Gluten- and casein-free diets for autistic spectrum disorder (Review)

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TABLE OF CONTENTS

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ABSTRACT

Background
It has been suggested that peptides from gluten and casein may have a role in the origins of autism and that the physiology and psychology of autism might be explained by excessive opioid activity linked to these peptides. Research has reported abnormal levels of peptides in the urine and cerebrospinal fluid of persons with autism. If this is the case, diets free of gluten or casein, or both, should reduce the symptoms associated with autism.

Objectives
To determine the efficacy of gluten and/or casein free diets as an intervention to improve behaviour, cognitive and social functioning in individuals with autism.

Search strategy
Electronic searching of abstracts from the Cochrane Central Register of Controlled Trials (*The Cochrane Library* Issue 3, 2003), PsycINFO (1971 to May 2003), EMBASE (1974 to May 2003), CINAHL (1982 to May 2003), MEDLINE (1986 to May 2003), ERIC (1965 to 2003), LILACS (to 2003) and the Cochrane Complementary Medicine Field Specialised Register (January 2004). Review bibliographies were also examined to identify potential trials.

Selection criteria
All randomised controlled trials involving programmes which eliminated gluten, casein or both gluten and casein from the diets of individuals diagnosed with autistic spectrum disorder.

Data collection and analysis
Abstracts of studies identified in searches of electronic databases were read and assessed to determine whether they might meet the inclusion criteria. The authors independently selected the relevant studies from the reports identified in this way. As only one trial fitted the inclusion criteria, no meta-analysis is currently possible and data are presented in narrative form.

Main results
The one trial included (n= 20) reported results on four outcomes. Unsurprisingly in such a small scale study, the results for three of these outcomes (cognitive skills, linguistic ability and motor ability) had wide confidence intervals that spanned the line of nil effect. However, the fourth outcome, reduction in autistic traits, reported a significant beneficial treatment effect for the combined gluten and casein free diet.

Authors' conclusions
This is an important area of investigation and large scale, good quality randomised controlled trials are needed.

PLAIN LANGUAGE SUMMARY

Extensive literature searches identified only one randomised control trial of gluten and/or casein free diet as an intervention to improve behaviour, cognitive and social functioning in individuals with autism. The trial was small scale, with only 10 participants in the treatment group and 10 participants in the control group. Results indicate that a combined gluten and casein free diet may reduce some autistic traits. This is an important area of investigation and large scale, good quality randomised control trials are needed.

BACKGROUND

The autistic spectrum disorders are characterised by the triad of impairments identified by Wing, including impairments of social functioning, communication and lack of flexibility of thought and behaviour (Wing 1996a). These impairments persist from childhood to adulthood and can have a severe impact on learning and social integration. Fombonne's review of the epidemiology of autistic spectrum disorders reports that these disorders affect between 0.7 to 21.1 per 10,000 children (Fombonne 1999).

Reichelt et al hypothesised that peptides from gluten and casein have an aetiological role in the pathogenesis of the disorder of autism (Reichelt 1991). It has been suggested that the pathophysiology and psychology of autism can be explained by excessive opioid activity linked with the above (Israngkun 1986; Reichelt 1981). Urine samples of people with autism have been reported to show an increased 24-hour low molecular weight peptide excretion (Israngkun 1986; Reichelt 1986; Shattock 1990) and increased opioid levels in cerebrospinal fluid (Israngkun 1986; Reichelt 1981). Based on analysis of urine samples, dietary intervention involving the exclusion of foods containing gluten or casein, or both, has been proposed to be effective in ameliorating some of the behavioural symptoms of autism. An investigation by Reichelt et al indicated that casein has a similar chemical structure to that of gluten (Reichelt 1991). Due to this similarity, it is hypothesised that if a person has a sensitivity to either they will have sensitivities to both; although these sensitivities need not be of equal severity. The inability adequately to process these substances can result in or exacerbate a variety of disorders including postpartum psychosis, schizophrenia, and autism (Reichelt 1990; Reichelt 1991; Reichelt 1995).

When these substances are not adequately metabolised the result is that peptides are absorbed across the dietary membranes into the body's systems. It is suggested that these peptides may become biologically active through a binding with opioid receptors. The resulting excess of opioids can lead to the behaviours noted in autistic spectrum disorders. Further, it is suggested that although high levels of peptides are appropriately deposited in the urine, a small proportion of the excess peptides will cross into the brain causing interference of signal transmission (Reichelt 1991). This can lead to a disruption of normal activity. One hypothesis surrounding the variation in behaviour of children and adults with autism is linked to food reactivity/sensitivity. It is postulated that the disruptive behaviour evidenced in many individuals with autism is directly linked to particular foods, for example, wheat and dairy products (Reichelt 1994). In addition to the various behavioural difficulties demonstrated, it is suggested that communicative ability and social and cognitive functioning are similarly affected (Knivsberg 2002).

Knivsberg et al have argued that the peptides probably derived from gluten and casein have a negative pharmacological effect on attention, brain maturation, social interaction and learning (Knivsberg 1995). Hence, they hypothesise that appropriate diets would facilitate learning, social behaviour, cognitive functioning and communicative skills in individuals with autism.

OBJECTIVES

To examine the effectiveness of gluten and/or casein free diets on the symptoms of individuals with autistic spectrum disorder.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All relevant randomised control trials involving diets including the elimination of gluten, casein and both gluten and casein.

Types of participants

Children, adolescents and adults who met the DSM-IV (APA 1994) or ICD-10 (WHO 1993) criteria for autism and who had received a formal diagnosis.

Types of intervention

- Gluten free diet versus placebo/no treatment.
- Casein free diet versus placebo/no treatment.
- Gluten and casein free diet versus placebo/no treatment.
- Gluten free diet versus casein free diet.

(NB: placebo can be particularly problematic in diet interventions; however, there are precedents for blinding participants to allocation. As an example of a blinded gluten free versus gluten challenge trial, see Vlissides 1986).

Types of outcome measures

- Concentration of peptides in urine samples.

- Behavioural observations and standardised assessments of autistic behaviours.
- Communication and linguistic ability.
- Cognitive functioning.
- Motor ability (this is a change to our previously published protocol).

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Developmental, Psychosocial and Learning Problems Group methods used in reviews.

Electronic searches

The following electronic databases were searched:
1. The Cochrane Central Register of Controlled Trials (*The Cochrane Library* Issue 3, 2003)
2. MEDLINE (1966 to May 2003)
3. EMBASE (1974 to May 2003)
4. CINAHL (1982 to May 2003)
5. PsycINFO (1971 to May 2003)
6. LILACS (2003)
7. ERIC (1965 to 2003)
8. The Cochrane Complementary Medicine Field Specialised Register (January 2004).
Search terms were chosen as appropriate for each database. Search terms for the Cochrane Library were as follows:

CHILD-DEVELOPMENT-DISORDERS-PERVASIVE*:ME
COMMUNICATION*:ME
AUTIS*
PDD
(PERVASIVE and (DEVELOPMENTAL and DISORDER*))
(LANGUAGE near DELAY*)
COMMUNICAT*
(SPEECH near DISORDER*)
(CHILDHOOD next SCHIZOPHRENIA)
KANNER*
ASPERG*
((((((((((#1 or #2) or #3) or #4) or #5) or #6) or #7) or #8) or #9) or #10) or #11)
GLUTEN*:ME
CASEINS*:ME
GLUTEN*
CASEIN*
(#13 or #14 or #15 or #16)
(#12 and #17)
Reference Searching
The references of all studies identified from electronic and handsearches were inspected for further studies, and experts in the field as well as research and consumer groups with an interest in autism and nutrition were contacted.

METHODS OF THE REVIEW

Selection of trials
Using titles and abstracts, the full text of all studies reporting treatment of autistic spectrum disorder with gluten or casein restricted diets were obtained. Once all potentially appropriate studies had been obtained, each trial was evaluated independently by two reviewers (MF and GCJ or CM and SC) for inclusion. Where there was a question as to the possible inclusion/exclusion of any individual trial, final consensus decision was reached by discussion between MF and GCJ. Reviewers were not blinded to the name(s) of the author(s), institution(s) or publication source at any level of review.

Assessment of methodological quality
Concealment of treatment allocation is important in minimising bias (Schulz 1995). Assessment and scoring were undertaken using standard Cochrane format where A = adequate, B = Inadequate and C = unclear, as described in the Cochrane Collaboration Handbook (Clarke 2003). The one included trial (Knivsberg 2002) was also critically appraised against the following criteria:

- Was the assignment to treatment condition truly random?
- Was allocation adequately concealed?
- How complete was the follow up?
- How were the outcomes of people who withdrew considered?
- Were those assessing outcomes blind to the treatment allocation?

The characteristics of the one study included in this review are reported in the 'Table of Included Studies' (Knivsberg 2002). One other study (Pontino 1998) is awaiting assessment as information concerning randomisation has been unobtainable from the authors.

Data extraction
Two reviewers (MF and GCJ) independently extracted the data for the one trial meeting the inclusion criteria identified above, and authors were contacted for additional information (see below)
.

Data Synthesis
All data analyses were conducted using RevMan 4.2. If additional trials are identified in updates of this review, and report binary data, the odds ratio with a 95% confidence interval (CI) will be applied. The one included trial presented continuous data and was therefore analysed using a weighted mean difference as the same outcome measures were reported for both groups. Had there been studies using different but conceptually similar outcomes the standardised weighted mean difference would have been used. Had a trial reported more than 30% attrition, data would have been reported but not included in a summary analysis.

As only one trial was included, an assessment for trial heterogeneity was unnecessary, and no meta-analysis was performed. Should studies be included in future updates of this review, we plan to assess the extent to which between-trial differences are

apparent and assess consistency of results both visually and by examining I^2 (Higgins 2002), a quantity which describes approximately the proportion of variation in point estimates that is due to heterogeneity rather than sampling error. This will be supplemented with a test of homogeneity, to determine the strength of evidence that the heterogeneity is genuine. If statistically significant heterogeneity is found, a meta-analysis will not be performed. If heterogeneity is found but not considered to be a serious source of bias, then a random-effects model will be used. If no heterogeneity is found then a fixed-effect model will be used for the purpose of data synthesis.

Publication bias
Insufficient trials currently exist to carry out a funnel plot to investigate the potentially biasing influence of sample size. If, in the future, further trials are identified, funnel plots will be evaluated to assess the relationship between effect size and trial precision. Such a relationship could be due to publication or related biases or due to systematic differences between small and large studies. If a relationship is identified, clinical diversity of the studies will be further examined as a possible explanation (Egger 1997).

DESCRIPTION OF STUDIES

One trial met the criteria for inclusion (Knivsberg 2002). This was a small, single-blind randomised trial of combined gluten and casein free diet versus a 'normal' diet. Participants had been recruited from all parts of Norway via journal announcements and school psychological services, and participation was based on written consent. Mean age range of the intervention group was 91 months (range 62 to 120); mean age range of the control group was 86 months (range 59 to 127). Entry criteria included a diagnosis of autism and the presence of abnormal urinary patterns of peptides. There were 10 participants in each arm of the trial and the duration of the trial was 12 months. Four outcomes were measured, namely: autistic traits, cognitive skills, linguistic ability and motor ability.

One small study (Pontino 1998, n = 8) awaits assessment, as authors have not responded to enquiries about randomisation. Our search also discovered review articles, case studies and a non-randomised controlled study. See 'Studies awaiting assessment' and 'Table of excluded studies' for further information.

METHODOLOGICAL QUALITY

The one trial included was a small scale single-blind trial. The participants were pair-wise matched by severity of autistic symptoms and randomly allocated, within each pair, to treatment or control group. Methods of randomisation and allocation concealment were not described in the published paper, but we established through contact with the authors that coin-tossing had been used and that both randomisation and allocation had been undertaken independently of the project team conducting the study and therefore merited scores of (A) in each case (Knivsberg 2004). The outcomes assessors were blinded.

Baseline scores were provided for all four outcomes. One participant is described as "not responding to the cognitive and linguistic tasks" and scores are not reported for these two outcomes for this participant. There was no loss to follow up.

RESULTS

Only one trial met the inclusion criteria (Knivsberg 2002). This trial compared the impact of gluten and casein free versus normal diet on children diagnosed with autistic syndrome and abnormal urinary peptide patterns. Participants were pair-wise matched by severity of autistic symptoms and randomly allocated to treatment or control group within each pair. The trial lasted one year. The four outcome measures investigated in this study were: number of autistic traits (see below for fuller description), linguistic age in months, non-verbal cognitive level and motor problems. Data are presented as both group means and standard deviations and as individual patient data for both before and after scores, and standard deviations were calculated and presented below.

(1) Concentration of peptides in urine samples
The one study included in this review did not report investigations of peptide concentrations in the urine samples of participants (Knivsberg 2002).

(2) Behavioural observations and standardised assessment
Number of autistic traits was assessed using DIPAB, a Danish instrument for measuring autistic traits (Haracopos 1975). 'Autistic traits' were defined and assessed by grading, on a scale from 0 to 4, higher scores indicating greater severity: verbal communication, non-verbal communication, reaction when spoken to, behaviour in learning situations, sharing of emotions, reaction to physical contact, eye contact and interaction with other children. In addition, presence of repetitive and peculiar language, echolalia, adult dependency, unusual emotional expression, unusual fear or anxiety, rigidity, peculiar handling of toys, attachment to particular items and peculiar gait or movements were registered. Post intervention, the diet group had a mean autistic trait score of 5.60 (standard deviation (SD) = 2.41) compared to the control group mean score of 11.20 (SD = 5.00). Weighted mean difference (WMD) = -5.6 (95% CI -9.04 to -2.16), z = 3.19, p=0.001 (Knivsberg 2002).

(3) Communication and linguistic ability
Linguistic age in months was assessed using one of two tests depending on the age and functional level of the participants. The tests were the Illinois Test of Psycholinguistic Ability (ITPA) (Gjessing 1975), as standardised for Norwegian children, or the

Reynells språktest (language-test) (Hagtvet 1986). Post intervention, the diet group had a mean linguistic age in months of 66.60 (SD = 35.10) compared to the control group mean age of 55.70 (SD = 28.30). WMD = 10.9 (95% CI -18.56 to 40.36), z = 0.73, p = 0.47 (Knivsberg 2002).

(4) Cognitive functioning
Non-verbal cognitive level was assessed using the Leiter International Performance Scale (LIPS) (Leiter 1979). Post intervention, the diet group had a LIPS mean score of 86.7 (SD = 38.5) compared to the control group mean score of 74.30 (SD = 31.40). WMD = 12.40 (95% CI -20.06 to 44.86), z = 0.75, p = 0.45 (Knivsberg 2002).

(5) Motor ability
The published protocol for this systematic review (Ferriter 2002) did not pre-specify that outcomes concerning motor ability would be sought; however, we will include this information both here and in future updates of the review. Knivsberg et al reported that motor problems were assessed using the Movement Assessment Battery for Children (Henderson 1992). Post intervention, the mean score for the diet group was 26.3 (SD = 11.50) compared to the control group mean score of 27.80 (SD = 12.20). WMD = -1.50 (95% CI -11.89 to 8.89), z = 0.28, p = 0.78) (Knivsberg 2002).

DISCUSSION

The one trial included within this systematic review (Knivsberg 2002) reported results on four outcomes. Unsurprisingly in such a small scale trial, the results for three of the four outcomes (cognitive skills, linguistic ability and motor ability) were not significant and had wide confidence intervals that spanned the line of nil effect. However, the fourth and perhaps most pertinent outcome, reduction in autistic traits, showed a significant beneficial treatment effect for the combined gluten and casein free diet. Triallists used a scale (the DIPAB (Haracopos 1975)) in which 'autistic traits' were defined and assessed with a global score, registering: verbal communication, non verbal communication, reaction when spoken to, behaviour in learning situations, sharing of emotions, reaction to physical contact, eye contact and interaction with other children. In addition, presence of repetitive and peculiar language, echolalia, adult dependency, unusual emotional expression, unusual fear or anxiety, rigidity, peculiar handling of toys, attachment to particular items and peculiar gait or movements were registered.

The one significant result lends tentative support to the anecdotal reports by families of improvements in behaviour and cognition of family members with autistic spectrum disorder following the introduction of a gluten and/or casein free diet. However, these regimes are not without cost in terms of inconvenience and extra financial cost, as well as limitations on foods of choice for the affected family member, and one cannot recommend the use of such diets on the basis of this one small trial alone.

Researchers in the field are attempting to explore the effectiveness of these dietary interventions on persons with autistic spectrum disorder but to date there has not been evidence of sufficient size to eliminate other explanations for these beneficial changes. Only good quality, adequately-powered randomised controlled trials will resolve this issue and we await, with interest, further developments in this field.

AUTHORS' CONCLUSIONS

Implications for practice

Though the results of one small trial adds weight to the existing anecdotal evidence for a gluten and/or casein free diet for autism, there is not yet sufficient evidence for clinicians to advise the use of such diets in cases of autistic spectrum disorder.

Implications for research

Well-conducted and adequately-powered randomised controlled trials are urgently needed in this area.

POTENTIAL CONFLICT OF INTEREST

One of the reviewers (MF) is the parent of a son with autism.

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Knivsberg 2002
Methods	Single-blind, randomised trial (method: coin-tossing).
Participants	Twenty children with autistic syndrome and abnormal urinary peptide patterns. Mean age range of the intervention group was 91 months (range 62 - 120); mean age range of the control group was 86 months (range 59-127).
Interventions	Gluten and casein free diet v normal diet. Duration of the study, 12 months.
Outcomes	Autistic traits (as measured by the DIPAB). Cognitive skills (Leiter International Performance Scale). Linguistic ability (ITPA & Reynells språktest. Motor ability (Movement Assessment Battery for Children).
Notes	
Allocation concealment	A – Adequate

Characteristics of excluded studies

Study	Reason for exclusion
Adams 1997	Review article
Ashkenazi 1980	Letter
Baghdaadli 2002	Review of research on intervention for autism including diet
Bird 1977	Case study
Bowers 2002	Audit
Brudnak 2001	Not RCT
Cocchi 1996	Discussion paper
Cook 1997	Review article
Cornish 2002	Non random postal survey
Ellis 1999	Review article
Fitzgerald 1999	Not RCT, not dietary intervention.
Garvey 2002	Review of diet and autism
Howling 1997	Review article
Howling 1999	Editorial

Characteristics of excluded studies (*Continued*)

Israngkun 1986	Not RCT
Kidd 2002a	Review
Kidd 2002b	Review
Knivsberg 1990	Not RCT
Knivsberg 1995	Not RCT
Knivsberg b	Review
Lucarell 1995	'Control' group did not have ASD; no randomisation
O'Banion 1978	Case study
Reichelt 1991	Not RCT
Reichelt 1997	Not RCT
Shattock 2002	A review of the opioid-excess theory.
Sponheim 1991	Groups were of different ages, received different interventions, no separate controls.
Torisky 1993	Not RCT
Whitely 1999	A non-randomised controlled trial of gluten-free diet. Controls did not have autistic spectrum disorder
Whitely 2000	Qualitative analysis of feeding problems of a random sample of persons with autistic spectrum disorder.

Characteristics of ongoing studies

Study	**NIMH 2004**
Trial name or title	Diet and Behavior in Young Children with Autism Clinical trials no.: NCT00090428
Participants	Expected enrollment: 30. Ages eligible: 30 to 54 Months, both genders eligible; Inclusion Criteria: Autism spectrum disorder or pervasive developmental disorder Participation in applied behavioral analysis classes for at least 4 months, with at least 20 hours per week of service, and at least 1 hour of service in the home A score higher than 30 on the Mullen Early Learning scale Ability to maintain a gluten- and casein-free diet during the study In order to maintain study integrity, and due to frequent child assessments, enrollment is limited to a select population within the Rochester NY (USA) area
Interventions	Gluten- and casein-free diet
Outcomes	Primary Outcomes: Safety and Efficacy of the gluten free casein free diet
Starting date	Study start: January 2004; Expected completion: April 2008
Contact information	University of Rochester Medical Center, Rochester, New York, 14642, United States; Recruiting Carol Stamm carol_stamm@urmc.rochester.edu
Notes	Sponsored by the NIMH

ANALYSES

Comparison 01. Gluten and casein free diet versus normal diet

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Autistic traits (measured by DIPAB)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
02 Linguistic age (measured in months)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
03 Cognitive functioning / skills (measured by LIPS)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
04 Motor ability (measured by MABC)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected

INDEX TERMS

Medical Subject Headings (MeSH)

Autistic Disorder [*diet therapy; etiology; psychology]; Caseins [administration & dosage; adverse effects]; Cognition; Communication; Gluten [administration & dosage; adverse effects]; Mental Disorders [diet therapy]; Motor Activity; Peptides [urine]; Randomized Controlled Trials

MeSH check words

Child; Humans

COVER SHEET

Title	Gluten- and casein-free diets for autistic spectrum disorder
Authors	Millward C, Ferriter M, Calver S, Connell-Jones G
Contribution of author(s)	All reviewers contributed to the writing of the protocol and to the selection of trials. Graham Connell-Jones and Mike Ferriter extracted data. Claire Millward and Mike Ferriter wrote the text of the review.
Issue protocol first published	2002/1
Review first published	2004/2
Date of most recent amendment	25 August 2005
Date of most recent SUBSTANTIVE amendment	27 January 2004
What's New	We have learned of an ongoing USA-based Phase I randomized, double-blind, placebo Control, parallel assignment, safety/efficacy study, which is now within the references of this review. The study is anticipated to be completed in April 2008.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author

Date authors' conclusions section amended	Information not supplied by author
Contact address	Dr Michael Ferriter Research Fellow, Department of Research Nottinghamshire Healthcare NHS Trust Rampton Hospital Woodbeck Retford Nottinghamshire DN22 0HU UK E-mail: Michael.Ferriter@nottshc.nhs.uk Tel: +44 1777 247 357 Fax: +44 1777 247 221
DOI	10.1002/14651858.CD003498.pub2
Cochrane Library number	CD003498
Editorial group	Cochrane Developmental, Psychosocial and Learning Problems Group
Editorial group code	HM-BEHAV

GRAPHS AND OTHER TABLES

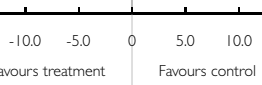
Analysis 01.01. Comparison 01 Gluten and casein free diet versus normal diet, Outcome 01 Autistic traits (measured by DIPAB)

Review: Gluten- and casein-free diets for autistic spectrum disorder

Comparison: 01 Gluten and casein free diet versus normal diet

Outcome: 01 Autistic traits (measured by DIPAB)

Study	Treatment		Control		Weighted Mean Difference (Fixed)	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	95% CI
Knivsberg 2002	10	5.60 (2.41)	10	11.20 (5.00)		-5.60 [-9.04, -2.16]



Analysis 01.02. Comparison 01 Gluten and casein free diet versus normal diet, Outcome 02 Linguistic age (measured in months)

Review: Gluten- and casein-free diets for autistic spectrum disorder

Comparison: 01 Gluten and casein free diet versus normal diet

Outcome: 02 Linguistic age (measured in months)

Study	Treatment		Control		Weighted Mean Difference (Fixed)	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	95% CI
Knivsberg 2002	9	66.60 (35.10)	9	55.70 (28.30)		10.90 [-18.56, 40.36]

Analysis 01.03. Comparison 01 Gluten and casein free diet versus normal diet, Outcome 03 Cognitive functioning / skills (measured by LIPS)

Review: Gluten- and casein-free diets for autistic spectrum disorder

Comparison: 01 Gluten and casein free diet versus normal diet

Outcome: 03 Cognitive functioning / skills (measured by LIPS)

Study	Treatment		Control		Weighted Mean Difference (Fixed)	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	95% CI
Knivsberg 2002	9	86.70 (38.50)	9	74.30 (31.40)		12.40 [-20.06, 44.86]

Analysis 01.04. Comparison 01 Gluten and casein free diet versus normal diet, Outcome 04 Motor ability (measured by MABC)

Review: Gluten- and casein-free diets for autistic spectrum disorder

Comparison: 01 Gluten and casein free diet versus normal diet

Outcome: 04 Motor ability (measured by MABC)

Study	Treatment		Control		Weighted Mean Difference (Fixed)	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	95% CI
Knivsberg 2002	10	26.30 (11.50)	10	27.80 (12.20)		-1.50 [-11.89, 8.89]