Zurich, Institute of Pharmacology & Toxicology, Winterthurerstrasse 190, 8057 Zurich, Switzerland.
[f] Forschungszentrum Jülich, Institute of Neuroscience and Medicine (INM-5), Wilhelm-Johnen-Straße, 52428 Jülich, North Rhine-Westphalia, Germany.
[g] Harvard Medical School, Division of Sleep Medicine, Suite BL-438, 221 Longwood Avenue, 02115 Boston, Massachusetts, United States of America.
[h] Rheinische Friedrich-Wilhelms-Universität Bonn, Faculty of Medicine, Venusberg-Campus 1, 53127 Bonn, North Rhine-Westphalia, Germany.
[i] Rheinische Friedrich-Wilhelms-Universität Bonn, Division of Medical Psychology, Venusberg-Campus 1, 53127 Bonn, North Rhine-Westphalia, Germany.
[j] University Hospital Cologne, Multimodal Neuroimaging Group, Department of Nuclear Medicine, Kerpener Strasse 62, 50937 Cologne, North Rhine-Westphalia, Germany.

Objectives:
Adenosine and cerebral adenosine A_1 (A_1AR) and A_{2A} receptors are important modulators of the sleep-wake cycle and regulate to some extent the sleep-wake homeostasis. Acute sleep deprivation has been shown to result in an upregulation of A_1ARs in human and rat brains. The stimulating effects of caffeine are evoked through non-selective antagonism at adenosine receptors. Using positron emission tomography (PET), we investigate the effect of repeated coffee consumption during chronic sleep restriction and subsequent coffee abstinence after recovery sleep on cerebral A_1AR availability and occupancy in humans.

Methods:
Thirty healthy volunteers (28±5 years, 15f) completed an in-lab study including three [^{18}F]CPFPX PET scans to determine cerebral A_1AR availability after subsequent exposure to rested (3 nights with 8h time in bed (TIB)), chronically sleep restricted (5 nights with 5h TIB), and recovery (one night with 8h TIB) conditions. Participants either consumed freshly brewed coffee (n = 17) or decaffeinated coffee (n = 13) during 5 days of sleep restriction (prior caffeine abstinence > 10 days). Regular coffee contained 200 mg caffeine at 7.30 a.m. and 100 mg caffeine at 2.00 p.m., decaffeinated coffee contained 4 mg and 2 mg, respectively. PET scans were conducted at the

same time of day under caffeine-abstinent rested conditions, roughly 7h after the latest coffee intake after sleep restriction, and after ~ 31h of coffee abstention after recovery. Caffeine levels in saliva were determined repeatedly. Cerebral A_1AR availability was quantified by distribution volume (V_T) and occupancy levels were calculated by applying the Lassen plot including cortical and subcortical areas, cerebellum, and pons.

Results:
In the decaffeinated coffee group, no differences in cerebral A_1AR availability were found between baseline condition, 5 days of sleep restriction and one night of recovery sleep. Repeated administration of regular coffee resulted in a displacement of [^{18}F]CPFPX binding of 19 ± 13 % on average. One day after coffee abstention and recovery sleep, V_T values did not differ from baseline.

Conclusions:
Our data suggest that neither chronic sleep restriction for 5 days nor combination with repeated caffeine consumption result in a persistent change in the regulation of cerebral A_1AR availability.

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