Bimuno GOS may also improve cognitive impairment in ageing, dementia and schizophrenia. Furthermore, the GOS composition may benefit the detrimental influence of maternal infection on the developing foetal brain.

The invention will be further described by way of reference to the following examples and figures.

Figure 1A shows the effect of FOS and GOS on levels of BDNF protein in extracts of rat frontal cortex and hippocampus.

Figure 1B shows the effect of FOS and GOS on levels of NRI subunits in the rat frontal cortex and the hippocampus. Western blot images of NRI and β-actin immunoreactivity in protein extracts are shown.

Figure 2A shows the effect of FOS and GOS on levels of NR2A subunits in the rat frontal cortex and the hippocampus. Western blot images of NR2A subunits and β-actin immunoreactivity are shown.

Figure 2B shows the effect of FOS and GOS on levels of NR2B subunits in the rat frontal cortex and the hippocampus. Western blot images of NR2B and β-actin immunoreactivity are shown.

Figures 3A to 3D are representative auto-radiographs of BDNF (A, C, E) and NRI subunit (B, D, F) mRNA expression in rat hippocampus following oral administration of water (A, B), FOS (C, D) or GOS (E, F). Arrows delineate increased expression and arrow head indicates reduced expression. DG = dentate gyrus, CA1 and CA3 = Cornu Ammons subfields of the hippocampus. Scale bar = 200 μM.

Figures 4A to 4D show the effect of FOS and GOS on levels of BDNF, NR1, NR2A and NR2B mRNAs in the dentate gyrus (DG) of and CA1 and CA3 (Cornu Ammons) subfields of the hippocampus.

Example 2

Syrup composition per 7.25g finished product:-

Galactooligosaccharide (GOS) mixture	2.75g	
Lactose	0.58g	
Monosaccharides (glucose, galactose)	1.69g	
Ash		0.23g
Moisture		1.95g
Protein		0.05g

Example 3

In vivo study of the effect of feeding prebiotics on central brain derived neurotrophic factor (BDNF) and N-methyl-D-aspartate (NMDA) receptor subunits.

MATERIALS AND METHODS

Prebiotic administration

All rat experiments were carried out in accordance with UK Home Office guide lines and under approved licences. Male Sprague Dawley rats (225-250g) were administered a daily oral administration (gavage) or either water, FOS (fructooligosaccharide) (4g/kg) or GOS (galactooligosaccharide [Bimuno]) (4g/kg), for 5 weeks (n=8/group). This dosing regimen was based on previous studies (Anthony et al; Food Chem Toxicol; 44 (6); 819-26 (2006)) and pilot data showing that these optimal prebiotic doses provides maximum microbiota growth (not shown). All animals were sacrificed, trunk blood collected and their brains removed, twenty-four hours after the last gavage. Blood was centrifuged to obtain plasma, and the frontal cortex and hippocampus were dissected out from half of the harvested brains. Whole brains and isolated regions were snap-frozen in isopentane on dry-ice and stored with plasmas at -80°C prior to use.

BDNF analysis

Cortex and hippocampus tissue from all groups were homogenized in RIPA (radio immunoprecipitation assay) buffer (1:10 w/v, Sigma Aldrich, UK) containing protease inhibitors ('Complete-Mini', Roche). Protein concentrations were determined using the Bradford reagent (Sigma, UK). Samples of protein extracts were diluted 1:5 v/v in deionised water, prior to their analysis with a commercial BDNF ELISA kit (BDNF Emax immunoassay system, Promega UK).

Western blotting

Equal concentrations of protein extracts of cortex, hippocampus or cerebellum (20□g) from prebiotic and control groups were mixed with loading buffer (50mM 1, 4-dithiothreitol and 0.025% bromophenol blue), and fractionated with a molecular weight marker (GE Healthcare, Buckinghamshire, UK) by electrophoresis on pre-cast 7.5% SDS/polyacrylamide gels (Biorad,UK), and trans-blotted onto polyvinyl difluoride (PVDF) membranes (Immobilon-P, Millipore, Watford, UK).

The membranes were blocked with 5% (w/v) non-fat milk in PBS (phosphate buffered saline) containing 0.1% Tween (PBST) for 45min, and then incubated for 1 h at room temperature in incubation buffer (PBST with 2% [w/v] milk) containing a primary antibody (diluted 1:1000) against one of three NMDAR subunits: NR1 (AB9864, Millipore, UK), NR2A (AB1555, Millipore, UK) and NR2B (AB15362, Millipore, UK), and b-actin (Sigma-Aldrich, UK, diluted 1:50,000). Membranes were then washed three times for ten minutes in PBST and incubated for 30min in HRP (horseradish peroxidise)-linked secondary antibody in blocking buffer. Immunoreactive bands were visualized by chemiluminescence using the ECL-Plus kit (GE Healthcare, Buckinghamshire, UK), and apposing membranes to X-ray film (Kodak BioMax AR film). All antibodies produced a single band of expected molecular weight. The optical densities (OD) of bands were measured using the AlphaImager 3400, and the data expressed as OD ratios of phosphorylated: total NMDAR subunit, or total NMDAR subunit:b-actin.

In situ hybridization histochemistry (ISHH)

The frozen rat brain hemispheres were coronally sectioned (14□m) on a cryostat, thaw mounted on to Superfrost-plus slides (Fisher Scientific) and stored at -80°C. Sections containing frontal cortex were pre-treated as described (Burnet et al; Mol. Cell. Neurosci.; 46; 167-75; (2011)).

Commercially synthesized (MWG, UK) oligodeoxyribonucleotides complementary to: BDNF (bases 883-927, NM001270630.1), NR1 (bases 746-780, NM008169.1), NR2A (bases 1642-1676, NM008170.2) or NR2B (bases 1758-1792, NM010350.2) were used in an establish ISHH method (Eastwood et al.; J. Psychopharmacol.; 21; 635-644; (2007)). Oligodeoxyribonucleotide probes were 3'-end labelled with [^{35}S]-dATP using terminal deoxynucleotidyl transferase (Promega, UK). Probes were diluted in hybridization buffer, pipetted onto the tissue sections

Results

Figure 11 shows that rats given BGOS for 3 weeks showed improved performance in the extra-dimensional (ED) component of the ASST that is a measure of flexible learning. Execution of the ED element as effortlessly as the intra-dimensional phase (ID/ED-shift) is indicative of increased cognitive flexibility, a parameter which is impaired in the elderly. In Figure 11 #$p<0.05$ compared to control ID and *$p<0.05$ compared to control ED.

Conclusion

Rats given BGOS show improved cognitive performance in a task dependent on the medical prefrontal cortex, which is often impaired in psychiatric disorder and ageing.

CLAIMS

1. A galactooligosaccharide composition comprising disaccharides Gal (β1-3)-Glc; Gal (β1-3)-Gal; Gal (β1-6)-Gal; Gal (α1-6)-Gal; trisaccharides Gal (β1-6)-Gal (β1-4)-Glc; Gal (β1-3)-Gal (β1-4)-Glc; tetrasaccharide Gal (β1-6)-Gal (β1-6)-Gal (β1-4)-Glc and pentasaccharide Gal (β1-6)-Gal (β1-6)-Gal (β1-6)-Gal (β1-4)-Glc for use in preventing or treating cognitive dysfunction and/or emotional disturbances in neuropsychiatric illnesses or ageing.

2. The composition according to claim 1 wherein the cognitive dysfunction is cognitive decline or impairment as a result of ageing, dementia or schizophrenia.

3. The composition according to claim 1 wherein the neuropsychiatric illnesses are depressive disorders or anxiety disorders.

4. The composition according to any one of claims 1 to 3 which is in the form of a powder, a tablet, a capsule, a liquid formulation such as a syrup or a soft pastille.

5. The composition according to claim 4 wherein when in powder form it comprises from 1.35 to 9.6g of galactooligosaccharides in 1.65g to 20g of the powdered composition, preferably from 1.96g to 4.9g of galactooligosaccharides in 2.5g to 10g of the powder, most preferably 2.7g to 2.75g galactooligosaccharides in 3.0g to 5.5g of the powder.

6. The composition according to claim 4 wherein when in syrup form it comprises from 1.35g to 9.6g of galactooligosaccharides in 2.1g to 25.29g of the syrup composition, preferably from 1.96g to 4.9g of galactooligosaccharides in 3.0g to 12.9g of the syrup, most preferably 2.7g to 2.75g of galactooligosaccharides in 4.1g to 7.25g of the syrup.

7. A method of preventing or treating cognitive dysfunction and/or emotional disturbances occurring in neuropsychiatric illnesses or in ageing comprising administering to an individual an effective amount of a galactooligosaccharide composition comprising disaccharides Gal (β1-3)-Glc; Gal (β1-3)-Gal; Gal (β1-6)-Gal; Gal (α1-6)-Gal; trisaccharides Gal (β1-6)-Gal (β1-4)-Glc; Gal (β1-3)-Gal (β1-4)-Glc; tetrasaccharide Gal (β1-6)-Gal (β1-6)-Gal (β1-4)-Glc and pentasaccharide Gal (β1-6)-Gal (β1-6)-Gal (β1-6)-Gal (β1-4)-Glc.

8. The method according to claim 7 wherein the individual is a human.

9. The method according to claim 7 wherein the composition is administered orally.

10. The method according to claim 7 wherein the effective amount of the galactooligosaccharide composition is administered daily as a single dose.

11. The method according to claim 7 wherein the effective amount of the galactooligosaccharide composition is administered daily as two separate doses from 4 to 12 hours apart, preferably from 6 to 10 hours apart, most preferably 8 hours apart.

12. The method according to claim 7 wherein the composition is in the form of a powder, a tablet, a capsule, a liquid such as a syrup formulation or a soft pastille.

13. The method according to claim 12 wherein the composition is in the form of a powder comprising from 1.35 to 9.6g of galactooligosaccharides in 1.65g to 20g of the powdered composition, preferably from 1.96g to 4.9g of galactooligosaccharides in 2.5g to 10g of the powder, preferably 2.7g to 2.75g of galactooligosaccharides in 3.0g to 5.5g of the powder.

14. The method according to claim 12 wherein the composition is in the form of a syrup comprising from 1.35g to 9.6g of galactooligosaccharides in 2.1g to 25.29g of the syrup composition, preferably from 1.96g to 4.9g of galactooligosaccharides in 3.0g to 12.9g of the syrup, most preferably 2.7g to 2.75g of galactooligosaccharides in 4.1g to 7.25g of the syrup.

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Rats given BGOS show improved cognitive performance in a task dependent on the medial prefrontal cortex, which is often impaired in psychiatric disorder and ageing.

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2. The use according to claim 1 wherein the neuropsychiatric illnesses are depressive disorders or anxiety disorders.

3. The use according to claim 1 or claim 2 where the medicament is in the form of a powder, a tablet, a capsule, a liquid formulation such as a syrup or a soft pastille.

4. The use according to claim 3 wherein when in powder form the medicament comprises from 1.35 to 9.6g of galactooligosaccharides in 1.65g to 20g of the powdered composition, preferably from 1.96g to 4.9g of galactooligosaccharides in 2.5g to 10g of the powder, most preferably 2.7g to 2.75g galactooligosaccharides in 3.0g to 5.5g of the powder.

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