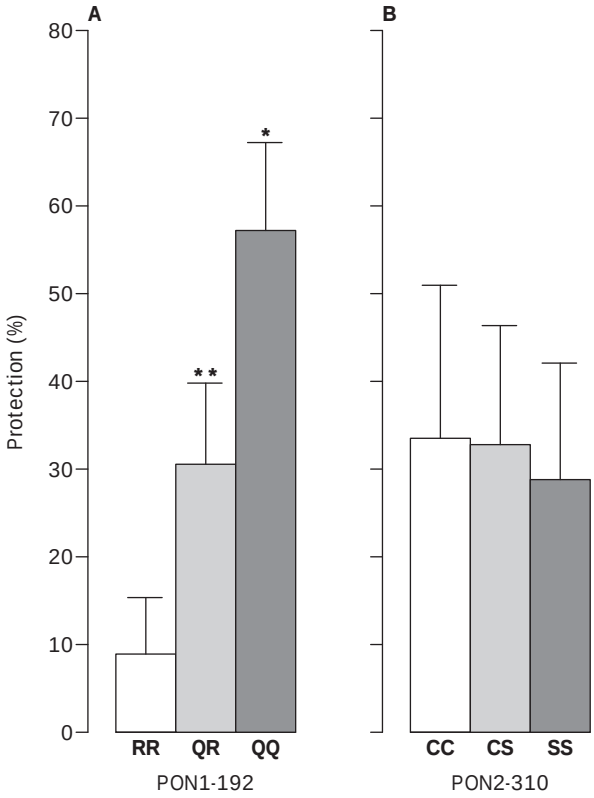

Effect of the PON1-192 (A) and PON2-310 (B) polymorphism on the ability of HDL to protect LDL against oxidative modification

LDL and autologous HDL prepared by ultracentrifugation were co-incubated at 37°C in presence of 5 μmol/L Cu^{2+} for 6 h. Lipid peroxides on LDL were analysed as described.[1] % protection is defined as amount of lipid-peroxides present in LDL incubated in presence of HDL subtracted from the amount of lipid-peroxide in LDL incubated in absence of HDL multiplied by 100. *p<0·005, **p<0·01 compared with RR genotype. Means (SD) of 36 measurements.

due to a differential inhibition of the PON1 alloenzymes by Cu^{2++}.[2] However, the PON2 polymorphism had no significant effect on the ability of HDL to protect against lipid peroxide generated on LDL (figure B).

Our results thus indicate that whilst PON1 polymorphisms are important in determining the capacity of HDL to protect LDL against oxidative modification in vitro, the PON2 polymorphism at position 310 has no effect on this action of HDL. If PON2 is involved in the genesis of CHD, it is likely therefore that it does so by a mechanism that does not involve HDL and is perhaps intracellular.

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Verbal self-monitoring and auditory hallucinations in schizophrenia

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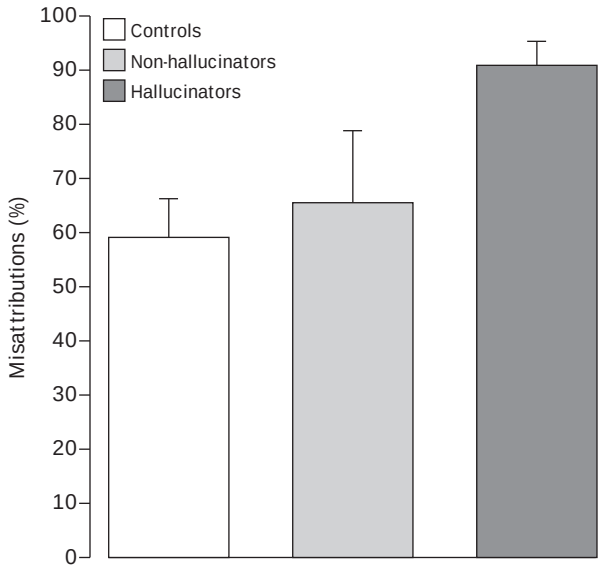
Auditory hallucinations are a major feature of schizophrenia, and typically involve patients hearing voices of other people saying derogatory things to them (such as "You're no good"). Cognitive psychological models propose that auditory hallucinations arise from a problem with monitoring one's own verbal thoughts (or inner speech), such that they are misidentified as not belonging to oneself and are perceived as external "voices".[1] Although this theory is widely held and is supported by neuroimaging data,[2,3] there is only limited psychological evidence specifically linking hallucinations with such a self-monitoring deficit.[4]

We addressed this issue using a cognitive task that engages verbal self-monitoring. Participants read out single words (complimentary, derogatory, or neutral adjectives) presented on a computer screen. They spoke into a microphone that was connected to an amplifier and an acoustic-effects unit, which allowed the investigators to alter the pitch of the speech. Altering the pitch of their speech introduced a disparity between what the participants expected to hear and what they actually perceived. Their speech was instantaneously fed back to them through headphones as they spoke. After articulating each word, participants were required to identify, by pressing a button, the source of the speech they had heard as "self", "someone else", or "unsure". The effects of "moderate" distortion (pitch lowered by three semitones) and "severe" distortion (pitch lowered by six semitones) on response choice were examined relative to reading aloud normally (no distortion). We tested ten patients with schizophrenia who had prominent auditory verbal hallucinations and delusions (hallucinators), who we referred to as eight patients with



Percentage of errors where participants misidentified their distorted speech as belonging to someone else

schizophrenia with prominent delusions alone (non-hallucinators), and 20 volunteers. The two groups of patients were matched for other psychotic symptoms, and all three groups were matched for age, education level, and premorbid IQ. All participants gave written informed consent to participate in the study.

Even though the pitch had been changed by only a few semitones, patients in both groups had difficulty recognising their own speech (p=0·037); they were either unsure about its source or misattributed it to someone else. The hallucinators were particularly prone to concluding that their distorted voice belonged to someone else, as opposed to simply being unsure (p=0·015): 91% of their errors were misattributions, compared with 65% for non-hallucinators, and 59% for controls (figure). Furthermore, the hallucinators were more likely to make errors when the words they read were derogatory, rather than neutral or complimentary (p=0·03).

These results show that patients with auditory hallucinations were not just uncertain about the source of their own speech when it was distorted, they positively misidentified it as belonging to someone else. This misrecognition of one's own verbal output is thought to be a fundamental deficit underlying auditory hallucinations. The tendency of hallucinators to make errors when articulating negative emotional material suggests that the typically derogatory content of auditory hallucinations might reflect a bias whereby the patient is particularly likely to attribute unpleasant thoughts about himself to somebody else.

We are grateful to Chris Frith who provided advice on the design of the task; and to Susan Rossell and Farooq Ahmad who helped to recruit and test some of the patients. The work was done at the Institute of Psychiatry.

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Haemopoietic, thrombopoietic, and vascular endothelial growth factor in space

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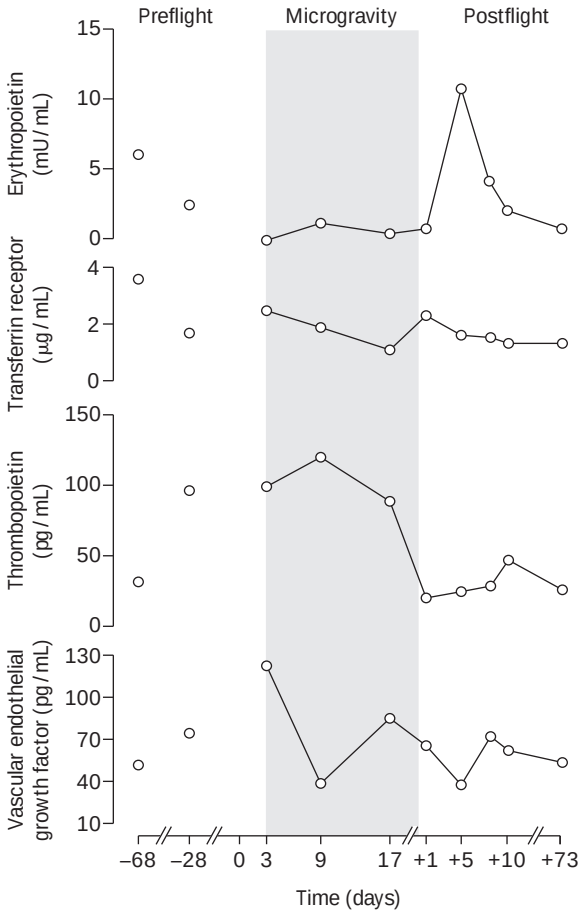
During November, 1998, the first components of the international space station were launched. Future research on board will include the effect of microgravity on the human body. Data concerning hormonal regulation in man under micro-gravity conditions are scanty or absent. We measured erythropoietin, the predominant regulator of the red blood cell mass,[1] transferrin receptors, thrombopoietin, and vascular endothelial growth factor, an important angiogenic factor,[2] before, during, and after a 21-day spaceflight. Serum samples from a 40-year-old male cosmonaut were analysed with standard ELISA techniques (figure). Before take-off the cosmonaut had normal



German Mir 97 mission
Measurements in a 40-year-old astronaut.

concentrations for a sedentary man except for thrombopoietin. In space, haemopoiesis is diminished, as indicated by the low erythropoietin and transferrin receptor concentrations. These data are consistent with earlier findings concerning erythropoietin concentrations and control of red blood cells under microgravity.[3,4] Increased erythropoietin concentrations after the flight restore diminished oxygen transport capacity of the blood. Preflight thrombopoietin concentrations varied but were increased in flight, and decreased after the flight. Vascular endothelial growth factor was increased early in the flight and returned to normal afterwards.

Erythropoietin and thrombopoietin were inversely related. Transferrin receptor concentrations were poorly related to erythropoietin changes. Vascular endothelial growth factor was doubled during the early stages of microgravity which might be related to intravascular fluid shifts under microgravity.

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