Cocaine dependence: a fast-track for brain ageing?

Cocaine-dependent individuals anecdotally appear aged and their mortality rates are estimated up to eight times higher than in the healthy population. Psychological and physiological changes typically associated with old age such as cognitive decline, brain atrophy, or immunodeficiency are also seen in middle-aged

**Figure 1.** Age-related changes in gray matter volume in 60 healthy volunteers and 60 cocaine-dependent individuals. The brain maps show regions of age-related gray matter volume loss separately in healthy volunteers (a) and cocaine-dependent individuals (b); the scatter plots next to the brain maps show age versus the gray matter volume in these regions for each participant in each group (black circles, cocaine-dependent individuals; gray circles, healthy volunteers). (c) A direct comparison of age-related gray matter decline between the two groups revealed a significant group-by-age interaction such that cocaine-dependent individuals showed significantly greater atrophy in prefrontal and temporal-brain regions (blue regions) compared with controls and they showed a lack of normal age-related volume loss in the striatum (red regions). The scatter plot shows the mean volumes of brain regions where there was a significant group-by-age interaction. Left side of the brain is shown on the left side of each slice; the numbers denote z-coordinates for each slice in standard stereotactic space.
coclamine-dependent individuals. These observations raise the
question of whether cocaine abuse might accelerate the process
of normal ageing. Although this is a little-studied area, there are
several reasons for assuming that chronic cocaine exposure
interferes with the processes of brain ageing.

We compared the effects of age on gray matter volume in 120
individuals aged 18–50 years (Supplementary Information). Half
of the sample met the standard diagnostic criteria for cocaine
dependence of the DSM-IV-TR whereas the other half had no
history of substance misuse disorders or major psychiatric
disorders. The two groups were matched for age (t_{118} = −0.12,
P = 0.905), gender (t = 2.8, P = 0.148), and verbal IQ (t_{115} = −0.36,
P = 0.716), as described elsewhere. All participants underwent a
structural MRI brain scan, which was analyzed using voxel-based
morphometry to produce whole-brain maps of age-related
change in gray matter volume.

All participants showed a reduction of gray matter volume in
cortical and subcortical regions as a linear function of increasing
calendar age (Figures 1a and b). However, the annual rate of
global gray matter volume loss in cocaine-dependent individuals
was almost twice the rate of healthy volunteers (that is, 3.08 ml per
year (standard error (s.e.): 0.49 ml) versus 1.69 ml per year (s.e.:
0.41 ml)). Consequently, the rate of age-related gray matter
volume loss in cocaine-dependent individuals was significantly
greater than in healthy volunteers (F_{1,116} = 4.7, P = 0.031); this
interaction remained significant after excluding 16 individuals
with comorbid alcohol dependence (F_{1,100} = 6.4, P = 0.013).
Accelerated ageing in cocaine-dependent individuals was also
demonstrated by a significant age-by-group interaction on
gray matter volume of the regions affected by age (P < 0.001,
see Figure 1c). Cocaine-dependent individuals showed a signifi-
cantly greater-than-normal age-related decline in gray matter
in prefrontal and temporal regions compared with healthy controls.
By contrast, parts of the striatum appeared resistant to age-related
volume decline in the cocaine-using group. Enlarged striatal
volume has frequently been reported in stimulant-dependent
individuals, possibly reflecting a marker of reduced dopamine
neurotransmission in this dopamine-rich brain region where drugs
like cocaine work. Decline in striatal dopamine receptor density
has been associated with normal age-related cognitive decline.
The relative absence of age-related changes in the striatum of
cocaine-dependent people may thus reflect another feature of an
abnormal brain ageing process.

Abnormal ageing in chronic cocaine users is an emerging public
health concern, which has received little attention. Approximately
1% (ref. 8) of the 21 million users of cocaine worldwide are
considered to develop cocaine dependence. These individuals
may potentially be at risk of premature brain ageing. Young
people taking cocaine today need to be educated about the long-
term risk of ageing prematurely, specifically at a time when many
developed economies are facing the demographic challenge of an
ageing population. Our findings also draw attention to the
increasing number of older drug users seeking treatment for drug
abuse. Drug-treatment services, however, mainly target drug use
in young people, focusing on prevention and harm reduction; the
needs of older drug users are not so well catered for. As the
psychological and physiological challenges of ageing may have
also accelerated in individuals with long-term drug dependence, the
effects of cocaine on the process of ageing should be
recognized in order to design and administer age-appropriate
treatments for older drug users.

**CONFLICT OF INTEREST**

This work was funded and sponsored by GlaxoSmithKline (RG45422) and conducted
within the GlaxoSmithKline Clinical Unit Cambridge (UK) and the Behavioural and
Clinical Neuroscience Institute at the University of Cambridge, which is jointly funded
by the Medical Research Council and the Wellcome Trust. KDE and PSJ, who are both
supported by an MRC research grant, declare no conflict of interest. GBW declares
that he has no potential conflict of interest. TWR consults for Cambridge Cognition,
Lilly, Lundbeck and GlaxoSmithKline, and is currently in receipt of research grants
from these companies. ETB is employed part-time by GlaxoSmithKline and part-time
by the University of Cambridge.

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Supplementary Information accompanies the paper on the Molecular Psychiatry website (http://www.nature.com/mp)