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A review of environmental contributions to childhood motor skills

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Abstract

Although much of children's motor skills have a heredity component, at least half of the variance is likely to be influenced by the environment It is important to ascertain features of the environment that are responsible so that toxins can be avoided, children at risk can be identified and beneficial interventions initiated. This review outlines the results of published studies and recommends the areas where further research is required. We found much confusion with little comparability concerning the ages or measures used. Few studies had sufficient power and few allowed for confounders. We found that research to date implicates associations with prenatal drinking ≥4 drinks of alcohol per day; diabetes; taking antidepressant drugs; being deficient in iodine or iron; dietary fish; and postnatal depression. The child appearing to be most at risk was born of low birth weight (but not due to preterm delivery); or with neonatal problems.

Keywords

motor coordination; environmental causation; neurotoxicants; socioeconomic factors

Introduction

There is growing interest in the importance of child development on the life chances of young people as they grow to adulthood.[1,2] The importance of early physical and cognitive development on the individual have been highlighted within the Marmot review, "Fair Society, Healthy Lives".[3] Dyson and colleagues concluded that early childhood development strongly influences many aspects of wellbeing progressing into adulthood including mental health, heart disease, competence in literacy and numeracy, criminality, and economic participation throughout life.[4]

Although considerable attention is paid to mental development, including features of speech and vocabulary, attention and memory, and other cognitive measures, development of motor

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skills tends to be neglected throughout childhood. Severe motor coordination difficulties can affect activities of daily living resulting in a diagnosis of developmental coordination disorder, which is associated with significant difficulties in other developmental domains, including mental health and educational attainment.[5–7] Early detection of a delay in motor development, whether of gross or fine motor skills, or of specific abnormalities can be of benefit to the child and family so that investigations can be undertaken and appropriate help given.[8] Even more useful would be the identification of factors that may be responsible for poor motor skills, so that primary preventive actions can be initiated.

In this paper we concentrate on the features that have been highlighted in the literature as being associated with motor skills as broadly defined. We do not consider cerebral palsy, or balance as a number of reviews have considered these.[9–11] Nor do we consider specific syndromes. Rather we concentrate on factors associated with motor skills in general.

General features of motor skills

Timing—The development of features of the human brain that influence motor development occur at various stages both during pregnancy, in the postnatal period, and during childhood.[12] The importance of timing is illustrated by a study that showed that if thyroid hormone deficiency occurs early in pregnancy, the offspring displays problems in gross motor skills; if it occurs later in pregnancy children are at additional risk of fine motor deficits.[13]

Nature or Nurture—Most studies of heritability estimate the genetic contribution to an outcome by comparing the concordance between monozygotic twins with that between dizygotic twins, or by assessing concordance between siblings in family studies. Estimates of heritability of hand motor skill are quoted as 41%[14] and 78%,[15] gross motor skill as 65%;[16] a review published in 1983 indicated that heritability of scores on different fine motor tests varies from 50% to 80% and of gross motor tests from 45% to 91%.[17] A different design tested twins who had been reared apart – they also demonstrated a very high heritability rate.[18] Although these twin studies indicate a strong genetic component, they do not preclude environmental influences on the development of motor skills. Below we examine the various environmental features that have been considered in the literature.

Methodology used in the literature search

A variety of sources were used to identify studies that had examined child motor skills in regard to aspects of the environment, including physical, psychological and psychosocial features. The major sources included: (a) an accumulated set of reprints that one of us [JG] had collected and key-worded since 1968 – this included chapters in books as well as academic papers (the keywords in this collection were derived from reading the full publication, not just the abstract); (b) a series of searches particularly of the more recent literature mainly using Google Advanced Scholar, with a variety of keywords, but always with ‘motor’ and ‘child’; (c) a search of PUBMED using keywords ‘motor skills’ or ‘motor development’ and ‘environment’. All articles were scanned for references to other publications of relevance.

It will be seen that a variety of different tests of motor skills have been used in the literature. These have been listed with appropriate references in the Appendix.

Chemical exposures

Toxic trace metals

Toxic metals such as lead, cadmium, mercury and arsenic are known to influence the development of the brain adversely. This has been shown using animal experiments, and also in humans after contamination from major accidents or exposure to high levels from occupations or residence near industrial plants. Less well studied are the possible effects of the range of exposures to which the general population may be exposed.

Lead—In Sydney, Australia, prenatal blood lead and yearly postnatal levels of 207 children were compared with the results of tests at age four years using the McCarthy. There was no significant relationship between lead levels at any age and motor or (mental) development.[19] There have been several studies in the USA: in 1984 Bellinger and colleagues[20] compared cord blood and six-month blood lead levels with scores on the Psychomotor Developmental Index on 249 six-month-old infants – they found no relationship with either measure of blood lead. A study in Cincinnati of 245 six-year-olds showed a negative association of neonatal blood levels but not maternal prenatal blood lead levels with fine motor coordination.[21]

Teeth were used in two studies. Grinding up the milk teeth enables an assessment of lead exposure of the child during early childhood, but mostly during the time period prior to shedding the teeth. Winneke and colleagues[22] collected teeth from 115 schoolchildren and reported that the level of lead was 'nearly' significantly negatively associated with speed of finger tapping. Needleman and colleagues[23] had tested 132 adults and shown that higher lead levels in their childhood teeth were significantly related to slower finger tapping and poorer hand-eye control.

Thus, of the studies available the evidence suggests an association between lead levels in the child and reduced fine motor skills which may continue into adulthood. There is currently insufficient evidence to implicate prenatal exposure.

Mercury—In contrast with lead there have been many studies on the possible effects of mercury. For example, in Boston 341 pregnant women were enrolled between 1999 and 2002. Blood levels of mercury were compared with their offspring's fine motor skills using WRAVMA at three years. The results showed that the children had lower average scores if the maternal blood mercury level was in the highest compared to the lowest decile.[24] A study of 374 children in Poland compared the level of mercury in cord blood with results on the Bayley at ages 12, 24 and 36 months: there was a reduction in motor development at 12 months but not thereafter as mercury levels increased.[25] In the Faroe Islands prenatal mercury levels measured in maternal hair were positively associated with adverse motor function at age seven years.[26] Of the 1022 children, 878 were contacted and tested again at age 14; there was an inverse association between the maternal prenatal mercury level and the speed of finger tapping, but there was no such association with postnatal levels of mercury in the child.[27] In the Seychelles a pilot study of 87 children for whom maternal prenatal mercury was measured were followed up at nine years: two tests of visuo-motor coordination showed improving scores with increasing prenatal mercury.[28] In the main study 779 children were followed up at nine years of age. Maternal hair mercury was not associated with any of the motor tests except one where it was adversely associated, but only in boys.[29] At age ten years in this cohort, no association was shown with visual motor coordination.[30]

In response to general anxiety in regard to the small doses of mercury in many vaccines, 1047 children were tested at ages 7–10 years and the results compared with the amount of thiomersal [the mercury compound used] that they had been exposed to prenatally, neonatally, and up to seven months of age. There were no signs of adverse effects - in fact beneficial effects associated with mercury levels were found with finger tapping in the dominant hand.[31]

There has been one primate experiment. Monkeys dosed with mercury from birth to age 7 years were compared with controls. By 13 years of age there was evidence that they had started to become clumsy. A second set of monkeys, treated from pregnancy to four years of age showed changes in manual sensitivity many years after the treatment had stopped. Both groups of monkeys had impaired vibration sensitivity.[32]

The delay in motor effects shown was also found in humans exposed to the Minamata pollution episode in Japan. This occurred when an industrial pollution incident resulted in high levels of mercury in the local seafood, especially shellfish,- eaten by the surrounding population; 40 years later tests showed increasing difficulty in performing daily activities compared with controls.[33]

Thus there is conflicting evidence in regard to prenatal and early child effects of mercury on motor development in childhood. However the evidence from primate studies and the Minimata accident raise the possibility of an adverse effect many years after exposure.

Arsenic—Most studies of the adverse effects of arsenic have occurred in developing countries where water drawn from a well can have high levels. Arsenic is known to cross the placenta; it occurs in seafood and other features of the diet as well as the water supply and soil.[34] In a major longitudinal study of around 2000 pregnancies in Bangladesh, with measures of arsenic at 8–9 and 30 weeks gestation, the Bayley tests of psychomotor development at seven months[35] and at 18 months[36] showed no association with maternal arsenic levels. One cross-sectional study has, however, shown an association: the arsenic levels in 304 children aged 8–11 were negatively associated with measures of motor function and fine motor coordination.[37]

Manganese—Manganese is both an essential nutrient and a known neurotoxicant. In animal experiments it produces motor abnormalities – and these are also found in adults occupationally exposed.[38] Given this, it is somewhat surprising that there have been few studies on infants and children. There have been two reviews of the literature concerning possible neurotoxic effects of exposures of the fetus or child to manganese. The first reviewed 12 studies,[39] only one of which had measured motor developmental outcomes. That indicated that the level of manganese in cord blood was associated negatively with psychomotor indices at age three years, but not at six years.[40] The second only reviewed studies published between January 2011 and July 2012.[38] Four studies had assessed effects on motor outcomes; only one of these was longitudinal – the authors had found no association between the child's manganese levels and motor development at 12 or 24 months as measured using the Bayley in 448 infants in Mexico.[41] The cross-sectional studies included an association in 11–14 year-olds between level of manganese in the soil and a reduction in motor coordination in Italy;[42] a further study in Mexico examined 195 children aged 7–11 years and found "a subtle negative association of manganese exposure with motor function and fine motor coordination";[43] in Bangladesh a study of levels of manganese in 8–11 year olds showed no association with motor function or fine motor coordination.[37]

Other toxic metals—Few studies have been carried out on other toxic metals. A review of cadmium effects on health in 2006 suggests a possible association with motor development, but indicates that there is very little in the way of information or research in the area.[44] In regard to aluminium, a study of offspring of rats exposed to aluminium lactate prenatally reported that locomotor coordination was reduced,[45] but there do not appear to have been any human studies.

Deficiencies of essential trace metals

In contrast to studies of potentially neurotoxic chemicals which cannot be used in confirmatory experiments on humans, studies of nutritional deficiencies may conduct randomised trials ethically.

Iron—A number of randomised controlled trials [RCTs] have been carried out during pregnancy and childhood. For example, in Nepal, a complex RCT design using several micronutrients found that fine motor functioning was positively associated with prenatal iron/folic acid supplementation in an area where iron deficiency is prevalent. There was no separate association with the other micronutrients.[46] Elsewhere a group of iron deficient formula-fed children were randomised to iron-fortified or non-fortified formulae; psychomotor development of the two groups differed at nine and 12 months but not at six or 18 months.[47] An RCT of iron supplementation in 614 preschool children in Zanzibar found that motor development 12 months later had improved in those who had been supplemented, but only in those children who had a Hb $<$90g/l.[48]

There have been a number of reviews: in 1989, Parks and Wharton concluded that iron deficiency in childhood affects psychomotor development – but can be reversed by giving iron.[49] In 2001 an editorial in the British Medical Journal stated that iron deficiency is associated with impaired psychomotor development.[50] In 2010 a systematic review of the literature concluded that iron supplementation of non-anaemic infants tends to result in improved psychomotor development, but seems to have no effect on mental development or behaviour.[51]

Iodine and thyroid hormone deficiency—An RCT using iodised oil and placebo (saline) injections to women prior to pregnancy in an area of Papua New Guinea with extreme iodine deficiency resulted in almost complete lack of cretinism and reduction of major motor problems in the offspring.[52] A follow-up study of children born to women in the trial showed a benefit in manual function in the group who had been born to women injected with the iodised oil.[53] Subsequently there have been trials of iodine supplementation in Europe that have found effects on motor skills; they include a Spanish trial that found improved scores on both gross and fine motor coordination at 18 months if the supplements were given in early compared with late pregnancy.[54] A study on 10–13 year old children living in a mildly iodine deficient area in Albania found that iodine supplementation at this age improved their fine motor skills.[55]

The mechanism by which iodine deficiency may have such an effect is thought to involve thyroid hormones. If thyroid hormone deficiency occurs early in pregnancy, the offspring display problems in visual attention, visual processing (i.e. acuity and strabismus) and gross motor skills. If it occurs later in pregnancy, children are at additional risk of subnormal visual (i.e. contrast sensitivity) and visuospatial skills, as well as slower response speeds and fine motor deficits.[13] A study of thyroid hormones in cord blood in 62 children followed up at 5–6 years found negative correlations between TSH and both general motor and fine motor abilities.[56]

The evidence for a beneficial effect of iodine supplementation in early pregnancy seems unequivocal, but Nyaradi and colleagues utter a note of caution since an RCT of high maternal prenatal iodine supplementation in Spain reportedly resulted in lower psychomotor infant development.[57]

Other deficiencies—Preterm infants are at high risk of sodium deficiency. A long-term follow-up at 10 –13 years of preterm (<33 weeks) infants involved in an RCT of sodium supplementation showed that the supplemented group performed better on motor function.[58]

Zinc deficiency has been studied mainly in relation to child health, and RCTs have been undertaken with regard to morbidity and mortality, but few, if any, studies have looked at child development in general and motor skills in particular.[57] However, in an area of common micronutrient deficiency in Bangladesh, an RCT of supplements was undertaken with 221 infants in five groups: (a) iron, (b) zinc, (c) iron + zinc, (d) multivitamins and minerals, (e) riboflavin. The results showed that at 12 months the two groups administered both zinc and iron (i.e. (c) and (d)) had better motor skills.[59]

Although selenium is recognised as being important for health, there have been few studies assessing the effect of selenium deficiency on child development. A cross-sectional study of selenium in children in Bangladesh showed a positive association with motor function at ages 8–11 years.[37] One of the potential benefits of a high selenium intake lies in its interactions with mercury; a recent review stated that “effects of high methylmercury exposures depend on dietary selenium intakes and selenium status”.[60]

Other pollutants

PCBs and other organohalogens and pesticides—Polychlorinated biphenyls (PCBs) are a group of chemicals that, although created in industrial processes, persist in the environment and are ingested in the food chain. They include dioxins. There were several summaries of the literature concerning effects on children prior to 2002. In 1989 a brief review reported associations of prenatal PCB levels with motor impairment in newborns, and motor delay at six months.[61] A review in 1997 of effects of prenatal PCBs in humans and animals demonstrated effects on psychomotor development.[62] Finally a 2001 review of the effect of prenatal PCBs on the infant demonstrated a decrease in motor skills in the first months of life in four of five studies that had examined this. There was no apparent adverse effect of PCBs in breast milk.[63] This finding has been queried by a study of 171 infants followed prospectively. The level of PCBs in breast milk was inversely related to the child's motor scores at 30 months.[64]

Several studies of PCBs have been published since 2001. In Japan the bloods of 134 pregnant women were assayed for dioxins and PCBs. The offspring were followed up and tested at age six months using the Bayley. Some of the dioxin isomer levels were negatively related to the motor development of the infant – with a stronger effect than shown for mental development.[65] In the Netherlands, levels of PCBs in prenatal blood and in breast milk were measured in 376 mothers; negative associations were found between PCBs and motor development in their children at school age in those with less optimal homes, but not in those raised in optimal environments.[66] A study of 917 births in the Faroes, with PCBs measured in cord blood, compared levels of different isomers with the results of a finger tapping test: no significant associations were found.[67] However, in Guadeloupe, the organochlorine insecticide chlordecone was detected in cord blood in 75 of 130 infants. They were shown at seven months to have reduced fine motor score on adjustment (P=0.002).[68]

A study of 62 children aged 5–6 years compared their motor skills with levels of 12 organohalogens in their mothers' blood in late pregnancy. Some associations were positive and some negative. For example, brominated flame retardant levels were associated with worse fine motor abilities but better motor coordination.[56]

Pesticides in general—The only studies we found on children used indirect measures as a proxy for exposure to pesticides. In Ecuador 121 children aged 1–2 years were assessed according to their mother's occupation. Children of those women who worked in the flower industry (and were presumed to be exposed to pesticides) had reduced fine motor skills compared to the other children.[69] In Mexico, Guillette et al[70] compared 33 children living in an area where multiple pesticides were used with 17 children of similar ages living in an area without such exposures. Those in the pesticide area had worse gross and fine motor ability.

Other Pollutants—There were two studies relating to other chemicals. Toluene is an important solvent used widely in industry. One study has shown that women exposed to toluene at work showed marked deficits themselves in manual dexterity.[71] Another study was concerned with 210 children exposed to nitrogen dioxide from traffic in urban and rural areas where NO_2 exposure was estimated by means of land use regression models. Gross motor ability was worse when there were higher levels of NO_2, though this was not statistically significant.[72]

Social drugs

Alcohol—Women drinking alcohol in excess during pregnancy are known to damage their children's neurocognitive development. A major study in Washington State of women drinking more than four drinks per day found that the offspring, examined at eight months of age, had impaired motor skills compared to those of non-drinkers.[73] Follow-up of the 402 offspring involved in the study included testing them as adults; their fine motor coordination showed no effect associated with moderate alcohol intake during pregnancy – but the group that were exposed heavily (>4 units per day) had poorer coordination scores.[74] The only other study that we could find involved children of 156 women in France who had been interviewed during pregnancy. At age 4.5 years, children born to the women who had drunk ≥21 glasses of alcohol per week had an excess of minor neurological signs compared to those born to non-drinkers.[75]

A systematic review suggests a negative effect of prenatal alcohol on motor coordination of the offspring but only when the maternal consumption exceeded a certain level. Of the six cohort studies reporting a maternal alcohol intake exceeding four drinks/day, all but one showed a negative effect of this on the motor function of the offspring; conversely of the three studies reporting total intakes <10 drinks/week, none showed a deleterious effect on the offspring's motor function. However, the authors pointed out that a possible adverse effect of binge drinking has still to be settled.[76]

The topic of breast feeding of women who drink alcohol (which is known to be transferred to the breast milk) has been considered in two studies. One, in Washington State, showed a negative effect of alcohol in breast milk on offspring motor development at 12 months.[77] The other, in the UK, with much larger numbers failed to replicate this finding when assessing the motor development of children using the Griffiths test at 18 months.[78]

Cigarette smoking—There is substantial evidence of the effects of maternal smoking on the development of the fetus resulting in adverse consequences in childhood and into adulthood. Strangely, although there have been a number of longitudinal studies assessing the effects of maternal prenatal cigarette smoking on child cognitive development, there have been few looking at motor skills. One study tested 282 neonates with the Neonatal Behaviour Assessment Scale; this showed an association between *in utero* exposure to both maternal smoking and her exposure to passive smoking and adverse scores on the 'motorsystem cluster' (which includes tests of motor performance, quality of movement and muscular tone).[79] The Streissguth study, although focussed on prenatal alcohol exposure, did look at the possible effects of prenatal smoking, but found no significant effect on motor coordination.[73] However, a UK study of 13207 children in the National 1958 Birth Cohort found smoking during pregnancy to be associated with subtly reduced motor competence of offspring, particularly on the non-dominant side, at age 11.[80] In Canada 503 adolescents aged 12–18 years were tested for motor dexterity; there was no association with history of fetal exposure to maternal smoking.[81] Elsewhere, 320 adolescents aged 16 who had been followed from birth were evaluated. There were significant and independent associations of maternal prenatal smoking with processing speed and deficits in visual–motor coordination.[82] Thus it is possible that there may be some deficits in motor skills with prenatal cigarette smoking. The likelihood of a complex association has been evidenced by the demonstration of gene-environment interaction (between maternal smoking measured using cord blood cotinine and genes associated with the metabolism of nicotine) and fine motor skills at two years of age.[83]

Cannabis and hard drugs—Willford and colleagues showed that maternal prenatal exposure to cannabis had similar adverse effects on processing speed and deficits in visual–motor coordination in offspring at age 16 as they had found with prenatal cigarette smoking (see above) – and since cannabis exposure usually involves using tobacco at the same time, it is possible that the mixture is important rather than the cannabis *per se*.[82]

Although a drug that is only taken intermittently, ecstasy (MDMA) is often taken in the early stages of pregnancy before the woman is aware that she is pregnant. A recent UK study reported on 12 month old children of 28 women who had taken ecstasy; they were examined using the Bayley and compared with 68 controls born to women with no such history. The exposed children were delayed in motor development, but only if their mothers had been heavier users (defined as taking more than the median of those exposed).[84]

Studies following up women who had used hard drugs in pregnancy have tended to concentrate on cocaine exposure. In spite of one study by Arendt et al comparing 98 prenatally exposed two year-olds with 101 controls which showed poorer fine and gross motor development in exposed children,[85] a systematic review in 2001found evidence of poorer motor scores only up to the age of seven months but not thereafter.[86] The Arendt study was excluded because recruitment was not prospective – in fact the authors had recruited the two year-olds and obtained the history of cocaine exposure from medical records and maternal interview. It is questionable as to whether that means it should have been discarded. A further study published in 2000 was not included. It compared two groups each of 25 children from poor socioeconomic backgrounds – one of these groups of children had been exposed to cocaine prenatally. Examination at 12 months showed better fine motor skills in those not exposed. In parallel, two groups of children, with similar prenatal exposures, who had been adopted by parents living in more advantaged circumstances, showed similar differences in fine motor skills.[87]

Caffeine—The Washington State study that had focussed on the adverse effects of alcohol also assessed whether there were any adverse consequences of maternal caffeine intake. No significant associations were found in offspring at eight months,[73] four years[88] or seven years.[89] There do not appear to be any other studies looking at the possibility of maternal caffeine exposure having an association with her offspring's motor skills. This is confirmed by a detailed review of the literature in 2002.[90] Animal studies have suggested that caffeine may have beneficial effects in regard to toxicants – Bjorklund and colleagues[91] for example showed that the adverse effect of prenatal exposure to mercury was reversed by giving the animals caffeine. They suggested that adenosine A_1 and A_{2A} receptors were involved in the alterations triggered by caffeine exposure during development and which reduced vulnerability to methylmercury.

Dietary factors

Studies of different aspects of the diet on the child's motor development tend to have concentrated on contaminants such as mercury, pesticides and PCBs (considered earlier), deficiencies (particularly iron and iodine) and seafood, particularly focussing on omega-3 fatty acids.

Seafood exposure—There have been several longitudinal birth cohorts that have looked at the association between maternal seafood consumption and the development of cognitive skills, but the child's motor skills have been considered less frequently. In the USA and the UK, there have been two studies that have considered motor skills. In Boston, 341 pregnant women, enrolled in 1999–2002, had provided information on fish intake in the second trimester; their offspring were tested at three years for fine motor skills using the WRAVMA. The study showed that the children had significantly higher scores if their mothers ate > 2 portions of fish per week.[24] A detailed study of the Avon Longitudinal Study of Parents and Children [ALSPAC] showed that maternal prenatal seafood consumption was strongly related to beneficial outcome in fine motor skills of her offspring at age 42 months assessed by parental questionnaire. It was assumed that this was likely to be influenced by the omega-3 fatty acids to be found in fish.[92]

A study in the Seychelles showed that fish in the diet of pregnant women was an important source of essential elements such as iron, zinc, selenium and iodine.[93] This has to be balanced against the toxicants found in fish, especially mercury and PCBs. Much of the research on the effects of seafood has concentrated on the neurotoxins, rather than the overall seafood intake. Nevertheless in 2006 Mozaffarian and Rimm concluded, after reviewing the evidence, that 'for women of childbearing age, benefits of modest fish intake … outweigh the risks'.[94]

Omega-3 fatty acids—There have been a number of studies that have looked at actual prenatal measurements of fatty acids. A cohort in the Seychelles measured the omega-3 and omega-6 levels in the mother's prenatal blood. On examining the offspring at ages nine and 30 months they found beneficial development using the Bayley PDI as the mother's prenatal omega-3 blood level increased.[95] In the Netherlands, 306 cord blood levels of the omega-3 fatty acid DHA were positively associated with the total motor and the quality motor scores as measured on the MMT when the children were aged seven, but there was no association between motor measures and the seven-year-old's blood level of DHA.[96]

There have been a few randomised controlled trials (RCTs) in pregnancy and early childhood:

i. 98 pregnant women in Australia were randomised to either: (a) fish oil, containing DHA and EPA or (b) olive oil. Seventy-two of the children were tested at age two and a half years using the Griffiths test. The results showed that group (a) had higher scores for hand-eye coordination than group (b). There was also a correlation between the omega-3 cord blood levels and this outcome.[97]

ii. 79 term infants aged ≤ 5 days in the USA were randomised to (a) formula + iron; (b) formula + iron + DHA; (c) Formula + iron + DHA +AA. Of these, 56 were tested at 18 months using the Bayley. The study showed that ability scores for both groups (b) and (c) were significantly greater than group (a) for motor development.[98] In 2003 Auestand and colleagues carried out a similar but larger RCT in the USA with three groups – formula/formula + DHA/formula + DHA + AA. Follow-up at 39 months showed no difference in visuo-motor coordination tested with the Beery Index.[99]

A treatment study of children aged 5–12 years with DCD in the UK randomised children to two groups: one was supplemented with omega-3 + omega-6 and the other with placebo for three months, there was then a cross-over for a further three months. The study showed no difference in motor skills as the result of the supplements.[100]

Breast feeding—There have been a number of relatively small follow-up studies concerned with breast feeding: In Brazil 232 infants were examined at age12 months. Breast feeding at one month was associated with mental but not motor development.[101] In Scotland an examination of 592 18-month-old infants using the Bayley found a significant benefit of breast feeding at two weeks on mental development, but no such effect for motor development.[102] Similarly in Spain a study of 249 infants aged 18 months showed benefits of duration of breast feeding on mental development, but not on psychomotor development.[103] In Groningen follow-up at age nine years of 135 breast-fed and 391 formula-fed infants found that, after adjustment, neurological abnormalities (which included motor coordination) were more likely in the formula-fed group.[104]

By far the largest study, that of the British Millennium cohort, using results collected at nine months, found a protective effect of any breastfeeding on the attainment of gross motor milestones to be "attributable to some component(s) of breast milk or feature of breastfeeding and not simply a product of advantaged social position, education, or parenting style, because control for these factors did not explain any of the observed association." In contrast, the association found with fine motor delay was explained statistically by biological, socioeconomic, and psychosocial factors.[105] In an earlier large cohort study (the 1970 British Births), examination of the children at age five years had demonstrated a benefit of breast feeding on visuomotor coordination skills that increased with duration of breast feeding and was resistant to adjustment for social confounders.[106]

Other dietary factors—A pregnancy RCT of supplementation with multiple micronutrients in Indonesia resulted in improved motor development among the offspring in the intervention group in the preschool period.[107] Earlier an RCT in Finland had recruited 1062 infants aged seven months in the years 1990–96. The intervention group had dietary advice on giving the child a low saturated fat and low cholesterol diet; the controls were given usual dietary advice. Less than half (496) were assessed at age five using failure on the Bender Gestalt Test. There were no differences in either gross motor or visual motor skills between the two groups.[108] In Nepal, 390 children aged 10–13 years were tested using the Movement ABC; their mothers had participated in a vitamin A/placebo trial during pregnancy. There was no significant difference between the two groups in overall score, but no analyses were published to enable the reader to assess whether there were differences in the fine or gross motor skills.[109]

Maternal disorders and medications

Maternal epilepsy—It is well known that many anticonvulsants have teratogenic effects (congenital defects include cleft lip/palate and spina bifida). Surprisingly few studies, however, have followed-up children born to women with epilepsy to assess possible associations with motor skills. One relatively old study of births in Berlin between 1976 and 1983 compared 15 month old infants of epileptic women on monotherapy during pregnancy with those on polytherapy and a control sample. The group with mothers on polytherapy had significantly lower scores on the Bayley motor test and the motor test within the McCarthy compared to both the other groups.[110,111] In Sweden, 100 infants born to epileptic women who had taken anticonvulsant medication during pregnancies between 1985 and 1995 were compared with 100 matched controls at nine months of age using the Griffiths: there was no difference between the two groups in psychomotor development.[112] More recently, a study of children prenatally exposed to sodium valproate (a treatment for epilepsy) in Australia found major reductions in IQ, but little difference in processing speed (a measure of graphomotor skills).[113]

Maternal diabetes—Maternal diabetes, especially insulin-dependent diabetes, is associated with a variety of adverse outcomes: in particular it has a teratogenic effect with an excess of specific congenital malformations. Although the mechanism is unproven it is likely to be related to blood glucose levels.[114] There have been some small studies following up the offspring of women with diabetes. For example, comparison of 4–5 year-olds born to women with insulin dependent diabetes (n=76) and controls (n=92) in Copenhagen in 1980–83, used the McCarthy test of motor ability as well as the Qualitative Motor Developmental Score. For both assessments the children born to the diabetic mothers scored worse than the controls ($P < 0.001$).[115] Two parallel studies in Israel examined school children born to mothers with either insulin-dependent (n=57) or gestational diabetes (n=32); each group was compared to 57 control children. The authors report that the offspring of the insulin-dependent women had similar IQs but had worse fine and gross motor development than the control group.[116] A review by Ornoy[116] confirmed that in follow-up studies, children born to diabetic mothers generally have normal IQ results, but motor function is often impaired.

Prenatal infections—Although we now know that acute infections in pregnancy (such as influenza) can have long-term effects on the offspring's brain, especially in regard to an increased risk of schizophrenia,[118] there have been no longitudinal studies that we could find that assessed whether such prenatal infections are associated with the offspring's motor skills. There was just one study that involved chronic prenatal exposure to infection: Foster and colleagues[119] examined 62 children born with HIV (by definition their mothers will have had HIV during pregnancy); they had increased gross motor difficulties and abnormal neurological signs compared with non-infected children.

Maternal depression—In Bangladesh a cohort study found no evidence of any effect of prenatal depression on infant motor development at 8–9 months;[120] in the USA a cohort study of 1021 births in Boston found no effect of exposure to prenatal depression on visuomotor skills of the offspring at three years of age using the WRAVMA.[121]

However there appear to be discernible effects if the depressed woman takes medication in pregnancy. For example, in the USA, of 44 pregnant women with severe depression, 13 had decided not to use medication and 31 were prescribed SSRIs (selective serotonin reuptake inhibitors). The offspring were tested using the Bayley at ages 6 – 40 months. This showed that children exposed *in utero* to the medication had lower psychomotor developmental indexes and reduced motor quality compared to the non-exposed.[122] In Canada, 32 pregnant women were prescribed an SSRI: compared with controls their offspring exhibited scores significantly lower on the gross motor subscale of the BSID-III, and this was not explained by underlying maternal depression.[123] In Australia 22 infants of women who had taken antidepressants in pregnancy were compared with 19 non-exposed. The authors report that 'children exposed to antidepressant medication in pregnancy scored lower on motor sub-scales in particular on fine motor scores than non-exposed children'; there was no association between maternal depression *per se* and neurodevelopment.[124] A small study of 6 neonates exposed to SSRIs *in utero* compared with 61 controls showed differences in autonomic and gross motor activity between those who were or were not exposed after controlling for active maternal psychiatric illness.[125]

The most reliable study on this topic used linked maternal prenatal prescription to offspring development data in Denmark.[126] There, routinely at age 7–10 months, the child undertakes the BOEL test, a psychomotor developmental test from which the items on hearing were excluded. The proportion of children failing this test was compared between 82 women who had taken benzodiazepines in pregnancy, 50 taking antidepressants, 145 anticonvulsants, 63 neuroleptic drugs and 722 controls. All the children born to women taking the drugs had elevated odds of failing the test – the adjusted odds ratios were 8.1 for the benzodiazepines, 8.0 for antidepressants, 15.5 for anticonvulsants and 4.1 for neuroleptics. However, the study was unable to assess whether the medications or the disorders were responsible.

A systematic review of offspring outcomes relating to mothers taking antidepressants prenatally, considered all publications from 1973 to February 2010.[127] Although the authors' overall conclusion was that there were few demonstrable adverse effects, they only found two studies that specifically examined motor function: both reported adverse effects as described above.[122,126]

Postnatal depression has been shown to have an adverse association with offspring motor development in Barbados, where 226 infants were studied at six months of age,[128] and in Bangladesh where 652 infants were examined at 8–9 months.[120] However no similar effects on motor development were found in Australia (n = 360),[129] but there were negative effects on fine motor skills reported from a study of 693 infants in Crete tested at 18 months of age using the Bayley.[130]

Stress—Depression is often a response to stress. A study in the USA measured beta-endorphins, a marker of stress, in maternal and cord bloods for 106 infants. The authors found that a complex and stressful delivery resulted in increased levels in cord blood. Contrary to expectation, follow-up at age three years showed that children born with lower cord blood levels had lower motor scores on psychometric tests.[131] There do not appear to have been any studies looking at prenatal stress as identified using life events, or measures of anxiety, in regard to motor development.

Prenatal aspirin—A large RCT was undertaken among pregnant women who were thought to be at risk of pre-eclampsia and/or fetal growth retardation (the CLASP study). A sample of the offspring was followed up at 18 months - although not statistically significant, a group in which the mothers had taken aspirin during pregnancy were less likely to fail to achieve the age-appropriate fine motor development test questions derived from the Denver test (28/2146 v. 39/2219).[132]

Obstetric and neonatal outcomes

Preterm delivery

There have been a large number of studies following up and examining very preterm infants (e.g. <32 weeks). All find major developmental problems, but will not be reviewed in this study. Here we have looked at broader definitions of preterm delivery. A follow-up at age six years of 156 children born at <35 weeks showed high levels of perceptual-motor problems; in addition 44% scored <15th centile of the Movement ABC.[133,134] There have been few studies that have looked at infants born at <37 weeks – in an American study, 134 children who were delivered <37 weeks were compared with 134 term deliveries and tested at age four. The preterm group were worse on fine motor, but not gross motor skills.[135] A study in Crete examined children at 18 months using the Bayley; the preterm infants had lower scores on both the fine and gross motor scales, but these results did not reach statistical significance.[130]

A study of 12–13 year olds in Australia compared their motor skills tested using the Movement ABC with their gestational age at birth: this showed a strong linear association for the total score, but that when divided into its subcategories, the association was predominantly due to an association with ball skills rather than manual dexterity.[136]

Birth weight

There are a large number of studies of very low birth weight infants (<1500g). In this review, however, we concentrate on infants of low birth weight defined as <2000g or <2500g. They mainly show the same results as for preterm studies – namely a higher level of poor motor coordination of various types. In 1986 a literature review indicated that low birth weight infants are more likely to have problems in visual motor integration.[137] More recently, examination of seven-year-olds demonstrated that low birth weight (<2000g) infants showed worse fine and gross motor coordination.[138] In Helsinki, 386 neonates recognised as being at high risk because of various conditions and 107 controls were given a test of motor impairment and a neurodevelopmental assessment at age nine years. The analysis demonstrated an association between increased impairment and low birthweight.[139] Also in Finland, parental questionnaires completed on over 8000 eight-year-old children in the North Finland Birth Cohort indicated that those born <2500g were poorer in motor skills than the rest of the cohort.[140] An ingenious study examined, at age nine years, 22 pairs of twins who had had a birth weight difference between the pair of at least 25%. In general the smaller of the twins had significantly poorer fine motor performance-balance-coordination, as well as of visuomotor perception.[141]

The assumption is made in these studies that the low birth weight is a marker of intrauterine growth retardation rather than preterm delivery. This was illustrated in the National Collaborative Perinatal Project.[142] Follow-up at seven years included testing using Bender-Gestalt score. Those defined as IUGR were defined as having a birth weight ≤2500g in infants born at term (gestation 37+ weeks): they had significantly lower visuo-motor scores (n= 33,000). However, when they compared the outcomes of 148 pairs of siblings where only one was IUGR, there was no difference in score. One study has looked at other markers of fetal growth: a follow up of 194 infants born at <1500g tested at age eight years showed that motor impairments in this group were closely related to head circumference at birth and subsequently.[143] In Pakistan, 1476 infants born in 1984–87 were examined monthly and assessed for milestones. Gross motor ability was defined by the age at onset of walking and fine motor development by the age at which they could build a tower of three cubes. Thinness at birth (birth weight for length) was negatively associated with both measures and birth length was positively associated with fine motor development.[144]

Labour and delivery

Most studies of features of labour and delivery that considered possible developmental harm to the offspring were undertaken many decades ago. For example the American NCPP, following births in the period 1958–65, showed that complex patterns of labour were correlated with eight month motor development scores using the Bayley.[145] An early RCT of vacuum extraction v forceps showed no difference in motor development or psychomotor features at age four.[146] Later, however, a study in Germany of 350 infants born 1986–88 and followed at ages three months, 24 months and four and a half years reported that complications of pregnancy and delivery were related to motor delay at each age.[147]

Birth asphyxia

There has often been an assumption that children with developmental defects are more likely to have had difficult deliveries leading to birth asphyxia and a stormy neonatal course. However few studies have examined children followed up after signs of birth asphyxia. One study compared 48 term infants with mild birth asphyxia with 43 term controls at 12 months using the psychomotor scales of the Bayley. There was no difference between the two groups.[148] A Norwegian study used the Norwegian Birth Registry to select infants with low five-minute Apgar scores, together with samples with higher scores; parents were sent questionnaires enquiring about the child's development. The children with low Apgar scores were more likely to have minor motor disabilities and to develop skills later than usual, but only if the neonate had had signs of an encephalopathy.[149]

Neonatal morbidity

In New Zealand the population-based Dunedin Birth Cohort Study assessed 986 children for their motor ability using the McCarthy Motor Scale at age five years: there was no relationship between motor ability and perinatal complications.[150] In Finland 386 children who had been recognised as being at high risk because of various conditions in the neonatal period were compared with 107 controls using a test of motor impairment and a neurodevelopmental assessment at age nine years. The children with neonatal problems scored significantly worse on motor impairment in particular if they had neonatal signs of cerebral depression, long duration of hyperbilirubinaemia or respiratory problems other than respiratory distress syndrome.[139] Furthermore, preterm infants tested at four years revealed that fine motor delay was greater if the infant had been ill in the neonatal period.[135] Children at age 12–14 years were shown to have different types of coordination disorder if they had had problems in the perinatal period.[151]

A more focussed study examined 111 children who had had meningitis in the neonatal period compared with two different sets of controls at age 9–10 years using the Movement ABC. Those who had had meningitis had significantly poorer motor skills.[152]

Childhood

Growth and nutrition

Studies relating growth and nutrition in childhood to motor skills have been based in low and middle income countries. In Pakistan, 1476 infants born between 1984 and 1987 were examined monthly. Postnatal stunting was linked to worse gross motor skills, and postnatal wasting to both worse gross and fine motor outcomes.[144] In Guatemala, follow-up of 357 children to age three years showed that those who were stunted had much poorer motor development (using the Bayley) and those who were severely stunted were even worse; the relationship with motor development was stronger than with mental development.[153] In a rural area of India, follow up of children who had been malnourished in the first five years showed, at age 10 – 12 years, marked deficits in mental performance, but no differences in manual dexterity.[154] In Bangladesh, a longitudinal study of over 2000 children showed that, in an area where stunting of growth is prevalent, the child's height-forage at 15 months was related to both the age at achievement of milestones and the results of the Movement ABC.[155]

Gross malnutrition is rare in high income countries, but examination of 51 individuals with anorexia nervosa and 51 matched controls at ages 16 and 21 years revealed a significant excess of cases with dysdiadochokinesis at each age ($P < 0.01$). *[Dysdiadochokinesis* is the inability to execute rapidly alternating movements, particularly of the limbs].[156]

General Health

A prospective American study starting in pregnancy [n=561 women] found that the infants who had had colic in the first three months showed no association with motor skills at age five years, but the children with prolonged crying of no known cause showed fine motor deficits at this age.[157] In New Zealand, the Dunedin Birth Cohort Study followed up 986 children and assessed their motor ability using the McCarthy Motor Scale at five years. There were significant negative associations of motor skills with maternally reported general health of the children at three years.[150] In Liverpool, 115 survivors of meningococcal infection were compared with 115 matched controls some 8–11 years later. The cases were more likely to have poor motor coordination [OR 4.1; 95% CI 1.4, 11.6].[158]

Other

Children were screened for hypermetropia (hyperopia or long-sight) at 8–9 months of age in the UK; those identified and a set of controls were tested at four years using the Movement ABC. The hypermetropic group were significantly worse in regard to fine and gross motor development.[159]

In a single study of 43 mother-infant dyads, motor development was assessed according to the use of equipment in the home, such as playpen, high chair; the results showed reduced development with increasing numbers of types of equipment for the child.[160]

Social circumstances

In Germany, 350 infants were examined at ages 3 months, 24 months and 4.5 years - significant associations with motor delay included low parental education, parental psychiatric disorder, poor coping skills, the study pregnancy being unwanted and overcrowding in the home.[147] In Northern Ireland social disadvantage using area deprivation measures was associated with reduced motor skills at ages 4–5 and 7–8years.[161] The five year assessment of motor ability in the New Zealand (Dunedin) Birth Cohort Study used the McCarthy Motor Scale. There were reduced motor skills with increased family adversity and poor child rearing attitudes.[150] In the British 1958 National Birth Cohort, visuomotor coordination was significantly worse in single parent families.[162] In the Netherlands, examination of children at 12 – 14 years reported that different types of coordination disorder were associated with low social class.[163] In Brazil, a community sample of 561 infants were followed until 18 months of age. Multivariable analysis showed positive independent associations between motor ability and both household income and the amount of space within the home.[164] An intriguing study of 50 children born to women living in socially deprived circumstances compared the 25 who were adopted into socioeconomically good homes, with the 25 who remained with their mother; the adopted group showed better fine motor skills at 12 months. However, follow-up of a separate 50 children who had been exposed to cocaine prenatally showed no improvement in the 25 who had been adopted.[87] A review article of social circumstances published in 2010 noted that children in lower social circumstances almost always had poorer motor development, the exception being in Argentina where the reverse was found, and has been attributed to different cultural practices in the more deprived groups.[165] In Crete, examination of 605 infants at 18 months using the Bayley demonstrated that fine motor development was increased when the mother had had longer years of education (compared with low levels), and gross motor skills were increased if the mother was employed but reduced if the child had siblings.[166] Other miscellaneous findings include a lack of association with advanced paternal age in the major American Collaborative Perinatal Project concerning 33,000 children tested at eight months.[167]

Ethnic background

The UK's Millennium Cohort Study (n=15,994) contacted their members for the first time at nine months. The results of examination at this time point demonstrated differences in impaired motor development according to ethnic background: infants with parents whose origins were Black Caribbean (OR 0.23; 95% CI 0.11, 0.48), Black African (OR 0.31, 95% CI 0.18, 0.55), or Indian (OR 0.55, 95% CI 0.33, 0.93) were less likely to show delay in the attainment of gross motor milestones compared with White infants after adjustment for a range of explanatory variables. Infants with a Pakistani or Bangladeshi background were more likely to have delays in fine motor development but this was accounted for by socioeconomic factors.[168]

Parenting

A Brazilian study of 561 infants aged 0–18 months showed, using backward regression analysis, that the child's motor skills were positively related to parenting behaviour as indexed by whether the parents engaged in games about body parts; surprisingly there was a negative association with whether the child played with other children.[164] A German study of 171 infants followed to 30 months showed a strong relationship between the Bayley measures of motor skills and parenting as measured with the HOME score.[64]

Discussion

The results of this literature review have illustrated the vast diversity of concepts used, measures undertaken and study designs. We have shown that if one study has shown a positive or negative result there is rarely a similar dataset with which to compare it. Thus meta-analyses have not been feasible.

As discussed below, there are two major difficulties in reviewing this topic: (i) the different types of measures used, and (ii) natural changes in motor function of the individual over time.

Measures used

In the Appendix we describe the different terms used and the tests employed. It is likely that different forms of motor skills are influenced by different types of exposure. We have shown that some of the measures incorporate a variety of different types of motor ability. This is likely to make it more difficult to identify important features of the environment that may influence a child's specific types of skills even when broadly categorised into fine and gross motor skills.

Continuity

In any study of motor skills and motor development, it is crucial to understand how stable the classification of both general abilities and motor skills may be. One detailed study of 45 children who were examined monthly until 18 months to assess their motor development showed wide variation from month to month, indicating that these children did not develop consistently along a steady trajectory; for example 31% were $<10^{th}$ centile of the distribution of motor skills at least once.[169] Children with poor motor skills studied at different ages had either continued with the problem,[170] had ceased to be affected[171] or the prevalence of the problem had increased with the child's age.[151] A much larger (n > 2000) longitudinal study in Bangladesh compared the motor ability of the child using (a) ages at achievement of gross motor milestones; (b) their results on the Bayley psychomotor development index at 18 months, and (c) the results on the Movement ABC tested at five years. Although there were significant positive associations, the levels of correlation were very low.[155]

Complexity

In most of the papers we have reviewed, the studies have been straight forward comparisons between one environmental measure and an outcome. As we have also shown it is likely that the aetiology of associations of motor skills with environmental factors vary not only with the age of the child but also with the types of motor skill measured.

To date there has been little attention paid to the possibility of gene-environment or environment-environment interactions. However, some more detailed analyses have been produced in regard to the inter-relationships between seafood intake and outcome. As we have shown, there are often positive associations between fish intake and motor skills. There are two major correlates of fish intake that have been considered – one is the presence of mercury, a neurotoxicant, and the other the presence of omega-3 fatty acids, particularly DHA. An analysis of the data collected in the Seychelles longitudinal project has shown that the negative effect of maternal prenatal mercury exposure is only demonstrable if the omega-3 fatty acid levels in the maternal blood are taken into account.[172] Conversely the benefits of omega-3 fatty acids become stronger if mercury is taken into account.[95] This allowance for positive confounding has been discussed by Choi and colleagues, and has the potential of detracting from the overall beneficial outcomes of prenatal fish consumption.[173]

We have assessed a large amount of literature collected over a period of 40 years by one of the authors (JG) with the express purpose of gathering information about environmental effects on child development. The studies recorded will not necessarily appear in search engines as they include details that occur in text rather than abstracts, tables rather than text, chapters as well as peer-reviewed articles, books as well as chapters. We have enhanced these records with searches on keywords in Google Advanced Scholar and PubMed. However we do not claim that this is a systematic review. We have tried to include all studies that are based on population samples followed longitudinally. However, it is unusual to find studies in this field that are comparable or longitudinal. We have therefore also quoted the results of studies that are less reliable, but are the only ones concerning a particular exposure.

Conclusions

Poor motor skills have deleterious effects on the child's self-esteem and may result in poor emotional and behavioural outcome.[6,7] The aim of this review was to determine the general environmental factors that have been considered in the literature and thence the environmental features that may have been neglected. We have shown that there is a dearth of well-designed studies in most fields. Primary or secondary prevention is of public health concern; identifying influences that will enable resilience is therefore important. There is a major requirement for further information. This need not mean that new studies need to be mounted, but rather that some of the major longitudinal birth cohort studies should be analysed in detail in an attempt to increase knowledge and understanding in the area of motor skills.

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Abbreviations used

AA	Arachidonic acid (an Omega 6 fatty acid)
ALSPAC	Avon Longitudinal Study of Pregnancy & Childhood
CHES	Child Health and Education Survey [the 1970 UK National Birth Cohort]
DCD	Developmental Conduct Disorder
DHA	Decosahexaenoic acid (an Omega 3 fatty acid)
EPA	Eicosapentaenoic acid (an Omega 3 fatty acid)
IUGR	Intrauterine growth retardation or restriction
NCPP	US National Collaborative Perinatal Project = the American Birth Cohort enrolling pregnancies 1959–1966
NO_2	Nitrogen dioxide
PCBs	Polychlorinated biphenyls
RCT	Randomised controlled trial
SGA	Small for gestational age
TSH	Thyroid Stimulating Hormone
SSRI/SRI	Serotonin re-uptake inhibitor

References

1. Hertzman C, Power C. Child Development as a determinant of health across the life course. Curr Pediatr. 2004; 14(5):438–443.
2. Allen, G. Early intervention: the next steps. London: Stationery Office Ltd; 2011.
3. Marmot, M. Fair Society, Healthy Lives: The Marmott Review. London: UCL; 2010.
4. Dyson, AH.; Roberts, C.; Tunstill, H.; Vaghri, J. Childhood development, education and health inequalities. London: UCL; 2010.
5. Kadesjo B, Gillberg C. Developmental coordination disorder in Swedish 7-year-old children. J Am Acad Child Adolesc Psychiatry. 1999; 38(7):820–828. [PubMed: 10405499]
6. Lingam R, Golding J, Jongmans MJ, et al. The association between developmental coordination disorder and other developmental traits. Pediatr. 2010; 126(5):e1109–e1118.
7. Lingam R, Jongmans MJ, Ellis M, et al. Mental Health Difficulties in Children With Developmental Coordination Disorder. Pediatr. 2012; 129(4):e882–e891.
8. Gibbs J, Appleton J, Appleton R. Dyspraxia or developmental coordination disorder? Unravelling the enigma. Arch Dis Child. 2007; 92(6):534–539. [PubMed: 17515623]
9. Blair E, Stanley F. Epidemiology of the cerebral palsies. Orthop Clin North Am. 2010; 41(4):441. [PubMed: 20868877]
10. Humphriss R, Hall A, Macleod J. Prenatal alcohol exposure and childhood balance: a systematic review. Paediatr Perinatal Epidemiol. 2010; 24(2):156–165.
11. O'Reilly RC, Morlet T, Nicholas BD, et al. Prevalence of vestibular and balance disorders in children. Otology & Neurotology. 2010; 31(9):1441–1444. [PubMed: 20729773]
12. Rice D, Barone S Jr. Critical periods of vulnerability for the developing nervous system: evidence from human and animal models. Environ Health Perspect. 2000; 108(3):511–533. [PubMed: 10852851]
13. Zoeller RT, Rovet J. Timing of thyroid hormone action in the developing brain: clinical observations and experimental findings. J Neuroendocrinol. 2004; 16:809–818. [PubMed: 15500540]
14. Francks C, Fisher SE, Marlow AJ, et al. Familial and genetic effects on motor coordination, laterality and reading-related cognition. Am J Psychiatr. 2003; 160:1970–1977. [PubMed: 14594743]
15. Stromswold K, Rosenthal M, Patel K, Molnar D. Development of visual-motor integration: the role of genetic and environmental factors. J Vis. 2011; 11(11):article 462.
16. Williams LR, Gross JB. Heritability of motor skill. Acta Genet Med Gemellol. 1980; 29(2):127. [PubMed: 7196128]
17. Bouchard C, Malina RM. Genetics of physiological fitness and motor performance. Exercise Sport Sci Rev. 1983; 11.1:306.
18. Fox PW, Hershberger SL, Bouchard TJ. Genetic and environmental contributions to the acquisition of a motor skill. Nature. 1996; 384:356–358. [PubMed: 8934520]
19. Cooney GH, Bell A, McBride W, Carter C. Low-level exposures to lead in the Sidney lead study. Dev Med Child Neurol. 1989; 31:640–649. [PubMed: 2478405]
20. Bellinger DC. Early sensory-motor development and prenatal exposure to lead. Neurobehav Toxicol Teratol. 1984; 6(5):387–402. [PubMed: 6514103]
21. Dietrich KN, Berger OG, Succop PA. Lead exposure and the motor development status of urban six-year-old children in the Cincinnati Prospective Study. Pediatr. 1993; 91:301–307.
22. Winneke G, Krämer U, Brockhaus A, et al. Neuropsychological studies in children with elevated tooth-lead concentrations. Int Arch Occup Environ Health. 1983; 51(3):231–252. [PubMed: 6852930]
23. Needleman HL, Schell A, Bellinger D, et al. The long-term effects of exposure to low doses of lead in childhood: an 11-year follow-up report. New Engl J Med. 1990; 322(2):83–88. [PubMed: 2294437]

24. Oken E, Radesky JS, Wright RO, et al. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. Am J Epidemiol. 2008; 167(10):1171–1181. [PubMed: 18353804]
25. Jedrychowski W, Perera F, Jankowski J, et al. Fish consumption in pregnancy, cord blood mercury level and cognitive and psychomotor development of infants followed over the first three years of life Krakow epidemiologic study. Environ Int. 2007; 33:1057–1062. [PubMed: 17643489]
26. Grandjean P, Weihe P, White RF, et al. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicol Teratol. 1997; 19:417–428. [PubMed: 9392777]
27. Debes F, Budtz-Jorgensen E, Weihe P, et al. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. Neurotoxicol Teratol. 2006; 28(3):363–375. [PubMed: 16647838]
28. Davidson PW, Palumbo D, Myers GJ, et al. Neurodevelopmental outcomes of Seychellois children from the pilot cohort at 108 months following prenatal exposure to methylmercury from a maternal fish diet. Environ Res Sect A. 2000; 84:1–11.
29. Myers GJ, Davidson PW, Cox C, et al. Prenatal methylmercury exposure from ocean fish consumption in the Seychelles Child Development Study. Lancet. 2003; 361:1686–1692. [PubMed: 12767734]
30. Davidson PW, Myers GJ, Hansen ON, et al. Association between prenatal exposure to methylmercury and visuospatial ability at 10.7 years in the Seychelles Child Development Study. Neurotoxicol. 2008; 29(3):453–459.
31. Thompson WW, Price C, Goodson B, et al. Early thiomersal exposure and neuropsychological outcomes at 7 to 10 years. N Engl J Med. 2007; 357(13):1281–1292. [PubMed: 17898097]
32. Rice DC. Evidence for delayed neurotoxicity produced by methylmercury. Neurotoxicol. 1996; 17(3–4):583–596.
33. Fujiki M, Tajima S. The pollution of Minamata Bay by mercury. Water Sci Technol. 1992; 25(11): 133–140.
34. Rodriguez W, August PV, Wang Y, et al. Empirical relationships between land use/cover and estuarine condition in the Northeastern United States. Landsc Ecol. 2007; 22(3):403–417.
35. Tofail F, Vahter M, Hamadani JD, et al. Effect of arsenic exposure during pregnancy on infant development at 7 months in rural Matlab, Bangladesh. Env Health Perspect. 2009; 117(2):288–293. [PubMed: 19270801]
36. Hamadani JD, Granthan-McGregor S, Tofail F, et al. Pre- and postnatal arsenic exposure and child development at 18 months of age: a cohort study in rural Bangladesh. Int J Epidemiol. 2010; 39:1206–1216. [PubMed: 20085967]
37. Parvez F, Wasserman GA, Factor-Litvak, et al. Arsenic exposure and motor function among children in Bangladesh. Env Health Perspect. 2011; 119(11):1665–1670. [PubMed: 21742576]
38. Zoni S, Lucchini RG. Manganese exposure: cognitive, motor and behavioural effects on children: a review of recent findings. Curr Opin Pediatr. 2013; 25(2):255–260. [PubMed: 23486422]
39. Menezes-Filho JA, Bouchard M, Sarcinelli P de N, Moreira JC. Manganese exposure and the neuropsychological effect on children and adolescents: a review. Rev Panam Publica Salud. 2009; 26(6):541–548.
40. Takser L, Mergler D, Hellier G, Sahuquillo J, Huel G. Manganese, monoamine metabolite levels at birth, and child psychomotor development. Neurotoxicol. 2003; 24:667–674.
41. Henn BC, Ettinger AS, Schwartz J, et al. Early postnatal blood manganese levels and children's neurodevelopment. Epidemiol. 2010; 21(4):433.
42. Lucchini RG, Guazzetti S, Zoni S, et al. Tremor, olfactory and motor changes in Italian adolescents exposed to historical ferro-manganese emission. Neurotoxicol. 2012; 33(4):687–696.
43. Hernandez-Bonilla D, Schilmann A, Montes S, et al. Environmental exposure to manganese and motor function of children in Mexico. Neurotoxicol. 2011; 32:615–621.
44. Schoeters G, Den Hond E, Zuurbier M, et al. Cadmium and children: exposure and health effects. Acta Paediatr. 2006; 95(Supplement 453):50–54. [PubMed: 16373296]
45. Muller G, Bernuzzi V, Desor D, et al. Developmental alterations in offspring of female rats orally intoxicated by aluminium lactate at different gestation. Teratol. 1990; 42:253–261.

46. Christian P, Murray-Kolb LE, Khatry SK, et al. Prenatal micronutrient supplementation and intellectual and motor function in early school-aged children in Nepal. JAMA. 2010; 304(24): 2716–2723. [PubMed: 21177506]
47. Moffatt MEK, Longstaffe S, Besant J. Prevention of iron deficiency and psychomotor decline in high-risk infants through use of iron-fortified infant formula: a randomized clinical trial. J Pediatrics. 1994; 125:527–534.
48. Stoltzfus RJ, Kvalsvig JD, Chwaya HM, et al. Effects of iron supplementation and anthelmintic treatment on motor and language development of preschool children in Zanzibar: double blind, placebo controlled study. Br Med J. 2001; 323:1389–1393. [PubMed: 11744561]
49. Parks A, Wharton BA. Iron deficiency and the brain. Acta Paediatr Scand (supplement). 1989; 361:71–77.
50. Saloojee H, Pettifor JM. Iron deficiency and impaired child development. Br Med J. 2001; 323:1377–1378. [PubMed: 11744547]
51. Szajewska H, Ruszczynski M, Chmielewska A. Effects of iron supplementation in nonanemic pregnant women, infants, and young children on the mental performance and psychomotor development of children: a systematic review of randomized controlled trials. Am J Clin Nutr. 2010; 91:1684–1690. [PubMed: 20410098]
52. Pharoah POD, Connolly KJ. A Controlled Trial of Iodinated Oil for the Prevention of Endemic Cretinism: A Long-Term Follow-Up. Int J Epidemiol. 1987; 16:68–73. [PubMed: 3032814]
53. Connolly K, Pharoah PD, Hetzel B. Fetal iodine deficiency and motor performance during childhood. Lancet. 1979; 314(8153):1149–1151. [PubMed: 91886]
54. Berbel P, Mestre JL, Santamaria A, et al. Delayed neurobehavioral development in children born to pregnant women with mild hypothyroxinemia during the first month of gestation: The importance of early iodine supplementation. Thyroid. 2009; 19(5):511–519. [PubMed: 19348584]
55. Zimmermann MB, Connolly K, Bozo M, et al. Iodine supplementation improves cognition in iodine-deficient school children in Albania: a randomised, controlled, double-blind study. Am J Clin Nutr. 2006; 83:108–114. [PubMed: 16400058]
56. Roze E, Meijer L, Bakker A, et al. Prenatal exposure to organohalogens, including brominated flame retardants, influences motor, cognitive and behavioural performance at school age. Environ Health Perspect. 2009; 117:1953–1958. [PubMed: 20049217]
57. Nyaradi A, Li J, Hickling S, et al. The role of nutrition in children's neurocognitive development, from pregnancy through childhood. Front Hum Neurosci. 2013; 7:article 97, 1–16.
58. Al-Dahhan J, Jannoun L, Haycock GB. Effect of salt supplementation of newborn premature infants on neurodevelopmental outcome at 10–13 years of age. Arch Dis Child Fetal Neonatal Ed. 2002; 86:F120–F123. [PubMed: 11882555]
59. Black MM, Baqui AH, Zaman K, et al. Iron and zinc supplementation promote motor development and exploratory behaviour among Bangladeshi infants. Am J Clin Nutr. 2004; 80:903–910. [PubMed: 15447897]
60. Raymond, LJ.; Seale, LA.; Ralston, NVC. Seafood selenium in relation to assessments of methylmercury exposure risks. In: Hatfield, DL., et al., editors. Selenium: Its Molecular Biology and Role in Human Health. Vol. Chapter 31. Springer Science + Business Media LLC; 2012. p. 399-408.
61. Rogan WJ, Miller RW. Prenatal exposure to polychlorinated biphenyls. Lancet. 1989; ii:1216. [PubMed: 2572923]
62. Rice DC. Neurotoxicity produced by developmental exposure to PCBs. Ment Retard. 1997; 3:223–229.
63. Ribas-Fito N, Sala M, Kogevinas M, Sunyer J. Polychlorinated biphenplys (PCBs) and neurological development in children: a systematic review. J Epidemiol Community Health. 2001; 55:537–546. [PubMed: 11449010]
64. Walkowiak J, Wiener J-A, Fastabend A, et al. Environmental exposures to polychlorinated biphenyls and quality of the home environment: Effects on psychodevelopment in early childhood. Lancet. 2001; 358:1602–1607. [PubMed: 11716887]

65. Nakajima S, Saijo Y, Kato S, et al. Effects of prenatal exposure to polychlorinated biphenyls and dioxins on mental and motor development in Japanese children at 6 months of age. Environ Health Perspect. 2006; 114(5):773–778. [PubMed: 16675436]

66. Vreugdenbil H, Lanting CI, Mulder P, Boersma R, Weisglas-Kuperus N. Effects of prenatal PCB and dioxin background exposure on cognitive and motor abilities in Dutch children at school age. J Pediatr. 2002; 140:48–56. [PubMed: 11815763]

67. Grandjean P, Weihe P, Nielson F, et al. Neurobehavioural deficits at age 7 years associated with prenatal exposure to toxicants from maternal seafood diet. Neurotoxicol Teratol. 2012; 34:466–472. [PubMed: 22705177]

68. Dallaire R, Muckle G, Rouget F, et al. Cognitive, visual and motor development of 7-month-old Guadeloupean infants exposed to chlordecone. Environ Res. 2012; 118:79–85. [PubMed: 22910562]

69. Handal AJ, Harlow SD, Breilh J, Lozoff B. Occupational exposure to pesticides during pregnancy and neurobehavioural development of infants and toddlers. Epidemiol. 2008; 19(6):851–859.

70. Guillette EA, Meza MM, Aquilar GM, et al. An anthropological approach to the evaluation of preschool children exposed to pesticides in Mexico. Environ Health Perspect. 1998; 106:347–353. [PubMed: 9618351]

71. Foo SC, Jeyaratnam J, Koh D. Chronic neurobehavioural effects of toluene. Br J Ind Med. 1990; 47:480–484. [PubMed: 2383518]

72. Freire C, Ramos R, Puertas R, Lopez-Espinosa M-J, et al. Association of traffic-related air pollution with cognitive development in children. J Epidemiol Community Health. 2010; 64(3):223–228. [PubMed: 19679705]

73. Streissguth AP, Barr HM, Martin DM. Effects of maternal alcohol, nicotine, and caffeine use during pregnancy on infant mental and motor development at eight months. Alcohol Clin Exp Res. 1980; 4:152–164. [PubMed: 6990818]

74. Connor PD, Sampson PD, Streissguth AP, et al. Effects of prenatal alcohol exposure on fine motor coordination and balance: a study of two adult samples. Neuropsychol. 2006; 44:744–751.

75. Larroque B, Kaminski M, Dehaene P, et al. Prenatal alcohol exposure and signs of minor neurological dysfunction at preschool age. Dev Med Child Neurol. 2000; 42:508–514. [PubMed: 10981927]

76. Bay B, Kesmodel US. Prenatal alcohol exposure–a systematic review of the effects on child motor function. Acta Obstetr Gynecol Scand. 2011; 90(3):210–226.

77. Little RE, Anderson KW, Ervin CH, Worthington-Roberts B. Maternal alcohol use during breast-feeding and infant mental and motor development at one year. N Engl J Med. 1989; 321(7):425–430. [PubMed: 2761576]

78. Little RE, Northstone K, Golding J. ALSPAC Study Team. Alcohol, breast feeding, and development at 18 months. Pediatr. 2002; 109(5):1–6.

79. Hernandez-Martinez C, Val VA, Subias JE, Sans JC. A longitudinal study on the effects of maternal smoking and secondhand smoke exposure during pregnancy on neonatal neurobehavior. Early Hum Dev. 2012; 88:403–408. [PubMed: 22099525]

80. Larsson M, Montgomery SM. Maternal smoking during pregnancy and physical control and coordination among offspring. J Epidemiol Community Health. 2011; 65(12):1151–1158. [PubMed: 20844292]

81. Kafouri S, Leonard G, Perron M, et al. Maternal cigarette smoking during pregnancy and cognitive performance in adolescence. Int J Epidemiol. 2009; 38:158–172. [PubMed: 19039007]

82. Willford JA, Chandler LS, Goldschmidt L, Day NL. Effects of prenatal tobacco, alcohol and marijuana exposure on processing speed, visual–motor coordination, and inter-hemispheric transfer. Neurotoxicol Teratol. 2010; 32(6):580–588. [PubMed: 20600845]

83. Hseih C-J, Liao H-F, Wu K-Y, et al. CYP1A1 Ile462Val and GSTT1 modify the effect of cord blood cotinine on neurodevelopment at 2 years of age. Neurotoxicol. 2008; 29:839–845.

84. Singer LT, Moore DG, Min MO, et al. One-year outcomes of prenatal exposure to MDMA and other recreational drugs. Pediatr. 2012; 130(3):407–413.

85. Arendt R, Angelopoulos J, Salvator A, Singer L. Motor development of cocaine-exposed children at age two years. Pediatr. 1999; 103:86–92.

86. Frank DA, Augustyn M, Knight WG, Pell T, Zuckerman B. Growth, development, and behaviour in early childhood following prenatal cocaine exposure. JAMA. 2001; 285:1613–1625. [PubMed: 11268270]

87. Van Beveren TT, Little BB, Spence MJ. Effects of prenatal cocaine exposure and postnatal environment on child development. Am J Hum Biol. 2000; 12:417–428. [PubMed: 11534032]

88. Barr HM, Streissguth AP, Darby BL, Sampson PD. Prenatal exposure to alcohol, caffeine, tobacco, and aspirin: Effects on fine and gross motor performance in 4-year-old children. Dev Psychol. 1990; 26(3):339.

89. Barr HM, Streissguth AP. Caffeine use during pregnancy and child outcome: A 7-year prospective study. Neurotoxicol Teratol. 1991; 13:441–448. [PubMed: 1921923]

90. Castellanos FX, Rapoport JL. Effects of caffeine on development and behavior in infancy and childhood: a review of the published literature. Food Chem Toxicol. 2002; 40(9):1235–1242. [PubMed: 12204387]

91. Bjorklund O, Kahlstrom J, Salmi P, et al. The effects of methylmercury on motor activity are sex- and age-dependent and modulated by genetic deletion of adenosine receptors and caffeine administration. Toxicol. 2007; 241:119–133.

92. Hibbeln JR, Davis JM, Steer C, et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. Lancet. 2007; 369(9561):578–585. [PubMed: 17307104]

93. Bonham MP, Duffy EM, Robson PJ, et al. Contribution of fish to intakes of micronutrients important for fetal development: a dietary survey of pregnant women in the Republic of Seychelles. Public Health Nutr. 2009; 12(9):1312. [PubMed: 18986594]

94. Mozaffarian D, Rimm EB. Fish intake, contaminants and human health: evaluating the risks and benefits. JAMA. 2006; 296(15):1885–1899. [PubMed: 17047219]

95. Stokes-Riner A, Thurston SW, Myers G, et al. A longitudinal analysis of prenatal exposure to methylmercury and fatty acids in the Seychelles. Neurotoxicol Teratol. 2011; 33(2):325–328. [PubMed: 21145963]

96. Bakker EC, Hornstra G, Blanco CE, Vles JSH. Relationship between long-chain polyunsaturated fatty acids at birth and motor function at 7 years of age. Eur J Clin Nutr. 2009; 63:499–504. [PubMed: 18091766]

97. Dunstan JA, Simmer K, Dixon G, Prescott SL. Cognitive assessment of children at age 2½ years after maternal fish oil supplementation in pregnancy: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed. 2008; 93:F45–F50. [PubMed: 17185423]

98. Birch EE, Garfield S, Hoffman DR, et al. A randomized controlled trial of early dietary supply of long-chain polyunsaturated fatty acids and mental development in term infants. Dev Med Child Neurol. 2000; 42:174–181. [PubMed: 10755457]

99. Auestand N, Scott DT, Janowsky JS, et al. Visual, cognitive and language assessments at 39 months: a follow-up study of children fed formulas containing long-chain polyunsaturated fatty acids to 1 year of age. Pediatr. 2003; 112:e177.

100. Richardson AJ, Montgomery P. The Oxford-Durham Study: A randomised controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. Pediatr. 2005; 115(5):1360–1366.

101. Eickmann SH, Cabral de Lira PI, de Carvalho Lima M, et al. Breast feeding and mental and motor development at 12 months in a low-income population in northeast Brazil. Paediatr Perinatal Epidemiol. 2007; 21:129–137.

102. Florey CDV, Leech AM, Blackhall A. Infant feeding and mental and motor development at 18 months of age in first born singletons. Int J Epidemiol. 1995; 24:521–526.

103. Gómez-Sanchiz M, Cañete R, Rodero I, Baeza JE, Avila O. Influence of breast-feeding on mental and psychomotor development. Clin Pediatr. 2003; 42(1):35–42.

104. Lanting CI, Fidler V, Huisman M, et al. Neurological differences between 9-year-old children fed breast-milk or formula-milk as babies. Lancet. 1994; 344:1319–1322. [PubMed: 7968027]

105. Sacker A, Quigley MA, Kelly YJ. Breastfeeding and developmental delay: findings from the Millennium Cohort Study. Pediatr. 2008:e682–e689.

106. Taylor B, Wadsworth J. Breast feeding and child development at five years. Dev Med Child Neurol. 1984; 26(1):73–80. [PubMed: 6698329]

107. Prado EL, Alcock KJ, Muadz H, et al. Maternal multiple micronutrient supplements and child cognition: a randomised trial in Indonesia. Pediatr. 2012; 130:e536.

108. Rask-Nissila L, Jokinen E, Terho P. Neurological development of 5-year-old children receiving a low-saturated fat, low-cholesterol diet since infancy. JAMA. 2000; 284:993–1000. [PubMed: 10944645]

109. Buckley GJ, Murray-Kolb LE, Khatry SK, et al. Cognitive and motor skills in school-aged children following maternal vitamin A supplementation during pregnancy in rural Nepal: a follow-up of a placebo-controlled, randomised cohort. Br Med J Open. 2013; 3:e002000.

110. Losche G, Steinhausen H-C, Koch S, et al. The psychological development of children of epileptic parents. II. The differential impact of intrauterine exposure to anticonvulsant drugs and further influential factors. Acta Paediatr. 1994; 83:961–966. [PubMed: 7529601]

111. Steinhausen HC, Losche G, Koch S. The psychological development of children of epileptic parents. I. Study design and comparative findings. Acta Paediatr. 1994; 83:955–960. [PubMed: 7529600]

112. Wide K, Winbladh B, Tomson T, et al. Psychomotor development and minor anomalies in children exposed to antiepilieptic drugs in utero: a prospective population-based study. Dev Med Child Neurol. 2000; 42:87–92. [PubMed: 10698324]

113. Nadebaum C, Anderson V, Vajda F, et al. The Australian Brain and Cognition and Antiepileptic Drugs Study: IQ in school age children exposed to sodium valporate and polytherapy. J Int Neuropsychol Soc. 2011; 17:133–142. [PubMed: 21092354]

114. Garne E, Loane M, Dolk H, et al. Spectrum of congenital anomalies in pregnancies with pregestational diabetes. Birth Defects Res A Clin Mol Teratol. 2012; 94:134–140. [PubMed: 22371321]

115. Petersen, MB. Carbohydrate Metabolism in Pregnancy and the Newborn IV. London: Springer Verlag; 1989. Status at 4–5 years in 90 children of insulin-dependent diabetic mothers. In: Sutherland HW, Stowers JM, Pearson DWM; p. 353-361.

116. Ornoy A, Ratzon N, Greenbaum C, et al. School-age children born to diabetic mothers and to mothers with gestational diabetes exhibit a high rate of inattention and fine and gross motor impairment. J Pediatr Endocrinol Metab. 2001; 14(Supplement):681–690. [PubMed: 11393563]

117. Ornoy A. Growth and neurodevelopmental outcome of children born to mothrs with pregestational and gestational diabetes. Pediatr Endocrinol Rev. 2005; 3(2):104–113. [PubMed: 16361984]

118. Brown AS, Patterson PH. Maternal infection and schizophrenia: implications for prevention. Schizophr Bull. 2011; 37(2):284–290. [PubMed: 21134972]

119. Foster CJ, Biggs RL, Melvin D, et al. Neurodevelopmental outcomes in children with HIV infection under 3 years of age. Dev Med Child Neurol. 2006; 48:677–682. [PubMed: 16836781]

120. Nasreen HE, Nahar Kabir Z, Forsell Y, Edhborg M. Impact of maternal depressive symptoms and infant temperament on early infant growth and motor development: Results from a population based study in Bangladesh. J Affect Disord. 2012; 146:254–261. [PubMed: 23063237]

121. Tse AC, Rich-Edwards JW, Rifas-Shiman SL, et al. Association of maternal prenatal depressive symptoms with child cognition at age 3 years. Paediatr Perinatal Epidemiol. 2010; 24(3):232–240.

122. Casper RC, Fleisher BE, Lee-Ancajas JC, et al. Follow-up of children of depressed mothers exposed or not exposed to antidepressant drugs during pregnancy. J Pediatr. 2003; 142:402–408. [PubMed: 12712058]

123. Hanley GE, Brain U, Oberlander TF. Infant developmental outcomes following prenatal exposure to antidepressants, and maternal depressed mood and positive affect. Early Hum Dev. 201310.1016/j.earlhumdev.2012.12.012

124. Galbally M, Lewis AJ, Buist A. Developmental outcomes of children exposed to antidepressants in pregnancy. Aust N Z J Psychiatry. 2011; 45(5):393–399. [PubMed: 21314237]

125. Smith MV, Sung A, Shah B, et al. Neurobehavioral assessment of infants born at term and in utero exposure to serotonin reuptake inhibitors. Early Hum Dev. 2012; 89(2):81–86. [PubMed: 22999988]
126. Mortensen JT, Olsen J, Larsen H, et al. Psychomotor development in children exposed in utero to benzodiazepines, antidepressants, neuroleptics and anti-epileptics. Eur J Epidemiol. 2003; 18:769–771. [PubMed: 12974552]
127. Gentile S, Galbally M. Prenatal exposure to antidepressant medications and neurodevelopmental outcomes: a systematic review. J Affect Disord. 2011; 128:1–9. [PubMed: 20303599]
128. Galler JR, Harrison RH, Ramsey F, et al. Maternal depressive symptoms affect infant cognitive development in Barbados. J Child Psychol Psychiatr. 2000; 41(6):747–757.
129. Piteo AM, Yelland LN, Makrides M. Does maternal depression predict developmental outcome in 18month old infants? Early Hum Dev. 2012; 88(8):651–655. [PubMed: 22361258]
130. Koutra K, Chatzi L, Bagkeris M, et al. Antenatal and postnatal maternal mental health as determinants of infant neurodevelopment at 18 months of age in a mother–child cohort (Rhea Study) in Crete, Greece. Soc Psychiatry Psychiatr Epidemiol. 2012a:1–11.
131. Rothenberg SJ, Chicz-DeMet A, Schnaas L, et al. Umbilical cord B-endorphin and early childhood motor development. Early Hum Dev. 1996; 46:83–95. [PubMed: 8899357]
132. CLASP Collaborative Group. Low dose aspirin in pregnancy and early childhood development: follow-up of the collaborative low dose aspirin study in pregnancy. Br J Obstetr Gynaecol. 1995; 102:861–868.
133. Jongmans M, Mercuri E, De Vries L, et al. Perceptual-motor difficulties and their concomitants in six-year-old children born prematurely. Hum Mov Sci. 1998; 17:629–653.
134. Jongmans M, Mercuri E, De Vries L, et al. Minor neurological signs and perceptual-motor difficulties in prematurely born children. Arch Dis Child Fetal and Neonatal Ed. 1997; 76:F9–F14. [PubMed: 9059179]
135. Sullivan MC, McGarth MM. Perinatal morbidity mild motor delay, and later school outcomes. Dev Med Child Neurol. 2003; 45:104–112. [PubMed: 12578236]
136. Pitcher JB, Schneider LA, Burns NR, et al. Reduced corticomotor excitability and motor skills development in children born preterm. J Physiol. 2012; 590(22):5827–5844. [PubMed: 22966161]
137. Cohen, SE. The low-birth weight infant and learning disabilities. In: Lewis, M., editor. Learning Disabilities and Prenatal Risk. Champaign Il: University of Illinois Press; 1986. p. 153-193.
138. Elliman AM, Bryan EM, Elliman AD, et al. Coordination in low birthweight seven-year-olds. Acta Paediatr Scand. 1991; 80:316–322. [PubMed: 1709772]
139. Lindahl E, Michelsson K, Helenius M, et al. Neonatal risk factors and later neurodevelopmental disturbances. Dev Med Child Neurol. 1988; 30:571–589. [PubMed: 2465930]
140. Yliherva A, Olsen P, Maki-Torkko E, et al. Linguistic and motor abilities of low-birthweight children as assessed by parents and teachers at 8 years of age. Acta Paediatr. 2001; 90:1440–1449. [PubMed: 11853344]
141. Ylitalo V, Kero P, Erkkola R. Neurological outcome of twins dissimilar in size at birth. Early Hum Dev. 1988; 17:245–255. [PubMed: 3208679]
142. Strauss RS, Dietz WH. Growth and development of term children born with low birth weight: effects of genetic and environmental factors. J Pediatr. 1998; 133:67–72. [PubMed: 9672513]
143. Cooke RWI. Are there critical periods for brain growth in children born preterm? Arch Dis Child Fetal and Neonatal Ed. 2006; 91:F17–F20. [PubMed: 16223756]
144. Cheung YB, Yip PSF, Karlberg JPE. Fetal growth, early postnatal growth and motor development in Pakistani infants. Int J Epidemiol. 2001; 30:66–74. [PubMed: 11171859]
145. Friedman, EA.; Neff, RK. Labor course and outcome: Lexicon approach. In: Friedman, EA.; Neff, RK., editors. Labor and Delivery: Impact on Offspring. Littleton MA: PSG Publishing Co; 1987. p. 88-104.
146. Bjerre I, Dahlin K. The long-term development of children delivered by vacuum extraction. Dev Med Child Neurol. 1974; 16:378–381. [PubMed: 4407631]

147. Laucht M, Esser G, Schmidt MH. Developmental outcome of infants born with biological and psychosocial risks. J Child Psychol Psychiatr. 1997; 38:843–853.

148. Handley-Derry M, Low JA, O'Burke S, et al. Intrapartum fetal asphyxia and the occurrence of minor deficits in 4-to 8-year-old children. Dev Med Child Neurol. 1997; 39:508–514. [PubMed: 9295845]

149. Moster D, Lie RT, Markestad T. Joint association of Apgar scores and early neonatal symptoms with minor disabilities at school age. Arch Dis Child Fetal Neonatal Ed. 2002; 86:F16–21. [PubMed: 11815542]

150. Stanton WR, McGee R, Silva PA. Indices of perinatal complications, family background, child rearing, and health as predictors of early cognitive and. Pediatr. 1991; 88:954–959.

151. Lunsing RJ, Hadders-Algra M, Huisjes HJ, et al. Minor neurological dysfunction from birth to 12 years: increase during late school-age. Dev Med Child Neurol. 1992; 34:399–403. [PubMed: 1375566]

152. Stevens JP, Eames M, Kent A, et al. Long term outcomes of neonatal meningitis. Arch Dis Child Fetal Neonatal Ed. 2003; 88:F179–F184. [PubMed: 12719389]

153. Kuklina EV, Ramakrishnan U, Stein AD, et al. Early childhood growth and development in rural Guatemala. Early Hum Dev. 2006; 82:425–433. [PubMed: 16431042]

154. Agarwal KN, Agarwal DK, Upadhyay SK. Impact of chronic undernutrition on higher mental functions in Indian boys aged 10–12 years. Acta Paediatr. 1995; 84:1357–1361. [PubMed: 8645950]

155. Hamadani JD, Tofail F, Cole T, Grantham-McGregor S. The relation between age of attainment of motor milestones and future cognitive and motor development in Bangladeshi children. Matern Child Nutr. 2013; 9(S1):89–104. [PubMed: 23167587]

156. Gillberg C, Rastam M, Gillberg IC. Anorexia nervosa: physical health and neurodevelopment at 16 and 21 years. Dev Med Child Neurol. 1994; 36:567–575. [PubMed: 8034118]

157. Rao MR, Brenner RA, Schisterman EF, et al. Long term cognitive development in children with prolonged crying. Arch Dis Child. 2004; 89:989–992. [PubMed: 15499048]

158. Fellick JM, Sills JA, Marzouk O, et al. Neurodevelopmental outcome in meningococcal disease: a case-control study. Arch Dis Child. 2001; 85:6–11. [PubMed: 11420186]

159. Atkinson J, Nardini M, Anker S, et al. Refractive errors in infancy predict reduced performance on the Movement Assessment Battery for children at 3½ and 5½ years. Dev Med Child Neurol. 2005; 47(4):243–251. [PubMed: 15832547]

160. Abbott AL, Bartlett DJ. Infant motor development and equipment use in the home. Child Care Health Dev. 2001; 27:295–306. [PubMed: 11350456]

161. McPhillips M, Jordan-Black J-A. The effect of social disadvantage on motor development in young children: a comparative study. J Child Psychol Psychiatr. 2007; 48(12):1214–1222.

162. Wadsworth J, Burnell J, Taylor B, Butler N. The influence of family type on children's behaviour and development at five years. J Child Psychol Psychiatr. 1985; 26:245–254.

163. Soorani-Lunsing RJ, Hadders-Algra M, Huisjes HJ. Minor neurological dysfunction after the onset of puberty: association with perinatal events. Early Hum Dev. 1993; 33:71–80. [PubMed: 8319556]

164. Saccani R, Valentini NC, Pereira KRG, Muller AB, Gabbard C. Associations of biological factors and affordances in the home with infant motor development. Pediatr Int. 2013; 55:197–203. [PubMed: 23279095]

165. Venetsanou F, Kambas A. Environmental factors affecting preschoolers' motor development. Early Child Educ J. 2010; 37:319–327.

166. Koutra K, Chatzi L, Roumeliotaki T, Vassilaki M, Giannakopoulou E, Batsos C, Koutis A, Kogevinas M. Socio-demographic determinants of infant neurodevelopment at 18 months of age: Mother-child cohort (Rhea Study) in Crete, Greece. Inf Behav Dev. 2012; 35:48–59.

167. Saha S, Barnett AG, Foldi C, et al. Advanced paternal age is associated with impaired neurocognitive outcomes during infancy and childhood. PLoS Med. 2009; 6(3):0001–9.

168. Kelly Y, Sacker A, Schoon I, Nazroo J. Ethnic differences in achievement of developmental milestones by 9 months of age: the Millennium Cohort Study. Dev Med Child Neurol. 2006; 48:825–830. [PubMed: 16978462]

169. Darrah J, Redfern L, Maguire TO, et al. Intra-individual stability of rate of gross motor development in full-term infants. Early Hum Dev. 1998; 52:169–179. [PubMed: 9783818]
170. Losse A, Henderson SE, Elliman D, et al. Clumsiness in children - do they grow out of it? A 10-year follow-up study. Dev Med Child Neurol. 1991; 33:55–68. [PubMed: 1704864]
171. Lunsing RJ, Hadders-Algra M, Huisjes HJ, et al. Minor neurological dysfunctions from birth to 12 years: Puberty is related to decreased dysfunction. Dev Med Child Neurol. 1992; 34:404–409. [PubMed: 1375567]
172. Strain JJ, Davidson PW, Bonham MP, et al. Associations of maternal long chain polyunsaturated fatty acids, methylmercury, and infant development in the Seychelles Child Development Nutrition Study. Neurotoxicol. 2008; 29(5):776–782.
173. Choi AL, Cordier S, Weihe P, Grandjean P. Negative confounding in the evaluation of toxicity: the case of methylmercury in fish and seafood. Crit Rev Toxicol. 2008; 38(10):877–893. [PubMed: 19012089]

Appendix

Descriptions of the different terms and tests used in the literature in regard to motor competence

Bayley test: Used to assess fine and gross motor skills, language (receptive and expressive) and cognitive development in children aged 0–3 years. Scores from the fine and gross motor skills tend to be combined to give the Psychomotor Development Index.[1,2]

Beery Test Visual-Motor Integration. This is used to screen for visual-motor deficits that can lead to learning, neuropsychological and behaviour problems.[3]

Bender Gestalt Test or Bender Visual Motor Gestalt Test evaluates "visual-motor maturity" to screen for developmental disorders, or to assess neurological function or brain damage.[4]

BOEL test. A test primarily used in Scandinavia; a modified version is used in the UK, Netherlands and Australia.[5]

BSID-III (current version): Bayley Scales Infant Development (See Bayley test above)

Denver Test (Denver Developmental Screening Test (DDST)) screens for cognitive and behavioural problems in pre-school children. It includes subscales for fine and gross motor development.[6]

Fine motor skills/coordination/ability: The coordination of small muscle movements e.g. in fingers, usually in coordination with the eyes (or Dexterity) e.g. drawing, threading a needle.

Graphomotor skills pertaining to the muscular movements used in handwriting.

Griffiths Mental Developmental Scales This test, which is administered by trained assessors, has a number of subscales including locomotor, hand and eye coordination, and performance.[7]

Gross motor skills/coordination/ability: The coordination of limb(s) or whole body as in walking, running, swimming.

Hand-eye control/coordination: *See* **Fine Motor Skills; Motor development**

Manual dexterity: *See* **Fine Motor skills; Motor development**

Maastricht Motor Test (MMT) which measures both quantitative (the ability to perform a movement) and qualitative (how the movement is performed) motor function.[8,9]

McCarthy test (MSCA or McCarthy Scales of Children's Abilities (pre-school) – a child test of test the child's abilities. It includes a motor scale which incorporates leg coordination, arm coordination, imitative action, draw-a-design, draw-a-child tests.[10]

Milestones: Age at achievement of developmental milestones – particularly age at starting to walk unaided (gross motor) and placing bricks upon one another (fine motor).

Motor development: usually denotes attainment of specific motor developmental milestones [see above].

Movement ABC (Movement Assessment Battery for Children). This set of tests provides an overall score, and scores for ball skills, manual dexterity, and balance.[11]

Neonatal Behaviour Assessment Scale. A scale developed by T. Berry Brazelton in 1973 for evaluating the neurological condition and behaviour of a newborn (recommended for use up to 2 months of age) by assessing the baby's alertness, motor maturity, irritability, consolability and interaction with people.[12]

Psychomotor Development Index (PDI) is most closely associated with the Bayley (see above). Test items include motor skills such as rolling, crawling, grasp and use of utensils. It refers to a measure of motor skills that also involve some aspects of conceptual or psychological functioning.

Qualitative Motor Development Score: This was developed for a Danish study; it incorporated observations during a standard test as to the quality of the child's response to each motor item.[13]

Speed of finger tapping: The tapping rate is a test given to assess the integrity of the neuromuscular system and examine motor control. The number of taps per second one month after a minor brain injury has been shown to be slower than in healthy people.

Visuo-motor coordination [or visual motor coordination]. The ability to coordinate vision with the movements of the body or parts of the body.

WRAVMA (Wide Range Assessment of Visual Motor Ability) used on ages 3–17 years.[14]

References

1. Bayley, N. Manual for the Bayley Scales of Infant Development. New York, NY: Psychological Corporation; 1969.
2. Bayley, N. Bayley Scales of Infant Development. 2. San Antonio, TX: The Psychological Corporation; 1993.
3. Beery, KE. The VMI: Developmental Test of Visual-Motor Integration. 3. Cleveland OH: Modern Curriculum Press; 1989.
4. Koppitz, EM. The Bender-Gestalt Test for Young Children. New York, NY: Grune & Stratton; 1963.
5. Junker KS, Barr B, Maliniemi S, Wasz-Hockert O. BOEL – a screening program to enlarge the concept of infant health. Paediatrician. 1982; 11:85–89. [PubMed: 7088576]
6. Frankenburg WK, Dodds JB. Denver Developmental Screening Test. J Pediatr. 1967; 71:181–191. [PubMed: 6029467]
7. Griffiths, R. The Abilities of Young Children. High Wycombe, UK: The Test Agency; 1970.
8. Kroes M, Kessels AG, Kalff AC, Feron FJ, et al. Quality of movement as predictor of ADHD: results from a prospective population study in 5- and 6-year old children. Dev Med Child Neurol. 2002; 44:753–760. [PubMed: 12418616]
9. Vles, J.; Kroes, M.; Feron, F. Maastrichtse Motoriek Test (MMT). Leiden: PITS; 2004.
10. McCarthy, D. McCarthy Scales of Children's Abilities. New York, NY: the Psychological Corporation; 1972.
11. Henderson, SE.; Sugden, DA. Movement Assessment Battery for Children. London: The Psychological Corporation; 1992.
12. Brazelton, TB.; Nugent, JK. The Neonatal Behavior Assessment Scale. Cambridge: Mac Keith Press; 1995.
13. Petersen, MB. Status at 4–5 years in 90 children of insulin-dependent diabetic mothers. In: Sutherland, HW.; Stowers, JM.; Pearson, DWM., editors. Carbohydrate Metabolism in Pregnancy and the Newborn IV. London: Springer Verlag; 1989. p. 353-361.
14. Adams, W.; Sheslow, D. Wide range assessment of visual motor abilities. Wilmington, DE: Wide Range, Inc; 1995.