MRS of the brain in patients with anorexia or bulimia nervosa

Barbara Rost, Werner Roser, Reinhard Bubl, Ernst W Radue, Dieter Buergin

Twenty patients with anorexia or bulimia nervosa were prospectively investigated by magnetic resonance spectroscopy (MRS) of the brain. Compared to healthy controls, MRS of those with eating disorders revealed metabolic changes, which seem to be a consequence of their nutritional deficiency.

Dr Barbara Rost is Senior Consultant in the Department of Child and Adolescent Psychiatry, University of Basel, Switzerland, **Dr Werner Roser** is Medical Physicist in the Department of Neuroradiology, University Hospitals, Basel, Switzerland, **Dr Reinhard Bubl** is Senior Consultant in University Children's Hospital, Basel, Switzerland, **Professor Ernst W Radue** is Head of the Department of Neuroradiology, University Hospitals, Basel, Switzerland, and **Professor Dieter Buergin** is Chief of Service and Head of Department of the Department of Child and Adolescent Psychiatry, University of Basel, Switzerland

Correspondence to: Dr B Rost

Morphological changes in the brain of patients with anorexia or bulimia nervosa, such as enlarged ventricles and/or sulcal widening (Krieg et al, 1989; Hoffman et al, 1989), have been previously detected by computed tomography (CT) and magnetic resonance imaging (MRI). These changes were reported to be reversible (Kornreich et al, 1991; Hentschel et al, 1995; Lambe et al, 1997). The cause of these changes and their potential relevance to the progression of the diseases can still not be satisfactorily explained.

By using magnetic resonance spectroscopy (MRS) non-invasive studies of cerebral metabolism in vivo are possible. The purpose of the present study was therefore to investigate different areas of the brain of patients with anorexia or bulimia nervosa by MRS and to search for alterations in brain metabolism by comparing patients and healthy controls.

SUBJECTS

We investigated 20 patients with anorexia and bulimia nervosa (19 females, one male, mean age 19±9 years, mean weight 42±9 kg, mean body mass index (BMI) 15.4±2.0 kg/m$^{2)}$ by localized proton MRS of the brain. Because of the limited patient number in the study, subjects with anorexia and bulimia nervosa were combined for data evaluation. This procedure seems to be justified since very similar morphological changes in the brain of patients with anorexia or bulimia nervosa have been reported (Hoffman et al, 1989; Krieg et al, 1989).

MATERIAL AND METHODS

All measurements were performed at a magnetic field strength of 1.5 Tesla on a Siemens Magnetom SP whole body system, in addition to clinical MRI using the standard head coil. Fifteen healthy volunteers (14 females, 1 male, mean age 24±8 years, mean weight 59±7 kg, mean BMI 20.9±1.9 kg/m^2) were investigated as controls.

MR spectra were acquired after image-guided localization using a stimulated echo acquisition mode (STEAM) sequence (Frahm et al, 1987) with a short echo time of 20 ms. The repetition time was 3000 ms, 128 echoes were averaged. Up to three volumes of interest, 2 x 2 x 2 cm^3 each, were investigated, depending on the patience of the subjects. The first was located frontally in predominantly white matter, the second in occipital gray matter and the third in the cerebellum.

In the spectra, we integrated the peaks of the neuronal marker N-acetyl-aspartate (NA), the energy supply marker creatine (Cr), the cell membrane component choline (Cho), the osmolyte myo-inositol (Ino), and lipid compounds (Lip). For data evaluation, we determined both metabolic ratios (spectral area of metabolite x divided by the spectral area of metabolite y, i.e. x:y; y = Cr or Cho in most MRS studies) and absolute metabolite concentrations (in mM) from the spectra using a special calibration procedure (Roser et al, 1997).

ETHICAL ASPECTS

The Ethical Committee of the Basel University Hospitals reviewed and approved the study protocols. All participants were informed of the purpose of the study and gave their written consent.

RESULTS

Figure 1 shows an MRS measurement in frontal white matter. The most prominent contributions to the spectra have been indicated. A clear reduction of lipid signals is evident in the patient's spectrum (*Figure 1a*) compared to the control's

spectrum (*Figure 1b*). *Figure* 2 shows the ratio of Lip:Cr for the different localizations in patients and controls. The reduction of Lip:Cr in frontal white matter is highly significant ($P<0.005$).

In *Figure 3*, the absolute concentrations of Ino are shown. Ino (and also Ino:Cr) is significantly reduced in the white matter area ($P< 0.05$). All other metabolite ratios and absolute concentrations of metabolites were found to be within the normal range, except the water signal, which was found to be increased in the cerebellum. No special marker peaks or lactate signals were observed in any subject. In MRI no lesions were found in the brain of any of the patients nor in any of the controls.

Taking together the data of both patients and healthy controls, we investigated whether the metabolic changes mentioned above vary with the BMI. Here we observed that Ino is further reduced with decreasing BMI ($r^2 = 0.21$).

DISCUSSION

In this study, we found metabolic changes in different areas of the brain of patients with anorexia or bulimia nervosa compared to healthy controls. These changes were found to be most prominent in the frontal white matter localization. Here, the lipid peaks, which can also contain protein signals (Kauppinen et al, 1993), were reduced to nearly half of the control level. For anorexic patients, it is well known that the contribution of proteins to basal energy expenditure is increased to maintain normal glucose oxidation (Franssila-Kallunki et al, 1991). Furthermore, fatty acid metabolism is significantly altered in these patients (Holman et al, 1995). This might explain the reduced intensity of the corresponding signals in MRS, caused by, as we suppose, a reduced concentration of free MRS visible lipoproteins within the investigated brain parenchyma.

As far as we know, reduced lipid concentrations in brain parenchyma have not been previously reported. Whether this is an important causal factor in brain pseudoatrophy — and even more important, whether this has relevance for brain functioning, remains unclear.

In the three locations investigated, we did not observe any significant changes in Cho or Cho:Cr. This is in contrast to Hanefeld et al (1993), who observed a significant decrease of Cho in the white matter of seven anorexic patients, and also in contrast to Schlemmer et al (1998), who found a significant increase of Cho:Cr by 26% in anorexic patients. However, in

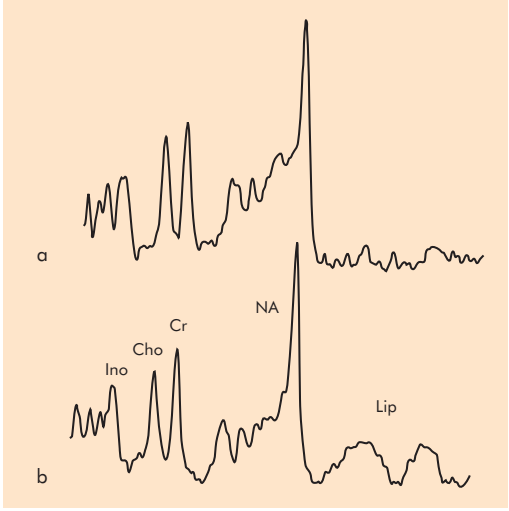

Figure 1. Magnetic resonance spectroscopy (MRS) measurement from frontal white matter. a. Anorexic patient. b. Healthy control. The evaluated metabolites have been indicated: Ino: myo-inositol, Cho: choline, Cr: creatine, NA: N-acetyl-aspartate, Lip: lipids. The patient's spectrum is characterized by reduced Lip and a slight reduction of Ino.

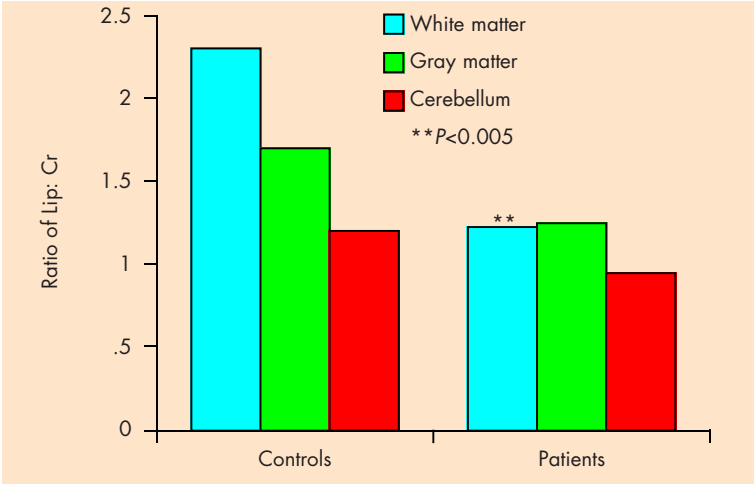

Figure 2. The ratio of lipids to creatine (Lip:Cr), for the different localizations in patients and controls. The reduction of Lip:Cr in frontal white matter is highly significant (P<0.005).

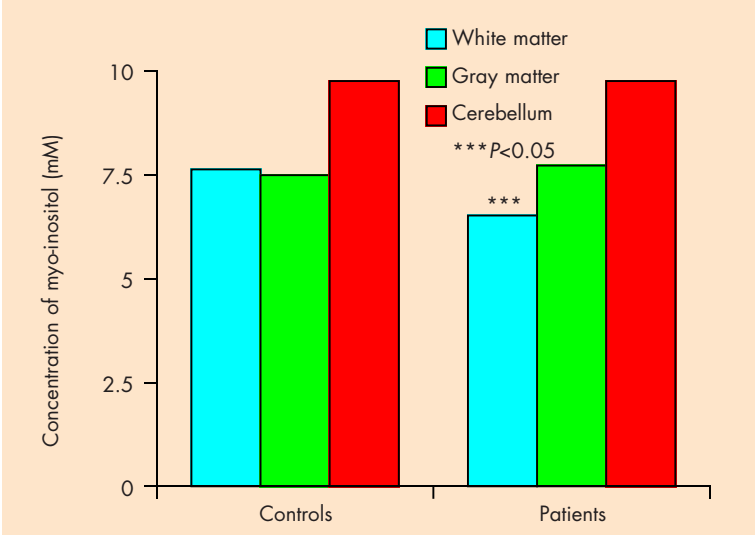

Figure 3. Absolute concentrations of myo-inositol (Ino) within the different localizations in patients and controls. Ino is significantly reduced in frontal white matter (P<0.05).

the latter study, it was unclear whether the increase of Cho:Cr is caused by an increase of Cho or a decrease of Cr or both, or by the use of different data acquisition parameters on two MR scanners with incomparable technology by Schlemmer et al. In the present study, we observed a slight increase of Cho in the cerebellar localization (8%, not significant). However, in this location, the concentration of all metabolites and of water was increased. Thus we suppose that the increase of Cho in the cerebellum could be merely the result of a slight shrinking of the cerebellum caused by brain pseudoatrophy rather than an increase in the concentration of Cho itself.

An interesting observation is the fact that Ino was reduced by 15% in frontal white matter. Ino is a metabolite which mainly occurs in glia cells (Brand and Leibfritz, 1992). It is also an osmolyte in the human brain and it has been shown that the signal intensity of Ino is drastically reduced in hyponatraemia (Videen et al, 1995). Since hyponatraemia can occur quite easily in anorectics (Alvin et al, 1993), reduced levels of Ino could be expected in these patients. Reduced levels of Ino have also been observed in a patient group treated with corticosteroids (Auer et al, 1997). Since cortisol levels are frequently increased in patients with eating disorders, we have found another possible relationship between the metabolic findings of the present study and other aspects of anorexia and bulimia nervosa.

In the patients, we observed no significant changes of NA nor NA:Cr. NA is believed to be a neuronal marker, and we therefore found no evidence of neuronal degeneration, which also corresponds to clinical, neuropsychological and electroencephalography data.

CONCLUSIONS

Previous CT and MRI studies on patients with anorexia or bulimia nervosa revealed structural brain abnormalities, while white and gray matter appeared macroscopically normal. This might have indicated that there are no alterations of the brain parenchyma.

However, the very few existing proton MRS studies reveal changes in brain metabolism, even if the results are still, to some extent, controversial (Hanefeld et al, 1993; Roser et al, 1996; Schlemmer et al, 1998). MRS in combination with routine MRI may serve as an investigative tool to observe metabolic changes in the brain of patients with anorexia and bulimia nervosa, leading to an improved characterization of the disease. It might help us to understand mechanisms which particularly promote chronic courses of the disease. HM

KEY POINTS

- Localized magnetic resonance spectroscopy (MRS) has shown metabolic changes in the brains of anorexic patients, such as a significant decrease of both myo-inositol (Ino) and lipid compounds within frontal white matter.
- The concentration of Ino in particular is further reduced with decreasing body mass index and reduced lipid signals have also been found in occipital gray matter.
- In the cerebellum the concentration of all metabolites including water, except lipids, was increased.
- The metabolic alterations seen in the present study seem to be a consequence of the nutritional deficiency, but further investigations are required to see if these findings have any relevance for brain functioning.
- MRS might serve as a valuable investigative tool to observe the cause of eating disorders and to follow the success of therapy.

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